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Research

Multidisciplinary, exercise-based oncology rehabilitation programs improve patient outcomes but their effects on healthcare service-level outcomes remain uncertain: a systematic review

Amy M Dennett [a,b], Mitchell Sarkies [c,d], Nora Shields [a], Casey L Peiris [a], Cylie Williams [d,e], Nicholas F Taylor [a,b]

[a] School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Australia; [b] Allied Health Clinical Research Office, Eastern Health, Melbourne, Australia; [c] School of Public Health, Curtin University, Perth, Australia; [d] School of Primary and Allied Health Care, Monash University, Melbourne, Australia; [e] Department of Allied Health, Peninsula Health, Melbourne, Australia

KEY WORDS

Cancer
Physical therapy
Exercise
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ABSTRACT

Question: What is the effect of multidisciplinary, exercise-based, group oncology rehabilitation programs on healthcare service outcomes and patient-level outcomes, including quality of life and physical and psychosocial function? **Design**: Systematic review with meta-analysis of randomised controlled trials. **Participants**: Adults diagnosed with cancer. **Intervention**: Multidisciplinary, group-based rehabilitation that includes exercise for cancer survivors. **Outcome measures**: Primary outcomes related to health service delivery, including costs, hospitalisations and healthcare service utilisation. Secondary outcomes were patient-level measures, including: the European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire, 30-second timed sit to stand and the Hospital Anxiety and Depression Scale. The evidence was evaluated using the PEDro Scale and the Grades of Research, Assessment, Development and Evaluation (GRADE) approach. **Results**: Seventeen trials (1,962 participants) were included. There was uncertainty about the effect of multidisciplinary, exercise-based rehabilitation on healthcare service outcomes, as only one trial reported length of stay and reported wide confidence intervals (MD 2.4 days, 95% CI −3.1 to 7.8). Multidisciplinary, exercise-based rehabilitation improved muscle strength (1RM chest press MD 3.6 kg, 95% CI 0.4 to 6.8; 1RM leg press MD 19.5 kg, 95% CI 12.3 to 26.8), functional strength (30-second sit to stand MD 6 repetitions, 95% CI 3 to 9) and reduced depression (MD −0.7 points, 95% CI −1.2 to −0.1) compared to usual care. There was uncertainty whether multidisciplinary rehabilitation programs are more effective when delivered early versus late or more effective than exercise alone. Adherence was typically high (mean weighted average 76% sessions attended) with no major and few minor adverse events reported. **Conclusion**: Multidisciplinary, exercise-based oncology rehabilitation programs improve some patient-level outcomes compared with usual care. Further evidence from randomised trials to determine their effect at a healthcare service level are required if these programs are to become part of standard care. **Trial registration**: PROSPERO CRD42019130593. **[Dennett AM, Sarkies M, Shields N, Peiris CL, Williams C, Taylor NF (2021) Multidisciplinary, exercise-based oncology rehabilitation programs improve patient outcomes but their effects on healthcare service-level outcomes remain uncertain: a systematic review. *Journal of Physiotherapy* 67:12–26]**

Introduction

Rehabilitation is an essential element of cancer survivorship care.[1] With growing numbers of cancer survivors,[2] there is a need to provide interventions that mitigate the adverse effects of cancer treatments and prevent future disease and cancer recurrence. The most commonly reported issues for cancer survivors are physical problems (such as pain and fatigue) and psychosocial problems (such as fear of recurrence).[3–5] Cancer survivors also have an increased risk of developing secondary comorbidities such as cardiovascular disease.[6] Oncology rehabilitation aims to address physical and psychological impairments to maintain or restore function, reduce symptom burden, maximise independence and improve quality of life.[7] Oncology rehabilitation programs may help manage cancer as a chronic disease, which in turn may improve patient and healthcare service outcomes.

Exercise is an important component of oncology rehabilitation. As a structured form of physical activity, exercise improves a variety of outcomes for cancer survivors, including fatigue, depression, cardiorespiratory fitness and quality of life.[8–10] Supervised exercise

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programs yield the greatest improvements in these outcomes.[8] Higher doses of exercise are also associated with greater reductions in cancer-related mortality, cancer recurrence and cardiovascular disease risk.[11,12] Given these benefits, guidelines support the integration of exercise into cancer supportive care.[9,13–15]

Multidisciplinary, oncology rehabilitation programs have been implemented for people with cancer.[16] These programs are based on exercise and supplemented by multidisciplinary education and lifestyle counselling. Similar to a cardiac rehabilitation model,[17] these programs reduce mortality and readmissions and improve quality of life in people with cardiovascular disease.[18] Exercise-based oncology rehabilitation shares similar goals to cardiac rehabilitation, including: reducing symptoms, managing risk factors and improving functional capacity and psychosocial well-being.[16,17] Oncology rehabilitation is also commonly delivered in groups to provide peer support to participants and offer greater access, efficiency and cost savings.[19,20] Delivering exercise-based oncology rehabilitation programs for cancer survivors is feasible,[16] and participants describe programs as helping them 'return to normal' after cancer diagnosis.[19]

Despite the similarities, there are important differences between oncology rehabilitation and cardiac rehabilitation. Unlike cardiac disease, the effects of cancer and its associated treatment may not be localised to one physiological system and patients may present with multiple complex impairments, suggesting that the role of the multidisciplinary team may be even more pertinent.[7] Two previous reviews have evaluated the effect of oncology rehabilitation programs generally.[21,22] Four of the 15 trials described across the two reviews were delivered in a multidisciplinary, exercise-based group model. These reviews concluded that multidimensional rehabilitation reduces fatigue among breast cancer survivors[21] and improves quality of life among a mixed cohort of cancer survivors.[22] No review has specifically evaluated the effect of multidisciplinary, exercise-based group oncology rehabilitation.

There are currently no standardised guidelines for the implementation of multidisciplinary, exercise-based oncology rehabilitation programs, and access to programs is poor.[20,23] For wider implementation of multi-disciplinary, exercise-based oncology rehabilitation programs into clinical practice, there is a need to evaluate programs at a healthcare service level. Healthcare service outcomes may include healthcare-related costs, hospital length of stay, hospital readmissions, emergency department presentations and healthcare service utilisation such as outpatient visits. Multidisciplinary, exercise-based oncology rehabilitation is a resource-intensive and complex intervention. Despite promising results about feasibility of exercise-based oncology rehabilitation from pre-to-post and retrospective studies,[16] there is limited evidence from randomised controlled trials on their effect on outcomes such as patient mortality, readmissions and costs to healthcare services. Only one systematic review has evaluated the costs of multidimensional, oncology rehabilitation broadly. This review of six studies (of which only one non-randomised study included a multidisciplinary, exercise-based oncology program) found preliminary evidence of potential cost savings for healthcare services (incremental cost-effectiveness ratios ranged from −€16,976 to €11,057 per quality-adjusted life year).[24] Costs were up to €793 per patient for a group-based exercise and psychosocial intervention.[25] Another review found conflicting evidence of cost-effectiveness of physiotherapy-only interventions (including exercise) for people with breast cancer.[26] Data relating to healthcare service costs of multidisciplinary exercise-based group oncology rehabilitation will help policy-makers and healthcare service providers make important decisions about implementing exercise-based oncology rehabilitation into practice.

Therefore, the research questions for this systematic review were:

1. What is the effect of multidisciplinary, exercise-based, group oncology rehabilitation programs on healthcare service outcomes?
2. What is the effect of multidisciplinary, exercise-based group oncology rehabilitation programs on patient-level outcomes, including quality of life and physical and psychosocial function?

Method

This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[27]

Identification and selection of studies

Studies were identified through electronic database searches of MEDLINE, CINAHL, Embase, Sport Discus, PsycINFO and PEDro from the earliest available time until April 2019. The search strategy used synonyms and MeSH terms focusing on the three key concepts of cancer, multidisciplinary rehabilitation and exercise (Appendix 1). Filters were applied to the search strategy to limit study design to only include randomised controlled trials.[28] Citation tracking of included trials was performed using Google Scholar and reference lists of all included papers were checked to supplement database searches.

Two reviewers independently screened the titles and abstracts of each study against predefined inclusion criteria. Any disagreement was discussed between the two reviewers until consensus was reached. Full-text articles were obtained and screened by two independent reviewers to determine final eligibility for study inclusion. Agreement between reviewers was assessed using the kappa statistic (κ).

To be included, randomised controlled trials needed to evaluate a multidisciplinary, group exercise-based, oncology rehabilitation program for adults with cancer. Comparison groups needed to be usual care or an alternative intervention (eg, exercise only). Trials could include any healthcare service or patient-level outcome. For the purpose of this review, healthcare service outcomes included healthcare-related costs, hospital length of stay, hospital readmissions, emergency department presentations and healthcare service utilisation such as outpatient visits. Trials were excluded if they were single-discipline programs (eg, support groups with no exercise component), unstructured exercise, alternative exercise/psychosocial groups (mindfulness meditation, yoga, Pilates, Qi-Gong), single-component programs (eg, exercise only supervised by a physiotherapist and exercise physiologist), individual (1:1) rehabilitation programs, tele-rehabilitation (unless broadcast simultaneously with a supervised centre-based group), home-based therapy, survivorship clinics or single assessment only with no group follow-up (Box 1).

Box 1. Inclusion criteria.

Design
- Randomised controlled trial

Participants
- Adults with cancer

Intervention
- Multidisciplinary ($\geq$ 2 disciplines) and multicomponent group-based rehabilitation that includes supervised exercise
- Exercise intervention with aerobic and/or resistance exercise as a core component
- The rehabilitation program is time-limited with a minimum of 2 weeks' duration

Outcome measures
- Healthcare service outcomes (costs, hospital re-admissions, length of stay, emergency department presentations, healthcare service utilisation)
- Patient-level outcomes (health-related quality of life; physical and psychosocial function; symptom and impairment measures; participation measures including physical activity levels)
- Process measures (adherence, adverse events)

Comparison
- Oncology rehabilitation compared to usual care
- Oncology rehabilitation compared to equivalent alternative intervention (eg, telehealth intervention, written/digital information materials, exercise only)
- Comparing two different models of cancer rehabilitation (eg, at two times or at two intensities)

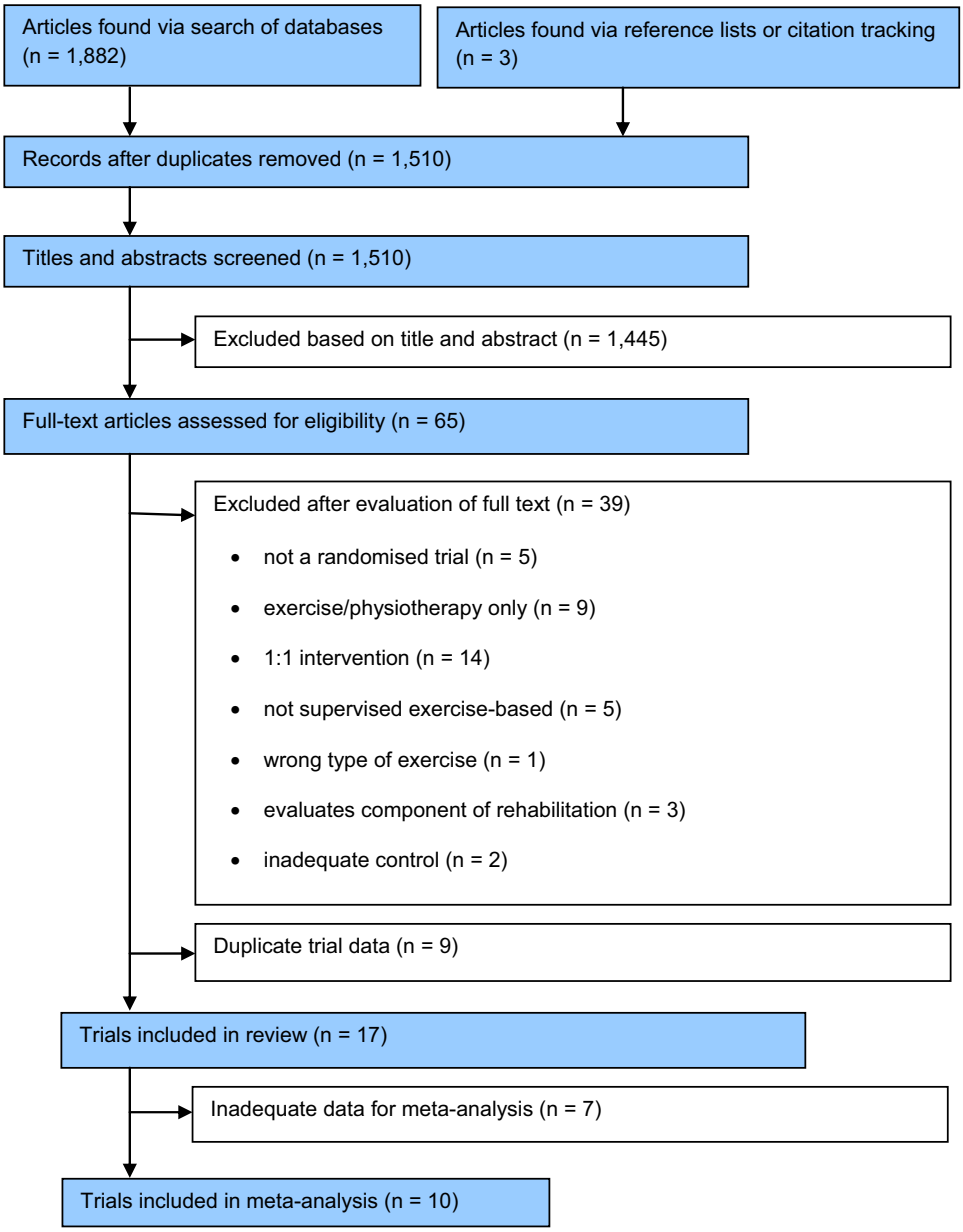

Figure 1. Flow of trials through the review.

Assessment of methodological quality

Two reviewers independently used the 11-item Physiotherapy Evidence Database (PEDro) scale to assess methodological quality. The PEDro scale comprises one item evaluating external validity and 10 items evaluating internal validity. The PEDro score demonstrates convergent and construct validity[29] and has moderate levels of inter-rater reliability (ICC 0.68, 95% CI 0.57 to 0.76).[30] A score of 8 on the PEDro scale is considered the highest possible score, as participants and therapists in exercise trials are unable to be blinded.

Data analysis

To compare groups, mean differences (MD) were calculated from post-intervention means and standard deviations (SD) for homogenous outcomes. If change scores were presented, post-intervention means were calculated in reference to the baseline mean and the post-intervention SD was imputed using baseline data.[31] Where there were insufficient data for analysis or inconsistency in data, authors were contacted to seek further information.

Meta-analysis was performed using a random-effects model with clinically homogenous data using RevMan software.[32] If more than low levels of statistical heterogeneity were observed ($I^2 > 25\%$), sensitivity analyses were completed excluding trials hypothesised to be contributing to heterogeneity. The Grades of Research, Assessment, Development and Evaluation (GRADE) approach was used to determine the overall quality of evidence (between 'high' and 'very low') presented in each meta-analysis. Evidence was downgraded based on predetermined criteria by one level if: PEDro score was < 6 for the majority of trials used in the meta-analysis;[33] there was greater than low levels of statistical heterogeneity between trials ($I^2 > 25\%$);[34] and there were large confidence intervals (exceeding the minimum clinically important difference). Results were summarised descriptively when data could not be pooled for meta-analysis.

Results

Study selection

Database searches identified 1,882 articles for screening. An additional two articles were identified by citation tracking and one

Table 1
PEDro scores of the included trials.

Trial	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor binding	< 15% dropout	Intention-to-treat analysis	Between-group comparisons reported	Point estimates and variability	Total *(0 to 10)*
Adamsen 2009 [42]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Bergland 1994 [43]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Bergland 2007 [40]	Y	N	Y	N	N	N	N	N	N	Y	3
Bourke 2011 [41]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Cho 2006 [47]	Y	N	Y	N	N	N	N	N	N	Y	3
Clark 2013 [44]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Ghavarmi 2017 [48]	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Hubbard 2016 [52]	Y	N	N	N	N	N	N	N	N	N	1
Korstjens 2008 [45]	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Midtgaard 2013 [36]	Y	N	Y	N	N	N	N	Y	Y	Y	5
O'Neill 2018 [37]	Y	Y	N	N	N	Y	Y	N	Y	Y	6
Quist 2018 [38]	Y	Y	Y	N	N	Y	N	Y	Y	Y	7
Rummans 2006 [46]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Sandmael 2017 [49]	Y	N	Y	N	N	N	N	N	Y	Y	4
Sheppard 2016 [50]	Y	N	Y	N	N	N	N	N	Y	Y	4
Spahn 2013 [51]	Y	Y	N	N	N	N	Y	Y	Y	Y	6
Uster 2017 [39]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8

Y = Yes, N = No.

article through checking reference lists. The total yield was reduced to 1,510 after duplicates were removed. Sixty-five full-text articles were screened and reduced to 26 articles after assessment against inclusion criteria. The inter-rater agreement between two reviewers for full text was 'very good' (κ = 0.835, 95% CI 0.697 to 0.972).[35] The 26 included articles reported data from 17 randomised controlled trials (Figure 1). Where duplicate trial data were presented, the first article published with participant outcome data was considered the primary trial throughout (Appendix 2). Four authors responded to requests for missing data.[36–39]

Methodological quality

The quality of trials included in this review was moderate, with a mean score of 5 (range 1 to 8) on the PEDro scale (Table 1). Inter-rater agreement on quality criteria was 'very good' (κ = 0.887, 95% CI 0.832 to 0.941).[35] Seven trials had concealed allocation (41%) and four trials (24%) had blinded assessors.

Study characteristics

Participants

Trials included 1,962 participants. The mean age of participants ranged from 46[36] to 69 years[40,41] and most were women (Table 2). Seven trials included participants with a mix of cancer types[36,39,42–46] and nine trials included people with early-stage cancer only.[37,38,43,45,47–51] Four trials evaluated rehabilitation exclusively in an advanced cancer cohort.[36,39,44,46] Trials were usually conducted after cancer treatment completion, with six trials including participants during treatment[39,42,44,46,49,52] and one trial including participants pre-surgery.[38] Only four trials reported baseline physical performance status,[39,44,46,49] which was described as fully active or restricted, in only strenuous activities for the majority of participants.

Intervention

Rehabilitation was delivered in outpatient hospital settings. Group sizes ranged from 3 to 25 participants and were often led by physiotherapists[36–40,42,44–46,49,52] (11 trials) and nurses[38,40–47,52] (10 trials). Dietitians (six trials)[37,39,43,47,49,50] also contributed to programs. Programs were supervised twice-weekly for 4 weeks to 1 year, with most being 10 to 12 weeks in duration. Nine trials included both aerobic and resistance training.[36–39,41–43,45,52] Exercise was described as individually tailored in 12 trials.[36–39,41–43,45,47–49,52] Exercise was supplemented by multidisciplinary information sessions (12 trials),[37,38,40,41,43,44,46,47,49–52] relaxation (seven trials)[40,42–44,46,51,52] and individual nutrition counselling (six trials) (Table 3).[37–39,48,49,51] Four trials included standardisation processes within the rehabilitation program comprising staff training[44–46] and written materials.[44,46,50] Two trials compared multidisciplinary rehabilitation with supervised, group-based exercise[45,51] and two trials compared early rehabilitation with late rehabilitation.[38,49] The other 13 trials compared multidisciplinary exercise-based cancer rehabilitation with usual care (Table 2).

Adverse events

Six trials reported on adverse events.[36–39,45,51] No serious adverse events were attributed to the rehabilitation interventions in these six trials. In one trial,[36] six participants in the rehabilitation group (of 214 total) developed lymphoedema. This did not limit group participation. Exacerbation of pre-existing musculoskeletal discomfort was reported by seven of 107 participants across two trials.[37,51] No other adverse events attributed to the intervention were reported in the remaining three trials. One trial comparing prehabilitation plus early rehabilitation with prehabilitation plus late rehabilitation found an overall postoperative pulmonary complication rate of 23% within 30 days after surgery, with complications highest in the early

Table 2
Characteristics of the included trials.

Trial Country	Participants	Intervention	Outcome measures
Adamsen 2009 [42] Denmark	n = 269 Age (*yr*) = 48 (11) Gender = 196 F, 73 M Cancer type = mixed Cancer stage = mixed Time since diagnosis = 12 wks Cancer treatment = during chemotherapy Baseline performance status = NR	Exp = Oncology rehab, 4/wk, 6 wks Con = Usual care: allowed to freely increase activity	• Muscle strength = 1RM • Fitness = VO_2 max (stationary cycle) • Fatigue = FACT An • Physical Activity = leisure time PA self-report • QoL = EORTC QLQ-C30, MOS SF-36 • Follow-up = 0, 6 wks
Bergland 1994 [43] Sweden	n = 199 Age (*yr*) = Exp 53 (NR), Con 54 (NR) Gender = 192 F, 7 M Cancer type = mixed Cancer stage = early Time since diagnosis = within 8 wks Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 11 sessions, 7 wks Con = Usual care: n = 65 had no intervention, n = 36 offered a session with dietitian and oncologist	• Strength and activity = self-reported • Psychological = Modified HADS, Mental Adjustment to Cancer Scale • Symptoms = Breast cancer symptoms • Activity = Activities of daily living • QoL = Global Quality of life • Follow-up = 0, 3, 6, 12 months
Bergland 2007 [40] Sweden	n = 211 Age (*yr*) = 69 (12) Gender = 0 F, 211 M Cancer type = prostate Cancer stage = mixed Time since diagnosis = within 6 months Cancer treatment = watchful waiting, during and post-treatment[a] Baseline performance status = NR	Exp = Oncology rehab, 7 sessions, 7 wks Con = Usual care: included two information leaflets and opportunity to phone nurse with questions	• Psychological = HADS • QoL = EORTC QLQ-C30 • Follow-up = 0, 6, 12 months
Bourke 2011 [41] UK	n = 18 Age (*yr*) = 69 (8) Gender = 6 F, 12 M Cancer type = colon Cancer stage = mixed Time since diagnosis = 6 to 24 months Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 1 to 2/wk, 12 wks Con = Usual care: included nurse-led follow-up	• Fatigue = FACT-F • Fitness = VO_2 peak (Bruce protocol) • Muscle strength = knee extensor strength, isometric muscle fatigue • Functional activity = 30-s STS • Physical Activity = Godin Leisure-time Index • QoL = FACT-C • Follow-up = 0, 12 wks
Cho 2006 [47] South Korea	n = 65 Age (*yr*) = 49 (NR) Gender = 65 F, 0 M Cancer type = breast Cancer stage = early Time since diagnosis = 15 months Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 2/wk, 10 wks Con = Usual care: no group rehabilitation	• ROM = Shoulder • Psychological = Psychosocial Adjustment Score • QoL = Quality of Life • Follow-up = 0, 10 wks
Clark 2013 [44] USA	n = 131 Age (*yr*) = 59 (NR) Gender = 45 F, 86 M Cancer type = mixed Cancer stage = advanced Time since diagnosis = within 12 months Cancer treatment = during radiotherapy Baseline performance status = ECOG 0 (n = 64), $\geq$ 1 (n = 67)	Exp = Oncology rehab, up to 4 wks Con = Usual care: including medical appointments and referrals to specialists when needed	• Psychological = POMS • Sleep = PSQI • Physical Activity = Exercise behaviour questionnaire • QoL = FACIT-Spiritual Wellbeing, FACT-G, Caregiver QoL questionnaire • Follow-up = 0, 4, 27 wks
Ghavarmi 2017 [48] Iran	n = 80 Age (*yr*) = 49 (9) Gender = 80 F, 0 M Cancer type = breast Cancer stage = early Time since diagnosis = 3 to 18 months post-treatment Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 5/wk, 24 wks Con = Usual care	• Body Composition = BMI • Fatigue = CFS • Sleep = PSQI • QOL = EORTC QLQ-C30, EORTC-BR23 • Follow-up = 0, 24 wks
Hubbard 2016 [52] UK	n = 41 Age (*yr*) = NR Gender = NR Cancer type = colorectal Cancer stage = NR Time since diagnosis = NR Cancer treatment = post-surgery Baseline performance status = NR	Exp = Cardiac rehab, 1 to 2/wk, 6 to 12 wks Con = Usual care: given booklet *Staying healthy after bowel cancer*	• Adverse events • Intervention adherence and attendance • Staff and patient experience • Follow-up = post-intervention, time period not stated

Table 2 (*Continued*)

Trial Country	Participants	Intervention	Outcome measures
Korstjens 2008 [45] Netherlands	n = 147 Age (*yr*) = 49 (11) Gender = 123 F, 24 M Cancer type = mixed Cancer stage = early Time since diagnosis = 1-year post-treatment Cancer treatment = post-treatment Baseline performance status = NR	Exp= Oncology rehab (physiotherapy, CBT), 2/wk, 12 wks Con = Active: physiotherapy only	• Cognition = SPSI-R • Psychological = HADS • Fitness = VO_2 max (Cycle ergometer) • Strength = MVC (Elbow and knee) hand held dynamometer • Fatigue = MFI • Physical Activity = PASE • QoL = MOS SF-36, EORTC QLQ-C30 • Follow-up = 0, 3, 6, 12 months
Midtgaard 2013 [36] Denmark	n = 214 Age (*yr*) = Exp 48 (10), Con 46 (12) Gender = 178 F, 36 M Cancer type = mixed Cancer stage = advanced Time since diagnosis = 80 d post-treatment Cancer treatment = post chemotherapy Baseline performance status = NR	Exp = Oncology rehab, 1/wk, 52 wks Con = Usual care: feedback and general exercise advice after fitness testing at each assessment	• Fitness = VO_2 max (cycle ergometer) • Muscle strength = 1RM chest and leg press • Fatigue = EORTC-QLQ C30 • Psychological = HADS • Physical activity = Saltin and Grimby Questionnaire • QOL = MOS SF-36, EORTC QLQ-C30 • Follow-up 0, 6, 12 months
O'Neill 2018 [37] Ireland	n = 43 Age (*yr*) = 66 (9) Gender = 8 F, 35 M Cancer type = upper gastrointestinal Cancer stage = early Time since diagnosis = 45 d post-surgery Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 2/wk, 12 wks Con = Usual care	• Fitness: VO_2 max (cycle ergometer) • Body composition = Anthropometric measurements • Physical activity = Actigraph GT3X+ • QoL = EORTC QLQ-C30 • Follow-up = 0, 3, 6 months
Quist 2018 [38] Denmark	n = 235 Age (*yr*) = early 66 (NR), late 65 (NR) Gender = 117 F, 118 M Cancer type = lung Cancer stage = early Time since diagnosis = 2 to 14 wks post-surgery Cancer treatment = post-surgery Baseline performance status = NR	Exp = Early rehabilitation: unsupervised training 2 wks preop and supervised training 2 wks postop, 2/wk, 12 wks Con = Active: late rehabilitation: started 6 wks post-op after 2 wks pre-op unsupervised training	• Fitness = VO_2 max (cycle ergometer) • Psychological = HADS, Distress thermometer • Lung capacity = FEV_1 • Muscle strength = 1RM chest and leg press • Functional activity = 6MWT • Physical Activity = Physical Activity Scale • QoL = MOS SF-36, FACT-L, EORTC QLQ-C30, MSPSS • Follow-up= 0, 14, 26, 52 wks
Rummans 2006 [46] USA	n = 115 Age (*yr*) = 60 (11) Gender = 37 F, 78 M Cancer type = mixed Cancer stage = advanced Time since diagnosis = NR Cancer treatment = during radiotherapy Baseline performance status = ECOG: 0 (n = 33), 1 (n = 66), 2 (n = 4)	Exp = Oncology rehab, 8 sessions, 4 wks Con = Usual care: usual outpatient appointments and any other support sought by the patient	• Psychological = POMS-SF • QoL = Spitzer QoL, LASA QoL, FACIT-Spiritual wellbeing • Follow-up = 0, 4, 8, 27 wks
Sandmael 2017 [49] Norway	n = 41 Age (*yr*) = 63 (9) Gender = 16 F, 25 M Cancer type = head and neck Cancer stage = early Time since diagnosis = 2 wks Cancer treatment = during radiotherapy Baseline performance status = KPS $\geq$ 90 (n = 33)	Exp = Oncology rehab during first wk of radiotherapy, 2/wk, 6 wks Con = Active: oncology rehab, 2 to 4 wks at end of radiotherapy, 3/wk and 2 voluntary sessions, 3 wk	• Body composition = CT • Physical Activity = HUNT PA-Q • Follow-up = 0, 6, 14 wks
Sheppard 2016 [50] USA	n = 31 Age (*yr*) = 55 (10) Gender = 31 F, 0 M Cancer type = breast Cancer stage = early Time since diagnosis $\geq$ 6 months post but $<$ 5 years Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 1/wk, 12 wks Con = Usual care: patients given the NCI booklet *Facing Forward Life After Cancer Treatment*	• Fitness = VO_2 peak (treadmill) • Body composition • Dietary intake • Physical activity = IPAQ-SF • Follow-up = 0, 12 wks
Spahn 2013 [51] Germany	n = 64 Age (*yr*) = Exp 58 (9), Con 55 (11) Gender = 64 F, 0 M Cancer type = breast Cancer stage = early Time since diagnosis = 50 months Cancer treatment = post-treatment Baseline performance status = NR	Exp = Oncology rehab, 1/wk, supervised walking 3/wk, 10 wks Con = Active: supervised walking training only, 30 min, 3/wk, 10 wks	• Fatigue = VAS 0-100 mm scale, MFI • Psychological = HADS • Symptoms = MRS • QoL = EORTC QLQ-C30 • Follow-up = 0, 10, 22 wks

Table 2 (*Continued*)

Trial Country	Participants	Intervention	Outcome measures
Uster 2017 [39] Switzerland	n = 58 Age (*yr*) = 63 (10) Gender = 18 F, 40 M Cancer type = mixed Cancer stage = advanced Time since diagnosis = 12 months Cancer treatment = during and post-treatment[a] Baseline performance status = ECOG: 0 (n = 4), 1 (n = 35), 2 (n = 16), 3 (n = 3)	Exp = Oncology rehab, 2/wk, 12 wks Con = Usual care: no exercise intervention offered to patients. Request to maintain physical activity level. Nutritional support by a dietician as needed.	• Length of stay of unplanned admissions • 3-month survival • Dietary intake • Strength = Grip, 1RM leg press • Body composition • Functional activity = 6MWT, 30-s STS • QoL = EORTC QLQ-C30 • Follow-up = 0, 3, 6 months

Age is mean (SD).

BMI = body mass index, CFS = Cancer Fatigue Scale, Con = control group, CT = computed tomography, ECOG = Eastern Cooperative Oncology Group Performance Status, EORTC BR23 = European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Breast, EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30, Exp = experimental group, FACT An = Functional Assessment of Cancer Therapy - Anaemia, FACT-C = Functional Assessment of Cancer Therapy - Colorectal Cancer, FACT-F = Functional Assessment of Cancer Therapy - Fatigue, FACT-G = Functional Assessment of Cancer Therapy - General, FACT-L = Functional Assessment of Cancer Therapy - Lung, FACIT = Functional Assessment of Chronic Illness Therapy, FEV = forced expiratory volume, HADS = Hospital Anxiety and Depression Scale, HUNT PAQ = Nord Trondelag Health Study Questionnaire, IPAQ-SF = International Physical Activity Questionnaire Short Form, KPS = Karnofsky Performance Status, LASA = Linear Analogue Scales of Assessment, MFI = Multidimensional Fatigue Inventory, MOS-SF 36 = Medical Outcomes Study Short Form 36, MRS = Menopausal Rating Scale, MSPSS = Multidimensional Scale Of Perceived Social Support, MVC = maximum voluntary contraction, NR = not reported, PA = physical activity, PASE = Physical Activity Scale for the Elderly, POMS = Profile of Mood States, PSQI = Pittsburgh Sleep Quality Index, QOL = quality of life, RM = repetition maximum, SPSI-R = Social Problem Solving Inventory, STS = sit to stand, VAS = visual analogue scale, 6MWT = 6-minute walk test.

[a] Studies included participants who were receiving treatment or had completed treatment at the time of trial. In the trial by Uster et al 2017, two participants received radiotherapy, 22 received chemotherapy.

rehabilitation group (33% compared with 14%).[38] The prevalence of cardiac complications was 13%, with no difference between groups.[38]

Adherence

Thirteen trials reported adherence to the rehabilitation programs. Adherence varied between 67%[36] and 94%,[37,49] with a mean weighted average of 76% of sessions attended. In one trial that included prehabilitation for lung cancer surgery, six participants allocated to prehabilitation did not receive the intervention due to 'lack of time' (mean 8, SD 3 days to surgery) and one participant chose not to attend due to low motivation.[38] Only 25% of participants accomplished daily preoperative exercise and there was high dropout among both early (39%) and late (42%) rehabilitation groups.[38]

Effects of multidisciplinary exercise-based cancer rehabilitation compared to usual care

Healthcare service outcomes

One trial evaluated the effect of multidisciplinary, exercise-based oncology rehabilitation on hospital length of stay for unplanned admissions.[39] The mean between-group difference was 2.4 days in favour of the intervention group (95% CI −3.1 to 7.8).

Patient-level outcomes

Quality of life: Meta-analysis of five trials,[36,37,39,42,48] including 557 participants, found low-quality evidence of a medium-sized, clinically significant observed mean effect for exercise-based oncology rehabilitation improving global quality of life measured by the European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORTC QLQ-C30) (MD 14 points, 95% CI −1 to 28; I^2 = 95%) when compared with usual care; however, the lower bound of the confidence interval indicated uncertainty (Table 4, Figure 2). For a more detailed forest plot, see Figure 3 on the eAddenda. Meta-analysis of two trials with longer term follow-up also demonstrated uncertainty of a clinically significant between-group effect at the 3-month follow-up (Table 4).

Sensitivity analysis was completed for quality of life due to high I^2 values. Removal of trials including any participants receiving cancer treatment from analysis[39,42] indicated uncertainty as to whether there were improvements in any quality of life-related outcome for the effect of exercise-based oncology rehabilitation compared with usual care (global quality of life subscale MD 18 points, 95% CI −4 to 40, I^2 = 97%). When trials including any participants with advanced cancer were removed from analysis,[36,39,42] exercise-based oncology rehabilitation compared with usual care improved global quality of life (MD 26, 95% CI 9 to 43, I^2 = 86%) and insomnia (MD −39 points, 95% CI −46 to −32, I^2 = 0%). When two trials implementing long-term interventions[36,48] (6 and 12 months, respectively) were removed from analysis, global quality of life may have improved compared with usual care (MD 9 points, 95% CI 1 to 16, I^2 = 51%).

Two short-term interventions (4 weeks) both completed in advanced cancer populations that were not included in meta-analysis due to heterogeneous outcomes found short-term improvements in quality of life that were not sustained at 6 months.[44,46] Another trial not included in meta-analysis comprising early and advanced colorectal cancer survivors found a clinically significant effect in favour of rehabilitation for improved quality of life using the FACT-C (MD 14 points, 95% CI 2 to 27) (Appendix 3).[41]

There were no significant differences between multidisciplinary, exercise-based oncology rehabilitation and usual care for other quality of life outcomes measured by the EORTC QLQ-C30 (Table 4, Appendix 4).

Physical outcomes: Meta-analysis of two trials[36,42] including 388 participants showed high-quality evidence of improvement in upper body muscle strength measured by 1RM chest press (MD 3.6 kg, 95% CI 0.4 to 6.8, I^2 = 18%) and moderate-quality evidence of improvement in lower body muscle strength measured by 1RM leg press (MD 19.5 kg, 95% CI 12.3 to 26.8, I^2 = 0%) when comparing exercise-based oncology rehabilitation with usual care (Figure 4). Meta-analysis of two trials[39,41] including 55 participants found low-quality evidence of improvement in functional strength measured with the 30-second sit to stand test (MD 6 repetitions, 95% CI 3 to 9, I^2 = 0%) when comparing exercise-based oncology rehabilitation with usual care (Figure 4). For a more detailed forest plot, see Figure 5 on the eAddenda. No differences between multidisciplinary, exercise-based oncology rehabilitation and usual care were found for fatigue, body composition or cardiorespiratory fitness (Table 4).

Psychological outcomes: Meta-analysis of two trials[36,43] including 465 participants found moderate-quality evidence of small reductions in depression (MD −0.7 points, 95% CI −1.2 to −0.1, I^2 = 0%) but not anxiety as measured by the Hospital Anxiety and Depression Scale after exercise-based oncology rehabilitation when compared with usual care (Figure 6). For a more detailed forest plot, see Figure 7 on the eAddenda. Additional outcomes relating to quality of life, physical activity levels, physical impairments and psychological status were not included in meta-analysis due to heterogeneity and/or insufficient data (Appendix 3).

Table 3
Characteristics of the multidisciplinary oncology rehabilitation programs.

Trial Country	Supervised exercise FITT	Non-exercise components		Disciplines involved	Group size	Program		Information topics
		core	additional			duration	sessions	
Adamsen 2009 [42] Hospital	F: 3/wk I: high T: RT, AT, balance T: 90 min	Relaxation (30 min, 4/wk), massage (30 min, 2/wk), body awareness and restoration (90 min, 1/wk)		Nurse specialist Physiotherapist	7 to 10	6 wk	4 d/wk	
Bergland 1994 [43] NR	F: 1/wk (4 wks) I: NR T: AT, RT, mobility T: 120 min	Information session (1/wk, 4 wks), coping training (1/wk, 3 wks)	Take-home info on progressive muscle relaxation	Nurse specialist Physical trainer Oncologist Psychologist Dietitian		7 wk	11 sessions	Side effects Crisis and emotional reactions Diet Alternative treatments Return to work Anxiety Handling situations and rights
Bergland 2007 [40] Hospital	F: 1/wk I: NR T: Pelvic floor, fitness training, relaxation, breathing T: 60 min	Information session (60 min/session)	Booster session 2 months after conclusion of program	Physiotherapist Nurse Urologist	3 to 10	7 wk	7 sessions	Prostate cancer Side effects Crisis and emotional reactions Incontinence and sexual function
Bourke 2011 [41] Hospital	F: 2/wk × 2 wks, 1/wk × 6 wks I: moderate to high T: AT, RT T: 30 mins	Information sessions (15 to 30 mins, 1/fortnight)	HEP 2/wk in last 6 wks, nutrition info pack	Nurse Exercise physiologist		12 wk	1 to 2 d/wk	Healthy eating
Cho 2006 [47] Cancer centre (tertiary hospital)	F: 2/wk I: low to moderate T: AT, flexibility T: 90 min	Information session (90 min, 1/wk), support group (60 min, 1/wk)	HEP booklets (wk 5 to 10) with education content and 2 elastic balls	Nurse Surgeon Dietitian Image consultant Physiatrist Exercise prescription Fitness instructor	15	10 wk	2 d/wk	Understanding breast cancer Treatment and complications Nutrition and diet Sexual and daily life Prevention and management Lymphoedema Breast reconstruction Image management Relationships/communication Latest cancer treatment
Clark 2013 [44] Cancer centre (tertiary hospital)	F: NR I: NR T: conditioning T: 20 min	Information session (60 min/session), relaxation (15 min/session)	Telephone counselling after structured intervention (10 calls), manual	Psychologist Physical Therapist Physiatrist Nurse Social worker Chaplain	4	up to 4 wk	6 sessions	Health behaviour change Radiation and chemotherapy Mood and coping Spirituality Problem solving Community resources Advanced care planning Record keeping Physical activity Defining quality of life Communication strategies
Ghavarmi 2017 [48] Cancer centre	F: 3 to 5/wk I: high T: AT T: 60 min	Individual diet advice (1/wk)	Diet diaries, written information	Researcher Exercise coach	≤ 15	24 wk	5 d/wk	Healthy eating
Hubbard 2016 [52] Hospital or sports centre	F: 1 to 2/wk I: moderate to high T: AT, RT, flexibility T: 75 to 90 min	Relaxation, information session (1/wk)	HEP written info	Physiotherapist Nurse Physiotherapy assistant	15 to 25	6 to 12 wk	1 or 2 d/wk	Diet Physical activity Relaxation/stress management Cardiac-specific information sessions

Table 3 (*Continued*)

Trial Country	Supervised exercise FITT	Non-exercise components		Disciplines involved	Group size	Program		Information topics
		core	additional			duration	sessions	
Korstjens 2008 [45] University medical centre, hospital, rehab centre	F: 2/wk I: moderate to high T: AT, RT, sports T: 120 min	CBT (120 min, 1/wk)	CBT homework (30 min)	Psychologist Nurse Physiotherapist Social worker	8 to 12	12 wk	2 d/wk	Experience with cancer Stress, relaxation and fatigue Exercise physiology Illness perceptions Optimism Self-management Goal setting Decision-making
Midtgaard 2013 [36] Hospital	F: 1/wk I: high T: AT, RT T: 90 min	Counselling (120 min, 3 individual sessions, tri-monthly; 6 group sessions, bi-monthly)		Psychologist Physiotherapist Exercise physiologist		52 wk	1 d/wk	
O'Neill 2018 [37] Cancer centre	F: 1 to 2/wk I: low to moderate T: AT, RT T: 20 to 35 min	Individual diet counselling, information sessions (7 sessions)	HEP (1/ wk in wks 1 to 2, then 5/wk in wks 10 to 12)	Surgeon Dietitian Physiotherapist Occupational therapist Psychotherapist		12 wk	2 d/wk	Mindfulness
Quist 2018 [38] Hospital	F: 2/wk I: moderate to high T: AT, RT T: 60 min	Group education (3 sessions), individual counselling (3 sessions)	Preop HEP, smoking cessation, diet advice as needed	Physiotherapist Nurse		12 wk	2 d/wk	Health promoting behaviour
Rummans 2006 [46] Cancer centre	F: NR I: NR T: conditioning T: 20 min	Information sessions (60 min/session), relaxation (10 to 20 min/session)		Psychologist Physical therapist Physiatrist Nurse Social worker Chaplain		4 wk	8 sessions	Symptom management Spiritual guidance Financial resources Advanced care planning CBT for coping Open discussion and support
Sandmael 2017 [49] Hospital	F: 2/wk I: moderate T: RT, AT T: 30 to 35 min	Nutrition counselling, (during group, 1 session, post group 1/wk), information session (1/wk)	Oral supplements	Physiotherapist Dietitian		6 wk	2 d/wk	Cancer treatment side effects Physical activity Mental health
Sheppard 2016 [50] Hospital	F: 1/fortnight I: moderate T: NR T: 30 min	Information session (60 min, 1/fortnight), MI phone coaching, (on wks in between, 15 min)	Pedometers and step goal, food diary, manual to store resources	Exercise Physiologist Nutritionist		12 wk	Fortnightly	Nutrition education
Spahn 2013 [51] Hospital	F: 3 in 10 wks I: high T: AT T: 30 min	Information sessions, guided discussion, stress, nutrition, relaxation, hydrotherapy, mindfulness (1 ×/wk, 6 hrs)	Walking HEP (30 min, 3/wk)	Sports therapist Other disciplines NR	20	10 wk	1 d/wk	Psyche and pain Relaxation response Stress management Cognitive restructuring Yoga Nutrition Social competence Coping with disease
Uster 2017 [39] Hospital	F: 2/wk I: moderate to high T: AT, RT, balance T: 60 min	Nutrition counselling (3 sessions)	Oral supplements (post exercise)	Physiotherapist Dietitian		12 wk	2 d/wk	

AT = aerobic training, CBT = Cognitive Behavioural Therapy, FITT = frequency, intensity, type, time (per session), HEP = home exercise program, MI = motivational interviewing; NR = not reported, RT = resistance training.

Effects of multidisciplinary exercise-based cancer rehabilitation compared with supervised group exercise programs

Meta-analysis of two trials[45,51] including 191 participants found low-to-moderate-quality evidence of no difference between multidisciplinary, exercise-based oncology rehabilitation and supervised group exercise for improving quality of life (MD 2.1 points, 95% CI −8.8 to 13.0) or reducing fatigue (Multidimensional Fatigue Inventory - General Fatigue MD −0.2 points, 95% CI −1.2 to 0.7) or depression (MD −0.6 points, 95% CI −2.9 to 1.6) and anxiety (MD −0.4 points, 95% CI −3.3 to 2.4) immediately post-intervention (Appendix 4).

Effect of timing of rehabilitation

One trial[38] compared early and delayed rehabilitation after lung cancer surgery. A 12-week supervised exercise program was initiated 2 or 6 weeks after surgery. There was less reduction in FEV_1 in the early rehabilitation group compared with late rehabilitation at week 26 (MD 0.15 L, 95% CI 0.05 to 0.25) and week 52 (MD 0.1 L, 95% CI 0 to 0.25). Due to wide confidence intervals there was uncertainty about whether there were any other between-group differences at week 26 (primary outcome VO_2 peak MD −3 ml/minute, 95% CI −88 to 82).[38] In another trial[49] comparing rehabilitation during and after radiotherapy in people with early head and neck cancer, there was uncertainty due to the relatively wide confidence intervals about the magnitude of the between-group differences with respect to body composition at week 14 (muscle mass MD 2.9 cm^2/m^2, 95% CI −4.5 to 10.3; body weight MD 8 kg, 95% CI −5 to 21).

Discussion

The main findings of this review of multidisciplinary, exercise-based oncology rehabilitation programs were: there was uncertainty about the impact of such programs on healthcare service outcomes from a single trial on length of stay, due to wide confidence intervals; there was high-quality evidence of improved muscle strength, improved functional strength and reduced depression in a mixed cohort of cancer survivors compared with usual care but uncertainty about improvements in short-term global quality of life compared with usual care; and typically, programs were well attended and safe. In addition, evidence from two trials demonstrated uncertainty about whether multidisciplinary, exercise-based oncology rehabilitation may be more or less effective than supervised group exercise rehabilitation alone in cancer survivors who have completed treatment. There is also uncertainty whether early rehabilitation after surgery for lung cancer or during radiotherapy for head and neck cancer is more or less effective than delayed rehabilitation.

This review highlights the lack of data relating to outcomes that are meaningful to healthcare services. While recommendations have been made to integrate exercise into standard cancer care,[14] this cannot be achieved without evidence of the impact of exercise-based rehabilitation programs at healthcare system level, particularly in public healthcare systems where resources are limited. The multidisciplinary, exercise-based oncology rehabilitation model is a complex and resource-intensive intervention. Cardiac and pulmonary rehabilitation interventions have extensive evidence relating to service outcomes, which has assisted the integration of such programs into standard care pathways. A review of 14,486 cardiac rehabilitation participants demonstrated reduced risk of hospital admission and reduced cardiovascular mortality, with four trials demonstrating cost savings.[18] Similarly, in a review of pulmonary rehabilitation, reductions in hospital admissions and mortality were also established.[53] In the present review, only one trial evaluated a healthcare service outcome. Only two reviews have previously included healthcare service outcomes by evaluating costs of oncology rehabilitation more broadly; data specifically relating to exercise-based interventions are inconclusive.[24,26] It should also be considered that demonstrating cost-effectiveness may be more difficult for oncology rehabilitation than for other chronic diseases. Unlike cardiac or pulmonary disease, cancer affects multiple systems and patients may not present as an inpatient at initial diagnosis or at any stage throughout their treatment continuum. Therefore, in evaluating cost-effectiveness, other healthcare service outcomes relating to economic benefits – such as return to work, medication adherence and outpatient healthcare service utilisation – also need to be considered in addition to hospitalisations.

There was uncertainty about whether multidisciplinary, exercise-based oncology rehabilitation has a positive impact on cancer survivors' quality of life. Improvements in global quality of life demonstrated a mean 14-point improvement on the EORTC QLQ-C30, indicating a clinically meaningful improvement, but this estimate came with substantial uncertainty.[54–56] However, there was more confidence in the results when only short-term interventions and people with early-stage cancer were included. Additionally, studies included in the review but not included in the meta-analyses also reported positive effects on quality of life. This may be explained by the nature of living with cancer as a chronic disease and the transient effect that interventions such as rehabilitation may have on outcomes. Participants also had reduced levels of depression and improved their muscle strength, which may have contributed to improved overall quality of life by enhancing their ability to participate in functional activity. Cancer treatment negatively affects quality of life among people with cancer and they report high levels of unmet physical and psychosocial need.[55,57] Oncology rehabilitation may mitigate these negative effects. Our results provide further explanation as to the effect of multidisciplinary rehabilitation on quality of life compared with previous reviews [21,22] and the findings are consistent with a qualitative analysis that exercise-based oncology rehabilitation helps people 'return to normal' after cancer diagnosis.[19] A key difference between this review and those previously published is that all trials included in this review implemented supervised group-based exercise. Supervision of exercise increases the likelihood of benefits related to quality of life.[8] This may be due to the additional benefits of attention from therapists, including guided exercise progression, and the potential for increased adherence to the exercise protocol resulting in the completion of a greater volume of exercise.[8]

Surprisingly, multidisciplinary, exercise-based oncology rehabilitation did not improve cardiorespiratory fitness or reduce cancer-related fatigue. These are two important endpoints of oncology rehabilitation known to improve with exercise alone.[10,58] Our results may be related to issues with exercise prescription. In order for physiological adaptations to occur to induce change in cardiopulmonary systems, exercise must be prescribed at the appropriate dosage in accordance with FITT (frequency, intensity, type and timing) training principles, with attention paid to exercise specificity and progressive overload. Moderate-intensity aerobic exercise improves cardiorespiratory fitness and fatigue levels of cancer survivors.[10,33,58] There was poor reporting of exercise interventions in this review's included trials, which was consistent with other exercise trials on cancer.[59] Moreover, supervised exercise was mostly completed once or twice a week, with only half of the included trials including specific details related to aerobic exercise intensity, varying from low-to-moderate to high-intensity aerobic exercise. To be able to translate interventions into practice, adequate reporting of trials is important for clinicians who practise in exercise-based oncology rehabilitation. Clinicians currently have difficulty prescribing exercise in oncology rehabilitation programs to the appropriate intensity required to improve outcomes.[20] Therefore, exercise-based oncology rehabilitation interventions used in trials need to be reported using recognised checklists such as TIDieR[60] and described appropriately using FITT principles, so that clinicians can provide effective exercise prescription in practice.

Another possible explanation for the absence of between-group differences in fatigue may be related to timing and baseline status of participants. Participants in this review had low-to-moderate levels of fatigue prior to commencing rehabilitation. The majority of participants in this review had completed treatment and had early stage cancer, which may explain why their fatigue did not

Table 4
Meta-analysis, effect of multidisciplinary, exercise-based oncology rehabilitation programs on patient-related outcomes versus usual care.

Outcome	Time point	Trials (*n*)	Participants (*n*)	MD (95% CI) I^2 Exp minus Con	MCID	GRADE
Quality of Life (*0 worst to 100 best*)						
EORTC QLQ-C30 Global	Post-intervention	5[36,37,39,42,48]	557	14 (−1 to 28) 95%	5 to 8	Low[a]
	Follow-up	2[37,39]	77	8 (−1 to 18) 0%		Moderate[b]
EORTC QLQ C30 Physical function	Post-intervention	5[36,37,39,42,48]	551	10 (−2 to 22) 97%	2 to 7	Low[a]
	Follow-up	2[37,39]	77	3 (−9 to 15) 41%		Low[a]
EORTC QLQ-C30 Role function	Post-intervention	5[36,37,39,42,48]	551	7 (−2 to 16) 82%	6 to 12	Low[a]
	Follow-up	2[37,39]	76	7 (−7 to 20) 0%		Moderate[b]
EORTC QLQ-C30 Emotional function	Post-intervention	5[36,37,39,42,48]	550	8 (−2 to 17) 86%	6 to 9	Low[a]
	Follow-up	2[37,39]	77	6 (−29 to 41) 89%		Low[a]
EORTC QLQ-C30 Cognitive function	Post-intervention	5[36,37,39,42,48]	551	4 (−5 to 13) 88%	3 to 7	Low[a]
	Follow-up	2[37,39]	76	−7 (−25 to 11) 60%		Low[a]
EORTC QLQ-C30 Social function	Post-intervention	5[36,37,39,42,48]	551	7 (−3 to 17) 88%	3 to 8	Low[a]
	Follow-up	2[37,39]	77	−8 (−56 to 40) 90%		Low[a]
Symptoms (*0 best to 100 worst*)						
EORTC QLQ-C30 Fatigue	Post-intervention	5[36,37,39,42,48]	674	−9 (−23 to 6) 94%	−4 to −9	Low[a]
	Follow-up	2[37,39]	77	−3 (−14 to 9) 90%		Low[a]
EORTC QLQ-C30 Nausea/vomiting	Post-intervention	5[36,37,39,42,48]	546	−7 (−14 to 0) 91%	−3 to −9	Low[a]
EORTC QLQ-C30 Pain	Post-intervention	5[36,37,39,42,48]	551	−10 (−23 to 3) 93%	−5 to −9	Low[a]
EORTC QLQ-C30 Dyspnoea	Post-intervention	5[36,37,39,42,48]	551	−5 (−13 to 2) 82%	−2 to −9	Low[a]
EORTC QLQ-C30 Insomnia	Post-intervention	5[36,37,39,42,48]	551	−15 (−33 to 4) 94%	−5 to −9	Low[a]
EORTC QLQ-C30 Appetite	Post-intervention	5[36,37,39,42,48]	550	0 (−1 to 0) 0%	−7 to −13	High
EORTC QLQ-C30 Constipation	Post-intervention	5[36,37,39,42,48]	551	−6 (−14 to 3) 70%	−4 to −10	Low[a]
EORTC QLQ-C30 Diarrhoea	Post-intervention	5[36,37,39,42,48]	551	−1 (−8 to 7) 83%	−3 to −11	Moderate[c]
EORTC QLQ-C30 Financial difficulty	Post-intervention	5[36,37,39,42,48]	551	−7 (−15 to 1) 78%	−3	Low[a]
Body composition						
BMI (kg/m^2)	Post-intervention	4[37,41,48,50]	159	−2.2 (−5.2 to 0.9) 67%	NA	Low[a]
Waist circumference (*cm*)	Post-intervention	2[37,50]	62	−0.7 (−6.9 to 5.6) 0%	NA	Moderate[b]
Physical capacity						
VO_2 peak (*ml/kg/min*)	Post-intervention	3[36,37,50]	215	1.08 (−0.52 to 2.68) 0%	NA	High
30-sec Sit to Stand (*repetitions*)	Post-intervention	2[39,41]	55	6 (3 to 9) 0%	2	Low[a]
Strength: 1RM chest (*kg*)	Post-intervention	2[36,42]	388	3.6 (0.4 to 6.8) 18%	NA	High
Strength: 1RM leg (*kg*)	Post-intervention	2[36,42]	388	19.5 (12.3 to 26.8) 0%	NA	Moderate[b]

Table 4 (*Continued*)

Outcome	Time point	Trials (*n*)	Participants (*n*)	MD (95% CI) I^2 Exp minus Con	MCID	GRADE
Psychological well-being (0 best to 21 worst)						
HADS Anxiety	Post-intervention	2[36,43]	338	−0.7 (−1.4 to 0.1) 0%	−1.8 to −1.3	Moderate[d]
HADS Depression	Post-intervention	2[36,43]	338	−0.7 (−1.2 to −0.1) 0%	−1.7 to −1.5	Moderate[d]

GRADE working group grades of evidence (see reason for downgrade). PEDro score < 6 was considered lower quality. MCID taken from pulmonary rehabilitation cohort for HADS[70] and 30-sec sit to stand[71] because no MCID was available for oncology rehabilitation. MCID for EORTC from Cocks et al 2012.[56] Range of scores available representing the smallest clinically relevant difference.
BMI = body mass index, EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30, GRADE = Grades of Research, Assessment, Development and Evaluation, HADS = Hospital Anxiety and Depression Scale, MCID = minimum clinically important difference, NA = not available, NR = not reported, 1RM = one repetition maximum.

[a] Reason for downgrade: heterogeneity, wide confidence intervals.
[b] Reason for downgrade: wide confidence intervals.
[c] Reason for downgrade: heterogeneity.
[d] Both trials rated lower quality.

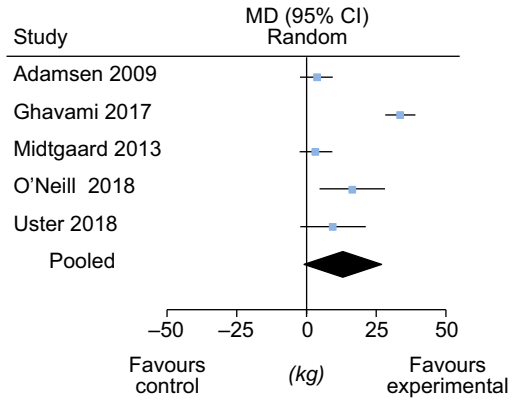

Figure 2. Mean difference (95% CI) in effect of multidisciplinary, exercise-based oncology rehabilitation compared with usual care on global quality of life measured with the European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORTC-QLQ C30) by pooling data from five trials.

significantly improve, given that the prevalence of cancer-related fatigue is higher among patients completing treatment and typically resolves within a year of treatment completion.[61,62] In addition, baseline physical performance of participants in relation to their disease status was largely unknown. Given that the greatest gains are made by participants with the highest needs,[63] it is possible that there was a ceiling effect of rehabilitation interventions with low baseline fatigue and high physical performance.

The results from this review provide preliminary evidence from two trials that multidisciplinary education in addition to exercise may

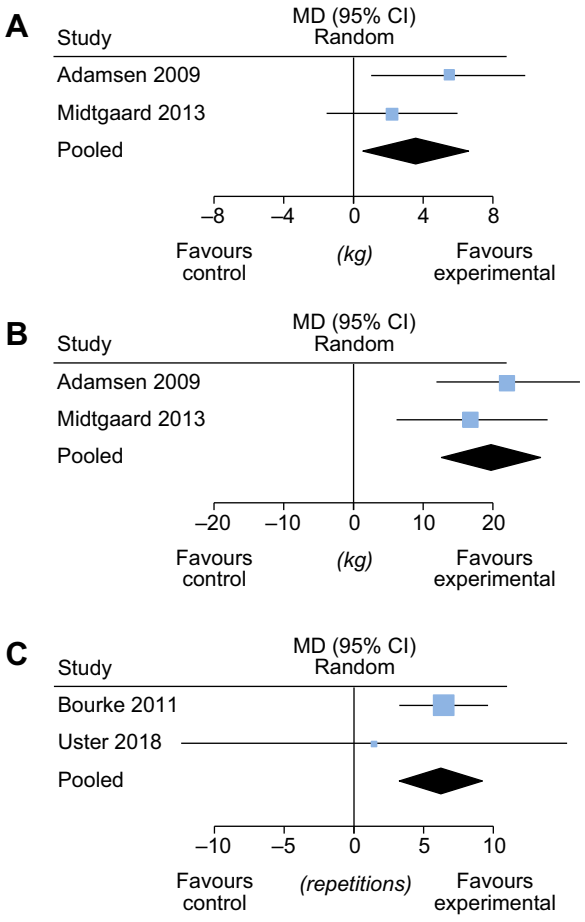

Figure 4. Mean difference (95% CI) in effect of multidisciplinary, exercise-based oncology rehabilitation compared with usual care on strength measured by the (A) 1 repetition maximum (1RM) chest press, (B) 1RM leg press and (C) 30-second sit to stand.

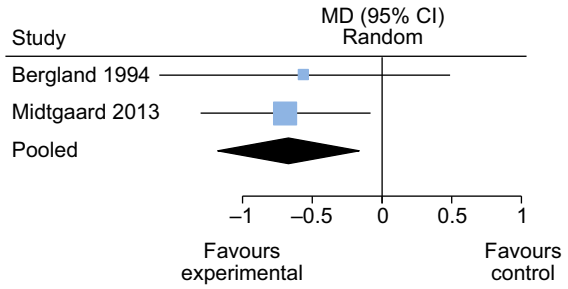

Figure 6. Mean difference (95% CI) in effect of multidisciplinary, exercise-based oncology rehabilitation compared with usual care on depression measured with the Hospital Anxiety and Depression Scale (HADS) by pooling data from two trials.

not provide additional benefit compared with exercise alone. This is consistent with previous findings related to oncology,[64] pulmonary[65] and cardiac rehabilitation.[18] It may be expected that a complex multidisciplinary rehabilitation intervention would be more effective than rehabilitation alone, as it can address multiple issues.[66] However, there is strong evidence that exercise alone improves cancer-related outcomes.[9,11] Therefore, routine addition of multidisciplinary education to exercise may need to be reconsidered. In the two trials that compared multidisciplinary rehabilitation and supervised group exercise, one multidisciplinary intervention was a 6-hour mind-body intervention, including guided discussion and lectures, and one comprised a 2-hour cognitive behavioural training session including education, discussion and problem solving. Adherence to specific elements of the rehabilitation program may be reduced due to participants needing to direct focus on multiple areas. Education may also not be delivered in a way that is consistent with adult learning needs, reducing its potential effectiveness.[65] As up to 80% of existing oncology rehabilitation programs include education sessions,[20] more research is required to justify their inclusion as a core element of cancer rehabilitation.

Timing of exercise-based oncology rehabilitation along the cancer continuum may not be as important as having access to services. Two trials comparing early and delayed treatment found no between-group difference in most outcomes. Moreover, in one trial offering early rehabilitation for lung cancer surgery there was high dropout, low adherence and higher complications in the earlier rehabilitation group.[38] These findings support qualitative data from participants of exercise-based cancer rehabilitation, suggesting that patients prefer flexible programs they can access when they feel ready to participate, especially when undergoing cancer treatment.[19,67] However, our findings are based on limited data. Recent guidelines have been released supporting the implementation of prehabilitation for people with cancer, where it may be more appropriate to provide individual multidisciplinary therapy than group-based therapies.[68]

To our knowledge, this review is the first to evaluate the effect of multidisciplinary, exercise-based oncology rehabilitation group programs. This review was reported in line with PRISMA guidelines and prospectively registered. It comprised randomised controlled trials and trials were not restricted to countries where English was the primary language. This inclusion reduced the risk of selection and publication bias, increasing confidence in the results. This review also included trials with participants with a variety of cancers, across the treatment continuum including people with advanced cancer, which is often underrepresented in exercise and cancer trials.

The methodological quality of most of the included trials was low, largely due to lack of allocation concealment and blinded assessment. We were unable to make strong recommendations relating to the duration and timing of exercise-based oncology rehabilitation programs due to the limited number and diversity of studies. Most included trials were short-term and completed after treatment in participants with early-stage cancer. There were insufficient trials to complete a moderator analysis. Furthermore, no trials examined multi-disciplinary, exercise-based prehabilitation, which is an area of increasing interest in cancer, particularly due to potential healthcare service cost savings.[69] There were also high levels of unexplained heterogeneity in the meta-analysis, which may limit the confidence in the estimate of the pooled effect. To account for this, sensitivity analysis was completed considering cancer type, treatment phase and program duration; however, further subgroup analysis was limited by lack of trials.

Only one randomised controlled trial reported the effect of multidisciplinary, exercise-based oncology rehabilitation programs on healthcare service outcomes. If exercise-based rehabilitation programs are to become part of standard care, more research is required to evaluate oncology rehabilitation at a healthcare service level. This review of 17 trials demonstrated moderate-to-high-quality evidence that multidisciplinary, exercise-based oncology rehabilitation improves strength and reduces depression, and low-quality evidence that it may improve quality of life compared with usual care. Strong recommendations relating to optimal content, timing and duration of programs were unable to be made. However, preliminary evidence suggests that exercise-based oncology rehabilitation that includes added multidisciplinary education may not provide additional benefit compared with supervised, group-based exercise alone, nor does providing early compared to late rehabilitation in head and neck and lung cancer survivors.

What was already known on this topic: Among people with cancer, exercise helps to reduce fatigue and depression, while improving cardiorespiratory fitness and quality of life. Supervised exercise programs with higher doses of exercise yield the greatest improvements. Multidisciplinary oncology rehabilitation programs supplement the exercise with lifestyle counselling and educational sessions from various healthcare professionals.

What this study adds: Multidisciplinary, exercise-based oncology rehabilitation programs offered in a group format increase limb muscle strength, improve performance on functional strength tasks and reduce depression. Current evidence does not confirm whether they improve outcomes at the healthcare service level, such as costs, hospitalisations and length of stay.

eAddenda: Figures 3, 5 and 7 and Appendices 1 to 4 can be found online at https://doi.org/10.1016/j.jphys.2020.12.008.

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Correspondence: Amy M Dennett, Allied Health Clinical Research Office, Eastern Health, Melbourne, Australia. Email: amy.dennett@easternhealth.org.au

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