**Exercise intervention in cancer patients undergoing surgery and adjuvant cancer treatment: A systematic review**

L Loughney1-2\*, MA West1-2,4, GJ Kemp2-3, MPW Grocott1-2, S Jack1-2

1Anaesthesia and Critical Care Research Area, NIHR Respiratory Biomedical Research Unit, University Hospital Southampton NHS Foundation Trust, CE93, MP24, Tremona Road, Southampton, SO16 6YD. UK

2Integrative Physiology and Critical Illness Group, Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, CE93, MP24, Tremona Road, Southampton, SO16 6YD. UK

3Department of Musculoskeletal Biology and MRC – Arthritis Research UK Centre for Integrated research into Musculoskeletal Ageing (CIMA), Faculty of Health and Life Sciences, University of Liverpool, Liverpool, UK

4 Academic Unit of Cancer Sciences, Faculty of Medicine, University of Southampton.

\*Corresponding author email: [lisa.loughney@gmail.com](mailto:lisa.loughney@gmail.com) & Lisa.Loughney@uhs.nhs.uk

\*Corresponding author tel/fax: +44 23 81205308

\*Corresponding author address: University Hospital Southampton, CE93 MP24, Tremona Road, Southampton SO16 6YD, UK

**ABSTRACT**

**Background:** Remaining physically active during and after cancer treatment is known to improve associated adverse effects, as well improve overall survival and reduce the probability of relapse. This systematic review focuses on the effect of an exercise training programme in cancer patients undergoing the “multiple hit” of adjuvant cancer treatment and surgery

**Methods:** A systematic database search of Embase, Ovid Medline without Revisions, SPORTDiscus, Web of Science, Cochrane Library and clinical trials.gov for any randomised controlled trials (RCT) or non-randomised controlled trial addressing the effect of an exercise training programme in those scheduled for adjuvant cancer treatment and surgery.

**Results:** The database search yielded 6,489 candidate abstracts of which 94 references included the required terms. A total of 17 articles were included in this review. Exercise training is safe and feasible in the adjuvant setting and furthermore can improve measures of physical fitness and health related quality of life.

**Conclusion:** This is the first systematic review of reports of exercise training interventions in cancer patients undergoing surgery and cancer treatment. Because of the lack of adequately powered RCTs in this area, it remains unclear what is the optimal time to initiate an exercise program and the kind of programme effective in improving clinical outcome measures. Initiating such exercise programmes at cancer diagnosis may have a long lasting effect in remaining physically active throughout the journey cancer patients endure.

**Introduction**

Higher aerobic capacity has been associated with longer cancer-specific survival and lower cancer related mortality [[1](#_ENREF_1)]. Remaining physically active during and after cancer treatment is known to improve associated adverse effects, as well improve overall survival and reduce the probability of relapse [[2](#_ENREF_2)]. Cancer patients are often treated with the “multiple hit” of surgery and a form of cancer treatment, both of which are associated with a decrease in physical fitness[[3](#_ENREF_3), [4](#_ENREF_4)]. The reduction in physical fitness appears to be related to the type of treatment they undergo, higher in those receiving surgery and radiotherapy in combination with chemotherapy compared to those who receive radiotherapy alone or surgery[[5](#_ENREF_5)].

Firstly, surgery has been associated with significant risk of morbidity and mortality as recently identified in the European Surgical Outcome Study[[6](#_ENREF_6)]. Morbidity has great impact on the recovery process post-operatively and is associated with long-term health implications for the patient. Poor physical fitness level following neoadjuvant chemotherapy in upper and lower gastrointestinal cancer has been associated to higher post-operative morbidity and mortality, respectively [[3](#_ENREF_3)] [[4](#_ENREF_4)]. Furthermore, a prolonged post-operative morbidity has been associated with an increased risk of death for up to 3 years after surgery [[7](#_ENREF_7)]. The decrease in physical fitness as a result of cancer treatment may have a lasting effect. In a series of cancer studies, cardiorespiratory fitness was ~30% below that of age-matched sedentary healthy women up to 3 years following completion of adjuvant cancer therapy [11, 12, 16].

The area of exercise oncology has gained great interest over recent years with a number of high quality systematic reviews conducted in this area of interest. In 2011, Granger and colleagues illustrated that it was safe to exercise non-small cell lung cancer (NSCLC) patients during and following cancer treatment [[8](#_ENREF_8)]. In 2014, Crandall and colleagues [[9](#_ENREF_9)] undertook a systematic review specifically investigating exercise interventions in NSCLC patients but in those requiring surgery which illustrated there was a lack of trials which influenced surgical outcome[[9](#_ENREF_9)]. To the best of our knowledge, there are currently no systematic reviews focussing on exercise interventions in cancer patients undergoing the “multiple hit” of surgery and adjuvant cancer treatment.

**Objectives**

The objective of this systematic review is to evaluate methods, safety and feasibility, outcome (both physical fitness and post-operative outcome) and health related quality of life (HRQoL), in studies that have utilised exercise interventions in cancer patients undergoing both surgery and adjuvant cancer treatment.

**Research questions**

i) Is exercise training in surgical cancer patients during cancer therapy safe and feasible? ii) Does it improve a measure of physical fitness (including physical capacity and physical activity)? iii) Does it improve HRQoL?

**Methods**

*Overview of methods and hypotheses*

We conducted a systematic search for all clinical trials that involved cancer patients who underwent surgical intervention and exercise-trained in the adjuvant setting. Abstracts were screened and reviewed against predefined inclusion and exclusion criteria by two independent assessors (LL and MW), and assessed using the Downs and Black quality assessment tool [[10](#_ENREF_10)]. Data was extracted by one investigator in accordance with predefined criteria.

The primary hypothesis was: exercise training in cancer patients undergoing both surgery and adjuvant cancer treatment is safe and feasible.

The secondary hypotheses were: exercise training in this patient cohort improves some measure of physical fitness (including physical capacity and physical activity), and quality of life.

Other exploratory outcomes included defining the structure of the exercise training programme, adherence and behaviour towards exercise and other clinically relevant outcomes such as fatigue.

*Search strategy*

Searches were performed on Embase, Ovid Medline without Revisions, SPORTDiscus, Web of Science, Cochrane Library database and clinical trials.gov using search terms defined by the reviewers. A comprehensive, systematic search was performed on 23 May 2013 and two further updated searches were performed on 1 October 2014 and 1 December 2014. Relevant keywords were categorised under five distinct headings: (i) cancer, (ii) cancer treatment, (iii) exercise, (iv) surgery and (v) outcome. (See Figure 1 for illustration of all search terms). First, each category was searched separately in the database. A combined search of all the categories was completed and duplicate results were removed. A manual title search of references from the previous review articles on exercise and cancer was also conducted. Data was extracted in accordance with predefined criteria.

*Inclusion and exclusion criteria*

Study design

The inclusion criteria were broad: RCTs and non-RCTs investigating exercise training in cancer patients undergoing surgery and adjuvant cancer treatment. Published abstracts, case reports and theses were excluded.

Participants

Studies recruited human adult (>18 years) cancer patients undergoing an exercise intervention receiving adjuvant cancer treatment following surgery were included.

Studies that recruited: cancer survivors (defined as cancer patients who completed all forms of cancer treatment); cancer patients receiving palliative treatment; patients with inoperable cancer; cancer patients undergoing an exercise programme during neoadjuvant cancer treatment, cancer patients undergoing an exercise programme following adjuvant treatment; and cancer patients receiving androgen therapy were excluded.

Exercise intervention

Interventions that consisted of any exercise intervention during cancer treatment before or after surgery were included. This also included interventions done alone or in combination: 1) aerobic training (defined as exercise that involves large muscle groups performing continuous or intermittent activity over an extended period of time) [[11](#_ENREF_11)]; 2) prescribed resistance training (defined as exercise that involves performing sets of repeated movements against a resistance during which neuromuscular fatigue occurs within 6-12 repetitions [[12](#_ENREF_12)]); 3) pelvic floor muscle exercise training; 4) pectoral exercise training; and 5) stretching programme.

Data extraction and analysis

All studies that met the inclusion criteria were independently assessed for descriptive characteristics such as participant characteristics, study design, types of cancer, length of study (intervention and follow-up times) and primary outcomes by different types of cancers. Descriptive data was extracted about the individual exercise programmes, including the frequency, intensity, time, type, supervision, location and adherence of the exercise sessions.

Assessment of methodological quality

Two reviewers (LL and MW) independently assessed the methodological quality of each study according to the Downs and Black quality appraisal checklist [[10](#_ENREF_10)]. This checklist consists of 27 questions to evaluate both randomised and non-randomised studies, evaluate study reports, internal validity and external validity. Each question was scored out of 1, except question 5 which was scored out of 2 and question 27 which was scored out of 5, giving a total score of 33. High scores reflect high-quality studies. All discrepancies were resolved by discussion between all authors (see appendix 1)

**Results**

*Database search*

The database search strategy which included exercise interventions in cancer patients undergoing both surgery and adjuvant treatment is shown in figure 1. This search yielded 6489 candidate abstracts. After review of the candidate abstracts by two independent reviewers (LL and MW), 94 references included the required terms, of which 72 references were excluded as they did not meet all inclusion criteria. 22 references were extracted for full text review, of which 7 references were included. A manual search through all the references from full text papers identified for inclusion resulted in an additional 17 full text papers extracted for review of which, 5 references were eligible for inclusion. A further database search was done from references on all published exercise and cancer related systematic reviews, which identified no further eligible articles for inclusion. 5 additional references were identified for inclusion following the most recent updated searches. After full text screening and application of all inclusion criteria, 17 articles were included in this review. Meta-analyses were not performed due to the clinical and statistical heterogeneity of the included studies.

Figure 1. **Search conducted for this systematic review**

*Study characteristics*

The characteristics of the studies are presented in Table 1. Of the 17 full text articles, 13 were reported as an RCT [[5](#_ENREF_5), [13-24](#_ENREF_13)] (note that all studies by Courneya and colleagues [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17)] are the results from one exercise training trial, the START trial) of which some are a pilot, 1 was a prospective single group design [[25](#_ENREF_25)] and 2 single group pilot study [[26](#_ENREF_26), [27](#_ENREF_27)]. Of these only 4 studies include >200 patients [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17), [22](#_ENREF_22)] and 3 studies 100-200 patients or more [[19](#_ENREF_19), [21](#_ENREF_21), [24](#_ENREF_24)]; the remaining 9 studies have 7-67 patients [[5](#_ENREF_5), [15](#_ENREF_15), [18](#_ENREF_18), [20](#_ENREF_20), [23](#_ENREF_23), [25-29](#_ENREF_25)]. All except 3 studies [[25-27](#_ENREF_25)] included a control group. 6 of the 17 studies were published within the last 5 years. The mean patient age ranged from 47 to 70 years.

*Study aims*

The study aims were very dependent on the type of cancer, especially in breast cancer studies where aims varied widely assessing the effects of an exercise intervention on; feasibility, tolerability, safety and exercise tolerance, cancer related fatigue (CRF), physical fitness and physical activity levels [[15](#_ENREF_15), [20](#_ENREF_20), [23-26](#_ENREF_23), [29](#_ENREF_29)] and other measures such as sleep disturbance, mood disturbance and symptom distress [[29](#_ENREF_29)]. Jones and colleagues [[25](#_ENREF_25)] aimed to assess feasibility of an exercise intervention in patients with NSCLC during adjuvant cancer treatment. Others investigated the effect of an exercise programme on HRQoL [[17](#_ENREF_17), [28](#_ENREF_28)], on muscular strength and fatigue with emphasis on resistance training [[18](#_ENREF_18)] and factors/moderators predicting exercise training response [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17)]. A study involving 21 different cancers aimed to decrease fatigue and improve general well-being [[22](#_ENREF_22)] whilst Hoffman and colleagues [[27](#_ENREF_27)] aimed to determine the effects of an exercise programme on CRF, other symptoms, functional status and HRQoL in NSCLC post-surgical intervention.

*Quality assessment*

The quality of each study was evaluated by using a checklist designed to assess randomized and non-randomized trials [[10](#_ENREF_10)]. Quality assessments are reported in Supplementary Appendix 1. The median methodological quality score for the included studies was x out of x. The X scored highest for methodological quality, X out of x. The smaller studies scored lowest for methodological quality. The external validity and statistical power sections of the checklist scored poorly across the studies.

*Participants*

The only mixed gender studies were Adamsen [[22](#_ENREF_22)], Jones [[25](#_ENREF_25)] and Hoffman[[27](#_ENREF_27)] and colleagues. All other studies involved breast cancer patients, including only females, with one study only including postmenopausal females.

*Type of cancer and cancer treatment*

The included studies involved patients with a variety of different cancer types undertaking an exercise intervention during adjuvant cancer treatment. Of the 17 studies included, 14 were of breast cancer [[5](#_ENREF_5), [14-21](#_ENREF_14), [23](#_ENREF_23), [24](#_ENREF_24), [26](#_ENREF_26), [28](#_ENREF_28), [29](#_ENREF_29)]), 2 of NSCLC [[25](#_ENREF_25), [27](#_ENREF_27)] and 1 study included 21 different cancer types which also included 4 malignant haematological diseases [[22](#_ENREF_22)].

*Exercise intervention Characteristics and Outcomes*

Exercise intervention characteristics are summarised in Table 1

Exercise Intervention

The breast cancer studies mainly included aerobic and resistance exercise/muscle strengthening training programmes [[5](#_ENREF_5), [14](#_ENREF_14), [17](#_ENREF_17), [20](#_ENREF_20), [23](#_ENREF_23), [25](#_ENREF_25), [26](#_ENREF_26), [29](#_ENREF_29)], 1 of a pectoral muscle stretching exercise programme [[13](#_ENREF_13)] and 1 of a progressive resistance training programme [[24](#_ENREF_24)]. Other studies incorporated a variety of exercises into their training protocols; cardiovascular, resistance and flexibility training [[18](#_ENREF_18)], walking, cycling, low-level aerobics, muscle-strengthening exercises and circuits [[15](#_ENREF_15), [18](#_ENREF_18)]. The study involving 21 different cancer types implemented a high and low intensity exercise programme involving aerobic and resistance exercises, relaxation and body awareness followed by a massage [[22](#_ENREF_22)]. One NSCLC study implemented a walking and balancing exercise programme utilising the Nintendo Wii Fit plus [[27](#_ENREF_27)].

Exercise Intervention Adherence

Adherence rates were reasonably high amongst studies included in this review. Among home-based exercise programmes, the stretching programme reported 90% and 72%[[19](#_ENREF_19)] adherence over 6 weeks [[13](#_ENREF_13)] whilst Husebo and colleagues [[23](#_ENREF_23)] reported an adherence rate of 17% and 15% to their walking programme and strength training programme, respectively. One breast cancer study reported an acceptable adherence as the weekly average steps walked as recorded by a pedometer (mean increase in steps of 5920 from baseline to 12-week post-intervention)[[29](#_ENREF_29)]. Supervised exercise training varied in adherence: 70.8%[[22](#_ENREF_22)] adherence over 6 weeks, 70% over 12 weeks [[15](#_ENREF_15)], 85% over 14 weeks [[25](#_ENREF_25)], 78% for 16 weeks [[26](#_ENREF_26)], 91% over 18-22 weeks [[5](#_ENREF_5)] and 71.5% over 26 weeks[[21](#_ENREF_21)]. Courneya and colleagues [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17)] reported similar adherence rates when comparing aerobic and resistance exercise training. Adherence rates in NSCLC patients undergoing chemotherapy at the time of the training programme were reported at 93% and 72% in those patients not receiving chemotherapy [[25](#_ENREF_25)]. Three studies did not report adherence rates [[18](#_ENREF_18), [20](#_ENREF_20), [27](#_ENREF_27)].

Exercise Intervention Frequency

Frequency of exercise training varied from daily sessions to 2 or 3 sessions per week. Some studies prescribed frequency of exercise differently; one study [[23](#_ENREF_23)] reported frequency of exercise training as a mean of 168 minutes of physical activity per week whilst another study prescribed exercise at home 5-6 times per week (6 weeks in the patients receiving radiotherapy or 3-6 months in patients receiving chemotherapy) [[19](#_ENREF_19)]. The home-based pectoral muscle strengthening programme was twice daily [[13](#_ENREF_13)]. Some reports were unclear regarding exercise frequency; one group reported 18-22 weeks [[5](#_ENREF_5)]. One study asked participants establish the correct intensity to train at; low-intensity to moderate-intensity exercise[[29](#_ENREF_29)]. The length of time the training programme varied widely from 6 to 26 weeks, as follows: 6 weeks [[20](#_ENREF_20), [22](#_ENREF_22), [27](#_ENREF_27), [28](#_ENREF_28)], 12 weeks [[15](#_ENREF_15), [24](#_ENREF_24), [29](#_ENREF_29)], 14 weeks[[25](#_ENREF_25)], 16 weeks, [[18](#_ENREF_18), [26](#_ENREF_26), [30](#_ENREF_30)], 17 weeks (median) [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17)], 17 weeks (average)[[23](#_ENREF_23)]and 26 weeks [[21](#_ENREF_21)]. Of note, Battaglini and colleagues [[18](#_ENREF_18)] exercise trained patients for a 3-week period prior to beginning cancer treatment and continued the exercise training during the cancer treatment.

Exercise Intervention Intensity

The *intensity of aerobic exercise training* was tailored to heart rate (HR), oxygen uptake at lactate threshold (o2 at L) and/or oxygen uptake at peak exercise (o2peak), or to workload based on individual exercise testing. Intensities varied amongst the home-based walking exercise programmes; 50-60% o2peak and 50-70% maximum heart rate (MHR) [[19-21](#_ENREF_19), [25](#_ENREF_25)] whilst one study [[23](#_ENREF_23)] instructed participants to categorise the walking intensity into four different intensity levels; light, moderate, vigorous and very vigorous and to log intensities in their exercise diary. Naraphrong and colleagues[[29](#_ENREF_29)] asked participants to establish an intensity to exercise train at; low-intensity to moderate-intensity exercise as measured by Borg scale (score 12-14) [[29](#_ENREF_29)]. In addition, participants were also asked to choose activities that involved walking on their own that required low to moderate intensity levels (<3-6 METs)[[29](#_ENREF_29)]. The aerobic supervised sessions were mainly moderate to high intensity: 40-60% maximum exercise capacity [[18](#_ENREF_18)] or 60-70/75% MHR [[5](#_ENREF_5), [14-17](#_ENREF_14)]; some entailed progressive training programmes [[17](#_ENREF_17), [25](#_ENREF_25), [26](#_ENREF_26)]. The circuits-based aerobics exercise programme used a low-level intensity. The pectoral stretching programme involved a low load intensity [[13](#_ENREF_13)]. One study implemented a multimodal high and low intensity exercise intervention which matched an average intensity of 9 metabolic equivalent of task (MET) (4.5 MET hours per training session) [[22](#_ENREF_22)]. The exercise programme for NSCLC patients initiated a progressive training programme beginning at 60% of peak workload achieved at baseline exercise test for weeks 1 and 2, 65% of peak workload for weeks 2 to 4, 60-65% for weeks 5 and 6 followed by a mixture of training intensities from week 7 onwards [[25](#_ENREF_25)]. In the post-surgical NSCLC patients, light intensity (less than 3.0 metabolic equivalents) was initiated 66 hours (on average) post-hospital discharge [[27](#_ENREF_27)].



The aerobic supervised sessions were mainly moderate to high intensity: 40-60% maximum exercise capacity [[18](#_ENREF_18)] or 60-70/75% MHR [[5](#_ENREF_5), [14-17](#_ENREF_14)]; some entailed progressive training programmes [[17](#_ENREF_17), [25](#_ENREF_25), [26](#_ENREF_26)]. The circuits-based aerobics exercise program used a low-level intensity. The pectoral stretching programme involved a low load intensity [[13](#_ENREF_13)]. One study implemented a multimodal high and low intensity exercise intervention which matched an average intensity of 9 metabolic equivalent of task (MET) (4.5 MET hours per training session) [[22](#_ENREF_22)]. The exercise programme for NSCLC patients initiated a progressive training programme beginning at 60% of peak workload achieved at baseline exercise test for weeks 1 and 2, 65% of peak workload for weeks 2 to 4, 60-65% for weeks 5 and 6 followed by a mixture of training intensities from week 7 onwards [[25](#_ENREF_25)]. In the post-surgical NSCLC patients, light intensity (less than 3.0 metabolic equivalents) was initiated 66 hours (on average) post-hospital discharge [[27](#_ENREF_27)].

The *intensity of resistance exercise training programmes* was mainly based on 1 repetition maximum (RPM) test was used to measure the maximum weight a patient can lift once on a specific machine. Intensities were reported as 40-60% of maximum exercise capacity [[18](#_ENREF_18)] or 60-70% [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17)] and 60-80%[[24](#_ENREF_24)] of estimated 1RPM. A progressive approach was also utilised aiming to accomplish three continuous series of 5-8 repetitions at 70-100% of the 1RPM test over the exercise training period [[22](#_ENREF_22)]. To ensure progression, all patients performed 1RPM test every other week with subsequent adjustments made to their training programmes; this was estimated to have an intensity of 5.5 METS (4 MET hours per training session). One study followed the American College of Sports Medicine (ACSM) progression model, increasing the set and repetitions over the exercise intervention training period [[18](#_ENREF_18)]. The breast cancer home based programme [[23](#_ENREF_23)] prescribed exercise with resistance bands for arms and legs and strength training for the upper body however no intensity level was reported.

Exercise Intervention Time

The structured aerobic sessions ranged from 15 to 60 minutes per session. Progressive walking programmes based at home began from 15 minute brisk walk increasing to 30-45 minutes [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17), [19](#_ENREF_19)]. NSCLC patients exercised for 15-30 minutes [[25](#_ENREF_25)] and 5-30 minutes [[27](#_ENREF_27)]. One study divided up the exercise programme to include high intensity for 90 minutes followed by 30 minutes relaxation training, 3 days per week [28]. One supervised study reported that the exercise specialist led a 7-10 minute warm-up and a standardised cool down but they did not report the time allocated for each session [[21](#_ENREF_21)]. The home based walking programme [[23](#_ENREF_23)] offered participants the opportunity to divide up the 30 minutes of exercise into bouts of 10-minute walks throughout the day.

Exercise Intervention Type

Aerobic exercise training was mainly undertaken on a cycle ergometer. Some studies used a mixture of modalities; cycle ergometer, treadmill or elliptical equipment [[14](#_ENREF_14), [16-18](#_ENREF_16)], or a combination of walking, cycling, step and dance movements and other aerobic activities [[26](#_ENREF_26)]. Walking exercise programmes were tailored to supervised treadmill exercise or home-based [[19](#_ENREF_19), [21](#_ENREF_21), [27](#_ENREF_27)]. Resistance exercise training was undertaken with resistance bands/dumbbells and resistance machines[[22](#_ENREF_22)]. The circuit class used a combination of both [[15](#_ENREF_15)]. Two studies additionally included muscle strengthening and upper extremity exercises to their program, however the mode was not specifically reported [[5](#_ENREF_5)].

Exercise Intervention Supervision

Supervised exercise training was undertaken either in hospital or in an exercise suite with a physical therapist/exercise physiologist [[5](#_ENREF_5)] [[14-18](#_ENREF_14), [20](#_ENREF_20), [22](#_ENREF_22), [24-26](#_ENREF_24)]. The breast cancer studies utilised a combination of supervised and home-based exercise programmes. Other studies were home-based, incorporating a pectoral stretching programme and a walking exercise programme [[13](#_ENREF_13), [19](#_ENREF_19)], a walking and balancing programme [[27](#_ENREF_27)] and a walking programme with strength exercises[[23](#_ENREF_23)]. Segal and colleagues [[21](#_ENREF_21)] compared self-directed exercises at home to supervised exercise. For the home-based pectoral stretching programme, participants were seen by a physical therapist at their weekly oncology appointment [[31](#_ENREF_31)]. Mock and colleagues [[19](#_ENREF_19)] asked participants to keep a diary monitoring exercise sessions reporting heart rate, perceived exertion rates and fatigue levels. They also provided a detailed booklet and a video to ensure standardisation across subjects and across the eight clinical sites [[19](#_ENREF_19)]. Both home-based exercise programmes provided participants with leaflets on exercise instructions to continue at home [[19](#_ENREF_19), [21](#_ENREF_21)]. Husebo and colleagues [[23](#_ENREF_23)] supported their participants with motivational telephone calls every second week. Furthermore, exercise volume was reported daily from both the exercise and control group in exercise diaries. They also conducted weekly phone calls throughout the 12-week exercise programme to monitor exercise participation and to make adjustments to participants walking prescription for the next week as needed [[29](#_ENREF_29)]. Both Mock and Segal and colleagues [[19](#_ENREF_19), [21](#_ENREF_21)] asked participants to send their diaries back every week and researchers contacted participants every 2 weeks to evaluate prescription and progress. In the NSCLC patients home-based programme, on average 66 hours post-hospital discharge, a nurse conducted a home visit on the first session and beginning week 2 of the 6-week programme, followed by a phone call at 24 hours post the first visit and additional calls at the start of week 3 and 6 of the exercise programme [[27](#_ENREF_27)].

Inclusion of a Control Group

Thirteen RCT studies included a control group [[5](#_ENREF_5), [13-21](#_ENREF_13), [32](#_ENREF_32)]. Four studies did not include a control group [[25-27](#_ENREF_25)].

The usual-care groups received general advice from their oncologists on the benefits of exercise before the beginning adjuvant treatment [[13](#_ENREF_13), [19](#_ENREF_19), [21](#_ENREF_21), [29](#_ENREF_29)]. One study requested that the usual care group in their RCT keep physical activity diaries, and they underwent a telephone consultation by the researchers every 1-2 weeks in a similar way to the exercise group [[19](#_ENREF_19), [23](#_ENREF_23)]. Schmidt and colleagues[[24](#_ENREF_24)] perscribed a progressive muscle relaxation programme to their control group. Other studies offered an exercise programme/advice to the control group following the completion of the study [[32](#_ENREF_32)] [[14-17](#_ENREF_14)]. One study telephoned the control groups on a bi-weekly basis[[29](#_ENREF_29)].

*Exercise intervention Outcomes*

Safety and Tolerability

Kolden, Jones and Naraphong and colleagues [[25](#_ENREF_25), [26](#_ENREF_26), [29](#_ENREF_29)] assessed feasibility, tolerability, safety and benefits of an exercise programme during adjuvant cancer treatment. All were reported as pilot studies.

Physical Fitness Outcomes

A measure of physical fitness was used as a primary outcome in only 4 breast cancer studies [[5](#_ENREF_5), [20](#_ENREF_20), [21](#_ENREF_21), [26](#_ENREF_26)]. One studies used CPET to measure their primary outcome; o2peak [[25](#_ENREF_25)]. One study measured range of movement as their primary outcome [[13](#_ENREF_13)]. A measure of physical fitness was used as a secondary outcome in majority of the studies: physical functioning (6 minute shuttle walk test[[23](#_ENREF_23)], 12 minute walking test[[15](#_ENREF_15), [29](#_ENREF_29)]; aerobic capacity (o2peak/max exercise or Bruce treadmill protocol [[18](#_ENREF_18)]); muscular strength (1 RPM test [[5](#_ENREF_5), [14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17), [32](#_ENREF_32)] or estimated sub-maximum bench press and leg press [[26](#_ENREF_26)]); maximum capacity for muscular strength [[18](#_ENREF_18)]; passive range of movement shoulder rotation [[13](#_ENREF_13)]; and others such as cardiopulmonary fitness endpoints (peak workload, ventilatory threshold, O2 pulse [[25](#_ENREF_25)]), flexibility (sit and reach test [[26](#_ENREF_26)]), and lean body mass and percent body fat/body weight [[16](#_ENREF_16), [17](#_ENREF_17)].

Only one study reported improvements in o2peak, as their primary endpoint, results did not reach statistical significance [[25](#_ENREF_25)]. The moderate intensity aerobic training during adjuvant radiotherapy was suggested that it may preserve or maintain exercise tolerance as measured by 6MWD, although this did not reach statistical significance [[20](#_ENREF_20)]. Two studies reported a significant increase in o2peak as their secondary outcome [[26](#_ENREF_26), [32](#_ENREF_32)]. Courneya and colleagues [[17](#_ENREF_17)] reported a statistical significant improvement in o2peak in the aerobic exercise training group but not in the resistance exercise training group or the usual care group. One home-based exercise programme illustrated a significant improvement in physical fitness as measured by 12-MWT[[29](#_ENREF_29)]. The pectoral stretching programme reported no statistical differences at the 7 month follow-up [[13](#_ENREF_13)]. Other studies illustrated improvements in a measure of physical fitness following the exercise programme although they report insignificant findings [[18](#_ENREF_18), [21](#_ENREF_21)] [[13](#_ENREF_13)].

Functional capacity and physical activity levels were primary outcomes for 2 breast cancer studies. Functional capacity was assessed as Karnofsky performance status [[5](#_ENREF_5)]. Physical functioning and activity levels were secondary outcome in several studies measured by 12 minute walk test (MWT) [[19](#_ENREF_19)], the Short Form (36) Health Survey (SF-36) [[15](#_ENREF_15), [19](#_ENREF_19), [27](#_ENREF_27)], physical activity questionnaire (PAQ) [[19](#_ENREF_19)], Scottish physical activity questionnaire (SPAQ) [[15](#_ENREF_15)],leisure time physical activity [[32](#_ENREF_32)] and International Physical Activity Questionnaire [[23](#_ENREF_23)]. One breast cancer study reported a slight worsening in Karnofsky performance status in both groups following chemotherapy, although insignificant [[5](#_ENREF_5)]. Furthermore, there was a significant decrease in physical functioning in women with high fatigue levels during breast cancer therapy [[19](#_ENREF_19)]. The small pilot study initiated 66 hours post-hospital discharge (on average) presented the following physical functional status; a decrease from 49.8 to 31.5 followed by an increase to 41.4 at pre- and post-surgery, and post 6-week exercise programme, respectively[[27](#_ENREF_27)]. Following the exercise intervention, three studies reported increased physical activity levels, although insignificant [[15](#_ENREF_15), [23](#_ENREF_23), [32](#_ENREF_32)].

Health Related Quality of life (HRQoL) Outcome

HRQoL, as the primary outcome, was measured by functional assessment of cancer therapy-anaemia (FACT-An scale) [[16](#_ENREF_16), [17](#_ENREF_17)] or physical functioning (SF-36) [[21](#_ENREF_21)]. HRQoL was used in almost all studies as a secondary outcome measure. This was assessed by changes in questionnaires such as SF-36 [[15](#_ENREF_15), [21](#_ENREF_21)], FACT-General [[15](#_ENREF_15), [21](#_ENREF_21)], FACT-Breast [[15](#_ENREF_15), [21](#_ENREF_21)], FACT functional subgroup [[26](#_ENREF_26)], FACT-Lung, Satisfaction with Life Scale (SWLS) [[15](#_ENREF_15)], fatigue and QoL subscales [[25](#_ENREF_25)], psychosocial functioning; Rosenberg Self-esteem scale, Centre for Epidemiological Studies Depression scale (CESD), Spielberger State-Trait Anxiety Inventory (STAI) [[17](#_ENREF_17)], the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [[5](#_ENREF_5), [32](#_ENREF_32)] and Ferrans and Powers Quality of Life Index (QLI) (assessing satisfaction and important aspects of life to the person) [[27](#_ENREF_27)]. General well-being was further assessed by Medical Outcomes Study Short Form (MOS SF-36) [[5](#_ENREF_5), [13](#_ENREF_13), [32](#_ENREF_32)], mood/distress; Beck Depression Inventory (BDI), STAI, Positive and Negative Affect Schedule (PANAS), Hamilton Rating Scale for Depression (HRSD), functioning; Cancer Rehabilitation Evaluation System (CARES), Global Assessment Scale (GAS) and the Life Functioning Scales (LFS) [[26](#_ENREF_26)].

Exercise training significantly improved different domains of HRQoL following circuit classes over a 12-week period [[15](#_ENREF_15)], a 16-week period [[26](#_ENREF_26)] and aerobic/resistance exercise program over a 17-week period [[16](#_ENREF_16)]. Following the START trial significant improvements in some HRQoL domains were reported, but no significant improvement in cancer-specific HRQoL (fatigue, depression or anxiety) [[16](#_ENREF_16)]. Following the multi-modal high intensity exercise programme, there was a mixture of HRQoL responses reported [[32](#_ENREF_32)]. There was a decrease in HRQol between pre- and post-surgery and an increase following the 6-week exercise program with the best results obtained at week-3 in the small NSCLC pilot study. However, 5 out of the 7 participants in this trial initiated chemotherapy at week 5 which may account for the slight decrease from week 3 to week 6 [[27](#_ENREF_27)]. There was no statistically significant differences in HRQoL reported following the pectoral training programme, self-directed versus supervised walking intervention or progressive resistance training programme [[13](#_ENREF_13), [21](#_ENREF_21), [24](#_ENREF_24)].

Fatigue and other Symptoms

Fatigue, as a primary outcome, was measured by total score of Piper Fatigue Scale (PFS) [[18](#_ENREF_18), [19](#_ENREF_19)], Schwartz Cancer Fatigue Scale-6[[23](#_ENREF_23)], Brief Fatigue Inventory (BFI) [[27](#_ENREF_27)] and Fatigue Assessment Questionnaire[[24](#_ENREF_24)]. Adamsen and colleagues [[32](#_ENREF_32)] reported that 65% of study population had a fatigue level greater than that of general population (mean >20) at baseline and that 29% reported severe fatigue (mean >60) as measured using EORTC QLQ-C30. Furthermore, they also report that 18% of the participants had a sedentary lifestyle at baseline and suggested that the fatigue may be primarily due to cancer or the chemotherapy. Schmidt and colleagues [[24](#_ENREF_24)] illustrated a change in fatigue levels from baseline to post intervention however the results did not reach statistical significance. Husebo and colleagues [[23](#_ENREF_23)]reported a statistical significant finding in fatigue levels 6 months following completing the exercise programme, initiated during cancer treatment, as measured using Schwartz Cancer Fatigue Scale-6. Fatigue as a secondary outcome was also measured by Revised Piper Fatigue Scale (PFS) [[15](#_ENREF_15), [29](#_ENREF_29)]. Symptom severity and interference was assessed using M.D. Anderson Symptom Inventory Core and Lung Module (MDASI) [[27](#_ENREF_27)]. Battaglini and colleagues reported significant improvements in PFS scores following exercise training [[18](#_ENREF_18)], compared to the control group. Moderate intensity home-based walking intervention was found to be effective in managing fatigue levels during both radiotherapy and chemotherapy [[19](#_ENREF_19)]. Moros and Campbell and colleagues [[5](#_ENREF_5), [15](#_ENREF_15)] reported no statistically significant changes following an aerobic exercise program. Hoffman and colleagues [[27](#_ENREF_27)] monitored CRF and symptom severity from pre-surgery to week-6 of their exercise programme, finding that on average participants experienced 7 symptoms pre-surgery, 10 symptoms post-surgery and 6 symptoms at week 6. In this study CRF increased from 3.5 to 4.8 pre- to post-surgery and decrease to 2.8 at week 6, with other symptom severity and interference results showing a similar trend (5 out of 7 participants commenced chemotherapy at week 5). Naraphong and colleagues demonstrated an improvement in CRF from baseline to the 10-week follow up although they reported insignificant findings[[29](#_ENREF_29)].

Naraphong and colleagues[[29](#_ENREF_29)] also assessed sleep disturbance (General Sleep Disturbance) and mood disturbance (Profile of Mood States-Brief Form). Although participants in the exercise group did demonstrate improvements in mood and symptom distress, results did not reach statistical significance.

Schmidt and colleagues[[24](#_ENREF_24)] assessed depression (20-item Center for Epidemiological Studies Depression scale) and cognitive function (concentration, cognitive flexibility). There was no statistical significance in either measure with no difference illustrated in depression in either control or exercise group however cognitive performance did improve in the exercise group only.

Behaviour

Only Courneya and colleagues [[14](#_ENREF_14)] investigated predictors of follow-up exercise behaviour 6 months following a RCT exercise trial as a primary outcome, finding a number of significant predictors such as; demographics, medical, fitness, psycho-social and motivational variables. Moreover, 58% of breast cancer survivors reported meeting at least one exercise guideline and 21% of those reported meeting both following the START trial. At baseline, only 23% were meeting either exercise guideline and only 5% of those were meeting both. The strongest predictor of those exercising at 6-month follow-up in their trial was pre-trial exercise levels. Additionally, other variables that predict the likelihood of meeting exercise guidelines at follow up included younger age, breast conserving surgery, strength improvements, lower post-intervention fatigue, a more positive attitude and lower post intervention BMI.

Table 1. Summary of exercise interventions

| Author,  year, (Country) | Study design | n | Cancer type,  Cancer treatment | Exercise Program | Supervision,  Location | Frequency | Intensity | Duration | Adherence | Outcome measure |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Segal et al[**[**21**](#_ENREF_21)**], 2001,** (Canada) | RCT | 123 | Breast,  Adjuvant chemo/other adjuvant therapies | Walking | Supervised &  home based | Home; 5times/week  x 26 weeks.  In-hospital; 3times x 26weeks | 50-60% VO2Peak | NR | 71.5% | \*Physical functioning  (in UC) |
| **Kolden et al**[[26](#_ENREF_26)]**, 2002**  (USA) | Pilot study | 40 | Breast cancer,  Adjuvant radiotherapy | Aerobic/  Resistance/ stretching | Supervised | 3times/week  x 16 weeks | Prog:  40-70% VO2Max | 60min | 78.4% | \*Fitness & Qol |
| **Campbell et al**[[15](#_ENREF_15)]**, 2005**  (UK) | Pilot  RCT | 22 | Breast,  Adjuvant radiotherapy/  chemotherapy | Circuit aerobics | Supervised | 2times/week  x 12 weeks | 60-75% MHR | NR | 70% | \* Qol measure (in EG) |
| **Mock et al**[[19](#_ENREF_19)]**, 2005**  (USA) | RCT | 119 | Breast  Adjuvant Radiotherapy | Walking | Home-based Unsupervised | 5-6times /week  x 6-weeks during RET or  3-6months | 50-70% MHR | 15-30  min | EG: 72% UG: 61% | Fatigue & physical functioning |
| **Battaglini et al**[[18](#_ENREF_18)]**, 2006**  (USA) | RCT | 20 | Breast  Adjuvant Chemo, radiation or both | CV/  Resistance/  flexibility | Supervised | 2times/week  x 16 weeks | 40-60% max exercise capacity | 60min | NR | \*Muscular strength, fatigue |
| **Courneya et al**[[17](#_ENREF_17)]**, 2007,** (Canada) | RCT | 242 | Breast  Adjuvant chemotherapy | Aerobic/ Resistance(RET) | Supervised  In-hospital | Duration of chemo | Prog:  60-80%  VO2Peak/1RM | 15-45min | 70.2% | ↑ QoL measure,  \*↑ chemo completion rate in RET |
| **Lee et al**[[13](#_ENREF_13)]**, 2007,** (Australia) | Single- blind RCT | 61 | Breast,  Adjuvant Radiotherapy | Pectoral muscle stretching program | Unsupervised  Home based | 2times/day  X 7days  x 6 weeks | NR | 10min | 90% | Range of motion |
| **Courneya et al**[[16](#_ENREF_16)]**, 2008,** (Canada) | RCT | 242 | Breast,  Adjuvant chemotherapy | Aerobic (A)/ Resistance (R) (#) | Supervised  In-hospital | 3 times/week x 17 weeks | 60-80% VO2Peak/ 60-70% 1RM | 15- 45 min | A; 72%  R; 68.2% | Measure of QoL |
| **Jones et al**[[25](#_ENREF_25)]**, 2008,** (Canada) | Pros. single group | 20 | Lung,  Adjuvant chemo © and some received no chemo (NC) | Cycle | Supervised: short term | 3 times/week  x14 weeks | Prog:  60-70% WRpeak | 15-45 min | ©93% and 72%, NC;85% | Feasible,  \*↑Qol and select CP (in NC only) |
| **Adamsen et al**[[32](#_ENREF_32)]**, 2009,**  (Denmark) | RCT | 269 | 21 different cancers,  59 different chemotherapy regiments | Resistance, relaxation, body awareness and massage | Supervised  In-hospital | 9hours/week x 6weeks | Low & high intensity | 90min | 70.8% | \*Fatigue,  Variety of QoL measures,  Other QoL measures |
| **Courneya et al**[[14](#_ENREF_14)] **2009,** (Canada) | Pros. RCT | 242 | Breast,  Adjuvant chemotherapy | Aerobic (A)/  Resistance (R ) | Supervised  In-hospital | 3 times/week x 17weeks | 60-80%  VO2Peak/ 60-70% IRM | 60min | A;72%  R;68.2% | Measure of exercise patterns |
| **Moros et al**[[5](#_ENREF_5)]**, 2010,** (Spain) | RCT | 22 | Breast,  Adjuvant chemotherapy | Aerobic / resistance | Supervised  In-hospital | 3 times week  x 18-22-weeks | 60-70% HR | 60min | 91% | Functional capacity,  \*QoL |
| **Milecki et al[**[**20**](#_ENREF_20)**], 2013**  (Poland) | RCT | 66 | Breast cancer,  Adjuvant radiotherapy | Aerobic  Endurance, Respiratory muscle training | Supervised,  In-Hospital | 5times / week x 6 weeks | 65-70% MHR | 40-45  min | NR | 6MWD |
| **Hoffman et al[**[**27**](#_ENREF_27)**], 2014**  (USA) | Pilot | 7 | NSCLC,  Chemotherapy (initiated week 5 in 5/7 patients) | Walking and balancing program  (Nintendo Wii Fit Plus) | Home based | 5times/week  X 6weeks | Prog:  5-30min | Light intensity | NR | CRF, other symptoms, functional status, QoL |
| **Schmidt et al[**[**24**](#_ENREF_24)**],**  **2014**  **Germany** | Prop. RCT | 101 | Breast cancer,  Adjuvant chemotherapy | Resistance exercise training | Supervised,  ? | 2/week x 12 weeks | 60-80% IRM | 60 min | 71% | Fatigue, QoL, depression, cognitive function, effect modification |
| **Naraphong et al[**[**29**](#_ENREF_29)**], 2014**  **(Thailand)** | Pilot | 23 | Breast cancer,  Adjuvant chemotherapy | Walking programme | Home based | 3-5 days/week x 12 weeks | Prog; 20-30min | Prog; light to moderate | Reported as increase in mean 5920 steps | Feasibility, CRF, physical fitness, mood and sleep disturbance |
| **Husebo et al[**[**23**](#_ENREF_23)**], 2014**  **(Norway)** | RCT | 67 | Breast cancer,  Adjuvant chemotherapy | Walking programme and strength exercise | Home based | Daily x 17weeks | Self-reported | 30 min | Walking-17%  Strength-15% | CRF, physical fitness, physical activity |

Abbreviations: \* - significant findings, RCT- randomised controlled trial, chemo-chemotherapy, VO2Peak – oxygen uptake at peak exercise, VO2max – oxygen uptake at max exercise, VO2 at LT- oxygen uptake at lactate threshold, 1RM – 1 rep maximum, UC- Usual care, Prog-progressive, IG/EG; Intervention group, CG; Control group, MHR- max heart rate, Min- minute, Prog – progressive increase, RET – resistance training, QoL; quality of life, CP –Cardiopulmoanry endpoints, Note# - UC offered 1month supervised exercise post intervention, AET- Aerobic exercise training, RET- resistance exercise training, Pros –prospective,WRpeak – peak work rate, 6MWD-6 minute walk distance test, CRT – chemoradiotherapy, CRF – cancer related fatigue

**Discussion**

*Main Findings*

This is the first systematic review of reports of exercise training intervention in cancer patients undergoing cancer treatment and surgery. The principal finding is that exercise training is safe and feasible in the adjuvant setting. There is evidence to suggest that exercise intervention during cancer treatment can improve measures of physical fitness and HRQoL. However, the question of which is the most effective exercise training programme aimed at improving physical fitness cannot be answered, with only 1 pilot study (of breast cancer) reporting statistical significant increases as a primary outcome measure of physical fitness [[26](#_ENREF_26)].

*Safety and Feasibility*

Overall, exercise training during cancer treatment is safe and feasible in several different patient groups. The papers reviewed here show that exercise programmes have been found to be safe +/ feasible in breast cancer patients [[15](#_ENREF_15), [26](#_ENREF_26)] and NSCLC during adjuvant cancer treatment [[25](#_ENREF_25)]. Cancer patients encounter worsening symptoms from cancer, cancer treatment and surgery yet these studies highlight the efficacy of implementing exercise programmes in this patient population [[25](#_ENREF_25)]. Considering NSCLC patients included in this review were older, had poor exercise tolerance, a diverse range of co-morbidities and recently underwent surgical excision of lung tissue highlights the feasibility of exercise programmes in such patients [[25](#_ENREF_25), [27](#_ENREF_27)]. Moreover, this review included participants of whom almost one third received platinum-based chemotherapy whilst undertaking the exercise programme [[25](#_ENREF_25)]. Additionally, one NCSLC study initiated exercise training 66-hours post hospital discharge [[27](#_ENREF_27)]. Only one study in this review documented a participant becoming unwell but quickly recovered during the exercise intervention [[17](#_ENREF_17)] suggesting intervening with an exercise program during this period is safe.

*Effect of exercise training on physical fitness*

A higher level of physical fitness has been related to longer cancer-specific survival and lower cancer-related mortality [[1](#_ENREF_1)]. Exercise training has been suggestive to playing a role in ameliorating toxicity, completion rate and cancer treatment efficacy [[33](#_ENREF_33)]. However, studies reviewed here provide little data relevant to deciding the training programme most effective on such outcomes. The studies included in this review were heterogeneous for the type of cancer (breast, NSCLC and one study including 21 different cancer types), cancer treatments and the initiation of the exercise training programme. The exercise training varied in the type of programme (mainly aerobic and resistance exercise training), supervision and setting (supervised in-hospital and unsupervised at home), frequency of the programme (2-26 weeks), intensity (mainly moderate aerobic with high intensity in two studies [[22](#_ENREF_22)]), time (15- 60 minutes) and type (mainly cycle ergometer) of exercise. Adherence ranged from 15 – 90% between home-based and in-hospital exercise training. For comparison, reported adherence rates for surgical prehabilitation studies also range widely, e.g. 16% in colorectal cancer [[34](#_ENREF_34)] and 81% in lung cancer patients[[35](#_ENREF_35)] for home-based training programmes and 100% for a supervised in-hospital program in abdominal aortic aneurysm repair patients [[36](#_ENREF_36)].

Remaining physically active during and after cancer treatment is known to improve associated adverse effects, as well improve overall survival and reduce the probability of relapse [[2](#_ENREF_2)]. Unfortunately, physical activity tends to decrease at diagnosis in cancer patients [[22](#_ENREF_22)]. However, 50% increase in physical activity following diagnosis has been shown to decrease both risk of colorectal cancer-specific and all-cause mortality [[37](#_ENREF_37)]. The first RCT (The CHALLENGE Trial) investigating physical activity levels and survival is currently being conducted among colon cancer survivors following completion of adjuvant chemotherapy [[38](#_ENREF_38)]. Encouragingly, Campbell [[15](#_ENREF_15)] and Adamsen [[22](#_ENREF_22)] and colleagues reported increased physical activity levels post-exercise training intervention.

Considering the role of strength/muscular training, a recent meta-analysis [[39](#_ENREF_39)] concluded that resistance training was associated with clinically important improvements in muscular function and body composition in patients undergoing cancer treatment and long term follow-up. Most of the studies included in this review did indeed incorporate a form of resistance exercise although only Battaglini and colleagues [[18](#_ENREF_18)] reported significant findings. Courneya and colleagues [[16](#_ENREF_16), [17](#_ENREF_17)] reported that chemotherapy moderated the effects of exercise training on muscular strength with patients receiving non-taxane based chemotherapy increasing muscular strength. Moreover, this resistance exercise training programme improved cancer treatment completion rate. Peripheral muscle strength is known to be related to physical activity in patients with chronic obstructive pulmonary disease (COPD) [[40](#_ENREF_40)], though this has not been studied in cancer patients.

*HRQoL*

Preparing for the “multiple hit” of surgery and adjuvant cancer treatment can cause unanticipated fear, anxiety and psychological stresses. HRQoL is much studied in oncology [[41](#_ENREF_41)]. The studies included in this review on the whole support the conclusion of Granger and colleagues [[8](#_ENREF_8)] such that exercise training is associated with positive benefits on some domains of HRQoL. Burke and colleagues [[42](#_ENREF_42)] explored experiences of participants in an in-hospital exercise programme using semi-structured interviews, finding that it promoted positive changes, as patients viewed their lives in a “fuller, richer and more meaningful way”. Campbell and colleagues [[15](#_ENREF_15)] found, over a 12-week exercise intervention period, a change in FACT G score of ~15 units, representing the difference between requiring bed rest half the waking day to being fully ambulatory with symptoms [[43](#_ENREF_43)].

*Exploratory outcomes (Fatigue and syymptoms, behaviour)*

Fatigue is one of the commonest symptoms of cancer and cancer treatment, manifested in the clinic as weakness and exercise intolerance, which can effect quality of life and physical activity [[42](#_ENREF_42)]. One exercise programme included in this review reported a small-to-medium clinically significant improvement in fatigue [[22](#_ENREF_22)], and found exercise training to be effective in managing fatigue levels during both radiation and chemotherapy [[19](#_ENREF_19)]. One other study included in this review reported a significant improvement in fatigue levels 6-months following participation following a home-based exercise programme however this study reported a poor adherence rate which would question whether such a significant finding is a result of participating in the exercise programme [[23](#_ENREF_23)]. Insight into strategies that help patients overcome barriers to exercise may help patients adopt and maintain physical activity [[44](#_ENREF_44)]. It has been suggested that patients interested in participating in physical activity preferred to receive information from a cancer centre or face to face as opposed to leaflets [[44](#_ENREF_44)]. Courneya and colleagues [[14](#_ENREF_14)] stressed the importance of fully considering demographic, medical, behavioural, fitness, psychosocial and motivational factors when designing behavioural support interventions to promote exercise during the important transition from breast cancer patient to survivor.

*Strengths and weaknesses*

The main strength of this article is that it provides an up-to-date comprehensive review of all studies using an exercise programme in cancer patients undergoing surgery and adjuvant cancer treatment. The review was conducted in a rigorous manner using selected search terms over several databases of which was updated over several time points. Furthermore, two independent assessors screened the candidate articles using the predefined search terms which minimised bias. The quality of each study was evaluated by using a checklist designed to assess randomized and non-randomized trials.

The main weakness of this article is the limited number of reports available (of which 3 referred to a single exercise program, the START trial [[14](#_ENREF_14), [16](#_ENREF_16), [17](#_ENREF_17)]). Not all studies reported initial baseline fitness levels, and some studies excluded patients who were already vigorously exercising 3 times a week for 20 minutes or more. Furthermore, not all studies specified the timing of assessments, duration of exercise programmes and the nature of the cancer treatment received. Some studies offered incentives such as massages [35] to continue the exercise programme which limits future application of such exercise interventions. Due to the nature of the literature, only three of the seventeen included studies included mixed genders, all other studies included female breast cancer. Finally, due to the clinical and statistical heterogeneity of the included studies, meta-analyses were not performed

**Conclusion**

To our knowledge, this is the first systematic review including all cancer patients undergoing both surgery and adjuvant cancer treatment. Consistent with findings presented in a recent review [[33](#_ENREF_33)], we agree that the majority of work conducted in the adjuvant setting mainly includes breast cancer patients. However, in comparison our review has focussed on all surgical patients and furthermore on those undergoing adjuvant cancer treatment. Of the 17 included studies, 6 have been conducted in the past 5 years. Because of the lack of adequately powered RCTs in this area, it remains unclear what is the optimal time to initiate an exercise program and the kind of programme effective in improving clinical outcome measures. Future studies will need to examine the mechanisms of cancer treatment and different exercise programmes. Initiating such exercise programmes at cancer diagnosis may have a long lasting effect in remaining physically active throughout the journey cancer patients endure.

**References:**

1. Brunelli A, P.C., Salati M, Refai M, Berardi R, Mazzanti P, Tiberi M., *Preoperative maximum oxygen consumption is associated with prognosis after pulmonary resection in stage I non-small cell lung cancer.* Ann Thorac Surg, 2014. **98**(1): p. 238-42.

2. Thomas RJ, H.M., AL-Adhami A, *Physical activity after cancer: An evidence review of the international literature.* BJMP, 2014. **7**(1): p. a708.

3. West M.A, L.L., Barben CP, Sripadam R, Kemp GJ, Grocott MP, Jack S., *The effects of neoadjuvant chemoradiotherapy on physical fitness and morbidity in rectal cancer surgery patients.* Eur J Surg Oncol, 2014.

4. Jack S, W.M., Raw D, Marwood S, Ambler G, Cope TM, Shrotri M, Sturgess RP, Calverley PM, Ottensmeier CH, Grocott MP., *The effect of neoadjuvant chemotherapy on physical fitness and survival in patients undergoing oesophagogastric cancer surgery.* Eur J Surg Oncol, 2014.

5. Moros MT, R.M., Caballero A, Serrano E, Martínez V, Tres A., *Effects of an exercise training program on the quality of life of women with breast cancer on chemotherapy.* Rev Med Chil., 2010. **138**(6): p. 715-22.

6. Pearse RM, M.R., Bauer P, Pelosi P, Metnitz P, Spies C, Vallet B, Vincent J-L, Hoeft A, Rhodes A., *Mortality after surgery in Europe: a 7 day cohort study.* The Lancet, 2012. **380**

7. Moonesinghe SR, H.S., Mythen MG, Rowan KM, Haddad FS, Emberton M, Grocott MP., *Survival after postoperative morbidity: a longitudinal observational cohort studydagger.* Br J Anaesth, 2014. **113**(6): p. 977-84.

8. Granger, C.L., et al., *Exercise intervention to improve exercise capacity and health related quality of life for patients with Non-small cell lung cancer: a systematic review.* Lung Cancer, 2011. **72**(2): p. 139-53.

9. Crandall K, M.R., Campbell A, Kearney N., *Exercise intervention for patients surgically treated for Non-Small Cell Lung Cancer (NSCLC): a systematic review.* Surg Oncol, 2014. **23**(1): p. 17-30.

10. Downs SH, B.N., *The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions.* J Epidemiol Community Health 1998. **52**: p. 377–384.

11. Kraemer WJ, F.S., Deschenes MR, *Exercise Physiology: Integrating Theory and Application*, ed. s. Ed. 2012, Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health.

12. Kraemer WJ, R., NA., *Fundamentals of Resistance Training: Progression and Exercise Prescription.* Medicine & Science in Sports & Exercise, 2004. **36**(4): p. 674-688.

13. Lee TS, K.S., Refshauge KM, Pendlebury SC, Beith JM, Lee MJ., *Pectoral stretching program for women undergoing radiotherapy for breast cancer.* Breast Cancer Res Treat, 2007. **102**(3): p. 313-21.

14. Courneya KS, F.C., Reid RD, Gelmon K, Mackey JR, Ladha AB et al., *Predictors of follow-up exercise behavior 6 months after a randomized trial of exercise training during breast cancer chemotherapy.* Breast Cancer Res Treat, 2009. **114**(1): p. 179-87.

15. Campbell A, M.N., White F, McGuire F, Kearney N., *A pilot study of a supervised group exercise programme as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment.* Eur J Oncol Nurs, 2005. **9**(1): p. 56-63.

16. Courneya KS, M.D., Mackey JR, Gelmon K, Reid RD, Friedenreich CM et al., *Moderators of the effects of exercise training in breast cancer patients receiving chemotherapy: a randomized controlled trial.* Cancer, 2008. **112**(8): p. 1845-53.

17. Courneya KS, S.R., Mackey JR, Gelmon K, Reid RD, Friedenreich CM et al., *Effects of Aerobic and Resistance Exercise in Breast Cancer Patients Receiving Adjuvant Chemotherapy: A Multicenter Randomized Controlled Trial.* Journal of Clinical Oncology, 2007. **25**(28): p. 4396-4404.

18. Battaglini C, B.M., Shields E, Kirk D, Dennehy C, Hackney AC, Barfoot D, *The effects of resistance training on musclar strength and fatigue levels in breast cancer patients.* Rev Bras Med Esporte, 2006. **12**(3).

19. Mock V, F.C., Davidson NE, Ropka ME, Pickett M, Poniatowski B et al., *Exercise manages fatigue during breast cancer treatment: a randomized controlled trial.* Psychooncology, 2005. **14**(6): p. 464-77.

20. Milecki P, H.K., Ozga-Majchrzak O, Molinska-Glura M., *Exercise tolerance in breast cancer patients during radiotherapy after aerobic training.* Contemp Oncol (Pozn), 2013. **17**(2): p. 205-9.

21. Segal R, E.W., Johnson D, Smith J, Colletta S, Gayton J et al., *Strucutred exercise improves physical functioning in women with stages I and II breast cancer results of a randomised controlled trial.* Journal of Clinical Oncology, 2001. **19**(3): p. 657-665.

22. Adamsen L, Q.M., Andersen C, Moller T, Herrstedt J, Kronborg D et al., *Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial.* BMJ, 2009. **339**.

23. Husebo AM, D.S., Mjaaland I, Soreide JA, Bru E., *Effects of scheduled exercise on cancer-related fatigue in women with early breast cancer.* ScientificWorldJournal, 2014. **2014**: p. 271828.

24. Schmidt ME, W.J., Armbrust P, Schneeweiss A, Ulrich CM, Steindorf, K., *Effects of resistance exercise on fatigue and quality of life in breast cancer patients undergoing adjuvant chemotherapy: A randomized controlled trial.* Int J Cancer, 2014.

25. Jones LW, E.N., Peterson BL, Garst J, Crawford J, West MJ et al., *Safety and feasibility of aerobic training on cardiopulmonary function and quality of life in postsurgical nonsmall cell lung cancer patients: a pilot study.* Cancer, 2008. **113**(12): p. 3430-9.

26. Kolden, G.G., et al., *A pilot study of group exercise training (GET) for women with primary breast cancer: feasibility and health benefits.* Psychooncology, 2002. **11**(5): p. 447-56.

27. Hoffman AJ, B.R., von Eye A, Jones LW, Alderink G, Patzelt LH, Brown JK., *Home-based exercise: promising rehabilitation for symptom relief, improved functional status and quality of life for post-surgical lung cancer patients.* J Thorac Dis, 2014. **6**(6): p. 632-40.

28. Lee, T.S., et al., *Pectoral stretching program for women undergoing radiotherapy for breast cancer.* Breast Cancer Research and Treatment, 2007. **102**(3): p. 313-321.

29. Naraphong W, L.A., Schafer J,Whitmer K, Wilson BR., *Exercise intervention for fatigue-related symptoms in Thai women with breast cancer: A pilot study.* Nurs Health Sci, 2014.

30. Jones LW, D.P., Eves ND, Marcom PK, Kraus WE, Herndon JE et al., *Rationale and design of the Exercise Intensity Trial (EXCITE): A randomized trial comparing the effects of moderate versus moderate to high-intensity aerobic training in women with operable breast cancer.* BMC Cancer, 2010. **10**: p. 531.

31. Chapman A, M.S., Ladd B, Muers MF., *Population based epidemiology and prognosis of mesothelioma in Leeds, UK.* Thorax, 2008. **63**(5): p. 435-439.

32. Adamsen L, Q.M., Andersen C, Moller T, Herrstedt J, Kronborg D et al., *Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial.* BMJ, 2009. **339**: p. 3410.

33. Jones L.W, A.C., *Exercise-oncology research: past, present, and future.* Acta Oncol, 2013. **52**(2): p. 195-215.

34. Carli F, C.P., Stein B, Feldman L, Zavorsky G, Kim DJ et al., *Randomized clinical trial of prehabilitation in colorectal surgery.* Br J Surg, 2010. **97**(8): p. 1187-97.

35. Coats V, M.F., Simard S,Fréchette E, Tremblay L, Ribeiro F, Saey D., *Feasibility and effectiveness of a home-based exercise training program before lung resection surgery.* Can Resp J, 2013. **20**(2).

36. Barakat HM, S.Y., Barnes R, Gohil R, Souroullas P, Khan J et al., *Supervised exercise program improves aerobic fitness in patients awaiting abdominal aortic aneurysm repair.* Ann Vasc Surg, 2014. **28**(1): p. 74-9.

37. Meyerhardt JA, G.E., Holmes MD, Chan AT, Chan JA, Colditz GA, Fuchs CS., *Physical activity and survival after colorectal cancer diagnosis.* J Clin Oncol, 2006. **24**(22): p. 3527-34.

38. Courneya KS, B.C., Gill S, O’Brien P, Vardy J, Friedenreich CM et al. , *The Colon Health and Life-Long Exercise Change trial: a randomized trial of the National Cancer Institute of Canada Clinical Trials Group.* Current Oncology. **15**(6).

39. Strasser B, S.K., Wiskemann J, Ulrich CM, *Impact of Resistance Training in Cancer Survivors.* Med Sci Sports Exerc., 2013. **45**(11): p. 2080-2090.

40. Rausch-Osthoff A-K, K.M., Sievi NA, Clarenbach CF,van Gestel A Jr, *Association between peripheral muscle strength, exercise performance, and physical activity in daily life in patients with Chronic Obstructive Pulmonary Disease.* Multidisciplinary Respiratory Medicine, 2014. **9**(37).

41. Costantini M, M.E., Giulio PD, Cortesi, Roila F, Ballatori E, *Cancer patients as experts in defining quality of life domains. A multicentre survey by the Italian group for the evaluation of outcomes in oncology (IGEO). .* Qual Life Res, 2000. **9**: p. 151-159.

42. Burke SM, B.J., Sabiston CM, Jack S, Grocott MP, West MA., *Patients' perceptions of quality of life during active treatment for locally advanced rectal cancer: the importance of preoperative exercise.* Support Care Cancer, 2013.

43. Brady MJ., C.D., Mo F, Bonomi A.M, Tulsky DS, Lloyd SR et al., *Reliability and validity of the functional assessment of cancer therapy breast quality of life assessment. .* Journal of Clinical Onocology 1997. **15**: p. 974–998.

44. Buffart, L.M., et al., *Evidence-based physical activity guidelines for cancer survivors: current guidelines, knowledge gaps and future research directions.* Cancer Treat Rev, 2014. **40**(2): p. 327-40.

**Appendix 1:**

**Appendix 2.**

|  |
| --- |
| **Search terms** |
| 1. **CANCER** |
| 1. expNeoplasm |
| 1. Canc\*.tw. |
| 1. Neoplasm\*.tw. |
| 1. expTumor |
| 1. Tumo\*.tw. |
| 1. expCarcinoma |
| 1. Carcin\*.tw. |
| 1. expMalignant |
| 1. expOncology |
| 1. Oncol\*tw. |
| 1. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 |
| 1. **CANCER TREATMENT** |
| 1. expNeoadjuvant |
| 1. Neoadjuvant\*.tw. |
| 1. expChemo |
| 1. Chemo\*.tw. |
| 1. expRadiotherapy |
| 1. expCancer treatment |
| 1. 12 or 13 or 14 or 15 or 16 or 17 |
| 1. **EXERCISE** |
| 1. expExercise |
| 1. Exercise\*.tw. |
| 1. expFitness |
| 1. Fit\*.tw. |
| 1. expOxygen consumption |
| 1. expAerobic |
| 1. Aerobic\*.tw. |
| 1. Anaerobic |
| 1. Anaerobic\*.tw. |
| 1. 19 or 20 or 21 or 21 or 22 or 23 or 24 or 25 or 26 or 27 |
| **i) and ii) and iii)** |
| 1. **SURGERY** |
| 1. Surgery |
| 1. Surg\*.tw. |
| 1. Surgical (including Anatomy, drainage, mortality, patient, science, stress, wound, ward all terms) |
| 1. 30 or 31 or 32 |
| 1. **I) and ii) and iii) and iv)** |
| 1. **OUTCOME** |
| 1. Morb\*.tw. |
| 1. Mort\*.tw. |
| 1. Recurrence\*.tw. |
| 1. Outcom\*.tw. |
| 1. 34 or 35 or 36 or 37 |
| 1. **and ii) and iii) and iv) and v)** |

Figure 2. **Search terms used in this systematic review**