

BMJ Open Prehabilitation in adult cancer patients: an overview of systematic reviews

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ABSTRACT

Objectives A growing body of evidence supports prehabilitation in cancer patients, but the findings have been inconsistent. This overview aimed to identify, evaluate and summarise the effect of prehabilitation on the clinical outcomes of cancer patients.

Design Overview of systematic reviews.

Data sources PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Library and the JBI Evidence Synthesis database (Joanna Briggs Institute, University of Adelaide, Australia; hosted on Ovid) were searched from inception to January 2025. The search was updated in May 2026, and no new articles were included.

Eligibility criteria We included systematic reviews of randomised controlled trials (RCTs) involving adult cancer patients with a clinically established diagnosis who received prehabilitation interventions prior to surgical treatment. We excluded abstract-only citations, narrative reviews and scoping reviews. Reviews were excluded if ≥50% of the included studies were postoperative interventions, or if preoperative subgroup data could not be extracted.

Data extraction and synthesis Two reviewers independently extracted data on participants' characteristics, types of interventions, outcomes, synthesising methods and pooled anticipated absolute/relative effects for outcomes meta-analysed. Two reviewers assessed methodological quality using the A MeaSurement Tool to Assess Systematic Reviews 2 (AMSTAR 2) tool and assessed the certainty of evidence for prehabilitation using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. Overlap among included systematic reviews was quantified using the corrected covered area (CCA).

Results Twenty systematic reviews (137 RCTs and 18 941 participants) were included. Low- to moderate-certainty evidence indicated that prehabilitation may improve preoperative physical fitness (eg, 6-minute walk test, preoperative cardiopulmonary function, preoperative lung function), reduce surgical complications and shorten the length of hospital stay. None of the included systematic reviews demonstrated a statistically significant effect on preoperative handgrip strength, 30-day readmission, mortality, anxiety or depression. Findings regarding physical activity and quality of life remained inconsistent. Overlap among included reviews was slight (CCA=4.15%).

Conclusions Low- to moderate-certainty evidence suggests that prehabilitation may improve preoperative physical fitness, reduce surgical complications and shorten the length of hospital stay in adult cancer patients

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We comply with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and the Preferred Reporting Items for Overviews of Reviews (PRIOR) statement, using a preregistered protocol.
- ⇒ Methodological quality and evidence certainty were evaluated using A MeaSurement Tool to Assess Systematic Reviews 2 (AMSTAR 2) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, respectively.
- ⇒ We included only systematic reviews of randomised controlled trials to reduce the risk of bias.
- ⇒ Only systematic reviews published in English were included, which may introduce language bias.
- ⇒ Substantial clinical and methodological heterogeneity across the included reviews, combined with partial overlap of primary studies, precluded quantitative re-pooling and required a structured narrative synthesis.

undergoing surgery, whereas current evidence does not support a beneficial effect on 30-day readmission, mortality, quality of life or psychological status. Given the predominantly low-to-moderate certainty of the evidence and the methodological heterogeneity across the included systematic reviews, these findings should be interpreted with caution. Methodologically robust and transparently reported RCTs and systematic reviews are needed to strengthen the certainty of evidence and to inform clinical implementation of prehabilitation.

PROSPERO registration number CRD 42024533214.

INTRODUCTION

Surgical treatment is crucial for improving the survival rates of cancer patients.¹ By the year 2040, it is projected that the global demand for surgical procedures related to cancer will increase by approximately 14 million cases.² Despite ongoing advancements in surgical oncology, postoperative complication rates among cancer patients remain alarmingly high, ranging from 20% to 60%. This negatively affects the quality of life (QoL) and functional status of patients to varying degrees,³ significantly impacting their overall recovery. Preoperative functional status is significantly

associated with perioperative outcomes in cancer patients, leading to a growing emphasis on prehabilitation.⁴

Prehabilitation was first proposed in 2002 to systematically assess the physical, psychological and social aspects of patients from the time of cancer diagnosis. It involves targeted interventions for high-risk patients up to the time of surgery to improve their health status and enhance their ability to cope with the surgery and subsequent treatment, thereby accelerating their recovery from the disease.⁵ A series of studies have demonstrated that implementing prehabilitation interventions before therapy in cancer patients provides statistically significant benefits, including improved clinical outcomes, enhanced physical and mental well-being, improved QoL and reduced healthcare costs.^{6–9}

To date, several systematic reviews and meta-analyses have been published examining the effects of prehabilitation on cancer patients.^{9–14} These studies investigated the effect of prehabilitation on perioperative outcomes, including physical function, complication rates, length of hospital stay (LOS) and QoL. Nevertheless, the heterogeneity in inclusion criteria and methodological rigour across these studies, coupled with their inconsistent findings, poses challenges for policymakers in interpreting the evidence and formulating best practices for clinical application. Therefore, this study was conducted as an overview of systematic reviews (ie, a systematic review of systematic reviews),¹⁵ which provides a comprehensive assessment of the effects of prehabilitation on clinical outcomes in cancer patients.

Objectives

This overview of systematic reviews aimed to identify, evaluate and summarise systematic reviews of prehabilitation interventions for cancer patients, providing evidence-based support for healthcare professionals in making decisions related to the adoption of prehabilitation for cancer patients.

METHODS

This overview of systematic reviews was conducted in accordance with recommended best practices,^{16–18} and the reporting of this overview adheres to both the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines¹⁹ for systematic reviews and the Preferred Reporting Items for Overviews of Reviews (PRIOR) statement,²⁰ which is the established reporting guideline specifically developed for overviews of systematic reviews. A protocol was prospectively registered on PROSPERO (CRD 42024533214, <https://www.crd.york.ac.uk/PROSPERO/#recordDetails>) (registered on 5 January 2024).

Eligibility criteria

The population, intervention, comparison and outcomes framework was used to develop the inclusion criteria. *Population*: patients (aged ≥18 years) diagnosed with

any type of cancer. *Intervention*: Prehabilitation can be unimodal or multimodal. Four types of prehabilitation interventions have been described: exercise, nutritional support, patient education and/or cognitive/psychological therapy.^{21 22} *Comparator*: usual care as defined in the clinical pathway. *Outcomes*: at least one health-related outcome, experience or cost.

Systematic reviews (with or without meta-analysis) that include randomised controlled trials (RCTs) were included. Systematic reviews including findings from other study designs were included if RCT findings were reported separately. We excluded abstract-only citations (ie, conference proceedings), narrative reviews and scoping reviews. Where eligible studies reported mixed preoperative and postoperative interventions, studies were excluded if ≥50% of included studies were postoperative or if preoperative subgroup data could not be extracted. Only systematic reviews available in English were included.

Literature search

Five databases, including PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Library and the JBI Evidence Synthesis database (Joanna Briggs Institute, University of Adelaide, Australia; hosted on Ovid), were comprehensively and systematically searched from inception to January 2025, and the search formula used was a combination of MeSH terms and free words. We updated the search in May 2026, and no new articles were included. Online supplemental material appendix S1 provides the complete search strategy for each of the above databases.

Data extraction

After excluding duplicate studies, two researchers independently screened titles and abstracts of all potentially eligible studies, followed by full-text review of those meeting preliminary inclusion criteria. Two authors independently extracted data using a standardised form developed before database searching, which included participants' characteristics, types of interventions, outcomes, synthesising methods and pooled anticipated absolute/relative effects for outcomes meta-analysed. Disagreements were resolved by consensus.

Quality assessment of included reviews

Two authors independently evaluated the methodological quality of the included systematic reviews using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR 2),²³ which is a valid and reliable tool for evaluating the quality of systematic reviews. The confidence in the evidence incorporated into the systematic evaluation of outcomes was independently evaluated by two evaluators using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence grading system.²⁴

Data synthesis

Our synthesis methodology comprised a series of well-defined steps. First, overlap among the original studies

included across different systematic reviews represents one of the main methodological challenges when conducting an overview of systematic reviews.²⁵ Multiple inclusions of endpoints with overlapping associations or duplicate populations may lead to bias in the final results of the systematic evaluation reappraisal. For finding overlapping associations, we quantitatively evaluated the degree of overlap using the corrected covered area (CCA). CCA between 0% and 5% is considered a slight overlap, 6% to 10% is moderate overlap, 11% to 15% is high overlap and 15% or more is very high overlap.²⁶ When two or more systematic reviews addressed the same research question and shared overlapping primary studies, a single review was retained for each outcome, selected hierarchically by (i) highest AMSTAR 2 rating, (ii) largest number of primary RCTs and (iii) most recent publication date. Next, we created tables to provide detailed overviews of available systematic reviews and their findings. We reported outcomes that were examined in more than one systematic review. The number of participants, types of interventions, anticipated absolute effects and relative effects were reported in tables. For overview-level visual summaries, pooled effect estimates were displayed in the original effect metric as reported by each source systematic review—namely, risk ratios (RRs) or ORs for binary outcomes and mean differences (MDs) or standardised mean differences (SMDs) for continuous outcomes. No cross-metric statistical pooling was performed. MD and SMD were presented in separate panels because they differ in scale interpretation. RR and OR were co-displayed on a single panel because both are relative ratio

measures of binary outcomes, share a common null of 1 and use a directionally consistent axis. Finally, we evaluated the certainty of evidence for prehabilitation using the GRADE framework.

Patient and public involvement

As the study is an overview of systematic reviews, there are no participants. There was no patient or public involvement in the design or conduct of this review

RESULTS

Search results

Our initial literature search was conducted in January 2025 and updated in May 2026, yielding no additional eligible articles. After removing duplicates, 758 of 1009 identified records underwent screening, resulting in the inclusion of 20 systematic reviews (see online supplemental material appendix S2 for reasons for exclusion). The PRISMA flow diagram is shown in figure 1.

Characteristics of the included systematic reviews

The basic characteristics of the included systematic reviews are reported in online supplemental material appendix S3. 20 systematic reviews^{27–46} were included, published between 2018 and 2024, and the resource search among the included reviews was from inception up to August 2023. There were a total of 137 unique RCTs, and the number of RCTs included in each systematic review ranged from 2 to 25. 15 of these systematic reviews included the findings of a meta-analysis.

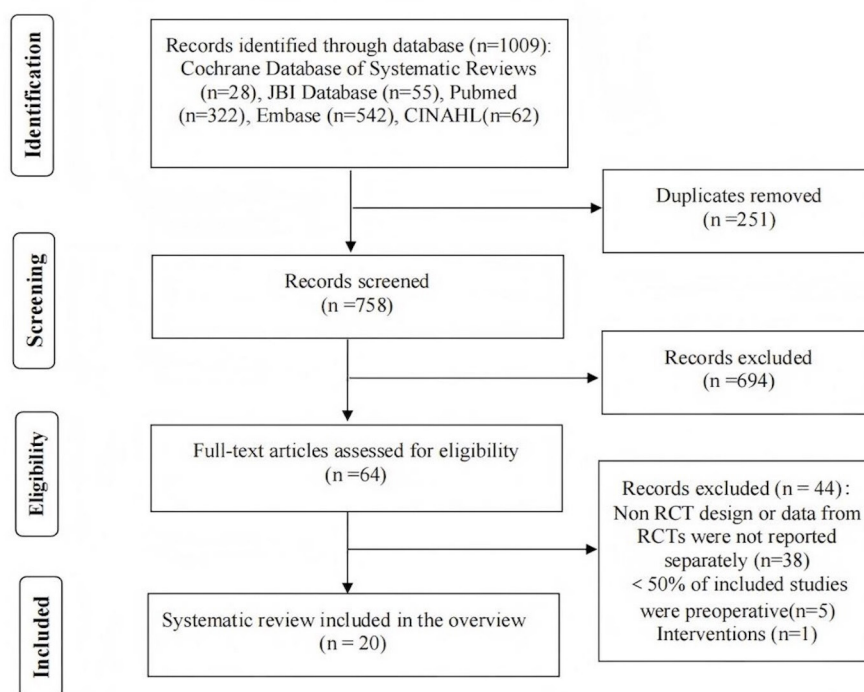


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart illustrating the selection of systematic reviews. CINAHL, Cumulative Index to Nursing and Allied Health Literature; JBI, Joanna Briggs Institute; RCT, randomised controlled trial.

Overlap of the included systematic reviews

The CCA calculation was 4.15% (see online supplemental appendix S4). This indicates a slight overlap of original studies (RCTs) included within this overview.

Participants characteristics

There were a total of 18941 participants, and the number of participants included in each systematic review ranged from 111 to 2682. Six (30%) systematic reviews included patients diagnosed with any type of cancer; six (30%) systematic reviews included patients diagnosed with gastrointestinal cancers; four (20%) systematic reviews included patients diagnosed with lung cancer; three (15%) systematic reviews included patients diagnosed with major abdominal cancer; and one (5%) systematic review included patients diagnosed with head and neck cancer. 14 of the 20 systematic reviews (70%) reported participant age, with the overall age span across reviews ranging from approximately 49 to 84 years. Notably, none of the 20 reviews synthesised sex/gender distribution or socioeconomic descriptors at the review level; such information resided only within the constituent primary trials and was therefore beyond the unit-of-analysis scope of an overview of systematic reviews. The basic characteristics of the participants are detailed in online supplemental appendix S3.

Baseline fitness was informatively but inconsistently reported across the 20 included systematic reviews. Frailty or its surrogates (ie, the Fried Frailty Index, sarcopenia or malnutrition) were explicitly addressed in approximately one-third of the reviews, while several others enriched for high-risk phenotypes such as advanced age, chronic obstructive pulmonary disease, or impaired lung function. Mobility was reported in 19 of the 20 reviews, most commonly through the 6-minute walk test (6MWT). The few reviews providing baseline 6MWT values reported in the 440–460 m range. Cardiopulmonary fitness, primarily indexed by peak oxygen uptake (VO_{peak}) (commonly 14–20 mL/kg/min), the anaerobic threshold and spirometric indices, was assessed in most reviews. However, pre-specified baseline-fitness-stratified subgroup analyses were uncommon, representing a notable reporting gap in the prehabilitation evidence base.

Prehabilitation interventions

Only four (20%) systematic reviews elaborated the definition of prehabilitation intervention in the eligibility criteria, of which two (10%) delineated the definition of prehabilitation, one (5%) delineated the definition of preoperative high-intensity interval training (HIIT) and one (5%) delineated the definition of preoperative exercise.

For the type of prehabilitation, most (12, 60%) systematic reviews were unimodal interventions, which included exercise (11, 55%) or nutrition (1, 5%). Seven (35%) systematic reviews were mixed interventions that included any form of prehabilitation. One (5%) systematic review was multimodal interventions.

For systematic reviews that included exercise intervention (ie, unimodal, mixed or multimodal; 19 systematic reviews, 95%), all but one systematic review included different types of exercise. For the type of exercise, 16 (80%) included aerobic and resistance training, 12 (60%) included inspiratory muscle training, 7 (35%) included HIIT, 3 (15%) included pelvic floor muscle training and 1 (5%) included yoga. The frequency, intensity and duration of the exercise varied considerably across systematic reviews.

Among the systematic reviews focusing on nutrition interventions, which encompassed unimodal, mixed or multimodal approaches, eight reviews (40%) were identified. Of these, two reviews (10%) exclusively addressed supplementation, while six reviews (30%) incorporated a combination of counselling and supplementation. Reporting of the nutrition interventions varied widely in the systematic reviews.

For systematic reviews that included psychological intervention (ie, mixed or multimodal; six systematic reviews, 30%), one (5%) included counselling only, one (5%) included stress management training (SMT) only, three (15%) included a mix of counselling and SMT and one (5%) included a motivational interview and interventions aimed at reducing preoperative anxiety. Two (10%) systematic reviews included education sessions in prehabilitation interventions.

18 (90%) systematic reviews reported the duration of prehabilitation. The overall range spanned 3 days to 16 weeks, with a mean of approximately 4.8 weeks (median 4.5 weeks). The most frequently reported duration ranges were 1–8 weeks (four reviews) and 1–4 weeks (three reviews), and 14 of 18 reviews (78%) synthesised programmes with an upper bound ≤ 8 weeks; only four reviews extended the upper bound to 14–16 weeks. The per-review intervention durations are detailed in online supplemental appendix S5. 13 (65%) systematic reviews reported the location of prehabilitation: 1 is home-based, 1 is hospital-based and the other 11 did not restrict the location (either home, hospital or both). Only three (15%) systematic reviews explicitly indicated the supervision procedure in the inclusion criteria. Seven (35%) systematic reviews reported the compliance rate of prehabilitation, ranging from 16% to 100%. More details of the prehabilitation interventions can be seen in online supplemental appendix S5.

Outcomes

Outcomes reported in the included systematic reviews are listed in online supplemental appendix S6. Outcomes were grouped into three broad categories: physical fitness, surgical complications and patient outcomes. The most common outcome in each outcome category was the 6MWT (11/20, 55%), postoperative complications (17/20, 85%) and LOS in the hospital (16/20, 80%), respectively.

Methodological quality of the included systematic reviews

Three (3/20, 15%) systematic reviews were rated as high quality, nine (9/20, 45%) were rated as moderate

quality, seven (7/20, 35%) were rated as low quality and one (1/20, 5%) was rated as critically low quality. A more detailed description is shown in online supplemental appendix S7.

Intervention effect and GRADE evidence quality

The GRADE summary of the findings table is shown in online supplemental appendix S8. Across approximately 65 outcome-level assessments derived from the 15 systematic reviews with meta-analyses, the certainty of evidence was rated as high for only 1 outcome (1.5%), moderate for 6 outcomes (9.2%), low for 24 outcomes (36.9%) and very low for 34 outcomes (52.3%). The principal reasons for downgrading were risk of bias arising from inadequate randomisation, allocation concealment and blinding in the primary RCTs; inconsistency due to substantial statistical heterogeneity ($I^2 > 50\%$ in many pooled estimates); imprecision related to small sample sizes and wide CIs crossing the null; and, for some outcomes, suspected publication bias indicated by funnel-plot asymmetry. Indirectness was generally not a concern. In broad terms, evidence regarding preoperative physical fitness outcomes (ie, 6MWT, VO_{2peak} , Forced Expiratory Volume (FEV_1), Forced Vital Capacity (FVC)) was of comparatively higher certainty, whereas evidence regarding patient-reported outcomes (QoL, anxiety, depression) and long-term clinical outcomes (30-day readmission, mortality) was almost uniformly of low to very low certainty.

6MWT

The effect of prehabilitation on 6MWT was assessed in 11 meta-analyses (figure 2). Seven meta-analyses showed statistically significant positive effects on the preoperative 6MWT (I^2 ranging from 0% to 99%), and three showed statistically significant positive effects on the postoperative 6MWT (I^2 ranging from 0% to 89%).

Preoperative cardiopulmonary function

The preoperative cardiopulmonary functions were assessed using VO_{2peak} and anaerobic threshold (figure 1 of online supplemental appendix S9). The effects of VO_{2peak} were examined in six meta-analyses (I^2 ranging from 0% to 78%), and three of them showed statistically significant positive effects. For the anaerobic threshold, two meta-analyses reported no statistically significant effect (³¹: $I^2=0\%$; ⁴⁵: $I^2=23\%$).

Preoperative lung function

The preoperative lung functions were measured by FEV_1 , the FVC and Peak Expiratory Flow (PEF); see figure 2 of online supplemental appendix S9. There was a statistically significant effect of prehabilitation on FEV_1 (³³: MD 5.87, 95% CI 4.46 to 7.28, $I^2=0\%$; ³⁴: MD 6.65, 95% CI 5.25 to 8.05, $I^2=0\%$) and on FVC (³³: MD 5.42, 95% CI 0.73 to 10.11, $I^2=53\%$; ³⁴: MD 4.71, 95% CI 0.95 to 8.47, $I^2=0\%$) in two meta-analyses. For PEF, only one primary study contributed to the pooled estimate (³³: MD 21.52, 95% CI -7.11 to 50.16, I^2 not applicable).

Preoperative handgrip strength

Four systematic reviews described that there was no statistically significant improvement between the prehabilitation group and the control group. Of them, one systematic review with meta-analysis provided very low-certainty evidence that prehabilitation may have no effect on preoperative handgrip strength improvement (³¹: MD 2.8, 95% CI -0.1 to 5.7, $I^2=49\%$); see figure 3 of online supplemental appendix S9.

Physical activity

Two systematic reviews without meta-analyses reported on the effect of prehabilitation on physical activity. Meneses-Echavez *et al*³⁷ found that it is uncertain whether prehabilitation with combined training improved physical activity levels. However, Thomas reported a statistically significant increase in physical activity after multimodal prehabilitation.

Surgical complications

Eleven systematic reviews with meta-analyses reported on the effect of prehabilitation on postoperative complication rates (I^2 ranging from 0% to 77%), and six of them showed a statistically significant reduction in postoperative complication rates (figure 3). Major complications (defined as Clavien-Dindo ≥ 3) were reported in four meta-analyses, and only one showed a statistically significant reduction in major complication rates (figure 3b). Postoperative pneumonia was reported in two meta-analyses ($I^2=0\%$ in both), and neither found a statistically significant difference (figure 3c).

LOS in the hospital

The effect of prehabilitation on the LOS was assessed in 12 meta-analyses (I^2 ranging from 0% to 85%) (figure 4a,b). Six of them showed a statistically significant decrease in LOS in the prehabilitation group.

A systematic review with meta-analysis provided very low-certainty evidence, indicating no significant differences in the length of stay in the intensive care unit (ICU) in days between the prehabilitation group and the control group. (²⁷: MD: -0.24 d, 95% CI: -0.94 to 0.47, $I^2=48\%$); see figure 4c. Additionally, another systematic review without meta-analysis also reported no benefit in ICU LOS.

The rates of 30-day readmission

Four systematic reviews reported the rates of 30-day readmission, and three of them performed meta-analyses (³⁵: RR 1.10, 95% CI 0.52 to 2.32, I^2 not applicable³⁹; RR 1.20, 95% CI 0.54 to 2.65, $I^2=0\%$ ⁴⁵; OR 1.07, 95% CI 0.61 to 1.90, $I^2=0\%$). None of the systematic reviews found a statistically significant difference in the rates of 30-day readmission (figure 4 of online supplemental appendix S9).

Mortality

Eight systematic reviews reported the rates of mortality, and five of them performed meta-analyses ($I^2=0\%$ in

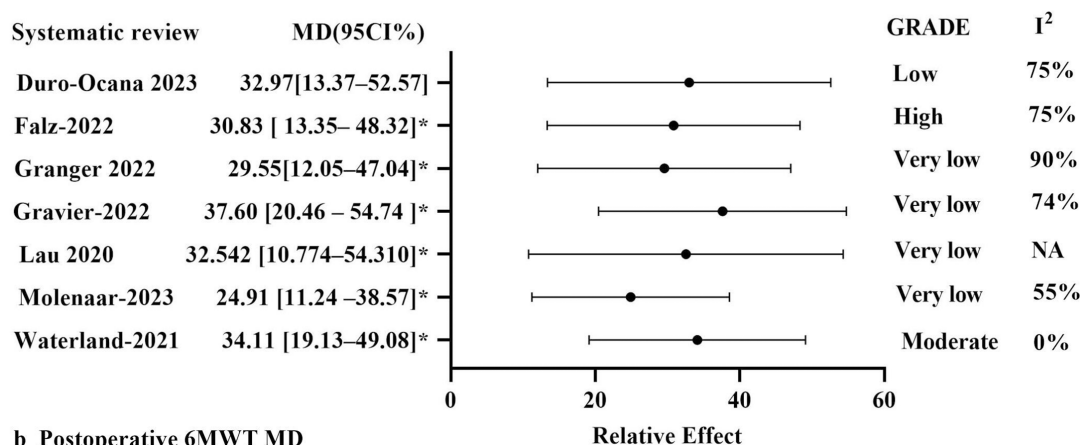
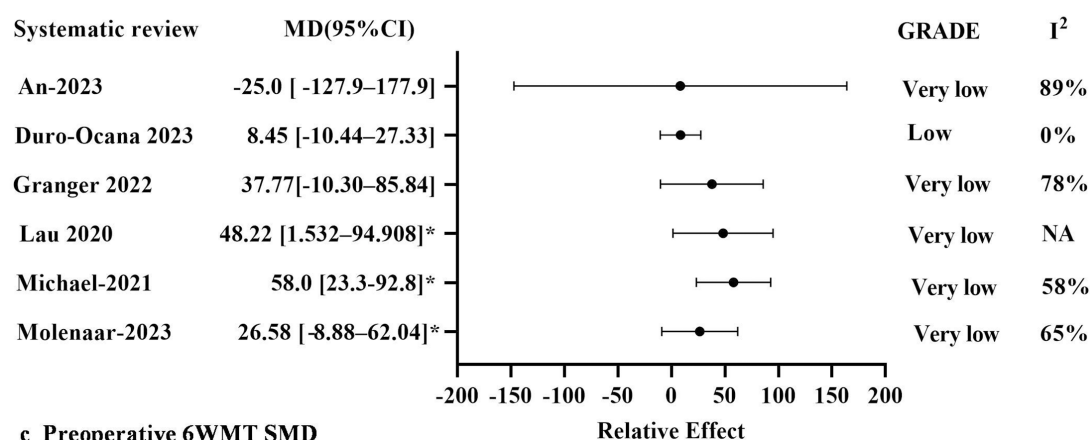
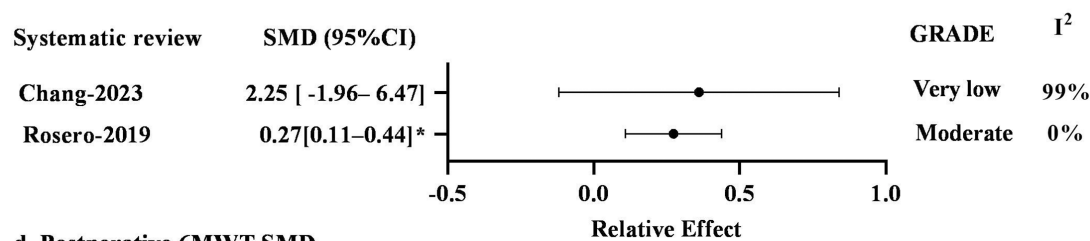
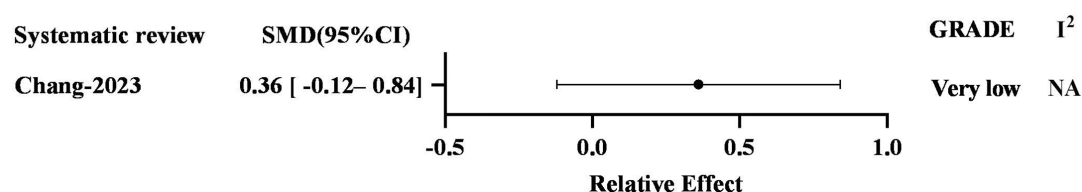
a Preoperative 6MWT MD**b Postoperative 6MWT MD****c Preoperative 6WMT SMD****d Postoperative 6MWT SMD**

Figure 2 Results of meta-analyses that assessed 6MWT. GRADE, the Grading of Recommendations Assessment, Development, and Evaluation evidence grading system; MD, mean difference; NA, not applicable; SMD, standard mean difference; 6MWT, 6-minute walk test.

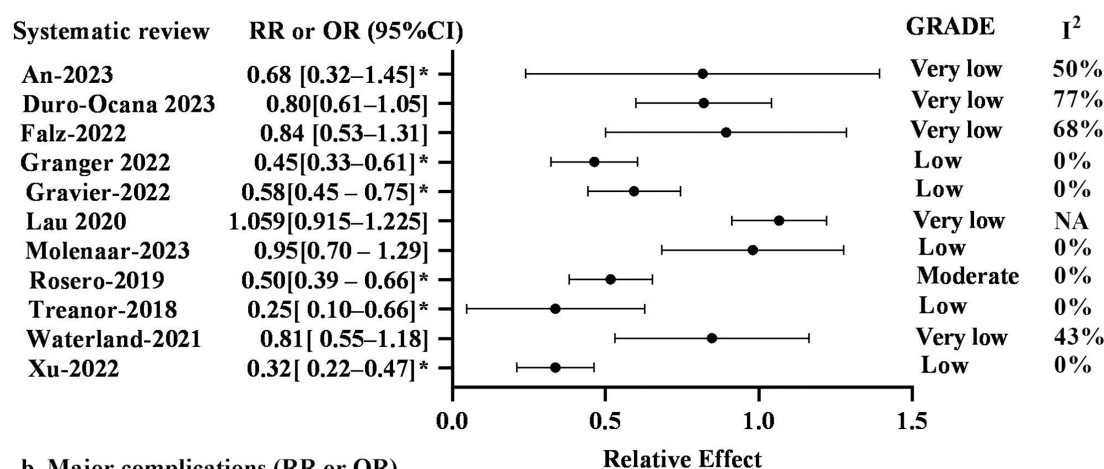
all four reviews that reported the statistic^{27 31 34 45}; not reported in³⁵. None of the systematic reviews found a statistically significant difference in the rates of mortality (figure 5 of online supplemental appendix S9).

Postoperative QoL

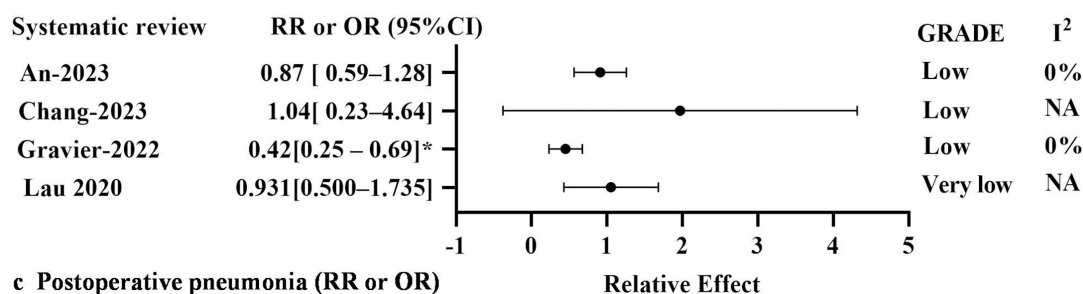
The effect of prehabilitation on postoperative QoL was reported in six systematic reviews, using the European Organisation for Research and Treatment of Cancer

QoL Questionnaire-Core 30 (EORTC QLQ-C30), 36-item Short-Form Health Survey (SF-36), or Functional Assessment of Cancer Therapy-Chemotherapy. Four systematic reviews reported no statistically significant difference, and two of them provided low or very low-certainty evidence that there were no differences between prehabilitation and control in postoperative EORTC QLQ-C30 scores (²⁷: MD 10.26, 95% CI –13.75 to 34.27, I²=84%³⁷; MD 1.10,

a Postoperative complications (RR or OR)



b Major complications (RR or OR)



c Postoperative pneumonia (RR or OR)

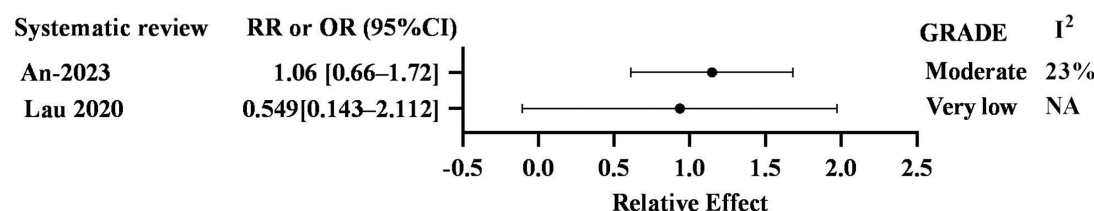


Figure 3 Results of meta-analyses that assessed surgical complications. GRADE, the Grading of Recommendations Assessment, Development, and Evaluation evidence grading system; NA, not applicable.

95% CI –1.90 to 4.20, I²=0%) (figure 6 of online supplemental appendix S9)

Anxiety and depression

The effect of prehabilitation on anxiety and depression was assessed in only one meta-analysis, using the Hospital Anxiety and Depression Scale. The meta-analysis provided very low-certainty evidence that there were no differences between the prehabilitation group and the control group on anxiety (³⁴: MD: –0.2 point, 95% CI: –1.3 to 1.0, I²=0%) or depression (³⁴: MD: –0.6 point, 95% CI: –1.6 to 0.5, I²=0%); see figure 7 of online supplemental appendix S9.

DISCUSSION

Summary of the evidence

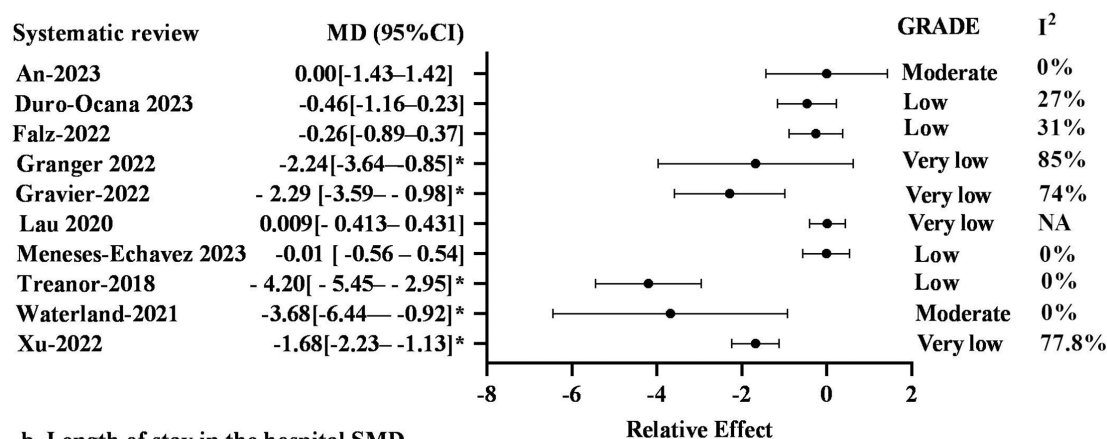
This overview appraised and summarised evidence from 20 systematic reviews (137 unique RCTs and 18941 participants) assessing the effects of prehabilitation interventions on adult cancer patients. Low- to moderate-certainty evidence indicated that prehabilitation interventions may improve preoperative physical fitness, reduce surgical

complications and shorten the LOS, whereas current evidence does not support a beneficial effect on 30-day readmission, mortality, QoL or psychological status. However, the effects varied among included systematic reviews, and the GRADE certainty of the evidence for most outcomes was low or very low; accordingly, definitive conclusions regarding the efficacy of prehabilitation cannot yet be drawn. The inconsistent results may be interpreted by differences in cancer types and stages, as well as heterogeneity between interventions and measurement instruments. To improve the certainty of evidence for prehabilitation, more methodologically robust and well-reported RCTs are needed.

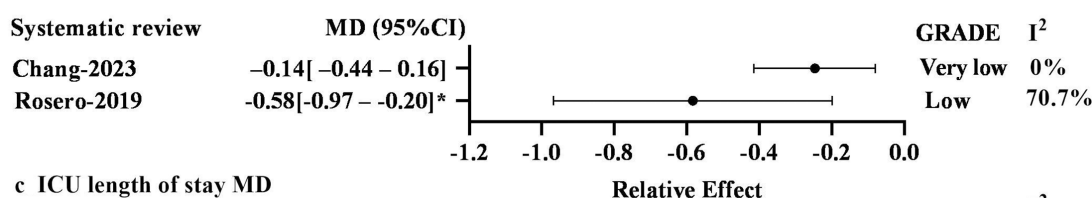
Effects of prehabilitation

Physical fitness is an important preoperative assessment factor, as it has been found to be strongly associated with surgical complications, LOS and mortality.⁴⁷ The 6MWT is the most common physical fitness outcome because of ease of use and cost,⁴⁸ and 11 systematic reviews included in this overview reported it. Seven of the nine (77.78%)

a Length of stay in the hospital MD



b Length of stay in the hospital SMD



c ICU length of stay MD

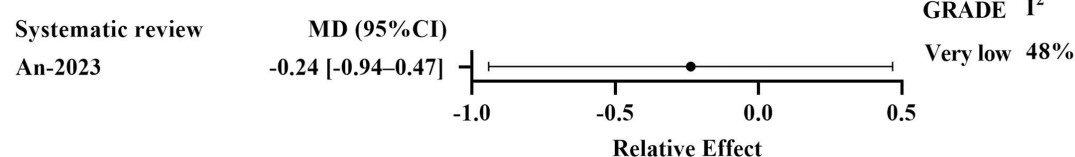


Figure 4 Results of meta-analyses that assessed length of stay in hospital. GRADE, the Grading of Recommendations Assessment, Development, and Evaluation evidence grading system; ICU, intensive care unit; MD, mean difference; NA, not applicable; SMD, standard mean difference.

systematic reviews reported statistically significant clinical improvement after prehabilitation interventions in preoperative 6MWT, and three of the seven (42.86%) systematic reviews reported statistically significant clinical improvement in postoperative 6MWT. Cardiopulmonary function testing, which measures $\text{VO}_{2\text{peak}}$, is more expensive and requires interpretation by an experienced operator, but may be more accurate than 6MWT.⁴⁹ Among the six systematic reviews that evaluated this parameter, three (50%) reported a statistically significant improvement. FEV_1 and FVC are considered the most widely accepted measures of lung function.⁵⁰ Our findings suggested that prehabilitation was effective at improving FEV_1 and FVC in two systematic reviews. Differences in measurement instruments among studies are possible explanations for the different results in physical fitness.

In addition to physical fitness, surgical complications and LOS are also outcome measures of great interest in cancer prehabilitation studies. Among the 17 systematic reviews that evaluated postoperative complications, 7 (41.2%) reported a statistically significant improvement. And 7 of the 16 (43.75%) studies reported a statistically significant reduction after intervention in LOS. The discrepancy may be due to the heterogeneity of prehabilitation interventions, such as the mode, duration and adherence. A recent meta-analysis found that only

multimodal prehabilitation could reduce postoperative complications compared with unimodal prehabilitation.⁵¹

Beyond differences in measurement instruments and intervention modalities, the magnitudes of the pooled effects reported above must be interpreted in light of the statistical heterogeneity observed across the included meta-analyses. While several pooled estimates demonstrated low heterogeneity, other pooled estimates exhibited substantial-to-considerable heterogeneity. The presence of such heterogeneity indicates that the true effect of prehabilitation is unlikely to be a single fixed value across populations, but rather varies according to cancer type, surgical setting, intervention components (unimodal vs multimodal), session frequency, total duration, supervision intensity and patient adherence. Consequently, the point estimates of these pooled effects should be interpreted with caution, and clinicians should not directly extrapolate the magnitude of benefit observed in one setting to a different patient population without considering these contextual factors.

Certainty of the evidence

This overview followed the GRADE system to evaluate the level of evidence for the outcome indicators of the included studies and found that the evidence was of low certainty; no economic evaluation studies were identified.

The main reasons for the reduced level of evidence were limitations, inconsistencies and imprecision. The systematic evaluation included original studies that did not fully implement allocation concealment and blinding, increasing the risk of bias and lowering the level of evidence. The inconsistency aspect was mainly due to the high heterogeneity of the included studies, which was analysed due to the non-uniformity of the frequency and periodicity of the prehabilitation interventions and the variety of tools for the evaluation of the outcome indicators, resulting in a lower level of evidence. The literature on some of the outcome indicator studies is too small, with small sample sizes and wide CIs, resulting in less precise results and lower quality of evidence. From a policy perspective, the lack of economic data means that cost-effectiveness cannot be incorporated into decisions regarding health insurance coverage or reimbursement. This is particularly problematic in settings with limited resources, where the opportunity cost of implementing interventions may be high. Future research should employ more rigorous designs to replicate existing studies and incorporate economic endpoints. Where feasible, it should also conduct in-trial or model-based cost-effectiveness analyses. Research funders and journal editors could accelerate progress by making GRADE grading and economic reporting a condition for publication.

Strengths and limitations

This overview has several strengths. First, we have a pre-specified protocol, and we included only systematic reviews of RCTs to reduce the risk of bias. This overview followed both the PRISMA 2020 guidelines and the PRIOR statement. A comprehensive literature search was conducted across multiple databases. Second, two reviewers independently performed all stages of the overview, which is the best practice method for an overview. We also used the standard assessment tool AMSTAR 2 to evaluate the methodological quality of the included systematic reviews and applied the GRADE score to determine the certainty of evidence, with discrepancies resolved by consensus or a third reviewer. Finally, including endpoints with overlapping associations or duplicate populations multiple times may introduce bias into the final results of the systematic evaluation reappraisal. To identify these, we quantitatively assessed the extent of overlap using the CCA calculation, which gave a result of 4.15%. This is considered to be slight overlap in the included RCTs, which increased our confidence in the findings.

This study has the following five limitations. First, despite searching multiple databases, we did not include grey literature or non-English-language databases. With respect to language restriction, available meta-epidemiological evidence suggests that, for healthcare interventions in high-resource settings such as surgical oncology, restriction to English-language reviews typically exerts only a modest influence on pooled effect estimates and rarely alters the direction of conclusions^{52 53}; nonetheless,

language-restriction bias remains a recognised limitation. Second, as an overview of systematic reviews, we did not conduct independent statistical tests for publication bias, owing to two methodological challenges specific to overviews: (i) heterogeneity in effect measures (RR vs OR) across included systematic reviews precludes pooling of effect estimates; and (ii) overlapping primary studies across reviews violate the independence assumption required for such tests. We instead mitigated and evaluated publication bias by assessing whether each included review appropriately addressed it under AMSTAR 2 item 15. Third, different systematic reviews may include the same primary studies, potentially resulting in the same evidence being counted more than once. We quantified overlap using the CCA method, but did not perform a meta-analysis to aggregate overlapping systematic reviews. Fourth, most of the evidence was rated as low or very low certainty based on GRADE scores. Finally, no included review reported health-economic outcomes, which prevented us from drawing conclusions regarding the cost-effectiveness of prehabilitation.

Future directions

As mentioned above in this overview, a considerable body of evidence exists evaluating the effects of prehabilitation interventions on adult cancer patients. However, it seems premature to draw robust conclusions due to the low quality of evidence for most outcomes. There are several suggestions for future studies. First, cancer patients most likely to benefit from prehabilitation need to be selected. Current evidence has shown that patients with decreased physiological function may benefit more from prehabilitation.⁵⁴ Future trials should therefore phenotype participants using standardised baseline assessments and pre-specify baseline-stratified subgroup analyses to identify the cancer-patient phenotypes most likely to benefit. Second, a consensus must be reached on the definition of prehabilitation, and the effects of single-mode or multi-modal prehabilitation need to be clarified. Third, adherence was rarely reported in included studies; however, adequate adherence is also very important for a successful prehabilitation programme. Fourth, an adequate duration of prehabilitation to enhance health status within acceptable waiting times for cancer patients needs to be explored. Finally, more methodologically robust and well-reported RCTs and systematic reviews are needed to improve the certainty of evidence for prehabilitation.

CONCLUSION

Low- to moderate-certainty evidence suggests that prehabilitation may improve preoperative physical fitness, reduce surgical complications and shorten LOS in adult cancer patients undergoing surgery, whereas current evidence does not support a beneficial effect on 30-day readmission, mortality, QoL or psychological status. Given the predominantly low-to-moderate certainty of evidence and the methodological heterogeneity across included

systematic reviews, these findings should be interpreted with caution. Methodologically robust and transparently reported RCTs and systematic reviews are needed to strengthen the certainty of evidence and to inform clinical implementation of prehabilitation.

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REFERENCES

- Are C, Murthy SS, Sullivan R, *et al.* Global Cancer Surgery: pragmatic solutions to improve cancer surgery outcomes worldwide. *Lancet Oncol* 2023;24:e472–518.
- Perera SK, Jacob S, Wilson BE, *et al.* Global demand for cancer surgery and an estimate of the optimal surgical and anaesthesia workforce between 2018 and 2040: a population-based modelling study. *Lancet Oncol* 2021;22:182–9.
- Gultekin SC, Cakir AB, Guc ZG, *et al.* The comparison of functional status and health-related parameters in ovarian cancer survivors with healthy controls. *Support Care Cancer* 2024;32:119.
- Coderre D, Brahmabhatt P, Hunter TL, *et al.* Cancer Prehabilitation in Practice: the Current Evidence. *Curr Oncol Rep* 2022;24:1569–77.
- Gillis C, Ljungqvist O, Carli F. Prehabilitation, enhanced recovery after surgery, or both? A narrative review. *Br J Anaesth* 2022;128:434–48.
- Gennuso D, Baldelli A, Gigli L, *et al.* Efficacy of Prehabilitation in cancer patients: an Rcts systematic review with meta-analysis. *BMC Cancer* 2024;24:1302.
- Bausys A, Luksta M, Anglickiene G, *et al.* Effect of home-based prehabilitation on postoperative complications after surgery for gastric cancer: randomized clinical trial. *Br J Surg* 2023;110:1800–7.
- Ikeda T, Toyama S, Harada T, *et al.* Effectiveness of prehabilitation during neoadjuvant therapy for patients with esophageal or gastroesophageal junction cancer: a systematic review. *Esophagus* 2024;21:283–97.
- Guo Y, Ding L, Miao X, *et al.* Effects of prehabilitation on postoperative outcomes in frail cancer patients undergoing elective surgery: a systematic review and meta-analysis. *Support Care Cancer* 2022;31:57.
- Franssen R, Voorn M, Jetten E, *et al.* Real-life effectiveness of prehabilitation to improve postoperative outcomes in patients with colorectal cancer approaching surgery: A systematic review and meta-analyses of observational studies versus randomized controlled trials. *European Journal of Surgical Oncology* 2024;50:108708.
- Voorn MJ, Franssen RFW, Hoogbeem TJ, *et al.* Evidence base for exercise prehabilitation suggests favourable outcomes for patients undergoing surgery for non-small cell lung cancer despite being of low therapeutic quality: a systematic review and meta-analysis. *Eur J Surg Oncol* 2023;49:879–94.
- Shen Y, Cong Z, Ge Q, *et al.* Effect of nutrition-based prehabilitation on the postoperative outcomes of patients with esophagogastric cancer undergoing surgery: A systematic review and meta-analysis. *Cancer Med* 2024;13:e70023.
- Marmol-Perez A, Corres P, Fernández-Escabias M, *et al.* Impact of Multidisciplinary Prehabilitation Interventions on Postoperative Hospital Length of Stay and Functional Capacity in Patients Undergoing Resection of Colorectal Cancer: A Systematic Review and Meta-analysis. *Dis Colon Rectum* 2024;67:1107–19.
- Laza-Cagigas R, Larumbe-Zabala E, Rampal T, *et al.* Effect of prehabilitation programmes on functional capacity in patients awaiting oncological resections: a systematic review and meta-analysis of randomised controlled trials. *Support Care Cancer* 2024;32:667.
- Aguilera-Eguía RA, Fuentes-Barria H, Serón-Silva P. When is an overview of systematic reviews necessary? *Nutr Hosp* 2023;40:895–6.
- Lunny C, Brennan SE, McDonald S, *et al.* Toward a comprehensive evidence map of overview of systematic review methods: paper 1—purpose, eligibility, search and data extraction. *Syst Rev* 2017;6:231.
- Lunny C, Brennan SE, McDonald S, *et al.* Toward a comprehensive evidence map of overview of systematic review methods: paper 2—risk of bias assessment; synthesis, presentation and summary of the findings; and assessment of the certainty of the evidence. *Syst Rev* 2018;7:159.
- Aromataris E, Fernandez R, Godfrey CM, *et al.* Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. *Int J Evid Based Healthc* 2015;13:132–40.
- Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
- Gates M, Gates A, Pieper D, *et al.* n.d. Reporting guideline for overviews of reviews of healthcare interventions: development of the PRIOR statement. *BMJ* 2018;378:e070849.
- Engel D, Testa GD, McIsaac DI, *et al.* Reporting quality of randomized controlled trials in prehabilitation: a scoping review. *Perioper Med* 2023;12:48.
- Wade-McBane K, King A, Urch C, *et al.* Prehabilitation in the lung cancer pathway: a scoping review. *BMC Cancer* 2023;23:747.
- Shea BJ, Reeves BC, Wells G, *et al.* AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008.
- Brozek JL, Akl EA, Alonso-Coello P, *et al.* Grading quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions. *Allergy* 2009;64:669–77.
- Ballard M, Montgomery P. Risk of bias in overviews of reviews: a scoping review of methodological guidance and four-item checklist. *Res Synth Methods* 2017;8:92–108.
- Pieper D, Antoine S-L, Mathes T, *et al.* Systematic review finds overlapping reviews were not mentioned in every other overview. *J Clin Epidemiol* 2014;67:368–75.
- An KR, Seijas V, Xu MS, *et al.* Does prehabilitation before esophagectomy improve postoperative outcomes? A systematic review and meta-analysis. *Dis Esophagus* 2024;37:doad066.

- 28 Cantwell LA, Fahy E, Walters ER, *et al.* Nutritional prehabilitation in head and neck cancer: a systematic review. *Support Care Cancer* 2022;30:8831–43.
- 29 Chang MC, Choo YJ, Kim S. Effect of prehabilitation on patients with frailty undergoing colorectal cancer surgery: a systematic review and meta-analysis. *Ann Surg Treat Res* 2023;104:313–24.
- 30 Chou YJ, Kuo HJ, Shun SC. Cancer Prehabilitation Programs and Their Effects on Quality of Life. *Oncol Nurs Forum* 2018;45:726–36.
- 31 Duro-Ocana P, Zambolin F, Jones AW, *et al.* Efficacy of supervised exercise prehabilitation programs to improve major abdominal surgery outcomes: A systematic review and meta-analysis. *J Clin Anesth* 2023;86:111053.
- 32 Falz R, Bischoff C, Thieme R, *et al.* Effects and duration of exercise-based prehabilitation in surgical therapy of colon and rectal cancer: a systematic review and meta-analysis. *J Cancer Res Clin Oncol* 2022;148:2187–213.
- 33 Granger C, Cavalheri V. Preoperative exercise training for people with non-small cell lung cancer. *Cochrane Database Syst Rev* 2022;9:CD012020.
- 34 Gravier F-E, Smondack P, Prieur G, *et al.* Effects of exercise training in people with non-small cell lung cancer before lung resection: a systematic review and meta-analysis. *Thorax* 2022;77:486–96.
- 35 Lau CSM, Chamberlain RS. Prehabilitation Programs Improve Exercise Capacity Before and After Surgery in Gastrointestinal Cancer Surgery Patients: A Meta-Analysis. *J Gastrointest Surg* 2020;24:2829–37.
- 36 Mareschal J, Hemmer A, Douissard J, *et al.* Surgical Prehabilitation in Patients with Gastrointestinal Cancers: Impact of Unimodal and Multimodal Programs on Postoperative Outcomes and Prospects for New Therapeutic Strategies-A Systematic Review. *Cancers (Basel)* 2023;15:1881.
- 37 Meneses-Echavez JF, Loaiza-Betancur AF, Díaz-López V, *et al.* Prehabilitation programs for individuals with cancer: a systematic review of randomized-controlled trials. *Syst Rev* 2023;12:219.
- 38 Michael CM, Lehrer EJ, Schmitz KH, *et al.* Prehabilitation exercise therapy for cancer: A systematic review and meta-analysis. *Cancer Med* 2021;10:4195–205.
- 39 Molenaar CJ, van Rooijen SJ, Fokkenrood HJ, *et al.* Prehabilitation versus no prehabilitation to improve functional capacity, reduce postoperative complications and improve quality of life in colorectal cancer surgery. *Cochrane Database Syst Rev* 2023;2022:CD013259.
- 40 Piraux E, Caty G, Reyckler G. Effects of preoperative combined aerobic and resistance exercise training in cancer patients undergoing tumour resection surgery: A systematic review of randomised trials. *Surg Oncol* 2018;27:584–94.
- 41 Rosero ID, Ramírez-Vélez R, Lucia A, *et al.* Systematic Review and Meta-Analysis of Randomized, Controlled Trials on Preoperative Physical Exercise Interventions in Patients with Non-Small-Cell Lung Cancer. *Cancers (Basel)* 2019;11:944:944–44:.
- 42 Smyth E, O'Connor L, Mockler D, *et al.* Preoperative high intensity interval training for oncological resections: A systematic review and meta-analysis. *Surg Oncol* 2021;38:101620.
- 43 Thomas G, Tahir MR, Bongers BC, *et al.* Prehabilitation before major intra-abdominal cancer surgery: A systematic review of randomised controlled trials. *Eur J Anaesthesiol* 2019;36:933–45.
- 44 Treanor C, Kyaw T, Donnelly M. An international review and meta-analysis of prehabilitation compared to usual care for cancer patients. *J Cancer Surviv* 2018;12:64–73.
- 45 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.
- 46 Xu X, Cheung DST, Smith R, *et al.* The effectiveness of pre- and post-operative rehabilitation for lung cancer: A systematic review and meta-analysis on postoperative pulmonary complications and length of hospital stay. *Clin Rehabil* 2022;36:172–89.
- 47 Del Bianco N, Borsati A, Toniolo L, *et al.* What is the role of physical exercise in the era of cancer prehabilitation? A systematic review. *Crit Rev Oncol Hematol* 2024;198:104350.
- 48 Pires IM, Denysyuk HV, Villasana MV, *et al.* Development Technologies for the Monitoring of Six-Minute Walk Test: A Systematic Review. *Sensors (Basel)* 2022;22:581.
- 49 Levett DZH, Jack S, Swart M, *et al.* Perioperative cardiopulmonary exercise testing (CPET): consensus clinical guidelines on indications, organization, conduct, and physiological interpretation. *Br J Anaesth* 2018;120:484–500: .
- 50 Miller MR. Choosing and using lung function prediction equations. *Eur Respir J* 2016;48:1535–7.
- 51 Daniels SL, Lee MJ, George J, *et al.* Prehabilitation in elective abdominal cancer surgery in older patients: systematic review and meta-analysis. *BJS Open* 2020;4:1022–41.
- 52 Nussbaumer-Streit B, Klerings I, Dobrescu AI, *et al.* Excluding non-English publications from evidence-syntheses did not change conclusions: a meta-epidemiological study. *J Clin Epidemiol* 2020;118:42–54.
- 53 Morrison A, Polisena J, Huseraue D, *et al.* The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *Int J Technol Assess Health Care* 2012;28:138–44.
- 54 Minnella EM, Awasthi R, Gillis C, *et al.* Patients with poor baseline walking capacity are most likely to improve their functional status with multimodal prehabilitation. *Surgery* 2016;160:1070–9.