Clinical guideline and recommendations on pre-operative exercise training in patients awaiting major non-cardiac surgery

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Summary

Despite calls for the routine implementation of pre-operative exercise programmes to optimise patient fitness before elective major surgery, there is no practical guidance for providing safe and effective exercise in this specific context. The following clinical guideline was developed following a review of the evidence on the effects of pre-operative exercise interventions. We developed a series of best-practice and, where possible, evidence-based statements to advise on patient care with respect to exercise training in the perioperative period. These statements include: patient selection for exercise training in surgical patients; integration of exercise training into multi-modal prehabilitation programmes; and advice on exercise prescription factors and follow-up. Although we acknowledge that further research is needed to identify the optimal exercise prescription in different clinical scenarios, we urge perioperative teams to embrace these recommendations.

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Summary of key recommendations

1. Pre-operative exercise training should be offered to patients undergoing major or complex elective surgery with a view to improving their physical fitness and health status and reducing the risk of perioperative morbidity and mortality. If resources are limited, priority of referral to pre-operative exercise training should go to patients who are at increased risk of perioperative complications, such as those with low cardiorespiratory fitness.

2. Pre-operative exercise training should be offered as part of a multi-modal prehabilitation programme that addresses a variety of perioperative risk factors including cigarette smoking, excessive alcohol consumption and anaemia.

3. Healthcare professionals making referrals to a pre-operative exercise programme should have basic knowledge about what the programme entails and its potential effects. A pre-operative exercise programme should be presented by the referring clinician as a fundamental part of the pre-operative optimisation of a patient, rather than an optional extra.

4. The referral process and/or the initial assessment for pre-operative exercise training offer an important opportunity to explore the patient’s understanding of exercise, address concerns, and to educate patients about the benefits of exercise training, both during the perioperative period and in the longer term. The referral/assessment stage also provides an opportunity to assess and refer for treatment of comorbidities before commencing exercise training.

5. The setting of the pre-operative exercise programme, skill mix of the team and other comorbidities should always be considered in the risk assessment of patients entering the programme.

6. Patients should undergo thorough assessment before commencing pre-operative exercise training. The assessment should identify: contraindications to exercise; current health status, including comorbidities; current treatments, including medications; ongoing investigations; and prior and current levels of physical activity. The assessment should also ideally include an objective evaluation of functional capacity and a questionnaire-based assessment of quality of life.

7. The patient’s response to exercise training should be evaluated using repeat assessments of functional capacity and quality of life. Clinical outcomes and patient experience should also be documented.

8. Early identification and referral of patients who may benefit from pre-operative exercise training is essential to allow sufficient time to intervene. Ideally, pre-operative exercise training should commence as early in the surgical pathway as possible, ensuring a minimum training duration of 4 weeks.

9. To ensure endurance, strength and respiratory muscle function benefits, a combination of aerobic training, resistance training and inspiratory muscle training should ideally be delivered during a pre-operative exercise programme. The frequency, intensity and duration of each exercise component should be tailored to each patient, taking into consideration their initial fitness and health status.

10. The pre-operative exercise programme should be supervised and delivered by individuals with relevant expertise. Self-managed (unsupervised) exercise training is feasible
but patients must be carefully selected. Mechanisms for offering remote support and provision of home exercise equipment should also be considered.

**Why was this clinical guideline developed?**

In the past few years, there have been several systematic reviews on the effects of pre-operative exercise training in patients awaiting elective major surgery [1-5]. These reviews highlight sufficient clinical trial data to support pre-operative exercise training as being safe and efficacious. However, to facilitate the translation of this evidence into clinical practice, clinicians must know sufficient details about the appropriate and effective exercise interventions and their components. Therefore, the aim of this document was to provide a practical, evidence-based guideline on how to deliver pre-operative exercise training to patients awaiting major, non-cardiac surgery. This guideline is aimed primarily at practitioners within the United Kingdom. This includes anaesthetists, surgeons, nurses, physiotherapists, general practitioners, and other healthcare professionals. It is intended to inform those conducting pre-operative exercise programmes and also those who manage surgical patients who may be referred into a prehabilitation scheme.

**Background to pre-operative exercise training**

The prevalence of physical inactivity is high worldwide, particularly in older adults [6,7]. Continuous physical inactivity accelerates the age-associated declines in maximal aerobic capacity and functional fitness [8,9] and increases the risk of developing several chronic health conditions, including cardiovascular disease, obesity, colon and breast cancer, and Type 2 diabetes [10].

The resultant effects of chronic physical inactivity may place individuals at an increased risk of complications when undergoing major or complex surgery. For example, there is developing evidence of an association between low cardiorespiratory fitness and adverse perioperative outcomes across a range of surgical specialties [11]. Although many surgical, anaesthetic, and patient-related factors contribute to outcome, a critical factor appears to be the body’s physiological reserve to cope with the neuroendocrine stress imposed by major surgery [12]. Individuals unable to meet this demand appear to be at highest risk of developing perioperative complications [13], as illustrated in Fig. 1.

<<Figure 1 here>>

Recently published data demonstrate the potential contextual relevance of perioperative fitness to meet this demand, with in-hospital mortality rates of 0.5 to 3.6% for patients undergoing major surgery in the United Kingdom [14,15]. Non-fatal complications occur far more frequently and may affect patients well beyond hospital discharge [16,17]. Reduced quality of life and independence, increased rates of readmission, reduced longer-term survival and an increased health economic burden may all follow. Healthcare professionals working across perioperative medicine should develop strategies to address this problem [18-20].

Improving patients’ fitness before surgery through exercise training seems a logical step in achieving this, and is termed ‘prehabilitation’ [21]. Prehabilitation initiatives aim to create
sufficient physiological reserve to deal with the subsequent surgical stress response, leading to a reduced risk of perioperative complications. This concept is detailed in Fig. 1. The idea of utilising the broader pre-operative encounter to optimise patient health is attractive, with patients potentially more responsive to lifestyle behaviour change at this time (i.e. surgery as a ‘teachable moment’ [22]).

**Referral and assessment of patients for pre-operative exercise training**

A number of recommendations can be made about the referral process for pre-operative exercise training. First, early identification and referral is essential to allow sufficient time to intervene. Ideally, prehabilitation initiatives should commence as early in the surgical pathway as possible, with a minimum of four weeks of exercise training being desirable for meaningful improvements in fitness to be achieved. Second, patients who are being referred for prehabilitation should be given oral and written information about what this will entail, and the potential benefits. Experience from pulmonary rehabilitation indicates that the uptake and effects of prehabilitation may be positively influenced by the initial clinician interaction and what information is provided about the programme [23-25]. Initial discussions with the patient should also seek to identify their goals for prehabilitation, which could then be recorded, and may aid motivation. The type of healthcare professional that undertakes these initial discussions and provides relevant information may differ between settings according to local patient pathways, but referrals should always be made by people who have at least a basic knowledge about what the programme entails and its potential effects. Furthermore, pre-operative exercise training should be presented by the referring clinician as a fundamental component of pre-operative preparation, rather than an optional extra.

Ideally, pre-operative exercise training should be offered to all patients undergoing elective major or complex surgery, with the aim of improving physiological and functional reserve to both reduce the risk of perioperative morbidity and mortality, and facilitate post-operative recovery of functional capacity. However, if resources are limited, priority of referral to pre-operative exercise training should go to patients who are at increased risk of perioperative complications, such as those with low cardiorespiratory fitness. Fig. 2 highlights a potential decision making tool for identifying those patients who may benefit most from a pre-operative exercise programme.

<<Figure 2 here>>

Patients should undergo thorough screening and baseline assessment before starting pre-operative exercise training. As a minimum, patient demographics, surgical indication and comorbidities, and any relevant investigations and treatments, should all be recorded. Any contraindications to exercise should be identified, such as unstable angina, uncontrolled hypertension, significant aortic stenosis, acute illness or fever, and uncontrolled cardiac arrhythmias (see [27] for full list). Risk assessment should be performed using recognised criteria. Objective baseline evaluation of physical fitness (e.g. cardiopulmonary exercise testing, six-minute walk distance), activity levels and health-related quality of life are recommended to inform the exercise prescription and the level of supervision required; however, an initial supervised period is recommended for most patients. Repeat assessments are recommended where possible at the end of the programme, before
surgery, to allow for monitoring of programme effectiveness, as with United Kingdom cardiac rehabilitation services [28].

Evaluation of other potentially harmful lifestyle factors, such as smoking status and alcohol consumption, is recommended as part of the initial evaluation as ‘clustering’ [29] is common. Where concerns are identified, referral to relevant services is recommended due to the cumulative potential negative effects on perioperative outcomes in at-risk individuals [30,31].

Pre-operative exercise training: evidence and recommendations

The recommendations included in this guideline were based on the best available evidence. A systematic search process was undertaken to identify systematic reviews and meta-analyses of randomised controlled trials that compared the effect of pre-operative exercise training with standard care or a ‘control condition’ on cardiorespiratory fitness and post-operative outcomes in adults awaiting elective major non-cardiac surgery. The study search and selection processes are presented in Appendices S1-S3 in the Online Supplementary Information.

The database search yielded 57 records, 42 of which were ineligible on title and abstract screening. Inspection of the reference lists and citations of the remaining 15 records yielded a further 28 potentially-eligible records. Thirty-four of the 43 records were systematic reviews of prehabilitation interventions before major surgery, and a further six were non-systematic literature reviews on this topic. However, 39 of the 43 records that underwent full-text screening were excluded, with reasons described in Appendix S3 in the Online Supplementary Information. Four systematic reviews were eligible for inclusion [2-5]. Four recently published randomised controlled trials that we were aware of were also included [32-35]. These studies had not been included in any of the included reviews, so their inclusion provided a more comprehensive representation of the current evidence base.

General characteristics of the four systematic reviews and four randomised controlled trials are shown in Table 1. All were published in 2016 or 2017. A total of 21 relevant individual randomised controlled trials including 1057 participants were identified. Two randomised controlled trials [36,37] overlapped across two of the systematic reviews [3,4]. A list of the included reviews and trials is presented in Appendix S4 in the Online Supplementary Information. Three systematic reviews included meta-analyses on the effects of pre-operative exercise training [2,4,5]: one Cochrane review had a target population of patients undergoing lung resection surgery for non small-cell lung cancer and co-primary outcomes of post-operative pulmonary complications and post-operative duration of intercostal catheter use [2]; one review focused on patients undergoing major abdominal surgery and had co-primary outcomes of post-operative mortality, durations of stay in hospital and the intensive care unit, and ‘all post-operative complications’ [4]; and one review was of people with cancer undergoing both neoadjuvant cancer treatment and surgery, which did not specify a primary outcome [5]. The remaining review included studies of patients undergoing major abdominal cancer surgery [3]. All reviews used recognised tools to assess methodological risk of bias in their included studies. Of the four additional trials we identified, two included patients awaiting elective abdominal aortic aneurysm repair [34,35], one included patients awaiting lung resection surgery for non-small-cell lung cancer [33], and one included adults aged ≥70 years undergoing major abdominal surgery [32].

<<Table 1 here>>
**The role and structure of pre-operative exercise programmes**

As highlighted, one of the main aims of pre-operative exercise training is to increase physiological reserve to minimise the risk of perioperative complications. However, through the literature appraisal process we identified that the rationale for pre-operative exercise training varied between the 21 trials, forming six categories: to reduce post-operative pulmonary complications by improving pulmonary function (four studies); to reduce post-operative pulmonary complications by improving pulmonary function and cardiorespiratory fitness (five studies); to reduce post-operative pulmonary complications and enhance the post-operative recovery of functional capacity (one study); to reduce post-operative complications and enhance the post-operative recovery of functional capacity (two studies); to reduce post-operative complications by improving cardiorespiratory fitness (seven studies); to improve or maintain cardiopulmonary/cardio-metabolic health during neoadjuvant chemotherapy (two studies).

Clarifying the rationale for prehabilitation is important because this will inform the exercise prescription. This relates to the training principle of specificity, whereby the exercises used should be relevant and appropriate to the desired outcome. With this in mind, it is perhaps unsurprising that all 10 interventions targeting a reduction in post-operative pulmonary complications included respiratory muscle training, either in isolation (four studies), in combination with aerobic exercise training (four studies), or in combination with aerobic and resistance exercise training (two studies). The remaining 11 interventions all included an aerobic exercise component, either in isolation (six studies), in combination with resistance training (four studies), or resistance training and respiratory muscle training (one study). Another example of specificity is that all interventions aimed at enhancing the post-operative recovery of functional capacity included resistance training, muscle strength being an important determinant of functional status.

Detailed descriptions of the interventions used in the 21 trials are provided in Appendix S5 in the Online Supplementary Information. Here, an overview of the three main exercise components (respiratory muscle training, aerobic training and resistance training) is provided. Specific recommendations for pre-exercise training are presented after the effects of pre-operative exercise training on important fitness and health outcomes have been summarised.

Inspiratory muscle training was the main form of respiratory muscle training, being clearly described in eight of the 11 respiratory muscle training components. The frequency of inspiratory muscle training ranged from three sessions per week to twice daily, with sessions typically lasting 15 minutes (range 10 to 30 minutes). The participants were trained to use an inspiratory threshold-loading device with a load typically in the range of 10 to 60% of maximal inspiratory pressure, although one study described an interval-training approach involving 6 cycles of 6 inspirations at 60 to 80% of maximum inspiratory pressure, interspersed by rest intervals of 5 to 60 seconds [38]. In at least three interventions, perceived exertion was used to guide the progression of training, aiming to maintain a moderate/somewhat hard (two studies) or hard (one study) intensity during each session.

The most common aerobic exercise modality was cycle ergometry, present in 10 of the 17 aerobic training components. Treadmill or normal overground walking was included in eight interventions. Other aerobic modalities included recumbent cross-trainer (n=2), rowing ergometry (n=1), and arm ergometry (n=1). Eight aerobic components involved continuous training, five involved interval training, one involved a combination of continuous and interval
training, and two involved circuit-based training. The specific format of aerobic training was unclear in the remaining study. In nine interventions, the intensity of exercise was guided using heart rate responses (n=3), perceived exertion (n=3), or using both approaches (n=3). Aerobic training was most commonly undertaken for 30 to 45 minutes per session (range 10 to 60 minutes) and 3 to 7 times per week (range 1 to 15 sessions).

Of the seven resistance training components, six included a combination of upper- and lower-body exercises, and one included only lower-body exercises. Details on the specific exercises used were poorly reported. Two interventions involved circuit-based training, two involved use of elastic resistance bands, two involved functional exercises (e.g. chair sit-to-stand), and three involved dumbbells or fixed resistance machines. One study reported using two sets of 10 to 12 repetitions for each exercise, whereas another used single-set training at an 8 to 15 repetition maximum. The frequency of resistance training ranged from 2 to 4 sessions per week.

Eleven of the 21 interventions were supervised, mostly in a clinical setting (n=9; e.g. hospital physiotherapy gym or outpatient clinic). Three interventions were unsupervised, and seven involved a mixture of supervised and unsupervised exercise training. The duration of pre-operative exercise training most commonly ranged from 2 to 4 weeks (n=15, 71%), but was 12 to 16 weeks in the two studies of patients undergoing neoadjuvant chemotherapy [29,30].

Cardiorespiratory fitness

The main findings and conclusions from each included review and trial are presented in Table 2. Seven trials reported data on changes in cardiorespiratory fitness following pre-operative exercise training, as measured using cardiopulmonary exercise testing. All seven of these studies reported data on peak oxygen uptake, with five studies demonstrating a statistically significant improvement following pre-operative exercise training. In those five studies, the improvement relative to control was consistently greater than 2.5 ml.kg\(^{-1}\).min\(^{-1}\); a change that is likely to be clinically important [35]. The limited effect on peak oxygen uptake in the two remaining studies may be due to the use of an active comparator in one study [36] and a lower-than-intended intensity of exercise in the other [35,39].

<<Table 2 here>>

Only two trials reported data on anaerobic threshold (expressed in ml.kg\(^{-1}\).min\(^{-1}\)), which is perhaps surprising given the interest that has been placed on this variable as an indicator of fitness for surgery [13]. In the study by Barakat et al. [34], which assessed the effects of circuit-based pre-operative exercise training before elective abdominal aortic aneurysm repair (n=124), anaerobic threshold increased from median (IQR) 12.0 (10.4 to 14.5) ml.kg\(^{-1}\).min\(^{-1}\) at baseline to 13.9 (10.6 to 15.1) ml.kg\(^{-1}\).min\(^{-1}\) at pre-surgery (p=0.012). There was no significant change in the control group (-0.2 ml.kg\(^{-1}\).min\(^{-1}\), p=0.532). These findings were limited by pre- and post-training cardiopulmonary exercise test data only being recorded for 33/62 exercise and 15/62 control participants and the analysis of within-group changes rather than between-group differences. In contrast, the study of Tew et al. [35], which also involved patients awaiting elective abdominal aortic aneurysm repair (n=53), showed no substantial between-group difference in anaerobic threshold following four weeks of pre-operative high-intensity interval training: adjusted mean difference (95% CI) = 0.3 ml.kg\(^{-1}\).min\(^{-1}\)
.min⁻¹ (-0.4 to 1.1). However, there was evidence of inter-individual heterogeneity, with one third of the exercise participants possibly to very likely being positive responders, defined as an improvement of >1.5 ml.kg⁻¹.min⁻¹. The authors suggested that their exercise safety criteria limited the progression of training, which, in turn, probably limited adaptations in cardiorespiratory fitness.

**Health-related quality of life**

Only two pilot trials reported data on health-related quality of life. The data of Tew et al. [35] suggest a small beneficial effect of pre-operative high-intensity interval training on general health status and physical functioning, but not mental health (Table 2). For example, the mean EQ-5D utility index value before surgery was 0.864 in the exercise group and 0.796 in the control group (mean difference [95% CI] = 0.068 [0.002 to 0.135]); this difference appeared to be maintained at 12 weeks post-discharge (0.837 vs. 0.760; mean difference [95% CI] = 0.077 [0.005 to 0.148]). In the study of Hornsby et al. [40], the effects of a 12-week aerobic exercise training programme were assessed in 20 patients receiving neoadjuvant chemotherapy for breast cancer. Quality of life was assessed using the Functional Assessment of Cancer Therapy-Breast and Functional Assessment of Cancer Therapy-General, and there was no significant differences between groups on either measure (p=0.685 and p=0.431, respectively).

**Perioperative clinical outcomes**

Small sample sizes and low event rates prevent conclusions being drawn about the effects of pre-operative exercise training on short-term (e.g. 30-day) perioperative mortality. For example, the two systematic reviews that included post-operative mortality as an outcome both stated that no post-operative deaths occurred in any study [2,4]. Across the four additional trials we included (485 patients in total), there were five 30-day deaths in each study group.

More data are available on perioperative complications, but the results appear inconsistent and potentially dependent on the type of surgical population and complication being studied (Table 2). Across all surgical populations, no study has reported that pre-operative exercise training increases post-operative complications. In people undergoing lung resection for non-small-cell lung cancer, there is evidence that pre-operative exercise training can reduce post-operative pulmonary complications (e.g. pneumonia, severe atelectasis). For example, a meta-analysis of four studies (158 patients) demonstrated a relative risk reduction of 67% (risk ratio [95% CI] = 0.33 [0.17 to 0.61]) [2]; however, the evidence was graded as low quality due to high risk of bias and small sample sizes in the included studies. The meta-analysis result is supported by a recent trial of 164 patients [33], which showed a lower incidence of post-operative pulmonary complications in the group allocated to interval-training-based prehabilitation versus usual care (23% vs 44%; p=0.018). In patients undergoing major intra-abdominal surgery (e.g., bowel resection, radical cystectomy, abdominal aortic aneurysm repair), the impact of pre-operative exercise training on perioperative complications is less clear, with interpretation clouded by lack of standardisation in outcome measures. In the systematic review of Hijazi et al. [3], three trials that included a variety of abdominal surgical populations recorded complications using the Clavien-Dindo classification, with none of them reporting significant between-groups differences [36,37,41]. A recent trial of 144 patients undergoing major abdominal surgery also reported no effect of pre-operative exercise training on the severity of complications assessed using the Clavien-Dindo classification [32]; however, the percentage of patients
with post-operative complications was lower (31% versus 62%; relative risk ratio [95% CI] = 0.5 [0.3 to 0.8]) when complications were defined as any deviation from the normal post-operative course according to the standards of the European Society of Anaesthesiology and European Society of Intensive Care Medicine [42]. Finally, of the two trials that have included patients undergoing elective abdominal aortic aneurysm repair [34,35], one showed a lower incidence of post-operative cardiac, pulmonary, and/or renal complications in the exercise group versus control (22.6% versus 41.9%, relative risk ratio = 0.54, p=0.021) [34], whereas the other showed no substantial difference in mean total Post-Operative Morbidity Survey count up to the point of discharge from hospital (2.3 versus 2.1; difference [95% CI] = 0.2 [-0.3 to 0.7]) [35].

**Hospital length of stay**

The effect of pre-operative exercise training on length of hospital stay also appears to be inconsistent. In the lung cancer literature, a meta-analysis of four studies (158 patients) showed that length of hospital stay was lower following prehabilitation versus control (mean difference [95% CI] = -4.24 days [-5.43 to -3.06]) [2]; however, this was not supported by the trial of Licker et al. [33], which showed a median (IQR) length of stay of 10 (8 to 12) days in the prehabilitation group versus 9 (7 to 13) days in the control group (p=0.223). In a systematic review of pre-operative exercise training before major intra-abdominal surgery [4], a meta-analysis of four studies (n=232) showed no significant difference in length of stay between exercise and control groups (mean difference [95% CI] = -1.62 days [-7.57 to 4.33]), with the quality of evidence rated as ‘very low’. Other trial evidence is mixed, with two studies showing some evidence of reduced length of stay [32,34], and one showing no substantial difference [35].

**Exercise-related adverse events**

Data on exercise-related adverse events were presented in one of the systematic reviews [5] and all four of the additional trials [32-35]. The review of Loughney et al. [5] cited the results of a study exploring the safety and efficacy of aerobic exercise training in people with operable breast cancer receiving neoadjuvant chemotherapy [40]. This study reported that three non-life threatening/non-ECG-related adverse events occurred during baseline exercise testing, which resulted in prematurely stopping the tests due to exercise-induced oxygen desaturation (SpO₂ = 84%), anxiety attack, and dizziness. All symptoms/signs resolved promptly upon cessation of exercise and did not preclude study participation. One aerobic training-related adverse event was observed, consisting of unexplained leg pain that quickly resolved following exercise cessation. Three of the additional trials reported that no adverse events occurred during pre-operative exercise training [32-34]. The remaining trial reported one exercise-related adverse event that resulted in the termination of an exercise session: a single episode of short-lived angina that was relieved through self-administration of glyceryl trinitrate [35].

**Limitations and issues of the current evidence base**

In the current literature regarding pre-operative exercise training in patients undergoing elective major non-cardiac surgery, several issues were identified that we recommend are addressed in future research:

First, there is a limited number of relevant randomised controlled trials, many of which have small sample sizes, and are from a single centre. There is a need for multi-centre
randomised controlled trials with specifically-designed pre-operative exercise training programmes and a carefully selected patient population to strengthen current evidence. Encouragingly, a search of the International Clinical Trials Registry Platform identified more than 30 on-going trials in this area. Second, there is heterogeneity of the included patient populations. Patients scheduled for different surgical procedures have different characteristics in terms of pre-operative physical status and comorbidities, which will likely influence the efficacy of pre-operative exercise training. Group-level analyses in trials may mask inter-individual differences in response. Research is needed to identify which type of pre-operative exercise training works best in different clinical scenarios. Only then will perioperative teams be able to provide evidence-based individualised programmes. Third, there is a lack of standardisation of pre-operative exercise programmes in terms of composition (physical/pulmonary), duration, and frequency. The aforementioned inconsistent effects of pre-operative exercise programmes may be partly due to heterogeneity in intervention design. In particular, there has been variation in the type of exercise used (e.g., high-intensity interval training vs. moderate-intensity continuous training, resistance training vs. aerobic training, inspiratory muscle training vs. whole-body training), the duration of exercise training, its frequency and timing. To some extent, variation in programme design is expected, as the specific goals of training may differ according to the type of surgical procedure and patient characteristics. Regardless, head-to-head trials of different pre-operative exercise interventions would be beneficial to identify optimal exercise prescriptions. Finally, there is also a lack of standardisation of outcome measures. Development of a core outcome set for prehabilitation trials would facilitate comparisons between studies and enhance evidence synthesis through maximum inclusion of studies into meta-analyses.

**Practical guidelines for pre-operative exercise training**

When prescribing any exercise training programme, consideration should be given to the frequency, intensity, time, type, volume and progression principles [43]. Pre-operative exercise training is principally aimed at increasing physiological and functional reserve through performing structured, purposeful exercise training; however, a combination of regular exercise training and general physical activity should be encouraged for longer-term fitness, health and wellbeing. In most cases, it would be appropriate for a pre-operative exercise programme to include a combination of aerobic training, resistance training and inspiratory muscle training to promote positives adaptations in cardiorespiratory fitness, muscular strength and endurance and respiratory muscle function, respectively. The frequency, intensity and duration of each exercise component should be tailored to each patient, taking into consideration their initial fitness and health status. As mentioned, a minimum of four weeks of exercise training is desirable for meaningful improvements in fitness to be achievable.

Sessions should be individualised, supervised by appropriately trained members of staff (at least initially), and include warm-up and cool-down sections before and after the main conditioning phase respectively. If considering the promotion of self-managed (unsupervised) exercise training, the following important factors need careful consideration: mechanisms to offer remote support, provision of home exercise equipment and patient selection.

The setting in which pre-operative exercise training is offered will depend on the available infrastructure and resources. Despite financial constraints within the current National Health Service, a range of potential settings exists. This includes cardiac and pulmonary
rehabilitation facilities, hospital- or community-based physiotherapy clinics, and community wellbeing centres.

Simply prescribing ‘exercise’, in a generic sense, to a patient is insufficient guidance and is unlikely to achieve the desired outcomes. To help clinicians prescribe/deliver evidence-based exercise interventions, we provide practical details for three pre-operative scenarios in Fig. 3 (intra-abdominal surgery), Fig. 4. (thoracic surgery), and Fig. 5 (neoadjuvant chemoradiotherapy and surgery for cancer). Uncertainties in the prehabilitation evidence base prevent presentation of a single intervention for each scenario. Therefore, a typical intervention or a range of practical options from various studies is presented. The information about each intervention is presented using key headings from the TIDieR (Template for Intervention Description and Replication) guide for intervention reporting [44].

<<Figure 3 here>>
<<Figure 4 here>>
<<Figure 5 here>>

**Multi-modal prehabilitation and rehabilitation**

Simultaneously addressing multiple lifestyle behaviours may yield greater rewards than solely focusing on exercise, and given the propensity for unhealthy behaviours (e.g. physical inactivity, smoking and excessive alcohol consumption) to co-occur or cluster in the population [29], a wider approach to prehabilitation appears important. The optimal package of interventions is currently unknown, but a multimodal prehabilitation programme that addresses both behavioural (e.g. exercise, nutrition, smoking) and clinical (e.g. anaemia, frailty) perioperative risk factors may harness the concept of aggregating marginal gains already well established in enhanced recovery initiatives. The ideal scenario may be a blurring of the lines between prehabilitation and enhanced recovery, such that one programme leads into the next, punctuated by surgery, with minimal interruption. This idea is particularly appealing in the case of exercise, where evidence suggests that early post-operative exercise rehabilitation enhances the recovery of functional status [57,58]. There is some evidence that the pre-operative period may represent a more appropriate time than the post-operative period to implement an intervention [59]; however, further research is needed to determine if a combination of prehabilitation plus early rehabilitation is superior to prehabilitation alone.

**Barriers and facilitators of implementation**

Successful implementation of prehabilitation programmes may prove challenging. A range of institutionalised cultural and attitudinal barriers exist that could affect pre-operative initiatives to varying degrees. Patient-related factors include motivation, time and financial worries, and limiting comorbidities. System-related barriers include lack of educational opportunities highlighting the benefits of exercise, insufficient infrastructure, and concerns about the feasibility of delivery and cost effectiveness of potential programmes. Paton et al. [60] reviewed 14 case studies utilising enhanced recovery programmes, identifying inherent differences in programme elements between surgical specialities and difficulty of incorporating certain components into established pathways. Several barriers to
implementation were discussed, the main ones being resistance to change from patients and staff and lack of funding or support from management. Based on evidence drawn from enhanced recovery initiatives [60], the development and implementation of successful and sustainable prehabilitation programmes may rely on several factors: effective leadership including a dedicated project lead to coordinate and sustain multi-disciplinary team working; continuity of the pathway; ongoing educational initiatives for staff, patients and patient representatives; collaborative decision making between primary and secondary care with agreement of objectives and goals to allow focused local planning and action, and the availability of dedicated resources.

References


Figure 1. The prehabilitation concept. Following major surgical intervention all patients experience an acute drop in physiological reserve/functional capacity followed by a recovery and rehabilitation phase (A). A low physiological reserve/functional capacity may increase the risk of perioperative complications and lead to a slower, sometimes incomplete recovery (B). A prehabilitated patient may possess greater physiological reserve/functional capacity at the time of surgery, facilitating a more rapid and complete recovery (C). Crucially, in the event of a complicated recovery, prehabilitated patients may be better placed to retain their functional independence and quality of life in the longer term (D).
Figure 2. Flowchart to assist clinicians in identifying patients who may benefit from pre-operative exercise training. This should be used in conjunction with clinical judgement and locally available options. See [26] for examples of major/complex elective surgery.
Figure 3. Pre-operative exercise training to reduce post-operative complications in patients undergoing major intra-abdominal surgery.
Figure 4. Pre-operative exercise training to reduce post-operative pulmonary complications in patients undergoing lung resection surgery.
Figure 5. Pre-operative exercise training in people with cancer undergoing neoadjuvant chemoradiotherapy and surgery.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design (No. of relevant RCTs/participants)</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome measures</th>
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<tbody>
<tr>
<td>Cavalheri [2]</td>
<td>Cochrane SR and meta-analysis of RCTs (5/167)</td>
<td>Patients undergoing lung resection surgery for NSCLC</td>
<td>PET; ≥7 sessions completed over ≥1 week pre-operatively; sessions could be supervised, unsupervised, or both, and include aerobic, resistance or respiratory muscle training, or a combination.</td>
<td>Post-operative mortality, post-operative complications, LOS, CRF, days intercostal catheter needed after surgery, functional capacity, fatigue, dyspnoea, pulmonary function</td>
</tr>
<tr>
<td>Hijazi [3]</td>
<td>SR of RCTs and non-randomised controlled trials (5/243)</td>
<td>Patients undergoing major abdominal cancer surgery</td>
<td>Prehabilitation programmes, which could include physical exercise, nutrition, and/or psychological support components.</td>
<td>Post-operative complications, CRF, HR-QoL, functional capacity, psychological status</td>
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<tr>
<td>Loughney [5]</td>
<td>SR of RCTs and non-randomised controlled trials with meta-analyses (2/30)</td>
<td>People with cancer undergoing both neoadjuvant cancer treatment and surgery</td>
<td>PET interventions during neoadjuvant cancer treatment</td>
<td>CRF, HR-QoL, adverse events, physical activity, fatigue, biomarkers</td>
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<td>Barberan-Garcia [32]</td>
<td>RCT (1/144)</td>
<td>Adults aged ≥70 years undergoing elective major abdominal surgery</td>
<td>4 weeks of PET comprising supervised cycle-based HIIT and promotion of unsupervised walking and functional exercises</td>
<td>In-hospital mortality, post-operative complications, LOS, HR-QoL, functional capacity, exercise capacity, physical activity, psychological status</td>
</tr>
<tr>
<td>Licker [33]</td>
<td>RCT (1/164)</td>
<td>Patients undergoing lung resection surgery for NSCLC</td>
<td>PET of varying duration (median 26 days); comprising supervised cycle-based HIIT and whole-body resistance training and promotion of unsupervised walking</td>
<td>Post-operative mortality, post-operative complications, CRF, adverse events, functional capacity, physical activity</td>
</tr>
<tr>
<td>Barakat [34]</td>
<td>RCT (1/124)</td>
<td>Adults undergoing elective repair of a large</td>
<td>6 weeks of thrice-weekly PET comprising circuit classes involving</td>
<td>Post-operative mortality, post-operative complications, LOS, CRF, functional capacity, physical activity</td>
</tr>
<tr>
<td>Tew [35]</td>
<td>Randomised feasibility trial (1/53)</td>
<td>Adults undergoing elective repair of a large (5.5 to 7.0 cm) abdominal aortic aneurysm</td>
<td>4 weeks of thrice-weekly PET comprising supervised cycle-based HIIT</td>
<td>Post-operative mortality, post-operative complications, LOS, CRF, HR-QoL, exercise enjoyment, healthcare resource use</td>
</tr>
</tbody>
</table>

CRF, cardiorespiratory fitness; HIIT, high-intensity interval training; HR-QoL, health-related quality of life; LOS, length of hospital stay; NSCLC, non-small-cell lung cancer; PET, pre-operative exercise training; RCT, randomised controlled trial; SIRS, systemic inflammatory response syndrome; SR, systematic review
Table 2. Main results and conclusions from included reviews and trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Post-operative mortality, complications and length of stay</th>
<th>Cardiorespiratory fitness and health-related quality of life</th>
<th>Main conclusions and limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavalheri [2]</td>
<td>One study reported no in-hospital deaths in either group [51]. Pooled data from 4 studies (n=158) showed PET reduced post-operative pulmonary complications by 67% (RR [95% CI] 0.33 [0.17 to 0.61]). Post-operative LOS was also lower in the exercise group (MD [95% CI] -4.24 days [-5.43 to -3.06]; 4 studies).</td>
<td>One study [61] reported an improvement in $\dot{V}O_2$peak from baseline to post-intervention in the PET group (14.9 ± 2.3 ml.kg$^{-1}$.min$^{-1}$ to 17.8 ± 2.1 ml.kg$^{-1}$.min$^{-1}$; p&lt;0.01), with no change in the control group (p&gt;0.05).</td>
<td>“[PET] may reduce the risk of developing a postoperative pulmonary complication, … length of hospital stay, and improve both exercise capacity and [pulmonary function] in people undergoing lung resection for NSCLC. The findings … should be interpreted with caution due to disparities between the studies, risk of bias, and small sample sizes.”</td>
</tr>
<tr>
<td>Hijazi [3]</td>
<td>Severity of post-operative complications was graded in 3 studies using the Clavien-Dindo classification. In one study [36], patients whose functional capacity deteriorated during PET were at higher risk of complications. There was no significant difference in complications between groups in the other studies [37,41].</td>
<td>In one study [62], PET increased $\dot{V}O_2$peak by 2.51 ml.kg$^{-1}$.min$^{-1}$ (p=0.002).</td>
<td>“delivery of such programs is feasible” “findings and recommendations are limited by the heterogeneity in the literature” Limitation: One of the included studies used an intervention that also included post-operative exercise training [41].</td>
</tr>
<tr>
<td>Moran [4]</td>
<td>No deaths were reported in any study. Pooled data from 9 studies showed a 41% reduction post-operative complications in PET vs. control (OR [95% CI] 0.59 [0.38 to 0.91]). There were no significant differences in LOS between exercise and control groups (MD [95% CI] -1.62 days [-7.57 to 4.33]; 4 studies).</td>
<td>In one study [36], $\dot{V}O_2$peak increased from 1,395 ± 76 to 1,529 ± 88 ml.min$^{-1}$ in a biking and strengthening group (p=0.003) and from 1,400 ± 71 to 1,511 ± 84 ml.min$^{-1}$ in a walking and breathing group (p=0.007).</td>
<td>“[PET] appears to be beneficial in decreasing the incidence of postoperative complications; however, more high-quality studies are needed to validate its use in the preoperative setting.” Limitation: The methodological quality of studies was very low, and 2 of the included studies did not isolate the effects of PET ([59] and [63]).</td>
</tr>
<tr>
<td>Loughney [5]</td>
<td>Not reported</td>
<td>In one study [40], 12 weeks of PET increased $\dot{V}O_2$peak by 2.6 ± 3.5 ml.kg$^{-1}$.min$^{-1}$ vs. a 1.5 ± 2.2 ml.kg$^{-1}$.min$^{-1}$ decrease in the control group.</td>
<td>“… is safe and feasible but that there are insufficient controlled trials in this area to draw reliable conclusions about the efficacy of such an intervention…”</td>
</tr>
<tr>
<td>Study</td>
<td>Description</td>
<td>HR-QoL Findings</td>
<td>PET Findings</td>
</tr>
<tr>
<td>-----------------------------</td>
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</tr>
<tr>
<td>Barberan-Garcia [32]</td>
<td>There was one in-hospital death in each group. The PET group showed a lower rate of post-operative complications: 31% vs. 62% (RR [95% CI] 0.5 [0.3 to 0.8], p=0.001). There was no effect on the severity of complications using the Clavien-Dindo classification. Mean (SD) LOS was 8 (8) vs. 13 (20) days (p=0.078) for intervention vs. control. Mean (SD) length of ICU stay was 1 (2) days for intervention versus 4 (1) days for control (p=0.078).</td>
<td>FACT-B (p=0.685) or FACT-G (p=0.431).</td>
<td>Limitation: Only 2 pilot RCTs</td>
</tr>
<tr>
<td>Licker [33]</td>
<td>There were two 30-day deaths in each group. The composite post-operative mortality-morbidity endpoint occurred less frequently in the PET group: 27/74 (35.5%) vs. 39/77 (50.6%) (RR [95% CI] 0.70 [0.48 to 1.02]; p=0.08). There were fewer post-operative pulmonary complications with PET (23% vs. 44%; p=0.018), but LOS did not differ between groups.</td>
<td>VO₂peak data were not reported. There was no meaningful change in the SF-36 physical or mental component summary scores from baseline to pre-surgery in either group (p≥0.146).</td>
<td>“[PET] enhanced post-operative clinical outcomes in high-risk candidates for elective major abdominal surgery...” Limitations: High attrition (24%), evidence of primary outcome switching, and VO₂peak data not reported.</td>
</tr>
<tr>
<td>Barakat [34]</td>
<td>There were two 30-day deaths in each group. The PET group showed a lower rate of post-operative complications (cardiac, pulmonary or renal) (22.6% vs. 41.9%; p=0.021). LOS was shorter with PET (median [IQR] 7 [5 to 9] vs. 8 [6 to 12.3] days; p=0.025).</td>
<td>In the PET group, median (IQR) VO₂peak increased from 18.4 (15.0 to 20.9) to 20.0 (16.9 to 21.3) ml.kg⁻¹.min⁻¹ (p=0.004). Median (IQR) AT increased from 12.0 (10.4 to 14.5) to 13.9 (10.6 to 15.1) ml.kg⁻¹.min⁻¹ (p=0.012). There were no significant changes in the control group (p≥0.532).</td>
<td>“[PET] was safe and effective in reducing postoperative complications and hospital stay.” Limitations: Incomplete description of the intervention and treatment fidelity; fitness data only recorded for 33 PET and 15 control participants.</td>
</tr>
</tbody>
</table>
Tew [35]  There were no in-hospital or 30-day deaths in either group. One PET-group participant died 12 weeks after hospital discharge. Mean total POMS count up to hospital discharge was 2.3 with PET and 2.1 in control (MD [95%CI] 0.2 [-0.3 to 0.7]). There was no substantial group × post-operative day interaction. Median (IQR) LOS was 7 (4.5 to 8.5) vs. 6 (4 to 8) days for PET and control groups, respectively.

For PET vs. control at pre-surgery:
AT = 11.7 vs. 11.4 ml.kg⁻¹.min⁻¹ (MD [95% CI] 0.3 ml.kg⁻¹.min⁻¹ [-0.4 to 1.1])
𝑉̇O₂peak = 16.8 vs. 16.3 ml.kg⁻¹.min⁻¹ (MD [95% CI] 0.5 ml.kg⁻¹.min⁻¹ [-0.6 to 1.7])
EQ-5D utility score = 0.864 vs. 0.796 (MD [95% CI] 0.068 [0.002 to 0.135])

For PET vs. control at 12 weeks post-discharge:
EQ-5D utility score = 0.837 vs. 0.760 (MD [95% CI] 0.077 [0.005 to 0.148])
SF-36 physical function = 49.4 vs. 46.5 (MD [95% CI] 2.9 [0.4 to 5.4]).

“the findings support the feasibility and acceptability of … pre-operative HIIT… A definitive trial is warranted.”

Limitations: Designed primarily to test feasibility rather than clinical and cost effectiveness.

AAA, abdominal aortic aneurysm; AT, anaerobic threshold; CI, confidence interval; CRF, cardiorespiratory fitness; FACT-B, Functional Assessment of Cancer Therapy-Breast; FACT-G, Functional Assessment of Cancer Therapy-General; HIIT, high-intensity interval training; HR-QoL, health-related quality of life; ICU, intensive care unit; IQR, inter-quartile range; LOS, length of hospital stay; MD, mean difference; NSCLC, non-small-cell-lung-cancer; OR, odds ratio; PET, pre-operative exercise training; POMS, Post-Operative Morbidity Survey PR, pulmonary rehabilitation; RCT, randomised controlled trial; RR, relative risk; 𝑉̇O₂peak, peak oxygen uptake.
Supporting Information (online only)

Appendix S1. Literature search and study selection processes

The PubMed Clinical Queries database was searched in July 2017 for systematic reviews using the following search: “prehabilitation” OR “pre* exercise”. Relevant reviews were also sourced by reference screening and citation tracking of included reviews. Our aim was to identify systematic reviews and meta-analyses of randomised controlled trials that examined the effects of pre-operative exercise training versus standard care or control condition on cardiorespiratory fitness and post-operative outcomes in adults awaiting elective major non-cardiac surgery. All studies with a sole focus on musculoskeletal prehabilitation, and no element of cardiorespiratory conditioning (e.g. orthopaedics) were excluded. Furthermore, we excluded studies of programmes that were multi-modal, included a post-operative training phase, or were focussed on pelvic floor exercises. When the same trials were included in more than one review, we only included either the most comprehensive or the most recently published review. The study selection process is summarised in Appendices 2 and 3.
**Appendix S2. Study selection process**

- **Records identified through database searching (n=57)**
  - Excluded after title and abstract screening (n=42)

- **Full-texts retrieved for detailed screening (n=15)**
  - Papers identified from reference lists and citation tracking (n=28)

- **Articles for full-text screening (n=43)**
  - Systematic reviews included (n=4)
  - Additional trials included (n=4)
  - Records excluded (n=39)
# Appendix S3: Excluded reviews

<table>
<thead>
<tr>
<th>Title of review</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kendall, F., Oliveira, J., Peleteiro, B., Pinho, P. and Bastos, P.T., 2017. Inspiratory muscle training is effective to reduce postoperative pulmonary complications and length of hospital stay: a systematic review and meta-analysis. Disability and rehabilitation, pp.1-22.</td>
<td>Relevant included trials represented in a more recent/comprehensive systematic review</td>
</tr>
<tr>
<td>Looijaard, S.M., Slet-Valentijn, M.S., Otten, R.H. and Maier, A.B., 2017. Physical and Nutritional Prehabilitation in Older Patients With Colorectal Carcinoma: A Systematic Review. Journal of Geriatric Physical Therapy.</td>
<td>Only included one relevant trial, which had been represented in one of the included reviews</td>
</tr>
<tr>
<td>Authors</td>
<td>Title</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>Cabillan, C.J., Hines, S. and Munday, J.,</td>
<td>The effectiveness of prehabilitation or preoperative exercise for surgical patients: a systematic review. JBI database of systematic reviews and implementation reports, 13(1), pp.146-187.</td>
</tr>
<tr>
<td>Halloway, S., Buchholz, S.W., Wilbur, J. and Schoeny, M.E.,</td>
<td>Prehabilitation interventions for older adults: an integrative review. Western journal of nursing research, 37(1), pp.103-123.</td>
</tr>
<tr>
<td>Katsura, M., Kuriyama, A., Takeshima, T., Fukuhara, S. and Furukawa, T.A.,</td>
<td>Preoperative inspiratory muscle training for postoperative pulmonary complications in adults undergoing cardiac and major abdominal surgery. The Cochrane Library.</td>
</tr>
<tr>
<td>Pouwels, S., Willigendael, E.M., van Sambeek, M.R.H.M., Nienhuijs, S.W., Cuypers, P.W.M. and Teijink, J.A.W.,</td>
<td>Beneficial effects of pre-operative exercise therapy in patients with an abdominal aortic aneurysm: a systematic review. European Journal of Vascular and Endovascular Surgery, 49(1), pp.66-76.</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Year, Month</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
</tr>
<tr>
<td>Olsén, M.F. and Anzén, H.</td>
<td>2012</td>
</tr>
<tr>
<td>Nagarajan, K., Bennett, A., Agostini, P. and Naidu, B.</td>
<td>2011</td>
</tr>
</tbody>
</table>
Appendix S4. Randomised controlled trials and systematic reviews used in the evidence section of this statement


Relevant RCTs included in this review:


Relevant RCTs included in this review:


Relevant RCTs included in this review:


Relevant RCTs included in this review:


Additional individual trials


### Appendix S5. Intervention details from included trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Materials/provider/setting</th>
<th>Delivery/dosage/tailoring</th>
<th>Adherence</th>
</tr>
</thead>
</table>
| van Adrichem 2014 (high-intensity IMT group) | **Materials**: Respifit S® IMT devices  
**Provider**: physiotherapist  
**Setting**: University Medical Center Groningen | Prehabilitation involved a minimum training period of 3 weeks that ended the day before surgery. In case of receiving neoadjuvant chemo-radiotherapy, training started 1 to 2 weeks after finishing treatment (depending on the side effects experienced). Patients performed three supervised training sessions per week, each consisting of six cycles of six inspiratory manoeuvres on an inspiratory threshold-loading device (Respifit S®). Resting time between cycles was progressively reduced from 60 to 45, 30, 15, and 5 seconds. Maximum inspiratory pressure (MIP) was measured weekly to adjust intensity adequately. Initial intensity was 60% of MIP and increased to 80% during the first week. In consecutive sessions, training intensity was 80% of MIP and increased by 5% if perceived exertion decreased below hard. Patients in both study groups also received the usual post-operative physical therapy comprising breathing exercises, coughing techniques, and early mobilisation. | The median number of weeks trained was 3.7 (2.9 to 4.4). Average compliance was 98.0% (range 84.6 to 100%). |
| Barbalho-Moulim 2011 | **Materials**: Threshold IMT® devices  
**Provider**: physiotherapist (two sessions per week) and unsupervised (four sessions per week)  
**Setting**: unclear | Training was performed 2 to 4 weeks before surgery using the Threshold IMT® device. The programme consisted of one daily session that lasted 15 minutes, six times per week (supervised by a physiotherapist on two occasions, unsupervised on the other four occasions). The initial load was calculated at 30% MIP, measured in the baseline evaluation and re-calculated after a new measure of this variable at each visit to the physiotherapist. | Not reported |
| Kulkarni 2010 (specific IMT group) | **Materials**: Powerbreathe® IMT device  
**Provider**: unsupervised  
**Setting**: participant’s home | Patients were instructed in the IMT technique by the researcher and were asked to train at home for 15 minutes twice daily for a minimum of 2 weeks. They undertook self-assessment of training completed and ease of training method (1 to 5, 1 being very easy and 5 being very difficult). Patients trained using a Powerbreathe® IMT device. The initial resistance was set at 20 to 30% of baseline MIP depending on ease of use in the first session. The load varied from 1 to 9 and was increased incrementally by half a level every day for the first week. For the remaining duration, patients trained at a level achieved at the end of the first week. | Patients trained for a median of 14 days (range 8 to 28 days) with a median difficulty of grade 3 (range 1 to 4). |
<p>| Dronkers 2008 | <strong>Materials</strong>: Threshold IMT® devices | The training programme, which was designed to increase the strength and endurance of the inspiratory muscles, involved six sessions of IMT per week for at least two weeks. Each session consisted of 15 minutes of IMT; one | Not reported |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Provider</th>
<th>Setting</th>
<th>Materials</th>
<th>Provider</th>
<th>Setting</th>
<th>Rationale for exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai 2017</td>
<td>“experienced physical therapist” (one session per week) and unsupervised (five sessions per week)</td>
<td>partly home-based</td>
<td>NuStep recumbent cross trainer, Voldyne 5000 respiratory training devices</td>
<td>physiotherapist</td>
<td>Hospital ward and rehabilitation centre</td>
<td>to reduce post-operative pulmonary complications by improving pulmonary function and cardiorespiratory fitness</td>
</tr>
<tr>
<td>Morano 2013</td>
<td>Threshold IMT® device</td>
<td>“teaching hospital”</td>
<td>Treadmill, Threshold IMT® device</td>
<td>not reported</td>
<td>“teaching hospital”</td>
<td>All patients completed 5 sessions per week for 4 weeks.</td>
</tr>
<tr>
<td>Study</td>
<td>Materials</td>
<td>Provider</td>
<td>Setting</td>
<td>Description</td>
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</tr>
<tr>
<td>Stefanelli 2013</td>
<td>Bench, mattress pad, wall bars, rowing ergometer, treadmill, cycle ergometer</td>
<td>Not reported</td>
<td>“outpatient”</td>
<td>Five sessions of respiratory exercise training and high-intensity upper- and lower-limb endurance exercise training per week for three weeks. The respiratory exercises were performed on a bench, mattress pad and wall bars. The endurance exercise training was performed on a rowing ergometer, treadmill, and cycle ergometer. The exercise workload for each patient was set according to the results of a cardiopulmonary exercise test, starting with 70% of the maximum level achieved, and increasing by 10 W when the patient was able to tolerate the set load for 30 minutes.</td>
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<tr>
<td>Benzo 2011 (second study)</td>
<td>Treadmill, NuStep recumbent cross training, arm ergometer, TheraBand, Threshold IMT® or P-Flex valve devices</td>
<td>unclear but weekend sessions were unsupervised</td>
<td>“Mayo Clinic”</td>
<td>One week of prehabilitation, involving two face-to-face sessions per day for five consecutive days and self-managed weekend exercise. The face-to-face sessions included: (1) up to 20 minutes of endurance training on a treadmill, NuStep recumbent cross trainer or arm ergometer; (2) strengthening exercises with Thera-band, alternating upper- and lower-body every other day. During this programme, patients were asked to perform two sets of 10 to 12 repetitions starting with the lowest Thera-band resistance. If the patient perception was ‘too easy’ or ‘requires no effort’, resistance was increased. (3) IMT was also conducted for 10 to 20 minutes daily, with patients asked to breathe through the training device at a ‘somewhat hard’ level of exertion. (4) The practice of slow breathing (prolonging expiratory time and thereby decreasing respiratory rate to less than 10 breaths/min) was also routinely included. Patients were instructed to ‘just watching their breath with pursed lips to prolong the expiratory phase’ for at least 10 minutes per session. The weekend exercise involved self-managed daily walking, IMT routine upper-limb resistance exercise. All 10 patients randomised to the intervention successfully completed 10 face-to-face sessions of treatment in one week.</td>
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</tr>
<tr>
<td>Pehlivan 2011</td>
<td>Incentive spirometer, treadmill, heart rate monitor, pulse oximeter</td>
<td>physical therapist from the surgery department</td>
<td>not reported</td>
<td>One week of twice-daily intensive physical therapy (chest physiotherapy and walking exercise) before the planned surgery. Chest physiotherapy consisted of diaphragmatic, pursed-lip, segmental breathing exercise, usage of incentive spirometry, coughing exercise. The walking exercise was done by the patient on a treadmill three times a day, according to the patient’s tolerance to exercise speed and time. A warm-up and cool-down was included, and heart rate, perceived exertion and oxygen saturation was measured throughout. The target heart rate was calculated as 0.65 – 0.8 × [220-age (year)]. Patients were also encouraged to walk around the surgical centre throughout the day. Session completion rate not reported. The duration of walking exercise was 18 ± 7 minutes during the first session compared with 40 ± 16 minutes in the last session. The maximum treadmill speed increased from 4.03 ± 0.97 km/h in the first session to 4.96 ± 1.15 km/h in the last session.</td>
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<tr>
<td>Soares 2013</td>
<td>Gym space, Threshold IMT® devices</td>
<td></td>
<td></td>
<td>Participants received pre-operative physical therapy during the two to three weeks preceding their surgical procedure. The protocol consisted of two supervised 50-minute physical therapy sessions per week, which consisted of Data not reported on adherence to the supervised sessions; however, authors state that all participants</td>
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<tr>
<td>Provider</td>
<td>Setting</td>
<td>Materials</td>
<td>Provider</td>
<td>Setting</td>
<td>Materials</td>
<td>Rationale for exercise</td>
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<tr>
<td>physical therapist (two sessions per week) and unsupervised (four sessions per week)</td>
<td>unclear, but partly home-based</td>
<td>stretching exercises, trunk rotation, deep breathing, respiratory muscle training, upper and lower extremity exercises, walking, and relaxation. Participants also received guidance and training on coughing and huffing. For respiratory muscle training, patients were trained to use an inspiratory threshold-loading device (Threshold IMT®), for 15 minutes daily. The initial load was set at 20% of MIP. This was increased by 2 cmH2O per week in the pre-operative period. Participants also completed 10 minutes of walking on flat ground at a perceived exertion of not exceeding “hard”. Additional respiratory muscle training and walking was carried out at home, four times a week, on days not coinciding with supervised physical therapy sessions.</td>
<td>reported full adherence with the home-based respiratory muscle training and walking.</td>
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<tr>
<td>Carli 2010 (cycling/strengthening group)</td>
<td>stationary cycle, heart rate monitor, “weights”</td>
<td>Participants were instructed to perform unsupervised cycling exercise initially at 50% of their maximal heart rate; this was increased by 10% each week, if tolerable. Weight training was also to be carried out three times a week. Patients were instructed to do push-ups, sit-ups and standing lunges until volitional fatigue, increasing this number to reach 12 repetitions. The weight chosen for strengthening of biceps, deltoids and quadriceps was based on what the person could lift to reach volitional fatigue with eight repetitions. Cycling was to start at 20 minutes per day, increasing to 30 minutes daily; weight-training exercises took 10 to 15 minutes per day. A fully adherent participant would do about 20 to 45 minutes per day for approximately 3.5 h per week, or 14 h over a 4-week period. A stationary cycle and weights were given to each participant for their use during the prehabilitation period, and afterwards if they desired. Participants were visited once at home to demonstrate the programme and at least once to verify the exercise programme; they were also telephoned weekly until surgery.</td>
<td>The mean increase in pre-surgery exercise/physical activity was 4.1 h (about 1 h per week). Only 16% of participants were fully-adherent (14 h of exercise in total; ~3.5 h per week), and a further 20% did 10 h or more (equivalent to 30 minutes daily for 4 weeks).</td>
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<tr>
<td>Dronkers 2010</td>
<td>free weights or resistance exercise machines, IMT devices, aerobic exercise machines, heart rate monitors</td>
<td>Participants were invited to attend two, 60-minute sessions per week for two to four weeks. Each supervised session involved a warm-up, resistance training of the lower-limb extensors (one set, 8 to 15 repetition maximum), IMT against a variable resistance (10 to 60% of MIP) for about 15 minutes (240 breathing cycles), aerobic training (55 to 75% of maximal heart rate or ‘light’ to ‘somewhat-hard’ perceived exertion) for 20 to 30 minutes, training “functional activities” according to the patients’ capabilities and interest, and a cool-down. Participants were also encouraged to perform a ‘light’-to-‘somewhat-hard’ self-managed 30-minute walk every day, as well as 15 minutes of daily IMT at ~20% MIP (gradually increasing the resistance to ensure an intensity of at least</td>
<td>The mean number of training sessions was 5.1 ± 1.9. The attendance at training sessions was 97%.</td>
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</tbody>
</table>
**Setting:** Hospital outpatient department of physical therapy

somewhat hard). Both groups also received instruction in diaphragmatic breathing, deep inspirations with the aid of incentive spirometry and coughing and forced expiration techniques.

<table>
<thead>
<tr>
<th>Rationale for exercise = to reduce post-operative complications by improving cardiorespiratory fitness</th>
</tr>
</thead>
</table>

Barberan-Garcia 2017

**Materials:** cycle ergometer, pulse oximeter, pedometers, elastic resistance bands

**Provider:** “specialised physiotherapist” (one to three sessions per week) and unsupervised

**Setting:** “mostly performed in the community setting”

**Supervised component:** one to three cycle-based exercise sessions per week for at least four weeks. Each session included five minutes of warm-up cycling at 30% of the peak power output, 37 minutes of interval training, and five minutes of cool-down pedalling at 20% of peak power output. The interval training combined two minutes of high-intensity pedalling and three minutes of active rest. Work-rate progress during the prehabilitation period was tailored on an individual basis, according to subjects’ symptoms, to maximise the training effect. During the first two weeks, high-intensity pedalling interval was at least 70% of peak power output and the active rest interval was at least 40% of peak power output. Thereafter, work-rate was increased by approximately 5% every week up to a maximum of 85% of peak power output during the last week for the high-intensity period and 50% of peak power output for the active rest. The cycling rate during the sessions was maintained at 60 to 70 revolutions per minute.

**Unsupervised component:** Promotion of increased daily steps measured by a pedometer and/or “optimisation of walking intensity”. “International recommendations on step-based physical activity were used as a theoretical frame to set up the objectives.” Patients with severely-reduced aerobic capacity and/or physical activity were empowered on home-based functional exercises (e.g. sit-to-stand exercise, stairs climbing, elastic bands, indoor walking, among others) to decrease sedentary behaviour at home.

Tew 2017

**Materials:** cycle ergometer, heart rate monitor, stethoscope and sphygmomanometer, CPET equipment to determine baseline power output at anaerobic threshold and \( \dot{V}O_2 \text{peak} \).

**Provider:** cardiac physiotherapist, research nurse

Three, 45-minute sessions per week for four weeks preceding the intended operation date. Weekly maintenance sessions were undertaken if surgery was delayed.

**Cycle-based high-intensity interval training:** Each of the first three sessions comprised a 10-minute warm-up of unloaded cycling, 8 × 2-minute intervals of high-intensity cycling interspersed with 2-minute rest periods of unloaded cycling, and then a 5-minute cool-down of unloaded cycling. In all subsequent sessions, participants had the choice of performing 8 × 2-minute or 4 × 4-minute “work” intervals for the main body of the workout. In the first exercise session, the 2-minute work intervals were performed at the power output corresponding to anaerobic threshold on a baseline cardiopulmonary exercise test. The power

The mean duration of the prehabilitation programme was 6 ± 2 weeks and during this period patients attended 12 ± 5 supervised exercise training sessions.

In total, 324 ‘main-phase’ and 40 maintenance exercise sessions were scheduled, of which 240 (74%) and 36 (90%) were completed, respectively (overall attendance rate = 76%). Mean perceived exertion was lower than intended (moderate-to-hard instead of hard). Twenty of the 27 exercise participants had at least one episode of cycling power output
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<th><strong>Setting:</strong> Hospital physiotherapy gym</th>
<th>Output in all subsequent sessions was guided by participants’ ratings of perceived exertion; the aim being for all work intervals to be undertaken at a “hard” to “very hard” level of exertion. However, for safety reasons, the power output of the work intervals was reduced if systolic blood pressure exceeded 180 mmHg or if heart rate exceeded 95% of the maximum observed on baseline CPET.</th>
<th>Reduction owing to safety criteria being triggered (such as systolic BP over 180 mmHg). Of all work intervals, there were 36 instances of power output reduction among the 17 adherent participants, and 40 instances among the ten non-adherent participants (rates of 3 and 10 per cent respectively).</th>
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<td><strong>Licker 2017</strong> <strong>Materials:</strong> cycle ergometer, resistance exercise machines <strong>Provider:</strong> physiotherapists (two to three sessions per week) and unsupervised (four sessions per week) <strong>Setting:</strong> Hospital outpatient clinic</td>
<td>Two-to-three sessions per week; number of weeks not standardised (the time delay from the date of enrolment to surgery was a median of 26 days [IQR 21 to 33] in the prehabilitation group). Cycle-based high-intensity interval training: After a 5-minute warm-up period at 50% of peak power output the patients completed two 10-minute long series of 15-second sprint intervals (at 80 to 100% of peak power output) interspersed by 15-second pauses and a 4-minute rest between the two series. The patients then cooled down with a 5-minute active recovery period at 30% peak power output. The work rate was adjusted by the physiotherapist on each session to target near maximal heart rates towards the end of each series of sprints based on the individual’s exercise response. Additional exercises were proposed on an individual basis, such as leg press, leg extension, back extension, seat row, biceps curls or chest-and-shoulder press. Patients in both groups were also encouraged to complete at least four 30-minute walks per week.</td>
<td>Adherence to the prescribed training sessions was 87±18% (median 8 sessions, IQR 7 to 10). The daily step count tended to be higher in the prehabilitation group (7,243 ± 3,934 steps versus 6,315 ± 3,690 steps in the usual care group, p=0.082).</td>
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<td><strong>Barakat 2016</strong> <strong>Materials:</strong> cycle ergometer, assorted-weight dumbbells, exercise steps, treadmill <strong>Provider:</strong> unclear <strong>Setting:</strong> Hospital physiotherapy gym</td>
<td>Three, 1-hour sessions per week for six weeks preceding the intended operation date. Each exercise class consisted of the following: 5-minute warm-up and stretching, cycle ergometer against moderate resistance for two minutes, heel-rise repetitions for two minutes, knee extensions against resistance for two minutes, dumbbell arm-curl repetitions for two minutes, step-up lunges for two minutes, bodyweight squats for two minutes, and five minutes for cool down and stretching. Between each of the exercise stations, patients either walked around the gym or on a treadmill, or rested for two minutes before moving on to the next exercise.</td>
<td>Attended 0 classes: n=11 Attended 6-12 classes: n=19 Attended 13-18 classes: n=32 (of which 18 attended all 18 classes)</td>
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<td><strong>Dunne 2014</strong> <strong>Materials:</strong> cycle ergometer, CPET equipment to determine VO2peak <strong>Provider:</strong> “clinicians”</td>
<td>Prehabilitation consisted of 12 cycle-based interval exercise sessions over a 4-week period. Two recovery exercise sessions were included at the end of the first and fourth weeks (i.e. sessions 3 and 12). The interval sessions included a warm-up and cool-down, and 30 minutes of interval training alternating</td>
<td>18 of 19 exercise-group participants completed 100% of the exercise sessions, with one patient missing two sessions whilst having</td>
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<td>Setting: tertiary hepatobiliary centre</td>
<td>between exercise of moderate (&lt;60% of (V\bar{O}_2)peak) and vigorous (&gt;90% (V\bar{O}_2)peak) intensity. The exercise programme was individualised to candidates following a standardised equation based on the work rate at their anaerobic threshold on baseline CPET.</td>
<td>emergency colonic stenting for an obstructing primary tumour.</td>
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<td><strong>Banerjee 2013</strong> Materials: cycle ergometer, heart rate monitor Provider: several individuals were thanked in the thesis for supporting the exercise sessions; however, their occupation and training was not reported Setting: exercise physiology laboratory at the University of East Anglia</td>
<td>Prehabilitation consisted of twice-weekly cycle-based interval exercise training over a 4-week period. A typical exercise session lasted for an hour, including 5- to 10-minute warm-up and cool-down periods of low-resistance cycling. The main part of each session involved 6 x 5-minute intervals at a target perceived exertion of 13 to 15 (‘somewhat hard’ to ‘hard’) on the Borg 6-20 scale, with 2.5-minute interpolated rest periods. Participants were instructed to maintain a steady pedalling cadence of 50 to 60 rev/min on the exercise bike during the work intervals and the exercise programme was progressed by gradually adding more load to the flywheel to maintain the target perceived exertion. Heart rate and perceived exertion were recorded in the final minute of each interval.</td>
<td>The median number of sessions attended was 8, which was the prescribed regimen as per the protocol. In four patients surgery was delayed by longer than 4 weeks, and they attended two more sessions than planned. Overall, 6 patients complete 1-4 sessions, 8 patients completed 5-7 sessions, and 16 patients completed 8 or more sessions.</td>
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<td><strong>Kim 2009</strong> Materials: cycle ergometer, heart rate monitor Provider: unsupervised Setting: participant’s home</td>
<td>Participants were given a cycle ergometer for home-based exercise training and encouraged to use it daily for four weeks pre-operatively. Exercise duration progressed from 20 to 30 minutes. The intensity of exercise progressed from 40% heart rate reserve (or ‘light’ perceived exertion) to 65% heart rate reserve (or ‘hard’ perceived exertion). Participants were given a training diary and asked to report whether they exercised or not for each day, and if they did exercise, what the exercise duration and average heart rate was. A physical therapist visited the participants at home on several occasions during the 4-week home-based exercise programme to make sure they followed the programme as prescribed and make sure they were properly recording their exercise training in their training diaries.</td>
<td>The prehabilitation group underwent 3.8 ± 1.2 weeks (27 ± 9 sessions) of pre-operative exercise training. The compliance was 74 ± 16%.</td>
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<td><strong>Hornsby 2014</strong> Materials: cycle ergometer, CPET equipment Provider: unclear Setting: unclear</td>
<td>Three, one-on-one supervised cycle ergometry sessions per week on non-consecutive days for 12 weeks. In week one, exercise intensity was initially set at 60% of baseline peak power output for 15 to 20 minutes duration. Duration and/or intensity were then subsequently increased throughout weeks two to four, up to 30 minutes at 65% peak power. In weeks five and six, exercise intensity varied between 60 to 65% of peak power for 30 to 45 minutes duration for two sessions; in the remaining session, participants cycled for 20 to 25 minutes at a power output equivalent to ventilatory threshold. From the seventh week onwards, participants performed two sessions at 60 to 70% peak power</td>
<td>Overall attendance to planned exercise sessions was 82% (296 attended/ 360 prescribed; range 0 to 100%). 66% of sessions were completed as planned, i.e. 102 sessions (34%) required dose modification. Specifically, 23% (68/296) of sessions required a reduction in exercise duration</td>
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with one threshold workout for 20 to 30 minutes. Finally, in weeks 10 to 12, participants performed two sessions at 60 to 70% peak power with one interval session at 100% peak power. Interval workouts consisted of 30 seconds at peak power followed by 60 seconds of active recovery for 10 to 15 intervals. and/or intensity, whereas 11% (34/296) required an increase in exercise duration and/or intensity. Major reasons for dose reductions were nausea, tiredness/fatigue, and not feeling well; major reasons for dose escalation were per exercise trainer adjustment or patient request.

| Rao 2012 | **Materials:** exercise balls, resistance bands, dumbbells up to 5 pounds  
*Provider:* “experienced personal trainer”  
*Setting:* the setting of the group-based sessions was unclear; there was an option for home-based training | The exercise regimen chosen involved a bootcamp programme that included both aerobic and resistance exercises. The bootcamp was started within one week of the first chemotherapy cycle, and a total of 48 sessions were prescribed. During each session patients engaged in intervals of activities such as jumping jacks, running in place, arm and leg work with exercise balls, bands, and weights up to 5 pounds. To optimise compliance, patients were allowed to choose whether they completed a home-based regimen where a personal trainer came to the patient’s house for one hour three times a week, or to attend group-based sessions three times per week. | All five patients in the bootcamp group completed >80% of the advised exercise sessions. |

CPET, cardiopulmonary exercise testing; IMT, inspiratory muscle training; MIP, maximum inspiratory pressure; $\dot{V}O_2$peak, peak oxygen uptake