Supportive Care in Cancer
https://doi.org/10.1007/s00520-021-06708-6

REVIEW ARTICLE

Efficacy of resistance training during adjuvant chemotherapy and radiation therapy in cancer care: a systematic review and meta-analysis

Aoife McGovern[1] · **Nicholas Mahony**[1] · **David Mockler**[2] · **Neil Fleming**[1]

Received: 14 July 2021 / Accepted: 16 November 2021

Abstract

Purpose To determine the effect of resistance training during adjuvant chemotherapy and radiation therapy in cancer patients on measures of lean mass and muscle strength. Secondary aims were to analyse the prescription and tolerability of supervised resistance training in this population.

Methods EMBASE, Medline, CINAHL, Cochrane Library and Web of Science were searched from inception until 29 March 2021. Eligible randomised controlled trials (RCTs) examining supervised resistance training > 6 weeks duration during adjuvant chemotherapy and/or radiation therapy in cancer patients with objective measurement of muscle strength and/or lean mass were included. The meta-analysis was performed using Revman 5.4.

Results A total of 1910 participants from 20 articles were included (mean age: 54 years, SD = 10) and the majority were female (76.5%). Resistance training was associated with a significant increase in upper body strength (standardised mean difference (SMD) = 0.57, 95% CI 0.36 to 0.79, $I2 = 64\%$, $P < 0.0001$), lower body strength (SMD = 0.58, 95% CI 0.18 to 0.98, $I2 = 91\%$, $P = 0.005$), grip strength (mean difference (MD) = 1.32, 95% CI 0.37 to 2.27, $I2 = 0\%$, $P < 0.01$) and lean mass (SMD = 0.23, 95% CI 0.03 to 0.42, $I2 = 0\%$, $P = 0.02$). A P value of < 0.05 was considered statistically significant. The quality of the studies included was moderate to high with low risk of bias as per the PEDro scale.

Conclusion Resistance training is an effective adjunct therapy to improve muscle strength and lean mass in cancer patients undergoing chemotherapy and/or radiation therapy.

PROSPERO Registration Number CRD42020180643

Keywords Cancer · Resistance exercise · Chemotherapy · Radiation therapy · Muscle strength · Lean mass

Introduction

The incidence of cancer is reported to be 442.4 per 100,000 men and women per year [1]. Cancer is the second leading cause of death globally, accounting for an estimated 9.6 million deaths, or one in six deaths, in 2018 [2]. Observational evidence from a meta-analysis of 71 studies suggests an inverse dose-response relationship between physical activity levels and cancer-specific mortality among the general population and cancer survivors [3]. Muscle mass specifically is an important predictor of overall survival across multiple cancer sites [4–7].

Cancer cachexia is a metabolic syndrome characterised by progressive muscle wasting that may partly but not fully be reversed by conventional nutritional support [8, 9]. Common adjuvant cancer therapies such as chemotherapy and radiation therapy increase the catabolic state leading to protein loss and abnormal metabolism which further promotes cancer cachexia [10, 11]. Resistance training interventions have shown improvements in lean body mass in cachectic cancer patients [12].

Whilst the American College of Sports Medicine (ACSM) recommends exercise during cancer treatment, there is no specific guideline regarding which type or volume of training is most effective during chemotherapy or radiation therapy. The safety of resistance training during

✉ Aoife McGovern
aomcgove@tcd.ie

[1] Department of Anatomy, School of Medicine, Trinity College, Dublin, Ireland

[2] John Stearne Library, Trinity Centre for Health Sciences, Dublin, Ireland

Published online: 07 January 2022

chemotherapy and radiation therapy has been well established [13–16]. However, little information is known about the attendance, adherence and loss-to-follow-up (LTF) rates of supervised resistance training during adjuvant cancer treatment. Adequate prescription of resistance training is required to stimulate a cellular response with subsequent improvements in muscle strength and increase in muscle mass.

This review focused on supervised exercise only as it has been shown to be more effective than unsupervised for improvements in muscle strength and lean muscle mass [17, 18]. Supervised resistance training in oncology patients also has the added benefit of ensuring safety, correct technique, progression and motivation, whilst allowing opportunity to measure attendance and adherence accurately.

This meta-analysis and systematic review was conducted to analyse the effects of supervised resistance training on muscle strength and lean muscle mass objective measures in patients actively undergoing chemotherapy and/or radiation therapy across cancer types. Secondary aims were to analyse the prescription of supervised resistance training, in this patient cohort. Finally, participant-reported attendance, adherence and LTF rates were analysed to assess tolerability to the resistance training prescription.

Methods

Data searches and sources

A systematic search was conducted by a research librarian (D. M.) of the databases EMBASE, Medline, CINAHL, Cochrane Library and Web of Science from foundation to the 29 of March 2021. The search strategy consisted of using search terms cancer OR neoplasm, patient OR survivor, resistance training (weight, strength, resistance weight-bearing, exercise) and their derivatives were entered as Medical Subject Heading terms and keywords combined with an "AND" term. See the Appendix for full search strategy. The search was then limited to English-language publications in peer-reviewed journals. Manual searches were also conducted using reference lists of other reviews in exercise oncology as well as reference lists of eligible articles. This analysis was conducted in accordance with the PRISMA guidelines (PROSPERO identifier: CRD42020180643).

Study eligibility criteria

Eligible studies must be RCT design, involving a resistance training or weight-bearing intervention that is supervised at least once a week lasting > 6 weeks in duration, participants must have a cancer diagnosis and actively receiving curative treatment with adjuvant chemotherapy and/or radiotherapy and participants must be aged ≥ 18 years of age. Studies must report an objective measure of muscle strength (e.g. %1RM, isometric/isokinetic test, handgrip) and or lean muscle mass (via imaging or muscle CS) reported at both baseline and follow-up. Only primary studies were included in the review. However, secondary studies were used to gain more information.

Study selection and data extraction

Title and abstract screening was conducted by two independent reviewers (A. Mc. G. and N. M.), with any conflicts being resolved by an independent team member (N. F.). The same process was repeated for full-text screening. The primary measures were change in strength and lean mass via objective assessment. Secondary measures of treatment effectiveness were also evaluated by assessing rates of attendance (i.e. percentage of total attended to planned treatments), adherence (i.e. percentage of planned sessions successfully completed at the planned duration and intensity to sessions attended) and LTF (percentage of patients who did not complete postintervention assessment to number randomly assigned) [19]. Safety was defined as report of any serious or nonserious adverse events of any grade [20].

In studies that met all inclusion criteria, baseline and post-intervention means and standard deviations (SDs) were extracted for all main outcome variables. As a wide range of strength tests were performed, upper and lower body composite strength scores were derived by combining and averaging strength values for each study. Change scores with resistance training were calculated and averaged by subtracting the baseline value from the post-training score.

Data extraction guidelines were developed to systematically extract data from each study under the following headings: the population studied, adjuvant cancer treatment, intervention, control, resistance training prescription, attendance at supervised sessions, adherence with the prescribed exercise programme and LTF.

Risk of bias

The PEDro scale was used to assess the risk of bias in included studies. The PEDro scale is an 11-point scale that has been shown to be reliable assessment of study quality in RCT [21]. Studies scoring ≥ 6 are considered high quality, 4–5 fair quality and ≤ 3 poor quality. Among exercise trials, blinding of participants is challenging and can result in a high risk of performance bias [22]. This foreseeable bias is acknowledged by the reviewers and should not infer poor methodological quality of the trial.

Data synthesis and analysis

For eligible studies, the effect size was calculated by using the mean and SD of change in strength or lean mass from baseline to postintervention for the exercise and control groups. All values were converted to the International System of Units (SI). Where baseline or post intervention data was missing, study authors were contacted to provide more information. The SMD and standardised deviation of the change were used to calculate effect size. Where the standardised deviation of the change was not reported, it was calculated. When SD pre and post intervention were available, SD was calculated via the below formula, where r is the correlation between baseline and follow-up score (r=0.5 was assumed) [23]:

$$SD = \sqrt{SD_b^2 + SD_f^2 - 2{*}r{*}SD_b * SD_f}$$

Where data was missing for mean and SD post intervention, the standard error (SE) was used to calculate the SD of the change by: SD = SE $\sqrt{n}$ [23]. Where SE was not reported, SE was calculated from the 95% CI [24]:

$$SE = \frac{UCB - LCB}{3.92}$$

Where data was available for more than one follow-up time, the timepoint closest to completion of the supervised resistance training programme was chosen. If there was no data collected within one month of completion of the supervised resistance training programme, it was not included in the meta-analysis as it was deemed not an accurate measure of the effect of the supervised exercise. For studies utilising a waitlist control or delayed intervention group, the timepoint before this group started the intervention was used [25, 26].

A random-effects model was used for analysis of handgrip strength, lean body mass, global lower limb strength and global upper limb strength due to differences between study populations, chemotherapy or radiation therapy treatment received, and the training stimulus. The random-effects model considers these additional sources of between study variability as well as within-study variability. Mean difference from baseline to post-intervention was used for analysing handgrip strength as the unit of measurement could be converted to the standard SI unit (kg) in all study groups included. Where data was presented for both right and left hands, the mean's and SD's pre- and post-interventions were summed and divided by 2 to get a mean and SD for just one hand. Where data was presented for treatment subgroups, both subgroups were included separately in analysis. SMD was used for analysis of lean body mass, upper limb strength and lower limb strength due to difference in data collection and units of measurement.

The I^2 statistic was used to estimate the percentage of variability across the pooled estimates attributable to heterogeneity beyond chance (where I^2 of 0 to 25% = low, I^2 of 26 to 75% = moderate, I^2 of 76 to 100% = high, severity of between-study heterogeneity). The potential for publication bias was evaluated visually by constructing a funnel plot to display the precision of the estimate of the effect size against the estimate of the effect size. All statistical analysis was conducted using Revman 5.4 (version 5.4, the Nordic Cochrane Centre, Copenhagen, Denmark). All results are presented as mean (SD) unless otherwise stated. A P value of 0.05 was considered statistically significant.

Results

Search results

A total 3921 references were found from initial search. After de-duplication, there were 1841 records to screen. After initial title and abstract screening, full-text review of 147 articles was carried out. A total of 20 articles, representing 18 independent RCTs, were included: 18 in qualitative analysis and 17 in quantitative analysis. Figure 1 presents the literature review in a PRISMA flowchart for study selection and reasons for exclusion based on full-text review.

Risk of bias assessment

Individual PEDro analysis of the included studies is shown in Table 1 below. PEDro scores ranged from 4 to 7. The majority of included studies were good quality with low risk of bias (score>6, 83%) [25–40], whilst three studies were fair quality (score 4–5, 17%) [41–44]. Funnel plots indicate that publication bias cannot be ruled out (see Figure 2).

Study and patient characteristics

A total of 20 articles from 18 different studies involving 1910 participants were included in the review. A description of the studies included is shown in Table 2. The mean (SD) age of participants was 54 (10) years. The majority of participants were female (n = 1461 female or 76.5%, n = 449 male or 23.5%). The control group was given usual care in 14 studies (77.7%). Usual care involved nutritional support in head and neck cancer studies at higher risk of weight loss [25, 33, 34]. One study specifically asked all participants in the usual care group not to start an exercise programme during the intervention period [28]; however, this was deemed unethical in later studies. One study asked participants in the control group to perform 3 sets

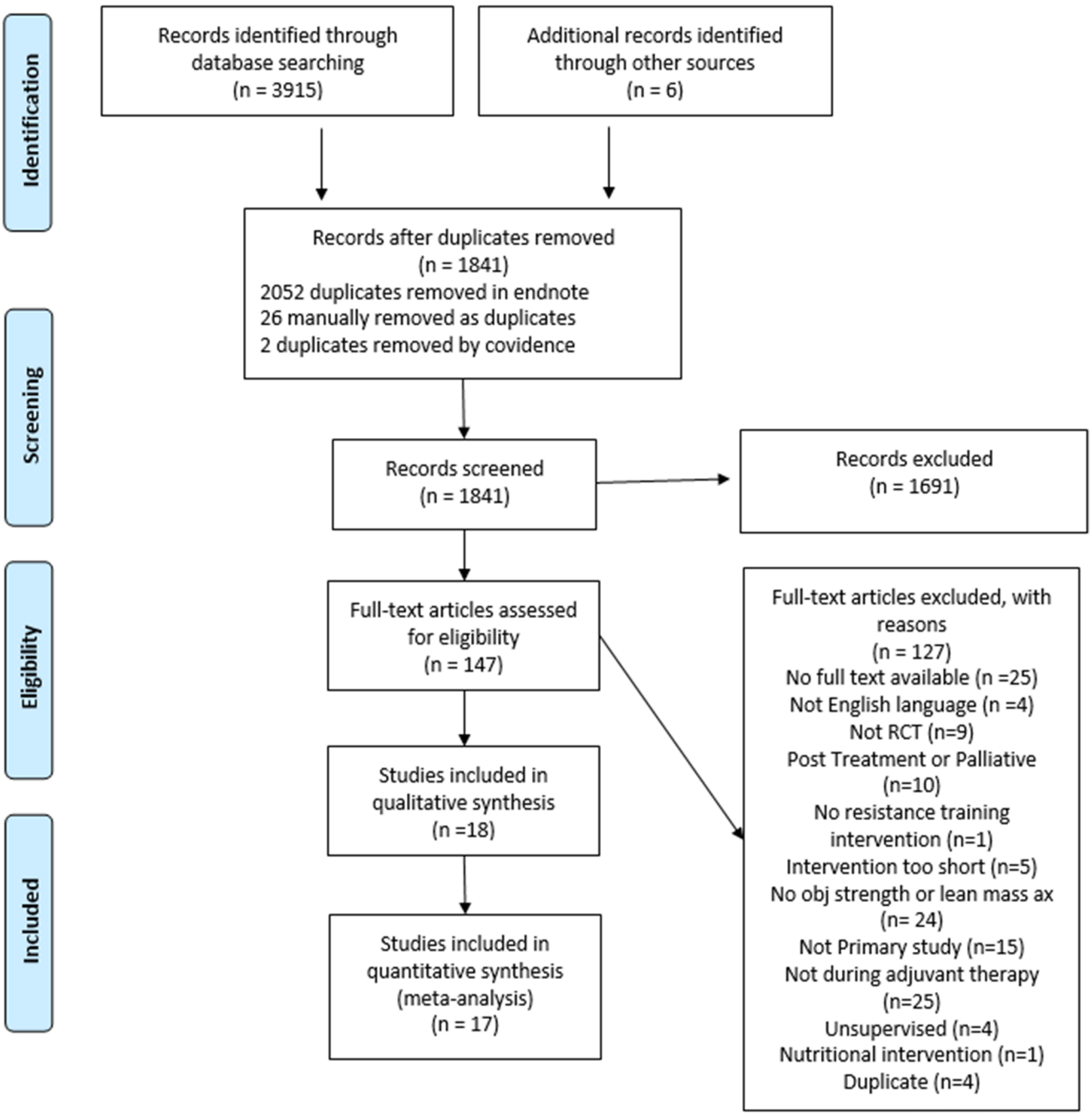


Figure 1 PRISMA flowchart of literature search and selection process

of 10 chair rises twice a week for 12 weeks to mitigate the placebo effect [39]. LTF rates reported were similar in intervention and control groups (intervention mean = 11.8 (10.5) %; control mean = 11.5 (8.5) %). No serious adverse events were reported relating to resistance training that resulted in participant drop out.

Resistance training principles

The reported resistance training prescriptions used in the individual studies are shown in Table 3. The mean (SD) duration of resistance training intervention was 13 (5) weeks. The most common frequency prescribed was two (55%) or

Table 1 Study quality on the PEDro scale

Study	1.*	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	Score
Courneya et al. 2007	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Adamsen et al. 2009	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Segal et al. 2009	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Hacker et al. 2011	✓	✓	✗	✗	✗	✗	✗	✓	✗	✓	✓	5
Rogers et al. 2013	✓	✓	✓	✓	✗	✗	✗	✓	✗	✓	✓	6
Christensen et al. 2014	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Schmidt et al. 2015	✓	✓	✓	✓	✗	✗	✗	✗	✗	✓	✓	5
Travier et al. 2015	✓	✓	✓	✗	✗	✗	✓	✗	✓	✓	✓	6
Zhou et al. 2015	✓	✓	✓	✗	✗	✗	✓	✓	✗	✓	✓	6
van Waart et al. 2015 van Waart et al. 2018	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Capozzi et al. 2016	✓	✓	✓	✗	✗	✗	✗	✓	✓	✓	✓	6
Wiskerman et al. 2017	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Grote et al. 2018	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✓	7
Mijwel et al. 2018a Mijwel et al. 2018b	✓	✓	✗	✓	✗	✗	✗	✗	✗	✓	✓	4
Ammitzboll et al. 2019	✓	✓	✓	✓	✗	✗	✓	✗	✓	✓	✓	7
CeŠeiko et al. 2020	✓	✓	✗	✓	✗	✗	✗	✓	✓	✓	✓	6
Hong et al. 2020	✓	✓	✓	✓	✗	✗	✓	✓	✗	✓	✓	7
Cheng et al. 2021	✓	✓	✗	✓	✗	✗	✓	✓	✗	✓	✓	6

(1) Eligibility criteria specified; (2) subjects randomly allocated; (3) allocation was concealed; (4) groups similar at baseline for the most important diagnostic indicators; (5) blinding of all subjects; (6) blinding of all therapists; (7) blinding of all assessors; (8) measures of at least one outcome measure were available from more than 85% of the subjects initially allocated to groups; (9) all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"; (10) The results of between-group statistical comparisons are reported for at least one key outcome; (11) The study provides both point measures and measures of variability for at least one key outcome

*This item is not used to calculate the PEDro score

three (39%) training sessions per week on non-consecutive days. Three studies also included additional unsupervised training [25, 30, 41]. There was considerable heterogeneity across prescribed exercise intensity, ranging from 1 to 10 sets, 4 to 20 repetitions at 45 to 100% 1RM reported. One study did not reported exercise intensity or sets completed [41]. Attendance at the supervised exercise sessions was reported in 14 studies with an average of 75.5%. Adherence to the prescribed resistance training programme was reported in three studies of breast cancer patients as 83% [42, 43], 96% [28] and 100% [39], respectively.

Lean mass assessment

Objective measures of lean mass were reported in seven studies [25, 28, 32–34, 36, 38]. Resistance training resulted in improvements in lean muscle mass following supervised resistance training intervention in six of the seven studies included resulting in a small effect size (SMD = 0.23, 95% CI 0.03 to 0.42, $I2 = 0\%$, $P = 0.02$) (see Figure 3).

Changes in cross sectional area (CSA) of the vastus lateralis via muscle biopsy were reported in two studies [36, 43]. Sixteen weeks following the onset of chemotherapy in breast cancer patients, the usual care control group demonstrated a significant reduction in vastus lateralis CSA for type I ($P = 0.01$) and type IIa muscle fibres ($P = 0.026$) based on 10 participants [43]. The intervention group of combined resistance training and high intensity interval training displayed a significant increase in type I muscle fibre CSA ($P = 0.049$) based on seven participants [43]. In germ cell cancer patients undergoing chemotherapy, the total CSA of the vastus lateralis decreased by −322 μm^2 (95% CI −899 to 255; $P = 0.473$) in the usual care control group ($n = 9$) and increased by +206 μm^2 (95% CI −384 to 796; $P = 0.257$) in the resistance training group ($n = 10$) after 9 weeks (adjusted mean difference (AMD), +625 μm^2, 95% CI −253 to 1503, $P = 0.149$) [36].

Strength assessment

Participant strength changes were measured objectively in all 18 of the included studies. The results of two studies were excluded from the meta-analysis. Ammitzboll et al. (2019) did not report results after the supervised 20-week

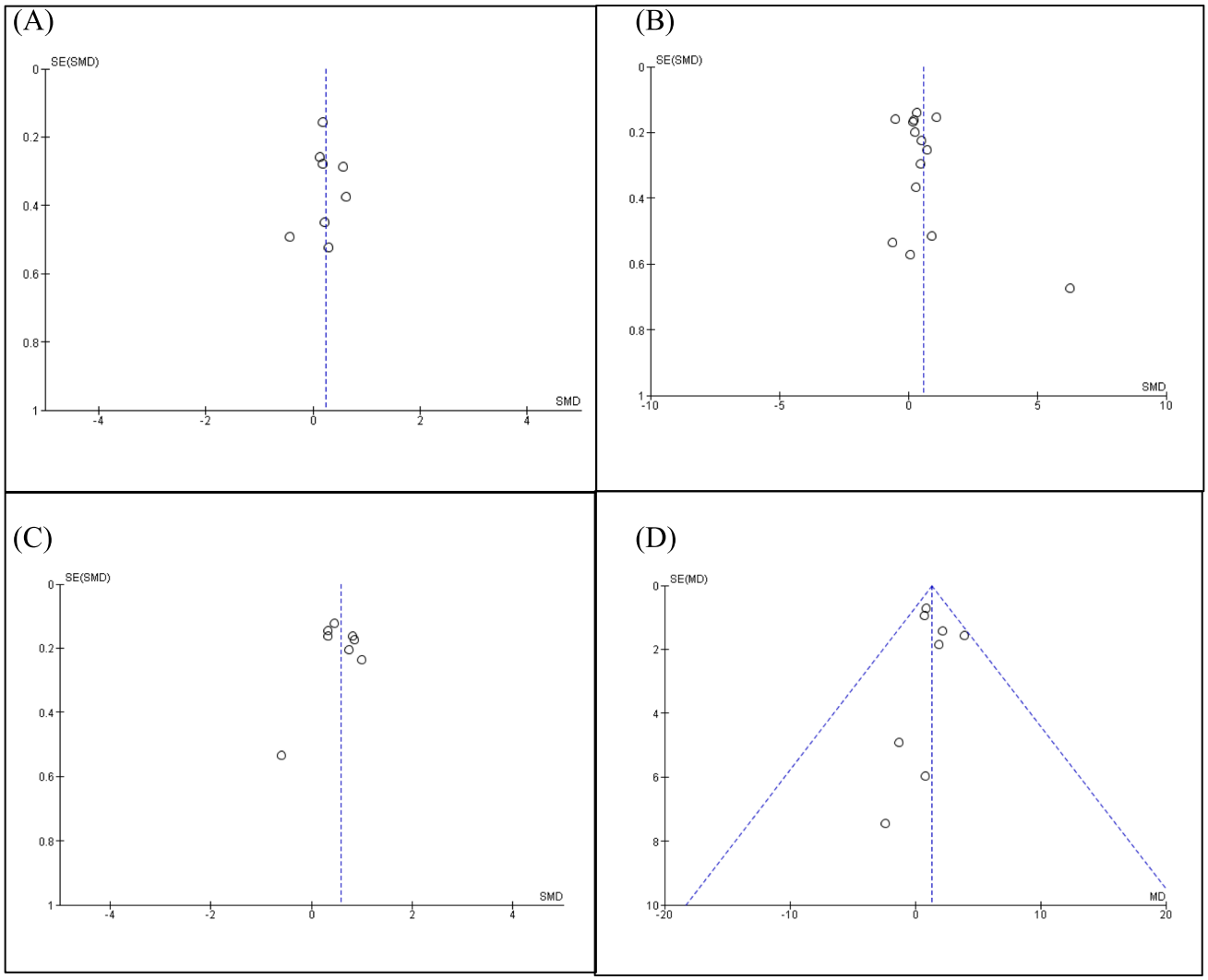


Figure 2 A Funnel plot of results for lean muscle mass. B Funnel plot of results of lower limb strength. C Funnel plot of results of upper limb strength. D Funnel plot of results of handgrip strength

intervention but only after a full year comprising 30 unsupervised weeks and therefore was not included in meta-analysis [30]. Results of this long-term follow-up found a significantly greater increase in strength in the intervention group than the control group for leg press (mean adjusted change = 7.2; 95% CI −0.3 to 14.6; *P*= 0.035), elbow flexion (mean adjusted change ipsilateral side = 0.8; 95% CI 0.2 to 1.2; *P*= 0.002; contralateral side = 0.7; 95% CI 0.2 to 1.1; *P*= 0.005) and contralateral shoulder abduction (mean adjusted change = 0.5; 95% CI 0.1 to 1.0; *P*= 0.014) [30]. There was no significant difference between groups in isometric muscle strength or grip strength [30]. Upper limb and grip strength results for one study were unable to be included in the meta-analysis due to insufficient reporting of results, reporting only that there was no significant change between groups across the study period [33]. Results from another study were excluded due to discrepancies in reporting of strength measures within the study and no reply from the principle author on contacting [38].

Objective measures of lower limb strength varied between studies (see Table 2). The pooled result of 13 studies (1283 participants) reported a significant improvement in lower limb strength following supervised resistance training with moderate heterogeneity (SMD = 0.58, 95% CI 0.18 to 0.98, $I2 = 91\%$, $P = 0.005$) (see Figure 3).

Upper limb strength was assessed objectively by a variety of different methods (see Table 2). The pooled result of 1116 participants (9 studies) found a significant improvement in upper limb strength with moderate effect size in favour of supervised resistance training compared to the control group and moderate levels of heterogeneity (SMD = 0.57, 95% CI 0.36 to 0.79, $I2 = 64\%$, $P < 0.0001$) (see Figure 3).

Grip strength was assessed via handheld dynamometer in nine articles involving eight independent studies. A pooled

Table 2 characteristics of included studies

Study First author, year, country.	Type of cancer	Adjuvant Treatment Type	Participants	Strength Assessment	Lean Mass Assessment	Other Outcome Measures
Mijwel et al. 2018a, Sweden.	Breast	Chemo	INT: RT HITT, n = 74 CON: UC, n= 60	Isometric mid-thigh pull, handgrip strength	-	VO_2peak, pressure-pain threshold, haemoglobin levels, and body mass
Mijwel et al. 2018b. Sweden.	Breast	Chemo	INT: RT, n = 7 CON: UC, n= 10	-	muscle biopsy of vastus lateralis: CSA	Protein extraction and immunoblot analysis, citrate synthase activity, immunohistochemistry analysis, myosin heavy chain typing
Travier et al. 2015, Netherlands.	Breast	Chemo	INT: RT, n = 102 CON: UC, n= 102	Cybex dynamometer assessed peak torque of knee extensors and flexors, handgrip strength	-	Fatigue, quality of life, anxiety, depression, and physical fitness
Schmidt et al. 2015, Germany.	Breast	Chemo	INT: RT, n = 52 CON: group-based relaxation, n= 49	Isometric muscular capacity of quadriceps, latts and pecs	-	Fatigue, QOL, depression, cognitive function, endurance performance
Courneya et al. 2007, Canada.	Breast	Chemo	INT: RT, n = 82 CON: UC* n= 82	8RM on the horizontal bench press and leg extension	DXA lean mass and % body fat	QOL, fatigue, psychosocial functioning, physical fitness, chemotherapy completion rate, and lymphedema
Wiskerman et al. 2017, Germany.	Breast	Radiation Therapy	INT: RT, n = 80 CON: group-based relaxation, n= 80	Isokinetic dynamometer: MVIC and MIPT for knee extensor and flexors, shoulder rotators	-	Fatigue
Ammitzboll et al. 2019, Denmark.	Breast[§]	Radiation Therapy +/- Chemo	INT: RT, n = 82 CON: UC, n= 76	7RM tests for shoulder abduction, elbow flexion, elbow extension, and leg press. Handgrip strength	DXA: interlimb difference	Interlimb volume difference by water displacement
CeŠeiko et al. 2020, Latvia.	Breast	Chemo or Radiation Therapy	INT: RT, n = 27 CON: Chair rises, n = 28	1 RM leg press	Skinfold measurement	Walking economy, time to exhaustion, 6MWT, 30 sec sit to stand, stair climb test.

Table 2 (continued)

Study First author, year, country.	Type of cancer	Adjuvant Treatment Type	Participants	Strength Assessment	Lean Mass Assessment	Other Outcome Measures
van Waart et al. 2015, Netherlands. van Waart et al. 2018, Netherlands.	Breast	Chemo	INT: RT, n = 76 CON: UC, n= 77	MicroFET† handheld dynamometer elbow flexion and knee extension, handgrip strength	-	Steep Ramp Test, 30-second chair stand test, fatigue, self-reported physical activity level, functioning in daily life, psychological distress, QOL, return to work, and chemotherapy completion rates
	Colon	Chemo	INT: RT = 7 CON: UC = 8	MicroFET† handheld dynamometer elbow flexion and knee extension, handgrip strength	-	Steep Ramp Test, 30-second chair stand test, fatigue, self-reported physical activity level, functioning in daily life, psychological distress, QOL, return to work, and chemotherapy completion rates
Grote et al. 2018, Germany.	Head and Neck	Radiation Therapy	INT: RT, n = 10 CON: UC, n= 10	Handgrip strength	BIA: %fat mass and % lean muscle mass	6MWT, fatigue, QOL
Zhou et al. 2015, USA.	Head and Neck	Chemo-radiation	INT: RT, n = 11 CON: UC, n= 9	Isokinetic dynamometer for elbow flexion and knee extension, handgrip strength	DXA: % lean muscle mass	6MWT, TUG, QOL, physician reported concurrent CRT toxicity
Capozzi et al. 2016, Canada.	Head and Neck	Radiation Therapy or Chemo-radiation	INT: RT, n = 31 CON: wait-list control, n= 29	Grip strength	DXA: % lean muscle mass	30 sec sit to stand, QOL, depression, nutrition status, 6MWT, sit and reach test
Rogers et al. 2013, USA.	Head and Neck	Radiation Therapy	INT: RT, n = 7 CON: UC, n= 8	Back and leg dynamometer, handgrip strength	Bioelectric impedance: % lean muscle mass	Physical functioning, fatigue, QOL
Hacker et al. 2011, USA.	Leukaemia	Chemo	INT: RT, n = 9 CON: UC, n= 10	Handgrip strength	-	Timed stair climb, 30-second chair-stand test, time needed to stand up from bedrest exam, fatigue, QOL
Hong et al. 2020, China.	Gastro-intestinal	Chemo	INT: RT, n = 102 CON: group-based relaxation = 102	1RM leg press, seated row, leg extension and chest press	-	Muscular endurance, 6m usual walk, 6m fast walk, 6m backwards walk, 400m walk, chair rise test, QOL

Table 2 (continued)

Study First author, year, country.	Type of cancer	Adjuvant Treatment Type	Participants	Strength Assessment	Lean Mass Assessment	Other Outcome Measures
Segal et al. 2009, Canada.	Prostate	Radiation Therapy	INT: RT, n = 40 CON: UC, n= 41	8RM horizontal bench and leg press	DXA: % BF	Fatigue, serum lipids, bloods, VO_2peak
Christensen et al. 2014, Denmark.	Germ cell	Chemo	INT: RT, n = 15 CON: UC, n = 15 REF: Healthy age + BMI matched controls n = 15	Maximum isometric torque of quadriceps, 1RM leg press†	muscle biopsies from vastus lateralis: CSA DXA: lean muscle mass (kg)	Fibre phenotype composition, blood biochemistry
Cheng et al. 2021, China	Mixed (lung, gastric or breast)	Chemo and/or Radiation Therapy	INT: Low intensity RT, n = 30 High intensity RT, n = 30 CON: UC, n= 30	-	Bioelectric impedance: % lean muscle mass	Fatigue, sleep quality, anxiety and depression
Adamsen et al. 2009, Denmark.	Mixed (21 different types)	Chemo	INT: RT, n = 135 CON: wait-list control, n= 134	1RM chest press, leg press, and pull down	-	Fatigue, QOL, VO_2max

INT= intervention, Chemo = chemotherapy, RT = resistance training, CON = control, Ref = reference group, UC = usual care, RM = repetition maximum, DXA = dual energy x-ray absorptiometry, BIA = Bioelectrical Impedance Analysis, CSA = cross-sectional area, QOL = Quality of life, 6MWT = six minute walk test, TUG = timed up and go, BMI = Body Mass Index

*asked not to initiate an exercise program and offered a one month exercise program postintervention.

§increased risk of lymphedema development.† only available for intervention group and healthy subjects.

Table 3: Description of Supervised Resistance Training Interventions

Study First author, year.	INT	Duration (weeks)	Freq (d/wk)	Intensity	Time (mins)	Type	Progression/ Modification	Attd (%)	Adh (%)	LTF (%)
Mijwel et al. 2018a; Mijwel et al. 2018b	RT + HIIT	16	2	2-3 sets of 8–12 reps at 70%-80% 1RM	NR	9 exercises involving the major muscle groups	Estimated 1RM tests were performed when participants could lift more than 12 reps of their estimated 80% 1RM.	68	83	INT = 17.7 CON = 29.6
Travier et al. 2015	RT + AE	18	2	2 × 10 reps at 65 % 1RM, increasing to 1 × 10 reps at 75 % 1RM and 1 × 20 reps at 45 % 1RM)	Total = 60 RT = 25	Exercises involving arms, legs, shoulder, and trunk	Repeating 1RM tests every 4 weeks.	83	NR	INT = 8.8 CON = 12.7
Schmidt et al. 2015	RT	12	2	3 sets of 8–12 reps at 60–80% of 1RM	60	8 different machine-based exercises	NR	71	NR	INT =12.5 CON = 7.1
Courneya et al. 2007	RT	Duration of chemo (median = 17)	3	2 sets of 8-12 reps at 60%-70% of estimated 1RM	NR	9 exercises involving machine and free weights.	Load increased by 10% when participants completed more than 12 reps	68.2	96	INT = 6.1 CON = 11
Wiskerman et al. 2017	RT	12	2	3 sets at 12RM	NR	8 different machine-based exercises	Progression by at least by 5% after successfully completing 3 sets of 12 reps	83	NR	INT = 1 CON = 2.5
Ammitzboll et al. 2019	RT	20	2*	2-3 sets of 10-20 reps at 10-25RM	NR	Exercises involved the major muscle groups in the upper limb, lower limb, and core.	Monthly strength tests, reducing rep range and increasing intensity every 4 weeks.	NR	NR	INT = 19.5 CON = 18.4
CeŠeiko et al. 2020	RT	12	2	4 sets of 4 reps at 90% 1 RM	20	Leg press machine only	NR	96	100	INT= 0 CON = 0
van Waart et al. 2015 van Waart et al. 2018	RT + AE	Duration of chemo: breast cancer mean = 17 Colon Cancer mean = 27	2	8 reps x 2 sets at 80% 1RM	RT = 20 AE = 30-50	6 exercises targeting large muscle groups	1RM testing was repeated every 3 weeks	Breast cancer =71 Colon cancer =61	NR	INT = 8.8 CON = 12.7 INT = 0 CON = 12.5

Table 3: (continued)

Study First author, year.	INT	Duration (weeks)	Freq (d/wk)	Intensity	Time (mins)	Type	Progression/ Modification	Attd (%)	Adh (%)	LTF (%)
Grote et al. 2018	RT	8	3	3 sets of 8-12 reps, RPE >7.	30	3 exercises for major muscle groups: leg press, latissimus pull-down and chest press	Based on patient reported RPE – The weight loading was increased at the next workout if RPE < 7. Modifications reported.	90	NR	INT = 0 CON = 0
Zhou et al. 2015	RT + walking	14	3	8-12 reps x 3 sets – intensity individualised	≥60	8 exercises using dumbbells and ankle weights	NR	72	NR	INT = 0 CON = 22
Capozzi et al. 2016	RT	12	2*	8 reps x 2 -3 sets at 8-10RM	NR	10 exercises based on the major muscle groups + home equipment provided	Progression was applied at 4, 6, and 9 weeks, as appropriate	45.2	NR	INT = 38.7 CON = 20.6
Rogers et al. 2013	RT	12	2	Up to 10 reps, intensity NR	60	9 exercises with resistance bands targeting the major muscle groups	Progressed resistance band strength pr rep range as appropriate every 2 weeks.	83	NR	INT = 28.6 CON = 0
Hacker et al. 2011	RT	6	1-2 *	8-10 reps x 1 set, RPE 13	NR	8 exercises using resistance bands and 3 bodyweight exercises	Increase to 2 sets, then increase resistance band	NR	NR	INT = 11.1 CON = 10
Hong et al. 2020	RT	12	2	3 sets of 8 to 12 reps at 60-80% 1RM	60	8 machine-based exercises: leg extension, leg curl, leg press, shoulder internal and external rotation, seated row, latissimus pull down, shoulder flexion and extension, butterfly and butterfly reverse	If 3 sets of 12 reps on an exercise completed, weight increased by at least 5% in the next session.	NR	NR	INT = 7.8 CON = 5.9
Segal et al. 2009	RT	24	3	2 sets of 8-12 reps at 60-70% estimated 1RM	NR	10 different exercises: incorporated machine based and free weights.	Resistance was increased by 5 lb when participants completed more than 12 repetitions.	85.5	NR	INT = 17.5 CON = 2.4

Table 3: (continued)

Study First author, year.	INT	Duration (weeks)	Freq (d/wk)	Intensity	Time (mins)	Type	Progression/ Modification	Attd (%)	Adh (%)	LTF (%)
Christensen et al. 2014	RT	9	3	3–4 sets of 10–15 reps at 12–15RM.	NR	4 machine-based exercises: leg press, knee extension, chest press and lateral pulldown	Load was progressed when a participant could perform more than 12 reps at a given load	70	NR	INT = 20 CON = 13.33
Cheng et al. 2021	RT	12	3	30% 1RM for low intensity group – reps NR, 10 sets total 60% 1RM for high intensity group – reps NR 10 sets total	30	6 exercises: standing row, bench press, standing dumbbell shoulder press, lying leg lifts, prone leg raises, and prone leg curls	NR	NR	NR	INT: low intensity group = 10 High intensity group = 16.6 CON = 13.3
Adamsen et al. 2009	RT + AE + BAL + CO-ORD	6	3	3 sets of 5-8 reps at 70-100% of their 1RM	RT= 45 AE =15	6 machine-based exercises targeting the major muscle groups	1RM testing was repeated every second week	70.8	NR	INT = 12.7 CON = 12.6

Attd=attendance, Adh = adherence, LTF = lost to follow up, INT = intervention group, RT = resistance training, HIIT = high intensity interval training, AE= aerobic exercise, BAL = balance, CO-ORD = co-ordination exercises, RM = repetition maximum, NR = not reported RPE = rate of perceived exertion, CON = control group,

*additional unsupervised training

significant mean difference in favour of the resistance training group was found with low heterogeneity based on 595 participants (MD = 1.32, 95% CI 0.37 to 2.27, $I^2 = 0\%$, $P = 0.006$) (see Figure 3).

Discussion

Findings of this meta-analysis demonstrate that supervised resistance exercise is an effective adjunctive strategy to improve or mitigate the loss of lower limb, upper limb, hand grip strength and lean mass in adult-onset cancer patients undergoing chemotherapy and/or radiation therapy. Resistance training was prescribed alone and in combination with high and moderate intensity aerobic exercise, balance and coordination exercises. The most common resistance training prescription was 2–3 non-consecutive days of the week with high levels of variance in sets, repetitions and prescribed intensity. The reported attendance of supervised exercise sessions was high at 75.5%. Adherence to the prescribed exercise prescription was only reported in three studies; therefore, an accurate estimation of this is unknown. LTF varied between studies but overall was similar between intervention and control groups.

Insufficient prescription of resistance training principles may result in underreporting of the benefits of resistance training during chemotherapy and radiation therapy. Progression of resistance training programmes is a key principle to achieve strength and lean mass improvements. Resistance bands were used in two of the included studies and may not be able to achieve appropriate overload for physiological changes in the muscle [34, 41]. Some studies did not adequately report how or if progression was applied. As cancer-related fatigue and other treatment side effects can exacerbate later into chemotherapy and radiation therapy treatment protocols, underreporting of adherence to the training prescriptions means we are unable to determine if patients in the intervention group were able to tolerate progressions to their programme or whether maintenance may be a more appropriate target during this time. A review of the exercise principles reported in exercise oncology studies found similar poor reporting of exercise principles with progression reported by 26% of the 33 included studies [45]. Only two (6%) studies reported participant adherence to each component of the exercise prescription [45]. Future exercise oncology research should follow previously published guidelines for reporting of exercise interventions prescribed and exercise completed [46].

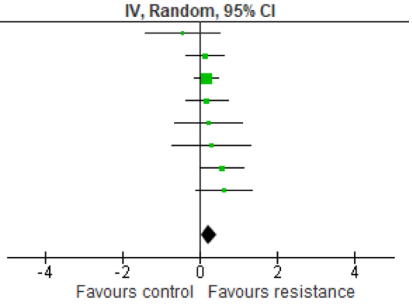
Whilst overall resistance training was found to increase or maintain lean mass compared to non-training control groups, the change reported had a low effect size (SMD = 0.23). This may be in part attributed to a lack of studies included, with only seven studies meeting our inclusion criteria for this part of the meta-analysis. A combined nutritional and resistance training intervention including protein supplementation may have greater results in improvements in lean mass [47]. The muscle biopsy studies further indicate improvements in CSA of *vastus lateralis* following resistance training intervention are likely [36, 43]. It is unclear if a greater difference in lean mass changes would emerge after a longer intervention period or may be cancer type dependent. Four studies included were in head and neck cancer patients who are at higher risk of developing cancer cachexia. Sub-group analysis excluding head and neck cancer patients revealed a slightly higher efficacy in support of improvements in lean mass (SMD = 0.28, 95% CI 0.05 to 0.51, P=0.02). The study with the largest sample size of 164 breast cancer patients also had the smallest increase in lean muscle mass [28]. Whilst the study with the largest effect size in favour of improvements in lean muscle was in male germ cell cancer patients [36]. Participants in this study were all males and had a younger mean age which may account for the larger effect size. Variations in resistance training programme prescribed (3–4 sets of 10–15 reps at 12–15RM on 4 machine-based exercises, 3 days a week) to the germ cell cancer patients versus breast cancer patients (2 sets of 8–12 reps at 60–70% of estimated 1RM on 9 exercises a combination of machine and free weight) may also have contributed to the superior results, whilst differences in the effect of chemotherapy vs radiation therapy on lean muscle mass need to be investigated. The only study to report an effect size in favour of the usual care control group was in head and neck cancer patients following 14 weeks of concomitant chemoradiation therapy (SMD = −0.44, 95% CI −1.40 to 0.52) [33]. A possible explanation for the change in favour of the usual care control group is a mismatch in the intake energy balance in the intervention group [33]. Results are limited by the small sample size included (n=20) [33]. One multi-group study found that higher intensity resistance training (HIRT) was superior to low intensity resistance training (LIRT) for improving lean mass in a mixed cancer patient group (HIRT SMD= 0.56, 95% CI −0.01 to 1.12 vs LIRT SMD= 0.18 −0.36 to 0.73) [38]. Further comparator studies with different resistance training prescriptions and larger sample sizes would allow the opportunity to evaluate the efficacy of different resistance training prescriptions.

Our meta-analysis results show significant improvements in lower body, upper body and grip strength. The increases in muscle strength reported in this review are likely due to neural adaptations [48–50]. The moderate heterogeneity found for upper limb and lower limb strength (I_2 = 64% and I_2 = 58%, respectively) may be explained by differences in the outcome measure used and interventions prescribed. Interestingly, the study which reported a slightly negative effect for changes in lean mass in the resistance trained group reported the largest increase in lower limb muscle

(A)

Study or Subgroup	Resistance training Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Zhao, 2015	0.2	1.66	11	1	1.85	7	4.1%	-0.44 [-1.40, 0.52]
Capozzi, 2016	-4.9	3.9	31	-5.4	3.77	29	14.9%	0.13 [-0.38, 0.64]
Courneya, 2007	1	4.7	82	0.1	5.46	82	40.6%	0.18 [-0.13, 0.48]
Cheng, 2021LIRT	0.5	6.2	27	-0.6	5.66	25	12.8%	0.18 [-0.36, 0.73]
Grote, 2018	0.5	6.3	10	-1.7	12.3	10	4.9%	0.22 [-0.66, 1.10]
Rogers, 2013	-0.3	16.33	8	-5.5	16.79	7	3.7%	0.30 [-0.73, 1.32]
Cheng, 2021HIRT	2.6	5.62	25	-0.6	5.66	25	11.9%	0.56 [-0.01, 1.12]
Christensen, 2014	-1.34	1.27	15	-2.56	2.42	15	7.1%	0.61 [-0.12, 1.35]
Total (95% CI)			**209**			**200**	**100.0%**	**0.23 [0.03, 0.42]**

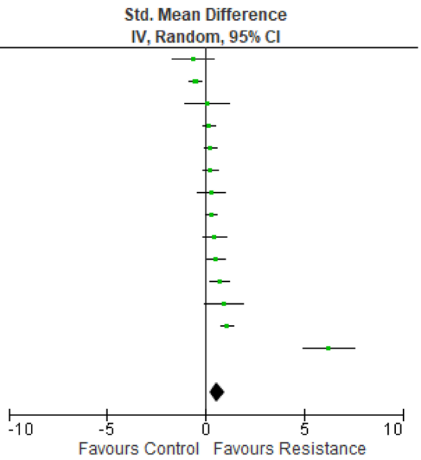
Heterogeneity: Tau² = 0.00; Chi² = 4.53, df = 7 (P = 0.72); I² = 0%
Test for overall effect: Z = 2.28 (P = 0.02)



(B)

Study or Subgroup	Resistance training Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
van Waart, 2018	-9.5	21.79	7	10.8	35.89	8	5.4%	-0.63 [-1.68, 0.42]
Courneya, 2007	8.4	11.96	82	13.41	6.8	82	8.3%	-0.51 [-0.82, -0.20]
Rogers, 2013	4.4	39.11	5	0.41	54.74	8	5.2%	0.07 [-1.04, 1.19]
Wiskemann, 2017	0.07	0.28	72	0.02	0.3	71	8.2%	0.17 [-0.16, 0.50]
van Waart, 2015	1.2	18.12	76	-3.4	21.43	77	8.3%	0.23 [-0.09, 0.55]
Schmidt, 2015	8.2	31.28	52	1.4	25.56	49	8.1%	0.24 [-0.16, 0.63]
Christensen, 2014	-5	62.79	15	-21	37.59	15	6.8%	0.30 [-0.42, 1.02]
Travier, 2015	6.45	22.9	102	-1.33	26.75	102	8.4%	0.31 [0.04, 0.59]
Mijwel, 2018NT	12.01	28.88	27	-2.29	31.44	21	7.4%	0.47 [-0.11, 1.05]
Segal, 2009	25.6	39.79	40	0.41	54.74	41	7.9%	0.52 [0.08, 0.96]
Mijwel, 2018T	16.32	33.34	38	-4.6	21.07	30	7.7%	0.72 [0.23, 1.22]
Zhao, 2015	1	36.48	11	-36	42.33	7	5.6%	0.91 [-0.10, 1.91]
Hong, 2020	27.45	31.53	94	-6.5	31.02	96	8.3%	1.08 [0.78, 1.39]
CeŠeiko, 2020	20	4.58	27	-9	4.58	28	4.5%	6.24 [4.92, 7.56]
Total (95% CI)			**648**			**635**	**100.0%**	**0.58 [0.18, 0.98]**

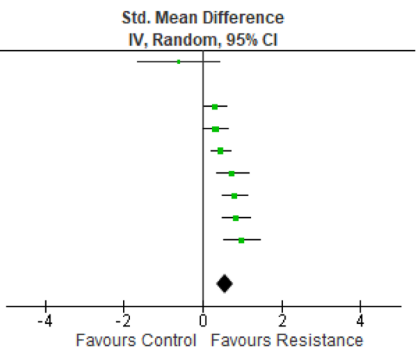
Heterogeneity: Tau² = 0.47; Chi² = 137.83, df = 13 (P < 0.00001); I² = 91%
Test for overall effect: Z = 2.83 (P = 0.005)



(C)

Study or Subgroup	Resistance training Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
van Waart, 2018	-0.4	16.48	7	11.7	20.59	8	3.5%	-0.61 [-1.65, 0.44]
Zhao, 2015	0	0	0	0	0	0		Not estimable
Hong, 2020	3	18.69	94	-3.2	20.18	96	15.2%	0.32 [0.03, 0.60]
van Waart, 2015	0.3	13.14	76	-3.9	12.57	77	14.3%	0.33 [0.01, 0.64]
Adamsen, 2009	7.45	15.52	135	0.15	16.91	134	16.5%	0.45 [0.21, 0.69]
Schmidt, 2015	35.49	46.19	52	4.18	35.91	49	12.0%	0.75 [0.34, 1.15]
Courneya, 2007	8.8	9.52	82	1.5	8.4	82	14.3%	0.81 [0.49, 1.13]
Wiskemann, 2017	6.48	0.76	71	-0.14	11	72	13.6%	0.84 [0.50, 1.18]
Segal, 2009	10.9	12.8	40	-2.5	14	41	10.6%	0.99 [0.53, 1.45]
Total (95% CI)			**557**			**559**	**100.0%**	**0.57 [0.36, 0.79]**

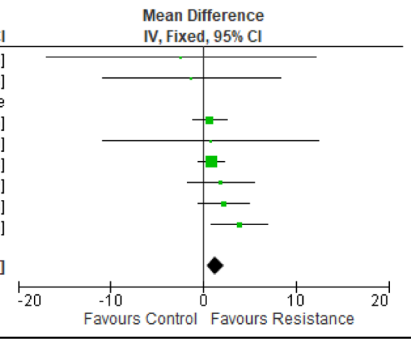
Heterogeneity: Tau² = 0.06; Chi² = 19.52, df = 7 (P = 0.007); I² = 64%
Test for overall effect: Z = 5.27 (P < 0.00001)



(D)

Study or Subgroup	Resistance training Mean [Kg]	SD [Kg]	Total	Control Mean [Kg]	SD [Kg]	Total	Weight	Mean Difference IV, Fixed, 95% CI
van Waart, 2018	3	12.2	8	5.4	16	7	0.4%	-2.40 [-16.96, 12.16]
Hacker, 2011	-2.6	11	8	-1.3	8.5	8	1.0%	-1.30 [-10.93, 8.33]
Zhao, 2015	0	0	0	0	0	0		Not estimable
van Waart, 2015	-1.2	5.9	77	-1.9	5.8	76	26.1%	0.70 [-1.15, 2.55]
Rogers, 2013	-1.6	9.4	8	-2.4	13.1	7	0.7%	0.80 [-10.89, 12.49]
Travier, 2015	0	4.9	102	-0.9	5.5	102	43.9%	0.90 [-0.53, 2.33]
Capozzi, 2016	-1.5	7.8	31	-3.4	6.5	29	6.8%	1.90 [-1.72, 5.52]
Mijwel, 2018NT	1.1	5.1	43	-1.1	6.4	29	11.6%	2.20 [-0.58, 4.98]
Mijwel, 2018T	0.5	5.5	31	-3.4	6.5	29	9.6%	3.90 [0.84, 6.96]
Total (95% CI)			**308**			**287**	**100.0%**	**1.32 [0.37, 2.27]**

Heterogeneity: Chi² = 4.52, df = 7 (P = 0.72); I² = 0%
Test for overall effect: Z = 2.73 (P = 0.006)



◂**Figure 3** A Forest plot of results for lean muscle mass. B Forest plot of results of lower limb strength. C Forest plot of results of upper limb strength. D Forest plot of results of handgrip strength

strength of the included studies [33]. However, its impact is limited by large 95% CI (SMD = 0.91, 95% CI −0.10 to 1.91) and a small sample size ($n = 18$). It is also important to consider the impact of Androgen Deprivation Therapy (ADT), a common prostate cancer treatment, as muscle atrophy is a common side effect [51]. Only one study involved prostate cancer patients and of them 61.2% of the overall sample were on ADT [35]. However, subgroup meta-analysis excluding prostate cancer patients resulted in minimal change in upper body or lower body strength (lower limb strength SMD = 0.59, 95% CI 0.16, 1.02, P =0.007; upper limb strength SMD = 0.53, 95% 0.31, 0.74, $P < 0.0001$).

The method and accuracy of strength assessment used must also be considered. High levels of reliability and reproducibility are reported with 1RM testing [52–54], and it is considered the gold standard field-based strength test [55]. A learning effect should be considered as to our knowledge no published protocols of included studies in this review described a familiarisation test for participants. Reliability studies recommend familiarisation sessions to ensure accurate baseline testing [56, 57]. Isokinetic dynamometry is considered the gold standard laboratory-based strength assessment [55] and is less likely to have a learning effect [58]. There is also some skill involved in carrying out strength tests such as the back and leg dynamometer used in one study [42]. Handheld dynamometry is limited by the strength and skill of the tester [59] but demonstrates high levels of reliability when compared to isokinetic dynamometry [60]. Grip strength assessment has been found to be unreliable in assessing changes in muscle strength following an exercise intervention in prefrail and frail older people (≥65 years of age) [61]. The National Cancer Institute reports that 66 is the median age of people diagnosed with cancer [62] and therefore many participants would fall into the category of prefrail or frail older people. Grip strength is also poorly correlated with changes in 1RM bench press in breast cancer survivors [63]. It is important for researchers and clinicians to consider that peripheral neuropathy, a common side effect of chemotherapy treatment, may negatively affect the participants' ability to grip. Standardisation of strength assessment in exercise oncology trials would greatly facilitate and support future meta-analysis.

A systematic review of exercise interventions during chemotherapy on muscle strength and endurance capacity reported improvements in leg press (4 to 33%) and chest press (12–38%) in intervention groups based on eight out of nine included studies [64]. Small improvements in muscle strength were also reported in 11 of 14 usual care control groups (1.3 to 6.5%). Results of this review are notably limited due to large heterogeneity between included studies by not defining intervention duration, supervised or unsupervised as part of its inclusion/exclusion criteria [64]. This review also made an error in its screening process by including a non-randomised control trial [65] in its analysis even though being an RCT is part of its inclusion criteria. Therefore, results should be interpreted with caution.

A Cochrane Review which included data from 912 female breast cancer patients found significant improvements in muscle strength following resistance training during adjuvant cancer treatment (SMD = 0.27; 95% CI 0.04 to 0.50; $I_2 = 59\%$) [66]. Adjuvant therapies included chemotherapy, radiation therapy and/or hormone therapy. This Cochrane review pooled all assessments of strength together and included both supervised and unsupervised exercise interventions for breast cancer patient which both have disadvantages as outlined previously [66].

A meta-analysis of six RCTs including patients both during and after cancer treatment found significant improvements in lean body mass with progressive resistance training (mean duration = 18 weeks) compared with usual care (WMD = +1.07kg, 95% CI 0.76–1.37, $P < 0.001$) [67]. The heterogeneity of the participants and interventions included makes interpretation difficult. Results of this meta-analysis are also limited as it did not consider baseline values. Only pooled post intervention values of the intervention and control groups were considered. Although the review included all cancer types, only early-stage breast cancer patients both during and after treatment were included in the meta-analysis of lean muscle mass [67].

Strengths of this review include the following: the librarian (D. M.) on the team has specialized training in literature searching and therefore an extensive search of the literature was carried out. Screeners (A. Mc. G., N. F. and N. M.) worked independently reducing risk of selection bias. Extensive documentation carried out ensures search methods can be fully reviewed and the study can be easily replicated. Only published RCTs were included in our meta-analysis to reduce selection bias and reduce risk of overestimation of effects [68]. We used mean change and SMD to take baseline values into consideration. We excluded studies that were not directly supervised to assess adherence more accurately.

There are several limitations of this review. No grey literature was searched for inclusion in this systematic review and meta-analysis and funnel plots suggest that publication bias may be present. There was high clinical heterogeneity in study design and moderate statistical heterogeneity for changes in lower limb and upper limb mass. There was a limited number of studies found meeting the inclusion and exclusion criteria. A significant majority of participants were female, diagnosed with breast cancer and treated with chemotherapy. Control group contamination and high LTF may

reduce the ability to detect significantly meaningful effect sizes between intervention and control groups.

Conclusions

This meta-analysis demonstrates the efficacy of resistance training for improving strength and lean mass during chemotherapy or radiation therapy in cancer patients. Further research is needed to determine its efficacy for changes in lean muscle mass in cancer populations at higher risk of muscle loss. Attention to the resistance training principles is critical to prescribing an optimal plan. The optimal resistance training prescription remains unclear.

Appendix 1

Search Strategy

EMBASE

1. 'Clinical trial'/de
2. 'Randomized controlled trial'/de
3. Randomization/de
4. 'Single blind procedure'/de
5. 'Double blind procedure'/de
6. 'Crossover procedure'/de
7. Placebo/de
8. 'Randomi?ed controlled trial*':ti,ab
9. Rct:ti,ab
10. 'Random allocation':ti,ab
11. 'Randomly allocated':ti,ab
12. 'Allocated randomly':ti,ab
13. (allocated NEAR/2 random):ti,ab
14. 'Single blind*':ti,ab
15. 'Double blind*':ti,ab
16. ((treble or triple) NEAR/1 (blind*)):ti,ab
17. Placebo*:ti,ab
18. 'Prospective study'/de
19. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
20. 'Case study'/de
21. 'Case report':ti,ab
22. 'Abstract report'/de or 'letter'/de
23. #20 OR #21 OR #22
24. #19 not #23
25. 'neoplasm'/exp OR 'cancer patient'/exp
26. (cancer NEAR/5 (patient* OR survivor*)):ti,ab
27. #25 OR #26
28. 'resistance training'/exp
29. ((resistance OR strength OR weight-bearing OR weight*) NEAR/3 (exercis* OR train*)):ti,ab
30. #28 OR #29
31. #24 AND #26 AND #30

Medline

1. Randomized controlled trials as Topic/
2. Randomized controlled trial/
3. Random allocation/
4. Double blind method/
5. Single blind method/
6. Clinical trial/
7. Exp Clinical Trials as Topic/
8. Or/1-7
9. (clinic$ adj trial$1).tw.
10. ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.
11. Placebos/
12. Placebo$.tw.
13. Randomly allocated.tw.
14. (allocated adj2 random).tw.
15. Or/9-14
16. 8 or 15
17. Case report.tw.
18. Letter/
19. Historical article/
20. Review of reported cases.pt.
21. Review, multicase.pt.
22. Or/17-21
23. 16 not 22
24. exp Neoplasms/
25. (Cancer adj5 (patient* OR survivor*)).ti,ab.
26. or/24-25
27. Resistance Training/
28. ((resistance OR strength OR weight-bearing OR weight*) adj3 (exercis* OR train*)).ti,ab.
29. or/27-28
30. and/23,26,29

CINAHL

1. MH randomized controlled trials
2. MH double-blind studies
3. MH single-blind studies
4. MH random assignment
5. MH pretest-posttest design
6. MH cluster sample
7. TI (randomised OR randomized)
8. AB (random*)
9. TI (trial)
10. MH (sample size) AND AB (assigned OR allocated OR control)

11. MH (placebos)
12. PT (randomized controlled trial)
13. AB (CONTROL W5 GROUP)
14. MH (CROSSOVER DESIGN) OR MH (COMPARATIVE STUDIES)
15. AB (CLUSTER W3 RCT)
16. MH ANIMALS+
17. MH HUMAN
18. S16 NOT S17
19. MH (ANIMAL STUDIES) NOT S17
20. TI (ANIMAL MODEL*) NOT MH (HUMAN)
21. S18 OR S19 OR S20
22. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15
23. S22 NOT S21
24. (MH "Neoplasms+") OR (MH "Cancer Patients") OR (MH "Cancer Survivors")
25. TI (Cancer N4 (patient* OR survivor*)) OR AB (Cancer N4 (patient* OR survivor*))
26. S24 OR S25
27. (MH "Resistance Training")
28. TI((resistance OR strength OR weight-bearing OR weight*) N2 (exercis* OR train*)) OR AB((resistance OR strength OR weight-bearing OR weight*) N2 (exercis* OR train*))
29. S27 OR S28
30. S23 AND S26 AND S29

Cochrane Library

1. [mh "Neoplasms"]
2. (Cancer NEAR/5 (patient* OR survivor*)):ti,ab,kw
3. #1 OR #2
4. [mh "Resistance Training"]
5. ((resistance OR strength OR weight-bearing OR weight*) NEAR/3 (exercis* OR train*)):ti,ab,kw
6. #4 OR #5
7. #3 AND #6

Web of Science

TS= ((Cancer NEAR/5 (patient* OR survivor*)) AND ((resistance OR strength OR weight-bearing OR weight*) NEAR/3 (exercise* OR train*))) AND (TS= clinical trial* OR TS=research design OR TS=comparative stud* OR TS=evaluation stud* OR TS=controlled trial* OR TS=follow-up stud* OR TS=prospective stud* OR TS=random* OR TS=placebo* OR TS=(single blind*) OR TS=(double blind)

Code availability Not applicable

Author contribution A. M. G. conceptualised the review. A. M. G., N. F. and N. M. were involved in the design and completion of the review. D. M. completed the search strategy. A. M. G. drafted the manuscript. N. F. edited and revised the manuscript prior to approval of the final version of the manuscript.

Data availability Any additional data required can be provided by corresponding author Aoife McGovern aomcgove@tcd.ie.

Declarations

Ethics approval Not applicable

Consent to participate Not applicable

Consent for publication Given.

Competing interests The authors declare no competing interests.

References

1. Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, Jemal A, Kramer JL, Siegel RL (2019) Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin 69:363–385
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394–424
3. Li T, Wei S, Shi Y, Pang S, Qin Q, Yin J, Deng Y, Chen Q, Wei S, Nie S (2016) The dose–response effect of physical activity on cancer mortality: findings from 71 prospective cohort studies. Br J Sports Med 50:339–345
4. Dolan RD, Almasaudi AS, Dieu LB, Horgan PG, McSorley ST, McMillan DC (2019) The relationship between computed tomography-derived body composition, systemic inflammatory response, and survival in patients undergoing surgery for colorectal cancer. J Cachexia Sarcopenia Muscle 10:111–122
5. Beuran M, Tache C, Ciubotaru C, Vartic M, Hostiuc S, Prodan A, Sartelli M, Griffiths EA, Hernandez M, Negoi I (2018) Sarcopenia is a predictive factor for postoperative morbidity and mortality in patients having radical gastrectomy for cancer. Chirurgia (Bucur) 113:678–686
6. Cushen SJ, Power DG, Murphy KP, McDermott R, Griffin BT, Lim M, Daly L, MacEneaney P, OS K, Prado CM, Ryan AM (2016) Impact of body composition parameters on clinical outcomes in patients with metastatic castrate-resistant prostate cancer treated with docetaxel. Clin Nutr ESPEN 13:e39–e45
7. Limpawattana P, Theerakulpisut D, Wirasorn K, Sookprasert A, Khuntikeo N, Chindaprasirt J (2018) The impact of skeletal muscle mass on survival outcome in biliary tract cancer patients. PLoS One 13:e0204985
8. Ni J, Zhang L (2020) Cancer cachexia: definition, staging, and emerging treatments. Cancer Manag Res 12:5597–5605
9. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, Jatoi A, Loprinzi C, MacDonald N, Mantovani G, Davis M, Muscaritoli M, Ottery F, Radbruch L, Ravasco P, Walsh D, Wilcock A, Kaasa S, Baracos VE (2011) Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 12:489–495

10. Fearon K, Arends J, Baracos V (2013) Understanding the mechanisms and treatment options in cancer cachexia. Nat Rev Clin Oncol 10:90–99
11. Inui A (2002) Cancer anorexia-cachexia syndrome: current issues in research and management. CA Cancer J Clin 52:72–91
12. Lønbro S, Dalgas U, Primdahl H, Johansen J, Nielsen JL, Aagaard P, Hermann AP, Overgaard J, Overgaard K (2013) Progressive resistance training rebuilds lean body mass in head and neck cancer patients after radiotherapy--results from the randomized DAHANCA 25B trial. Radiother Oncol 108:314–319
13. Cheema BS, Kilbreath SL, Fahey PP, Delaney GP, Atlantis E (2014) Safety and efficacy of progressive resistance training in breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat 148:249–268
14. Cormie P, Newton RU, Spry N, Joseph D, Taaffe DR, Galvao DA (2015) Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. Prostate Cancer Prostatic Dis 18:196
15. Heywood R, McCarthy AL, Skinner TL (2017) Safety and feasibility of exercise interventions in patients with advanced cancer: a systematic review. Support Care Cancer 25:3031–3050
16. Piraux E, Caty G, Aboubakar Nana F, Reychler G (2020) Effects of exercise therapy in cancer patients undergoing radiotherapy treatment: a narrative review. SAGE Open Medicine 8:2050312120922657
17. Storer TW, Dolezal BA, Berenc MN, Timmins JE, Cooper CB (2014) Effect of supervised, periodized exercise training vs. self-directed training on lean body mass and other fitness variables in health club members The Journal of Strength & Conditioning Research 28
18. Lacroix A, Hortobágyi T, Beurskens R, Granacher U (2017) Effects of supervised vs. unsupervised training programs on balance and muscle strength in older adults: a systematic review and meta-analysis. Sports Med 47:2341–2361
19. Sasso JP, Eves ND, Christensen JF, Koelwyn GJ, Scott J, Jones LW (2015) A framework for prescription in exercise-oncology research. Journal of Cachexia, Sarcopenia and Muscle 6:115–124
20. Boutron I, Altman DG, Moher D, Schulz KF, Ravaud P (2017) CONSORT statement for randomized trials of nonpharmacologic treatments: a 2017 update and a CONSORT extension for nonpharmacologic trial abstracts. Ann Intern Med 167:40–47
21. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M (2003) Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther 83:713–721
22. Day SJ, Altman DG (2000) Blinding in clinical trials and other studies. BMJ 321:504
23. Fu R, Vandermeer BW, Shamliyan TA, O'Neil ME, Yazdi F, Fox SH, Morton SC (2013) Handling continuous outcomes in quantitative synthesisMethods Guide for Effectiveness and Comparative Effectiveness Reviews [Internet]. Agency for Healthcare Research and Quality (US)
24. Friedrich JO, Adhikari NKJ, Beyene J (2008) The ratio of means method as an alternative to mean differences for analyzing continuous outcome variables in meta-analysis: a simulation study. BMC Med Res Methodol 8:32
25. Capozzi LC, McNeely ML, Lau HY, Reimer RA, Giese-Davis J, Fung TS, Culos-Reed SN (2016) Patient-reported outcomes, body composition, and nutrition status in patients with head and neck cancer: results from an exploratory randomized controlled exercise trial. Cancer 122:1185–1200
26. Adamsen L, Quist M, Andersen C, Moller T, Herrstedt J, Kronborg D, Baadsgaard MT, Vistisen K, Midtgaard J, Christiansen B, Stage M, Kronborg MT, Rorth M (2009) Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. BMJ 339:b3410
27. Travier N, Velthuis MJ, Steins Bisschop CN, van den Buijs B, Monninkhof EM, Backx F, Los M, Erdkamp F, Bloemendal HJ, Rodenhuis C, de Roos MA, Verhaar M, ten Bokkel HD, van der Wall E, Peeters PH, May AM (2015) Effects of an 18-week exercise programme started early during breast cancer treatment: a randomised controlled trial. BMC Med 13:121
28. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, Ladha AB, Proulx C, Vallance JKH, Lane K, Yasui Y, McKenzie DC (2007) Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. J Clin Oncol 25:4396–4404
29. Wiskemann J, Schmidt ME, Klassen O, Debus J, Ulrich CM, Potthoff K, Steindorf K (2017) Effects of 12-week resistance training during radiotherapy in breast cancer patients. Scand J Med Sci Sports 27:1500–1510
30. Ammitzboll G, Johansen C, Lanng C, Andersen EW, Kroman N, Zerahn B, Hyldegaard O, Wittenkamp MC, Dalton SO (2019) Progressive resistance training to prevent arm lymphedema in the first year after breast cancer surgery: results of a randomized controlled trial. Cancer 125:1683–1692
31. van Waart H, Stuiver MM, van Harten WH, Geleijn E, Kieffer JM, Buffart LM, de Maaker-Berkhof M, Boven E, Schrama J, Geenen MM, Meerum Terwogt JM, van Bochove A, Lustig V, van den Heiligenberg SM, Smorenburg CH, Hellendoorn-van Vreeswijk JA, Sonke GS, Aaronson NK (2015) Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial. J Clin Oncol 33:1918–1927
32. Grote M, Maihoefer C, Weigl M, Davies-Knorr P, Belka C (2018) Progressive resistance training in cachectic head and neck cancer patients undergoing radiotherapy: a randomized controlled pilot feasibility trial Radiation Oncology 13
33. Zhao SG, Alexander NB, Djuric Z, Zhou J, Tao Y, Schipper M, Feng FY, Eisbruch A, Worden FP, Strath SJ, Jolly S (2016) Maintaining physical activity during head and neck cancer treatment: results of a pilot controlled trial. Head Neck 38(Suppl 1):E1086–E1096
34. Rogers LQ, Anton PM, Fogleman A, Hopkins-Price P, Verhulst S, Rao K, Malone J, Robbs R, Courneya KS, Nanavati P et al (2013) Pilot, randomized trial of resistance exercise during radiation therapy for head and neck cancer. Head Neck 35:1178–1188
35. Segal RJ, Reid RD, Courneya KS, Sigal RJ, Kenny GP, Prud'Homme DG, Malone SC, Wells GA, Scott CG, Slovinec D'Angelo ME (2009) Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 27:344–351
36. Christensen JF, Jones LW, Tolver A, Jorgensen LW, Andersen JL, Adamsen L, Hojman P, Nielsen RH, Rorth M, Daugaard G (2014) Safety and efficacy of resistance training in germ cell cancer patients undergoing chemotherapy: a randomized controlled trial. Br J Cancer 111:8–16
37. van Waart H, Stuiver MM, van Harten WH, Geleijn E, de Maaker-Berkhof M, Schrama J, Geenen MM, Meerum Terwogt JM, van den Heiligenberg SM, Hellendoorn-van Vreeswijk JAJH, Sonke GS, Aaronson NK (2018) Recruitment to and pilot results of the PACES randomized trial of physical exercise during adjuvant chemotherapy for colon cancer. Int J Color Dis 33:29–40
38. Cheng DW, Hu X, Dai J, L L, Lv Y, Feng H, Zhang Y, Guo Y, Wang L (2021) Effect of tai chi and resistance training on cancer-related fatigue and quality of life in middle-aged and elderly cancer patients Chinese Journal of Integrative Medicine
39. CeSeiko RT, Tomsone SN, Eglītis J, Vetra A, Srebnijs A, Timofejevs M, Purmalis E, Wang E (2020) Heavy resistance training

in breast cancer patients undergoing adjuvant therapy. Med Sci Sports Exerc 52:1239–1247
40. Hong YW, Wu CB (2020) Effects of resistance exercise on symptoms, physical function, and quality of life in gastrointestinal cancer patients undergoing chemotherapy Integrative Cancer Therapies 19
41. Hacker ED, Larson J, Kujath A, Peace D, Rondelli D, Gaston L (2011) Strength training following hematopoietic stem cell transplantation. Cancer Nurs 34:238–249
42. Mijwel S, Backman M, Bolam KA, Olofsson E, Norrbom J, Bergh J, Sundberg CJ, Wengstrom Y, Rundqvist H (2018) Highly favorable physiological responses to concurrent resistance and high-intensity interval training during chemotherapy: the OptiTrain breast cancer trial. Breast Cancer Res Treat 169:93–103
43. Mijwel S, Cardinale DA, Norrbom J, Chapman M, Ivarsson N, Wengström Y, Sundberg CJ, Rundqvist H (2018) Exercise training during chemotherapy preserves skeletal muscle fiber area, capillarization, and mitochondrial content in patients with breast cancer. FASEB J 32:5495–5505
44. Schmidt T, Weisser B, Duerkop J, Jonat W, Van Mackelenbergh M, Roecken C, Mundhenke C (2015) Comparing endurance and resistance training with standard care during chemotherapy for patients with primary breast cancer. Anticancer Res 35:5623–5629
45. Winters-Stone KM, Neil SE, Campbell KL (2014) Attention to principles of exercise training: a review of exercise studies for survivors of cancers other than breast British Journal of Sports Medicine 48: 987-+
46. Slade SC, Dionne CE, Underwood M, Buchbinder R, Beck B, Bennell K, Brosseau L, Costa L, Cramp F, Cup E, Feehan L, Ferreira M, Forbes S, Glasziou P, Habets B, Harris S, Hay-Smith J, Hillier S, Hinman R et al (2016) Consensus on Exercise Reporting Template (CERT): modified Delphi Study. Phys Ther 96:1514–1524
47. Morton RW, Murphy KT, McKellar SR, Schoenfeld BJ, Henselmans M, Helms E, Aragon AA, Devries MC, Banfield L, Krieger JW, Phillips SM (2018) A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. Br J Sports Med 52:376–384
48. Balshaw TG, Massey GJ, Maden-Wilkinson TM, Morales-Artacho AJ, McKeown A, Appleby CL, Folland JP (2017) Changes in agonist neural drive, hypertrophy and pre-training strength all contribute to the individual strength gains after resistance training. Eur J Appl Physiol 117:631–640
49. Eklund D, Pulverenti T, Bankers S, Avela J, Newton R, Schumann M, Häkkinen K (2015) Neuromuscular adaptations to different modes of combined strength and endurance training. Int J Sports Med 36:120–129
50. Gabriel DA, Kamen G, Frost G (2006) Neural adaptations to resistive exercise: mechanisms and recommendations for training practices. Sports Med 36:133–149
51. Rhee H, Gunter JH, Heathcote P, Ho K, Stricker P, Corcoran NM, Nelson CC (2015) Adverse effects of androgen-deprivation therapy in prostate cancer and their management. BJU Int 115(Suppl 5):3–13
52. Barbalho M, Gentil P, Raiol R, Del Vecchio FB, Ramirez-Campillo R, Coswig VS (2018) High 1RM tests reproducibility and validity are not dependent on training experience, muscle group tested or strength level in older women Sports (Basel) 6: 171
53. Grgic J, Lazinica B, Schoenfeld BJ, Pedisic Z (2020) Test–retest reliability of the one-repetition maximum (1RM) strength assessment: a systematic review. Sports Medicine - Open 6:31
54. Rydwik E, Karlsson C, Frändin K, Akner G (2007) Muscle strength testing with one repetition maximum in the arm/shoulder for people aged 75 + - test-retest reliability. Clin Rehabil 21:258–265
55. Miller TA (2012) NSCA's guide to tests and assessments. Human Kinetics
56. Levinger I, Goodman C, Hare D, Toia D, Selig S (2007) The reliability of the 1RM strength test for untrained middle-aged individuals. Journal of science and medicine in sport / Sports Medicine Australia 12:310–316
57. Amarante do Nascimento M, Borges Januário RS, Gerage AM, Mayhew JL, Cheche Pina FL, Cyrino ES (2013) Familiarization and reliability of one repetition maximum strength testing in older women. The Journal of Strength & Conditioning Research 27:1636–1642
58. Glenn J, Gray M, Moyen N, Vincenzo J, Harmon K, Brown L (2018) Test-retest reliability and the learning effect on isokinetic fatigue in female master's cyclists. International Journal of Kinesiology and Sports Science 6:1–9
59. Bohannon RW, Kindig J, Sabo G, Duni AE, Cram P (2012) Isometric knee extension force measured using a handheld dynamometer with and without belt-stabilization. Physiother Theory Pract 28:562–568
60. Bohannon R (1990) Hand-held compared with isokinetic dynamometry for measurement of static knee extension torque (parallel reliability of dynamometers) Clinical physics and physiological measurement : an official journal of the Hospital Physicists' Association. Deutsche Gesellschaft für Medizinische Physik and the European Federation of Organisations for Medical Physics 11:217–222
61. Tieland M, Verdijk LB, de Groot LC, van Loon LJ (2015) Handgrip strength does not represent an appropriate measure to evaluate changes in muscle strength during an exercise intervention program in frail older people. Int J Sport Nutr Exerc Metab 25:27–36
62. Islami F, Ward EM, Sung H, Cronin KA, Tangka FKL, Sherman RL, Zhao J, Anderson RN, Henley SJ, Yabroff KR, Jemal A, Benard VB (2021) Annual Report to the Nation on the Status of Cancer, Part 1: National Cancer Statistics JNCI: Journal of the National Cancer Institute
63. Rogers BH, Brown JC, Gater DR, Schmitz KH (2017) Association between maximal bench press strength and isometric handgrip strength among breast cancer survivors. Arch Phys Med Rehabil 98:264–269
64. Van Moll CCA, Schep G, Vreugdenhil A, Savelberg HHCM, Husson O (2016) The effect of training during treatment with chemotherapy on muscle strength and endurance capacity: a systematic review. Acta Oncol 55:539–546
65. Lin K-Y, Shun S-C, Lai Y-H, Liang J-T, Tsauo J-Y (2014) Comparison of the Effects of a supervised exercise program and usual care in patients with colorectal cancer undergoing chemotherapy. Cancer Nurs 37:E21–E29
66. Furmaniak AC, Menig M, Markes MH (2016) Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev 9:CD005001
67. Strasser B, Steindorf K, Wiskemann J, Ulrich CM (2013) Impact of resistance training in cancer survivors: a meta-analysis. Med Sci Sports Exerc 45:2080–2090
68. Schulz KF, Chalmers I, Hayes RJ, Altman DG (1995) Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA 273:408–412