Physical activity for cancer survivors: meta-analysis of randomised controlled trials


CRD summary
Authors concluded physical activity was associated with clinically important effects on physical function and quality of life. Most data was on breast cancer patients but a similar benefit was found in patients who had different types of cancer. Substantial proportion of low quality studies and potential for non-specific (placebo) effects means the conclusions may not be reliable.

Authors' objectives
To examine the impact of physical activity on adult cancer patient survivors who had completed their main cancer treatment.

Searching
PubMed and CINAHL were searched to September 2011; search terms were reported and no language restrictions were applied. Google Scholar was also searched up to 2011. A manual search of references of included articles, and reviews identified from The Cochrane Library was undertaken.

Study selection
Eligible studies were randomised controlled trials (RCTs) of patients diagnosed with cancer who had completed their primary treatment (those receiving hormonal treatment were not excluded). Each trial was required to include a physical activity intervention and to measure health outcomes.

Mean age was 55 years and ranged from 39.1 to 74 years. Most studies focused on patients with breast cancer (65%), a small number of studies also included only patients with colorectal or endometrial cancer. Approximately a quarter of studies included patients with different types of cancer. Most physical activity interventions were aerobic exercise programmes (63%). Other interventions included both aerobic and resistance/strength training and resistance/strength training based on personal preference. The duration of interventions ranged from three to 60 weeks with most performed between two and five times per week. Control group mainly included no exercise or a sedentary activity.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
Two reviewers independently assessed the quality of included studies with any differences resolved by discussion. The Scottish Intercollegiate Guidelines Network (SIGN) checklist was used. This was based on 10 criteria including items on randomisation, allocation concealment blinding and attrition. An overall judgement was then made concerning the risk of bias: ++ (very unlikely), + (unlikely) and – (likely).

Data extraction
Data were extracted from each study to calculate mean differences (MD) and estimate 95% confidence intervals (CIs).

Two reviewers independently extracted data with any differences resolved through discussion.

Methods of synthesis
Data were pooled using a DerSimonian-Laird random-effects model. For studies with more than one intervention group each comparison with the control group was entered in the meta-analysis as a separate data point. Substantial heterogeneity was identified using \( X^2 \) (p less than 0.1) and \( I^2 \) (50% or greater) statistics.

Sources of heterogeneity were examined using meta-regression for study quality, publication year, percentage of female participants, mean age of participants, number of subjects, duration of intervention, type of physical activity, percentage of patients with breast cancer.

Publication bias was assessed using Egger's test (p less than 0.1 was considered evidence of bias).
Results of the review
Thirty-four RCTs (providing data on 4,108 participants) were included in the meta-analysis. Fifteen trials were judged to contain bias that was likely to impact conclusions. For all other trials any bias identified was judged either unlikely or very unlikely to impact conclusions. No information was reported on the duration of the follow-up period.

Physiological markers
There was a statistically significant reduction in insulin-like growth factor-I (ng/ml) for patients with breast cancer in the physical activity group (MD = -11.9 ng/ml; 95% CI -23.3 to -0.5; four data points from four studies; I²=0%) compared with the control group. No other statistically significant effects were found on other physiological markers.

Body composition: There was a small reduction in BMI (MD = -0.4; 95% CI -0.6 to -0.2; 16 data points from 15 studies; I²=0%) and body weight (MD = -1.1Kg; 95% CI -1.6 to -0.6; 14 data points from 14 studies) for the physical activity group compared with the control group. But no difference was found for waist-to-hip ratio (MD -0.01; 95% CI -0.04 to 0.02; three data points from three studies; I²=0.5%).

Physical function: Physical activity was also associated with benefit for a number of physical function outcomes such as distance walked in six minutes (MD= 29mins; 95% CI 4 to 55.5 data points from 4 studies; I²= 20%) and increased peak oxygen consumption (MD = 2.2ml/Kg/min; 95% CI 1.0 to 3.4; seven data points from seven studies; I²=18%).

Depression: There was a large reduction in depression (Beck Depression Inventory) for the physical activity group but with relatively high heterogeneity (MD-4.1, 95% CI -6.5 to -1.8; four data points from four studies; I² =47%).

Fatigue: There was a statistically significant reduction in fatigue (Piper fatigue scale) for the physical activity group (MD -1.0, 95% CI -1.8 to 0.01; three data points from two studies; I²= 0%).

Quality of life: The physical activity intervention was associated with benefit on mental health (MD 2.4; 95% CI 0.7 to 4.1; two data points from two studies; I²=0%), physical function (MD 3.0, 95% CI 0.7 to 5.3; two data points from two studies; I²=0%) and social function (MD 3.4, 95% CI 0.4 to 6.4; two data points from two studies; I²=0%) on the short form 36 quality of life measure.

Investigating heterogeneity and publication bias
Substantial heterogeneity was identified on physical function for the following outcomes: leg press, left hand grip and right hand grip. Meta-regression analyses suggested high quality studies reported smaller effects on leg press. For left hand and right hand grip, age of patients and year of publication impacted effect estimates. For most other outcomes there was low heterogeneity.

Small study effects/publication bias was identified for the waist-to-hip ratio outcome. For all other outcomes no such bias was found.

Authors’ conclusions
There were clinically important effects on physical function and quality of life for patients with cancer who had completed cancer treatment. Most of the data was for breast cancer patients but similar benefits were found for a broader group of cancer patients.

CRD commentary
The review question and inclusion criteria were clear. An adequate search of relevant sources was undertaken. However unpublished material was not searched for. Study selection, data extraction and quality assessment were carried out with sufficient attempts to minimise error and bias.

Only overall quality assessment ratings were presented for individual studies. Therefore ratings for each individual item (such as blinding) was not provided, nor examined as predictors of effectiveness estimates. The overall results of the quality assessment found almost half of all studies included bias likely to impact conclusions. There was also some evidence that study quality impacted results of the meta-analyses. This raises questions about the reliability of the effect estimates.
Although a number of covariates were examined in the meta-regression there were further potential factors that may have influenced results not included in the analysis, including whether physical activity was supervised, and adherence to the intervention. The meta-analysis included some double counting of studies where a study involved more than one intervention and this doesn't appear to have been taken into account. This could result in an underestimate of variability (such as standard errors and confidence intervals, and therefore on p-values) although this was only the case for three of the 34 included studies. This was more likely to have an impact on outcomes with a relatively small number of trials included in the meta-analysis such as distance walked in six minutes and fatigue. There was no evidence of publication bias except for the waist-to-hip ratio outcome, however since there was no statistically significant benefit found for physical activity interventions on this outcome this was unlikely to have an important impact on the reliability of the findings. A further limitation acknowledged by the authors was that their results related only to short-term benefit.

The substantial proportion of study results which may have been subject to bias or to the impact of non-specific (placebo) effects, means that the authors’ conclusions may not be reliable, particularly for outcomes where there was limited data.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated future research should be conducted on patients with cancers other than breast cancer. In addition, they recommended greater consistency in use of outcome measures and for the intensity of physical activity interventions in future trials.

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