Effect of exercise interventions on hospital length of stay and admissions during cancer treatment: a systematic review and meta-analysis

David Mizrahi ,[1,2] Jonathan King Lam Lai,[3,4] Hayley Wareing,[3] Yi Ren,[3] Tong Li ,[1,3] Christopher T V Swain ,[5,6] David P Smith ,[1] Diana Adams,[7] Alexandra Martiniuk ,[1,8,9] Michael David[1,10]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bjsports-2023-107372).

For numbered affiliations see end of article.

Correspondence to
Dr David Mizrahi, The University of Sydney, Sydney, Australia; david.mizrahi@sydney.edu.au

Accepted 12 October 2023
Published Online First
21 November 2023

ABSTRACT

Objective To assess the effect of participating in an exercise intervention compared with no exercise during cancer treatment on the duration and frequency of hospital admissions.

Design Systematic review and meta-analysis.

Data sources MEDLINE, EMBASE, PEDro and Cochrane Central Registry of Randomized Controlled Trials.

Eligibility criteria for selecting studies Randomised studies published until August 2023 evaluating exercise interventions during chemotherapy, radiotherapy or stem cell transplant regimens, compared with usual care, and which assessed hospital admissions (length of stay and/or frequency of admissions).

Study appraisal and synthesis Study quality was assessed using the Cochrane Risk-of-Bias tool and Grading of Recommendations Assessment, Development and Evaluation assessment. Meta-analyses were conducted by pooling the data using random-effects models.

Results Of 3918 screened abstracts, 20 studies met inclusion criteria, including 2635 participants (1383 intervention and 1252 control). Twelve studies were conducted during haematopoietic stem cell transplantation regimens. There was a small effect size in a pooled analysis that found exercise during treatment reduced hospital length of stay by 1.40 days (95% CI: −2.26 to −0.54 days; low-quality evidence) and lowered the rate of hospital admission by 8% (difference in proportions=−0.08, 95% CI: −0.13 to −0.03, low-quality evidence) compared with usual care.

Conclusion Exercise during cancer treatment can decrease hospital length of stay and admissions, although a small effect size and high heterogeneity limits the certainty. While exercise is factored into some multidisciplinary care plans, it could be included as standard practice for patients as cancer care pathways evolve.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Exercise in patients diagnosed with cancer has been shown to improve quality of life, functional capacity, cardiorespiratory fitness, reduce symptom burden and lower the risk of recurrence and mortality.

⇒ Numerous oncology organisations internationally now endorse exercise during and after cancer treatment.

⇒ It is unknown whether participating in a structured exercise intervention during chemotherapy, radiotherapy or stem cell transplant regimens reduces the duration and frequency of hospital admissions.

WHAT THIS STUDY ADDS

⇒ This systematic review and meta-analysis evaluate the evidence regarding the association between participating in exercise interventions during cancer treatment and reductions in the duration and frequency of hospital admissions.

⇒ There was a small but significant effect size in a pooled analysis that structured exercise during treatment reduced hospital length of stay by 1.40 days compared with usual care.

⇒ Structured exercise during cancer treatment was demonstrated to be safe, and contributed to an 8% lower rate of hospital admission.

INTRODUCTION

In 2020, there were approximately 19.3 million new cancer diagnoses worldwide.[1] Cancer treatment typically involves prolonged regimens that can result in extended hospitalisation due to adverse treatment-effects and reduced physical function.[2] The number of patients with cancer requiring systemic therapies is projected to increase by 53% from 9.8 million in 2020 to 15 million in 2040,[3] so interventions that reduce complications from treatment are warranted.

Different cancer treatments have varying levels of supportive care needs which can impact the risk of repeated and prolonged hospital stays. For example, haematopoietic stem cell transplantation (HSCT) is a common treatment for haematological malignancies in adults and children.[4] HSCT typically requires staying in a single-bed isolation room for 4–6 weeks due to the risk of bleeding complications and infection caused by immunodeficiency and neutropenia.[5] Treatments including surgery, chemotherapy, radiotherapy and immune or targeted therapies also carry a risk of hospital admission to manage common side effects such as dyspnoea, pain, cachexia and fatigue.[6] Repeated and prolonged hospitalisation remains a significant physical, psychosocial, logistical and economic burden for patients, caregivers and healthcare systems. Lengthy periods of hospitalisation can disrupt the rest–activity cycle with

To cite: Mizrahi D, Lai JKL, Wareing H, *et al. Br J Sports Med* 2024;**58**:97–109.

associated physical deconditioning and sleep deprivation, while also increasing the risk of falling, infections,[7] impeding quality of life (QoL),[8] alongside reducing satisfaction with care.[9] The physical deconditioning from extended sedentary periods, which can cause fatigue, muscle wasting and reduced physical function can further worsen QoL.[10]

Hospital length of stay for patients with cancer varies by age, cancer type, insurance, treatment, comorbidity and country.[11] In a high-income country such as Australia in 2019–2020, there were 1.3 million cancer-related hospitalisations, accounting for one in nine of all hospitalisations, with the age-standardised admission rate increasing by 20% in the past 20 years.[12 13] In the USA in 2017, the average duration for adults who were admitted to hospital principally for their cancer was for 6.5 days.[14] A population-wide analysis in a middle-income country such as Brazil found that patients with breast, prostate, colorectal, cervix, lung and stomach cancer in 2010–2014 spent a median of 6 days in hospital during their first year after diagnosis.[15] For patients treated for advanced cancers or haematological malignancies, the hospital length of stay is typically prolonged to 29 and 26 days, respectively.[16 17] Extended and repeated hospital stays can be costly for healthcare systems and individual payers, with the average cost of US$3400 per day.[14] A recent systematic review found no hospital-initiated intervention (eg, clinical pathways, multidisciplinary care, case management, hospitalist services) exhibited significantly reduced hospital length of stay across high-risk populations.[18] However, this systematic review did not include any studies incorporating exercise as an intervention. Therefore, appraising the evidence around the effectiveness of exercise-based interventions in reducing hospital length of stay and admissions is critical among patients undergoing cancer treatment who may experience reduced physical function, and numerous side effects and comorbidities.[6]

In the past two decades, physical activity (ie, any movement resulting in energy expenditure, such as leisure-time activities) and exercise (ie, planned and structured physical activity with the aim to improve fitness) have become increasingly recognised as an important intervention for patients with cancer to engage in during and following treatment.[19] Leading oncology organisations now recommend incorporating regular aerobic and resistance exercise into standard practice during and after treatment, however the optimum dose and intensity recommended during treatment is still unknown.[20 21] For patients with more complex medical attention, such as those with advanced cancer, exercise has been evidenced to be feasible, safe and beneficial.[22] Exercise in patients with cancer has been shown to improve QoL, functional capacity, cardiorespiratory fitness, reduce symptom burden (eg, fatigue) and modulate systemic inflammation.[23 24] Furthermore, epidemiological analyses show that patients with cancer with higher doses of moderate-to-vigorous physical activity have a reduced risk of cancer recurrence and mortality.[25] Patients with reduced cardiorespiratory fitness before treatment have been shown to have lower chemotherapy completion rates, thus improving this modifiable risk factor in deconditioned patients by exercising during treatment may improve clinical outcomes.[26] Although there is a growing body of evidence supporting the role of exercise in cancer care, it remains unclear whether exercising during prolonged cancer treatment regimens can reduce hospital length of stay. This study proposed to fill the gap in the literature regarding the effect of exercise during frequently prescribed cancer treatments on hospital outcomes, and by specific exercise parameters (type, frequency, and level of supervision), in adults and children with cancer. The primary aim of this study examined the effect of exercise interventions on the hospital length of stay and admissions rate for patients with cancer undergoing HSCT, chemotherapy and/or radiotherapy treatment regimens, with secondary aims examining specific exercise parameters and by age group.

METHODS

Search strategy and selection criteria

This systematic review was conducted in accordance with the Cochrane Collaboration methods for systematic reviews,[27] and reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses checklist (online supplemental table 1).[28] The review protocol was registered with PROSPERO (2022 CRD42022309639). Electronic database searches using combinations of keywords for 'cancer', 'treatment', 'exercise' and 'hospitalization' were undertaken in MEDLINE via PubMed, EMBASE, Cochrane Central Register of Controlled Trials and PEDro (full search details are shown in online supplemental table 2). The initial search included studies published in peer-reviewed journals from inception to 23 March 2022. All databases were searched again on 9 August 2023 to ensure the articles included in this manuscript were current prior to publication. No additional eligible studies identified between March 2022 and August 2023. Reference lists of relevant reviews were manually searched for any additional articles which were not identified in the database searches.

Eligibility criteria

The Participant, Intervention, Comparator and Outcome framework[29] was used to organise the inclusion criteria. The inclusion criteria included studies encompassing: (1) patients with adult or childhood cancer of any age, cancer type and disease stage, (2) undergoing cancer treatment regimens including chemotherapy, radiotherapy or stem cell/bone marrow transplant as individual therapy modality or combined regimens, (3) randomised controlled trials (RCTs) which implemented an exercise intervention (ie, repeated bouts of exercise) during the period of the cancer treatment regimen (eg, chemotherapy protocol), be it aerobic-based, resistance-based or mixed, which could be delivered as a supervised in-hospital intervention by an exercise professional or other member of the medical team, or an unsupervised intervention where a programme is created for the participant to complete by themselves in hospital or at home, or a combination, compared with a usual care control group and (4) studies assessing the hospital length of stay and/or number of hospital admissions. Studies were included when interventions other than exercise were also applied as part of the study (eg, education, meditation, nutritional interventions), and studies published in any language were permitted. Single-arm and non-randomised studies, systematic reviews, case studies and conference abstracts were excluded.

Study selection and data extraction

Studies identified during the electronic database search were imported in the data management software for systematic reviews, Covidence (Veritas Health Innovation, Melbourne, Australia; available at www.covidence.org). Duplicate titles were removed. Abstract and title screening were screened initially, followed by full-text review and then data extraction, with each step dual-screened between three independent authors (100% by DM, and 50% each by HW and YR). Authors (DM, AM, MD, CTVS, DPS and TL) have prior experience with conducting systematic reviews and meta-analyses. To ensure consistency, reviewing coauthors (DM, HW and YR) received guidance from a university librarian with expertise in systematic reviews, and underwent weekly meetings over 12 weeks to discuss progress and challenges. Conflicts were resolved by discussion among these three authors, with an external reviewer consulted if consensus could not be achieved (CTVS). Study details extracted included country, recruitment dates, age, sex, type of cancer diagnosis and treatment type (ie, chemotherapy, radiotherapy, HSCT) of participants. Data extraction for exercise intervention characteristics included type (eg, aerobic, resistance), dose (eg, sessions, repetitions, intensity), frequency (eg, times per week), setting (eg, supervised in-hospital, home-based), duration (eg, minutes, weeks), compliance (ie, number of sessions completed compared with prescribed) and what the control group was instructed to do. Hospital length of stay data was reported as days spent in hospital and proportion of the study group admitted to hospital. Authors from studies with incomplete data on hospital length of stay outcomes were contacted on up to two occasions.

Quality assessment

The Cochrane Risk of Bias 2 tool (RoB 2) was used to assess the risk of bias of the RCTs.[30] The RoB 2 evaluates sources of bias from random sequence generation, allocation concealment, blinding of personnel, patients and outcome assessors, incomplete outcome data, selective outcome reporting and other sources. Each bias category was ranked as 'low', 'high' or 'some concerns. All studies were dual-assessed for bias between independent researchers (100% by JKLL, and 50% each by TL and CTVS), with disagreements resolved by discussion with the lead author (DM).

The quality of evidence was determined using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system,[31] categorising the level of evidence as 'high', 'moderate', 'low' or 'very low,' using the criteria: risk of bias, inconsistency (ie, unexplained heterogeneity), indirectness (ie, population, intervention and/or outcome differences), imprecision (ie, wide CIs leading to uncertainty) and other considerations (eg, publication bias).

Outcomes

The primary outcome of interest was the potential effect of participating in an exercise intervention during cancer treatment on hospital length of stay, frequency of hospital admissions or proportion of study group admitted to hospital, compared with a usual-care control group. Adverse events of the exercise interventions were reported as a secondary outcome.

Data synthesis and analysis

Descriptive statistics were used to summarise study characteristics. Tables and figures were also used to present the data. Inter-rater reliability for all dual-screened processes was assessed by calculating the proportional agreement between assessors. Hospital length of stay was reported as a continuous outcome (days), while rate of hospital admission was reported as a dichotomous outcome. In the initial stage of the meta-analysis, means and SD were extracted from the included studies where the outcome was continuous. If not reported, we derived means and SD from sample size, median, IQR, minimum and maximum values.[32] When the outcome was dichotomous, the number of events and total number of participants were extracted. Effect sizes in the form of mean difference or differences in proportions with their 95% CIs were then calculated for each study, which were presented by treatment type. To handle heterogeneity from study effects were pooled using restricted maximum likelihood random effects estimation. Furthermore, statistical heterogeneity was assessed by means of an I^2 test and was categorised as low (<50%), moderate (51–75%) or high according to predefined criteria.[33] This was calculated to estimate how much the total variability in the effect size estimates was due to heterogeneity among the true effects.[34] To further assess heterogeneity, subgroup analyses were performed by the cancer treatment (ie, chemotherapy only, chemotherapy and radiation, HSCT), with sensitivity analyses conducted by exercise type, number of sessions and level of supervision. Additionally, we tested the association between the mean difference effect and each subgroup using meta-regression. The possible presence of publication bias was assessed using Egger's test.[35] All analyses were conducted using Stata V.18 (StataCorp, College Station, Texas, USA).

Protocol deviations

Our final manuscript deviated from the original PROSPERO registration by focusing only on RCTs, adding adverse events as a secondary outcome, conducting sensitivity analyses investigating the effect of different exercise doses on hospitalisation outcomes, and searching four rather than six electronic databases (details listed in online supplemental table 3).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting of this research, however the authorship team will disseminate the findings through their established consumer networks (ie, oncology community and non-government organisations).

Equity, diversity, and inclusion statement

The author group is gender-balanced and consists of junior, mid-career and senior researchers from different disciplines (including exercise physiology, implementation science, medical oncology, epidemiology and biostatistics). Although the research was conducted in Australia, some of the research teams are from different countries and a range of ethnicities. All the studies reported in this manuscript were conducted in high-income countries, with the small number of studies reporting ethnicity having a high Caucasian representation, and thus we acknowledge the findings may not be generalisable to low-income and middle-income countries and other ethnicities, warranting addressing in future studies.

RESULTS

Literature search

A total number of 4349 studies were retrieved through the initial search strategy. After removing 430 duplicates, 3919 abstracts were initially screened. After screening the titles and abstracts, 118 full-text articles were read. Following the full-text review of these publications, 98 studies were excluded based on the inclusion and exclusion criteria. Finally, 20 articles were included in the systematic review,[36–55] and 19 articles in the meta-analyses (figure 1).[36–42 44–55] One study was not included in the meta-analysis because it did not include data about hospital length of stay despite conducting a between-group comparison.[43] There was good inter-rater agreement in the initial abstract screening (96% proportional agreement) and 72% agreement at the assessment for full text inclusion.

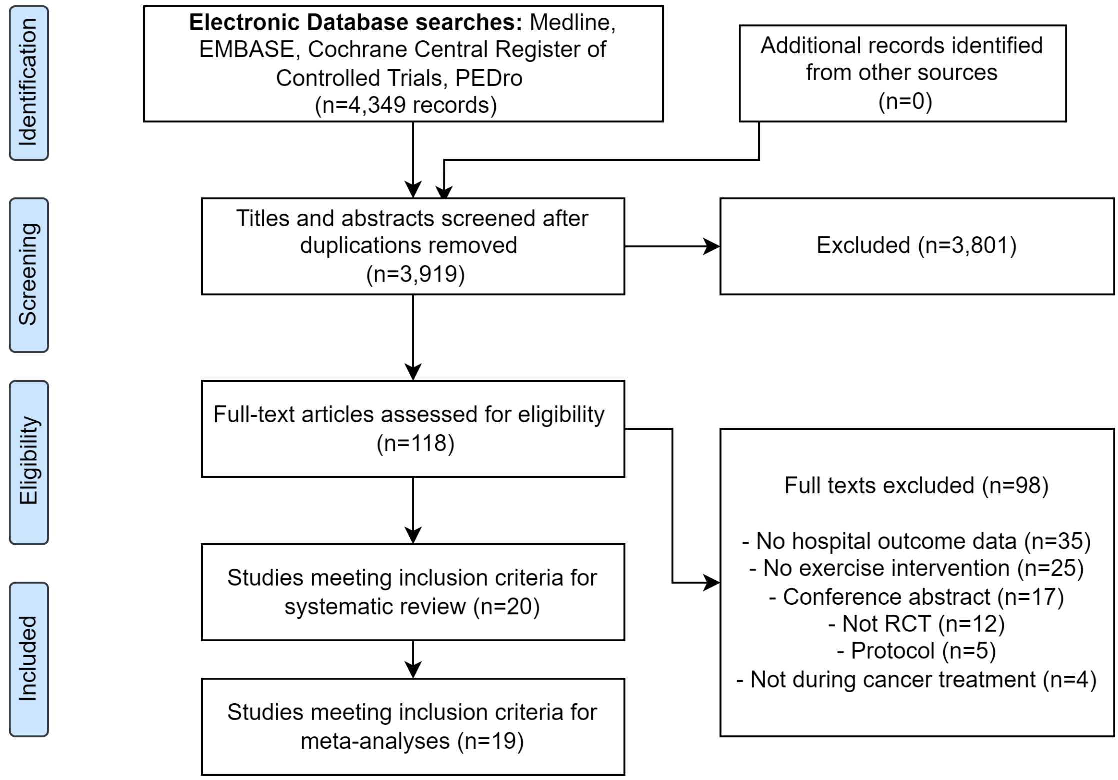

Figure 1 Flow chart of included studies.

Study characteristics

Study characteristics are reported in table 1. The systematic review included data from 2635 participants recruited (1383 in exercise interventions and 1252 in control groups), with a median sample size across studies of 70 (range: 29–711). Sixty-two per cent of participants were women. Eighteen studies were conducted in adults (mean age=52.2±10.9 years)[37–40 42–55] and two studies in children (mean age=11.0±3.5 years).[36 41] Studies were conducted in Germany (n=7),[38 41 42 49 52–54] the USA (n=5),[36 43 44 51 55] Canada (n=2),[37 40] Sweden (n=1),[50] Denmark (n=1),[39] France (n=1),[47] Scotland (n=1),[45] Switzerland (n=1)[48] and Netherlands (n=1).[46] Studies were conducted in patients with haematological cancers (n=14),[36–41 43 44 49 51–55] breast cancer (n=2)[45 50] and mixed solid tumours (n=4).[42 46–48] Studies were conducted during HSCT (n=12),[36 38–41 43 44 51–55] chemotherapy (n=3),[37 49 50] chemoradiation (n=4)[45–48] and across both chemotherapy and HSCT (n=1).[42] The median recruitment rate was 71% (range 18–99%). There is clear evidence of clinical heterogeneity in the included studies as shown by the diversity in the study populations, both in age and sex.

EXERCISE INTERVENTIONS

Type of exercise interventions

Data regarding the exercise interventions are presented in table 2. Exercise interventions were combined aerobic, resistance and stretching (n=6),[36–41] aerobic only (n=4),[42–44 55] aerobic and resistance (n=2),[45 46] aerobic, resistance and balance (n=2),[47 48] aerobic versus resistance (n=2),[49 50] resistance only (n=1),[51] aerobic, stretching and activities of daily living (n=1),[52] aerobic, resistance, stretching and activities of daily living (n=1)[53] and whole body vibration (n=1).[54] In summary, aerobic exercise (n=17/20) and resistance exercise (n=14/20) were the most commonly used interventions in the included trials.

Exercise programme details

The median exercise intervention length was 5.5 weeks (range 2–52). Most interventions included moderate intensity exercise (n=18),[36–53] with one study being low intensity[54] and one not reporting intensity.[55] The mean length of sessions was 38 min (SD: 14, range: 10–70) and 4.4 sessions/week (SD: 1.7, range: 2–7). Interventions were fully supervised (n=11)[36 37 39 41 42 48–50 52–54] or partially supervised with a home-based component (n=7),[38 40 44–46 51 55] and unsupervised (n=2).[43 47] Of supervised programmes, n=15 were delivered one-on-one,[36–42 44 49–55] and n=3 were group-based sessions.[45 46 48] Median compliance with exercise interventions, which was reported in 15 studies, was 70.7% (SD: 22.3%, range: 54–94.4%). The average withdrawal rate was 28% and 24% in exercise and control groups, respectively.

Additional interventions delivered

In addition to delivering the exercise intervention, some intervention groups also received relaxation (n=3),[39 40 43] dietary guidance (n=2)[48 49] and motivational interviewing (n=1).[45]

Control groups

While three control groups received usual care only,[42 46 48] other control groups received other interventions including resources (n=5),[40 43 45 47 50] physiotherapy (n=4),[39 49 53 54] exercise education (n=2),[39 51] mental relaxation (n=2),[36 41] bike access (n=2),[40 55] a pedometer (n=2)[38 44] and stretching and gymnastics sessions (n=1).[52] Additionally, two control groups were offered the study exercise intervention after the control period.[40 45]

Hospital length of stay and rate of admissions

All 20 included studies described the length of stay (n=17) or rate of admission (n=5) in the exercise intervention and

Table 1 Clinical characteristics of included studies

	Country	Date of recruitment	Age range, years (mean±SD)	Total number of participants (% of eligible, consented, and randomised)	Female	Diagnosis, stage (if known)
Haematopoietic stem cell transplantation						
Potiaumpai (2021)	USA	NR	40–80 (58.8±7.6)	35 (61)	16 (46)	AML, ALL, CLL, MDS, MM, other lymphomas
Pahl (2020)	Germany	Jun 2016 – Oct 2017	32–63 Exercise: 50–63 (55), Control: 32–63 (56)	44 (NR)*	14 (32)	AML, ALL, CLL, CMML, MDS, MM, myelofibrosis, SG, severe aplastic anaemia
Santa Mina (2020)	Canada	Oct 2014 – Oct 2018	>17 Exercise: 50.4±18.1, Control: 48.4±13.0	30 (15)	15 (50)	Leukaemia, lymphoma, MDS, MNGIE
Senn-Malashonak (2019)	Germany	Jan 2011 – Dec 2014	Median (range). Exercise: 5–17 (11), Control: 6–18 (12)	70 (42)	48 (69)	Leukaemia, MDS, lymphoma, neuroblastoma, nephroblastoma, nasopharynx carcinoma, soft tissue sarcoma
Wallek (2018)	USA	Jan 2011 – Dec 2014	5–17 (10.9±3.5)	53 (32)	18 (34)	Leukaemia, MDS, solid tumour, lymphoma
Hacker (2017)	USA	May 2013 – Aug 2015	19–73 (53.3±12.2)	67 (37)	26 (39)	Haematological cancer
Jacobsen (2014)	USA	Jan 2011 – Jun 2012	18–76 Median: Exercise: 58 (20±76) Exercise+Stress management: 57 (20±75) Stress management: 57 (18±75) CON: 55 (19±76)	711 (NR)	306 (43)	AML, ALL, CML, CLL, MDS, MPS, MM, PCD, lymphoma
Wiskemann (2011)	Germany	May 2007 – Oct 2007	18–71 (48.8)	105 (94)	34 (32)	AML, ALL, CML, CLL, MDS, secondary AML, MPS, MM, other lymphomas, aplastic anaemia
Baumann (2011)	Germany	2002–2005	Exercise: 41.41±11.78 Control: 42.81±14.04	47 (NR)	17 (52)†	AML, ALL, CML, CLL, MPS, MDS, CMML, MM, PID
Baumann (2010)	Germany	Mar 2002 – Jul 2004	Exercise: 44.9 ±12.4 Control: 44.1±14.2	64 (NR)§	29 (45)	AML, ALL, CML, multiple myeloma, NHL/CLL, MDS/MPS, solid tumour
Jarden (2009)	Denmark	Apr 2005 – Nov 2007	18–65 (39.1±12.2)	42 (51)	16 (38)	AML, ALL, CML, AA, MDS, WM, PNH, myelofibrosis
DeFor (2007)	USA	Jul 2003 – Aug 2005	18–68 (47)	100 (82)	39 (39)	Haematological cancer
Chemotherapy alone						
Mijwel (2020)	Sweden	Mar 2013 – Jul 2016	18–70 Aerobic: NR (54.4±10.3) Resistance: NR (52.7±10.3) Control: NR (52.6±10.2)	240 (28)	240 (100)	Breast cancer Stage I-IIIa
Wehrle (2019)	Germany	Jun 2010 – Feb 2013	Aerobic: 47.7 (21.9±63.4)	29 (74)	9 (41)‡	Acute leukaemia
Alibhai (2015)	Canada	Jun 2011 –Feb 2013	23–80 (57±14.7)	81 (71)	37 (46)	AML Mixed cytogenetic risk group
HSCT+chemotherapy						
Dimeo[42]	Germany	NR	18–60 EX: NR (39±10) CON: NR (40±11)	70 (88)	51 (73)	Solid tumours
Chemo- and radiotherapy						
Arrieta[47]	France	Oct 2011 – May 2016	76.7±5.0	301 (67)	180 (60)	Breast cancer Colon cancer Hepatocellular carcinoma, Adenocarcinoma, Lymphoma
May (2017)	Netherlands	2010–2013	25–75 Breast (Exercise: 50±7.9, Control: 49.4±7.6), Colorectal (Exercise: 57.4±11.2, Control: 59.1±8.9)	194 (82)	176 (91)	Breast cancer Colon cancer Stage I-III
Mutrie (2007)	Scotland	Jan 2004 – Jan 2005	29–76 (51.9±9.5)	201 (65)	201 (100)	Breast cancer Stage 0-III

Continued

Table 1 Continued

	Country	Date of recruitment	Age range, years (mean±SD)	Total number of participants (% of eligible, consented, and randomised)	Female	Diagnosis, stage (if known)
Uster (2018)	Switzerland	Mar 2012 – Oct 2014	32–81 (63.0)	58 (48)	18 (31)	Gastrointestinal cancer Lung cancer Stage IV

Data presented as range (mean) or number (%). NR denotes not reported.
*Per-protocol analysis.
†14 patients deceased during hospitalisation, leaving behind 33 survivors.
‡Reasons for prematurely terminating study participation were mental overload (n=3), change in diagnosis (n=2), persistent thrombocytopenia <10/nL (n=1) or death (n=1), none of which were associated with exercise—leaving behind 22 participants.
§15 (8 of the treatment arm and 7 of the control arm) deceased during hospitalisation for HSCT.
AA, aplastic anaemia; ALL, acute lymphocytic leukaemia; AML, acute myeloid leukaemia; AT-HIIT, moderate-intensity aerobic and high-intensity interval training; CLL, chronic lymphocytic leukaemia; CML, chronic myeloid leukaemia; CMML, chronic myelomonocytic leukaemia; HSCT, haematopoietic stem cell transplantation; MDS, myelodysplastic syndrome; MM, multiple myeloma; MNGIE, mitochondrial neurogastrointestinal encephalopathy syndrome; MPS, myeloproliferative syndrome; NHL, non-Hodgkin's lymphoma; PCD, primary ciliary dyskinesia; PID, primary immune deficiency; PNH, paroxysmal nocturnal haemoglobinuria; RT-HIIT, resistance and high-intensity interval training; SAA, severe aplastic anaemia; SG, septic granulomatosis; WM, Waldenstrom macroglobulinaemia.

control groups (table 3). Of the 17 studies reporting on length of stay (days), only one study presented statistically significant reductions in hospital length of hospital stay, with Dimeo *et al* that identifying that participants who cycled for 30 min/day for 4 weeks, averaged 13.6 (2.2) days in hospital versus 15.2 (3.6) days in the control group ($p=0.03$).[42] In the five studies reporting the proportion of patients admitted to hospital in the study period,[37 45 47 50 51] two reported statistically lower rates of hospital admission among the exercise groups. Mijwel *et al* found that 2/74 (3%) and 4/72 (6%) of participants, who received two 60min/week resistance, or aerobic exercise, respectively, plus high-intensity interval exercise for 16 weeks, were hospitalised throughout their treatment compared with 8/60 (13%) of the control group ($p=0.02$).[37] Mutrie *et al* found that participants who undertook three sessions/week of moderate multimodal exercise for 12 weeks were hospitalised at half the rate throughout treatment compared with the control group (10/99 (10%) vs 20/102 (20%), $p=0.04$).[36]

Meta-analysis

Sixteen studies reporting hospital length of stay were included in the meta-analysis (522 in exercise interventions and 473 in control groups).[36–46 48 49 51–55] For hospital length of stay, there was a small effect size for all pooled studies favouring the exercise groups spending 1.40 days less (95% CI: −2.26 to −0.54, $p<0.01$) in hospital compared with the control groups (figure 2). Subanalyses found a small effect that the exercise groups spent 1.55 days less (95% CI: −2.61 to −0.50) for HSCT compared with usual care. In other treatment protocols, the exercise groups spent 0.67 days less (95% CI: −4.24 to 2.91) for chemotherapy) and 0.86 days less (95% CI: −2.09 to 0.36) for combined chemotherapy and radiation compared with usual care, however these subanalyses were not statistically significant. Egger's test suggested no evidence of publication bias ($p=0.68$). The amount of statistical heterogeneity was low with overall $I^2=22.86\%$ and subgroup I^2 not exceeding 24.82%.

Five studies reporting the rate of hospital admission were included in the meta-analysis (446 in exercise interventions and 360 in control groups).[37 45 47 50 51] There was a small effect size in the pooled analysis favouring exercise (figure 3). There was an 8% reduced risk of hospital admission in the exercise group (difference in proportions: −0.08, 95% CI: −0.13 to −0.03, $p<0.01$). As only five studies were pooled, Egger's test was not conducted for this meta-analysis. There was no evidence of statistical heterogeneity, as $I^2=0$.

In sensitivity-analyses, meta-regression on main outcomes mean difference and exercise type, number of sessions and level of supervision, removing studies with a control groups which were offered exercise equipment but no prescribed intervention, and separating by adult and child studies, did not explain the variation in either hospital length of stay or admission outcomes (online supplemental file 1).

Adverse events from exercise interventions

Ten studies reported investigating adverse events. Of these, eight reported no adverse events from the exercise interventions.[37 39–41 45 48 49 53] One study reported no serious adverse events, however documented two exercise sessions that ceased early due to two minor adverse events, including knee pain and discomfort.[54] One study, which reported no adverse events from the exercise intervention, had one participant fall during the baseline 6-minute walk test, and subsequently withdrew from the study.[40] Finally, one study reported that participants kept a daily log which included self-reporting of adverse events, however these findings were not presented in the article.[38]

Quality assessment

Over two-thirds of included studies had at least one risk of bias domain that was judged to be high risk (online supplemental figures 1 and 2). These trials were at high or unclear risk for selection bias relating to the randomisation, deviations from the intended interventions, missing outcome data, measurement of the outcome or selective reporting. Based on the GRADE rating system, the evidence for the effect of exercise on hospital length of stay was low quality, and low quality for rate of admissions (online supplemental table 4). The quality of evidence was downgraded because of risk of bias due to methodological limitations identified using the RoB 2, and imprecision, due to the confidence intervals being close to the no difference line. Due to the variability of bias assessments, which ranged from low to high across the five domains, especially for the second domain (ie, bias due to deviations from intended interventions), the presence of methodological heterogeneity is highly likely.

Table 2 Exercise intervention characteristics of the included studies

Author	Days/week, duration	Intensity	Exercise	Control	Co-interventions	Duration	Compliance/adherence
Haematopoietic stem cell transplantation							
Potiaumpai *et al*	4 days/week (3×supervised, 1×unsupervised) (Duration increased gradually from 5 to 30 min)	5-6/10 RPE (moderate) for multidirectional drills and 7-8/10 RPE (high) for walking	Multidirectional walking drills: ► A weighted eight-rung agility ladder ► Forward, backward, sideways, and diagonal walking	Physical activity counselling Given encouragement to be physically active Self-monitor their daily steps using a pedometer	No	1 month	Walk: 79
Pahl *et al*	Daily, one-on-one training (20 mins/each)	Low	Whole-body vibration training of the legs standing on the side-alternating vibration plate	Conducted mobilisation of the spine and stretching of the whole body	No	5.5 weeks	NR
Santa Mina *et al*	3 days/week: 1×supervised facility-based and 2×unsupervised home-based sessions (90–150 min per week)	Aerobic: 60% hour reserve	Resistance bands and exercise diary were given 3 to 5 min aerobic warm-up 30 to 45 min resistance training involved the use of free weights and/or resistance bands 10 to 15 min aerobic exercise: stationary bike, treadmill, or elliptical trainer Aerobic exercise in the home setting involved brisk walking Sessions concluded with yoga-based stretching and relaxation breathing	Stationary bikes and exercise placards (in-door exercise recommendations) were provided	No	3 months	Inpatient phase Aerobic: 50 Resistance: 99 Control: NR
Senn-Malashonak *et al*	5 days/week (30–60 mins/each)	Aerobic: Moderate (12-14/20 RPE) Resistance: 1–3×7–15 reps of 3–5 exercises	Resistance, endurance, and flexibility training	Mental and relaxation training	No	3 months	Exercise: 94 Control: 68
Wallek *et al*	5 days/week (40–60 min/each)	Aerobic: 60–80% HRmax, 12-14/20 RPE. Resistance: 1–3×8–15 reps for 3–6 exercises	Use of barbells, balls, rubber bands, steps, and bicycle ergometer. Training intensity was controlled via self-reported rating of perceived exertion	Mental and relaxation training	No	2 months	Exercise: 94 (3.1±0.6 sessions per week)
Hacker *et al*	3 days/week (1×supervised and 2 x unsupervised) 18 strength training sessions	Moderate, 13/20 RPE	Progressive resistance and strength training using: ► Elastic resistance bands ► Body weight (be it sit-ups or wall push-ups)	During hospitalisation, two visits per week during which hospital experience was discussed. After discharge, 1-on-1 health education sessions (1 /week, 6 weeks).	Education included health protection, working with doctors, finances, recommendations after HSCT	2.5 weeks	83 for exercise sessions 97 for education sessions
Jacobsen *et al*	3–5 days/week (20–30 min/each)	Moderate: 50%–75% hour reserve	One of four interventions: self-directed exercise, self-administered stress management, combinatorial exercise and stress management training, or usual care A pamphlet, a digital video disc (DVD) and a diary were given. Stress management training involved targeted-paced abdominal breathing, muscle relaxation, and coping strategies	A DVD, alongside brief discussion with an interventionist, were provided. Only general advice regarding exercise and stress management was offered (such that physical activity patterns and participants' own stress management techniques were maintained).	Pedometer and a relaxation CD were provided. Patients were re-contacted at 30 and 60 days post HSCT to review goals, barriers, and offer encouragement.	Duration of inpatient stay	67: self-guided relaxation. 34: deep breathing 12: relaxation audiotapes 4: videos

Continued

Table 2 Continued

Author	Days/week, duration	Intensity	Exercise	Control	Co-interventions	Duration	Compliance/adherence
Wiskemann *et al*	In-patient intervention: 3–5 x endurance sessions during hospitalisation 2 x resistance sessions per week (20–40 min/each)	Moderate-high Aerobic: 12-14/20 RPE for 20–40 mins Resistance: 14-16/20 RPE for 2–3 x 8–20 repetitions	Endurance training: 20 to 40 min walking in the outpatient setting. Cycling and treadmill walking during hospitalisation Strength training involved the use of stretch bands and focuses on the upper or lower extremities, the whole body, or bed exercises (inpatient settings)	Step counters were given to record daily physical activity. Controls were visited at the same frequency by research staff. Controls had access to treadmills and stationary cycles to complete themselves (but not prescribed)	No	6 weeks	Before admission: 88 During hospitalisation: 83 After discharge (for 6–8 weeks): 87
Baumann *et al* (2011)[53]	Twice a day Endurance training (10–20 min/day) Activities of daily living training (ADL-training) (20 min/day)	Exercise: 'slightly strenuous' or 'strenuous' (Borg scale) Control: low intensity, 'not strenuous' (Borg scale)	Endurance training was conducted on a cycle ergometer; if unable to complete this for 10 to 20 min without disruption, then interval training was conducted. ADL-training was performed during chemotherapy and post-engraftment and involved strength, coordination, stretching, walking, and stair climbing exercises.	Standard physiotherapy Individual active and passive mobilisation treatment – 10 min gymnastic, 5 min stretching, and massages – performed by a physiotherapist (5 days a week, 20 min each)	No	7.5 weeks	NR
Baumann *et al* (2010)[52]	Activities of daily living training (ADL-training): 5 days/week (20 min/each) Aerobic endurance training: 5–7 days/week (10–20 min each)	'Slight strenuous' to 'strenuous' (Borg Rate f Perceived Exertion scale)	Aerobic endurance training on a bicycle ergometer combined with activities of daily ADL-training	10 min gymnastics, low-intensity coordination training, and massages Controls underwent low-intensity active and passive mobilisation, which consists of gymnastics, massages, extensions, and coordination training. 5 days/week (20 min/each)	No	3.5 weeks	NR
Jarden *et al*	Dynamic exercise: 5 days/week (60±10 min/each) Resistance training:3 days/week	Stationary cycling: low to moderate intensity, 10-13/20 RPE Resistance training: low to moderate intensity, 10-13/20 RPE Relaxation: low intensity, 6-9/20 RPE	A multimodal intervention encompassing exercise, relaxation, and psychoeducation regarding capacity, functional performance. Dynamic exercises consisted of neck movements, shoulder rotations, hip flexion and extension, calf raise, ankle dorsi-flexion and plantar-flexion, in addition to abdominal and back muscle exercises. After cycling, stretching was conducted. Resistance training was comprised of 'free hand and ankle weights, bicep curl, shoulder press, triceps extension, chest press, flyer, squat, hip flexion, knee extension, and leg curl and extension'	'Modified logbook' was given to document the mode, frequency, and duration of exercise during hospitalisation. Physiotherapy was given after HSCT for up to 1.5 hours weekly. There was no stationary cycling ergometer given unless otherwise requested. All outcome measures needed to be completed within the same time frame as the exercise group.	Psychoeducation was based on behavioural and cognitive therapy techniques to facilitate adjustment to diagnosis and treatment. The aim was to foster personal control and increase motivation and self-efficacy.	four to 6 weeks	81 completed all requirements. Questionnaires at 3 months: Exercise: 81 Control: 62 Questionnaires at 6 months: Exercise: 76 Control: 62

Continued

Mizrahi D, *et al*. *Br J Sports Med* 2024;**58**:97–109. doi:10.1136/bjsports-2023-107372

Table 2 Continued

Author	Days/week, duration	Intensity	Exercise	Control	Co-interventions	Duration	Compliance/adherence
DeFor *et al*	Twice a day (15 min/each)	NR	During hospitalisation: 15 min walk on a treadmill twice a day and cycling for<20 mins/ day every other day. After discharge, participants would walk at a comfortable speed for>30 min/day	Controls were not told to do any exercise and not given a treadmill unless otherwise requested.	No	5 months	Adherence to physical activity for at least five times/week: Exercise: 62 Control: 38
Chemotherapy alone							
Mijwel *et al*	2 days/week (60 min/each)	Aerobic: 20 mins moderate intensity 13-15/20 RPE+3×3 mins (high-intensity), RPE=16–18/20 on cycle Resistance: 70–80% 1RM, 2–3x 8–12 reps + 3x3 mins (high-intensity) RPE=16–18/20 on cycle.	Interval training, combined with endurance or resistance training	Exercise recommendations were given (American College of Sports Medicine guidelines)	No	16 weeks	Adherence to the exercise intervention: RT-HIIT: 68 AT-HIIT: 63 Adherence to intensity: RT-HIIT: 83 AT-HIIT: 75
Wehrle *et al*	3 days/week (30–45 min/each)	Aerobic: 60–70% HRmax, RPE=12–14/20. Resistance: 4–6 x Body weight, bands/ dumbbell machines. RPE=12–14/20.	Endurance group: training on an upright stationary bicycle Resistance group: bodyweight exercises	Low-intensity mobilisation and stretching were given to avoid psychosocial bias	Nutritional counselling was offered by dieticians and physiotherapists to all participants	2 months	Endurance group: 69 Resistance group: 76 Control: 60
Alibhai *et al*	4–5 days/week (30–60 min/each)	Light-moderate, RPE=3–6/10	Aerobic, resistance, and flexibility training exercises Exercise was documented using weekly tracking sheets	Walking on a regular basis Any exercise was documented using weekly tracking sheets	No	5 months	54
Haematopoietic stem cell transplantation and chemotherapy							
Dimeo *et al*	Daily (30 min/each)	50% cardiac reserve 15×1 min (mean workload=32±5 Watts)	Aerobic exercise (cycling ergometer in the supine position)	Usual care without changing daily physical activity level	No	4 weeks	82 (±10%)
Chemotherapy and radiation therapy							
Arrieta *et al*	2 days/week	Low to high and focused on avoiding pain and exhaustion	Balance and proprioception exercises, aerobic training, and stretching exercises	French National Nutrition Health Programme (PNNS) booklet was given, which recommends 30 min of exercise per day	No	NR 1 year follow-up 2 year follow-up	Planned phone calls: 81 Exercise: 70
May *et al*	5 days/week (2×supervised, 3×unsupervised) (supervised: 60 min/each, home-based: 30 mins each)	Aerobic: either '3× 2 min increasing to 2× 7 min' or below '3× 4 min decreasing to 1× 7 min' ventilatory threshold. Resistance: 45–75% 1RM Home exercise at moderate intensity	5 min warming up, 50 min strength training, and 5 min cooling down	Usual care Habitual physical activity pattern	No	18 weeks	Breast cancer: 83 Colon cancer: 89
Mutrie *et al*	3 days/week (2×supervised, 1×unsupervised) 14 exercise classes (45 min each)	Moderate intensity, 50–75% HRmax	45 min supervised group exercise: 5 to 10 min warm up 20 min walking and cycling, low-level aerobics, or muscle strengthening exercises. Relaxation exercises	Usual care Exercise guideline leaflet entitled 'exercise after cancer diagnosis'	No	12 weeks	Breast cancer: 83 Colon cancer: 89
Uster *et al*	2 days/week (60 min each) 24 sessions in total	Aerobic: 10 mins warm up. Resistance: 60–80% 1RM	Warm-up, strength and balance training	Usual care without changing their daily physical activity level	Protein-rich snacks and oral nutritional supplements post-session	12 weeks	Mean: 67 Median: 75

Data are range (mean) or number (%).
Adherence is defined as the percentage of hospital days of exercise completed under supervision.
AT-HIIT, moderate-intensity aerobic and high-intensity interval training; 1RM, 1-repetition maximum (ie, maximal weight that a participant can lift for a single repetition); RPE, rating of perceived exertion; RT-HIIT, resistance and high-intensity interval training.

Table 3 Hospital length of stay and admission rate among patients in exercise and control groups of included studies

Hospital length of stay (days) Mean (SD)			
	Exercise group	**Control group**	**P value**
Haematopoietic stem cell transplantation			
Potiaumpai *et al*	12.9 (4.3)	11.7 (4.0)	0.41
Pahl *et al*	38.0 (range: 35–43.5)	41 (range: 37–44)	NR
Santa Mina *et al*	27.4 (3.8)	28.6 (3.5)	0.81
Senn-Malashonak *et al*	39.0 (range: 22–74)	42.0 (range: 26–93)	NR
Wallek *et al*	Intervention group (fit): 36 (range: 22–74) Intervention group (unfit): 40.5 (range: 26–57)	Control group (fit): 39 (range: 27–53) Control group (unfit): 43.5 (range: 26–93)	>0.05
Hacker *et al*	16.7 (4.2)	18.1 (5.5)	NR
Jacobsen *et al*	NR	NR	0.42
Wiskemann *et al*	45.0 (range: 24–92)	43.0 (range: 22–120)	0.64
Baumann *et al*[53]	56.1 (20.7)	51.4 (16.4)	NR
Baumann *et al*[52]	41 (25)	43 (33)	NR
Jarden *et al*	34.7 (5.6)	35.0 (6.1)	0.88
DeFor *et al*	32 (IQR: 15–42)	35.5 (IQR: 24.5–38.5)	0.37
Dimeo *et al*	13.6 (2.2)	15.2 (3.6)	.03
Chemotherapy			
Wehrle *et al*	Aerobic: 33 (IQR: 31–41) Resistance: 35 (IQR: 33–52)	37 (IQR: 34–43)	0.50
Alibhai *et al*	36.5*	35.8*	0.76
Chemotherapy and radiotherapy			
May *et al*	Breast cancer: 1.9 (3.1) Colon cancer: 2.6 (4.6)	Breast cancer: 1.6 (2.8) Colon cancer: 8.8 (11.8)	NR
Uster *et al*	5.9 (10.3)	8.3 (10.3)	0.18
Rate of hospital admission (%)			
Hacker *et al*	3/33 (9%) readmitted post- intervention	8/34 (23%) readmitted post-intervention	NR
Mijwel *et al*	RT+HIIT: 2/74 (3%) of the group AT+HIIT: 4/72 (6%) of the group	8/60 (13%) of the group	RT vs control: .02 AT vs control: >0.05
Alibhai *et al*	3/57 (5.6%) of group	3/24 (12.5%) of the group	0.26
Arrieta *et al*	22/121 (18%) at 1-year follow-up 21/86 (25%) at 2-year follow-up	20/128 (16%) at 1-year follow-up 29/100 (29%) at 2-year follow-up	1 year: >0.05 2 years: >0.05
Mutrie *et al*	10/99 (10%)	20/102 (20%)	0.04

Hospital length of stay data listed as mean (SD) days, unless otherwise indicated as median with range or IQR.
*SD not reported.
AT, aerobic training; HIIT, high-intensity interval training; NR, not reported; RT, resistance training.

DISCUSSION

Our study reviewed and synthesised data from 20 RCTs examining the impact of participating in exercise interventions during chemotherapy, radiotherapy or stem cell transplant cancer treatment regimens on hospital length of stay and rate of admissions. It found that patients who participated in exercise interventions during treatment spent 1.40 days less in hospital and had an 8% lower risk of hospital admission than non-exercising controls. However, findings should be evaluated with caution due to the low quality of evidence using the GRADE rating system. This systematic review and meta-analysis are important as it evaluates a potential low-cost intervention to mitigate a major concern among patients with cancer, this being lengthy and repeated hospital stays.

Prolonged hospital stays are associated with increased risk of readmission and mortality.[56] Our findings of reduced time spent in hospital and reduced risk for admissions may have important implications for the healthcare system, as there can be a high financial burden imposed on individuals and institutions bearing the costs of repeated and prolonged hospitalisation.[57] In-patient hospital costs have been shown to account for 68% of all cancer-related costs in the first year after diagnosis[58] and are steadily increasing. Embedding exercise into treatment plans could deliver significant health system savings through earlier discharge as well as improving individual patient outcomes. Recent calls have been made to make hospital care more efficient and less costly,[59] so our findings to potentially prevent admissions and reduce the burden on hospital bed pressure and the healthcare system are timely. Our study adds to the literature a potential intervention to combat hospital length of stay, with a recent systematic review, which did not investigate exercise interventions, unable to identify any interventions to reduce hospital length of stay.[18] Although our study was not a health economic analysis, future studies should investigate whether the cost of delivering exercise programmes offsets the money saved from preventing patient admissions and reduced hospital length of stay. Given a converging international consensus on incorporating exercise into standard cancer care,[20 21] exercise during treatment may allow patients to optimise their health and reduce their likelihood of hospital admission. Organisational limitations have been identified as the key barrier to implementing exercise into routine cancer care, using the expertise of a multidisciplinary team in implementing and/or prescribing exercise, and preparing broader community-based exercise groups and settings will likely assist.[60 61]

Mizrahi D, *et al*. *Br J Sports Med* 2024;**58**:97–109. doi:10.1136/bjsports-2023-107372

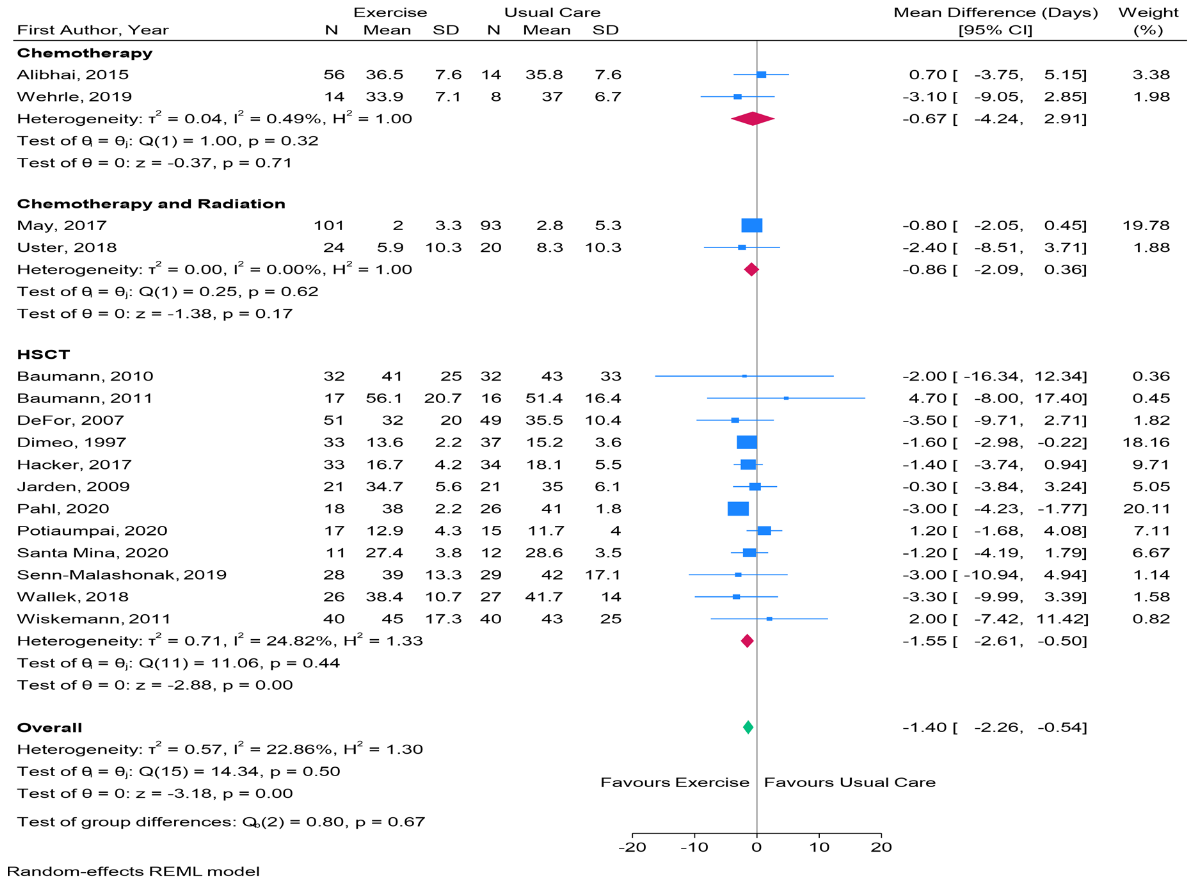

Figure 2 Meta-analysis of the difference in days spent in hospital between those patients with cancer participating in an exercise intervention versus control. Negative values favour exercise. HSCT, haematopoietic stem cell transplantation. REML, restricted maximum likelihood.

Given the known psychological, physical and financial burden of repeated admissions and prolonged hospital stays, supportive care interventions are urgently required to reduce the likelihood or duration of hospitalisation. Exercise before cancer treatment, termed 'prehabilitation', has been shown to improve clinical outcomes including reduced hospital length of stay. Prehabilitation studies, commonly conducted prior to cancer surgery, have been shown to reduce hospital length of stay by up to 4 days following gastrointestinal cancer surgery[62] and 4–8 days before lung cancer surgery.[63 64] Additionally, there is moderate-quality evidence that preoperative exercise halved the amount of postoperative complications in patients with lung cancer, and improved postoperative QoL in oral and patients with prostate cancer.[65] Although our study identified a smaller effect size regarding length of hospital stay compared with exercise interventions delivered prior to cancer surgery, the difference identified in our study applied on a population-level may still provide a cost-effective intervention to assist with reducing pressure on

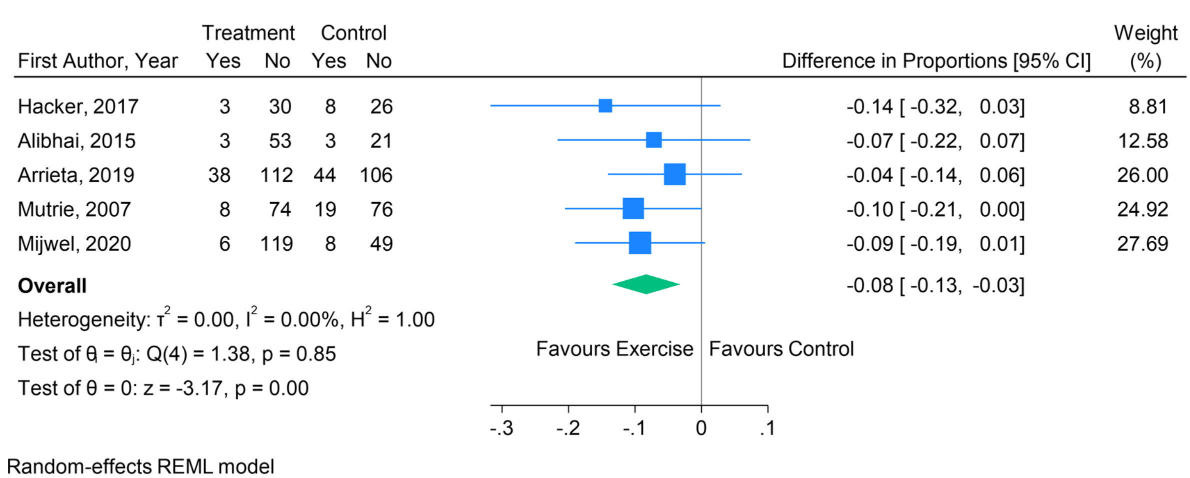

Figure 3 Meta-analysis of the difference in the proportion of participants with cancer admitted to hospital in exercise and control groups. Negative values favour exercise. REML, restricted maximum likelihood.

the healthcare system, while concurrently applying numerous health benefits. Further, reducing unplanned hospital admissions has been shown to reduce healthcare costs,[66] which can add to the importance of our study findings. Several issues need to be resolved to adapt current models of cancer care to implement exercise, including developing a trained workforce, overcoming barriers such as payments and ensuring exercise is recommended by the patient's medical oncologist.[67] One example is by adapting oncology models of care from other chronic diseases such as the WHO's 'Package of interventions for rehabilitation' for cardiopulmonary conditions, which recommends incorporating exercise, healthy lifestyle education and stress management to improve function and clinical outcomes,[68] a model demonstrating reduced risk and duration of hospital readmissions and mortality.[69]

There are likely multiple mechanisms regarding the effect of different exercise types during cancer treatment on risk of admission and hospital length of stay. Exercise can improve physical function by adaptations in cardiovascular (particularly aerobic exercise) and skeletal muscle systems (particularly resistance exercise).[23] Greater physical function has been shown to decrease hospital length of stay, while patients with reduced physical function can be referred for risk-reduction interventions such as exercise to improve their tolerance of treatment and side effects.[70] Physical therapy programmes focused on mobility have also displayed evidence to reduce hospital length of stay and risk of readmissions,[71] with potential reduction in falls risk a contributing factor. Exercise has also been shown to reduce depressive and anxious symptoms,[23] which may be important clinically given poor psychological health associated with longer hospital length of stay and higher likelihood of readmissions.[72] People with cancer have displayed a 15–30% increased risk of being admitted to hospital for a falls-related injury due to their symptoms and deconditioning.[73] Balance and muscle strengthening exercises have numerous clinical benefits, particularly in older patients, to reduce their falls and fracture risk,[74] which forms one common mechanism of reducing the risk of being admitted to hospital as identified in our study. When discussing the potential effect of different exercise types, most studies in our review included an aerobic exercise component, so comparisons between exercise types were not possible. Additionally, sensitivity analyses conducted as part of this study did not identify that there was an optimal exercise type, dose or level of supervision to reduce time or risk of being admitted to hospital. Given the current exercise-oncology guidelines recommend a combination of aerobic and resistance exercise,[20 21] we recommend a combined exercise programme in-line with the guidelines is likely to be beneficial.

Exercise during cancer treatment has been shown to be safe. For instance, in children with cancer, an evaluation of 35 110 exercise sessions found severe adverse events occurred at a rate of 0.02%.[75] Half the studies in our review reported on safety, in which most reported no adverse events from exercise. As 10% (2/20) of our included studies offered no exercise supervision, a small risk of both adverse events, and under-reporting of adverse events remains. Supervision should be encouraged during treatment to minimise such possibilities, particularly in the early stages of habituating participants to a consistent exercise programme. Future studies should systematically report exercise-related adverse events to improve the evidence of harms assessment, and could incorporate measurable methods to better understand patient, caregiver and staff experiences and challenges.[76]

This is the first systematic review and meta-analysis to investigate the effect of exercise during chemotherapy, radiotherapy and stem cell transplant cancer treatments on hospital length of stay and admission rates. Our methods have multiple strengths including protocol registration in PROSPERO, a comprehensive database search strategy, dual-screening of the abstract and full-text selection, data extraction, risk of bias assessments and pooling of data using meta-analysis of RCTs, representing the gold standard of evidence generation. However, our findings should be interpreted with caution. While statistical heterogeneity was assessed to be low, clinical and methodological heterogeneity was not, due to variability in the age and sex of study populations and quality of study evidence. Our study was not able to account for any possible missing data from the included studies, which may have affected the statistical calculations and produced biased estimates.[77] Many studies had high risk of bias, mostly due to high drop-out, low adherence to the exercise interventions and lack of blinding, highlighting the challenges in conducting allied health interventions[78] and presenting potential difficulties for patients to commit to interventions requiring additional visits during the treatment period where they are susceptible to various adverse events. Only one study in our review had a primary outcome assessing the effect of exercise on hospitalisation admissions,[50] thus future studies that are adequately powered to measure hospital length of stay are required to confirm our findings. There may be confounders our study could not include in the analysis that may have affected the relationship between exercise during treatment and hospital length of stay, including prediagnosis physical activity levels, baseline fitness, demographic characteristics or insurance status. Future research which includes analyses by age, sex, cancer type and other details on potential confounders or effect modifiers, as well as including other therapies such as immunotherapy and hormone therapies, will be beneficial. Further data on implementation, cost-effectiveness and cost-utility of different exercise programmes will also be useful.

CONCLUSION

Our systematic review and meta-analysis of RCTs found that exercising during treatment led to a significant reduction in days spent in hospital and rate of hospital admission. While the effect size of this difference was small, there may be important clinical relevance to patients wanting to stay out of hospital, which also may have economic benefits to healthcare systems. The heterogeneity of exercise interventions, patient characteristics, and quality assessment of the included studies suggested that these findings should be interpreted cautiously. While exercise is factored into some multidisciplinary care plans, its inclusion as standard practice for most patients who would benefit should be considered as cancer care pathways evolve.

Author affiliations
[1]The Daffodil Centre, The University of Sydney, a joint venture with Cancer Council NSW, Sydney, New South Wales, Australia
[2]Discipline of Exercise and Sport Science, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia
[3]School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia
[4]Medical Sciences Division, The University of Oxford, Oxford, UK
[5]Department of Physiotherapy, University of Melbourne, Melbourne, Victoria, Australia
[6]Cancer Epidemiology Division, Cancer Council Victoria, Melbourne, Victoria, Australia
[7]Macarthur Cancer Therapy Centre, Campbelltown Hospital, Sydney, New South Wales, Australia
[8]Office of the Chief Scientist, The George Institute for Global Health, Sydney, New South Wales, Australia
[9]Dalla Lana School of Public Health, The University of Toronto, Toronto, Ontario, Canada

[10]School of Medicine & Dentistry, Griffith University, Gold Coast, Queensland, Australia

Twitter David Mizrahi @davemiz_EP, Tong Li @TongLiUSYD, Christopher T V Swain @ctvswain, David P Smith @SmithDavidP, Diana Adams @Drdhadams and Alexandra Martiniuk @AlexMartiniuk

Acknowledgements The authors thank Paul Grogan and Rehana Abdus Salam from The Daffodil Centre, The University of Sydney, a joint venture with Cancer Council NSW, for providing internal review and methodological and strategic feedback on the manuscript.

Contributors DM was responsible for the conceptualisation and design of the study, and is responsible for the overall content as guarantor. DM, HW and YR were responsible for the selection of articles and data extraction. JKLL, TL and CTVS were responsible for further data extraction and risk of bias assessment with justification. DM, JKLL, CTVS and AM were responsible for assessing study methodologies. DM and JKLL were responsible for preparing the tables. MD was responsible for the meta-analysis. All authors were responsible for writing and editing of the manuscript. All authors approved the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
David Mizrahi http://orcid.org/0000-0003-1174-2248
Tong Li http://orcid.org/0000-0003-4956-765X
Christopher T V Swain http://orcid.org/0000-0002-0158-2511
David P Smith http://orcid.org/0000-0002-1474-3214
Alexandra Martiniuk http://orcid.org/0000-0003-1368-8206

REFERENCES

1. World Health Organization. Cancer. 2022. Available: https://www.who.int/news-room/fact-sheets/detail/cancer
2. Lage DE, El-Jawahri A, Fuh C-X, *et al*. Functional impairment, symptom burden, and clinical outcomes among hospitalized patients with advanced cancer. *J Natl Compr Canc Netw* 2020;18:747–54.
3. Wilson BE, Jacob S, Yap ML, *et al*. Estimates of global chemotherapy demands and corresponding physician workforce requirements for 2018 and 2040: a population-based study. *Lancet Oncol* 2019;20:769–80.
4. Steinberg A, Asher A, Bailey C, *et al*. The role of physical rehabilitation in stem cell transplantation patients. *Support Care Cancer* 2015;23:2447–60.
5. Tabbara IA, Zimmerman K, Morgan C, *et al*. Allogeneic hematopoietic stem cell transplantation: complications and results. *Arch Intern Med* 2002;162:1558–66.
6. Numico G, Cristofano A, Mozzicafreddo A, *et al*. Hospital admission of cancer patients: avoidable practice or necessary care? *PLoS One* 2015;10:e0120827.
7. NHS England. Reducing length of stay; 2023.
8. Sultan A, Pati AK, Choudhary V, *et al*. Hospitalization-induced exacerbation of the ill effects of chemotherapy on rest-activity rhythm and quality of life of breast cancer patients: a prospective and comparative cross-sectional follow-up study. *Chronobiol Int* 2018;35:1513–32.
9. Singer ES, Merritt RE, D'Souza DM, *et al*. Patient satisfaction after lung cancer surgery: do clinical outcomes affect hospital consumer assessment of health care providers and systems scores? *Ann Thorac Surg* 2019;108:1656–63.
10. Alibhai SMH, Breunis H, Timilshina N, *et al*. Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age. *J Geriatr Oncol* 2015;6:262–71.
11. Buttigieg SC, Abela L, Pace A. Variables affecting hospital length of stay: a scoping review. *JHOM* 2018;32:463–93.
12. Mahumud RA, Alam K, Dunn J, *et al*. Emerging cancer incidence, mortality, hospitalisation and associated burden among Australian cancer patients, 1982 - 2014: an incidence-based approach in terms of trends, determinants and inequality. *BMJ Open* 2019;9:e031874.
13. Australian Institute of health and welfare (AIHW). Cancer in Australia 2021; 2021.
14. Roemer M. Cancer-related hospitalizations for adults, 2017. In: *HCUP Statistical Brief #270*. Rockville, MD: Agency for Healthcare Research and Quality, 2021.
15. Feliciana Silva F, Macedo da Silva Bonfante G, Reis IA, *et al*. Hospitalizations and length of stay of cancer patients: a cohort study in the Brazilian public health system. *PLoS One* 2020;15:e0233293.
16. Schneider N, Dreier M, Amelung VE, *et al*. Hospital stay frequency and duration of patients with advanced cancer diseases - differences between the most frequent tumour diagnoses: a secondary data analysis. *Eur J Cancer Care (Engl)* 2007;16:172–7.
17. Godara A, Siddiqui NS, Munigala S, *et al*. Length of stay and hospital costs for patients undergoing allogeneic stem-cell transplantation. *JCO Oncol Pract* 2021;17:e355–68.
18. Siddique SM, Tipton K, Leas B, *et al*. Interventions to reduce hospital length of stay in high-risk populations: a systematic review. *JAMA Netw Open* 2021;4:e2125846.
19. Watson G, Coyne Z, Houlihan E, *et al*. Exercise oncology: an emerging discipline in the cancer care continuum. *Postgrad Med* 2022;134:26–36.
20. Ligibel JA, Bohlke K, May AM, *et al*. Exercise, diet, and weight management during cancer treatment: ASCO guideline. *J Clin Oncol* 2022;40:2491–507.
21. Cormie P, Atkinson M, Bucci L, *et al*. Clinical oncology society of Australia position statement on exercise in cancer care. *Med J Aust* 2018;209:184–7.
22. Toohey K, Chapman M, Rushby A-M, *et al*. The effects of physical exercise in the palliative care phase for people with advanced cancer: a systematic review with meta-analysis. *J Cancer Surviv* 2023;17:399–415.
23. Campbell KL, Winters-Stone KM, Wiskemann J, *et al*. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. *Med Sci Sports Exerc* 2019;51:2375–90.
24. Alizadeh AM, Isanejad A, Sadighi S, *et al*. High-intensity interval training can modulate the systemic inflammation and Hsp70 in the breast cancer: a randomized control trial. *J Cancer Res Clin Oncol* 2019;145:2583–93.
25. Cormie P, Zopf EM, Zhang X, *et al*. The impact of exercise on cancer mortality, recurrence, and treatment-related adverse effects. *Epidemiol Rev* 2017;39:71–92.
26. Groen WG, Naaktgeboren WR, van Harten WH, *et al*. Physical fitness and chemotherapy tolerance in patients with early-stage breast cancer. *Med Sci Sports Exerc* 2022;54:537–42.
27. Higgins JPT, Thomas J, Chandler J, *et al*. *Cochrane Handbook for Systematic Reviews of Interventions*. Chichester (UK): John Wiley & Sons, 23 September 2019.
28. Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;151:264–9,
29. Schardt C, Adams MB, Owens T, *et al*. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak* 2007;7:16.
30. Higgins JPT, Altman DG, Gøtzsche PC, *et al*. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
31. Balshem H, Helfand M, Schünemann HJ, *et al*. GRADE guidelines: 3. rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.
32. Wan X, Wang W, Liu J, *et al*. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;14:135.
33. Higgins JPT, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
34. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
35. Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
36. Wallek S, Senn-Malashonak A, Vogt L, *et al*. Impact of the initial fitness level on the effects of a structured exercise therapy during pediatric stem cell transplantation. *Pediatr Blood Cancer* 2018;65.
37. Alibhai SMH, Durbano S, Breunis H, *et al*. A phase II exercise randomized controlled trial for patients with acute myeloid leukemia undergoing induction chemotherapy. *Leuk Res* 2015;39:1178–86.
38. Wiskemann J, Dreger P, Schwerdtfeger R, *et al*. Effects of a partly self-administered exercise program before, during, and after allogeneic stem cell transplantation. *Blood* 2011;117:2604–13.
39. Jarden M, Baadsgaard MT, Hovgaard DJ, *et al*. A randomized trial on the effect of a multimodal intervention on physical capacity, functional performance and quality of life in adult patients undergoing allogeneic SCT. *Bone Marrow Transplant* 2009;43:725–37.
40. Santa Mina D, Dolan LB, Lipton JH, *et al*. Exercise before, during, and after hospitalization for allogeneic hematological stem cell transplant: a feasibility randomized controlled trial. *J Clin Med* 2020;9:1854.
41. Senn-Malashonak A, Wallek S, Schmidt K, *et al*. Psychophysical effects of an exercise therapy during pediatric stem cell transplantation: a randomized controlled trial. *Bone Marrow Transplant* 2019;54:1827–35.
42. Dimeo F, Fetscher S, Lange W, *et al*. Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood* 1997;90:3390–4.

43 Jacobsen PB, Le-Rademacher J, Jim H, *et al*. Exercise and stress management training prior to hematopoietic cell transplantation: blood and marrow transplant clinical trials network (BMT CTN) 0902. *Biol Blood Marrow Transplant* 2014;20:1530–6.
44 Potiaumpai M, Cutrono S, Medina T, *et al*. Multidirectional walking in hematopoietic stem cell transplant patients. *Med Sci Sports Exerc* 2021;53:258–66.
45 Mutrie N, Campbell AM, Whyte F, *et al*. Benefits of supervised group exercise programme for women being treated for early stage breast cancer: pragmatic randomised controlled trial. *BMJ* 2007;334:517.
46 May AM, Bosch MJC, Velthuis MJ, *et al*. Cost-effectiveness analysis of an 18-week exercise programme for patients with breast and colon cancer undergoing adjuvant chemotherapy: the randomised PACT study. *BMJ Open* 2017;7:e012187.
47 Arrieta H, Astrugue C, Regueme S, *et al*. Effects of a physical activity programme to prevent physical performance decline in Onco-geriatric patients: a randomized multicentre trial. *J Cachexia Sarcopenia Muscle* 2019;10:287–97.
48 Uster A, Ruehlin M, Mey S, *et al*. Effects of nutrition and physical exercise intervention in palliative cancer patients: a randomized controlled trial. *Clinical Nutrition* 2018;37:1202–9.
49 Wehrle A, Kneis S, Dickhuth HH, *et al*. Endurance and resistance training in patients with acute leukemia undergoing induction chemotherapy-a randomized pilot study. *Support Care Cancer* 2019;27:1071–9.
50 Mijwel S, Bolam KA, Gerrevall J, *et al*. Effects of exercise on chemotherapy completion and hospitalization rates: the Optitrain breast cancer trial. *Oncologist* 2020;25:23–32.
51 Hacker ED, Larson J, Kujath A, *et al*. Strength training following hematopoietic stem cell transplantation. *Cancer Nurs* 2011;34:238–49.
52 Baumann FT, Kraut L, Schüle K, *et al*. A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplant* 2010;45:355–62.
53 Baumann FT, Zopf EM, Nykamp E, *et al*. Physical activity for patients undergoing an allogeneic hematopoietic stem cell transplantation: benefits of a moderate exercise intervention. *Eur J Haematol* 2011;87:148–56.
54 Pahl A, Wehrle A, Kneis S, *et al*. Whole body vibration training during allogeneic hematopoietic cell transplantation-the effects on patients' physical capacity. *Ann Hematol* 2020;99:635–48.
55 DeFor TE, Burns LJ, Gold E-MA, *et al*. A randomized trial of the effect of a walking regimen on the functional status of 100 adult allogeneic donor hematopoietic cell transplant patients. *Biol Blood Marrow Transplant* 2007;13:948–55.
56 Han X, Robinson LA, Jensen RE, *et al*. Factors associated with health-related quality of life among cancer survivors in the United States. *JNCI Cancer Spectr* 2021;5:pkaa123.
57 Smith TJ, Hillner BE. Bending the cost curve in cancer care. *N Engl J Med* 2011;364:2060–5.
58 Goldsbury DE, Yap S, Weber MF, *et al*. Health services costs for cancer care in Australia: estimates from the 45 and up study. *PLoS One* 2018;13:e0201552.
59 de Oliveira C, Cheng J, Chan K, *et al*. High-cost patients and preventable spending: a population-based study. *J Natl Compr Canc Netw* 2020;18:23–31.
60 Kennedy MA, Bayes S, Newton RU, *et al*. Implementation barriers to integrating exercise as medicine in oncology: an ecological Scoping review. *J Cancer Surviv* 2022;16:1504–7.
61 Kennedy MA, Bayes S, Newton RU, *et al*. We have the program, what now? development of an implementation plan to bridge the research-practice gap prevalent in exercise oncology. *Int J Behav Nutr Phys Act* 2020;17:128.
62 Waterland JL, McCourt O, Edbrooke L, *et al*. Efficacy of prehabilitation including exercise on postoperative outcomes following abdominal cancer surgery: a systematic review and meta-analysis. *Front Surg* 2021;8:628848.
63 Sekine Y, Chiyo M, Iwata T, *et al*. Perioperative rehabilitation and physiotherapy for lung cancer patients with chronic obstructive pulmonary disease. *Jpn J Thorac Cardiovasc Surg* 2005;53:237–43.
64 Pehlivan E, Turna A, Gurses A, *et al*. The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. *Ann Thorac Cardiovasc Surg* 2011;17:461–8.
65 Steffens D, Beckenkamp PR, Hancock M, *et al*. Preoperative exercise halves the postoperative complication rate in patients with lung cancer: a systematic review of the effect of exercise on complications, length of stay and quality of life in patients with cancer. *Br J Sports Med* 2018;52:344.
66 Abel J, Kingston H, Scally A, *et al*. Reducing emergency hospital admissions: a population health complex intervention of an enhanced model of primary care and compassionate communities. *Br J Gen Pract* 2018;68:e803–10.
67 Coletta AM, Basen-Engquist KM, Schmitz KH. Exercise across the cancer care continuum: why it matters, how to implement it, and motivating patients to move. *Am Soc Clin Oncol Educ Book* 2022;42:1–7.
68 World Health Organization. Package of interventions for rehabilitation. Module 4 cardiopulmonary conditions. Geneva World Health Organization; 2023.
69 Dunlay SM, Pack QR, Thomas RJ, *et al*. Participation in cardiac rehabilitation, readmissions, and death after acute myocardial infarction. *Am J Med* 2014;127:538–46.
70 Valsangkar N, Wei JW, Binongo JN, *et al*. Association between patient physical function and length of stay after thoracoscopic lung cancer surgery. *Semin Thorac Cardiovasc Surg* 2021;33:559–66.
71 Aronson JH, Allen OS, Berkalieva A, *et al*. Benefits of an early mobility program for hospitalized patients with cancer. *JCO Oncol Pract* 2023;19:421–6.
72 Nipp RD, El-Jawahri A, Moran SM, *et al*. The relationship between physical and psychological symptoms and health care utilization in hospitalized patients with advanced cancer. *Cancer* 2017;123:4720–7. 10.1002/cncr.30912 Available: https://acsjournals.onlinelibrary.wiley.com/toc/10970142/123/23
73 Galet C, Zhou Y, Eyck PT, *et al*. Fall injuries, associated deaths, and 30-day readmission for subsequent falls are increasing in the elderly US population: a query of the WHO mortality database and national readmission database from 2010 to 2014. *Clin Epidemiol* 2018;10:1627–37.
74 Winters-Stone KM, Horak F, Jacobs PG, *et al*. Falls, functioning, and disability among women with persistent symptoms of chemotherapy-induced peripheral neuropathy. *J Clin Oncol* 2017;35:2604–12.
75 Gauß G, Beller R, Boos J, *et al*. Adverse events during supervised exercise interventions in pediatric oncology-A nationwide survey. *Front Pediatr* 2021;9:682496.
76 Spence RR, Sandler CX, Jones TL, *et al*. Practical suggestions for harms reporting in exercise oncology: the exercise harms reporting method (Exharm). *BMJ Open* 2022;12:e067998.
77 Kang H. The prevention and handling of the missing data. *Korean J Anesthesiol* 2013;64:402–6.
78 Armijo-Olivo S, Fuentes J, Rogers T, *et al*. How should we evaluate the risk of bias of physical therapy trials?: a psychometric and meta-epidemiological approach towards developing guidelines for the design, conduct, and reporting of Rcts in physical therapy (PT) area: a study protocol. *Syst Rev* 2013;2:88.