# Exercise for the management of cancer-related fatigue in adults (Review)

**Cramp F, Byron-Daniel J**


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## TABLE OF CONTENTS





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[Intervention Review]

# Exercise for the management of cancer-related fatigue in adults

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**Editorial group:** Cochrane Pain, Palliative and Supportive Care Group.
**Publication status and date:** New search for studies and content updated (conclusions changed), published in Issue 11, 2012.
**Review content assessed as up-to-date:** 19 April 2012.

**Citation:** Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 11. Art. No.: CD006145. DOI: 10.1002/14651858.CD006145.pub3.

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## ABSTRACT

### Background

Cancer-related fatigue is recognised as an important symptom associated with cancer and its treatment. A number of studies have investigated the effects of physical activity in reducing cancer-related fatigue. This is an updated version of the original Cochrane review published in *The Cochrane Library* (2008, Issue 1). The original review identified some benefits of physical activity on fatigue in cancer both during and after adjuvant treatment. We identified a number of limitations in the evidence, providing clear justification for an updated review.

### Objectives

To evaluate the effect of exercise on cancer-related fatigue both during and after cancer treatment.

### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 1, 2011), MEDLINE (1966 to March 2011), EMBASE (1980 to March 2011), CINAHL (1982 to March 2011), British Nursing Index (January 1984 to March 2011), AMED (1985 to March 2011), SIGLE (1980 to March 2011) and Dissertation Abstracts International (1861 to March 2011) using key words. We also searched reference lists off all studies identified for inclusion and relevant reviews. In addition, we handsearched relevant journals and contacted experts in the field of cancer-related fatigue.

### Selection criteria

We sought and included randomised controlled trials (RCTs) that investigated the effect of exercise on cancer-related fatigue in adults.

### Data collection and analysis

Two review authors independently assessed the risk of bias of studies and extracted data based upon predefined criteria. Where data were available we performed meta-analyses for fatigue using a random-effects model.


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**Main results**

For this update we identified a total of 56 studies (4068 participants) for inclusion (28 from the original search and 28 from the updated search), with the majority carried out in participants with breast cancer (28 studies). A meta-analysis of all fatigue data, incorporating 38 comparisons, provided data for 1461 participants who received an exercise intervention and 1187 control participants. At the end of the intervention period exercise was seen to be statistically more effective than the control intervention (standardised mean difference (SMD) -0.27, 95% confidence interval (CI) -0.37 to -0.17). Benefits of exercise on fatigue were observed for interventions delivered during or post-adjuvant cancer therapy. In relation to diagnosis, we identified benefits of exercise on fatigue for breast and prostate cancer but not for those with haematological malignancies. Finally, aerobic exercise significantly reduced fatigue but resistance training and alternative forms of exercise failed to reach significance.

**Authors' conclusions**

The findings of the updated review have enabled a more precise conclusion to be made in that aerobic exercise can be regarded as beneficial for individuals with cancer-related fatigue during and post-cancer therapy, specifically those with solid tumours. Further research is required to determine the optimal type, intensity and timing of an exercise intervention.

## PLAIN LANGUAGE SUMMARY

**The effect of exercise on fatigue associated with cancer**

Fatigue, or tiredness, is recognised as a side effect of cancer and its treatment. In the past people with cancer were encouraged to rest if they felt fatigued. It is important that individuals with cancer receive appropriate support and advice to help them cope with any side effects of the treatment or disease. Physical exercise has been suggested as helpful in reducing the fatigue that is associated with cancer. A number of studies have been carried out to investigate the effects of exercise both during and after treatment. The current review was carried out to evaluate the effect of physical exercise on fatigue related to cancer. Fifty-six studies, involving a total of 4068 participants, were included in this review. Results suggest that physical exercise such as aerobic walking and aerobic cycling can help to reduce fatigue both during and after treatment for cancer. The benefits of exercise on fatigue were observed specifically for people with breast cancer and prostate cancer.

## BACKGROUND

This review is an update of a review previously published in *The Cochrane Library* (2008, Issue 1) on exercise for the management of cancer-related fatigue (Cramp 2008). As a result of improved therapy, people with cancer are surviving longer and having to deal with the long-term consequences of the disease and its therapy. Consequently there has been an increasing number of individuals who need supportive care to enhance their quality of life (Lucia 2003). This has led to an increasing recognition of the symptoms associated with cancer and cancer management with relief of these symptoms emerging as an important dimension of cancer patient care.

### Description of the condition

Cancer-related fatigue is an abstract, multidimensional subjective experience, affecting 70% to 100% of the cancer patient population (Mock 2001b). It has a profound effect on the whole person, physically, emotionally and mentally (Ahlberg 2003), and can persist for months or even years following completion of treatment. It can have a phenomenal impact on a patient's life, interfering with daily activities (Curt 2000) and may also potentially have devastating social and economic consequences (Fletchner 2002). It can hinder a patient's chance of remission or even cure, owing to the effect it can have on the desire to continue with treatment (Morrow 2001).

In spite of the prevalence and impact of cancer-related fatigue there are limited data available with regards to the precise aetiology, pattern over time and exacerbating and relieving factors (Fletchner 2002), thus complicating the development of effective management interventions (Dimeo 2002). The aetiology of cancer-related fatigue remains to be fully established and a number of causes have been suggested, such as the effect of tumour and cancer treatment, comorbid medical conditions including anaemia, hy-


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pothyroidism, cytokines and sleep problems, psychological factors such as anxiety and depression, and loss of functional status (Lucia 2003; Wagner 2004; Mustian 2007). The cause of cancer-related fatigue may also differ between individuals as well as according to the phase of the disease and the type of treatment received (Ryan 2007).

### Description of the intervention

The National Comprehensive Cancer Network (NCCN 2012) has developed guidelines for the management of cancer-related fatigue. Initially any treatable factors that may cause fatigue should be identified and treated. The panel identified several factors that are treatable namely: pain, emotional distress, sleep disturbance, anaemia, nutrition, activity level, medication side effects, alcohol/substance abuse and comorbidities. If the patient does not have any treatable contributing factors or cancer-related fatigue persists, then additional treatment is recommended depending on the patient's clinical status. This incorporates education and counselling, general strategies for the management of fatigue, and pharmacological and non-pharmacological interventions. In line with these guidelines the role of non-pharmacological interventions in the management of cancer-related fatigue is supported by Mustian 2007 and colleagues who have identified psychosocial therapies, physical exercise and a range of other interventions as potentially beneficial. Activity enhancement is also recommended by the NCCN as one of the non-pharmacological interventions at all stages of the disease process: during active treatment, in disease-free patients on long-term follow-up and at the end of life (NCCN 2012).

The physical dimension of cancer-related fatigue is likely to have an organic aetiology (Dimeo 2001). The effect of treatment and a reduction in physical activity can lead to a reduction in physical performance (NCCN 2012). Thus, the patient requires an increased effort to accomplish normal everyday activities, which leads to the perception of fatigue. This is further exacerbated by impairment of skeletal muscle function intensified by a lack of activity (Lucia 2003).

### How the intervention might work

Exercise has been demonstrated to be effective in reducing fatigue and improving the exercise tolerance of healthy individuals as well as those with long-term conditions (Mock 2005). It has been suggested that changes brought about by physical activity may counteract the negative effects the tumour and toxic therapy have on the capacity for physical performance (Dimeo 2002). Activity could reduce cancer-related fatigue by improving functional capacity, resulting in a reduced effort and improvement in the perception of fatigue (NCCN 2012). Rest, the preferred recommendation for cancer-related fatigue in the past, is likely to be counterproductive as inactivity leads to muscle wasting and a loss of cardiorespiratory fitness, leading to increased fatigue (Dimeo 2001). Winningham 1992 developed a theoretical framework for cancer-related fatigue (Winningham's Psychobiological-Entropy model) which proposes that a balance between rest and activity can reduce fatigue, whereas an imbalance can lead to deterioration suggesting that too little or too much exercise may exacerbate it. More recently a biobehavioural model has been suggested to explain the benefits that exercise may have upon cancer-related fatigue (Al-Majid 2009). The model encompasses biological, psycho-behavioral and functional variables that are implicated in the induction of cancer-related fatigue.

The benefit of exercise may not be limited to the improvement of the physical dimension of fatigue. It could also relieve the emotional and mental dimensions. Exercise has been demonstrated to improve mood and reduce anxiety and fear in patients (Dimeo 2001).

### Why it is important to do this review

There are two complementary Cochrane systematic reviews focusing on the treatment of cancer-related fatigue at all stages of cancer. These complementary reviews have examined the role of drugs (Minton 2010) and psychosocial interventions (Goedendorp 2009) in modifying cancer-related fatigue. However, there is currently no definitive stand on exercise for cancer-related fatigue from the American College of Sports Medicine, with minimal detail given on exercise prescription in those that do recommend it (Lucia 2003; Mustian 2007). Furthermore there is limited information on specific groups of cancer patients where caution may be required (Mustian 2007). This review update was conducted to analyse the increasing number of trials and where possible to identify the optimal exercise for reducing cancer-related fatigue.

## OBJECTIVES

To evaluate the effect of exercise on cancer-related fatigue both during and after cancer treatment.

A secondary objective, subject to available data, was to explore the effect of exercise in different types of cancer populations. Groupings were determined based on tumour type, type of cancer treatment received and stage of cancer treatment, that is, either during or after treatment. Based upon the findings of the previous review it was also proposed to explore the effects of different modes of exercise.

## METHODS


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## Criteria for considering studies for this review

### Types of studies

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

### Types of participants

We included studies that evaluated the effect of exercise on cancer-related fatigue in adults of any age, regardless of gender, tumour type, tumour stage and type of cancer treatment. Participants may have been actively receiving treatment, be in long-term follow-up or receiving palliative care.

### Types of interventions

Included studies needed to evaluate and report the effect of physical exercise on cancer-related fatigue. The studies should compare exercise with no exercise, a usual care group (i.e. no specific exercise programme prescribed) or an alternative treatment or exercise regime for fatigue associated with cancer. The intervention could take place in any setting and be delivered to a group or individual participant. All types of physical exercise were considered for inclusion, including aerobic exercise, strength training and flexibility exercises. Studies that investigated an exercise programme accompanied by attempts to promote participant engagement were included. In contrast, studies that explored multi-dimensional programmes in which the effects of exercise alone could not be determined were excluded. Studies were also excluded if a specific exercise programme was not described and participants were only given advice or education about the potential benefits of exercise.

### Types of outcome measures

The outcomes of interest were:

1. patient-reported fatigue measured using reliable and valid assessment tools;
2. exercise maintenance on follow-up;
3. time spent exercising;
4. valid and reliable measures of aerobic capacity;
5. quality of life measures;
6. anxiety;
7. depression;
8. self efficacy (the individual's belief in their own ability to be physically active).

## Search methods for identification of studies

### Electronic searches

Please see Appendix 1 for the search strategy.

We used the following databases to obtain relevant studies for this review (the original search was conducted up to July 2007):

- The Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 1, 2011);
- MEDLINE (1966 to March 2011);
- EMBASE (1980 to March 2011);
- CINAHL (1982 to March 2011);
- British Nursing Index (January 1984 to March 2011);
- AMED (1985 to March 2011);
- SIGLE (1980 to March 2011);
- Dissertation Abstracts International (1861 to March 2011).

### Searching other resources

- We checked the reference lists of all articles obtained for additional studies.
- We handsearched the following journals up to April 2011: *Cancer*, *Journal of Clinical Oncology*, *Psycho-Oncology*, *Cancer Practice*, *Oncology Nursing Forum*.
- We contacted four experts in the field of cancer-related fatigue in order to identify any research that may not have been published.
- We obtained unpublished literature through searches of conference proceedings up to June 2011.
- We attempted to communicate with the study authors to secure information not presented in the studies.
- There were no language restrictions.

## Data collection and analysis

We retrieved all studies in which the abstract made reference to an exercise trial in a population of cancer participants in full. Where abstracts were not available and the study could not be excluded based upon the title alone we retrieved the full text. For a study to be included it had to include fatigue as an outcome measure and at least one treatment arm had to be exercise. Two independent review authors screened all the retrieved full-text articles for inclusion criteria. Although there was initially some discrepancy based upon the appropriateness of the outcome measures, following discussion there was 100% agreement.

Two review authors extracted data from the included studies. If there was disagreement we proposed that there would be a meeting with a third independent reviewer to reach a consensus.

For the original review we assessed the methodological quality of each study using the Oxford quality scale, which is concerned with the presence and adequacy of randomisation, the presence and adequacy of blinding, and description of participant withdrawals (Jadad 1996).

In addition, for each study we extracted:

- number of participants in each arm;
- type of control group;


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- demographic characteristics, including age and gender;
- type of cancer;
- type of treatment and stage of treatment, for example during or after treatment;
- the exercise undertaken in each intervention group;
- duration of intervention, intensity and total number of exercise sessions;
- duration of follow-up;
- outcome measures employed, including means and standard deviations;
- attrition rates.

### Assessment of risk of bias in included studies

For the update of the review we adapted the methods from those described by the Cochrane Pregnancy and Childbirth Group 2012. The authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) with any disagreements resolved by discussion. We assessed the following for each study:

1. Random sequence generation (checking for possible selection bias). We assessed the method used to generate the allocation sequence as: low risk of bias (any truly random process, e.g. random number table, computer random number generator); high risk of bias (any non-random process, e.g. odd or even date of birth, hospital or clinic record number); unclear risk of bias.

2. Allocation concealment (checking for possible selection bias). We assessed the method used to conceal allocation to interventions prior to assignment for whether intervention allocation could have been foreseen in advance of, or during, recruitment, or changed after assignment. We assessed the methods as: low risk of bias (e.g. telephone or central randomisation, consecutively numbered sealed opaque envelopes); high risk of bias (open random allocation, unsealed or non-opaque envelopes, alternation, date of birth); unclear risk of bias.

3. Blinding of outcome assessment (checking for possible detection bias). We assessed the methods used to blind study participants and outcome assessors from knowledge of which intervention a participant received. We considered studies to be at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect the results. We assessed blinding specifically in relation to the fatigue outcome.

4. Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data). We assessed the completeness of fatigue outcome data including attrition and exclusions from the analysis. We assessed methods as: low risk of bias (e.g. no missing outcome data, missing outcome data balanced across groups); high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups, intention-to-treat analysis not performed); unclear risk of bias.

5. Selective reporting (checking for reporting bias). We assessed the methods as: low risk of bias (where it is clear that all of the study's pre-specified fatigue outcomes have been reported); high risk of bias (where not all the study's pre-specified fatigue outcomes have been reported); unclear risk of bias.

### Measures of treatment effect

Fatigue outcomes were likely to be reported in different ways in the identified studies. It was therefore difficult to predict what data would be available to be combined. If the data were available, and it was appropriate to do so, we proposed that the studies would be combined in a meta-analysis. We proposed to calculate the mean difference in fatigue intensity between exercise and control groups including usual care and alternative treatment groups. Subgroup analysis would also be conducted if the data were available. Separate analysis would be implemented according to tumour type, for example breast cancer participants; treatment received, for example chemotherapy or radiotherapy; and the stage of treatment the participant was at when the exercise programme was administered, that is either during or after cancer treatment. If heterogeneity between studies was suspected, the possibility of utilising a random-effects model of meta-analysis would be considered. Further to this and if the information was available, we proposed to calculate the number of participants who experienced at least a 50% reduction in fatigue. This would be used to calculate the number needed to treat to benefit (NNTB) for a 50% reduction in fatigue.

### Assessment of heterogeneity

Where appropriate, heterogeneity of the data was formally assessed using the $I^2$ statistic (Higgins 2003). A value greater than 50% may represent substantial heterogeneity.

## RESULTS

### Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

In the original review, following a comprehensive literature search including screening of titles and abstracts (where available), we retrieved 51 full-text references. From these, we excluded 23 publications and identified 28 (2083 participants) as appropriate for inclusion in the current review. In the updated search we retrieved a further 58 full-text references following screening of titles and abstracts (where available). From these publications, we excluded 23, a further seven were found to be linked to previous studies


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and we identified 28 (n = 1985 participants) as appropriate for inclusion in the updated review. The 28 studies from the original review and the 28 new studies provided a total of 56 studies (4068 participants) for inclusion in the review. In addition, through correspondence with study authors, we identified two protocols for appropriate studies; both studies were still in progress and not yet published and are therefore included in the Characteristics of ongoing studies table.

## Included studies

The final selection, based on consensus, resulted in 28 studies being identified for inclusion in the original review and a further 28 identified in the update providing 56 studies for inclusion. Trial characteristics and outcomes can be seen in the Characteristics of included studies table. Five of the included studies incorporated two separate exercise groups and are therefore entered twice for the purposes of statistical analysis.

### Participants

Participants had various cancer diagnoses although the majority of studies investigated breast cancer only (Mock 1994; Mock 1997; Segal 2001a; Galantino 2003; Courneya 2003b; McKenzie 2003; Pinto 2003; Headley 2004; Campbell 2005; Drouin 2005; Mock 2005; Pinto 2005; Courneya 2007a; Daley 2007; Heim 2007; Moadel 2007 Mutrie 2007; Yuen 2007a; Battaglini 2008; Hwang 2008; Milne 2008; Payne 2008; Carson 2009; Danhauer 2009; Rogers 2009; Chandwani 2010; Lee 2010; Sequeira 2012). Thirty-eight studies investigated participants with a specific cancer diagnosis, whereas 18 studies included participants with different diagnoses. The time since diagnosis varied widely between studies and in some cases within studies. Stage of treatment also varied between the included studies, with 25 of the studies investigating participants during cancer treatment (Mock 1994; Mock 1997; Dimeo 1999; Segal 2001a; Coleman 2003a; Segal 2003; Headley 2004; Windsor 2004; Campbell 2005; Drouin 2005; Mock 2005; Courneya 2007a; Monga 2007; Mutrie 2007; Battaglini 2008; Chang 2008; Hwang 2008; Payne 2008; Adamsen 2009; Mustian 2009; Rogers 2009; Segal 2009a; Chandwani 2010; Culos-Reed 2010; Dodd 2010a), 18 following treatment (Burnham 2002; Courneya 2003b; Galantino 2003; McKenzie 2003; Pinto 2003; Dimeo 2004; Pinto 2005; Thorsen 2005; Culos-Reed 2006; Daley 2007; Heim 2007; McNeely 2008; Milne 2008; Carson 2009; Shelton 2009; Lee 2010; van Weert 2010; Sequeira 2012) and the remaining 13 studies including participants both during and post-cancer treatment (Courneya 2003a; Courneya 2003c; Cohen 2004; Brown 2006; Moadel 2007; Yuen 2007a; Courneya 2008; Oh 2008; Courneya 2009; Danhauer 2009; Galvão 2010; Oh 2010; Santa Mina 2012).

The mean age of participants ranged from 39 to 70 years, with the majority of studies reporting a mean age that fell within the fifth decade. Twenty-nine of the studies recruited females only, which is perhaps not surprising given that 28 of the studies investigated breast cancer only. Twenty studies included a mixed sample of males and females with the remaining seven studies recruiting males only. For detailed information on study participants see the Characteristics of included studies table.

### Interventions

Mode, intensity and timing of exercise differed across studies. Nineteen studies investigated home-based/unsupervised exercise programmes (Mock 1994; Mock 1997; Segal 2001a; Coleman 2003a; Courneya 2003a; Courneya 2003c; Galantino 2003; Headley 2004; Windsor 2004; Drouin 2005; Mock 2005; Pinto 2005; Thorsen 2005; Heim 2007; Yuen 2007a; Payne 2008; Mustian 2009; Culos-Reed 2010; Dodd 2010a), whereas 37 studies investigated supervised, institution-based exercise programmes (Dimeo 1999; Segal 2001b; Burnham 2002; Courneya 2003b; McKenzie 2003; Pinto 2003; Segal 2003; Cohen 2004; Dimeo 2004; Campbell 2005; Brown 2006; Culos-Reed 2006; Courneya 2007a; Daley 2007; Moadel 2007; Monga 2007; Mutrie 2007; Battaglini 2008; Chang 2008; Courneya 2008; Hwang 2008; McNeely 2008; Milne 2008; Oh 2008; Adamsen 2009; Carson 2009; Courneya 2009; Danhauer 2009; Rogers 2009; Segal 2009a; Chandwani 2010; Galvão 2010; Lee 2010; Oh 2010; van Weert 2010; Santa Mina 2012; Sequeira 2012). However, some studies investigating supervised exercise programmes encouraged participants to undertake additional home-based exercise. The remaining study compared a supervised and unsupervised exercise programme (Shelton 2009).

The mode of aerobic exercise varied between studies with 14 studies prescribing a walking programme (Mock 1994; Mock 1997; Segal 2001a; Galantino 2003; Windsor 2004; Drouin 2005; Mock 2005; Heim 2007; Monga 2007; Chang 2008; Payne 2008; Mustian 2009; Rogers 2009; Culos-Reed 2010), six prescribing stationary cycling (leg: Courneya 2003b; Dimeo 2004; Courneya 2008; Courneya 2009; arm: Dimeo 1999; McKenzie 2003) and a further 23 studies incorporating a range of modalities or allowing the participant to choose their preferred mode of aerobic exercise. One study did not report the mode of exercise carried out by participants (Sequeira 2012). Thirteen studies incorporated resistance training as a component of the exercise programme (Coleman 2003a; McKenzie 2003; Heim 2007; Battaglini 2008; Hwang 2008; Milne 2008; Adamsen 2009; Mustian 2009; Shelton 2009; Culos-Reed 2010; Galvão 2010; van Weert 2010; Santa Mina 2012) and four studies investigated resistance training in isolation (Segal 2003; Courneya 2007a; McNeely 2008; Lee 2010). Further to this, two studies included an aerobic training arm in addition to a resistance training arm (Yuen 2007a; Segal 2009a). Seven studies included flexibility training as a component of the exercise programme (Courneya 2003a; Courneya 2003c; Heim 2007; Battaglini 2008; Hwang 2008; Culos-Reed 2010; Lee 2010) al-


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though a number of studies incorporated routine stretching as part of the warm-up or cool-down, or both. Yoga was investigated in six studies (Cohen 2004; Culos-Reed 2006; Moadel 2007; Carson 2009; Danhauer 2009; Chandwani 2010), qigong in two studies (Oh 2008; Oh 2010) and seated exercise in one study (Headley 2004). The intensity of exercise varied greatly across studies with comparison complicated by the method used to monitor intensity in each study. This included methods such as heart rate monitoring, predicted oxygen uptake, patient perceived effort using the Borg scale and self paced exercise intensity. The frequency and duration of the exercise sessions also varied greatly between studies with participants encouraged to exercise between two times per week and daily for 10 to 120 minutes per session. In some studies the frequency or duration, or both, was increased incrementally each week whereas in other studies the duration was based upon individual tolerance. The overall time spent exercising for each of the groups was rarely reported.

In the majority of studies (k = 34) the comparison arm was described as a 'no intervention' or 'usual care' control group although in three of the 34 studies the participants received a weekly phone call regarding their symptom experience (Windsor 2004; Pinto 2005; Dodd 2010a). In a further 10 cases the comparison arm was a 'wait list' control (that is, the control group participants remained on a waiting list and were offered the intervention once the study was complete). Alternative comparison groups included relaxation training (Dimeo 2004), general stretching or range of movement exercises (Drouin 2005; Hwang 2008), light weights and stretching (McNeely 2008), Tai Chi (Galantino 2003) and group psychotherapy (Courneya 2003c). In two studies the participants in the control group received usual care but were also encouraged to remain active (Segal 2001a; Coleman 2003a) and in a further study the control arm patients were given written materials relating to general physical activity (Rogers 2009). In addition to the 'usual care' comparison group Daley 2007 also included a placebo group in which participants performed light intensity body conditioning exercises. No details were provided relating to the comparison group in the study by Burnham 2002. In two studies both arms received an exercise intervention, the first of these compared physical activity with physical activity delivered alongside a cognitive behavioural therapy to reduce fatigue (van Weert 2010); the second compared a group-based intervention to personal training (Santa Mina 2012).

The intervention period varied greatly between studies with a range from three weeks (Dimeo 2004) to one year (Dodd 2010a) and a mode of 12 weeks (k = 17 studies). In some studies duration of the intervention varied between participants, being based upon the duration of cancer treatment. Stratification during randomisation was carried out in the majority of studies in attempt to account for this variation.

For detailed information on interventions see the Characteristics of included studies table.

### Outcome measures

Fatigue was assessed using a wide range of outcome measures including the Functional Assessment of Cancer Therapy (FACT) (Courneya 2003a; Courneya 2003b; Courneya 2003c; Segal 2003; Courneya 2007a; Mutrie 2007; Courneya 2008; McNeely 2008; Courneya 2009; Danhauer 2009; Rogers 2009; Segal 2009a; Oh 2010; Santa Mina 2012), a linear analogue self assessment scale (Mock 1994; Mock 1997; Burnham 2002; Pinto 2005; Brown 2006), a numerical rating scale (Carson 2009), the fatigue sub scale of the Profile of Mood States (POMS) (Dimeo 1999; Coleman 2003a; Pinto 2003; Brown 2006; Culos-Reed 2006), the Piper Fatigue Scale (Mock 1997; Campbell 2005; Drouin 2005; Mock 2005; Daley 2007; Monga 2007; Yuen 2007a; Battaglini 2008; Payne 2008; Dodd 2010a), the Brief Fatigue Inventory (BFI) (Galantino 2003; Cohen 2004; Windsor 2004; Chang 2008; Hwang 2008; Mustian 2009; Shelton 2009; Chandwani 2010), the EORTC-QLQ-C30 fatigue sub scale (Dimeo 2004; Thorsen 2005; Culos-Reed 2006; Oh 2008; Adamsen 2009; Galvão 2010; Lee 2010; Sequeira 2012), the SF-36 vitality scale (Segal 2001a; McKenzie 2003; Adamsen 2009; Galvão 2010), the Functional Assessment of Chronic Illness Therapy-fatigue scale (Headley 2004; Moadel 2007; Mustian 2009), the Fatigue Severity Scale (FSS) (Culos-Reed 2010), the Multidimensional Fatigue Inventory (MFI) (Heim 2007; van Weert 2010) and the Schwartz Cancer Fatigue Scale (Milne 2008). Six studies incorporated more than one fatigue outcome measure (Mock 1997; Brown 2006; Culos-Reed 2006; Adamsen 2009; Mustian 2009; Galvão 2010).

In addition to measuring fatigue the following outcomes were recorded the most frequently: aerobic capacity/cardiovascular function (k = 36), quality of life (k = 38), body composition (k = 18), physical activity levels (k = 15), general mood (k = 11), depression (k = 20) and anxiety (k = 13). Other outcomes assessed included flexibility, sleep variables, distress, symptom stress, strength, well-being, happiness, self esteem, satisfaction with life, chemotherapy completion rates, lymphoedema, self perception, psychosocial adjustment, body image and motivational readiness for change.

For detailed information on outcomes measures see the Characteristics of included studies table.

## Excluded studies

The 56 publications retrieved and subsequently excluded did not meet the review inclusion criteria for the following reasons: two were reviews, 25 were not randomised controlled clinical trials, 10 did not report fatigue as an outcome measure, eight did not include an appropriate exercise intervention and one study did not report the results based upon the original group allocation. Details of the excluded studies can be found in the Characteristics of excluded studies table.


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## Risk of bias in included studies

We initially assessed the included studies for quality using the Oxford Quality Score (Jadad 1996) and in the updated review we also assessed studies using the Cochrane 'Risk of bias' tool (Higgins 2011). Following discussion there was 100% agreement in scores between the two review authors. The majority of studies scored two or three on the Oxford Quality Score. All studies lost two points due to the inability to conceal group allocation of study participants to the exercise intervention. It was also noted that observer blinding was rarely reported in the included studies. Studies that scored two lost a further point due to an incomplete description of drop-outs or an inadequate description of the method of randomisation. In general the Oxford Quality Score was higher in studies that were published more recently. However, it should also be noted that only five of the 56 studies were published prior to 2003. Oxford Quality Scores and 'Risk of bias' tables for each study are presented in the Characteristics of included studies table and a summary of the risk of bias is presented in Figure 1 and Figure 2.


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**Figure 1. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.**

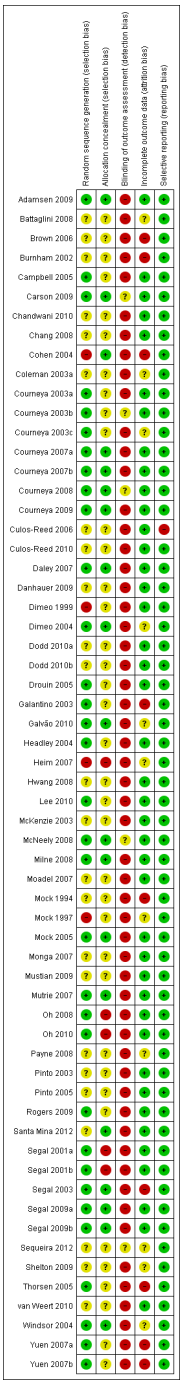



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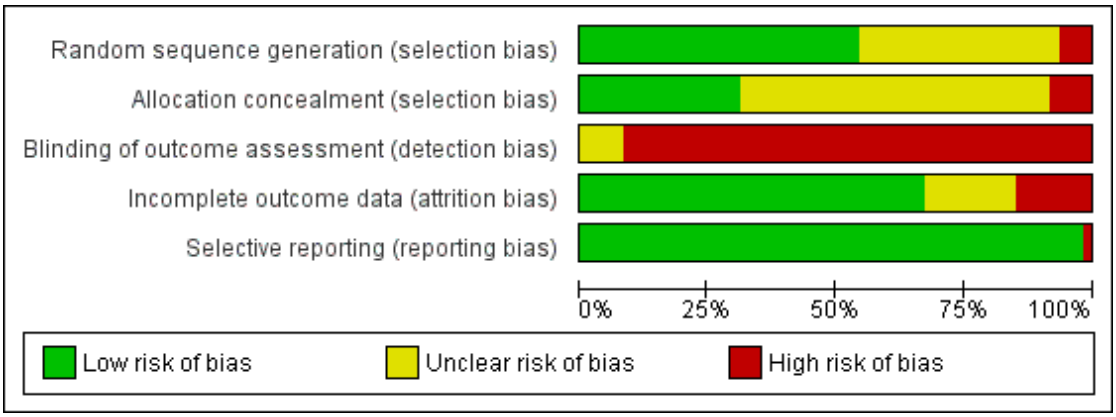
**Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**




### Allocation

Approximately half of the included studies reported appropriate random sequence generation. Allocation concealment was less well reported with over half the studies judged to be unclear.

### Blinding

Unsurprisingly blinding of the fatigue outcome assessment was not performed adequately in any study. This is due to the self report nature of a subjective outcome such as fatigue combined with the complexity of blinding participants to a physical exercise intervention.

### Incomplete outcome data

The majority of studies accounted for all participants and where appropriate performed intention-to-treat analysis.

### Selective reporting

Fatigue outcomes as reported in the methods for each study were provided for the majority of the included studies.

### Other potential sources of bias

A number of the included studies were limited by a small sample size with 24 studies recruiting fewer that 40 participants. Sample size ranged from 10 to 242 with a mean sample size of 69 participants and a median of 52.5. Thirty of the 56 studies either did not carry out or did not report a sample size calculation. The remaining 26 studies carried out a sample size calculation although only 10 of these recruited the required number of participants. Nine studies used fatigue as the basis of the sample size calculation with only four of the nine achieving their recruitment target.

Sixteen of the identified studies either provided no information regarding adherence to the prescribed intervention or did not report it in a meaningful way. The remaining 40 studies provided data on adherence to the exercise intervention with some of the studies also reporting exercise levels for the comparison group. Methods for reporting adherence varied between studies, for example, some studies reported the percentage of supervised sessions attended whereas others were based upon subjective reporting of exercise. Comparison between studies was complicated by the different methods used for reporting, however, for the studies that reported the percentage of supervised sessions attended adherence varied between 61% (Milne 2008) and 98.4% (Courneya 2003b). A few of the studies monitored activity in the comparison group and acknowledged that the level of exercise may have resulted in some participants in the control group carrying out similar levels of activity to individuals in the intervention group. Three studies compared time spent exercising between the intervention and comparison group; all three reported that the intervention group performed exercise for a statistically longer period during the intervention period (Courneya 2003c; Pinto 2005; Mutrie 2007). For analysis purposes all studies considered participants in the group to which they had been assigned, regardless of adherence, hence the estimated benefit of exercise did not take into consideration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whether or not the participants adhered to the prescribed activity. Only 11 of the 56 studies failed to provide adequate information regarding participants who withdrew or dropped out of the study. In the majority of cases participants who dropped out or withdrew were not included in the analysis although this was not entirely clear in all studies. Definition of intention-to-treat analysis varied between studies with some studies using this term to describe the inclusion of non-adherent participants in the analysis, whereas others used the term to describe the inclusion of participants who failed to complete the outcome measures or lost contact with the investigators, or both.

Follow-up assessment of long-term outcomes was poor with 35 of the 56 studies failing to assess outcomes beyond the end of the intervention period. From the remaining studies that did include a follow-up assessment, four did not present the follow-up data in the original publication (Headley 2004; Pinto 2005; Courneya 2007a; Culos-Reed 2010). The length of follow-up for the remaining studies varied from four weeks (Windsor 2004) to one year (Dodd 2010a) following the end of the intervention period.

The primary outcome was not identified in all studies, with the majority of studies employing multiple outcome measures. Fatigue reduction alone was the main purpose of the intervention in only eight studies (Dimeo 1999; Dimeo 2004; Mock 2005; Heim 2007; Yuen 2007a; Chang 2008; Adamsen 2009; Dodd 2010a). In the remaining studies fatigue was either one of two or more main outcomes, a secondary outcome or reported as a sub scale of a quality of life measure. In 11 of the studies improvement in quality of life was identified as the single main purpose of the intervention (Courneya 2003a; Courneya 2003c; Campbell 2005; Brown 2006; Courneya 2007a; Daley 2007; Moadel 2007; Mutrie 2007; Milne 2008; Chandwani 2010; Oh 2010). Thirteen studies identified two primary outcomes (Mock 1994; Mock 1997; Segal 2001a; Coleman 2003a; Courneya 2003b; Galantino 2003; McKenzie 2003; Segal 2003; Headley 2004; Windsor 2004; Monga 2007; McNeely 2008; Santa Mina 2012) and 13 studies identified three or more outcomes without identifying the primary purpose of the intervention (Pinto 2003; Drouin 2005; Pinto 2005; Thorsen 2005; Hwang 2008; Oh 2008; Payne 2008; Danhauer 2009; Mustian 2009; Segal 2009a; Culos-Reed 2010; Galvão 2010; van Weert 2010). The tools used to assess each of the outcomes of interest varied greatly between studies making comparisons difficult. Some of the included studies did not report the results in full and often only where statistically significant differences were identified.

## Effects of interventions

Twenty-eight studies were identified for inclusion in the original review and an additional 28 in the updated review, providing 56 studies for inclusion (n = 4068 participants). For the purposes of meta-analysis, where data were not reported in full, we made an attempt to contact the corresponding author (n = 30). Twelve of the 30 authors subsequently provided post-test mean data +/- standard deviation (SD) for the fatigue outcome employed. The remaining authors either did not respond, could not be located or reported that the data were not available. In the original review we carried out separate meta-analyses on fatigue data using post-test means and change data. The two comparisons provided very similar results and we subsequently decided to base the remaining comparisons on the post-test means as the data were more readily available. For the purposes of the updated review all comparisons were based upon post-test means.

Five studies were not appropriate for inclusion in the meta-analyses as they did not incorporate an acceptable control arm. The five studies excluded compared specific exercise with a general exercise control arm (Lee 2010), individually supervised versus a group exercise control (Santa Mina 2012), supervised exercise versus an unsupervised control (Shelton 2009), resistance exercise versus aerobic exercise (van Weert 2010) and finally exercise versus exercise and education (Sequeira 2012).

### Fatigue

#### All studies: exercise versus control, post-test means

We used a meta-analysis to combine the post-test results of the 51 remaining studies providing 56 possible comparisons due to the inclusion of two intervention arms in five studies. However, post-test means +/- SD were not available for 18 of the 56 comparisons. The remaining 38 comparisons provided data for 1461 participants who received an exercise intervention and 1187 participants in the control arm. At the end of the intervention period exercise was statistically more effective than the control intervention (standardised mean difference (SMD) -0.27, 95% confidence interval (CI) -0.37 to -0.17) with moderate statistical heterogeneity identified (P = 0.03; $I^2$ = 33.0%) (Analysis 1.1).

#### Intervention timing

Twenty-five studies provided separate data for participants receiving an exercise intervention during cancer treatment. We used a meta-analysis to combine the post-test results of the 25 studies with 28 comparisons possible due to the inclusion of two intervention groups in three studies. However, post-test means +/- SD were not available for 10 of the 28 comparisons. The remaining 18 comparisons provided data for 824 participants who received an exercise intervention and 642 participants in the control arm. At the end of the intervention period exercise was statistically more effective than the control intervention (SMD -0.23, 95% CI -0.33 to -0.12) with no evidence of statistical heterogeneity (P = 0.94; $I^2$ = 0%) (Analysis 2.1).

Nineteen studies investigated participants post-cancer treatment, however, four of these studies were not appropriate for inclusion in a meta-analysis due to the lack of an appropriate control arm (Shelton 2009; Lee 2010; van Weert 2010; Sequeira 2012). We


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also used a meta-analysis to combine the post-test results of the remaining 15 studies in which participants received an exercise intervention following cancer treatment with 15 comparisons possible. However, post-test means +/- SD were not available for five of the 15 comparisons. The remaining 10 comparisons provided data for 272 participants who received an exercise intervention and 267 participants in the control arm. At the end of the intervention period exercise was statistically more effective than the control intervention (SMD -0.44, 95% CI -0.79 to -0.09) with a high level of statistical heterogeneity detected (P < 0.0002; $I^2$ = 72.0%) (Analysis 3.1).

The remaining studies recruited a mixed sample of participants during and post-treatment for cancer and did not provide separate results.

#### Disease-specific comparisons

The majority of studies were carried out in breast cancer populations (k = 28 studies that only recruited breast cancer participants; n = 1671 participants). Two of these studies were not appropriate for inclusion in a meta-analysis due to the lack of an appropriate control arm (Lee 2010; Sequeira 2012). We used a meta-analysis to combine the post-test results of the remaining 26 studies, with 29 comparisons possible due to the inclusion of two intervention groups in three studies. However, post-test means +/- SD were not available for 11 of the 29 comparisons. The remaining 18 comparisons provided data for 672 participants who received an exercise intervention and 511 participants in the control arm. At the end of the intervention period exercise was statistically more effective than the control intervention (SMD -0.35, 95% CI -0.51 to -0.19) with a moderate level of statistical heterogeneity detected (P = 0.06; $I^2$ = 36.0%) (Analysis 4.1).

Seven studies were carried out in prostate cancer populations with an overall total of 491 participants. One study was not appropriate for inclusion in the meta-analysis due to the lack of an appropriate control arm (Santa Mina 2012). We used a meta-analysis to combine the post-test results of the remaining six studies, with seven comparisons possible due to the inclusion of two intervention groups in one study. However, post-test means +/- SD were not available for one of the seven comparisons. The remaining six comparisons provided data for 239 participants who received an exercise intervention and 176 participants in the control arm. At the end of the intervention period exercise was statistically more effective than the control intervention (SMD -0.45, 95% CI -0.78 to -0.11) although a high level of statistical heterogeneity was detected (P = 0.03; $I^2$ = 59.0%) (Analysis 5.1).

Five studies were carried out in populations with haematological malignancies (lymphoma, myeloma and leukaemia) with an overall total of 260 participants. One study was not appropriate for inclusion in the meta-analysis due to the lack of an appropriate control arm (Shelton 2009). We used a meta-analysis to combine the post-test results of the remaining four studies providing four comparisons. The comparisons provided data for 114 participants who received an exercise intervention and 106 participants in the control arm. At the end of the intervention period there was no statistically significant difference between the exercise and the control arm (SMD -0.15, 95% CI -0.42 to 0.11) with no evidence of statistical heterogeneity detected (P = 0.91; $I^2$ = 0%) (Analysis 6.1).

Two further studies recruited disease-specific cohorts, specifically a colorectal cancer population (Courneya 2003a) and a head and neck cancer population (McNeely 2008). The remaining studies (k = 14) recruited participants from more than one diagnostic group.

#### Mode of exercise

The majority of studies incorporated an aerobic exercise arm (k = 30), although one of the studies was not appropriate for inclusion in a meta-analysis due to the lack of an appropriate control arm (van Weert 2010). The remaining 29 studies provided 31 possible comparisons due to the inclusion of two intervention groups in two studies. However, post-test means +/- SD were not available for nine of the 31 comparisons. The remaining 22 comparisons provided data for 832 participants who received an aerobic exercise intervention and 701 participants in the control arm. At the end of the intervention period aerobic exercise was statistically more effective than the control intervention (SMD -0.22, 95% CI -0.34 to -0.10) with a moderate level of statistical heterogeneity detected (P = 0.20; $I^2$ = 20.0%) (Analysis 7.1).

Six studies included a resistance exercise arm although one of the studies was not appropriate for inclusion in a meta-analysis due to the lack of an appropriate control arm (Lee 2010). The remaining five studies provided data for 237 participants who received a resistance exercise intervention and 164 participants in the control arm. At the end of the intervention period resistance exercise was not statistically more effective than the control intervention (SMD -0.18, 95% CI -0.39 to 0.02) with no evidence of statistical heterogeneity detected (P = 0.91; $I^2$ = 0%) (Analysis 8.1).

Eight studies investigated low-intensity mind-body exercises, specifically yoga or qigong, providing eight possible comparisons for inclusion in a meta-analysis. However, post-test means +/- SD were not available for five of the eight comparisons. The remaining three comparisons provided data for 117 participants who received a mind-body exercise intervention and 77 participants in the control arm. At the end of the intervention period mind-body exercise was not statistically different to the control (SMD -0.10, 95% CI -0.39 to 0.19) with no evidence of statistical heterogeneity detected (P = 0.53; $I^2$ = 0%) (Analysis 9.1).

The remaining studies investigated multimodal exercise interventions, usually incorporating aerobic and resistance training.

#### Long-term outcomes


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The above results were based upon post-intervention data as only 12 of the included studies recorded and presented follow-up data. Five of these studies investigated the effects of an exercise programme delivered during cancer therapy (Windsor 2004; Mutrie 2007; Mustian 2009; Chandwani 2010; Dodd 2010a). Four of the five studies reported that the differences in fatigue levels between intervention and control arm were not significant post-intervention or at follow-up (Windsor 2004; Mutrie 2007; Chandwani 2010; Dodd 2010a). Duration of follow-up was one month (Windsor 2004), three months (Chandwani 2010), six months (Mutrie 2007) and one year (Dodd 2010a) following the intervention. In contrast Mustian 2009 reported that statistically significant improvements in fatigue in the intervention group compared to the control arm were maintained at three months.

Four of the studies that included a long-term follow-up investigated the effects of an exercise programme delivered post-cancer therapy (Daley 2007; Heim 2007; Milne 2008; Sequeira 2012). Daley 2007, Milne 2008 and Sequeira 2012 reported no differences between study arms with regard to fatigue immediately post-intervention or at 24 week/six-month follow-up. In contrast Heim 2007 reported that statistically significant improvements in fatigue in the intervention group compared to the control arm were maintained at three months.

The remaining three studies that included a long-term follow-up investigated a mixed sample of patients during and post-cancer therapy (Cohen 2004; Brown 2006; Courneya 2009). Cohen 2004 stated that outcomes were recorded at one and three months after baseline although there is no differentiation between the two time points in the reported results. Brown 2006 implemented a four-week intervention and participants were followed up post-intervention, at eight weeks and at 27 weeks. At eight weeks statistically fewer participants in the control arm reported clinically significant fatigue compared to the intervention arm. No statistically significant differences were reported between groups at eight or 27 weeks. The final study reported no significant differences in fatigue between study arms at the end of the intervention or at the six-month follow-up (Courneya 2009).

### Exercise Maintenance on Follow-up

Exercise maintenance was rarely reported and the methods employed were mainly self report and only completed by a small number of study participants.

### Time Spent Exercising

Time spent exercising was rarely reported and the methods employed were mainly self report and only completed by a small number of study participants.

### Aerobic capacity

Thirty-eight of the 56 studies measured aerobic capacity or physical fitness, or both. The measures used varied between studies with seven studies employing $VO_2$ max (an indicator of cardio-respiratory endurance and aerobic fitness) and the remaining studies employing alternative measures of physical fitness or endurance. Fifteen of the 38 studies reported no difference between the intervention and control groups for post-test aerobic capacity (Segal 2001a; Burnham 2002; Coleman 2003a; Courneya 2003a; Courneya 2003c; Galantino 2003; Mock 2005; Culos-Reed 2006; Heim 2007; Mustian 2009; Rogers 2009; Shelton 2009; Culos-Reed 2010; Galvão 2010; Santa Mina 2012) although it should be noted that two of these studies compared exercise interventions rather than a no exercise control arm (Shelton 2009; Santa Mina 2012). Seventeen of the 38 studies demonstrated a statistically significant difference in aerobic capacity or physical fitness between the intervention and control arm in favour of the intervention (Mock 1994; Mock 1997; Courneya 2003b; Windsor 2004; Campbell 2005; Pinto 2005; Thorsen 2005; Courneya 2007a; Daley 2007; Monga 2007; Mutrie 2007; Chang 2008; Courneya 2008; Milne 2008; Adamsen 2009; Courneya 2009; Segal 2009a). Four of the remaining six studies reported improvements over time but no between-group comparisons were provided (Pinto 2003; Dimeo 2004; Drouin 2005; Yuen 2007a). One study did not provide any statistical analysis of the aerobic capacity data (Dodd 2010a) and the final study did not reassess aerobic capacity post-intervention (Battaglini 2008).

Five studies investigated the relationship between aerobic capacity and fatigue; three reported no statistically significant correlation between change in aerobic performance and fatigue (Courneya 2003a; Dimeo 2004; Drouin 2005), whereas Mock 2005 and Milne 2008 reported a statistically significant association between improvements in aerobic fitness and subjective fatigue.

### Quality of life

Twenty of the 56 studies did not measure quality of life (QoL) and a further study did not report the quality of life outcome data within the results (Galantino 2003). The remaining 35 studies most frequently used the Functional Assessment of Cancer Therapy to assess QoL, although the version used varied between studies, for example, eight studies used the FACT-Breast (FACT-B) and eight the FACT-general (FACT-G). Other measures used to assess QoL included the Satisfaction with Life Scale (SWLS), SF-36, the EORTC-QLQ-C30, the QoL Index for Cancer and the Functional Assessment of Chronic Illness Therapy-Fatigue. Six studies used two measures to assess QoL and one study employed three different QoL measures. The findings were not always consistent between measures.

Sixteen studies reported no statistically significant difference in post-test QoL between the intervention and control arms (Segal 2001a; Dimeo 2004; Thorsen 2005; Courneya 2007a; Moadel 2007; Courneya 2008; McNeely 2008; Oh 2008; Adamsen 2009;


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Danhauer 2009; Rogers 2009; Segal 2009a; Culos-Reed 2010; Lee 2010; Santa Mina 2012; Sequeira 2012), whereas 17 studies reported that exercise was statistically more beneficial to QoL than the control intervention (Burnham 2002; Courneya 2003a; Courneya 2003b; Courneya 2003c; Segal 2003; Headley 2004; Culos-Reed 2006; Daley 2007; Heim 2007; Monga 2007; Hwang 2008; Milne 2008; Courneya 2009; Mustian 2009; Chandwani 2010; Galvão 2010; Oh 2010).

Campbell 2005 assessed QoL using the FACT-G, FACT-B and the SWLS although the FACT-G was identified as the primary outcome of interest. The FACT-G as the primary outcome demonstrated a statistically significant improvement in QoL pre-post test in the exercise arm compared to the control arm. However, the FACT-B and SWLS did not demonstrate statistically significant differences between arms. Mutrie 2007 employed the FACT-G as the primary measure of QoL in addition to the FACT-B. Results demonstrated no statistically significant differences between arms in the FACT-G although the FACT-B showed a statistically significant difference between arms post-intervention in favour of the exercise arm.

### Anxiety

Twenty-one of the 56 studies measured anxiety by means of the State Trait Anxiety Inventory (k = 7), the Profile of Mood State (POMS) Tension-Anxiety sub scale (k = 7), a visual analogue scale (VAS) (k = 3), the Hospital Anxiety and Depression Scale (HADS) (k = 2), or the Distressed Mood Index (k = 1). In addition, one study measured Social Physique Anxiety which assesses an individual's anxiety in regard to real or perceived evaluation of their physique by others (Milne 2008). One of the 21 studies only measured anxiety at baseline (Brown 2006) and a further study only reported a total HADS score with no separate anxiety data (Heim 2007). Thirteen of the remaining 19 studies that measured anxiety reported no statistically significant benefits of exercise compared to a control arm (Mock 1994; Coleman 2003a; Courneya 2003a; Courneya 2003c; Cohen 2004; Drouin 2005; Pinto 2005; Thorsen 2005; Courneya 2007a; Moadel 2007; Chang 2008; Courneya 2009; Chandwani 2010). Further to this, Burnham 2002 reported that anxiety improved over time in the exercise intervention arm but there was no statistically significant difference in anxiety compared to the control arm. Dimeo 1999 also reported a statistically significant improvement over time in the exercise arm but no comparison with the control arm was reported. Mock 1997, Culos-Reed 2006 and Oh 2010 reported a statistically beneficial effect of exercise on anxiety compared to a control. In relation to social physique anxiety Milne 2008 also reported exercise to be statistically more effective than a control.

### Depression

Twenty-eight of the 56 studies incorporated an outcome measure for depression including the Centre for Epidemiological Studies-Depression Scale (CES-D) (k = 10), POMS-depression sub scale (k = 9), the Beck Depression Inventory (k = 4), a VAS (k = 3) and the HADS (k = 2). Nineteen of the 28 studies that measured depression reported no statistically significant difference between the intervention and control arm post-test (Mock 1997; Dimeo 1999; Burnham 2002; Coleman 2003a; Courneya 2003a; Courneya 2003c; Pinto 2003; Cohen 2004; Thorsen 2005; Culos-Reed 2006; Courneya 2007a; Monga 2007; Mutrie 2007; Chang 2008; Payne 2008; Chandwani 2010; Culos-Reed 2010; Dodd 2010a; Lee 2010). A further two studies did not report the results from the depression outcome measure (Pinto 2005; Brown 2006) and one study only reported a total HADS score (Heim 2007). Three studies reported a significant improvement in depression in the exercise arm compared to the control arm at the end of the intervention (Courneya 2009; Danhauer 2009; Oh 2010). Daley 2007 also reported statistically less depression following exercise compared to the control arm, however, depression was also statistically less in the placebo exercise group compared to the control arm. Drouin 2005 reported a statistically significant improvement in depression pre-post test with no corresponding improvement in the control arm, however, statistical analysis for arm by time interaction was not reported. Finally, Mock 1994 reported statistically worse depression in the control arm compared to the intervention arm mid-way through chemotherapy treatment. This difference was not maintained one month following chemotherapy.

### Self efficacy

Only one of the included studies measured exercise self efficacy (Pinto 2005) with the results reported in a separate publication. No statistically significant mediating relationship was demonstrated between self efficacy and minutes of moderate-intensity activity undertaken.

## DISCUSSION

This review provides evidence that exercise is beneficial in the management of cancer-related fatigue. Statistically significant improvements in fatigue were identified following an exercise programme carried out either during cancer therapy or following cancer therapy. Further to this, statistically significant beneficial effects were identified specific to breast cancer and prostate cancer populations but not for those with haematological malignancies. It remains to be determined whether the type of cancer treatment alters the beneficial effect of exercise on cancer-related fatigue. Statistically beneficial effects were identified following aerobic training but not following resistance training or low-intensity mind-body interventions.


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## Limitations of the review

This review has incorporated a diverse range of studies with small numbers in several of them. There is a considerable degree of clinical heterogeneity between studies in terms of adjuvant therapy, mode and intensity of exercise, and stage and type of cancer. In addition, moderate statistical heterogeneity was present for the total fatigue (P = 0.03; $I^2$ = 33.0%), breast cancer fatigue (P = 0.06; $I^2$ = 36.0%) and the aerobic exercise (P = 0.20; $I^2$ = 20.0%) meta-analyses. A high level of statistical heterogeneity was present in the meta-analyses of studies investigating exercise after cancer therapy (P < 0.0002; $I^2$ = 72.0%) and in the prostate cancer population (P = 0.03; $I^2$ = 59.0%). However, the meta-analysis of studies carried out during cancer therapy (P = 0.94; $I^2$ = 0%), in haematological patients (P = 0.91; $I^2$ = 0%), for resistance exercise (P = 0.91; $I^2$ = 0%) and for mind-body exercise (P = 0.53; $I^2$ = 0%) provided no evidence of statistical heterogeneity. The lack of statistical heterogeneity does not exclude heterogeneity, given the small numbers.
Despite a comprehensive search strategy all studies included were published in the English language. This may reflect selective publication of English language studies with statistically significant findings.
Data were not available for the purpose of meta-analysis for all studies retrieved and identified as suitable. The studies which have not reported the data in full tended to be those that have not identified a favourable outcome for exercise, therefore the results of the meta-analysis may have been biased in the direction of a positive outcome, making exercise appear more effective. Selective reporting of statistically significant outcomes may also have occurred.
For the purpose of inclusion in the review all studies recorded fatigue as an outcome, however, the primary purpose of the exercise interventions varied between studies. The exercise may therefore have been designed for an alternative purpose, resulting in a lack of beneficial effect for fatigue.
The results of the review should not be considered in isolation as there are a range of non-pharmacological interventions that may be considered beneficial in the management of cancer-related fatigue. Interventions that may be delivered in conjunction with an exercise programme include, but are not limited to, psychosocial therapies (Jacobsen 2007; Goedendorp 2009), stress management, nutrition therapy and sleep therapy (Mustian 2007).

## Limitations of the included studies

The quality of the included studies was variable with the more recent studies generally being of better quality. It is acknowledged that blinding participants to an exercise intervention may not be a feasible option although methods to reduce this risk of bias should be carefully considered in future trials.
Few of the included studies provided information about people who refused participation in the trial. It is possible that the included participants differed statistically to those who refused participation, particularly in relation to their attitudes towards an exercise programme. It is possible that those who declined to participate would not have achieved the same benefits from an exercise programme as those who chose to participate. Some studies did indicate the main reasons for individuals refusing to participate which included a lack of interest in the study, a refusal or inability to travel, being too busy or having other commitments, a refusal to be randomised and not wanting to be reminded of their cancer.
Statistical power was limited by the small number of participants in several studies. Furthermore, in several studies, fatigue was not identified as the primary outcome, thus sample size calculations (where reported) were based upon a different outcome measure.
The majority of studies were carried out with breast cancer populations. Further research in this area needs to include participants with various cancer diagnoses or other specific cancer populations at various stages of disease, including those receiving palliative care.
In some studies the control groups received less attention from healthcare or research staff, or both, in comparison to the intervention groups. The additional attention may have resulted in a systematic bias (Hawthorne effect) in favour of the intervention.
Few studies included long-term follow-up measures and these were not always reported. Further to this a number of studies implemented short-term interventions (approximately three weeks) which may not have been long enough to produce any statistically significant effects in relation to fatigue.
According to the most recent recommendations from the American College of Sports Medicine (ACSM) (Garber 2011) adults should undertake moderate-intensity aerobic physical activity for at least 30 minutes on five days per week or vigorous intensity aerobic physical activity for at least 20 minutes on three days each week. The majority of exercise interventions reviewed did not reach these recommendations as exercise was only undertaken two to three times per week at moderate intensity. Twelve of the studies included an intervention that met these recommendations although the participants may have been advised to start at a lower level and progress to 30 minutes on five days per week (Mock 1994; Mock 1997; Segal 2001a; Courneya 2003a; Courneya 2003c; Dimeo 2004; Drouin 2005; Mock 2005; Pinto 2005; Adamsen 2009; Mustian 2009; Rogers 2009). This stepwise progression is in line with the recommendations from the ACSM (Garber 2011). It should be noted that the ACSM guidelines were developed for healthy individuals and may need to be adapted for cancer survivors according to the stage of disease and adjuvant treatment. ACSM have developed guidelines for older adults which highlight the importance of combined aerobic, resistance and flexibility exercises (Chodzko-Zajko 2009). These guidelines may be more appropriate for cancer survivors but due to insufficient evidence the optimal exercise programme has not yet been established (Chodzko-Zajko 2009). This is in line with the ACSM Roundtable Consensus Statement that recognised the need to adapt exercise programmes for the individual cancer sur-


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vivor according to health status, adjuvant treatment and anticipated disease trajectory (Schmitz 2010). The statement does, however, recommend that all cancer survivors should maintain and increase muscle mass (Schmitz 2010). The effect of resistance training upon fatigue is inconclusive as although there was a trend observed in favour of resistance training this failed to reach significance. In agreement with the current review the consensus group concluded that there was insufficient evidence to recommend alternative forms of exercise such as yoga and tai chi (Schmitz 2010).

### Outcome measures

A wide range of unidimensional and multidimensional outcome measures were used in the included studies which has prevented direct comparisons between studies. Data regarding fatigue were not always reported in full or adequately for the purposes of combining outcomes in a meta-analysis. We made attempts to contact authors where data were not available. It is recommended that multidimensional measures should be used to accurately assess fatigue to ensure that the effects of the intervention are captured in full. For example, an exercise intervention may have beneficial effects on mental and emotional fatigue levels but not physical fatigue levels. These effects would not be captured with a unidimensional tool.

The fatigue measures that were used do not have validated cut-off scores for mild/moderate/severe fatigue. In addition only one of the outcome measures used had validated minimal clinically important differences (MCIDs) (FACT-F; Cella 2002), hence it was not possible to determine the number needed to treat to benefit (NNTB) from the data obtained. Included studies did not provide estimates of effect size that could be pooled.

### Adherence and contamination

Several studies indicated that participants completed exercise diaries although the results of these were frequently not reported. The accuracy of reporting in exercise diaries has also been questioned (Montoye 1996). Group contamination has previously been reported in studies investigating exercise. This may occur when the control participants undertake exercise or the exercise group do not adhere to the programme. Further contamination may occur when participants do not undertake the exercise at the prescribed intensity or for the prescribed duration. Monitoring of exercise is more difficult when the prescribed programme is home-based or unsupervised, or both. It is possible that implementation of an exercise programme should be accompanied by a behavioural change intervention to ensure that participants are supported. Only one study monitored participants' self efficacy, which may be an important predictor of adherence to the exercise intervention (Pinto 2005). Adherence to an exercise programme may be lower during cancer treatment as a result of associated adverse effects (Oldervoll 2004), hence patients may require additional support to remain active at this time. Recent research has indicated that providing cancer patients with supporting printed material regarding the exercise or with physical activity monitoring devices may increase levels of physical activity (Vallance 2007).

## AUTHORS' CONCLUSIONS

### Implications for practice

Thirty studies provided overall evidence that aerobic exercise is beneficial in the management of fatigue both during and after cancer treatment and should therefore be considered as one component of a management strategy for fatigue that may include a range of other interventions and education. These findings related specifically to those with solid tumours.

### Implications for research

Further work is necessary to determine the most effective parameters of exercise for fatigue management including multi-modal exercise (combined aerobic and resistance), frequency and duration of each exercise session, and intensity of exercise. Future studies should also incorporate a long-term follow-up. Twenty eight of the included studies were carried out in breast cancer populations therefore future research needs to be undertaken with a broad range of diagnoses, including patients with advanced disease and those receiving palliative care.

Consensus is also needed on the most appropriate multi-dimensional outcome measure to use. Further work is required to determine cut-off scores and minimal clinically important differences (MCID) for each of the selected measures.

Future research also needs to consider issues of maximising adherence and promoting self efficacy to exercise as well as identifying the barriers and facilitators to exercise in people with a cancer diagnosis. Other limitations of the existing research that need to be addressed include concealment of group allocation and observer blinding. Trials also need to be adequately powered to detect a change in fatigue. It is likely that the large number of studies with small numbers of participants may be due to limited funding available for non-commercial trials. Funding agencies may therefore like to consider funding large studies to determine optimal exercise parameters for this patient group.

## ACKNOWLEDGEMENTS

This research was supported in part by the National Institute for Health Research (NIHR) Health Technology Assessment programme. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the funding agency.


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The search strategy was developed with the assistance of Sylvia Bickley and the review update search was supported by Jane Hayes, Trials Search Co-ordinator for the Cochrane Pain, Palliative and Supportive Care Review Group.

Gillian Prue and Dr Jackie Gracey contributed to the development of the initial review protocol.

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* *Indicates the major publication for the study*


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## CHARACTERISTICS OF STUDIES

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

**Adamsen 2009**

| | |
|---|---|
| Methods | RCT; 2 group parallel design |
| Participants | 235 participants with 21 different cancer diagnoses, median of 84 days since diagnosis, were receiving chemotherapy |
| Interventions | Multimodal supervised groups; aerobic, resistance and relaxation/body awareness. 6 weeks with 4 sessions/week (24 total), 9 hours/week.<br>Control: usual care |
| Outcomes | Fatigue<br>QoL<br>Side effects<br>Aerobic capacity<br>Muscle strength<br>Leisure time physical activity |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: fatigue was the primary outcome |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomisation was done by computer" |
| Allocation concealment (selection bias) | Low risk | "The allocation sequence was executed by the clinical research unit and concealed from the project team." |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All patients were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Battaglini 2008**

| | |
|---|---|
| Methods | RCT; 2-group parallel design |
| Participants | 20 breast cancer patients due to receive adjuvant therapy |
| Interventions | Aerobic and resistance training at 40% to 60% maximum exercise capacity and stretching; twice per week for 15 weeks, up to 60 minutes per session<br>Control: usual care |
| Outcomes | Fatigue<br>Total caloric intake<br>Cardiovascular endurance<br>Dynamic muscular endurance<br>Body composition |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: total calorie intake |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Stated to be randomised |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Not clear if all participants completed the study |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Brown 2006**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification by tumour type, age, gender and Eastern Co-operative Oncology Group Score |
| Participants | 103 cancer patients diagnosed within past 12 months and due to receive radiotherapy |
| Interventions | Structured multidisciplinary sessions incorporating self paced exercise. 8 sessions over 4 weeks with 20 mins of exercise per session. Control: usual care |
| Outcomes | Fatigue<br>Mood<br>Anxiety |


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**Brown 2006** (*Continued*)

| | | |
|---|---|---|
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to improve quality of life | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but methods not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Drop-outs not accounted for and unclear whether an intention-to-treat analysis was undertaken |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Burnham 2002**

| | |
|---|---|
| Methods | RCT; 3 groups, stratification by aerobic capacity and quality of life |
| Participants | 21 breast or prostate cancer survivors minimum 2 months post-treatment |
| Interventions | Moderate-intensity exercise: 40% to 50% HR reserve rising to 60% by week 10<br>Low-intensity exercise: 25% to 35% HR rising to 40% by week 10<br>Both groups supervised exercise 3 times/week for 10 weeks. Sessions initially 14 minutes increasing to 32 by week 10. Treadmill, stationary bicycle and stair climbing.<br>Control: no exercise prescribed |
| Outcomes | Aerobic capacity<br>Body composition<br>Flexibility<br>Quality of life<br>Fatigue<br>Anxiety<br>Confusion<br>Depression<br>Energy<br>Anger |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve physiological and psychological function |


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**Burnham 2002** (*Continued*)

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but no method described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Intention-to-treat not applied as one participant from the control arm was excluded as they took part in exercise training |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Campbell 2005**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification by type of adjuvant cancer therapy |
| Participants | 22 breast cancer patients post-surgery, receiving therapy. Not exercising vigorously 3 times/week for 20 mins or more |
| Interventions | Exercise: supervised, 2 times/week for 12 weeks. Warm up, 10 to 20 mins of various exercises, cool down. Approximate 60% to 75% age-adjusted HRmax.<br>Control: no intervention until week 12 |
| Outcomes | Quality of life<br>Fatigue<br>Physical activity levels |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve quality of life |

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "randomly allocated by computer-generated numbers" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |


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**Campbell 2005** (*Continued*)

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Carson 2009**

| | |
|---|---|
| Methods | RCT; 2 groups, wait list control |
| Participants | 37 breast cancer patients, diagnosed at least 2 years previously. Had received a variety of adjuvant treatments |
| Interventions | Exercise: yoga; supervised in groups (5 to 10 per group) for 120 minutes once/week for 8 weeks, and encouraged to practise daily with CD and illustrated handbook<br>Control: wait list, received usual care |
| Outcomes | Fatigue<br>Hot flashes<br>Joint pain<br>Mood<br>Sleep disturbance<br>Bother |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce hot flashes |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomization...random number table" |
| Allocation concealment (selection bias) | Low risk | "Assignments were concealed in envelopes that were not opened until all patients had completed their baseline assessment." |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | "The research assistant collecting assessment data was kept blind with regard to patient condition assignments". Fatigue was self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All patients were accounted for |


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**Carson 2009** (*Continued*)

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Chandwani 2010**

| | |
|---|---|
| Methods | RCT; 2 groups, wait list control |
| Participants | 58 breast cancer patients, due to receive radiotherapy |
| Interventions | Exercise: yoga; 2 x 60 min classes/week for 6 weeks, supervised, mainly on a one to one basis. Encouraged to practice daily<br>Control: wait list, received usual care |
| Outcomes | Quality of life (SF36 provided vitality data)<br>Depression<br>Anxiety<br>Sleep disturbance<br>Tendency to ruminate<br>Finding meaning in cancer |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but process not clear |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Chang 2008**

| | |
|---|---|
| Methods | RCT; 2 groups, parallel design |
| Participants | 22 patients with acute myelogenous leukaemia, due to commence chemotherapy |
| Interventions | Exercise: walking exercise programme during inpatient CT, 12 minutes of supervised walking on 5 days/week for 3 weeks. Aimed to reach a target intensity of resting heart rate plus 30<br>Control: attention control, no additional intervention specific to fatigue |
| Outcomes | Fatigue<br>Walk distance<br>Symptom distress<br>Mood (including anxiety and depression) |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to reduce fatigue |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not stated |
| Allocation concealment (selection bias) | Unclear risk | Allocation not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Cohen 2004**

| | |
|---|---|
| Methods | CCT; 2 groups |
| Participants | 39 lymphoma patients either during treatment or up to 12 months post-treatment |
| Interventions | Exercise: yoga class once per week for 7 weeks.<br>Control: wait list |
| Outcomes | Distress<br>Anxiety<br>Depression<br>Fatigue |


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**Cohen 2004** (*Continued*)

| | |
|---|---|
| | Sleep disturbance |
| Notes | Methodological quality score: 0<br>Main purpose of exercise: to reduce stress |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "Group assignment was conducted sequentially using minimization" |
| Allocation concealment (selection bias) | Low risk | "The allocation process was concealed from all investigators because all the relevant information was entered into a computer program and group assignment was determined by the program." |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | 1 participant dropped out of the study, no data were available for the individual and intention-to-treat analysis was not undertaken |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Coleman 2003a**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 24 multiple myeloma patients receiving high-dose chemotherapy and tandem peripheral blood stem cell transplantation |
| Interventions | Exercise: individualised home-based programme of strength and aerobic training<br>Control: no individual programme, advised to remain active and walk for 20 mins at least 3 times/week |
| Outcomes | Fatigue<br>Mood disturbance<br>Sleep variables<br>Body composition<br>Strength<br>Aerobic capacity |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve fatigue and sleep |


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**Coleman 2003a** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method of sequence generation not described |
| Allocation concealment (selection bias) | Unclear risk | "having a research assistant draw a sealed envelope containing group assignment", envelope not described as 'opaque' |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Not all participants accounted for and not clear whether intention-to-treat analysis was undertaken |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Courneya 2003a**

| | |
|---|---|
| Methods | RCT (wait list control); 2 groups |
| Participants | 102 colorectal cancer survivors following surgery within past 3 months |
| Interventions | Exercise: personalised home-based cardiovascular and flexibility programme lasting 16 weeks. Received a weekly phone call.<br>Control: no intervention, requested not to commence a structured exercise programme |
| Outcomes | Quality of life<br>Fatigue<br>Depression<br>Anxiety<br>Cardiovascular fitness<br>Body composition<br>Flexibility |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve quality of life |

| *Risk of bias* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "participants were randomly assigned to an exercise group or wait-list control group using a random-numbers table" |


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**Courneya 2003a** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment (selection bias) | Unclear risk | Allocation not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Courneya 2003b**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification by type of adjuvant cancer therapy |
| Participants | 53 breast cancer patients post anti-cancer treatment |
| Interventions | Exercise: supervised cardiovascular programme using cycle ergometers. 3 sessions/week for 15 weeks. Intensity - 70% to 75% max oxygen consumption. Time increased from 15 mins to 35 mins with 5 mins warm up and cool down.<br>Control: no intervention |
| Outcomes | Peak oxygen consumption and secondary cardiopulmonary outcomes<br>Quality of life<br>Happiness<br>Self esteem<br>Fatigue<br>Body composition |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve cardiopulmonary function and quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned to the exercise or control group using a random-numbers table" |
| Allocation concealment (selection bias) | Unclear risk | "allocation sequence and group assignments were generated by a research assistant and then enclosed in sequentially numbered and sealed envelopes" - unclear as not stated as 'opaque' |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | Outcome assessors were blind to group allocation but fatigue was self report |


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**Courneya 2003b** (*Continued*)

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Courneya 2003c**

| | |
|---|---|
| Methods | RCT; 2 groups, groups stratified for content |
| Participants | 108 cancer survivors with various diagnoses |
| Interventions | Exercise: group psychotherapy plus individualised home-based cardiovascular and flexibility exercises. 3 to 5 times/week for 20 to 30 mins at 65 to 75% HRmax.<br>Control: group psychotherapy only<br>Both groups 10 weeks |
| Outcomes | Quality of life<br>Satisfaction with life<br>Depression<br>Anxiety<br>Fatigue<br>Cardiovascular fitness<br>Body composition<br>Flexibility<br>Physical activity levels |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "classes were randomized to experimental conditions using a random numbers table" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias) All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias) All outcomes | Unclear risk | 12 participants did not complete the study or provide post-test data and were not included in intention-to-treat analysis |


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**Courneya 2003c** (*Continued*)

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Courneya 2007a**

| | |
|---|---|
| Methods | RCT; 3 groups, stratified by treatment centre and chemotherapy protocol |
| Participants | 242 women with breast cancer initiating chemotherapy |
| Interventions | Aerobic exercise: supervised 3 times/week during chemotherapy. Resistance exercise: supervised 3 times/week during chemotherapy. Control: usual care |
| Outcomes | Quality of life<br>Fatigue<br>Anxiety<br>Depression<br>Self esteem<br>Physical fitness<br>Body composition<br>Chemotherapy completion rate<br>Lymphoedema |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned...using a computer generated program" |
| Allocation concealment (selection bias) | Low risk | "The allocation sequence was...concealed from the project directors at each site who assigned participants to groups" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Courneya 2007b**

| | |
|---|---|
| Methods | see Courneya 2007a |
| Participants | see Courneya 2007a |
| Interventions | see Courneya 2007a |
| Outcomes | see Courneya 2007a |
| Notes | see Courneya 2007a |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned...using a computer generated program" |
| Allocation concealment (selection bias) | Low risk | "The allocation sequence was...concealed from the project directors at each site who assigned participants to groups" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Courneya 2008**

| | |
|---|---|
| Methods | RCT; 2 groups, parallel design |
| Participants | 55 patients with non-myeloid cancer, receiving darbepoetin alfa therapy for anaemia |
| Interventions | Exercise: darbepoetin alfa plus individually tailored exercise programme to improve cardiorespiratory fitness. 3 supervised cycle ergometry sessions/week for 12 weeks. Intensity 60% to 100% baseline peak power output<br>Control: darbepoetin alfa as per exercise group. Requested not to commence exercise programme during intervention period |
| Outcomes | Fatigue<br>Quality of life<br>Aerobic capacity<br>Haemoglobin |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve cardiorespiratory fitness |


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**Courneya 2008** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "randomly assigned to either DAL or DEX in a 1:1 ratio using a computer generated program." |
| Allocation concealment (selection bias) | Low risk | "The allocation sequence was concealed from the project director who assigned participants to groups." |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | "Oncologists to group assignments" but self reported fatigue |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Courneya 2009**

| | |
|---|---|
| Methods | RCT; 2 groups, parallel design |
| Participants | 122 patients with Hodgkin's or non-Hodgkin's lymphoma, 44% receiving adjuvant therapy, 56% post-adjuvant therapy |
| Interventions | Exercise: aerobic on a cycle ergometer; supervised, 3 times/week for 12 weeks. 15 to 20 mins for first 4 weeks then increased by 5 mins/week to 40 to 45 mins in week 9. In week 7 interval training above ventilatory threshold was introduced. Week 9 $VO_2$ peak training introduced. Intensity: commenced at 60% of peak power output, increased by 5% each week to a maximum of 75% by week 4<br>Control: usual care, asked not to exercise above baseline |
| Outcomes | Fatigue<br>Physical function<br>Quality of life<br>Happiness<br>Depression<br>Anxiety<br>Lymphoma symptoms<br>Cardiovascular fitness<br>Body composition<br>Chemotherapy completion<br>Treatment response<br>Adverse events |


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**Courneya 2009** (*Continued*)

| | | |
|---|---|---|
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve cardiorespiratory fitness | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "randomly assigned to AET or UC by using a computer-generated program" |
| Allocation concealment (selection bias) | Low risk | "The allocation sequence was generated independently and concealed in opaque envelopes" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | "Outcome assessors were not always blinded to group assignment" |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Culos-Reed 2006**

| | | |
|---|---|---|
| Methods | RCT; 2 groups | |
| Participants | 38 cancer survivors, minimum of 3 months post-treatment | |
| Interventions | Exercise: yoga<br>Control: wait list | |
| Outcomes | Fatigue<br>Mood<br>Symptom stress<br>Quality of life<br>Physical fitness<br>Physical activity | |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to improve physical and psychological health | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method not reported |


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**Culos-Reed 2006** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | High risk | Fatigue outcomes not reported and authors focused upon significant results |

**Culos-Reed 2010**

| | |
|---|---|
| Methods | RCT; 2 groups, wait list control |
| Participants | 61 prostate cancer patients receiving androgen deprivation therapy |
| Interventions | Exercise: supervised and unsupervised 16-week programme of walking, stretching, light resistance and core strengthening. Supervised group session once/week included 1 hour of exercise and 30 minutes of education and goal setting. Encouraged to exercise unsupervised 3 to 5 times/week<br>Control: wait list, no other details provided |
| Outcomes | Quality of life<br>Fatigue<br>Depression<br>Physical activity behaviour<br>Fitness<br>Body mass index<br>Bone mineral density<br>Blood work<br>Urinary N-telo-peptide<br>Prostate specific antigen level |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to increase physical activity levels, enhance quality of life, improve fitness and physiological variables |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |


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**Culos-Reed 2010** (*Continued*)

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Daley 2007**

| | |
|---|---|
| Methods | RCT; 3 groups, stratification by chemotherapy and tamoxifen |
| Participants | 108 women 12 to 36 months post-treatment for breast cancer |
| Interventions | Exercise: supervised aerobic exercise 3 times per week for 8 weeks<br>Placebo exercise: light intensity body conditioning/stretching<br>Control: usual care |
| Outcomes | Quality of life<br>Fatigue<br>Depression<br>Self perception<br>Physical activity<br>Aerobic fitness<br>Body composition |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "A telephone randomization service was provided by an independent trials unit. Randomization to the three treatment arms was on a 1:1:1 ratio and was performed using stratified random permutated blocks" |
| Allocation concealment (selection bias) | Low risk | "A telephone randomization service was provided by an independent trials unit. Randomization to the three treatment arms was on a 1:1:1 ratio and was performed using stratified random permutated blocks" |


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**Daley 2007** (*Continued*)

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Danhauer 2009**

| | |
|---|---|
| Methods | RCT; 2 groups, wait list control |
| Participants | 27 patients with breat cancer at various different stages of treatment |
| Interventions | Exercise: yoga, 75-minute supervised group class once/week for 10 weeks. Average of 6.6 women/session. No home practice required<br>Control: usual care, wait list |
| Outcomes | Physical health status<br>Quality of life<br>Fatigue<br>Spiritual well-being<br>Depression<br>Sleep quality<br>Mood |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to reduce fatigue and psychological distress, and improve sleep and quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |


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**Danhauer 2009** (*Continued*)

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Dimeo 1999**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 62 cancer patients with various diagnoses due to receive high does chemotherapy followed by autologous peripheral blood stem cell transplantation |
| Interventions | Exercise: supervised daily biking with a bed ergometer. 15 x 1-min at 50% cardiac reserve with 1-min rest between.<br>Control: no intervention |
| Outcomes | Mood (including depression, fatigue, anger and vigour)<br>Symptoms |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to reduce fatigue |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "patients recruited in odd weeks were included in the training group and patients recruited in the even weeks were included in the control group" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Dimeo 2004**

| | |
|---|---|
| Methods | RCT; 2 groups, stratified for tumour location |
| Participants | 72 various cancer diagnoses, post anti-cancer treatment |
| Interventions | Exercise: supervised stationary bike, 30 mins/per session, 5 days/week. 80% HRmax or 13 to 14 on Borg scale.<br>Control: relaxation training 45 mins, 3 times/week |


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**Dimeo 2004** (*Continued*)

| | |
|---|---|
| | Both groups lasted 3 weeks |
| Outcomes | HRQOL (including fatigue)<br>Physical performance |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce fatigue severity |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomisation was carried out using a computer-generated random number list" |
| Allocation concealment (selection bias) | Low risk | "randomisation sequence was concealed until assignment of interventions" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | 3 participants dropped out of the study; unclear if intention-to-treat analysis was performed |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Dodd 2010a**

| | |
|---|---|
| Methods | RCT; 3 groups |
| Participants | 106 patients, majority with breast cancer but patients with ovarian and colorectal cancer also included. All patients were due to commence chemotherapy |
| Interventions | Exercise during chemotherapy: home-based for 1 year, 3 to 5 times/week, 20 to 30-minute/session at 60% to 80% $VO_2$ peak or 12 to 14 on Borg scale (somewhat hard). Weekly follow-up calls to assess progress and adjust intensity<br>Exercise post-chemotherapy: home-based for 6 to 8 months, 3 to 5 times/week, 20 to 30-minute/session at 60 to 80% $VO_2$ peak or 12 to 14 on Borg scale (somewhat hard). Weekly follow-up calls to assess progress and adjust intensity<br>Control: usual care, no exercise prescription. Telephoned weekly to enquire about health and general response to cancer treatment |
| Outcomes | Fatigue<br>Sleep disturbance<br>Depression<br>Pain |


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**Dodd 2010a** (*Continued*)

| | |
|---|---|
| | Physical ability<br>Quality of life (not included in the analysis) |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to reduce fatigue |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not stated |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Dodd 2010b**

| | |
|---|---|
| Methods | See Dodd 2010a |
| Participants | See Dodd 2010a |
| Interventions | See Dodd 2010a |
| Outcomes | See Dodd 2010a |
| Notes | See Dodd 2010a |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not stated |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |


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**Dodd 2010b** (*Continued*)

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Drouin 2005**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 23 stage 0-III breast cancer patients prior to radiotherapy, sedentary |
| Interventions | Exercise: home-based individualised walking programme. 20 to 45 mins of walking 3 to 5 times/week at 50% to 70% max HR.<br>Control: stretching 3 to 5 times/week |
| Outcomes | Aerobic capacity<br>Fatigue<br>Mood |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve cardiorespiratory fitness, fatigue and psychological factors |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned...using a random number table" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias) All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Galantino 2003**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 11 stage II-IV breast cancer patients reporting cancer-related fatigue and having received adjuvant therapy within past year |
| Interventions | Exercise: Tai Chi, initial instruction and supporting video, then home-based 3 times/ week for 6 weeks. Weekly phone calls.<br>Control: walking booklet, advised to walk 3 times/week for 6 weeks. Weekly phone calls |
| Outcomes | Fatigue<br>Body composition<br>6-minute walk test<br>Physical well-being<br>Emotional well-being<br>Social/family well-being |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve fatigue and body mass index |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomized...by the use of a table of random numbers" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Number of participants varies with no explanation |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Galvão 2010**

| | |
|---|---|
| Methods | RCT; 2 groups parallel design |
| Participants | 57 patients with prostate cancer, some were receiving radiotherapy |
| Interventions | Exercise: combined progressive resistance and aerobic training twice/week for 12 weeks, supervised in small groups (n = 1 to 5). Resistance progressed from 12 to 6 repetition maximum with 2 to 4 sets/exercise. Aerobic training: 15 to 20 minutes of cycling, walking or jogging at 65% to 80% HRmax, perceived exertion 11 to 13 on Borg scale<br>Control: usual care |


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**Galvão 2010** (*Continued*)

| | |
|---|---|
| Outcomes | Fatigue<br>Quality of life<br>Aerobic capacity<br>Balance and falls self efficacy<br>Functional performance<br>Muscle strength<br>Muscle endurance<br>Body composition<br>Blood profile |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to increase muscle mass and strength, physical function, cardiorespiratory capacity and health status |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "participants were randomly assigned...1:1 using a computer random assignment program" |
| Allocation concealment (selection bias) | Low risk | "The allocation sequence was concealed from the project coordinator and exercise physiologist" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Some missing data |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Headley 2004**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 38 stage IV breast cancer patients due to initiate chemotherapy |
| Interventions | Exercise: 30-min seated exercises, 3 times/week with at least 1 day between each session. Consisted of 5-min warm-up, 20-min moderate intensity repetitive motion exercises, 5-min cool down.<br>Control: no intervention |
| Outcomes | Quality of life<br>Fatigue |


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**Headley 2004** (*Continued*)

| | | |
|---|---|---|
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life and reduce fatigue | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "Participants were assigned randomly to either the control or intervention group by computer" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Heim 2007**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 63 breast cancer patients at least 6 weeks post-surgery and chemotherapy |
| Interventions | Exercise: combined resistance exercises, stretching and aerobic walking in combination with a complex rehabilitation programme. Unsupervised, strengthening and stretching 3 times/week, aerobic walking 30 minutes, twice/week<br>Control: complex rehabilitation programme only |
| Outcomes | Fatigue<br>Quality of life<br>Aerobic capacity<br>Anxiety<br>Depression<br>Physical activity<br>Physical activity motivation<br>Muscle strength |
| Notes | Methodological quality score: 0<br>Main purpose of exercise: to reduce fatigue |
| ***Risk of bias*** | |
| **Bias** | **Authors' judgement** | **Support for judgement** |


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**Heim 2007** (*Continued*)

| | | |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "randomized according to their admission to hospital: depending on the alternating weeks" |
| Allocation concealment (selection bias) | High risk | Not done |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | No description of drop-outs |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Hwang 2008**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 37 patients with breast cancer, post-surgery and due to receive radiotherapy |
| Interventions | Exercise: supervised aerobic (treadmill walking and bicycling), some stretching (shoulder) and strengthening exercises, 50 minutes, 3 times/week for 5 weeks during radiation therapy. Target heart rate 50% to 70% HRmax<br>Control: shoulder range of movement exercises, encouraged to continue normal activities |
| Outcomes | Fatigue<br>Quality of life<br>Shoulder range of movement<br>Pain |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life and shoulder mobility and reduce fatigue and pain |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method not reported |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |


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**Hwang 2008** (*Continued*)

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Lee 2010**

| | |
|---|---|
| Methods | RCT; 3 groups; intervention groups stratified by operation type, historical control |
| Participants | 39 patients with breast cancer post-treatment (includes 18 drawn from a historical control cohort) |
| Interventions | Scapula exercise: supervised shoulder stretching and strengthening for 40 minutes once/week for 8 weeks<br>General exercise: supervised range of motion and body conditioning for 40 minutes once/week for 8 weeks<br>Control: historical group |
| Outcomes | Fatigue<br>Quality of life<br>Depression<br>Shoulder disability, function and range of movement<br>Pain |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to reduce upper limb dysfunction |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomization to the two treatment arms was achieved on a 1:1 ratio" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias) All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**McKenzie 2003**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 14 stage I-II breast cancer patient at least 6 months post-treatment with unilateral lymphoedema |
| Interventions | Exercise: 3 times per week supervised resistance training, strengthening, aerobic arm ergometry. Warm-up, 5 minutes stretching, strength exercises then cool down. Strength exercise 2 x 10 reps week one the 3 x 10 reps. Week 3 arm ergometry added |
| Outcomes | Fatigue<br>Arm volume<br>Quality of life |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to reduce lymphoedema |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**McNeely 2008**

| | |
|---|---|
| Methods | RCT; 2 groups parallel design |
| Participants | 52 patients following treatment for head and neck cancer |
| Interventions | Exercise: progressive resistance exercise training; 2 supervised sessions/week with an optional 3rd session either at home or in the centre for 12 weeks. Initially 2 sets of 10 to 15 reps of 5 to 8 exercises at 25% to 30% 1 RM and slowly progressing to 60% to 70% 1 RM by week 12<br>Control: standardised therapeutic protocol with light weights and stretching |


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**McNeely 2008** (*Continued*)

| | |
|---|---|
| Outcomes | Fatigue<br>Quality of life<br>Shoulder pain, disability and range of movement<br>Upper limb strength and muscle endurance |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce upper extremity pain and dysfunction |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Participants were assigned randomly...using a computer generated code" |
| Allocation concealment (selection bias) | Low risk | "allocation sequence...sequentially numbered and sealed (opaque) envelopes." |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | "Independent assessors who were blinded to group" but fatigue was self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Milne 2008**

| | |
|---|---|
| Methods | RCT; 2 group cross-over design |
| Participants | 58 breast cancer patients within 2 years of completing adjuvant therapy |
| Interventions | Exercise: 2 times per week supervised group programme including aerobic and resistance training for 12 weeks<br>Control: usual care and phone call every 3 weeks |
| Outcomes | Quality of life<br>Fatigue<br>Anxiety<br>Aerobic capacity |
| Notes | Methodological quality score: 3.<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***


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**Milne 2008** (*Continued*)

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Participants were randomly assigned...using a computer-generated program" |
| Allocation concealment (selection bias) | Low risk | "Group assignments were concealed from the project director who recruited participants to the trial" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Moadel 2007**

| | |
|---|---|
| Methods | RCT; 2 groups, wait-list control, stratification by cancer treatment |
| Participants | 128 breast cancer patients diagnosed between 2 weeks and 5 years previously; 48% received adjuvant therapy during the study |
| Interventions | Exercise: yoga, 12 weeks of one 1.5 hour group class/week, asked to practice at home daily. Were also permitted to attend additional classes<br>Control: wait list |
| Outcomes | Fatigue<br>Quality of life<br>Distress including anxiety<br>Spiritual well-being |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "Randomly assigned" but method not stated |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |


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| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Mock 1994**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 18 stage I or II breast cancer post-surgery, prior to adjuvant chemotherapy |
| Interventions | Exercise: home-based walking and support group. Walking: brisk incremental walk 10 to 45 mins with 5 min cool down, 4 to 5 times/week. Support group: 90 mins every 2 weeks. Continued throughout chemotherapy treatment.<br>Control: no intervention |
| Outcomes | Physical function<br>Psychosocial adjustment<br>Self concept<br>Body image<br>Symptom intensity (nausea, vomiting, fatigue, hair loss, difficulty sleeping, anxiety, depression, mouth sores, irritability, diarrhoea and pain) |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to improve physical and psychological adaptation |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias) All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias) All outcomes | High risk | Not all participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Mock 1997**

| | |
|---|---|
| Methods | CCT, 2 groups |
| Participants | 46 stage I and II breast cancer patients, post-surgery, receiving radiotherapy |
| Interventions | Exercise: individualised brisk 20 to 30-min incremental walk followed by 5-min cool down 4 to 5 times/week in own setting<br>Control: no intervention |
| Outcomes | Physical function (12-min walk test)<br>Symptoms<br>Fatigue |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to increase physical function and reduce symptom intensity |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "Following random assignment of the first subject, subsequent subjects were alternately assigned" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | 4 participants withdrew or dropped out of the study and were not included in the analysis |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Mock 2005**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification by type of adjuvant cancer therapy |
| Participants | 119 breast cancer patients post-surgery prior to any other adjuvant therapy. Exercising less than 45 mins per week |
| Interventions | Exercise: home-based walking programme during treatment. 5 to 6 times/week at ~50% to 70% HRmax. 15 mins per session initially increasing to 30 mins. Booklet and video provided. Contacted fortnightly.<br>Control: no intervention |
| Outcomes | Fatigue<br>Physical function<br>12-min walk |


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**Mock 2005** (*Continued*)

| | | |
|---|---|---|
| | Activity levels | |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce fatigue | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "computer-generated randomization assignments" |
| Allocation concealment (selection bias) | Low risk | "Consecutively numbered sealed opaque envelopes...were prepared at the co-ordinating centre and opened at the site following baseline testing for each participant." |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Monga 2007**

| | |
|---|---|
| Methods | RCT; 2 groups, stratified by activity level |
| Participants | 21 patients with prostate cancer due to receive radiotherapy |
| Interventions | Exercise: supervised aerobic exercise (walking on a treadmill), 3 times/week for 8 weeks. 10-min warm-up, 30 aerobic, 5 to 10-min cool down. Target HR = (0.65) (HRmax) + resting HR<br>Control: usual care |
| Outcomes | Fatigue<br>Aerobic fitness<br>Quality of life<br>Depression<br>Flexibility<br>Strength |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to prevent fatigue and improve quality of life |
| ***Risk of bias*** | |


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**Monga 2007** (*Continued*)

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Mustian 2009**

| | |
|---|---|
| Methods | RCT; 2 group, stratified by diagnosis |
| Participants | 38 patients with breast or prostate cancer receiving radiotherapy |
| Interventions | Exercise: home-based aerobic and resistance training every day for 4 weeks. Target was to increase steps by 5% to 20% each day up to 10,000 steps at a moderate intensity (60% to 70% HR reserve). Plus 11 resistance exercises, increasing repetitions up to 4 sets of 15 with moderate resistance<br>Control: usual care, requested not to commence formal exercise programme |
| Outcomes | Fatigue<br>Quality of life<br>Aerobic capacity<br>Strength<br>Body composition<br>Adherence |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to increase aerobic capacity, strength, muscle mass, fatigue and quality of life |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized, using a randomization scheme with blocks of four", not other details provided |
| Allocation concealment (selection bias) | Unclear risk | Not stated |


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**Mustian 2009** (*Continued*)

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Mutrie 2007**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification for hospital and treatment |
| Participants | 203 breast cancer patients during treatment |
| Interventions | Exercise: supervised 12-week group exercise 2 times/week, 45 mins/session at moderate intensity. Participants encouraged to exercise once/week at home<br>Control: usual care |
| Outcomes | Quality of life<br>Fatigue<br>Depression<br>Mood<br>Body composition<br>Physical activity<br>12-minute walk |
| Notes | Methodological quality score: 3.<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomisation was done by telephone to an interactive voice response system" |
| Allocation concealment (selection bias) | Low risk | "Randomisation was done by telephone to an interactive voice response system" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |


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| | | |
|---|---|---|
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Oh 2008**

| | |
|---|---|
| Methods | RCT; 2 group; stratified by treatment (ongoing or complete) |
| Participants | 18 cancer patients with various diagnoses and at various stages of treatment |
| Interventions | Exercise: Qigong, supervised groups, 1 to 2 sessions/week for 8 weeks, 90 mins/session and practice at home for 1 hour/day<br>Control: usual care, asked to refrain from joining a Qigong class |
| Outcomes | Quality of life (including a fatigue sub scale)<br>Symptom experience<br>Inflammation |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life, reduce treatment symptoms and inflammation |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomization was done by a computer program" |
| Allocation concealment (selection bias) | High risk | Not done |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Oh 2010**

| | |
|---|---|
| Methods | RCT; 2 group; stratified by treatment (ongoing or complete) |
| Participants | 108 cancer patients with various diagnoses and at various stages of treatment |
| Interventions | Exercise: Qigong, supervised groups, 2 sessions/week for 10 weeks, 90 mins/session and practice at home for 30 minutes/day<br>Control: usual care, asked to refrain from joining a Qigong class |


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**Oh 2010** (*Continued*)

| | |
|---|---|
| Outcomes | Fatigue<br>Quality of life<br>Mood<br>Inflammation |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomization, by computer, was stratified by treatment at baseline" |
| Allocation concealment (selection bias) | High risk | Not done |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Payne 2008**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 18 patients with breast cancer |
| Interventions | Exercise: aerobic, unsupervised, home-based walking at a moderate intensity for 20 minutes, 4 times/week for 12 weeks<br>Control: usual care |
| Outcomes | Fatigue<br>Depression<br>Sleep disturbance<br>Biomarkers<br>Exercise |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to reduce fatigue, sleep disturbances and depressive symptoms |

***Risk of bias***


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**Payne 2008** (*Continued*)

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Unclear |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Pinto 2003**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 24 stage 0 to II sedentary breast cancer patients post-treatment |
| Interventions | Exercise: 60% to 70% HRmax, supervised, 3 times/week for 12 weeks, increased up to 10-min warm-up, to 30-min cardiovascular activity and 10-min cool down. Various activities included.<br>Control: wait-list, no intervention |
| Outcomes | Mood (including anger, tension, depression, vigour, fatigue and confusion)<br>Positive and negative affect<br>Body esteem |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to reduce distress and improve body image and fitness |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not stated |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |


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**Pinto 2003** (*Continued*)

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Pinto 2005**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification for age, cancer stage and adjuvant therapy received |
| Participants | 86 stage 0 to II sedentary breast cancer patients post-treatment |
| Interventions | Exercise: moderate-intensity home-based activities, 55% to 65% HRmax. 10 mins twice/ week increasing to 30 mins at least 5 days/week over 12 weeks. Weekly phone calls during exercise.<br>Control: weekly phone call to monitor symptoms |
| Outcomes | Body composition<br>Activity levels<br>1-mile walk<br>Motivational readiness for exercise<br>Mood<br>Fatigue<br>Body esteem |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to increase physical activity, fitness; improve mood, physical symptoms and body esteem |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not stated |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias) All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Rogers 2009**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 37 patients with breast cancer receiving hormone therapy, all other adjuvant therapy complete |
| Interventions | Exercise: aerobic walking, supervised session once/week for 12 weeks in an individual basis in addition to home-based walking. Supervised sessions also included behaviour change counselling. Participants aimed to achieve 150 minutes of walking/week<br>Control: usual care plus received written material relating to physical activity |
| Outcomes | Fatigue<br>Aerobic fitness<br>Strength<br>Body composition<br>Physical activity<br>Diet<br>Endocrine symptoms<br>Cognitive function<br>Sleep dysfunction<br>Pain<br>Lower extremity function |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to increase physical activity |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomization was computer generated" |
| Allocation concealment (selection bias) | Unclear risk | "...and kept in sealed envelopes until randomization" - not clear as envelopes not stated as "opaque" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Santa Mina 2012**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 10 patients with prostate cancer either during or post-androgen deprivation therapy |
| Interventions | Exercise (group): combined aerobic and resistance training in a supervised group for 60 minutes/session, 3 times/week for 8 weeks. Aerobic intensity: 70% to 85% HRmax, resistance: 6 to 12 RM<br>Exercise (individual): combined aerobic and resistance training with a personal trainer for 60 minutes/session, 3 times/week for 8 weeks. Aerobic intensity: 70% to 85% HRmax, resistance: 6 to 12 RM |
| Outcomes | Fatigue<br>Quality of life<br>Aerobic fitness<br>Strength<br>Balance<br>Body composition<br>Blood pressure<br>Patient satisfaction |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce fatigue and improve quality of life |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not described |
| Allocation concealment (selection bias) | Low risk | "Concealed...sequentially numbered opaque envelopes" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Segal 2001a**

| | |
|---|---|
| Methods | RCT; 3 group, stratified for adjuvant treatment, random numbers table |
| Participants | 123 stage I to II breast cancer, within 2 weeks of commencing adjuvant therapy |


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**Segal 2001a** (*Continued*)

| | |
|---|---|
| Interventions | Supervised exercise: 3 times per week progressive walking, further 2 times unsupervised.<br>Unsupervised exercise: 5 times per week progressive walking at 50% to 60% maximal predicted oxygen uptake.<br>Control: usual care |
| Outcomes | HRQOL<br>Fatigue<br>Aerobic capacity<br>Body composition |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to improve physical function and HRQOL |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned participants to one of three groups using a random numbers table" |
| Allocation concealment (selection bias) | High risk | "A study coordinator revealed group assignment after baseline testing" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Segal 2001b**

| | |
|---|---|
| Methods | See Segal 2001a |
| Participants | See Segal 2001a |
| Interventions | See Segal 2001a |
| Outcomes | See Segal 2001a |
| Notes | See Segal 2001a |

***Risk of bias***


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**Segal 2001b** (*Continued*)

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned participants to one of three groups using a random numbers table" |
| Allocation concealment (selection bias) | High risk | "A study coordinator revealed group assignment after baseline testing" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Segal 2003**

| | |
|---|---|
| Methods | RCT; 2 groups, random numbers table, stratification for centre and intent of treatment |
| Participants | 155 prostate cancer patients, due to receive androgen deprivation therapy |
| Interventions | Exercise: individualised resistance training. 9 exercises at 60% to 70% 1 RM, 3 times/ week for 12 weeks.<br>Control: wait list |
| Outcomes | Fatigue<br>HRQOL<br>Muscular fitness<br>Body composition |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve quality of life and reduce fatigue |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomization, performed using a table of random numbers" |
| Allocation concealment (selection bias) | Low risk | "The treatment allocation was concealed from the study coordinator until completion of baseline testing and stratification" |


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**Segal 2003** (*Continued*)

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Reasons for drop-out not provided and data not included within an intention-to-treat analysis |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Segal 2009a**

| | |
|---|---|
| Methods | RCT; 3 groups; stratified by intended duration of androgen deprivation therapy |
| Participants | 212 patients with prostate cancer receiving radiotherapy |
| Interventions | Exercise (resistance): supervised, 3 times/week for 24 weeks. 2 times 8 to 12 reps of 10 exercises at 60% to 70% estimated 1 RM, increased by 5 lb when > 12 reps completed<br>Exercise (aerobic): supervised, 3 times/week for 24 weeks. Cycle ergometer, treadmill or elliptical trainer, 15 minutes/session initially, increased by 5 minutes every 3 weeks up to 45 minutes; started at 50% to 60% of $VO_2$ peak for 4 weeks then 70% to 75% for weeks 5 to 24.<br>Control: usual care, asked not to initiate exercise and offered a post-study intervention |
| Outcomes | Fatigue<br>Quality of life<br>Aerobic fitness<br>Strength<br>Body composition<br>Blood profile<br>Prostate specific antigen and testosterone |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce fatigue, improve cancer-specific quality of life, physical fitness, body composition, prostate specific antigen, testosterone and serum lipid levels |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned...using computer-generated numbers" |
| Allocation concealment (selection bias) | Low risk | Central random assignment was used, with allocation concealment before assignment. To ensure blinding of the research co-or- |


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**Segal 2009a** (*Continued*)

| | | |
|---|---|---|
| | | dinator, an exercise specialist handled the random assignments" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Segal 2009b**

| | |
|---|---|
| Methods | See Segal 2009a |
| Participants | See Segal 2009a |
| Interventions | See Segal 2009a |
| Outcomes | See Segal 2009a |
| Notes | See Segal 2009a |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned...using computer-generated numbers" |
| Allocation concealment (selection bias) | Low risk | Central random assignment was used, with allocation concealment before assignment. To ensure blinding of the research co-ordinator, an exercise specialist handled the random assignments" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Sequeira 2012**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 20 patients with breast cancer post-treatment |
| Interventions | Exercise: exercise programme in addition to physiotherapy, twice per week supervised in the hospital and once/week at home<br>Control: usual physiotherapy |
| Outcomes | Quality of life (including fatigue)<br>Physical activity level<br>Body mass index<br>Side effects of cancer therapy |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to increase physical activity level |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomized" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | Blinding unclear |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Unclear |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Shelton 2009**

| | |
|---|---|
| Methods | RCT; 2 groups |
| Participants | 53 patients with leukaemia within 6 months of allogenic stem cell transplant |
| Interventions | Exercise (supervised): combined aerobic and resistance training 3 times/week for 4 weeks. Individualised, aerobic exercise included upper and lower extremity ergometry and treadmill for at least 20 minutes at 60% to 75% age predicted HRmax. Various resistance exercises, 1 to 3 sets of 10 reps with intensity determined by fatigue. Intensity of aerobic and resistance training increased every third session unless extreme fatigue was reported<br>Exercise (unsupervised): combined aerobic (walking) and resistance training for 4 weeks. Walking time increased to 30 mins over the 4 weeks. Various resistance exercises 1 to 3 sets of 10 to 15 reps. Intensity of the exercise was not reported |


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**Shelton 2009** (*Continued*)

| | |
|---|---|
| Outcomes | Fatigue<br>Aerobic capacity<br>Physical performance |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve functional outcome |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "randomly assigned" but method not described |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Unclear |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Thorsen 2005**

| | |
|---|---|
| Methods | RCT; 2 groups, stratification for gender and diagnosis, randomised by computer |
| Participants | 111 various cancer diagnoses, 1 month following chemotherapy at baseline |
| Interventions | Exercise: personalised home-based training programme. Patient selected mode of exercise. 14 weeks, twice/week for at least 30 minutes per session. Intensity: 13 to 15 on Borg scale or 60% to 70% HRmax based on patient choice. Contacted fortnightly.<br>Control: no intervention |
| Outcomes | Physical function<br>HRQOL (including physical and emotional function and fatigue)<br>Anxiety<br>Depression<br>Activity level |
| Notes | Methodological quality score: 2<br>Main purpose of exercise: to improve cardiorespiratory fitness, mental distress and HRQOL |

***Risk of bias***


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**Thorsen 2005** (*Continued*)

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "randomly assigned...The...Hospital was responsible for the computerized random assignment" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Drop-outs were not accounted for and unclear how intention-to-treat was analysis was undertaken |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**van Weert 2010**

| | |
|---|---|
| Methods | RCT; 3 groups, wait list control recruited outside the randomisation process |
| Participants | 136 cancer patients at least 3 months following final treatment for cancer. In addition data from 60 patients were incorporated to provide a historical control (not reported here) |
| Interventions | Exercise: combined aerobic and strength training delivered through 12 1-hour individually supervised and 12 1-hour group sports sessions over 12 weeks. Individual aerobic training target was 40% to 50% HRmax for 4 weeks, increased to 50% to 80% HRmax during the remaining 8 weeks. Resistance training started at 30% of 1-RM and increased to 60% by week 12.<br>Comparison: exercise as above in combination with 12 hours of cognitive behavioural therapy |
| Outcomes | Fatigue<br>Quality of life |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce fatigue, improve quality of life and physical function |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "Randomization was conducted at the group level by an independent researcher using a randomization list" |


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**van Weert 2010** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants were accounted for |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Windsor 2004**

| | |
|---|---|
| Methods | RCT; 2 groups, independent telephone randomisation service |
| Participants | 66 men with localised prostate carcinoma on waiting list for radical conformed radiotherapy |
| Interventions | Exercise: home-based walking 60% to 70% HRmax, 30 mins/session at least 3 times/week during radiotherapy<br>Control: no intervention<br>Both groups contacted weekly |
| Outcomes | Fatigue<br>Physical function<br>Exercise adherence |
| Notes | Methodological quality score: 3<br>Main purpose of exercise: to reduce fatigue and prevent deterioration of physical function |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Patients were randomized to trial group by telephone call to the Scottish Cancer Therapy Network randomization line before baseline tests were performed" |
| Allocation concealment (selection bias) | Low risk | "Patients were randomized to trial group by telephone call to the Scottish Cancer Therapy Network randomization line before baseline tests were performed" |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |


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**Windsor 2004** (*Continued*)

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Unclear risk | Follow-up data were not available for 1 participant that withdrew; no intention-to-treat analysis |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

**Yuen 2007a**

| | |
|---|---|
| Methods | RCT; 3 groups |
| Participants | 22 patients with breast cancer |
| Interventions | Exercise (aerobic): home-based walking or alternative aerobic exercise at a Borg rating of 10 to 13 (fairly light to somewhat hard) for 20 to 30 minutes, 3 times/week for 12 weeks<br>Exercise (resistance): home-based, 8 exercises on non-consecutive days. One set of each exercise in weeks 1 to 3, 2 sets in weeks 4 to 6 and 3 sets in week 7 onwards. 8 to 12 reps per exercise. Once 12 reps could be repeated with good form resistance was increased. Advised to exercise at a Borg rating or 10 to 13 (fairly light to somewhat hard)<br>Control: advised to continue normal activities |
| Outcomes | Fatigue<br>Aerobic capacity |
| Notes | Methodological quality score: 1<br>Main purpose of exercise: to reduce fatigue |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "participants were assigned, based on computer generated random sequence, to one of three groups" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias) All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias) All outcomes | High risk | Intention-to-treat analysis not performed and reasons for drop-out not provided |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |


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**Yuen 2007b**

| | |
|---|---|
| Methods | See Yuen 2007a |
| Participants | See Yuen 2007a |
| Interventions | See Yuen 2007a |
| Outcomes | See Yuen 2007a |
| Notes | See Yuen 2007a |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "participants were assigned, based on computer generated random sequence, to one of three groups" |
| Allocation concealment (selection bias) | Unclear risk | Not stated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding not done |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Intention-to-treat analysis not performed and reasons for drop-out not provided |
| Selective reporting (reporting bias) | Low risk | Fatigue outcome reported |

CCT: controlled clinical trial
HR: heart rate
HRmax: maximum heart rate
HRQOL: health-related quality of life
RCT: randomised controlled trial
RM: repetition maximum
$VO_2$: an indicator of cardio-respiratory endurance and aerobic fitness

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

| Study | Reason for exclusion |
|---|---|
| Aghili 2007 | Not a randomised controlled trial |
| Barinow-Wojewódzki 2008 | Not a randomised controlled trial |
| Barsevick 2004 | No exercise intervention |


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(*Continued*)

| | |
|---|---|
| Battaglini 2007 | Outcomes reported do not meet the study inclusion criteria |
| Berglund 1994 | Outcomes reported do not meet the study inclusion criteria |
| Buss 2010 | Not a randomised controlled trial |
| Cella 2004 | No clinical trial; review of studies |
| Coleman 2003b | Outcomes reported do not meet the study inclusion criteria |
| Coleman 2008 | Outcomes reported do not meet the study inclusion criteria |
| Culos-Reed 2007 | Not a randomised controlled trial |
| Decker 1989 | Not a randomised controlled trial |
| Dimeo 1996 | Not a randomised controlled trial |
| Dimeo 1997a | Not a randomised controlled trial |
| Dimeo 1997b | Outcomes reported do not meet the study inclusion criteria |
| Dimeo 2008 | Not a randomised controlled trial |
| Fillion 2008 | Multimodal intervention therefore effects may not be attributed specifically to physical exercise |
| Goedendorp 2010 | Intervention did not meet study inclusion criteria |
| Hansen 2009 | Not a randomised controlled trial |
| Hartvig 2006 | Intervention did not meet study inclusion criteria |
| Hayes 2004 | Outcomes reported do not meet the study inclusion criteria |
| Hsieh 2008 | Not a randomised controlled trial |
| Jarden 2009 | Intervention did not meet study inclusion criteria. |
| Kim 2005 | Intervention did not meet study inclusion criteria |
| Kim 2009 | Outcomes reported do not meet the study inclusion criteria |
| Köhler 2008 | Not a randomised controlled trial |
| MacVicar 1989 | Outcomes reported do not meet the study inclusion criteria |
| Mock 2001 | Results not based upon original group allocation |


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(*Continued*)

| | |
|---|---|
| Oldervoll 2003 | Not a randomised controlled trial |
| Ozalevli 2010 | Not a randomised controlled trial |
| Pickett 2002 | Outcomes reported do not meet the study inclusion criteria |
| Poorkiani 2010 | Multimodal intervention therefore effects may not be attributed specifically to physical exercise |
| Riesenberg 2010 | Not a randomised controlled trial |
| Rummans 2006 | Multimodal intervention therefore effects may not be attributed specifically to physical exercise |
| Schneider 2007a | Not a randomised controlled trial |
| Schneider 2007b | Not a randomised controlled trial |
| Schneider 2007c | Not a randomised controlled trial |
| Schwartz 1999 | Not a randomised controlled trial |
| Schwartz 2000a | Not a randomised controlled trial |
| Schwartz 2000b | Not a randomised controlled trial |
| Schwartz 2001 | Not a randomised controlled trial |
| Schwartz 2002 | Not a randomised controlled trial |
| Sprod 2010 | Not a randomised controlled trial |
| Turner 2004 | Not a randomised controlled trial |
| Vadiraja 2009 | Outcomes reported do not meet the study inclusion criteria |
| Watson 2004 | No clinical trial, literature review |
| Wilson 2005 | Not a randomised controlled trial |

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

**Fisher-Schlombs 2010**

| | |
|---|---|
| Trial name or title | A pilot study of a home-based exercise intervention for adult patients with acute myeloid leukaemia |
| Methods | RCT |
| Participants | Post-treatment acute myeloid leukaemia patients |


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**Fisher-Schlombs 2010** (*Continued*)

| | |
|---|---|
| Interventions | 12-week home-based exercise programme |
| Outcomes | Fitness, quality of life, fatigue, anxiety and depression |
| Starting date | |
| Contact information | Shabbir M.H. Alibhai: shabbir.alibhai@uhn.ca |
| Notes | |

**Santa Mina 2010**

| | |
|---|---|
| Trial name or title | Aerobic versus resistance exercise training for prostate cancer patients on ADT |
| Methods | RCT |
| Participants | Prostate cancer patients receiving ADT |
| Interventions | Aerobic versus resistance exercise |
| Outcomes | Primary outcomes include fatigue, HRQOL and exercise adherence. Secondary outcomes include aerobic and musculoskeletal fitness, body composition and biomarkers associated with tumorigenesis |
| Starting date | |
| Contact information | Daniel Santa Mina: dstamina@gmail.com |
| Notes | |

ADT: androgen deprivation therapy
HRQOL: health-related quality of life
RCT: randomised controlled trial


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## DATA AND ANALYSES

### Comparison 1. Fatigue: all data

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 38 | 2646 | Std. Mean Difference (IV, Random, 95% CI) | -0.27 [-0.37, -0.17] |

### Comparison 2. Fatigue: during anti-cancer therapy

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 18 | 1456 | Std. Mean Difference (IV, Random, 95% CI) | -0.23 [-0.33, -0.12] |

### Comparison 3. Fatigue: post anti-cancer therapy

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control | 10 | 539 | Std. Mean Difference (IV, Random, 95% CI) | -0.44 [-0.79, -0.09] |

### Comparison 4. Fatigue: breast cancer

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no intervention control; post-test means | 18 | 1183 | Std. Mean Difference (IV, Random, 95% CI) | -0.35 [-0.51, -0.19] |


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### Comparison 5. Fatigue: prostate cancer

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 6 | 415 | Std. Mean Difference (IV, Random, 95% CI) | -0.45 [-0.78, -0.11] |

### Comparison 6. Fatigue: haematological malignancies

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 4 | 220 | Std. Mean Difference (IV, Random, 95% CI) | -0.15 [-0.42, 0.11] |

### Comparison 7. Fatigue: aerobic training

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 22 | 1533 | Std. Mean Difference (IV, Random, 95% CI) | -0.22 [-0.34, -0.10] |

### Comparison 8. Fatigue: resistance training

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 5 | 401 | Std. Mean Difference (IV, Random, 95% CI) | -0.18 [-0.39, 0.02] |


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## Comparison 9. Fatigue: mind-body exercise

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Exercise versus no exercise control; post-test means | 3 | 194 | Std. Mean Difference (IV, Random, 95% CI) | -0.10 [-0.39, 0.19] |

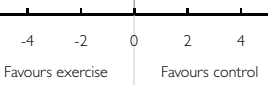
### Analysis 1.1. Comparison 1 Fatigue: all data, Outcome 1 Exercise versus no exercise control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 1 Fatigue: all data

Outcome: 1 Exercise versus no exercise control; post-test means

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Adamsen 2009 | 118 | 34.6 (24.3) | 117 | 41 (22.7) | | 5.6 % | -0.27 [ -0.53, -0.01 ] |
| Burnham 2002 | 12 | 15.3 (21.4) | 6 | 32.2 (34.5) | | 0.9 % | -0.61 [ -1.62, 0.39 ] |
| Chang 2008 | 11 | 4.6 (3) | 11 | 4.8 (3.5) | | 1.3 % | -0.06 [ -0.89, 0.78 ] |
| Cohen 2004 | 20 | 3.1 (1.5) | 19 | 3.1 (1.5) | | 2.0 % | 0.0 [ -0.63, 0.63 ] |
| Coleman 2003a | 23 | 14.4 (7.6) | 14 | 15 (5.6) | | 1.8 % | -0.08 [ -0.75, 0.58 ] |
| Courneya 2003a | 62 | -12.7 (10.9) | 31 | -12.1 (10.8) | | 3.4 % | -0.05 [ -0.49, 0.38 ] |
| Courneya 2003b | 25 | 8.3 (7.9) | 26 | 8.8 (8.1) | | 2.4 % | -0.06 [ -0.61, 0.49 ] |
| Courneya 2003c | 60 | 19.67 (11.31) | 48 | 22.37 (9.84) | | 3.9 % | -0.25 [ -0.63, 0.13 ] |
| Courneya 2007a | 78 | -36.8 (10.4) | 41 | -34.9 (12.5) | | 3.9 % | -0.17 [ -0.55, 0.21 ] |
| Courneya 2007b | 82 | -36.3 (9.4) | 41 | -34.9 (12.5) | | 4.0 % | -0.13 [ -0.51, 0.24 ] |
| Courneya 2008 | 26 | -37.6 (9.6) | 29 | -36.6 (9.8) | | 2.6 % | -0.10 [ -0.63, 0.43 ] |
| Courneya 2009 | 60 | -40.5 (9.4) | 62 | -38 (11.1) | | 4.2 % | -0.24 [ -0.60, 0.12 ] |
| Culos-Reed 2010 | 37 | 4.15 (1.68) | 24 | 4.46 (1.12) | | 2.7 % | -0.21 [ -0.72, 0.31 ] |
| Daley 2007 | 33 | 2.14 (1.75) | 33 | 3.44 (1.85) | | 2.8 % | -0.71 [ -1.21, -0.21 ] |
| Danhauer 2009 | 13 | -39.8 (11.5) | 14 | -32.6 (15.5) | | 1.4 % | -0.51 [ -1.28, 0.26 ] |
| Dimeo 1999 | 27 | 11.7 (8.9) | 32 | 11.5 (8.6) | | 2.7 % | 0.02 [ -0.49, 0.53 ] |
| Dimeo 2004 | 34 | 34 (21) | 35 | 39 (26) | | 3.0 % | -0.21 [ -0.68, 0.26 ] |

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(. . . *Continued*)

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Drouin 2005 | 13 | 60.9 (36.95) | 8 | 86 (55.55) | | 1.1 % | -0.54 [ -1.44, 0.36 ] |
| Galv o 2010 | 29 | 14.8 (13.8) | 28 | 30.6 (17.6) | | 2.4 % | -0.99 [ -1.54, -0.44 ] |
| McKenzie 2003 | 7 | -82.86 (9.51) | 7 | -55 (27.99) | | 0.7 % | -1.25 [ -2.43, -0.07 ] |
| McNeely 2008 | 25 | -36.7 (9) | 27 | -34.3 (11.1) | | 2.5 % | -0.23 [ -0.78, 0.31 ] |
| Milne 2008 | 29 | 11.9 (3.2) | 29 | 17.4 (4.7) | | 2.3 % | -1.35 [ -1.92, -0.78 ] |
| Moadel 2007 | 84 | -34.37 (11.26) | 44 | -33.82 (12.97) | | 4.1 % | -0.05 [ -0.41, 0.32 ] |
| Mock 2005 | 54 | 3.5 (2.4) | 54 | 3.7 (2.6) | | 4.0 % | -0.08 [ -0.46, 0.30 ] |
| Monga 2007 | 11 | 0.8 (1.8) | 10 | 3.8 (2.2) | | 0.9 % | -1.44 [ -2.42, -0.46 ] |
| Mustian 2009 | 19 | 1.6 (1.36) | 19 | 2.44 (2.08) | | 1.9 % | -0.47 [ -1.11, 0.18 ] |
| Mutrie 2007 | 82 | -40.3 (10.4) | 92 | -36 (12.1) | | 5.0 % | -0.38 [ -0.68, -0.08 ] |
| Pinto 2003 | 12 | 7.16 (6.4) | 12 | 9 (6.4) | | 1.3 % | -0.28 [ -1.08, 0.53 ] |
| Pinto 2005 | 43 | 27.08 (21.41) | 43 | 42.28 (26.2) | | 3.4 % | -0.63 [ -1.06, -0.20 ] |
| Rogers 2009 | 20 | -12.4 (10.42) | 19 | -10.29 (6.743) | | 2.0 % | -0.23 [ -0.86, 0.40 ] |
| Segal 2001a | 40 | 58.8 (22.8) | 20 | 62.6 (17.4) | | 2.5 % | -0.18 [ -0.71, 0.36 ] |
| Segal 2001b | 42 | 57 (23.9) | 21 | 62.6 (17.4) | | 2.6 % | -0.25 [ -0.78, 0.27 ] |
| Segal 2003 | 82 | -41.6 (10.5) | 73 | -40.3 (9.4) | | 4.7 % | -0.13 [ -0.45, 0.19 ] |
| Segal 2009a | 40 | -44.2 (8.9) | 21 | -42.1 (8.8) | | 2.6 % | -0.23 [ -0.76, 0.30 ] |
| Segal 2009b | 40 | -45.1 (9.1) | 20 | -42.1 (8.8) | | 2.5 % | -0.33 [ -0.87, 0.21 ] |
| Thorsen 2005 | 52 | 33.8 (21.2) | 49 | 25.9 (20.7) | | 3.8 % | 0.37 [ -0.02, 0.77 ] |
| Yuen 2007a | 8 | 2.79 (1.85) | 3 | 4.16 (1.67) | | 0.5 % | -0.69 [ -2.07, 0.68 ] |
| Yuen 2007b | 7 | 3.9 (1.71) | 4 | 4.16 (1.67) | | 0.6 % | -0.14 [ -1.37, 1.09 ] |
| **Total (95% CI)** | **1460** | | **1186** | | | **100.0 %** | **-0.27 [ -0.37, -0.17 ]** |

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 55.14$, df = 37 (P = 0.03); $I^2 = 33\%$

Test for overall effect: Z = 5.27 (P < 0.00001)

Test for subgroup differences: Not applicable



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## Analysis 2.1. Comparison 2 Fatigue: during anti-cancer therapy, Outcome 1 Exercise versus no exercise control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 2 Fatigue: during anti-cancer therapy

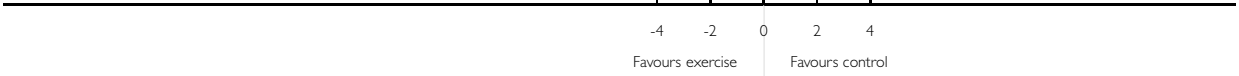
Outcome: 1 Exercise versus no exercise control; post-test means

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Adamsen 2009 | 118 | 34.6 (24.3) | 117 | 41 (22.7) | | 16.9 % | -0.27 [ -0.53, -0.01 ] |
| Chang 2008 | 11 | 4.6 (3) | 11 | 4.8 (3.5) | | 1.6 % | -0.06 [ -0.89, 0.78 ] |
| Coleman 2003a | 23 | 14.4 (7.6) | 14 | 15 (5.6) | | 2.5 % | -0.08 [ -0.75, 0.58 ] |
| Courneya 2007a | 78 | -36.8 (10.4) | 41 | -34.9 (12.5) | | 7.8 % | -0.17 [ -0.55, 0.21 ] |
| Courneya 2007b | 82 | -36.3 (9.4) | 41 | -34.9 (12.5) | | 7.9 % | -0.13 [ -0.51, 0.24 ] |
| Culos-Reed 2010 | 37 | 4.15 (1.68) | 24 | 4.46 (1.12) | | 4.2 % | -0.21 [ -0.72, 0.31 ] |
| Dimeo 1999 | 27 | 11.7 (8.9) | 32 | 11.5 (8.6) | | 4.2 % | 0.02 [ -0.49, 0.53 ] |
| Drouin 2005 | 13 | 60.9 (36.95) | 8 | 86 (55.55) | | 1.4 % | -0.54 [ -1.44, 0.36 ] |
| Mock 2005 | 54 | 3.5 (2.4) | 54 | 3.7 (2.6) | | 7.8 % | -0.08 [ -0.46, 0.30 ] |
| Monga 2007 | 11 | 0.8 (1.8) | 10 | 3.8 (2.2) | | 1.2 % | -1.44 [ -2.42, -0.46 ] |
| Mustian 2009 | 19 | 1.6 (1.36) | 19 | 2.44 (2.08) | | 2.7 % | -0.47 [ -1.11, 0.18 ] |
| Mutrie 2007 | 82 | -40.3 (10.4) | 92 | -36 (12.1) | | 12.3 % | -0.38 [ -0.68, -0.08 ] |
| Rogers 2009 | 20 | -12.4 (10.42) | 19 | -10.29 (6.743) | | 2.8 % | -0.23 [ -0.86, 0.40 ] |
| Segal 2001a | 40 | 58.8 (22.8) | 20 | 62.6 (17.4) | | 3.8 % | -0.18 [ -0.71, 0.36 ] |
| Segal 2001b | 42 | 57 (23.9) | 21 | 62.6 (17.4) | | 4.0 % | -0.25 [ -0.78, 0.27 ] |
| Segal 2003 | 82 | -41.6 (10.5) | 73 | -40.3 (9.4) | | 11.2 % | -0.13 [ -0.45, 0.19 ] |
| Segal 2009a | 40 | -44.2 (8.9) | 21 | -42.1 (8.8) | | 4.0 % | -0.23 [ -0.76, 0.30 ] |
| Segal 2009b | 40 | -45.1 (9.1) | 20 | -42.1 (8.8) | | 3.8 % | -0.33 [ -0.87, 0.21 ] |
| **Total (95% CI)** | **819** | | **637** | | | **100.0 %** | **-0.23 [ -0.33, -0.12 ]** |

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 10.65$, df = 17 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 4.26 (P = 0.000021)

Test for subgroup differences: Not applicable





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## Analysis 3.1. Comparison 3 Fatigue: post anti-cancer therapy, Outcome 1 Exercise versus no exercise control.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 3 Fatigue: post anti-cancer therapy

Outcome: 1 Exercise versus no exercise control

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Burnham 2002 | 12 | 15.3 (21.4) | 6 | 32.2 (34.5) | | 6.6 % | -0.61 [ -1.62, 0.39 ] |
| Courneya 2003b | 25 | 8.3 (7.9) | 26 | 8.8 (8.1) | | 10.8 % | -0.06 [ -0.61, 0.49 ] |
| Daley 2007 | 33 | 2.14 (1.75) | 33 | 3.44 (1.85) | | 11.4 % | -0.71 [ -1.21, -0.21 ] |
| Dimeo 2004 | 34 | 34 (21) | 35 | 39 (26) | | 11.6 % | -0.21 [ -0.68, 0.26 ] |
| McKenzie 2003 | 7 | -82.86 (9.51) | 7 | -55 (27.99) | | 5.4 % | -1.25 [ -2.43, -0.07 ] |
| McNeely 2008 | 25 | -36.7 (9) | 27 | -34.3 (11.1) | | 10.9 % | -0.23 [ -0.78, 0.31 ] |
| Milne 2008 | 29 | 11.9 (3.2) | 29 | 17.4 (4.7) | | 10.5 % | -1.35 [ -1.92, -0.78 ] |
| Pinto 2003 | 12 | 7.16 (6.4) | 12 | 9 (6.4) | | 8.2 % | -0.28 [ -1.08, 0.53 ] |
| Pinto 2005 | 43 | 27.08 (21.41) | 43 | 42.28 (26.2) | | 12.1 % | -0.63 [ -1.06, -0.20 ] |
| Thorsen 2005 | 52 | 33.8 (21.2) | 49 | 25.9 (20.7) | | 12.5 % | 0.37 [ -0.02, 0.77 ] |
| **Total (95% CI)** | **272** | | **267** | | | **100.0 %** | **-0.44 [ -0.79, -0.09 ]** |

Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 32.36$, df = 9 (P = 0.00017); $I^2 = 72\%$

Test for overall effect: Z = 2.49 (P = 0.013)

Test for subgroup differences: Not applicable



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## Analysis 4.1. Comparison 4 Fatigue: breast cancer, Outcome 1 Exercise versus no intervention control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 4 Fatigue: breast cancer

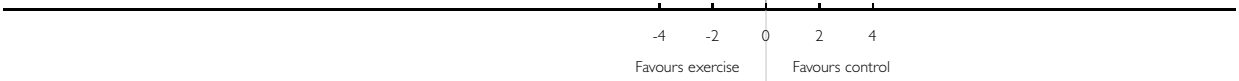
Outcome: 1 Exercise versus no intervention control; post-test means

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Courneya 2003b | 25 | 8.3 (7.9) | 26 | 8.8 (8.1) | | 5.6 % | -0.06 [ -0.61, 0.49 ] |
| Courneya 2007a | 78 | -36.8 (10.4) | 41 | -34.9 (12.5) | | 8.6 % | -0.17 [ -0.55, 0.21 ] |
| Courneya 2007b | 82 | -36.3 (9.4) | 41 | -34.9 (12.5) | | 8.7 % | -0.13 [ -0.51, 0.24 ] |
| Daley 2007 | 33 | 2.14 (1.75) | 33 | 3.44 (1.85) | | 6.3 % | -0.71 [ -1.21, -0.21 ] |
| Danhauer 2009 | 13 | -39.8 (11.5) | 14 | -32.6 (15.5) | | 3.4 % | -0.51 [ -1.28, 0.26 ] |
| Drouin 2005 | 13 | 60.9 (36.95) | 8 | 86 (55.55) | | 2.6 % | -0.54 [ -1.44, 0.36 ] |
| McKenzie 2003 | 7 | -82.86 (9.51) | 7 | -55 (27.99) | | 1.6 % | -1.25 [ -2.43, -0.07 ] |
| Milne 2008 | 29 | 11.9 (3.2) | 29 | 17.4 (4.7) | | 5.3 % | -1.35 [ -1.92, -0.78 ] |
| Moadel 2007 | 84 | -34.37 (11.26) | 44 | -33.82 (12.97) | | 9.0 % | -0.05 [ -0.41, 0.32 ] |
| Mock 2005 | 54 | 3.5 (2.4) | 54 | 3.7 (2.6) | | 8.7 % | -0.08 [ -0.46, 0.30 ] |
| Mutrie 2007 | 82 | -40.3 (10.4) | 92 | -36 (12.1) | | 10.6 % | -0.38 [ -0.68, -0.08 ] |
| Pinto 2003 | 12 | 7.16 (6.4) | 12 | 9 (6.4) | | 3.2 % | -0.28 [ -1.08, 0.53 ] |
| Pinto 2005 | 43 | 27.08 (21.41) | 43 | 42.28 (26.2) | | 7.5 % | -0.63 [ -1.06, -0.20 ] |
| Rogers 2009 | 20 | -12.4 (10.42) | 19 | -10.29 (6.743) | | 4.6 % | -0.23 [ -0.86, 0.40 ] |
| Segal 2001a | 40 | 58.8 (22.8) | 20 | 62.6 (17.4) | | 5.7 % | -0.18 [ -0.71, 0.36 ] |
| Segal 2001b | 42 | 57 (23.9) | 21 | 62.6 (17.4) | | 5.9 % | -0.25 [ -0.78, 0.27 ] |
| Yuen 2007a | 8 | 2.79 (1.85) | 3 | 4.16 (1.67) | | 1.2 % | -0.69 [ -2.07, 0.68 ] |
| Yuen 2007b | 7 | 3.9 (1.71) | 4 | 4.16 (1.67) | | 1.5 % | -0.14 [ -1.37, 1.09 ] |
| **Total (95% CI)** | **672** | | **511** | | ♦ | **100.0 %** | **-0.35 [ -0.51, -0.19 ]** |

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 26.60$, df = 17 (P = 0.06); $I^2$ =36%

Test for overall effect: Z = 4.34 (P = 0.000014)

Test for subgroup differences: Not applicable





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## Analysis 5.1. Comparison 5 Fatigue: prostate cancer, Outcome 1 Exercise versus no exercise control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 5 Fatigue: prostate cancer

Outcome: 1 Exercise versus no exercise control; post-test means

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Culos-Reed 2010 | 37 | 4.15 (1.68) | 24 | 4.46 (1.12) | | 17.5 % | -0.21 [ -0.72, 0.31 ] |
| Galv o 2010 | 29 | 14.8 (13.8) | 28 | 30.6 (17.6) | | 16.5 % | -0.99 [ -1.54, -0.44 ] |
| Monga 2007 | 11 | 0.8 (1.8) | 10 | 3.8 (2.2) | | 8.4 % | -1.44 [ -2.42, -0.46 ] |
| Segal 2003 | 82 | -41.6 (10.5) | 73 | -40.3 (9.4) | | 23.6 % | -0.13 [ -0.45, 0.19 ] |
| Segal 2009a | 40 | -44.2 (8.9) | 21 | -42.1 (8.8) | | 17.1 % | -0.23 [ -0.76, 0.30 ] |
| Segal 2009b | 40 | -45.1 (9.1) | 20 | -42.1 (8.8) | | 16.8 % | -0.33 [ -0.87, 0.21 ] |
| **Total (95% CI)** | **239** | | **176** | | | **100.0 %** | **-0.45 [ -0.78, -0.11 ]** |

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 12.21$, df = 5 (P = 0.03); $I^2 = 59\%$

Test for overall effect: Z = 2.60 (P = 0.0093)

Test for subgroup differences: Not applicable



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## Analysis 6.1. Comparison 6 Fatigue: haematological malignancies, Outcome 1 Exercise versus no exercise control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 6 Fatigue: haematological malignancies

Outcome: 1 Exercise versus no exercise control; post-test means

| Study or subgroup | Experimental N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Chang 2008 | 11 | 4.6 (3) | 11 | 4.8 (3.5) | | 10.1 % | -0.06 [ -0.89, 0.78 ] |
| Cohen 2004 | 20 | 3.1 (1.5) | 19 | 3.1 (1.5) | | 18.0 % | 0.0 [ -0.63, 0.63 ] |
| Coleman 2003a | 23 | 14.4 (7.6) | 14 | 15 (5.6) | | 16.0 % | -0.08 [ -0.75, 0.58 ] |
| Courneya 2009 | 60 | -40.5 (9.4) | 62 | -38 (11.1) | | 55.8 % | -0.24 [ -0.60, 0.12 ] |
| **Total (95% CI)** | **114** | | **106** | | | **100.0 %** | **-0.15 [ -0.42, 0.11 ]** |

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.55$, df = 3 (P = 0.91); $I^2 = 0.0\%$

Test for overall effect: Z = 1.14 (P = 0.26)

Test for subgroup differences: Not applicable



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## Analysis 7.1. Comparison 7 Fatigue: aerobic training, Outcome 1 Exercise versus no exercise control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 7 Fatigue: aerobic training

Outcome: 1 Exercise versus no exercise control; post-test means

| Study or subgroup | Experimental N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Chang 2008 | 11 | 4.6 (3) | 11 | 4.8 (3.5) | | 1.8 % | -0.06 [ -0.89, 0.78 ] |
| Courneya 2003a | 62 | -12.7 (10.9) | 31 | -12.1 (10.8) | | 5.7 % | -0.05 [ -0.49, 0.38 ] |
| Courneya 2003b | 25 | 8.3 (7.9) | 26 | 8.8 (8.1) | | 3.9 % | -0.06 [ -0.61, 0.49 ] |
| Courneya 2003c | 60 | 19.67 (11.31) | 48 | 22.37 (9.84) | | 6.8 % | -0.25 [ -0.63, 0.13 ] |
| Courneya 2007a | 78 | -36.8 (10.4) | 41 | -34.9 (12.5) | | 6.9 % | -0.17 [ -0.55, 0.21 ] |
| Courneya 2008 | 26 | -37.6 (9.6) | 29 | -36.6 (9.8) | | 4.1 % | -0.10 [ -0.63, 0.43 ] |
| Courneya 2009 | 60 | -40.5 (9.4) | 62 | -38 (11.1) | | 7.5 % | -0.24 [ -0.60, 0.12 ] |
| Daley 2007 | 33 | 2.14 (1.75) | 33 | 3.44 (1.85) | | 4.5 % | -0.71 [ -1.21, -0.21 ] |
| Dimeo 1999 | 27 | 11.7 (8.9) | 32 | 11.5 (8.6) | | 4.3 % | 0.02 [ -0.49, 0.53 ] |
| Dimeo 2004 | 34 | 34 (21) | 35 | 39 (26) | | 4.9 % | -0.21 [ -0.68, 0.26 ] |
| Drouin 2005 | 13 | 60.9 (36.95) | 8 | 86 (55.55) | | 1.6 % | -0.54 [ -1.44, 0.36 ] |
| Mock 2005 | 54 | 3.5 (2.4) | 54 | 3.7 (2.6) | | 6.9 % | -0.08 [ -0.46, 0.30 ] |
| Monga 2007 | 11 | 0.8 (1.8) | 10 | 3.8 (2.2) | | 1.4 % | -1.44 [ -2.42, -0.46 ] |
| Mutrie 2007 | 82 | -40.3 (10.4) | 92 | -36 (12.1) | | 9.4 % | -0.38 [ -0.68, -0.08 ] |
| Pinto 2003 | 12 | 7.16 (6.4) | 12 | 9 (6.4) | | 2.0 % | -0.28 [ -1.08, 0.53 ] |
| Pinto 2005 | 43 | 27.08 (21.41) | 43 | 42.28 (26.2) | | 5.6 % | -0.63 [ -1.06, -0.20 ] |
| Rogers 2009 | 20 | -12.4 (10.42) | 19 | -10.29 (6.743) | | 3.0 % | -0.23 [ -0.86, 0.40 ] |
| Segal 2001a | 40 | 58.8 (22.8) | 20 | 62.6 (17.4) | | 4.0 % | -0.18 [ -0.71, 0.36 ] |
| Segal 2001b | 42 | 57 (23.9) | 21 | 62.6 (17.4) | | 4.1 % | -0.25 [ -0.78, 0.27 ] |
| Segal 2009a | 40 | -44.2 (8.9) | 21 | -42.1 (8.8) | | 4.1 % | -0.23 [ -0.76, 0.30 ] |
| Thorsen 2005 | 52 | 33.8 (21.2) | 49 | 25.9 (20.7) | | 6.5 % | 0.37 [ -0.02, 0.77 ] |
| Yuen 2007a | 7 | 3.9 (1.71) | 4 | 4.16 (1.67) | | 0.9 % | -0.14 [ -1.37, 1.09 ] |
| **Total (95% CI)** | **832** | | **701** | | | **100.0 %** | **-0.22 [ -0.34, -0.10 ]** |

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 26.20$, df = 21 (P = 0.20); $I^2 = 20\%$

Test for overall effect: Z = 3.66 (P = 0.00025)

Test for subgroup differences: Not applicable



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## Analysis 8.1. Comparison 8 Fatigue: resistance training, Outcome 1 Exercise versus no exercise control; post-test means.

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 8 Fatigue: resistance training

Outcome: 1 Exercise versus no exercise control; post-test means

| Study or subgroup | Experimental N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Courneya 2007b | 82 | -36.3 (9.4) | 41 | -34.9 (12.5) | | 29.1 % | -0.13 [ -0.51, 0.24 ] |
| McNeely 2008 | 25 | -36.7 (9) | 27 | -34.3 (11.1) | | 13.7 % | -0.23 [ -0.78, 0.31 ] |
| Segal 2003 | 82 | -41.6 (10.5) | 73 | -40.3 (9.4) | | 41.0 % | -0.13 [ -0.45, 0.19 ] |
| Segal 2009b | 40 | -45.1 (9.1) | 20 | -42.1 (8.8) | | 14.0 % | -0.33 [ -0.87, 0.21 ] |
| Yuen 2007b | 8 | 2.79 (1.85) | 3 | 4.16 (1.67) | | 2.2 % | -0.69 [ -2.07, 0.68 ] |
| **Total (95% CI)** | **237** | | **164** | | | **100.0 %** | **-0.18 [ -0.39, 0.02 ]** |

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.02$, df = 4 (P = 0.91); $I^2 = 0.0\%$

Test for overall effect: Z = 1.79 (P = 0.074)

Test for subgroup differences: Not applicable



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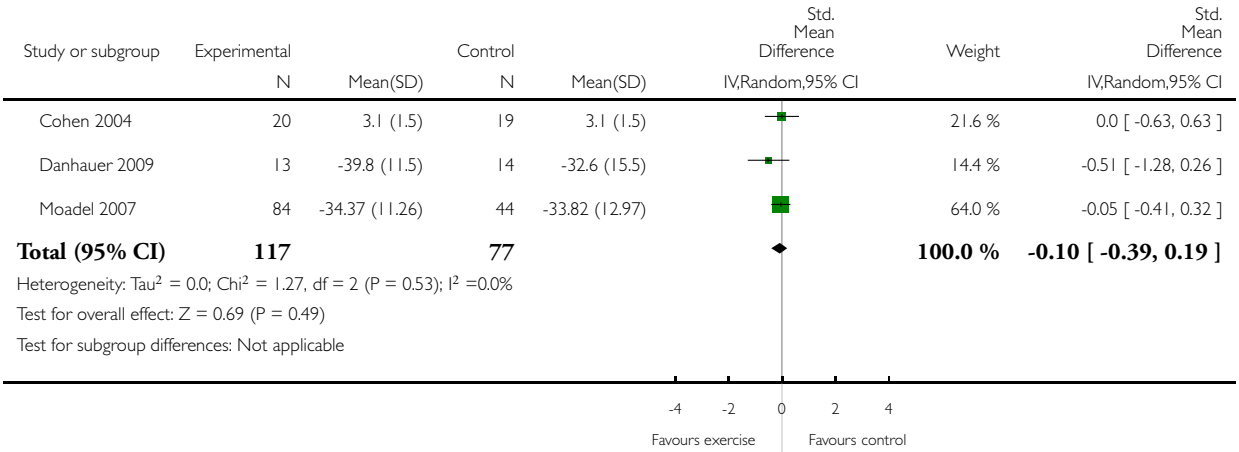
**Analysis 9.1. Comparison 9 Fatigue: mind-body exercise, Outcome 1 Exercise versus no exercise control; post-test means.**

Review: Exercise for the management of cancer-related fatigue in adults

Comparison: 9 Fatigue: mind-body exercise

Outcome: 1 Exercise versus no exercise control; post-test means




# APPENDICES

## Appendix 1. Search strategy

We used the following search strategy for this review, using text and keyword and MeSH terms in each database, with an RCT filter applied:

1. exp NEOPLASMS/
2. exp LEUKEMIA/
3. exp LYMPHOMA/
4. exp RADIOTHERAPY/
5. BONE MARROW TRANSPLANTATION/
6. neoplasm$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
7. cancer$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
8. (leukaemi$ or leukemi$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
9. (tumour$ or tumor$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
10. malignan$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
11. neutropeni$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
12. carcino$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
13. adenocarcinoma$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
14. lymphoma$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]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15. (radioth$ or radiat$ or irradiat$ or radiochemo$ or chemotherapy$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
16. (bone adj marrow adj5 transplant$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
17. or/1-16
18. exp EXERCISE MOVEMENT TECHNIQUES/
19. ((exercise$ or resistance or strength or flexibility or endurance) adj6 (train$ or program$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
20. ((resistance or aerobic$ or endurance$) adj3 exercise$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
21. (physical$ adj3 (activ$ or therap$ or exercise$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
22. (interval training or sport$ or movement therap$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
23. stretching.mp.
24. (dance therap$ or exercis$ or "Tai Ji" or "Tai Chi" or "Tai-Ji" or "Tai-Chi" or walking or yoga).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
25. or/18-24
26. FATIGUE/
27. fatigue.mp.
28. (tired$ or weary or weariness or exhaustion or exhausted or lacklustre or ((astenia or asthenic) and syndrome) or ((lack or loss or lost) adj3 (energy or vigour))).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
29. (apathy or apathetic or lassitude or weakness or lethargy or lethargic or (feeling adj3 (drained or sleepy or sluggish))).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
30. or/26-29
31. 17 and 25 and 30

The search was adapted as follows for each database:

**CENTRAL**

#1 MeSH descriptor Neoplasms explode all trees
#2 MeSH descriptor Leukemia explode all trees
#3 MeSH descriptor Lymphoma explode all trees
#4 MeSH descriptor Radiotherapy explode all trees
#5 MeSH descriptor Bone Marrow Transplantation explode all trees
#6 neoplasm* or cancer* or leukaemi* or leukemi* or tumour* or tumor* or malignan* or neutropeni* or carcino* or adenocarcinoma* or lymphoma*
#7 radioth* or radiat* or irradiat* or radiochemo* or chemotherap*
#8 bone next marrow near/5 transplant*
#9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)
#10 MeSH descriptor Exercise Movement Techniques explode all trees
#11 (exercise* or resistance or strength or flexibility or endurance) near/6 (train* or program*)
#12 (resistance or aerobic* or endurance*) near/3 exercise*
#13 physical* near/3 (activ* or therap* or exercise*)
#14 interval training or sport* or movement therap*
#15 stretching
#16 dance therap* or exercis* or "Tai Ji" or "Tai Chi" or "Tai-Ji" or "Tai-Chi" or walking or yoga
#17 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)
#18 MeSH descriptor Fatigue, this term only
#19 fatigue
#20 tired* or weary or weariness or exhaustion or exhausted or lacklustre or ((astenia or asthenic) and syndrome) or ((lack or loss or lost) near/3 (energy or vigour))
#21 apathy or apathetic or lassitude or weakness or lethargy or lethargic or (feeling near/3 (drained or sleepy or sluggish))
#22 (#18 OR #19 OR #20 OR #21)
#23 (#9 AND #17 AND #22)

**MEDLINE Ovid**


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1 exp NEOPLASMS/
2 exp LEUKEMIA/
3 exp LYMPHOMA/
4 exp RADIOTHERAPY/
5 Bone Marrow Transplantation/
6 neoplasm$.mp.
7 cancer$.mp.
8 (leukaemi$ or leukemi$).mp.
9 (tumour$ or tumor$).mp.
10 malignan$.mp.
11 neutropeni$.mp.
12 carcino$.mp.
13 adenocarcinoma$.mp.
14 lymphoma$.mp.
15 (radioth$ or radiat$ or irradiat$ or radiochemo$ or chemotherap$).mp.
16 (bone adj marrow adj5 transplant$).mp.
17 or/1-16
18 exp Exercise Movement Techniques/
19 ((exercise$ or resistance or strength or flexibility or endurance) adj6 (train$ or program$)).mp.
20 ((resistance or aerobic$ or endurance$) adj3 exercise$).mp.
21 (physical$ adj3 (activ$ or therap$ or exercise$)).mp.
22 (interval training or sport$ or movement therap$).mp.
23 stretching.mp.
24 (dance therap$ or exercis$ or "Tai Ji" or "Tai Chi" or "Tai-Ji" or "Tai-Chi" or walking or yoga).mp.
25 or/18-24
26 Fatigue/
27 fatigue.mp.
28 (tired$ or weary or weariness or exhaustion or exhausted or lacklustre or ((astenia or asthenic) and syndrome) or ((lack or loss or lost) adj3 (energy or vigour))).mp.
29 (apathy or apathetic or lassitude or weakness or lethargy or lethargic or (feeling adj3 (drained or sleepy or sluggish))).mp.
30 or/26-29
31 17 and 25 and 30
32 randomized controlled trial.pt.
33 controlled clinical trial.pt.
34 randomized.ab.
35 placebo.ab.
36 clinical trials as topic.sh.
37 randomly.ab.
38 trial.ti.
39 32 or 33 or 34 or 35 or 36 or 37 or 38
40 31 and 39
key:
mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer
ab = abstract
pt = publication type
sh = subject heading
ti = title

**EMBASE Ovid**

1 exp neoplasm/
2 exp leukemia/
3 exp lymphoma/
4 exp radiotherapy/ or exp cancer radiotherapy/
5 exp bone marrow transplantation/


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6 (neoplasm* or cancer* or leukaemi* or leukemi* or tumor* or tumour* or malignan* or neutropeni* or carcino* or adenocarcinoma* or lymphoma*).mp.
7 (radioth* or radiat* or irradiat* or radiochemo* or chemotherap*).mp.
8 (bone adj marrow adj5 transplant*).mp.
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10 exp kinesiotherapy/
11 ((exercise* or resistance or strength or flexibility or endurance) adj6 (train* or program*)).mp.
12 ((resistance or aerobic* or endurance*) adj3 exercise*).mp.
13 (physical* adj3 (activ* or therap* or exercise*)).mp.
14 (interval training or sport* or movement therap*).mp.
15 stretching.mp.
16 (dance therap* or exercis* or "Tai Ji" or "Tai Chi" or "Tai-Ji" or "Tai-Chi" or walking or yoga).mp.
17 10 or 12 or 13 or 14 or 15 or 16
18 exp fatigue/
19 fatigue.mp.
20 (tired* or weary or weariness or exhaustion or exhausted or lacklustre or ((astenia or asthenic) and syndrome) or ((lack or loss or lost) adj3 (energy or vigour))).mp.
21 (apathy or apathetic or lassitude or weakness or lethargy or lethargic or (feeling adj3 (drained or sleepy or sluggish))).mp.
22 18 or 19 or 20 or 21
23 9 and 17 and 22
24 crossover procedure/
25 double blind procedure/
26 randomized controlled trial/
27 single blind procedure/
28 random*.mp.
29 factorial*.mp.
30 crossover*.mp.
31 cross over*.mp.
32 cross-over*.mp.
33 placebo*.mp.
34 (doubl* adj blind*).mp.
35 (single* adj blind*).mp.
36 assign*.mp.
37 allocat*.mp.
38 volunteer*.mp.
39 24 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38
40 23 and 39
key:
[mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

## WHAT'S NEW

Last assessed as up-to-date: 19 April 2012.

| Date | Event | Description |
|---|---|---|
| 19 April 2012 | New search has been performed | We ran update searches for studies in March 2011. |


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(*Continued*)

| | | |
|---|---|---|
| 19 April 2012 | New citation required and conclusions have changed | The updated review includes an additional 28 studies; a further 22 were identified but excluded. We have also added 'Risk of bias' tables. The conclusions have been further developed to identify the 'type' of exercise (aerobic) necessary to reduce cancer-related fatigue |

## HISTORY

Protocol first published: Issue 3, 2006

Review first published: Issue 2, 2008

| Date | Event | Description |
|---|---|---|
| 24 September 2010 | Amended | Contact details updated. |
| 30 October 2008 | Amended | Converted to new review format. |

## CONTRIBUTIONS OF AUTHORS

FC led the review from the initiation of the protocol and has been responsible for the retrieval, screening and data extraction process as well as writing the review. In the updated review FC was responsible for the retrieval of new studies, screening and data extraction and re-writing the review.

JB-D screened all the studies, carried out data extraction for comparison purposes and contributed to the writing of the review. In the updated review JB-D screened all the studies, carried out data extraction on the new studies that were identified for inclusion and contributed to the writing of the final review.

## DECLARATIONS OF INTEREST

None known.

## SOURCES OF SUPPORT


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### Internal sources

- Faculty of Health and Social Care, University of the West of England, UK.

### External sources

- National Institute for Health Research (NIHR) Health Technology Assessment programme, UK.

HTA Project: 10/81/01 - Exercise interventions for the management of health related quality of life and fatigue in cancer survivors during and after treatment.

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the updated review it was decided a priori to carry out separate subgroup analysis based upon the mode of exercise. We also added 'Risk of bias' tables for all studies. There were no other changes between the protocol and review.

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Exercise; Fatigue [*therapy]; Neoplasms [*complications; therapy]; Randomized Controlled Trials as Topic

### MeSH check words

Adult; Humans


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