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Research

Supervised exercise reduces cancer-related fatigue: a systematic review

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KEYWORDS

Physical exercise
Cancer
Fatigue

CrossMark

Question: Does supervised physical activity reduce cancer-related fatigue? **Design:** Systematic review with meta-analysis of randomised trials. **Participants:** People diagnosed with any type of cancer, without restriction to a particular stage of diagnosis or treatment. **Intervention:** Supervised physical activity interventions (eg, aerobic, resistance and stretching exercise), defined as any planned or structured body movement causing an increase in energy expenditure, designed to maintain or enhance health-related outcomes, and performed with systematic frequency, intensity and duration. **Outcome measures:** The primary outcome measure was fatigue. Secondary outcomes were physical and functional wellbeing assessed using the Functional Assessment of Cancer Therapy Fatigue Scale, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, Piper Fatigue Scale, Schwartz Cancer Fatigue Scale and the Multidimensional Fatigue Inventory. Methodological quality, including risk of bias of the studies, was evaluated using the PEDro Scale. **Results:** Eleven studies involving 1530 participants were included in the review. The assessment of quality showed a mean score of 6.5 (SD 1.1), indicating a low overall risk of bias. The pooled effect on fatigue, calculated as a standardised mean difference (SMD) using a random-effects model, was –1.69 (95% CI –2.99 to –0.39). Beneficial reductions in fatigue were also found with combined aerobic and resistance training with supervision (SMD = –0.41, 95% CI –0.70 to –0.13) and with combined aerobic, resistance and stretching training with supervision (SMD = –0.67, 95% CI –1.17 to –0.17). **Conclusion:** Supervised physical activity interventions reduce cancer-related fatigue. These findings suggest that combined aerobic and resistance exercise regimens with or without stretching should be included as part of rehabilitation programs for people who have been diagnosed with cancer. **Registration:** PROSPERO CRD42013005803. **[Meneses-Echávez JF, González-Jiménez E, Ramírez-Vélez R (2015) Supervised exercise reduces cancer-related fatigue: a systematic review. *Journal of Physiotherapy* 61: 3–9]**

Introduction

The number of people diagnosed worldwide with cancer has been estimated to be as high as 10 million, with another 25 million having survived cancer.[1] In Colombia, the National Cancer Institute reported that malignant tumours are the third biggest cause of mortality, increasing their mortality burden from 6 to 15% in the six decades before 2002.[2] This increase in cancer diagnoses is an important public health problem, with the number of new cases diagnosed in 2020 expected to be approximately 1.7 million.[3]

Cancer-related fatigue is a common problem for people with cancer. Approximately 80 to 100% of people with cancer report that they experience cancer-related fatigue.[4] Furthermore, many people continue to experience fatigue for months or years after successful treatment.[4] Several concepts of cancer-related fatigue have been published in the biomedical literature. Stone and colleagues found that 75% of people with various solid tumours (among whom 48 out of 95 had metastatic disease) had a significantly increased cancer-related fatigue score compared with a matched control population.[4] The Colombian National Cancer Institute[2] and the National Comprehensive Cancer Network[5] define cancer-related fatigue as 'a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning'. Cancer-related fatigue also has a severe impact on daily activities, social relationships, reintegration and overall quality of life.[6] Some evidence suggests that cancer-related fatigue may be a predictor of survival for people with cancer.[7]

Physical activity has been proposed as an effective non-pharmacologic intervention to promote psychological wellbeing during and following cancer treatment.[8] A growing body of evidence indicates that physical activity improves muscle strength and body composition in people with cancer.[9,10] Recent systematic reviews examining the effect of physical activity on psychological and functional outcomes have tended to study particular types of cancer instead of all cancer types, with lung and breast cancer being the most widely studied.[11–13] A recent Cochrane systematic review[14] about exercise and cancer-related fatigue concluded that aerobic exercise reduces cancer-related fatigue and encouraged further research of other exercise modalities; however, this review only included data published before March 2011 and did not examine supervised physical activity interventions in isolation from unsupervised interventions.

Supervision plays an important role in the effects of exercise interventions in chronically ill people.[15,16] This value of supervision

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has been attributed to improvements in adherence and intensity,[17] perhaps because of greater encouragement or confidence to work when the help of a health professional is at hand. A supervising health professional may also help to individualise the exercise regimen to the specific condition of the person, such as the complex sequelae of cancer and its treatment.[17,18] Whitehead and Lavelleand[19] and Spence et al[20] reported that breast and colon cancer survivors prefer supervised exercise training over unsupervised exercise. In light of this, Lin et al[21] compared the effects of a supervised exercise intervention with those of usual care for 12 weeks in colorectal cancer patients during chemotherapy, and found significant improvements in the supervised exercise group on fatigue, physical activity, physical functioning, social functioning, hand-grip strength, cardiorespiratory fitness, and pain subscales of quality of life. Similarly, in a sample of 113 breast cancer patients, Schneider et al[18] reported that moderate-intensity individualised exercise improved cardiopulmonary function and fatigue during and after treatment. This apparent value of supervision and the lack of subgroup analysis of supervised physical activity interventions in isolation from unsupervised interventions in previous reviews necessitated a systematic review to determine the effectiveness of supervised physical activity. The current systematic review therefore aimed to answer two questions:

1. Does supervised physical activity improve cancer-related fatigue and physical and functional wellbeing among people with current or previous cancer?
2. What are the effects of specific modalities of supervised physical activity on these outcomes among people with current or previous cancer?

Methods

This systematic review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions,[22] analysed using Review Manager Software version 5.2,[23] and reported according to the PRISMA statement.[24]

Identification and selection of studies

Four electronic databases were searched (PubMed, CENTRAL, EMBASE and OVID) to September 2013. The search strategy incorporated the recommendations for a highly sensitive search strategy for the retrieval of clinical trials on PubMed.[25] The final search strategy followed the format: (*randomized controlled trial* OR *controlled clinical trial* OR *randomized* OR *trial* OR "clinical trials as topic") AND (*cancer* OR *neoplasm** OR *tumour** OR *tumor** OR *carcino** OR *leukaemi** OR *leukemi**) AND (*physical activity* OR *exercise* OR *aerobic* OR *resistance* OR *strength* OR *flexibility* OR *stretching*) AND (fatigue). See Appendix 1 on the eAddenda for further details of search strategy.

Two authors (JFM-E and RR-V) independently reviewed all of the retrieved studies against the inclusion criteria (Box 1). The title and abstract were examined and full text was obtained if there was ambiguity regarding eligibility. When the two authors could not reach an agreement, a third author arbitrated in cases of disagreement (EG-J). Additionally, the authors searched for other relevant trials listed in the reference lists of the retrieved articles, and in journals specialised in oncology for other possible relevant trials (ie, *Cancer*, *Journal of Clinical Oncology*, *Breast Cancer Research*, *Journal of Oncology Practice* and *The Lancet Oncology*). No language restrictions were applied.

Box 1. Inclusion criteria.

Design
- Randomised controlled trial

Participants
- Patients with any type of cancer, without restriction to a particular stage of diagnosis or treatment

Intervention
- Supervised physical activity interventions (aerobic, resistance or stretching)

Outcome measures
- Cancer-related fatigue (primary outcome)
- Physical wellbeing
- Functional wellbeing

Comparisons
- Supervised physical activity versus conventional care

Assessment of the characteristics of the studies

Quality

The methodological quality of the studies including their risk of bias was assessed using the Physiotherapy Evidence Database (PEDro) scale.[26] The PEDro scale rates the methodological quality of randomised trials out of 10. A trained assessor determined the score for each included study (JFM-E). Scores were based on all information available from both the published version and from communication with the authors. A score of 5 out of 10 was set as the minimum score for inclusion in the review.

Participants

This systematic review included studies involving people diagnosed with any type of cancer, without restriction to a particular stage of diagnosis or treatment. Participants may have received active treatment regardless of therapeutic approach (eg, chemotherapy, radiotherapy).

Intervention

The experimental intervention was supervised physical activity. Physical activity was considered as any body movement causing an increase in energy expenditure, and involving a planned or structured movement of the body performed in a systematic manner in terms of frequency, intensity, and duration and is designed to maintain or enhance health-related outcomes.[27] The control intervention was sham or conventional care. Physical activity interventions such as aerobic, resistance and/or stretching training were included. All interventions had to be supervised by health professionals; therefore, home-based physical activity, telephone monitoring and cognitive approaches were excluded from the analysis. Yoga and Tai Chi interventions were not included due to excessive variation in their mode, frequency, duration and intensity. Subgroup analysis was performed to explore the specific effect of supervised physical activity modalities (ie, aerobic, resistance and stretching training). The pooled statistical analysis and effect size was calculated for each physical activity training modality.

Outcome measures

The primary outcome measure was cancer-related fatigue measured using the Functional Assessment of Cancer Therapy (FACT)-Fatigue Scale, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), Piper Fatigue Scale (PFS), Schwartz Cancer Fatigue Scale (SCFS) and the Multidimensional Fatigue Inventory (MFI). The secondary outcomes were physical and functional wellbeing measured with the EORTC QLQ-C30 and FACT, and adverse events.

Data analysis

Relevant data were extracted independently from the eligible trials by two reviewers (JFM-E and RR-V) using a standard form, and the third author (EG-J) arbitrated in cases of disagreement. The reviewers extracted information about the methods (ie, design, participants and intervention) and the outcome data for the experimental and control groups. A random-effects model was used when there was substantial heterogeneity ($I^2 > 50\%$). Continuous outcomes were reported as standardised mean

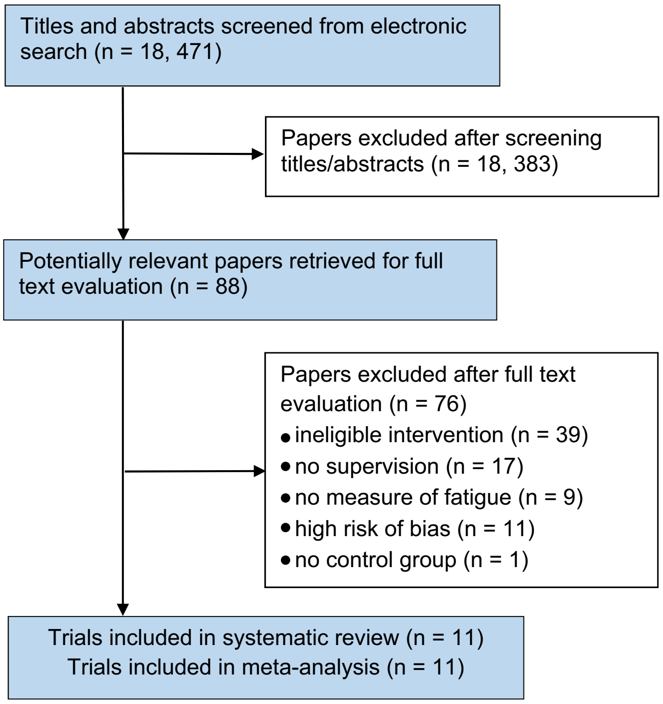

Figure 1. Flow of studies through the review.

differences (SMD) with 95% CI, with statistical significance set at a *p*-value < 0.05.

Results

Flow of trials through the review

Eleven randomised controlled trials involving 1530 participants were included (Figure 1).[28–38] The majority of studies were conducted in Canada (n = 4, 36%), Australia (n = 2, 18%) and UK (n = 2, 18%).

Characteristics of the included studies

Quality

The assessment of risk of bias showed a mean PEDro score of 6.5 (SD 1.1), indicating consistent methodological quality and a low risk of most biases except blinding (Table 1).

Participants

The mean age of participants in the included studies ranged from 47 to 66 years. Most participants were female (n = 1192, 78%). All participants were receiving treatment at the time of the study interventions and the most frequent treatment procedure was chemotherapy (n = 1028). The average time since cancer diagnosis was 8 months (SD 11). Breast cancer was the most investigated cancer type (six trials, 55%),[29,30,34–37] followed by prostate cancer (two trials, 18%),[33,38] and lymphoma (one trial, 9%).[31] Two trials (18%) included diverse types of cancer.[28,32]

Interventions

The interventions had a mean duration of 17 weeks (SD 12) with an average of three sessions (SD 1) per week. The mean session duration was 45 minutes (SD 29). The interventions included aerobic exercise (ie, walking and stationary cycling) in all trials, resistance training in six trials (55%) and stretching/flexibility exercises in four trials (36%). Training intensity varied considerably among studies, ranging from 50 to 90% maximum heart rate. All studies reported pre-exercise screening before high-intensity physical training. Table 2 summarises the characteristics of the included studies.

Outcome measures

The primary outcome – cancer-related fatigue – was measured using the FACT-Fatigue Scale in 55% of the included trials, the EORTC QLQ-C30 in 36% of trials, the PFS in 9% and the SCFS in 9%.

Effect of intervention

Primary outcome

Data from all of the included trials were used in the meta-analysis of the primary outcome.[28–38] The pooled SMD was –1.69 (95% CI –2.99 to –0.39), indicating a moderate reduction in fatigue from supervised physical activity (Figure 2, see Figure 3 on the eAddenda for a detailed forest plot). Due to considerable statistical heterogeneity ($p < 0.001$, $I^2 = 99\%$), this result was calculated using a random-effects model, which was mostly due to a single outlying trial.[36]

Secondary outcomes

Physical wellbeing was reported in seven studies.[28,30,32–35,37] The pooled effect was not statistically significant (SMD = 0.27 in favour of exercise, 95% CI –0.19 to 0.74), with considerable statistical heterogeneity ($p < 0.001$, $I^2 = 88\%$). Functional wellbeing was reported in six studies.[28,32,32–35] The pooled effect was not statistically significant (SMD = 0.47 in favour of exercise, 95% CI 0.00 to 0.95), again with considerable statistical heterogeneity ($p < 0.001$, $I^2 = 87\%$).

Three studies (27%) reported adverse events related to supervised physical activity interventions. Courneya et al[30] reported five adverse events in the exercise group (lymphoedema, gynaecologic complaints and influenza) and two in the control group (foot fracture and bronchitis). Courneya et al[31] reported one case each of back, hip and knee pain in the exercise group only. Segal et al[38] reported adverse events related to exercise: chest pain during resistance training (cardiologic investigations were negative), a syncopal episode before a treadmill exercise test in the aerobic group (no cause was identified), and a myocardial infarction 15 minutes after an exercise session in the aerobic group (full recovery).

Table 1
PEDro Scale scores for the included trials (n = 11).

Study	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor Blinding	< 15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0 to 10)
Adamsen[28]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Campbell[29]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Courneya[30]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Courneya[31]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Dimeo[32]	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Galvão[33]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Milne[34]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Mutrie[35]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Saarto[36]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Segal[37]	Y	N	Y	N	N	N	N	Y	Y	Y	5
Segal[38]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7

N = No, Y = Yes, PEDro = Physiotherapy Evidence Database.

Table 2
Characteristics of the included trials (n = 11).

Study	Cancer type Cancer treatment	Participants	Intervention[a]	Outcome measures
Adamsen[28]	Mixed types of cancer Chemotherapy	n = 235 (171 female) Exp: n = 118, age (yr) = 47 (SD 11) Con: n = 117, age (yr) = 47 (SD 11)	Exp: aerobic, resistance and stretching; 120 min x 5/wk x 6 wk; intensity 85 to 95% Con: conventional care	EORTC QLQ-C30, MOS SF-36, Leisure Time Physical Activity Questionnaire, 1RM
Campbell[29]	Breast: early stage (I-II) Chemotherapy, radiotherapy	n = 22 (22 female) Exp: n = 12, age (yr) = 48 (SD 10) Con: n = 10, age (yr) = 47 (SD 5)	Exp: aerobic and resistance; 20 min x 2/wk x 12 wk; intensity 60 to 75% Con: conventional care	FACT-G, FACT-B, SWLS, PFS, SPAQ, 12-minute walk test
Courneya[30]	Breast: early stage Chemotherapy, radiotherapy	n = 52 (52 female) Exp: n = 24, age (yr) = 59 (SD 5) Con: n = 28, age (yr) = 58 (SD 6)	Exp: aerobic; 35 min x 3/wk x 15 wk; intensity 70 to 75% Con: conventional care	FACT- G, FACT-B, FACT-F
Courneya[31]	Lymphoma: stages I-IV; Hodgkin's (18%) and non-Hodgkin's (82%) Chemotherapy	n = 122 (72 male) Exp: n = 60, age (yr) = 53 (range 18 to 77) Con: n = 62, age (yr) = 54 (range 18 to 80)	Exp: aerobic; 45 min x 3/wk x 12 wk; intensity 60 to 75% Con: conventional care	FACT-G, FACT-F
Dimeo[32]	Mixed: tumour stages I-IV Chemotherapy, radiotherapy	n = 69 (49 male) Exp: n = 34, age (yr) = 55 (SD 10) Con: n = 35, age (yr) = 60 (SD 10)	Exp: aerobic; 30 min x 5/wk x 3 wk; intensity ~80% Con: progressive relaxation training; 45 min x 3/wk x 3 wk	EORTC QLQ-C30
Galvão[33]	Prostate: localised (93%), nodal metastases (7%) Chemotherapy, radiotherapy	n = 57 (57 male) Exp: n = 29, age (yr) = 54 (SD 9) Con: n = 28, age (yr) = 52 (SD 12)	Exp: aerobic, resistance, stretching; 20 min x 2/wk x 12 wk; intensity 60 to 80% Con: conventional care	EORTC QLQ-C30, MOS SF-36, DEXA, 1 RM
Milne[34]	Breast: early stage Chemotherapy, radiotherapy	n = 58 (58 female) Exp: n = 29, age (yr) = 55 (SD 8) Con: n = 29, age (yr) = 55 (SD 8)	Exp: aerobic, resistance, stretching; 30 min x 3/wk x 12 wk; intensity ~75% Con: delayed the same exercise program until week 13	FACT-B, SCFS, PARQ, Aerobic Power Index
Mutrie[35]	Breast: early stage Chemotherapy, radiotherapy	n = 174 (174 female) Exp: n = 82, age (yr) = 51 (SD 10) Con: n = 92, age (yr) = 52 (SD 9)	Exp: aerobic, resistance; 45 min x 2/wk x 12 wk; intensity 50 to 75% Con: conventional care	FACT-G, FACT-B, FACT-F, BDI, PANAS, SPAQ Leisure time, BMI, 12-min walk test
Saarto[36]	Breast: early stage Chemotherapy, radiotherapy	n = 500 (500 female) Exp: n = 263, age (yr) = 52 (range 36 to 68) Con: n = 237, age (yr) = 52 (range 35 to 68)	Exp: aerobic; 60 min x 1/wk x 48 wk; intensity 86 to 92% Con: encouragement to maintain their previous level of physical activity and exercise habits	EORTC QLQ-C30, FACIT-F, RBDI, WHQ
Segal[37]	Breast: early stage Chemotherapy	n = 123 (123 female) Exp: n = 42, age (yr) = 51 (SD 9) Con1: n = 41, age (yr) = 50 (SD 9) Con2: n = 40, age (yr) = 51 (SD 9)	Exp: aerobic; session duration not stated; 3/wk x 26 wk; intensity 50 to 60% Con1: conventional care Con2: self-directed progressive walking; 5/wk x 26 wk; intensity 50 to 60%	FACT-G, FACT-B, MOS SF-36
Segal[38]	Prostate: stages I-IV Radiotherapy	n = 121 (121 male) Exp1: n = 40, age (yr) = 66 (SD 7) Exp2: n = 40, age (yr) = 66 (SD 8) Con: n = 41, age (yr) = 65 (SD 8)	Exp1: aerobic, resistance, stretching; 45 min x 3/wk x 24 wk; intensity 70 to 75% Exp2: supervised resistance exercise; 2 x 8–12 reps of 10 exercises; 3/wk x 24 wk; 60 to 70% of estimated 1RM Con: conventional care	FACT-G, FACT-P, FACT-F, VO_2max, 1RM, DEXA scan (percent body fat)

BDA = Beck Depression Inventory; BMI = Body mass index; DEXA = Dual-energy X-ray absorptiometry; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; FACT = Functional Assessment of Cancer Therapy, FACT-B = FACT – Breast; FACT-F = FACT – Fatigue; FACT-G = FACT – General; FACT-P = FACT – Prostate; FACIT = Functional Assessment of Chronic Illness Therapy; FACIT-F = FACIT questionnaire for fatigue; MFSI-SF = Multidimensional Fatigue Inventory; MOS SF-36 = Medical Outcomes Study Short Form; PANAS = Positive And Negative Affect Scale; PARQ = Physical Activity Readiness Questionnaire; PFS = Piper Fatigue Scale; RBDI = Finnish modified version of Beck's 13-item depression scale; SCFS = Schwartz Cancer Fatigue Scale; SPAQ = Scottish Physical Activity Questionnaire; SWLS = Satisfaction with Life Scale; VO_2max = maximal oxygen uptake; WHQ = Women's Health Questionnaire; 1RM = one repetition maximum.

[a] Supervised physical activity interventions usually consisted of a warm-up period, aerobic training (walking, cycle ergometers and circuits), muscle strength training, stretching exercises and a cool-down and relaxation period. The prescribed exercise intensities are reported as a percentage of maximal predicted oxygen uptake, unless otherwise stated.

Outcomes beyond the intervention period

At the 6-month follow-up, Courneya et al[31] reported that the favourable effect of aerobic exercise training on physical functioning was no longer statistically significant (mean difference 5.5 points, 95% CI –1.5 to 12.4). Similarly, overall quality of life (including fatigue) was no longer statistically significant (mean difference 7.6 points, 95% CI –0.1 to 15.4); however, regular exercise was significantly more common among the experimental group (p = 0.017). Conversely, Mutrie et al[35] stated that most of the benefits of exercise observed at 12 weeks continued to the 6-month follow-up. In addition, a beneficial effect of exercise on the primary outcome of breast-cancer-specific quality of life was observed, even though it had not been significant at the end of the intervention.

Subgroup analyses

Aerobic

Aerobic exercise was the only component of the physical activity intervention in five trials.[30–32,36,37] The effect of supervised aerobic exercise on cancer-related fatigue was non-significant (SMD = –2.99, 95% CI –6.49 to 0.51) with considerable statistical heterogeneity ($p < 0.001$, I^2 = 100%) (Figure 4, see Figure 5 on the eAddenda for a detailed forest plot).

Resistance

Only one trial had a group that undertook supervised resistance training only.[38] The authors analysed the effect of supervised resistance exercise on cancer-related fatigue using a mixed-model

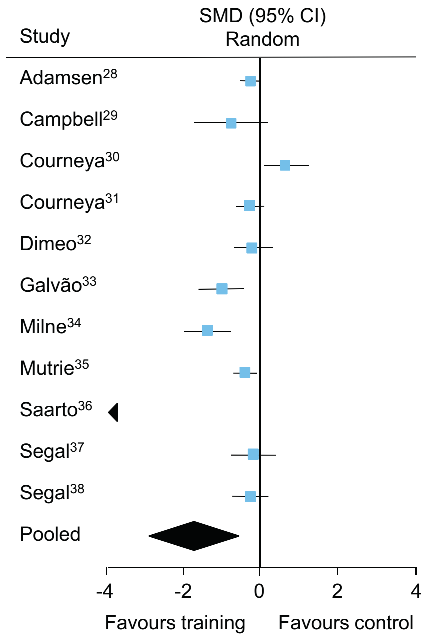

Figure 2. Standardised mean difference (SMD) of the effect of supervised physical activity on cancer-related fatigue.

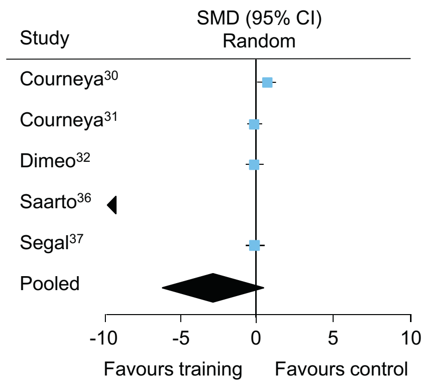

Figure 4. Standardised mean difference (SMD) of the effect of supervised aerobic exercise on cancer-related fatigue.

repeated measures analysis, which showed a benefit of 4.8 points on the FACT-Fatigue, which was statistically significant (95% CI 1.9 to 7.7).

Aerobic and resistance

The physical activity intervention involved both aerobic and resistance training in two studies.[29,35] The effect of supervised aerobic and resistance exercise on cancer-related fatigue was statistically significant (SMD = –0.41, 95% CI –0.70 to –0.13) with no statistical heterogeneity ($p = 0.47$, $I^2 = 0\%$) (Figure 6, see Figure 7 on the eAddenda for a detailed forest plot).

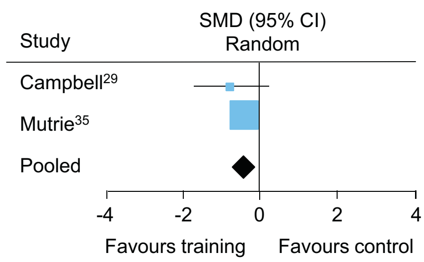

Figure 6. Standardised mean difference (SMD) of the effect of combined aerobic and resistance exercise with supervision on cancer-related fatigue.

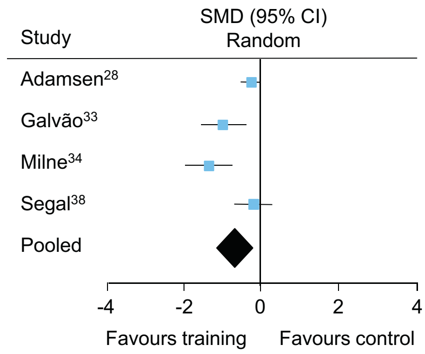

Figure 8. Standardised mean difference (SMD) of the effect of combined aerobic, resistance and stretching exercise with supervision on cancer-related fatigue.

Aerobic, resistance and stretching

The physical activity intervention involved aerobic and resistance training and stretching in four studies.[28,33,34,38] This supervised exercise regimen reduced cancer-related fatigue significantly (SMD = –0.67, 95% CI –1.17 to –0.17) with considerable statistical heterogeneity ($p = 0.001$, $I^2 = 81\%$) (Figure 8, see Figure 9 on the eAddenda for a detailed forest plot).

Discussion

The present review identified a substantial amount of information about the effects of supervised exercise on cancer-related fatigue. These data were from trials that were rated above average on the PEDro Scale for trials in physiotherapy.[39] These ratings were evaluated by one author, but they can be confirmed against the ratings on the PEDro website; therefore, there is confidence in the quality of the trials and in the included data.

The overall meta-analysis showed that supervised physical activity has a favourable effect on cancer-related fatigue when compared with conventional care. The final analysis of the results revealed that supervised physical activity interventions are effective in the management of cancer-related fatigue for all types of cancer (SMD = –1.69, 95% CI –2.99 to –0.39). The considerable statistical heterogeneity in this meta-analysis (Figure 2) is due to the outlying result of Saarto et al.[36] This trial had the largest sample size (n = 500) and the longest intervention program (48 weeks). Similar beneficial effects have been reported in meta-analyses of the effect of physical activity on depression,[40] fatigue[9,17] and quality of life[41] among cancer survivors. The results of the present study are in line with those published by Fong et al[42] where physical activity, with or without supervision, was positively associated with body composition, physical functioning and psychological outcomes, including fatigue. Nevertheless, there still is insufficient information available to define the physiological mechanism for any potential benefit of exercise in reducing fatigue during cancer therapy or decreasing cancer risk.[43–48]

In contrast to other systematic reviews in this area, the trials included in the present review all analysed participants during an active treatment stage – the most frequent treatment was chemotherapy (n = 1028). Oechsle et al,[49] in a recent prospective randomised pilot trial, found that supervised exercise improved fatigue among 48 participants receiving myeloablative chemotherapy. The exercise was ergometer training and strength exercises for 20 minutes each, five times a week during hospitalisation for chemotherapy. This trial is consistent with the finding of the present systematic review: that supervised physical activity improves fatigue during cancer treatment, especially in people receiving chemotherapy; however, further trials are warranted to strengthen this evidence.

Our subgroup analysis showed that supervised aerobic exercise did not provide significant benefits to cancer-related fatigue (SMD = –2.99, 95% CI –6.49 to 0.51). This finding is inconsistent with recent evidence suggesting that physical activity reduces fatigue in breast cancer survivors,[50] although that study analysed data from unsupervised interventions. Interestingly, our subgroup analysis revealed that combined aerobic and resistance training leads to a significant reduction in fatigue in cancer survivors (SMD = –0.41, 95% CI –0.70 to –0.13). Only one study examined the effects of resistance training alone, although this was also beneficial.[38] The effects of resistance exercise have not been addressed by the American Cancer Society[3] but have been examined recently in people undergoing cancer treatment.[51] However, the present review indicates that more evidence about resistance training alone would be helpful in advising people with cancer who are undergoing cancer therapy whether this type of training is helpful in isolation. To understand the possible mechanisms, more information is required regarding the effects of initial chemotherapy and radiation therapy on muscle satellite (progenitor) cells that are activated to proliferate in response to resistance exercise.[9,51]

A further and interesting finding of the present review was the positive effect of combined aerobic, resistance and stretching exercise with supervision for reducing fatigue in people who have been diagnosed with cancer. The stretching training consisted of slow muscle movements that had neither aerobic nor muscle resistance components.

It is not clear whether previously sedentary people can or will adhere to an exercise program, and, if they cannot, whether the amount of exercise they do engage in will still be of benefit in terms of symptom relief (ie, anxiety, depression, lack of sleep, mood change) and reduction of the risk of adverse events.[52]

The present review had some limitations. Publication bias may have been present, but it was not possible to test for it due to the small number of included studies. Also, heterogeneity was present in most of the meta-analyses. This may be due to the range of sample sizes, the diverse exercise regimens (in terms of length, duration and intensity) evaluated, and the wide variety in outcome measurement tools used in the included studies.

While further research is necessary in order to determine the optimal exercise program for people with cancer, the results of the present review indicate that physiotherapists should conduct careful pre-screening and prescribe appropriate physical activity programs, adjusting for each person's specific variables, such as physiological responses and physical disturbances related to the cancer and its treatment. The findings of the present systematic review reinforce the value of physiotherapy supervision in clinical practice for people with cancer and reinforce the concept that physical activity reduces cancer-related fatigue in this population.

What is already known on this topic: Supervised physical activity improves muscle mass, muscle function and quality of life among people who have been diagnosed with cancer. The optimal exercise program for adults who have been diagnosed with cancer has not yet been established.
What this study adds: In general, supervised physical activity reduces fatigue among people who have been diagnosed with cancer. Specifically, combined aerobic and resistance training with or without stretching are effective exercise regimens for reducing cancer-related fatigue. Supervised resistance exercise alone appears to be beneficial, based on one study. Current evidence does not make it clear whether supervised aerobic exercise alone or supervised stretching alone are beneficial in this population.

eAddenda: Figures 3, 5, 7 and 9 and Appendix 1 can be found online at doi:10.1016/j.jphys.2014.08.019.

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