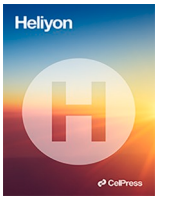
Heliyon 10 (2024) e29193

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Review article

Efficacy of aerobic and resistance exercises on cancer pain: A meta-analysis of randomised controlled trials

Philip D. Austin [a,*,1], Wei Lee [a,c,d], Daniel SJ. Costa [b,e,f,g], Alison Ritchie [a], Melanie R. Lovell [a,b]

[a] Department of Palliative Care, HammondCare, Greenwich Hospital, Sydney, New South Wales, Australia
[b] Sydney Medical School-Northern, University of Sydney, Sydney, New South Wales, Australia
[c] Improving Care for Palliative Aged, and Chronic Care through Clinical Research and Translation (IMPACCT), Faculty of Health, University of Technology Sydney, Sydney, New South Wales, Australia
[d] St Vincent's Clinical School, Faculty of Medicine, University of New South Wales, Sydney, New South Wales, Australia
[e] Kolling Institute, Northern Sydney Local Health District, Sydney, NSW, Australia
[f] School of Psychology, University of Sydney, Sydney, NSW, Australia
[g] The University of Sydney, Sydney, NSW, Australia

A B S T R A C T

Purpose: To evaluate effects of aerobic and resistance exercises for cancer-related pain in adults with and surviving cancer. Secondary objectives were to a) evaluate the effect of exercise on fatigue, psychological function, physical function, b) assess fidelity to exercise.
Design: A systematic search of MEDLINE, EMBASE, AMED, CINAHL and Cochrane Central Register of Controlled Trials was conducted to identify randomised controlled trials (RCTs) comparing aerobic and/or resistance exercise to control groups. The primary endpoint were changes in cancer-related pain intensity from baseline to post intervention. Meta-regression analysis evaluated predictors for heterogeneity between study findings. Tolerability was defined as reporting of exercise-induced adverse events while fidelity evaluated by reported intervention dropout.
Results: Twenty-three RCTs including 1954 patients (age 58 ± 8.5 years; 78 % women); 1087 (56 %) and 867 (44 %) allocated to aerobic/resistance exercise therapy and control group, respectively. Exercise therapy was associated with small to moderate decreases in cancer-related pain compared to controls (SMD = 0.38, 95 % CI: 0.17, 0.58). Although there was significant heterogeneity between individual and pooled study effects (Q = 205.25, $p < 0.0001$), there was no publication bias. Meta-regression including supervision, age, duration and exercise type as moderators showed no significant differences in reported outcomes. Analysis of secondary outcomes revealed a moderate effect for improvements in physical function, fatigue and psychological symptoms.
Conclusions: Aerobic and resistance exercises are tolerable and effective adjunct therapies to reduce cancer-related pain while also improving physical function, fatigue and mood. Future RCTs of dose, frequency, compliance and exercise type in specific cancer settings are required.

1. Introduction

Over 50 % of cancer patients experience pain both during and after anti-cancer treatments [1,2]. As cancer detection and treatments improve and survivorship increases, the management of cancer-related pain is becoming an increasing challenge for patients and treating oncologists [3,4]. Cancer-related pain is defined as pain caused by the primary cancer itself or metastases, its treatment in people with cancer or surviving cancer [5]. Tumours, surgery, chemotherapy, radiation therapy, targeted therapies, supportive care therapies including bisphosphates and diagnostic procedures can all cause pain in people with cancer [6]. Psychosocial factors also

* Corresponding author. Department of Palliative Care, HammondCare, Greenwich Hospital, 97-115 River Road, NSW, 2065, Australia.
E-mail address: paustin@hammond.com.au (P.D. Austin).
[1] Twitter handle: @PhilipAustin18.

https://doi.org/10.1016/j.heliyon.2024.e29193
Received 13 February 2023; Received in revised form 19 February 2024; Accepted 2 April 2024
Available online 6 April 2024

contribute to the experience of pain. Psychological morbidity and poor social support are common factors in cancer patients and are shown to significantly increase pain severity and pain-related disability. These multifactorial mechanisms further generate acute transient flare ups of ongoing pain known as breakthrough pain [7]. Although breakthrough pain can be attributed to non-malignant events, it is shown in cancer patients to be related to neoplastic lesions in 70–80 % of cases [8].

Despite the availability of guidelines such as the World Health Organisation [9] or Australian Cancer Pain Guidelines [10], cancer-related pain is often inadequately managed. Overall. Guidelines are not adequately adhered to over concerns that they are outdated and/or not specific to pharmacological and interventional options used with current cancer-related pain management [11]. Additionally, guideline recommendations for physical therapies may not be adhered to due to multiple patient, health practitioner and system barriers [12]. Thus, given the multifactorial contributors associated with cancer-related pain, non-pharmacological interventions are now being investigated and accessed by cancer patients and cancer survivors.

Exercise plays an increasing role in the management of cancer. Although current evidence shows exercise interventions have beneficial effects on physical and quality-of-life outcomes in cancer patients and survivors [13,14], their effects on cancer-related pain severity have been less thoroughly explored. For example, aerobic and resistance training are associated with improvements in physical, psychological, and behavioural symptoms in cancer patients and survivors [15,16]. Similarly, these exercises are shown to have anti-inflammatory effects such as decreases in IL-6, TNF-α and C-reactive protein [17,18], all of which are associated with increased levels of pain in people with cancer [19]. With increased attention by patients, clinicians and researchers towards the use of exercise interventions, it is important to identify the effectiveness of resistance and aerobic exercises in people reporting cancer-related pain. Given the multi-dimensional nature of pain and its impact on other symptoms and physical function, it is important to also consider the effects of aerobic and resistance exercise on the physical and psychological functional outcomes of pain during pain assessments [20,21]. Although previous reviews report the positive effects of exercise on pain in people with cancer, and survivors, findings are related to specific cancer types and are not systematic in design. Thus, the need for a systematic review and meta-analysis on the clinical effectiveness of aerobic and resistance exercises on pain and outcomes associated with cancer-related pain across cancer settings is required.

Thus, to identify the scope of data across cancer settings and subsequent clinical and research implications, our objective was to investigate the effects of aerobic and/or resistance exercise on cancer-related pain with people receiving anti-cancer treatment and those surviving cancer compared to control groups. Our secondary objective was to a) analyse the effect of aerobic and/or resistance exercise programs on fatigue, physical function and psychological symptoms in people with cancer-related pain compared to control

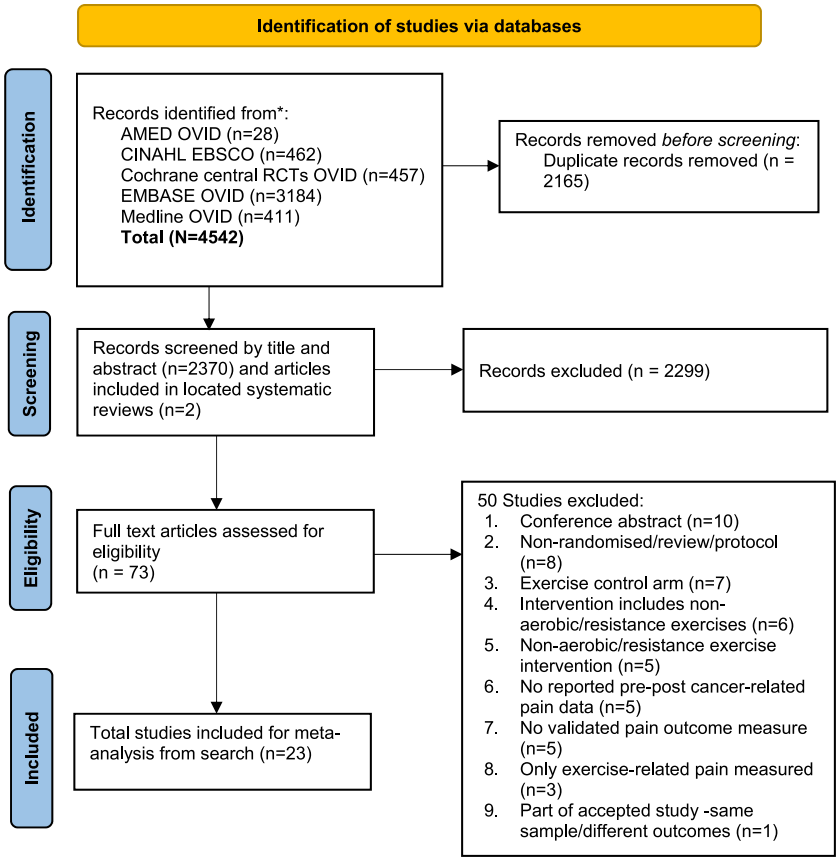


Fig. 1. PRISMA flow diagram of study identification and selection.

Table 1
Demographic data from included trials for meta-analysis (N-23).

Variable	No. of Trials (%)
Publication year	23
2000–2022	
Region of research	7 [31]
Americas	5
USA	1
Canada	1
Brazil	11 [47]
Europe	5
Germany	2
Sweden	1
Netherlands	1
Spain	1
Switzerland	1
UK	2 [9]
Asia	1
India	1
South Korea	3 [13]
Australia	
Sample size	4 [24]
≤50	12 [48]
51–100	7 [28]
≥101	
No. of participants	1954 (100.0)
Group Allocation	1087 [56]
Exercise	867 [44]
Control	
Mean age years (SD)	58.4 (8.3)
Female sex	1520 [74]
Cancer site	10 [44]
Breast	2 [12]
Head, neck and oral	2 [8]
Prostate	1 [4]
Leukemia	1 [4]
Lung	1 [4]
Pancreatic	6 [24]
Mixed	
Exercise type	10 [44]
Aerobic & resistance	7 [30]
Aerobic alone	6 [26]
Resistance alone	
Clinical settings	24 [75]
Oncology outpatient clinic	1 [4]
Hospital inpatient	

groups and b) to assess the tolerability and fidelity to these exercise programs.

2. Methods

2.1. Data searches and sources

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [22] to identify, screen and describe the protocols in this review. With registration at the international prospective register of systematic reviews register (PROSPERO identifier CRD42020208180) (https://www.crd.york.ac.uk/PROSPERO/), we conducted searches only for randomised controlled trials and randomised controlled pilot trials written in English identified by title and abstract in Ovid (Medline, Embase, AMED, Cochrane Central Register of Controlled Trials) and CINAHL (Supplementary File 1) published from January 2000 to August 2022. Additional studies referenced in related reviews were also included.

2.2. Study eligibility criteria

RCTs involving adults (age ≥18 years) analysing the effects of aerobic and/or resistance interventions on cancer-related pain versus control arms including waitlist, treatment as usual (TAU) and other interventions including passive physical therapy and breathing exercises. Studies were included regardless of exercise intensity, duration, mode of supervision (individual, group, unsupervised) or delivery of intervention (e.g., supervised versus home-based or mixed). Studies focusing on other cancer-related outcomes where pain was reported as a secondary outcome were also included. Studies examining the effects of exercise on chemotherapy-induced

Table 2
Characteristics of included studies.

Author/ year	RCT design	Setting	Patients (N)	Age means (SD)	Female (%)	Cancer type	Tumour stage	Exercise intervention	Exercise dose	Frequency/ Duration	Control intervention(s)	Pain outcome(s)	P values
Backman/ 2014	2-arm (non-blind)	Outpatient (MS)	77	54	90	BR/CRC	I-IV	Part supervised progressive walking	10k steps	Daily for 10 weeks	TAU/no restriction on physical activity	EORTC QLQ-C30	0.04
Bade/2021	2-arm (non-blind)	Outpatient (SS)	40	64.9 (8.7)	75	Lung	III-IV	Progressive walking (home-based)	Increase of 400 steps per day from baseline	Daily for 3 months	TAU/no additional advice	EORTC-QLQ-C30	0.95
Baglia/ 2019	2-arm (single blind)	Outpatient (SS)	121	61.3 [7]	100	BR + AI	I-III	Supervised progressive aerobic (walk)/RET (up/low body)	Aerobic – 150 min (60–80 % HRM) RET – 8–12 reps for 3 sets	RET – 2/week, Aerobic – 150 min/week for 12 months	TAU/no additional advice	SF-36	<0.001
Cantarero/ 2012	2-arm (single blind)	Outpatient (SS)	66	47.5 (8.5)	100	BR survivors	I–III	Supervised progressive aerobic/RET (water)	1-h sessions	3/week for 8 weeks	Healthy lifestyle recommendations	VAS (0–10) - neck pain/ shoulder/ axillary pain	0.001
Chatterjee/ 2017	2-arm (single blind)	Outpatient (SS)	94	45.5	10	Oral	I–IV	Supervised PRET – shoulder	2 sets – 10 reps at 25 % of 1 rep 100 %	Daily for 6 weeks	Daily active ROM exercises	SPADI	0.02
Cormie/ 2013	2-arm (single blind)	Outpatient (SS)	20	72.2 (7.2)	0	Prostate	> III	Supervised PRET Major muscle groups)	2-4 sets of 12-8 rep max for 8 exercises	X2/week for 12 weeks	TAU/no additional advice	VAS (0–10)/ FACT Bone pain	VAS - 0.6 FACT - 0.3
Dimeo. 2004	2-arm (non-blind)	Outpatient (SS)	69	58	28	Lung/GI	I–IV	Supervised progressive aerobic (bike)	5 × 3 mins/ day to 3 × 8 mins/day at 50 RPM (80 % HRM)	X5/week for 3 weeks	Muscle relaxation program	EORTC QLQ-C30	0.8
Fields/ 2016	2-arm (non-blind)	Outpatient (SS)	40	63 [8]	100	BR + AI	< III	Brisk walking (Home)	Progressing from 1 to 4 × 30 min	3-5/week for 12 weeks	TAU + physical activity booklet	BPI/SF-36	Not reported
Galvao/ 2013	2-arm (non-blind)	Outpatient (MS)	100	71.7 (10.6)	0	Prostate	II–IV	Supervised aerobic (walk bike) PRET (up/low body	Aerobic – 20–30 min PRET – progressing from 12 to 6 rep max for 2–4 sets	2/week for 12 months	Physical activity booklet/pedometer (150 mis/week)	SF-36	0.5
Hayes/ 2013	3-arm (single blind)	Outpatient (MS)	194	52.4 (8.4)	100	BR	0 - III	Supervised progressive aerobic/RET (up/low body)	20-30 to 45+ mins	4/week for 8 months	TAU/encouraged to maintain physical activity	NRS (0–100)	0.4
Irwin/2015	2-arm (non-blind)	Outpatient (MS)	121	61.3	100	BR survivors + AI	0-III	Supervised progressive aerobic	Aerobic – 150 min (60–80 % HRM)	RET – 2/week, Aerobic – 150	TAU/continue usual activities	BPI/ WOMAC	0.001

(*continued on next page*)

Table 2 (*continued*)

Author/ year	RCT design	Setting	Patients (N)	Age means (SD)	Female (%)	Cancer type	Tumour stage	Exercise intervention	Exercise dose	Frequency/ Duration	Control intervention(s)	Pain outcome(s)	P values
								(walk)/RET (up/low body)	RET – 8–12 reps for 3 sets	min/week for 12 months			
Knols/ 2011	2-arm (single blind)	Outpatient (SS)	131	61 (7.7)	41	Leukemia/ lymphoma	Not stated	Supervised aerobic (bike)/ PRET (up/low body	Aerobic - 20 min at 50–60 % to 70–80 % HRM RET – not reported	2/week for 12 weeks	TAU/no additional advice	EORTC QLQ-C30 (pain)	0.4
McNeely/ 2004	2-arm (non-blind)	Outpatient (SS)	17	52 [32–73, 76–78]	18	H/N	I–IV	Supervised PRET (up body)	Session duration not reported	3/week for 12 weeks	Passive ROM/ stretching	SPADI	0.04
Mijwel/ 2018	3-arm (non-blind)	Outpatient (SS)	206	63.8 (8.3)	100	BR Ca (pre-CT)	I-IIIa	Supervised progressive aerobic (bike)/ RET (major muscle groups)	Aerobic – 20 min with increasing effort PRET – 2–3 sets of 12 reps (70–80 % max of 1 rep max	2/week for 16 weeks	Written physical advice sheet	PPTs	Trapezius/ gluteus (non-taxanes side - <0.001
Nyrop/ 2017	2-arm (non-blind)	Outpatient (SS)	62	53.7 (4.5)	100	BR survivors + AI	I -IV	Supervised aerobic (walk)	150 min/week	150 min/week for 6 weeks	Waitlist control	VAS (0–10)/ WOMAC	No P values Effect size – 0.14/0.25
Park JH/ 2017	2-arm (single blind)	Inpatient (SS)	63	64.9 (8.4)	100	BR Ca	I–III	Supervised progressive aerobic (walk)/RET (arm strength)	3 × 20 min	5/week for 4 weeks	Manual lymphatic drainage	VAS (0–100)	<0.0001
Paulo/ 2019	2-arm (non-blind)	Community	36	46.7 (7.9)	100	BR Ca survivors + AI	I–III	Supervised progressive aerobic (walk)/RET (up/low body)	Aerobic – 30 min/day at 60–80 % HRM RET – 40 min/ day	3/week for 9 months	Stretch/relaxation	EORTC QLQ-C30	0.001
Rief/2014	2-arm (non-blind)	Outpatient (SS)	60	62.7 (10.5	45	Mixed	IV	Initial supervised/ then home paraspinal RET	30 min	3/week over course of radiotherapy	Passive physical therapy and breathing exercises	VAS (0–100)	0.4
Rief/2014a	2-arm (non-blind)	Outpatient (SS)	60	62.7 (10.5)	45	Mixed	IV	Initial supervised/ then home Paraspinal RET	30 min	3/week for 12 weeks	Passive physical therapy and breathing exercises	VAS (0–10)	<0.001
Rief/2014b	2-arm (non-blind)	Outpatient (SS)	60	54.3 (11.3)	45	Mixed	IV	Initial supervised/ then home Paraspinal RET	30 min	3/week over course of radiotherapy	Passive physical therapy and breathing exercises	EORTC QLQ-BM22	<0.001
Schmidt/ 2015	3-arm (non-blind)	Outpatient (SS)	67	46.0	100	BR Ca	Not stated	Supervised progressive aerobic/RET (up/low body)	Aerobic/RET – 60 min	2/week for 12 weeks	TAU	EORTC QLQ-C30	ET – 0.07 PRET – 0.54

(*continued on next page*)

Table 2 (*continued*)

Author/ year	RCT design	Setting	Patients (N)	Age means (SD)	Female (%)	Cancer type	Tumour stage	Exercise intervention	Exercise dose	Frequency/ Duration	Control intervention(s)	Pain outcome(s)	P values
van Waart/ 2015	3-arm (non-blind)	Outpatient (MS)	230	50.7 (9.1)	99	BR/CRC	I–III	Supervised vs home progressive aerobic (steep ramp) RET – (6 large muscle groups)	Aerobic – 30 min RET – 2 sets of 8 reps at 80 % of 1 rep max		Care guidelines/no exercise advice	EORTC QLQ-C30	Supervised <0.001 Home – 0.11
Yeo/2012	2-arm (non-blind)	Outpatient (SS)	102	66.5	50	Pancreatic	Ia, b - III	Brisk walking (Home)	10 progressing to 25–30 min		Usual activities/ exercise	VAS (0–10)/SF-36	0.05

Abbreviations AI – Aromatase inhibitors, BR Ca – breast cancer, CP – cancer-related pain BPI – Brief Pain Inventory, CRC – colorectal cancer, EORTC QLQ - European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire, ET – endurance training, GI – gastrointestinal, HRM – heart rate maximum, MS – multi-site, NP – neuropathic pain, NRS – numerical rating scale, PPTs – pressure point thresholds, PRET – progressive resistance exercise training, RET – resistance exercise training, ROM – range of motion, SF-36 – Short Form 36, SPADI - Shoulder Pain and Disability Index, SS – single site, TAU – treatment as usual, WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index, VAS - Visual analogue scaleRisk of Bias.

peripheral neuropathies were excluded as this cluster of signs and symptoms has been previously reviewed [23,24]. We included studies where at least one trial arm used either aerobic and/or resistance-type exercise interventions with at least one non-exercise, passive physical therapy, TAU, non-aerobic/resistance exercises (see excluded interventions), or waitlist control. Typical aerobic interventions include walking, jogging, aerobic classes, cycling, swimming, aqua-aerobics, or organised sports (e.g., tennis, football). Typical resistance exercises include weight training (e.g., dumbbells, barbells), resistance elastic band, participant bodyweight or a combination of both. Studies were excluded if exercises such as Pilates, mind-body practices including Yoga, Tai-chi and Qigong, dancing and stretching were included in intervention protocols. Further studies were not included if they were 1) published as conference abstracts, 2) non-randomised, review, study protocol or case-report design, 3) none or exercise control arm(s), 4) duplicates, 5) mixed aerobic and/or resistance with non-aerobic and/or resistance exercises, 6) non-aerobic/resistance exercise intervention (e.g., yoga, dance, Pilates), 7) no reported pre-post cancer-related pain data, 8) no validated pain outcome-measure, 9) pain measured due to exercise intensity rather than due to cancer and 10) Part of an accepted study with the same sample but different outcomes.

2.3. Study selection process and risk-of-bias assessment

To determine inclusion eligibility, titles and abstracts from results of the search were independently screened and data extracted by three authors (PA, AR, WL) using Covidence systematic review software [25]. All reviewers read and agreed on the included articles. At each stage disagreements were resolved through discussion between PA, AR, WL and ML. To ensure accurate study selection, we followed The American College of Sports Medicine definitions for aerobic and resistance exercise [26]. PA and AR independently assessed selected studies for risk of bias using Cochrane Risk of Bias tool for randomized trials (RoB2) for individual studies [27]. Conflicts of agreement were resolved by discussion with third and fourth review authors (WL, ML). For risk of bias assessment across studies, we used the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework measures of treatment effect [28].

2.4. Primary outcomes

All studies accepted for this review included pre-exercise scores at baseline to post exercise scores reported at the end of each study intervention. For primary outcomes, we included self-reported pain-rating measures validated in cancer settings including the visual analogue scale (VAS) [29], numerical pain rating scale (NPRS) [29], Brief Pain Inventory (BPI) [30], 36-Item Health Survey Instrument (SF-36), European Research and Treatment for Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) [31] and the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) pain scale [32]. We also included outcome measures reporting pain intensity in specific locations such as the Shoulder Pain and Disability Index (SPADI) [33] as well as outcome measures reporting pain with sensory testing such as Pressure Pain Thresholds (PPT), also validated in cancer settings [34]. To adjust for the effects of delayed onset muscle soreness after initial exercise sessions, we analysed baseline pain scores prior to initial exercise sessions and pain scores after the final exercise session of the program [35].

2.5. Secondary outcomes

We did not include search criteria for any associated cancer or exercise outcomes. However, we included secondary symptom and exercise-related outcomes analysed in accepted studies as they often assessed and managed together [36] while showing strong interrelationships with or impact pain in people with cancer [37–39]. For example, people with moderate to severe cancer-related pain report greater levels of fatigue [38] and psychological distress [39] compared to those reporting only mild cancer-related pain. Thus, given the associations between cancer-related pain and these variables, we further assessed the effects of aerobic and resistance exercises on fatigue and psychological outcomes including anxiety, stress and depression as analysed in accepted studies. We further assessed exercise-related outcomes including muscle strength, joint range of motion, heart rate, VO2 max/peak (gold-standard test for determining oxygen consumed per kilogram per minute), power and endurance.

2.6. Data analysis

We conducted meta-analysis using the *metafor* package in R [40], using a random-effects model due to expected heterogeneity in study characteristics. The estimate of exercise effect size was the standardised mean difference (SMD) in pre-post intervention change scores between intervention and control groups [41]. Because the included studies reported standard deviations at pre-intervention and post-intervention separately rather than standard deviations of the change scores, we estimated the standard deviations of the change scores using the formula $SD_{change} = \sqrt{SD_{pre}{}^2 + SD_{post}{}^2 - 2(r \times SD_{pre} \times SD_{post})}$, where r is the correlation between pre- and post-measures. To calculate this, we used three estimates of this correlation (0.5, 0.6, 0.7). Because most studies contributed multiple outcomes to each meta-analysis, and most had multiple interventions, we analysed the data using a multivariate model, where study identification number was modelled as a random effect. We examined the pooled SMD and its 95 % confidence interval, as well as a heterogeneity statistic, Cochran's *Q*. Results of the meta-analyses are summarised in forest plots, and funnel plots were used to examine publication bias (the Egger test and trim-and-fill method were, at the time of writing, not available for multivariate models in the Metafor package. On PRISMA recommendations for systematic review reporting, we performed a meta-regression analysis to determine possible predictors for heterogeneity between study findings across all outcomes [42]. Separate meta-analyses were run for

Table 3
Risk of bias.

Study	Sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of assessors	loss to follow-up/ ITT analysis reported	Free of selective reporting	Free of other bias sources	Appraisal of quality	Comment
Backman et al.	Yes	Unclear	No	No	Unclear	Yes	Unclear	High risk	High and unclear RoB for one or more key domains
Bade et al.	Unclear	unclear	No	No	Unclear	yes	Unclear	High Risk	High and unclear RoB for one or more key domains
Baglia et al.	Yes	Yes	No	Yes	Yes	Yes	Yes	Unclear risk	High RoB in only 1 domain
Cantarero et al.	Yes	unclear	No	Yes	Yes	Yes	Unclear	High risk	High and unclear RoB for one or more key domains
Chatterjee et al.	Yes	Unclear	No	Yes	Yes	Yes	Unclear	High risk	Unclear and high RoB for one or more key domains
Cormie et al.	Yes	Yes	No	Yes	Yes	Yes	unclear	Unclear risk	High and unclear RoB in only 1 domain
Dimeo et al.	Yes	Yes	No	No	Yes	Yes	Yes	High risk	High RoB for one or more key domains
Fields et al.	Yes	Yes	No	No	Unclear	Yes	unclear	High risk	High RoB for one or more key domains
Galveo et al.	Yes	Unclear	No	No	Yes	Yes	Yes	High risk	High RoB for one or more key domains
Hayes et al.	Yes	Yes	No	Yes	Yes	Yes	unclear	Unclear risk	High and unclear RoB in only 1 domain each
Irwin et al.	Yes	Unclear	No	No	Yes	Yes	Yes	High risk	High and unclear RoB for one or more key domains
Knols et al.	Yes	Yes	No	Yes	Yes	Yes	Yes	Unclear risk	High RoB in only 1 domain
McNeely et al. 04	Yes	Unclear	No	No	Yes	Yes	Yes	High risk	High RoB for one or more key domains
Mijwel et al.	Yes	Yes	No	No	Yes	Yes	Unclear	High risk	High RoB for one or more key domains
Nyrop et al.	Unclear	No	No	No	Yes	Yes	Yes	High risk	High RoB for one or more key domains
Park et al.	Unclear	Yes	No	Yes	Yes	Yes	Unclear	High risk	High and unclear RoB for more than key domain
Paulo et al.	Unclear	Unclear	No	No	Yes	Yes	Unclear	High risk	High and unclear RoB for more than key domain
Rief et al.	Unclear	Unclear	No	No	Unclear	Yes	Unclear	High risk	High and unclear RoB for more than key domain
Rief et al. (a)	Unclear	Unclear	No	No	Unclear	Yes	Unclear	High risk	High and unclear RoB for more than key domain

(*continued on next page*)

Table 3 (*continued*)

Study	Sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of assessors	loss to follow-up/ ITT analysis reported	Free of selective reporting	Free of other bias sources	Appraisal of quality	Comment
Rief et al. (b)	Unclear	Unclear	No	No	Unclear	Yes	Unclear	High risk	High and unclear RoB for more than key domain
Schmidt et al.	Yes	Yes	No	No	Unclear	Yes	Unclear	High risk	High and unclear RoB for more than key domain
Van Waart et al.	Yes	Unclear	No	No	Yes	Yes	Yes	High risk	High and unclear RoB for more than key domain
Yeo et al.	Yes	Unclear	No	No	Yes	Unclear	Unclear	High risk	High and unclear RoB for more than key domain

secondary outcome variables (fatigue, psychological function, ROM, strength, exercise, and physiological measures). In all analyses, a higher positive SMD indicates the superiority of the intervention over the control groups. We also included meta-regression analysis to determine predictors for heterogeneity between study findings across all outcomes. Where meta-regression was not possible due to a lack of within-trial sub-group analysis we included a narrative review.

3. Results

3.1. Study selection

Our systematic search retrieved 4542 potential articles (Fig. 1). After removing duplicates using EndNote citation management software [43] we retained 2377 articles. Using Covidence systematic review management software [44], we excluded 2299 studies based on titles and abstracts and retained 78 full-text records for assessment. A further 57 studies were deemed ineligible. Of these, seven studies did not report pre-post intervention mean pain outcome scores. After contacting corresponding authors, one returned relevant data [45], Three reported no access to data [46–48] and three did not respond [49–51]. Twenty-one RCTs were included [45, 52–71] while two hand-searched studies were further included from excluded systematic reviews [72,73]. A total of 23 studies were included for analysis.

3.2. Study characteristics

The 23 trials included a total of 1954 participants; 1087 (56 %) and 867 (44 %) were allocated to exercise and control groups respectively (Table 1). Seventy-eight percent of participants were women across all studies. Mean age across all studies was 57.9 years (SD = 8.5), while the mean sample size was 85 (exercise n = 47, control n = 38). Nineteen studies had two arms with four studies using three arms. Most studies (n = 10) investigated the effects of exercise on cancer-related pain in women with breast cancer, four of which recruited cancer survivors. Two studies recruited patients with head, neck and oral cancers, two with prostate and one for pancreatic and lung cancers. Six further studies reported mixed cancer diagnoses among their samples. All but one study recruited from hospital oncology outpatient settings, five of which were multisite and two enrolled participants directly from the community. Ten studies delivered a combination of progressive aerobic and resistance exercise while seven investigated aerobic exercise with walking and cycling or a combination of these exercises. Six studies delivered progressive resistance exercises for muscles in upper, lower extremities or paraspinal regions. Nine studies reported pain as their primary outcome, while 14 reported cancer-related pain as a secondary outcome [52,53,57,59–62,66,67,69–73]. In these studies, most reported a combination of primary outcomes including fatigue, quality of life (QoL), physical function/performance, and feasibility/efficacy. Specific study characteristics are found in Table 2.

3.3. Exercise attrition and program adherence

Attrition rates ranged from 0 % to 31 % with a mean attrition rate across exercise arms of 11 % and 14 % among control arms. Across exercise arms, most participants withdrew due to effects of cancer treatment (especially aromatase inhibitors and chemotherapy), tumour progression, non-exercise related accidents and death. Only two studies (9 % of included studies) cited exercise-related adverse events due to pre-existing musculo-skeletal conditions (n = 5) [58,59] and reported fatigue (n = 1) [52], thus showing that aerobic and resistance exercise programs are feasible and well-tolerated across a many cancer settings. Thirteen of the 23 accepted studies reported exercise intervention adherence rates that ranged from 70 % to 100 % with a mean adherence rate of 86 %

across intervention arms.

All trials were at substantial risk of performance bias where RCTs showed research personnel and participants knew assigned interventions (Table 3). Adequate sequence generation and allocation concealment was reported in 16/23 articles (70 %) and 9/23 (39 %) respectively. Nine of 23 articles (39 %) reported blinding of assessors while 16/23 (70 %) reported intention-to-treat analysis. The quality of evidence (GRADE) was rated as 'low quality' due to the trial design where it was difficult to blind in all trials, study personnel; and in two thirds of trials, assessors. Publication bias and heterogeneity are reported for cancer-related pain and secondary outcomes below.

3.3.1. *Meta-analysis on the effects of aerobic and resistance exercise on cancer-related pain intensity*

Meta-analysis of 45 outcomes across 23 studies [45,52–73] show that pain intensity after exercise programs were significantly lower in intervention groups compared to control groups (SMD = 0.38, 95 % CI: 0.17, 0.58) (Fig. 2). There was significant heterogeneity between individual study effects and the pooled effect across studies ($Q = 142.09$, $p < 0.0001$). The funnel plot (Fig. 3) is symmetric, indicating the absence of publication bias, although both plots show two extreme values, one favouring control over intervention, and the other favouring intervention over control. A wide range of validated pain outcome measures for pain in people with cancer were used across included studies, as illustrated in Table 1.

3.4. *Meta-analysis on the effects of aerobic and resistance exercise on secondary outcome measures*

All standard mean differences for primary and secondary outcome measures are found in supplementary file 1 while forest and funnel plots for secondary outcomes are in supplementary file 2.

3.5. *Changes in fatigue*

Meta-analysis of 13 studies [52–54,57,60,63,65,66,69–72], with 20 outcomes show that fatigue after exercise studies were significantly lower in intervention groups compared to control groups (SMD = 0.23, 95 % CI: 0.01, 0.4). There was significant heterogeneity between individual study effects and pooled effects across studies ($Q = 54.21$, $p < 0.0001$). Both funnel and forest plots show more values that favour intervention over control.

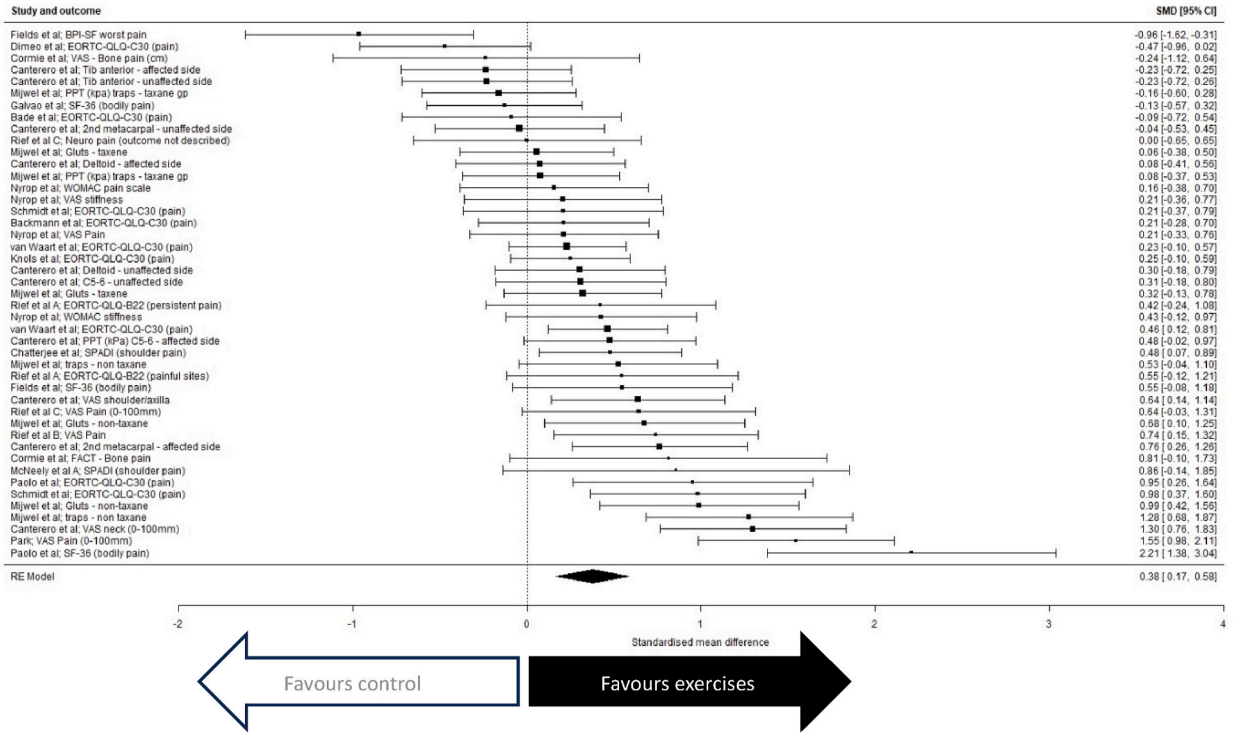


Fig. 2. Pooled effects of aerobic and resistance exercise compared with control groups on cancer-related pain severity (**please note, several studies used multiple self-report pain related outcomes while two studies also include pressure pain threshold measures**).

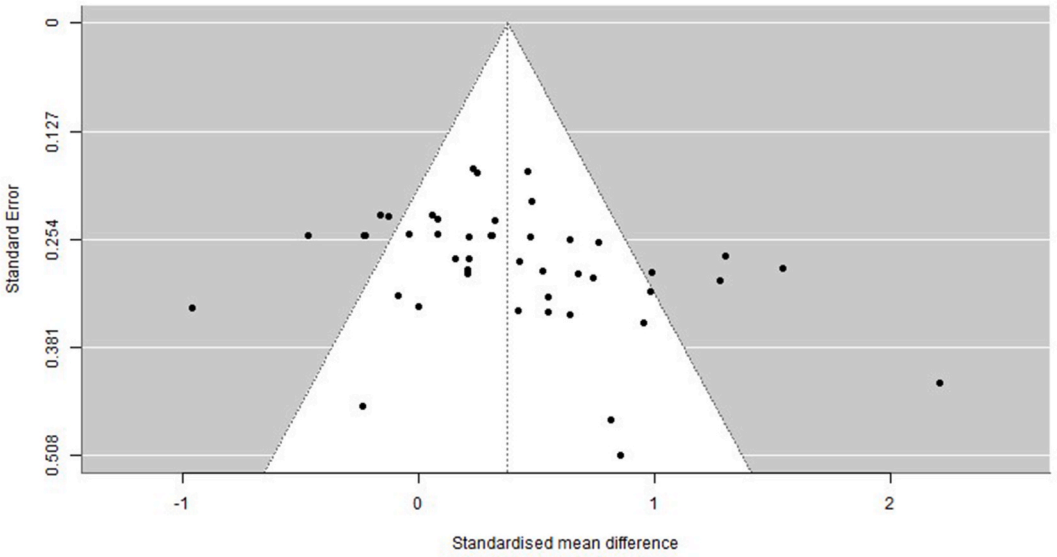


Fig. 3. A funnel plot showing absence of publication bias of studies investigating effects of aerobic and/or resistance exercise for cancer-related pain relief.

3.6. Changes in psychological symptoms

Meta-analysis of nine studies [52,53,58,59,61,63,65,66,69] with 11 outcomes showed that psychological symptoms after exercise study periods were significantly reduced in intervention groups compared to control groups (SMD = 0.21, 95 % CI: 0.04, 0.39). Heterogeneity was not significant between individual study effects and the pooled study effect ($Q = 7.5$, $p = 0.68$). The funnel plot is symmetric, although both plots show one extreme value that favours intervention over control.

3.7. Changes in range of motion

Meta-analysis of 3 studies [56,61,64], with 19 outcomes showed that ROM after exercise study periods were significantly greater in intervention groups compared to control groups (SMD = 0.79, 95 % CI: 0.04, 1.63). Heterogeneity was significant between individual study effects and the pooled effect across studies ($Q = 189.1$, $p < 0.0001$). The funnel plot is asymmetric, mostly driven by two large effects favouring the intervention in a small study.

3.8. Changes in strength

Meta-analysis of five studies [57,62,69,70,73], with 27 outcomes showed that strength after exercise study periods were significantly greater in intervention groups compared to control groups (SMD = 0.33, 95 % CI: 0.!7, 0.49). Heterogeneity was not significant between individual study effects and the pooled effect across studies ($Q = 35.1$, $p = 0.11$). The funnel plot is symmetric, although with one extreme observation that favoured the intervention.

3.9. Physical performance

Meta-analysis of seven studies [45,53,63,67,70,71,73], using nine outcomes showed that physical performance after exercise programs were significantly greater in intervention groups compared to control groups (SMD = 0.74, 95 % CI: 0.32, 1.16). Heterogeneity was significant between individual study effects and the pooled effect across studies ($Q = 35.3$, $p < 0.0001$). The funnel plot shows some asymmetry.

3.10. Changes in physiological function

Meta-analysis of six studies [45,52,62,69,70,72], with 13 outcomes showed that physiological outcomes (VO2-peak, power maximum, endurance-70 % maximum, heart-rate) after exercise study periods were significantly higher in intervention groups compared to control groups (SMD = 0.37, 95 % CI: 0.24, 0.51). Heterogeneity was not significant between individual study effects and pooled effects across studies ($Q = 16.7$, $p = 0.16$). The funnel plot is symmetric, although with one extreme observation that favoured the intervention.

3.11. Predictors for effects of exercise on primary and secondary outcomes

In each meta-regression model, there were four predictors: supervision status (unsupervised vs. supervised), type of exercise (resistance vs. aerobic vs. both), duration of exercise (2 months vs. 2–6 months vs. >6 months), and age (<50, 50–61, >61). years Unfortunately, although demographic data in most included studies show cancer staging sub-groups, these sub-groups were not independently analysed in any included study. Additionally, only 13/23 studies included adherence to exercise programs and would have substantially reduced the number of studies available for meta-regression, so we decided to exclude adherence as a moderator. The only outcome variables with significant predictors in the meta-regression were for psychological symptoms and exercise performance. Resistance exercise had a significantly lower mean effect size compared to aerobic exercise for both psychological symptoms (−1.05, $p = .03$) and exercise performance (−1.00, $p = 0.03$). Additionally, participants aged 51–60 show significantly lower mean effect size on exercise performance compared to those under 50 (−1.10, p = 0.001).

4. Discussion

Our findings show that aerobic and resistance exercise therapies are efficacious adjuncts in relieving pain in in adults with ongoing cancer and surviving cancer across a wide range of patient populations. Although this heterogeneity challenges interpretation of results for specific cancer-types and cancer stages, our findings concerning the beneficial effects of aerobic and resistance exercise can be generalised across a wide range of cancer settings while further highlighting sampling areas where research is needed. Importantly, the dropout rate across exercise intervention groups regardless of cancer setting was only 11 %. where, only six participants across three studies (0.6 % of intervention groups) reported the effects of exercise for withdrawal. We analysed pre-post exercise data for 45 pain-related outcomes across 23 studies, more than double the number of included studies in previous reviews and thus report a larger pooled effect of exercise on pain than in previous reviews. 16/23 studies (69 %) show significant decreases in cancer-related pain intensity.

An important strength of this study was its inclusion of physical and psychological functional outcomes. Cancer-related pain is typically measured as part of a broader symptom assessment to evaluate their individual and collective effects on QoL and distress [76]. Thus, we also included physical function outcomes (i.e. muscle strength, joint range of motion, heart rate, VO2 max/peak, power, endurance and fatigue) and psychological (i.e. anxiety, stress, depression) as part of the overall pain assessment [20,21]. A table summarising the effects sizes (standardised mean differences) for primary and secondary outcome measures can be found in supplementary file 2. Our findings support current evidence that aerobic and resistance exercise show benefits for increases in muscle strength, physical performance, ROM and physiological function in people with cancer-related pain [77]. Studies investigating the effects of aerobic and resistance exercise on physical function in people with cancer also show that moderate and vigorous exercise results in increases in general physical function and endurance, VO2 max and muscle strength [78]. Importantly from a time course perspective, Stout and colleagues also found that the effect of exercises on physical strength and physical function is greater when exercise programs are introduced after the completion of cancer treatment. Encouragingly, positive effects of exercise on strength and muscle mass are also shown in people with advanced-stage cancer [79]. Lastly, meta-analysis of individual patient data [74] from 34 RCTs assessing 4519 people with cancer, the authors found small but significant benefits exercise on physical function (βdifference in effect = 0.18, 95%CI = 0.01; 0.20) with a larger effect for supervised interventions.

Our findings also suggest that in people with cancer-related pain, the effects of exercise on psychological function and fatigue components of individuals' cancer-related pain are significant but showing modest effect sizes. Concerning fatigue, our findings concur with current literature where recent studies show a) positive associations between decreased fatigue and pain with exercise programs [80] and b) negative associations where people with cancer reporting decreased levels of exercise/physical activity report increased fatigue and pain [37]. Similarly, participation in exercise and physical activity are shown decrease levels anxiety, depression and pain in cancer patients [81,82]. These observations were consistent across timeframes, as measured by change from baseline to post intervention.

The magnitude of exercise-induced cancer-related pain relief observed in this meta-analysis is higher than previous systematic reviews. First, Nakano and co-workers reported that aerobic and resistance exercise therapies provide a small but positive effect on cancer-related pain (SMD = −0.17, 95 % CI = −0.32 to −0.03) compared to controls [13]. Earlier, Mishra and colleagues in a Cochrane Review of the therapeutic effect of exercise on QoL in cancer survivors, reported insignificant reductions in cancer-related pain ($Chi^2 = 2.99$, df = 2 (P = .22), $I^2 = 33.2$ %) [83]. A third systematic review investigated the efficacy of exercise on people with advanced cancer. While no meta-analysis was performed, the authors show only two of seven studies assessing pain (25 %) reporting significant pain relief, one of which we included in our meta-analysis [14,67].

Explanations for these conflicting findings are not clear but likely due to differences in cohorts, such as inclusion of a broad range of cancers and/or cancer staging in the same cohort (greater heterogeneity in exercise response), investigation of different exercise therapies both within and between studies and differing sample sizes. However, the most likely reason may be the inability of researchers to prevent control groups from freely participating in physical activities or who were given supplementary exercise advice/programs as part of control protocols. In 16 of 23 accepted studies, control group protocols included advice or encouragement for physical activity, muscle relaxation and exercises for stretching, ROM and breathing. Furthermore, checking participants' compliance in studies investigating home-based exercise interventions may have also been difficult to manage. Thus, participants across intervention and control groups in some studies may have gained similar levels of exercise-induced pain relief. Indeed, researchers stated these factors when describing their study limitations.

Only 13 of 23 studies reported adherence to intervention rates, with a mean of over 86 %. Importantly, 10 of the 11 not reporting

exercises adherence were home-based where several authors cited difficulty in getting participants to document what they had done. Given that exercise requires high levels of motivation, it is less likely that home-based participants, especially those who are sedentary will adopt or maintain exercise routines [84]. Thus, methods of a) retrieving this data and b) effective promotion and monitoring of interventions need to be investigated [85] as it has been recently shown that exercise improve a range of functional outcomes in people with cancer when adherence rates are 80 % or over [86].

4.1. Future research on predictors for effects on exercise on pain in people with cancer

Although our findings show exercise is beneficial for people with cancer-related pain, we found no significant predictors for cancer-related pain relief. This lack of data should be addressed in future studies where additional therapeutic benefits may exist. Recent meta-analysis of aerobic and resistance exercise on chronic non-cancer-related pain suggest that varying exercise dose as measured by time (e.g., minutes), frequency (e.g., per week) and program duration (weeks/months) significantly influences study effect size [87]. Hong and colleagues also show that largest benefits cancer symptoms including pain are observed where exercise sessions were 45–90 min in duration [88]. Our findings show average duration for each exercise session to be 30 min which may suggest greater exercise effect may be gained if session times were increased. Thus, future research should aim to detect the analgesic effects of exercise on cancer-related pain by varying session duration, dose, frequency and exercise intensity depending on patient age and stage of cancer. For example, exercise-induced analgesia for older patients or those with advanced cancer may require closer supervision and lower levels of exercise intensity as previously reported by Arancini and colleagues [89] compared to younger patients and those with early-stage disease who may be more able to complete higher intensity exercise programs. Concerning the effect of exercise intensity in cancer settings, recent meta-analysis shows that both high and low-intensity exercise are effective for cancer-related pain relief, and other cancer-related symptoms including fatigue [90,91].

4.2. Study limitations and strengths

Our study had several limitations. First, 18 % (5/28) of trials that met inclusion criteria did not report pre-post pain outcome data that could be pooled and thus were not included in the meta-analysis. Interestingly, findings from these studies were inconsistent with our current meta-analysis results where estimates of exercise effect [48,50,51,92] or mean change in reported pain [47] were insignificant compared to control groups. Second, 11 studies were excluded where aerobic/resistance interventions included additional therapeutic modalities. Here, six studies included stretching [77,75,93–96], two included psychosocial interventions [97,98] while single studies included additional breathing techniques [99], Pilates [100] and passive physical therapy [101]. Importantly, five of the six studies including stretch exercises show significant reductions in cancer-related pain intensity. Interestingly, these findings suggest that stretching may be a useful addition to exercise interventions, however, evidence for its analgesic effect alone or as part of multimodal exercise interventions in cancer and non-cancer settings is poor [102,103]. Furthermore, mind-body therapies such as yoga and to a lesser extent stretching are effective for improving physical function and fatigue in cancer patients, however, its efficacy for pain relief is not significant [104]. Thus, the effects of stretching alone or as part of multimodal exercise programs needs further investigation. Third, no included studies reported subgroup or individual patient-level analysis for cancer staging while 12 studies did not report baseline cancer-staging demographic data. Given the high prevalence of pain in people with advanced cancers and recent evidence showing exercise to be safe and feasible in these patients [105], it is crucial that research is undertaken to determine appropriate exercise dose, frequency, intensity, content and reporting of short-term exercise effects. The reporting of between and within-group and importantly, patient-level data in these cohorts will be key in elucidating the heterogeneity in analgesic response to aerobic and resistance exercise therapies and thus inform a more precision clinical approach [106]. Fourth, we must note that secondary outcome data in this review reflects changes in these outcomes only in people with cancer-related pain [107,108]. Lastly, we did not examine the effects of aerobic and resistance exercises on health-related quality of life as a secondary outcome. Here, recent meta-analyses show significant benefit of exercise for this multidimensional construct of which pain assessment is a component [109,110].

5. Clinical and research implications

Our findings show that aerobic and resistance exercise therapies are efficacious, feasible and tolerable while showing high therapeutic fidelity for reducing cancer-related pain both during and after anti-cancer treatments. Encouragingly, only three participants across all studies reported the effects of exercise for withdrawal. Based on our review, exercise should be recommended for people with cancer-related pain both during and after cancer treatments. Here, clinicians are encouraged to refer patients with cancer-related pain to exercise professionals for aerobic and resistance exercise programs to reduce cancer-related pain and improve physical function. Future studies should also aim to identify elderly patients and those in advanced care settings who may benefit for example from short-duration low intensity exercise programs, especially those that are supervised. Although our findings add evidence that patients in cancer settings can participate in and benefit from exercise programs, the exercise prescription (frequency, intensity, time, and type) across all settings is not yet defined especially in advanced care settings. At a pragmatic and policy level, future findings may allow for more cost-effective analgesia and reduced healthcare utilisation in both hospital and community settings.

6. Conclusions

In summary, aerobic and resistance exercises are effective adjunct therapies to reduce cancer-related pain intensity in people with and surviving cancer. Our findings also support recommendations that aerobic and resistance exercises are tolerable and feasible during and after cancer treatments. Further research is needed to determine the type, dose, frequency, compliance and immediate effects of these types of exercise in specific cancer settings including cancer type and staging.

CRediT authorship contribution statement

Philip D. Austin: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Wei Lee:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Daniel SJ. Costa:** Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Alison Ritchie:** Resources, Methodology, Conceptualization. **Melanie R. Lovell:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Philip Austin reports financial support, article publishing charges, and statistical analysis were provided by The Taylor Foundation. Philip Austin reports a relationship with The Taylor Foundation that includes: funding grants, non-financial support, and speaking and lecture fees. I have no competing interests to declare If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to thank 1) The University of Sydney librarian; Yulia Ulyannikova for her advice on search protocol development 2) The Taylor Foundation for their financial support in grant funding PA over the course of this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e29193.

References

[1] B.L. Schmidt, D.T. Hamamoto, D.A. Simone, G.L. Wilcox, Mechanism of cancer pain, Mol. Interv. 10 (3) (2010) 164–178.
[2] S.M. Makhlouf, S. Pini, S. Ahmed, M.I. Bennett, Managing pain in people with cancer-a systematic review of the attitudes and knowledge of professionals, patients, caregivers and public, J. Cancer Educ. 35 (2) (2020) 214–240.
[3] S. Falk, A.H. Dickenson, Pain and nociception: mechanisms of cancer-induced bone pain, J. Clin. Oncol. 32 (16) (2014) 1647–1654.
[4] M.S. Gallaway, J.S. Townsend, D. Shelby, M.C. Puckett, Pain among cancer survivors, Prev. Chronic Dis. 17 (2020) E54.
[5] M.I. Bennett, S. Kaasa, A. Barke, B. Korwisi, W. Rief, R.D. Treede, The IASP classification of chronic pain for ICD-11: chronic cancer-related pain, Pain 160 (1) (2019) 38–44.
[6] National Cancer Institute, Cancer Pain (PDQ®)–Health Professional Version Maryland, National Cancer Institute, 2022 [Available from: https://www.cancer.gov/about-cancer/treatment/side-effects/pain/pain-hp-pdq.
[7] S. Mercadante, P. Marchetti, A. Cuomo, M. Mammucari, A. Caraceni, Breakthrough pain and its treatment: critical review and recommendations of IOPS (Italian Oncologic Pain Survey) expert group, Support. Care Cancer : official journal of the Multinational Association of Supportive Care in Cancer 24 (2) (2016) 961–968.
[8] K.B. Svendsen, S. Andersen, S. Arnason, S. Arnér, H. Breivik, T. Heiskanen, et al., Breakthrough pain in malignant and non-malignant diseases: a review of prevalence, characteristics and mechanisms, Eur. J. Pain 9 (2) (2005) 195–206.
[9] World Health Organisation, WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents, Geneva: World Health Organisation, 2019, pp. 1–138. ISBN-ISBN 978-92-4-155039-0.
[10] Australian Adult Cancer Pain Management Guideline Working Party, Cancer Pain Management in Adults: Evidence-Based Clinical Practice Guidelines Adapted for Use in Australia,. Sydney Australia, 2021.
[11] C.L. Carlson, Effectiveness of the World Health Organization cancer pain relief guidelines: an integrative review, J. Pain Res. 9 (2016) 515–534.
[12] B.M. Scarborough, C.B. Smith, Optimal pain management for patients with cancer in the modern era, CA A Cancer J. Clin. 68 (3) (2018) 182–196.
[13] J. Nakano, K. Hashizume, T. Fukushima, K. Ueno, E. Matsuura, Y. Ikio, et al., Effects of aerobic and resistance exercises on physical symptoms in cancer patients: a meta-analysis, Integr. Cancer Ther. 17 (4) (2018) 1048–1058.
[14] R. Heywood, A.L. McCarthy, T.L. Skinner, Efficacy of exercise interventions in patients with advanced cancer: a systematic review, Arch. Phys. Med. Rehabil. 99 (12) (2018) 2595–2620.
[15] K.L. Syrjala, M.P. Jensen, M.E. Mendoza, J.C. Yi, H.M. Fisher, F.J. Keefe, Psychological and behavioral approaches to cancer pain management, J. Clin. Oncol. : official journal of the American Society of Clinical Oncology 32 (16) (2014) 1703–1711.
[16] T. Bouillet, X. Bigard, C. Brami, K. Chouahnia, L. Copel, S. Dauchy, et al., Role of physical activity and sport in oncology: scientific commission of the National Federation Sport and Cancer CAMI, Crit. Rev. Oncol.-Hematol. 94 (1) (2015) 74–86.
[17] M. Kruijsen-Jaarsma, D. Révész, M.B. Bierings, L.M. Buffart, T. Takken, Effects of exercise on immune function in patients with cancer: a systematic review, Exerc. Immunol. Rev. 19 (2013) 120–143.
[18] B.K. Pedersen, Anti-inflammatory effects of exercise: role in diabetes and cardiovascular disease, Eur. J. Clin. Invest. 47 (8) (2017) 600–611.
[19] I. Vendrell, D. Macedo, I. Alho, M.R. Dionísio, L. Costa, Treatment of cancer pain by targeting cytokines, Mediators Inflamm 2015 (2015) 984570.

[20] D.A. Scott, A. Stewart, Assessment and measurement of pain and pain treatment, in: D.A. Scott (Ed.), Acute Pain Management: Scientific Evidence, fifth ed. fifth ed., ANZCA, Melbourne, Australia, 2020.
[21] L. Broemer, A. Hinz, U. Koch, A. Mehnert-Theuerkauf, Prevalence and severity of pain in cancer patients in Germany, Front Pain Res (Lausanne) 2 (2021) 703165.
[22] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, PLoS Med. 6 (7) (2009) e1000097.
[23] Whalen L. Brett, W. Zachary Wright, P. Kundur, S. Angadi, S.C. Modesitt, Beneficial effects of exercise on chemotherapy-induced peripheral neuropathy and sleep disturbance: a review of literature and proposed mechanisms, Gynecol Oncol Rep 39 (2022) 100927.
[24] G.A. Kanzawa-Lee, J.L. Larson, K. Resnicow, E.M.L. Smith, Exercise effects on chemotherapy-induced peripheral neuropathy: a comprehensive integrative review, Cancer Nurs. 43 (3) (2020). E172-e85.
[25] Covidence Systematic Review Software. Veritas Health Innovation [Available from: www.covidence.org.
[26] American College of Sports Medicine, ACSM's Guidelines for Exercise Testing and Prescription, Lippincott Williams & Wilkins, USA, 2017.
[27] Covidence Systematic Review Software [Internet], Available from:, Veritas Health Innovation, 2021 www.covidence.org.
[28] H. Schunemann, J. Brozek, G. Guyatt, A. Oxman (Eds.), Handbook for Grading the Quality of Evidence and the Strength of Recommendations Using the GRADE Approach, The GRADE Working Group, 2013.
[29] F. de Conno, A. Caraceni, A. Gamba, L. Mariani, A. Abbattista, C. Brunelli, et al., Pain measurement in cancer patients: a comparison of six methods, Pain 57 (2) (1994) 161–166.
[30] V. Andersson, S. Bergman, I. Henoch, H. Simonsson, K. Ahlberg, Benefits of using the Brief Pain Inventory in patients with cancer pain: an intervention study conducted in Swedish hospitals, Support. Care Cancer 28 (8) (2020) 3721–3729.
[31] J.M. Giesinger, W. Kuijpers, T. Young, K.A. Tomaszewski, E. Friend, A. Zabernigg, et al., Thresholds for clinical importance for four key domains of the EORTC QLQ-C30: physical functioning, emotional functioning, fatigue and pain, Health Qual. Life Outcome 14 (2016) 87.
[32] T.J. Schnitzer, R. Easton, S. Pang, D.J. Levinson, G. Pixton, L. Viktrup, et al., Effect of Tanezumab on joint pain, physical function, and patient global assessment of osteoarthritis among patients with osteoarthritis of the hip or knee: a randomized clinical trial, JAMA 322 (1) (2019) 37–48.
[33] L. Ortiz-Comino, C. Fernández-Lao, C.M. Speksnijder, M. Lozano-Lozano, I. Tovar-Martín, M. Arroyo-Morales, et al., Upper body motor function and swallowing impairments and its association in survivors of head and neck cancer: a cross-sectional study, PLoS One 15 (6) (2020) e0234467.
[34] G.H.F. Rasmussen, M. Kristiansen, M. Arroyo-Morales, M. Voigt, P. Madeleine, Absolute and relative reliability of pain sensitivity and functional outcomes of the affected shoulder among women with pain after breast cancer treatment, PLoS One 15 (6) (2020) e0234118.
[35] K. Mizumura, T. Taguchi, Delayed onset muscle soreness: involvement of neurotrophic factors, J. Physiol. Sci. 66 (1) (2016) 43–52.
[36] K. Kwekkeboom, Y. Zhang, T. Campbell, C.L. Coe, E. Costanzo, R.C. Serlin, et al., Randomized controlled trial of a brief cognitive-behavioral strategies intervention for the pain, fatigue, and sleep disturbance symptom cluster in advanced cancer, Psycho Oncol. 27 (12) (2018) 2761–2769.
[37] S.A.D. Romero, L. Jones, J.M. Bauml, Q.S. Li, R.B. Cohen, J.J. Mao, The association between fatigue and pain symptoms and decreased physical activity after cancer, Support. Care Cancer : official journal of the Multinational Association of Supportive Care in Cancer 26 (10) (2018) 3423–3430.
[38] D. Liu, J.-S. Weng, X. Ke, X.-Y. Wu, S.-T. Huang, The relationship between cancer-related fatigue, quality of life and pain among cancer patients, Int. J. Nurs. Sci. 10 (1) (2023) 111–116.
[39] X.-M. Li, W.-H. Xiao, P. Yang, H.-X. Zhao, Psychological distress and cancer pain: results from a controlled cross-sectional survey in China, Sci. Rep. 7 (1) (2017) 39397.
[40] W. Viechtbauer, Conducting meta-analyses in R with the metafor package, J. Stat. Software 36 (3) (2010) 1–48.
[41] S.V. Faraone, Interpreting estimates of treatment effects: implications for managed care, P t 33 (12) (2008) 700–711.
[42] S. Arya, A.H. Kaji, M.A. Boermeester, PRISMA reporting guidelines for meta-analyses and systematic reviews, JAMA Surgery 156 (8) (2021) 789–790.
[43] EndNote. Philadelphia, PA: Clarivate, 2020.
[44] Veritas Health Innovation, 2022 [cited July 2022]. Available from: https://support.covidence.org/.
[45] M.L. Irwin, B. Cartmel, C.P. Gross, E. Ercolano, F. Li, X. Yao, et al., Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer survivors, J. Clin. Oncol. 33 (10) (2015) 1104–1111.
[46] G. Ammitzbøll, K.G. Andersen, P.E. Bidstrup, C. Johansen, C. Lanng, N. Kroman, et al., Effect of progressive resistance training on persistent pain after axillary dissection in breast cancer: a randomized controlled trial, Breast Cancer Res. Treat. 179 (1) (2020) 173–183.
[47] K. Griffith, J. Wenzel, J. Shang, C. Thompson, K. Stewart, V. Mock, Impact of a walking intervention on cardiorespiratory fitness, self-reported physical function, and pain in patients undergoing treatment for solid tumors, Cancer 115 (20) (2009) 4874–4884.
[48] M. Ibrahim, T. Muanza, N. Smirnow, W. Sateren, B.P.K. Fournier, et al., The long-term effects of posttreatment exercise on pain in young women with breast cancer, JCSO 16 (3) (2018) e145–e151.
[49] A.L. Cheville, J. Kollasch, J. Vandenberg, T. Shen, A. Grothey, G. Gamble, et al., A home-based exercise program to improve function, fatigue, and sleep quality in patients with Stage IV lung and colorectal cancer: a randomized controlled trial, J. Pain Symptom Manag. 45 (5) (2013) 811–821.
[50] M.J. Dodd, M.H. Cho, C. Miaskowski, P.L. Painter, S.M. Paul, B.A. Cooper, et al., A randomized controlled trial of home-based exercise for cancer-related fatigue in women during and after chemotherapy with or without radiation therapy, Cancer Nurs. 33 (4) (2010) 245–257.
[51] F. Streckmann, S. Kneis, J.A. Leifert, F.T. Baumann, M. Kleber, G. Ihorst, et al., Exercise program improves therapy-related side-effects and quality of life in lymphoma patients undergoing therapy, Ann. Oncol. 25 (2) (2014) 493–499.
[52] M. Backman, Y. Wengström, B. Johansson, I. Sköldengen, S. Börjesson, S. Tärnbro, et al., A randomized pilot study with daily walking during adjuvant chemotherapy for patients with breast and colorectal cancer, Acta Oncol. 53 (4) (2014) 510–520.
[53] B.C. Bade, G. Gan, F. Li, L. Lu, L. Tanoue, G.A. Silvestri, et al., Randomized trial of physical activity on quality of life and lung cancer biomarkers in patients with advanced stage lung cancer: a pilot study, BMC Cancer 21 (1) (2021) 352.
[54] M.L. Baglia, I.H. Lin, B. Cartmel, T. Sanft, J. Ligibel, D.L. Hershman, et al., Endocrine-related quality of life in a randomized trial of exercise on aromatase inhibitor-induced arthralgias in breast cancer survivors, Cancer 125 (13) (2019) 2262–2271.
[55] I. Cantarero-Villanueva, C. Fernández-Lao, Fernández-de-Las, C. Peñas, I.B. López-Barajas, R. Del-Moral-Ávila, A.I. de la-Llave-Rincón, et al., Effectiveness of water physical therapy on pain, pressure pain sensitivity, and myofascial trigger points in breast cancer survivors: a randomized, controlled clinical trial, Pain Med. 13 (11) (2012) 1509–1519.
[56] M. Chatterjee, V. Murthy, S. Nikam, S. Kannan, T. Gupta, S.G. Laskar, et al., Effect of progressive resistive exercise training (PRET) on shoulder joint abduction range of motion, pain and disability in post operative oral cancer patients undergoing radiation therapy: a randomized controlled trial, Indian J. Physiother Occup. Ther. 11 (1) (2017) 57.
[57] P. Cormie, R.U. Newton, N. Spry, D. Joseph, D.R. Taaffe, D.A. Galvão, Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases, Prostate Cancer Prostatic Dis. 16 (4) (2013) 328–335.
[58] J. Fields, A. Richardson, J. Hopkinson, D. Fenlon, Nordic walking as an exercise intervention to reduce pain in women with aromatase inhibitor-associated arthralgia: a feasibility study, J. Pain Symptom Manag. 52 (4) (2016) 548–559.
[59] D.A. Galvão, N. Spry, J. Denham, D.R. Taaffe, P. Cormie, D. Joseph, et al., A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR, Eur. Urol. 65 (5) (2014) 856–864.
[60] S.C. Hayes, S. Rye, T. Disipio, P. Yates, J. Bashford, C. Pyke, et al., Exercise for health: a randomized, controlled trial evaluating the impact of a pragmatic, translational exercise intervention on the quality of life, function and treatment-related side effects following breast cancer, Breast Cancer Res. Treat. 137 (1) (2013) 175–186.

[61] M.L. McNeely, M. Parliament, K.S. Courneya, H. Seikaly, N. Jha, R. Scrimger, et al., A pilot study of a randomized controlled trial to evaluate the effects of progressive resistance exercise training on shoulder dysfunction caused by spinal accessory neurapraxia/neurectomy in head and neck cancer survivors, Head Neck 26 (6) (2004) 518–530.
[62] S. Mijwel, M. Backman, K.A. Bolam, E. Olofsson, J. Norrbom, J. Bergh, et al., Highly favorable physiological responses to concurrent resistance and high-intensity interval training during chemotherapy: the OptiTrain breast cancer trial, Breast Cancer Res. Treat. 169 (1) (2018) 93–103.
[63] K.A. Nyrop, L.F. Callahan, R.J. Cleveland, L.L. Arbeeva, B.S. Hackney, H.B. Muss, Randomized controlled trial of a home-based walking program to reduce moderate to severe aromatase inhibitor-associated arthralgia in breast cancer survivors, Oncol. 22 (10) (2017) 1238–1249.
[64] J.H. Park, The effects of complex exercise on shoulder range of motion and pain for women with breast cancer-related lymphedema: a single-blind, randomized controlled trial, Breast Cancer 24 (4) (2017) 608–614.
[65] T.R.S. Paulo, F.E. Rossi, J. Viezel, G.T. Tosello, S.C. Seidinger, R.R. Simões, et al., The impact of an exercise program on quality of life in older breast cancer survivors undergoing aromatase inhibitor therapy: a randomized controlled trial, Health Qual. Life Outcome 17 (1) (2019) 17.
[66] H. Rief, M. Akbar, M. Keller, G. Omlor, T. Welzel, T. Bruckner, et al., Quality of life and fatigue of patients with spinal bone metastases under combined treatment with resistance training and radiation therapy- a randomized pilot trial, Radiat. Oncol. 9 (2014) 151.
[67] H. Rief, G. Omlor, M. Akbar, T. Welzel, T. Bruckner, S. Rieken, et al., Feasibility of isometric spinal muscle training in patients with bone metastases under radiation therapy - first results of a randomized pilot trial, BMC Cancer 14 (2014) 67.
[68] H. Rief, T. Welzel, G. Omlor, M. Akbar, T. Bruckner, S. Rieken, et al., Pain response of resistance training of the paravertebral musculature under radiotherapy in patients with spinal bone metastases–a randomized trial, BMC Cancer 14 (2014) 485.
[69] T. Schmidt, B. Weisser, J. Dürkop, W. Jonat, M. Van Mackelenbergh, C. Röcken, et al., Comparing endurance and resistance training with standard care during chemotherapy for patients with primary breast cancer, Anticancer Res. 35 (10) (2015) 5623–5629.
[70] H. van Waart, M.M. Stuiver, W.H. van Harten, E. Geleijn, J.M. Kieffer, L.M. Buffart, et al., 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. : official journal of the American Society of Clinical Oncology 33 (17) (2015) 1918–1927.
[71] T.P. Yeo, S.A. Burrell, P.K. Sauter, E.P. Kennedy, H. Lavu, B.E. Leiby, et al., A progressive postresection walking program significantly improves fatigue and health-related quality of life in pancreas and periampullary cancer patients, J. Am. Coll. Surg. 214 (4) (2012) 463–475. ; discussion 75-7.
[72] F.C. Dimeo, F. Thomas, C. Raabe-Menssen, F. Pröpper, M. Mathias, Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial, Support. Care Cancer : official journal of the Multinational Association of Supportive Care in Cancer 12 (11) (2004) 774–779.
[73] R.H. Knols, E.D. de Bruin, D. Uebelhart, G. Aufdemkampe, U. Schanz, F. Stenner-Liewen, et al., Effects of an outpatient physical exercise program on hematopoietic stem-cell transplantation recipients: a randomized clinical trial, Bone Marrow Transplant. 46 (9) (2011) 1245–1255.
[74] L.M. Buffart, J. Kalter, M.G. Sweegers, K.S. Courneya, R.U. Newton, N.K. Aaronson, et al., Effects and moderators of exercise on quality of life and physical function in patients with cancer: an individual patient data meta-analysis of 34 RCTs, Cancer Treat Rev. 52 (2017) 91–104.
[75] M.L. McNeely, M.B. Parliament, H. Seikaly, N. Jha, D.J. Magee, M.J. Haykowsky, et al., Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial, Cancer 113 (1) (2008) 214–222.
[76] M.N. Verkissen, M.J. Hjermstad, S. Van Belle, S. Kaasa, L. Deliens, K. Pardon, Quality of life and symptom intensity over time in people with cancer receiving palliative care: results from the international European Palliative Care Cancer Symptom study, PLoS One 14 (10) (2019) e0222988.
[77] A.D. Reis, P. Pereira, R.R. Diniz, J.G.L. de Castro Filha, A.M. Dos Santos, B.T. Ramallo, et al., Effect of exercise on pain and functional capacity in breast cancer patients, Health Qual. Life Outcome 16 (1) (2018) 58.
[78] N.L. Stout, J.C. Brown, A.L. Schwartz, T.F. Marshall, A.M. Campbell, L. Nekhlyudov, et al., An exercise oncology clinical pathway: screening and referral for personalized interventions, Cancer 126 (12) (2020) 2750–2758.
[79] S. Rodríguez-Cañamero, A.I. Cobo-Cuenca, J.M. Carmona-Torres, D.P. Pozuelo-Carrascosa, E. Santacruz-Salas, J.A. Rabanales-Sotos, et al., Impact of physical exercise in advanced-stage cancer patients: systematic review and meta-analysis, Cancer Med. 11 (19) (2022) 3714–3727.
[80] X. Chen, J. Li, C. Chen, Y. Zhang, S. Zhang, Y. Zhang, et al., Effects of exercise interventions on cancer-related fatigue and quality of life among cancer patients: a meta-analysis, BMC Nurs. 22 (1) (2023) 200.
[81] C.D. Rethorst, T.J. Carmody, K.E. Argenbright, T.L. Mayes, H.A. Hamann, M.H. Trivedi, Considering depression as a secondary outcome in the optimization of physical activity interventions for breast cancer survivors in the PACES trial: a factorial randomized controlled trial, Int. J. Behav. Nutr. Phys. Activ. 20 (1) (2023) 47.
[82] P. Marconcin, A. Marques, G. Ferrari, É.R. Gouveia, M. Peralta, A. Ihle, Impact of exercise training on depressive symptoms in cancer patients: a critical analysis, Biology 11 (4) (2022).
[83] S.I. Mishra, R.W. Scherer, P.M. Geigle, D.R. Berlanstein, O. Topaloglu, C.C. Gotay, et al., Exercise interventions on health-related quality of life for cancer survivors, Cochrane Database Syst. Rev. 2012 (8) (2012) Cd007566.
[84] S.J. Hardcastle, P.A. Cohen, Effective physical activity promotion to survivors of cancer is likely to Be home based and to require oncologist participation, J. Clin. Oncol. 35 (32) (2017) 3635–3637.
[85] C. Lopez, J. Jones, S.M.H. Alibhai, D.S. Mina, What is the "home" in home-based exercise? The need to define independent exercise for survivors of cancer, J. Clin. Oncol. 36 (9) (2018) 926–927.
[86] M.B. Kraemer, D.G. Priolli, I.G.M. Reis, A.C. Pelosi, A.L.P. Garbuio, L.H.D. Messias, Home-based, supervised, and mixed exercise intervention on functional capacity and quality of life of colorectal cancer patients: a meta-analysis, Sci. Rep. 12 (1) (2022) 2471.
[87] A.M. Polaski, A.L. Phelps, M.C. Kostek, K.A. Szucs, B.J. Kolber, Exercise-induced hypoalgesia: a meta-analysis of exercise dosing for the treatment of chronic pain, PLoS One 14 (1) (2019) e0210418.
[88] F. Hong, W. Ye, C.H. Kuo, Y. Zhang, Y. Qian, M. Korivi, Exercise intervention improves clinical outcomes, but the "time of session" is crucial for better quality of life in breast cancer survivors: a systematic review and meta-analysis, Cancers 11 (5) (2019).
[89] A. Avancini, V. Pala, I. Trestini, D. Tregnago, L. Mariani, S. Sieri, et al., Exercise levels and preferences in cancer patients: a cross-sectional study, Int. J. Environ. Res. Publ. Health 17 (15) (2020).
[90] A.M. Lavín-Pérez, D. Collado-Mateo, X. Mayo, G. Liguori, L. Humphreys, R.J. Copeland, et al., Effects of high-intensity training on the quality of life of cancer patients and survivors: a systematic review with meta-analysis, Sci. Rep. 11 (1) (2021) 15089.
[91] K. Toohey, M. Chapman, A.M. Rushby, K. Urban, G. Ingham, B. Singh, The effects of physical exercise in the palliative care phase for people with advanced cancer: a systematic review with meta-analysis, J Cancer Surviv 17 (2) (2023) 399–415.
[92] G. Ammitzboll, K.G. Andersen, P.E. Bidstrup, C. Johansen, C. Lanng, N. Kroman, et al., Effect of progressive resistance training on persistent pain after axillary dissection in breast cancer: a randomized controlled trial, Breast Cancer Res. Treat. 179 (1) (2020) 173–183.
[93] J. Bruce, E. Williamson, C. Lait, H. Richmond, L. Betteley, R. Lall, et al., Randomised controlled trial of exercise to prevent shoulder problems in women undergoing breast cancer treatment: study protocol for the prevention of shoulder problems trial (UK PROSPER), BMJ Open 8 (3) (2018) e019078.
[94] A.C. McGarvey, G.R. Hoffman, P.G. Osmotherly, P.E. Chiarelli, Maximizing shoulder function after accessory nerve injury and neck dissection surgery: a multicenter randomized controlled trial, Head Neck 37 (7) (2015) 1022–1031.
[95] T.-L. Su, A.-N. Chen, C.-P. Leong, Y.-C. Huang, C.-W. Chiang, I.H. Chen, et al., The effect of home-based program and outpatient physical therapy in patients with head and neck cancer: a randomized, controlled trial, Oral Oncol. 74 (2017) 130–134.
[96] J.H. Do, K.H. Choi, J.S. Ahn, J.Y. Jeon, Effects of a complex rehabilitation program on edema status, physical function, and quality of life in lower-limb lymphedema after gynecological cancer surgery, Gynecol. Oncol. 147 (2) (2017) 450–455.
[97] L.J. Frensham, G. Parfitt, J. Dollman, Effect of a 12-week online walking intervention on health and quality of life in cancer survivors: a quasi-randomized controlled trial, Int. J. Environ. Res. Publ. Health 15 (10) (2018).

[98] J.A. Stigt, S.M. Uil, S.J.H. van Riesen, F.J.N.A. Simons, M. Denekamp, G.M. Shahin, et al., A randomized controlled trial of postthoracotomy pulmonary rehabilitation in patients with resectable lung cancer, J. Thorac. Oncol. 8 (2) (2013) 214–221.
[99] C.C. Henke, J. Cabri, L. Fricke, W. Pankow, G. Kandilakis, P.C. Feyer, et al., Strength and endurance training in the treatment of lung cancer patients in stages IIIA/IIIB/IV, Support. Care Cancer 22 (1) (2014) 95–101.
[100] K.P. Barbosa, L.G.T. da Silva, P.A. Garcia, C.A. Freitas, E.C.F. da Silva, T.V. Pereira, et al., Effectiveness of Pilates and circuit-based exercise in reducing arthralgia in women during hormone therapy for breast cancer: a randomized, controlled trial, Support. Care Cancer : official journal of the Multinational Association of Supportive Care in Cancer 29 (10) (2021) 6051–6059.
[101] I. Cantarero-Villanueva, C. Fernández-Lao, E. Caro-Morán, J. Morillas-Ruiz, N. Galiano-Castillo, L. Díaz-Rodríguez, et al., Aquatic exercise in a chest-high pool for hormone therapy-induced arthralgia in breast cancer survivors: a pragmatic controlled trial, Clin. Rehabil. 27 (2) (2013) 123–132.
[102] F.B. Rangon, J. da Silva, A.V. Dibai-Filho, RRdJ. Guirro, ECdO. Guirro, Effects of complex physical therapy and multimodal approaches on lymphedema secondary to breast cancer: a systematic review and meta-analysis of randomized controlled trials, Arch. Phys. Med. Rehabil. 103 (2) (2022) 353–363.
[103] A. Kechichian, S. Lafrance, E. Matifat, F. Dubé, D. Lussier, P. Benhaim, et al., Multimodal interventions including rehabilitation exercise for older adults with chronic musculoskeletal pain: a systematic review and meta-analyses of randomized controlled trials, J. Geriatr. Phys. Ther. 45 (1) (2022) 34–49.
[104] K.D. Chandwani, G. Perkins, H.R. Nagendra, N.V. Raghuram, A. Spelman, R. Nagarathna, et al., Randomized, controlled trial of yoga in women with breast cancer undergoing radiotherapy, J. Clin. Oncol. 32 (10) (2014) 1058–1065.
[105] N. De Lazzari, T. Niels, M. Tewes, M. Götte, A systematic review of the safety, feasibility and benefits of exercise for patients with advanced cancer, Cancers 13 (17) (2021).
[106] F.S. Collins, H. Varmus, A new initiative on precision medicine, N. Engl. J. Med. 372 (9) (2015) 793–795.
[107] M. Al Maqbali, Sinani M. Al, Naamani Z. Al, Badi K. Al, M.I. Tanash, Prevalence of fatigue in patients with cancer: a systematic review and meta-analysis, J. Pain Symptom Manag. 61 (1) (2021), 167-89.e14.
[108] Y.-H. Wang, J.-Q. Li, J.-F. Shi, J.-Y. Que, J.-J. Liu, J.M. Lappin, et al., Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies, Mol. Psychiatr. 25 (7) (2020) 1487–1499.
[109] M.B. Kraemer, D.G. Priolli, I.G.M. Reis, A.C. Pelosi, A.L.P. Garbuio, L.H.D. Messias, Home-based, supervised, and mixed exercise intervention on functional capacity and quality of life of colorectal cancer patients: a meta-analysis, Sci. Rep. 12 (1) (2022) 2471.
[110] A.M. Lavín-Pérez, D. Collado-Mateo, X. Mayo, G. Liguori, L. Humphreys, R.J. Copeland, et al., Effects of high-intensity training on the quality of life of cancer patients and survivors: a systematic review with meta-analysis, Sci. Rep. 11 (1) (2021) 15089.