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

G.A. Tew[1], R. Ayyash[2], J. Durrand[3], G.R. Danjoux[4,5]

1 Associate Professor, Department of Sport, Exercise and Rehabilitation, Northumbria University, Newcastle-upon-Tyne, UK. 2 Consultant Anaesthetist, Department of Anaesthesia, James Cook University Hospital, Middlesbrough, UK. 3 Academic Clinical Fellow in Anaesthesia (ST4), Northern School of Anaesthesia and Intensive Care Medicine and Newcastle University, Newcastle, UK. Consultant Anaesthetist and Research Lead, Department of Anaesthesia, James Cook University Hospital, Middlesbrough, UK. 5 Visiting Professor, School of Health and Social Care, Teesside University, Middlesbrough UK.

Running Title: Pre-operative exercise training before major non-cardiac surgery

Keywords: Prehabilitation, Physical exercise, Guideline, Surgery, Postoperative complications

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.

Correspondence to: G. Danjoux

Email: gerard.danjoux@nhs.net

Accepted: 13 November 2017

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/cardiometabolic 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} (-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 (SpO_2 = 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 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

1. Pouwels S, Hageman D, Gommans LN, et al. Preoperative exercise therapy in surgical care: a scoping review. *Journal of Clinical Anesthesia* 2016; **33:** 476-90.
2. Cavalheri V, Granger C. Preoperative exercise training for patients with non-small cell lung cancer. *Cochrane Database of Systematic Reviews* 2017; **6:** CD012020.
3. Hijazi Y, Gondal U, Aziz O. A systematic review of prehabilitation programs in abdominal cancer surgery. *International Journal of Surgery* 2017; **39:** 156-62.
4. Moran J, Guinan E, McCormick P, et al. The ability of prehabilitation to influence postoperative outcome after intra-abdominal operation: A systematic review and meta-analysis. *Surgery* 2016; **160:** 1189-201.
5. Loughney L, West MA, Kemp GJ, Grocott MP, Jack S. Exercise intervention in people with cancer undergoing neoadjuvant cancer treatment and surgery: A systematic review. *European Journal of Surgical Oncology* 2016; **42:** 28-38.
6. Hallal PC, Andersen LB, Bull FC, et al. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet* 2012; **380:** 247-57.
7. Rhodes RE, Janssen I, Bredin SSD, Warburton DER, Bauman A. Physical activity: Health impact, prevalence, correlates and interventions. *Psychology & Health* 2017; **32:** 942-75.
8. Hawkins S, Wiswell R. Rate and mechanism of maximal oxygen consumption decline with aging: implications for exercise training. *Sports Medicine* 2003; **33:** 877-88.
9. Milanović Z, Pantelić S, Trajković N, Sporiš G, Kostić R, James N. Age-related decrease in physical activity and functional fitness among elderly men and women. *Clinical Interventions in Aging* 2013; **8:** 549-56.
10. Booth FW, Roberts CK, Thyfault JP, Ruegsegger GN, Toedebusch RG. Role of Inactivity in Chronic Diseases: Evolutionary Insight and Pathophysiological Mechanisms. *Physiological Reviews* 2017; **97:** 1351-402.
11. Moran J, Wilson F, Guinan E, McCormick P, Hussey J, Moriarty J. Role of cardiopulmonary exercise testing as a risk-assessment method in patients undergoing intra-abdominal surgery: a systematic review. *British Journal of Anaesthesia* 2016; **116:** 177-91.
12. Desborough JP. The stress response to trauma and surgery. *British Journal of Anaesthesia* 2000; **85:** 109-17.
13. Older P. Anaerobic threshold, is it a magic number to determine fitness for surgery? *Perioperative Medicine (London)* 2013; **2:** 2.
14. The International Surgical Outcomes Study. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. *British Journal of Anaesthesia* 2016; **117:** 601-9.
15. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012; **380:** 1059-65.
16. Khuri SF, Henderson WG, DePalma RG, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Annals of Surgery* 2005; **242:** 326-41.

17. Moonesinghe SR, Harris S, Mythen MG, et al. Survival after postoperative morbidity: a longitudinal observational cohort study. *British Journal of Anaesthesia* 2014; **113:** 977-84.
18. Royal College of Anaesthetists. Perioperative Medicine: The Pathway to Better Surgical Care, 2014. https://www.rcoa.ac.uk/sites/default/files/PERIOP-2014.pdf (accessed 30/08/2017).
19. Carlisle JB, White SM, Tobin AE. The anaesthetist and peri-operative medicine: migration and evolution. *Anaesthesia* 2016; **71:** 1-2.
20. Bougeard AM, Brent A, Swart M, Snowden C. A survey of UK peri-operative medicine: pre-operative care. *Anaesthesia* 2017, **72:** 1010-5.
21. Durrand J, Hackett R, Yates D, Danjoux G. Prehabilitation. In: Stuart-Smith K, ed. *Perioperative Medicine Current Controversies*. Springer Publications, 2016: 16-47.
22. Warner DO. Surgery as a teachable moment: lost opportunities to improve public health. *Archives of Surgery* 2009; **144:** 1106-7.
23. Arnold R, Ranchor AV, Koëter GH, et al. Changes in personal control as a predictor of quality of life after pulmonary rehabilitation. *Patient Education and Counseling* 2006; **61:** 99-108.
24. Harris D, Hayter M, Allender S. Improving the uptake of pulmonary rehabilitation in patients with COPD: qualitative study of experiences and attitudes. *British Journal of General Practice* 2008; **58:** 703-10.
25. Bulley C, Donaghy M, Howden S, Salisbury L, Whiteford S, Mackay E. A prospective qualitative exploration of views about attending pulmonary rehabilitation. *Physiotherapy Research International* 2009; **14:** 181-92.
26. National Institute for Health and Care Excellence. NICE Guideline 45: Routine preoperative tests for elective surgery, 2016. https://www.nice.org.uk/guidance/ng45 (accessed 02/11/2017).
27. American College of Sports Medicine. *ACSM's guidelines for exercise testing and prescription*, Eighth edn. Philadelphia: Lippincott Williams & Wilkins, 2009.
28. British Heart Foundation. The National Audit of Cardiac Rehabilitation Annual Statistical Report 2016. https://www.bhf.org.uk/publications/statistics/national-audit-of-cardiac-rehabilitation-annual-statistical-report-2016 (accessed 30/08/2017).
29. Buck D, Frosini F. Clustering of unhealthy behaviours over time: Implications for policy and practice. London: The King's Fund, 2012.
30. Schmid M, Sood A, Campbell L, et al. Impact of smoking on perioperative outcomes after major surgery. *American Journal of Surgery* 2015; **210:** 221-9.e6.
31. Eliasen M, Grønkjær M, Skov-Ettrup LS, et al. Preoperative alcohol consumption and postoperative complications: a systematic review and meta-analysis. *Annals of Surgery* 2013; **258:** 930-42.
32. Barberan-Garcia A, Ubré M, Roca J, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. *Annals of Surgery* 2017.
33. Licker M, Karenovics W, Diaper J, et al. Short-Term Preoperative High-Intensity Interval Training in Patients Awaiting Lung Cancer Surgery: A Randomized Controlled Trial. *Journal of Thoracic Oncology* 2017; **12:** 323-33.
34. Barakat HM, Shahin Y, Khan JA, McCollum PT, Chetter IC. Preoperative Supervised Exercise Improves Outcomes After Elective Abdominal Aortic Aneurysm Repair: A Randomized Controlled Trial. *Annals of Surgery* 2016; **264:** 47-53.
35. Tew GA, Batterham AB, Colling K, et al. Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair. *British Journal of Surgery* 2017.
36. Carli F, Charlebois P, Stein B, et al. Randomized clinical trial of prehabilitation in colorectal surgery. *British Journal of Surgery* 2010; **97:** 1187-97.
37. Dronkers JJ, Lamberts H, Reutelingsperger IM, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. *Clinical Rehabilitation* 2010; **24:** 614-22.

38. van Adrichem EJ, Meulenbroek RL, Plukker JT, Groen H, van Weert E. Comparison of two preoperative inspiratory muscle training programs to prevent pulmonary complications in patients undergoing esophagectomy: a randomized controlled pilot study. *Annals of Surgical Oncology* 2014; **21:** 2353-60.
39. Weston M, Batterham AM, Tew GA, et al. Patients Awaiting Surgical Repair for Large Abdominal Aortic Aneurysms Can Exercise at Moderate to Hard Intensities with a Low Risk of Adverse Events. *Frontiers in Physiology* 2016; **7:** 684.
40. Hornsby WE, Douglas PS, West MJ, et al. Safety and efficacy of aerobic training in operable breast cancer patients receiving neoadjuvant chemotherapy: a phase II randomized trial. *Acta Oncologica* 2014; **53:** 65-74.
41. Jensen BT, Petersen AK, Jensen JB, Laustsen S, Borre M. Efficacy of a multiprofessional rehabilitation programme in radical cystectomy pathways: a prospective randomized controlled trial. *Scandinavian Journal of Urology* 2015; **49:** 133-41.
42. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures: ESA-ESICM joint taskforce on perioperative outcome measures. *European Journal of Anaesthesiology* 2015; **32:** 88-105.
43. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Medicine and Science in Sports and Exercise* 2011; **43:** 1334-59.
44. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014; **348:** g1687.
45. Weston M, Weston KL, Prentis JM, Snowden CP. High-intensity interval training (HIT) for effective and time-efficient pre-surgical exercise interventions. *Perioperative Medicine (London)* 2016; **5:** 2.
46. Barbalho-Moulim MC, Miguel GP, Forti EM, Campos FoA, Costa D. Effects of preoperative inspiratory muscle training in obese women undergoing open bariatric surgery: respiratory muscle strength, lung volumes, and diaphragmatic excursion. *Clinics (Sao Paulo)* 2011; **66:** 1721-7.
47. Dronkers J, Veldman A, Hoberg E, van der Waal C, van Meeteren N. Prevention of pulmonary complications after upper abdominal surgery by preoperative intensive inspiratory muscle training: a randomized controlled pilot study. *Clinical Rehabilitation* 2008; **22:** 134-42.
48. Bolton CE, Bevan-Smith EF, Blakey JD, et al. British Thoracic Society guideline on pulmonary rehabilitation in adults. *Thorax* 2013; **68 Suppl 2:** ii1-30.
49. Jones LW, Peddle CJ, Eves ND, et al. Effects of presurgical exercise training on cardiorespiratory fitness among patients undergoing thoracic surgery for malignant lung lesions. *Cancer* 2007; **110:** 590-8.
50. Benzo R, Wigle D, Novotny P, et al. Preoperative pulmonary rehabilitation before lung cancer resection: results from two randomized studies. *Lung Cancer* 2011; **74:** 441-5.
51. Pehlivan E, Turna A, Gurses A, Gurses HN. The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. *Annals of Thoracic and Cardiovascular Surgery* 2011; **17:** 461-8.
52. do Nascimento Junior P, Módolo NS, Andrade S, Guimarães MM, Braz LG, El Dib R. Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery. *Cochrane Database of Systemic Reviews* 2014**; 2:** CD006058.

53. Swallow EB, Reyes D, Hopkinson NS, et al. Quadriceps strength predicts mortality in patients with moderate to severe chronic obstructive pulmonary disease. *Thorax* 2007; **62:** 115-20.
54. Jack S, West MA, Raw D, et al. The effect of neoadjuvant chemotherapy on physical fitness and survival in patients undergoing oesophagogastric cancer surgery. *Eur J Surg Oncol* 2014; **40:** 1313-20.
55. West MA, Loughney L, Barben CP, et al. The effects of neoadjuvant chemoradiotherapy on physical fitness and morbidity in rectal cancer surgery patients. *European Journal of Surgical Oncology* 2014; **40:** 1421-8.
56. Stefani L, Galanti G, Klika R. Clinical Implementation of Exercise Guidelines for Cancer Patients: Adaptation of ACSM's Guidelines to the Italian Model. *Journal of Functional Morphology and Kinesiology* 2017; **2:** 4.
57. Ibrahim MS, Khan MA, Nizam I, Haddad FS. Peri-operative interventions producing better functional outcomes and enhanced recovery following total hip and knee arthroplasty: an evidence-based review. *BMC Medicine* 2013; **11:** 37.
58. Batterham AM, Bonner S, Wright J, Howell SJ, Hugill K, Danjoux G. Effect of supervised aerobic exercise rehabilitation on physical fitness and quality-of-life in survivors of critical illness: an exploratory minimized controlled trial (PIX study). *British Journal of Anaesthesia* 2014; **113:** 130-7.
59. Gillis C, Li C, Lee L, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology* 2014; **121:** 937-47.
60. Paton F, Chambers D, Wilson P, et al. Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis. *BMJ Open* 2014; **4:** e005015.
61. Stefanelli F, Meoli I, Cobuccio R, et al. High-intensity training and cardiopulmonary exercise testing in patients with chronic obstructive pulmonary disease and non-small-cell lung cancer undergoing lobectomy. *European Journal of Cardiothoracic Surgery* 2013; **44:** e260-5.
62. Banerjee S, Manley K, Thomas L, et al. Preoperative exercise protocol to aid recovery of radical cystectomy: results of a feasibility study. *European Urology* 2013; **Suppl. 12:** 125.
63. Kaibori M, Ishizaki M, Matsui K, et al. Perioperative exercise for chronic liver injury patients with hepatocellular carcinoma undergoing hepatectomy. *American Journal of Surgery* 2013; **206:** 202-9.

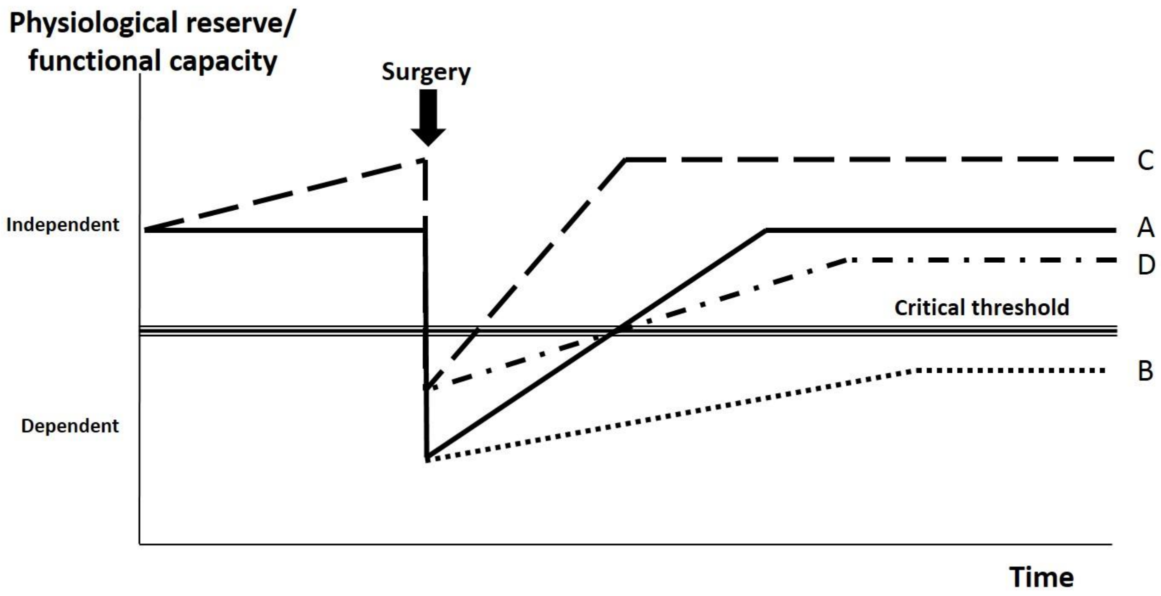


Figure 1. The prehabilitation concept. Following major surgical intervention all patients experience an acute drop in physiological reserve/functional capacity followed by a recovery and rehabilitation phase (A). A low physiological reserve/functional capacity may increase the risk of perioperative complications 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).

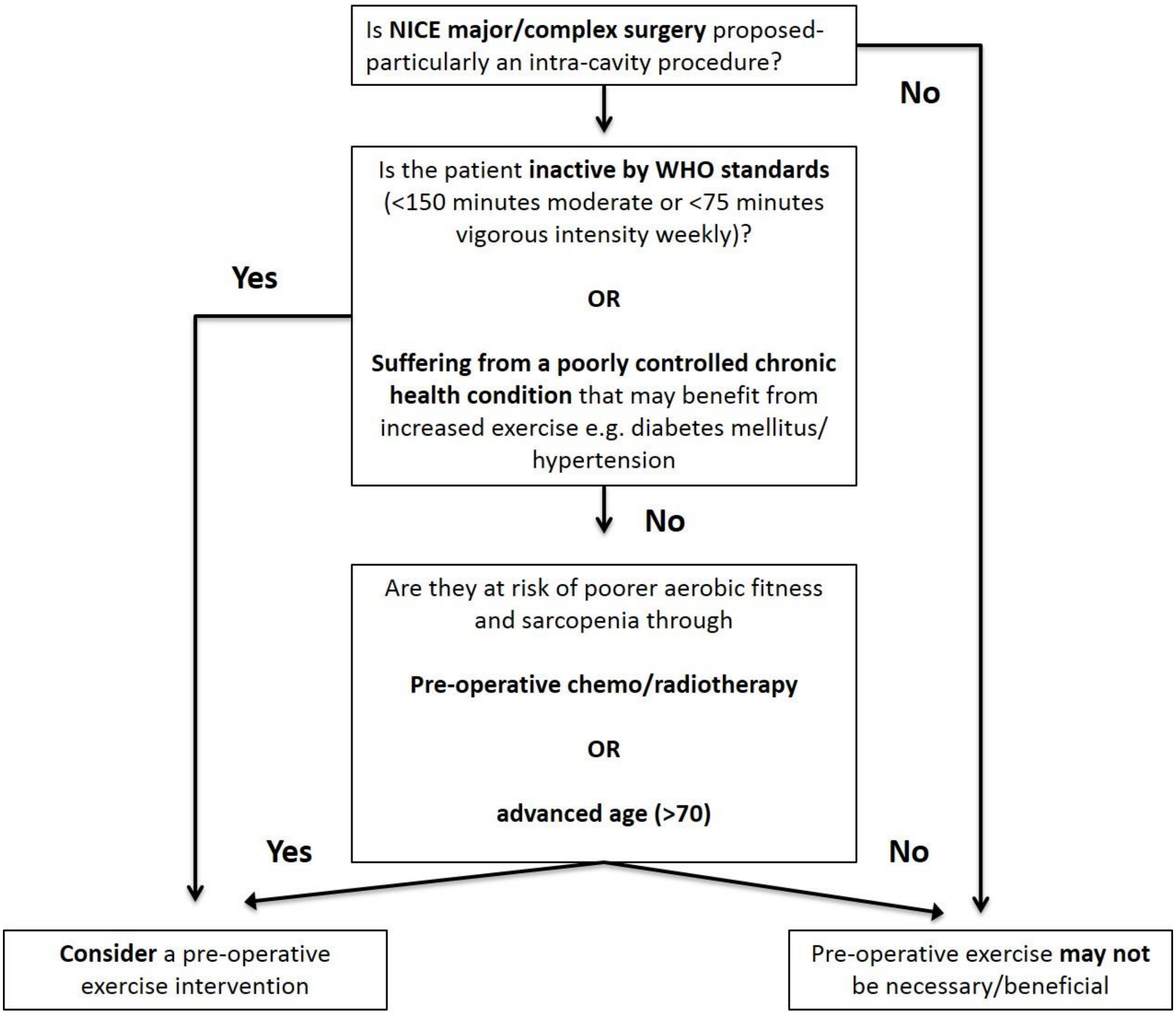


Figure 2. Flowchart to assist clinicians in identifying patients who may benefit from pre-operative exercise training. This should be used in conjunction with clinical judgement and locally available options. See [26] for examples of major/complex elective surgery.

Provider: Physiotherapist, physical therapist or clinical exercise specialist
Mode of delivery: The exercise should ideally be delivered face-to-face, although some sessions can be performed unsupervised in the home/community setting. The exercise prescription should be individually tailored based on an initial assessment; however, several patients can be supervised at the same time.
Setting: Can be delivered in various settings including hospital- or community-based physiotherapy clinics or community wellbeing facilities
Materials: Assessment tools: Cardiopulmonary exercise testing equipment (or, if unavailable, procedures and instructions for an alternative functional capacity test, e.g. 6-minute walk test) and condition-specific quality of life questionnaire(s). Exercise equipment: flat walking track (preferably indoor and air-conditioned) and inspiratory muscle training devices (e.g., Threshold IMT® [Philips Respironics, Inc., Murrysville, PA, USA] or POWERbreathe® [POWERbreathe International Ltd., Warwickshire, UK]). Optional for aerobic exercise – cycle ergometers, treadmills, arm-crank ergometers (e.g. for people with limited ability to perform lower-limb exercise), cross trainers. Optional for resistance exercise – resistance bands, dumbbells, weight machines. Intensity-monitoring equipment: heart rate monitors, manual sphygmomanometer and stethoscope, exertion scales (e.g. 6–20 point Borg Rating of Perceived Exertion Scale). Safety equipment: resuscitation equipment immediately available with staff appropriately trained in use, supplemental oxygen in the presence of co-morbid cardiorespiratory disease, glucose monitoring device for people with diabetes.
Aerobic exercise (based on [43]): Frequency: ≥5 day.week^{-1} of moderate-intensity exercise, or ≥3 day.week^{-1} of vigorous-intensity exercise, or a combination of moderate and vigorous exercise on ≥3–5 day.week^{-1}. Intensity: Moderate intensity (40–59% peak oxygen uptake reserve [the difference between the rate of oxygen consumption at rest and at maximal exercise] or heart rate reserve, or 55–69% of maximum heart rate or Borg exertion rating of 12–13) and/or vigorous intensity (60–84% peak oxygen uptake reserve or heart rate reserve, or 70–89% maximum heart rate or Borg exertion rating of 14–16) is recommended for most adults. Time: 30–60 min.day^{-1} (150 min.week^{-1}) of purposeful moderate exercise, or 20–60 min.day^{-1} (75 min.week^{-1}) of vigorous exercise, or a combination of moderate and vigorous exercise per day is recommended for most adults. Type: Regular, purposeful exercise that involves major muscle groups (e.g., walking, cycling, cross training), is repetitive and rhythmic in nature, and is tailored to preferences and comorbidities. Normal overground walking is particularly practical, and cycle ergometry allows for precise manipulation of the load. Pattern: Exercise may be performed in one continuous session per day or in multiple bouts of ≥10 min to accumulate the desired duration and volume of exercise per day. Interval training can also increase cardiorespiratory fitness, and may be more time-efficient than moderate continuous training [45] – see Tew et al. [35] for an example protocol. Progression: If the patient is adherent and tolerating the exercise programme, the exercise volume should be gradually increased by adjusting the duration, frequency, and/or intensity of exercise.
Inspiratory muscle training: Some studies have explored the benefit of inspiratory muscle training in people undergoing upper abdominal surgery [46,47], with the rationale that it may reduce post-operative pulmonary complications. More research is needed, but in the meantime, inspiratory muscle training may be considered as a potential adjunct to aerobic exercise training. Inspiratory muscle training consists of two distinct types of specific respiratory muscle training: respiratory muscle strength (resistive/threshold) and respiratory muscle endurance (hyperpnoea) training. Various protocols have been proposed; the following represents a typical approach. Frequency: 5–7 day.week^{-1}. Intensity: Initial load of 20–30% maximum inspiratory pressure, with gradual progression in subsequent sessions to 60% maximum inspiratory pressure or to a load that provides a moderate-to-hard level of exertion. Time: 15–30 min.session^{-1}. Type/Pattern: Most protocols involve continuous training using a handheld variable-resistance device (e.g., Threshold IMT® or POWERbreathe®). However, one study described an interval-training approach [38]. Other: Initial sessions should ideally be supervised to ensure that the correct technique and dose is being adhered to. Subsequently, sessions may be performed unsupervised (assuming equipment is available for home use).
Resistance exercise: May be considered as complementary (e.g., targeting improved strength, reduced falls risk or enhanced post-operative recovery of functional capacity), but not as a replacement for other exercise components. Guidelines: Moderate-to-vigorous intensity (Borg exertion rating of 14–16), 8–10 exercises targeting the major muscle groups, 2–4 sets of 10–15 repetitions per set), 2–3 sessions per week. Note: United Kingdom pulmonary rehabilitation guidelines [48] recommend that resistance exercise should not be undertaken by individuals with an abdominal aortic aneurysm >5.5 cm; however, one study [34] that included resistance training as part of a circuit-based exercise prehabilitation programme for this patient group reported no adverse effects.

Figure 3. Pre-operative exercise training to reduce post-operative complications in patients undergoing major intra-abdominal surgery.

Provider: Respiratory physiotherapist or exercise specialist trained in pulmonary rehabilitation

Mode of delivery: The exercise should ideally be delivered face-to-face, although some sessions can be performed unsupervised in the home/community setting. The exercise prescription should be individually tailored based on an initial assessment; however, several patients can be supervised at the same time.

Setting: Can be delivered in various settings including hospital- or community-based physiotherapy or pulmonary rehabilitation facilities

Materials: Assessment tools: Cardiopulmonary exercise testing equipment or procedures and instructions for 6-minute walk test, dyspnoea scale, pulse oximeter, device to measure blood pressure, spirometer, disease-specific quality of life questionnaire (e.g., St. George's Respiratory Questionnaire or Chronic Respiratory Disease Questionnaire). Exercise equipment: flat walking track (preferably indoor and air-conditioned) and inspiratory muscle training devices (e.g., Threshold IMT® [Philips Respironics, Inc., Murrysville, PA, USA] or POWERbreathe® [POWERbreathe International Ltd., Warwickshire, UK]). Optional for aerobic exercise – cycle ergometers, treadmills, arm-crank ergometers (e.g. for people with limited ability to perform lower-limb exercise), cross trainers. Optional for resistance exercise – resistance bands, dumbbells, weight machines. Intensity-monitoring equipment: heart rate monitors, manual sphygmomanometer and stethoscope, exertion scales (e.g. 6–20 point Borg Rating of Perceived Exertion Scale). Safety equipment: resuscitation equipment immediately available with staff appropriately trained in use, supplemental oxygen in the presence of co-morbid cardiorespiratory disease, glucose monitoring device for people with diabetes.

Aerobic exercise (based on [43]): Frequency: ≥5 day.week^{-1} of moderate-intensity exercise, or ≥3 day.week^{-1} of vigorous-intensity exercise, or a combination of moderate and vigorous exercise on ≥3–5 day.week^{-1}. Intensity: Moderate intensity (40–59% peak oxygen uptake reserve [the difference between the rate of oxygen consumption at rest and at maximal exercise] or heart rate reserve, or 55–69% of maximum heart rate or Borg exertion rating of 12–13) and/or vigorous intensity (60–84% peak oxygen uptake reserve or heart rate reserve, or 70–89% maximum heart rate or Borg exertion rating of 14–16) is recommended for most adults. Time: 30–60 min.day^{-1} (150 min.week^{-1}) of purposeful moderate exercise, or 20–60 min.day^{-1} (75 min.week^{-1}) of vigorous exercise, or a combination of moderate and vigorous exercise per day is recommended for most adults. Type: Regular, purposeful exercise that involves major muscle groups (e.g., walking, cycling, cross training), is repetitive and rhythmic in nature, and is tailored to preferences and comorbidities. Normal overground walking is particularly practical, and cycle ergometry allows for precise manipulation of the load. Pattern: Exercise may be performed in one continuous session per day or in multiple bouts of ≥10 min to accumulate the desired duration and volume of exercise per day. Interval and continuous training can be applied safely and effectively within the context of pulmonary rehabilitation to patients with chronic obstructive pulmonary disease [48]. This also appears to be the case in exercise prehabilitation studies of patients undergoing thoracic surgery [33,49]. Therefore, the choice of interval or continuous training should be based on patient and therapist preference. See Tew et al. [35] for an example interval training protocol. Progression: If the patient is adherent and tolerating the exercise programme, the exercise volume should be gradually increased by adjusting the duration, frequency, and/or intensity of exercise.

Inspiratory muscle training: Although inspiratory muscle training is not recommended as a routine adjunct to pulmonary rehabilitation [48], there is promising evidence to support its use for reducing post-operative pulmonary complication in people awaiting thoracic surgery [2]. Therefore, it may be considered as a potential adjunct to aerobic exercise training. Guidelines: 15–30 min.session^{-1} performed 5–7 day.week^{-1}; initial load of 20–30% maximum inspiratory pressure, with gradual progression in subsequent sessions to 60% maximum inspiratory pressure or to a load that provides a moderate-to-hard level of exertion; most published protocols involve continuous training using a handheld variable-resistance device (e.g., Threshold IMT® or POWERbreathe®). Some studies have used inspiratory muscle training as part of a broader respiratory therapy programme that also included deep-breathing exercises, thoracic physiotherapy and/or incentive spirometry (e.g. [50,51]). However, a recent systematic review of incentive spirometry alone or incentive spirometry with physiotherapy did not support the effectiveness of incentive spirometry for the prevention of post-operative pulmonary complications after upper abdominal surgery [52].

Resistance exercise: Resistance training may be of higher priority in thoracic surgery patients (relative to other surgical populations) given that lower-limb weakness is common in patients with respiratory disease and an indicator of poor prognosis [53]. However, it should be considered as complementary rather than as a replacement for other exercise components. Guidelines: Moderate-to-vigorous intensity (Borg exertion rating of 14–16), 8–10 exercises targeting the major muscle groups, 2–4 sets of 10–15 repetitions per set), 2–3 sessions per week. Note: Although United Kingdom pulmonary rehabilitation guidelines recommend a combination of progressive resistance and aerobic training [48], they state that resistance training should be avoided by individuals with an abdominal aortic aneurysm >5.5 cm. However, one study [34] that included resistance training as part of a circuit-based exercise prehabilitation programme for this patient group reported no adverse effects.

Figure 4. Pre-operative exercise training to reduce post-operative pulmonary complications in patients undergoing lung resection surgery.

Provider: Specialist trained in exercise rehabilitation for people with cancer, physiotherapist, or other allied health professional or nurse with advanced training in exercise testing and training

Mode of delivery: The exercise should ideally be delivered face-to-face, although some sessions can be performed unsupervised in the home/community setting. The exercise prescription should be individually tailored based on an initial assessment; however, several patients can be supervised at the same time.

Setting: Can be delivered in various settings including: outpatient physiotherapy department, community leisure centre, and/or at home

Materials: Assessment tools: Cardiopulmonary exercise testing equipment (or, if unavailable, procedures and instructions for an alternative functional capacity test, e.g. 6-minute walk test) and condition-specific quality of life questionnaire(s). Exercise equipment: flat walking track (preferably indoor and air-conditioned) and inspiratory muscle training devices (e.g., Threshold IMT® [Philips Respironics, Inc., Murrysville, PA, USA] or POWERbreathe® [POWERbreathe International Ltd., Warwickshire, UK]). Optional for aerobic exercise – cycle ergometers, treadmills, arm-crank ergometers (e.g. for people with limited ability to perform lower-limb exercise), cross trainers. Optional for resistance exercise – resistance bands, dumbbells, weight machines. Intensity-monitoring equipment: heart rate monitors, manual sphygmomanometer and stethoscope, exertion scales (e.g. 6–20 point Borg Rating of Perceived Exertion Scale). Safety equipment: resuscitation equipment immediately available with staff appropriately trained in use, supplemental oxygen in the presence of co-morbid cardiorespiratory disease, glucose monitoring device for people with diabetes.

Aerobic exercise (based on [43]): Neoadjuvant chemo- and chemo-radio-therapy decreases cardiorespiratory fitness, and this decrease is associated with poor surgical outcome (i.e. increased post-operative morbidity and mortality) in people with gastrointestinal cancer [54,55]. Initiating exercise training in the neoadjuvant setting, particularly aerobic exercise training, may therefore be important for reducing the adverse effects of cancer treatment and improving surgical outcome [5]. Frequency: ≥5 day.week^{-1} of moderate-intensity exercise, or ≥3 day.week^{-1} of vigorous-intensity exercise, or a combination of moderate and vigorous exercise on ≥3–5 day.week^{-1}. Intensity: Moderate intensity (40–59% peak oxygen uptake reserve [the difference between the rate of oxygen consumption at rest and at maximal exercise] or heart rate reserve, or 55–69% of maximum heart rate or Borg exertion rating of 12–13) and/or vigorous intensity (60–84% peak oxygen uptake reserve or heart rate reserve, or 70–89% maximum heart rate or Borg exertion rating of 14–16) is recommended for most adults. Time: 30–60 min.day^{-1} (150 min.week^{-1}) of purposeful moderate exercise, or 20–60 min.day^{-1} (75 min.week^{-1}) of vigorous exercise, or a combination of moderate and vigorous exercise per day is recommended for most adults. Type: Regular, purposeful exercise that involves major muscle groups (e.g., walking, cycling, cross training), is repetitive and rhythmic in nature, and is tailored to preferences and comorbidities. Normal overground walking is particularly practical, and cycle ergometry allows for precise manipulation of the load. Pattern: Exercise may be performed in one continuous session per day or in multiple bouts of ≥10 min to accumulate the desired duration and volume of exercise per day. Interval training can also increase cardiorespiratory fitness, and may be more time-efficient than moderate continuous training [45] – see Tew et al. [35] for an example protocol. Progression: If the patient is adherent and tolerating the exercise programme, the exercise volume should be gradually increased by adjusting the duration, frequency, and/or intensity of exercise. Note: See Stefani et al. [56] for contraindications to exercise training among cancer patients

Inspiratory muscle training: There is promising evidence to support the use of inspiratory muscle training for reducing post-operative pulmonary complication in people awaiting lung resection surgery for non-small-cell lung cancer [2]. Therefore, it may be considered as a potential adjunct to aerobic exercise training. Guidelines: 15–30 min.session^{-1} performed 5–7 day.week^{-1}; initial load of 20–30% maximum inspiratory pressure, with gradual progression in subsequent sessions to 60% maximum inspiratory pressure or to a load that provides a moderate-to-hard level of exertion; most published protocols involve continuous training using a handheld variable-resistance device (e.g., Threshold IMT® or POWERbreathe®). Other: Initial sessions should ideally be supervised to ensure that the correct technique and dose is being adhered to. Subsequently, sessions may be performed unsupervised (assuming equipment is available for home use).

Resistance exercise: To ensure strength and endurance benefits, a combination of progressive resistance and aerobic training should be delivered. Guidelines: Moderate-to-vigorous intensity (Borg exertion rating of 14–16), 8–10 exercises targeting the major muscle groups, 2–4 sets of 10–15 repetitions per set), 2–3 sessions per week.

Figure 5. Pre-operative exercise training in people with cancer undergoing neoadjuvant chemoradiotherapy and surgery.

Table 1. General characteristics of included reviews and trials

Study	Study design (No. of relevant RCTs/participants)	Population	Intervention	Outcome measures
Cavalheri [2]	Cochrane SR and meta-analysis of RCTs (5/167)	Patients undergoing lung resection surgery for NSCLC	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.	Post-operative mortality, post-operative complications, LOS, CRF, days intercostal catheter needed after surgery, functional capacity, fatigue, dyspnoea, pulmonary function
Hijazi [3]	SR of RCTs and non-randomised controlled trials (5/243)	Patients undergoing major abdominal cancer surgery	Prehabilitation programmes, which could include physical exercise, nutrition, and/or psychological support components.	Post-operative complications, CRF, HR-QoL, functional capacity, psychological status
Moran [4]	SR and meta-analysis of RCTs (7/307)	Patients undergoing major abdominal surgery	PET including aerobic, resistance and/or inspiratory muscle training	Post-operative mortality, post-operative complications, LOS
Loughney [5]	SR of RCTs and non-randomised controlled trials with meta-analyses (2/30)	People with cancer undergoing both neoadjuvant cancer treatment and surgery	PET interventions during neoadjuvant cancer treatment	CRF, HR-QoL, adverse events, physical activity, fatigue, biomarkers
Barberan-Garcia [32]	RCT (1/144)	Adults aged ≥70 years undergoing elective major abdominal surgery	4 weeks of PET comprising supervised cycle-based HIIT and promotion of unsupervised walking and functional exercises	In-hospital mortality, post-operative complications, LOS, HR-QoL, functional capacity, exercise capacity, physical activity, psychological status
Licker [33]	RCT (1/164)	Patients undergoing lung resection surgery for NSCLC	PET of varying duration (median 26 days); comprising supervised cycle-based HIIT and whole-body resistance training and promotion of unsupervised walking	Post-operative mortality, post-operative complications, CRF, adverse events, functional capacity, physical activity
Barakat [34]	RCT (1/124)	Adults undergoing elective repair of a large	6 weeks of thrice-weekly PET comprising circuit classes involving	Post-operative mortality, post-operative complications, LOS, CRF,

		(≥5.5 cm) abdominal aortic aneurysm	a mixture of aerobic and resistance exercises	adverse events, SIRS, post-operative bleeding
Tew [35]	Randomised feasibility trial (1/53)	Adults undergoing elective repair of a large (5.5 to 7.0 cm) abdominal aortic aneurysm	4 weeks of thrice-weekly PET comprising supervised cycle-based HIIT	Post-operative mortality, post-operative complications, LOS, CRF, HR-QoL, exercise enjoyment, healthcare resource use

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

Study	Post-operative mortality, complications and length of stay	Cardiorespiratory fitness and health-related quality of life	Main conclusions and limitations
Cavalheri [2]	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).	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 $ml.kg^{-1}.min^{-1}$; $p<0.01$), with no change in the control group ($p>0.05$).	*"[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."*
Hijazi [3]	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].	In one study [62], PET increased $\dot{V}O_2$peak by 2.51 $ml.kg^{-1}.min^{-1}$ ($p=0.002$).	*"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].
Moran [4]	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).	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 ($p=0.007$).	*"[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]).
Loughney [5]	Not reported	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	*"… 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..."*

		(p<0.001). For HR-QoL, PET had no significant effect on FACT-B (p=0.685) or FACT-G (p=0.431).	Limitation: Only 2 pilot RCTs
Barberan-Garcia [32]	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).	$\dot{V}O_2$peak 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).	*"[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 $\dot{V}O_2$peak data not reported.
Licker [33]	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.	Median change in $\dot{V}O_2$peak from baseline to pre-surgery was +2.9 $ml.kg^{-1}.min^{-1}$ in the PET group and -1.5 $ml.kg^{-1}.min^{-1}$ in the control group (p=0.004).	*"preoperative HIIT resulted in significant improvement in aerobic performances but failed to reduce early complications after lung cancer resection"* Limitations: Trial was stopped early after an interim analysis; original sample size target = 362.
Barakat [34]	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).	In the PET group, median (IQR) $\dot{V}O_2$peak 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).	*"[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.

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.	<u>For PET vs. control at pre-surgery:</u> 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]) $\dot{V}O_2$peak = 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]) <u>For PET vs. control at 12 weeks post-discharge:</u> 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."* <u>Limitations:</u> Designed primarily to test feasibility rather than clinical and cost effectiveness

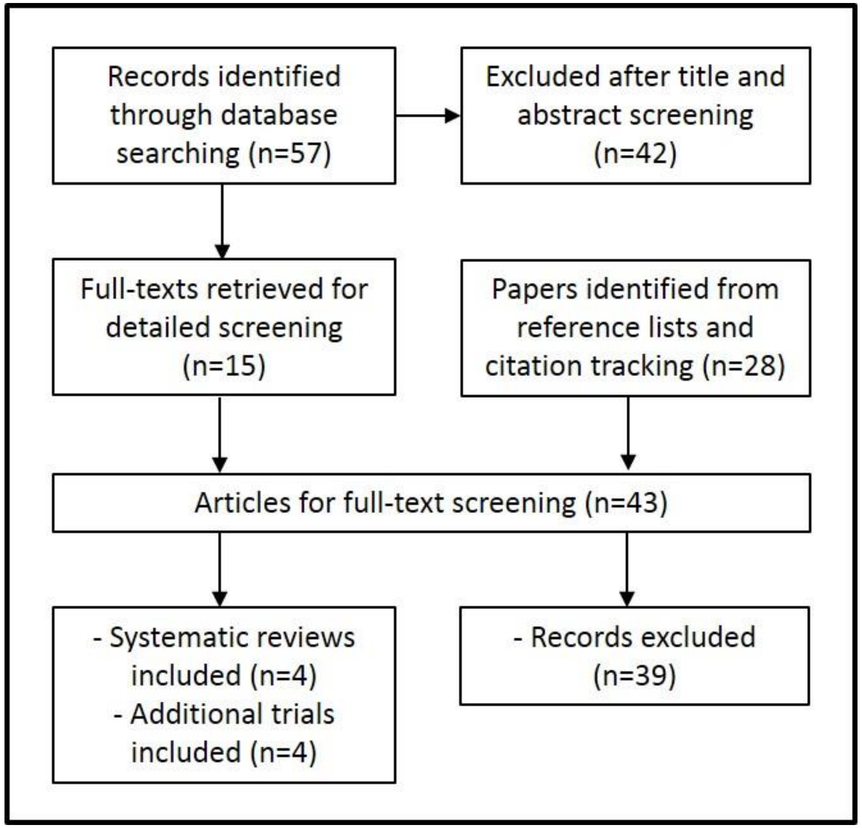
AAA, abdominal aortic aneurysm; AT, anaerobic threshold; CI, confidence interval; CRF, cardiorespiratory fitness; FACT-B, Functional Assessment of Cancer Therapy-Breast; FACT-G Functional Assessment of Cancer Therapy-General; HIIT, high-intensity interval training; HR-QoL, health-related quality of life; 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; $\dot{V}O_2$peak, 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



Appendix S3. Excluded reviews

Title of review	Reason for exclusion
Driessen, E.J., Peeters, M.E., Bongers, B.C., Maas, H.A., Bootsma, G.P., van Meeteren, N.L. and Janssen-Heijnen, M.L., 2017. Effects of prehabilitation and rehabilitation including a home-based component on physical fitness, adherence, treatment tolerance, and recovery in patients with non-small cell lung cancer: A systematic review. Critical Reviews in Oncology/Hematology.	No relevant trials included in the review
Hoffman, M., Chaves, G., Ribeiro-Samora, G.A., Britto, R.R. and Parreira, V.F., 2017. Effects of pulmonary rehabilitation in lung transplant candidates: a systematic review. BMJ Open, 7(2), p.e013445.	Only one randomised trial, which was from 1994, included just 9 patients, and did not report on post-operative outcomes
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.	Relevant included trials represented in a more recent/ comprehensive systematic review
Kendall, F., Abreu, P., Pinho, P., Oliveira, J. and Bastos, P., 2017. The role of physiotherapy in patients undergoing pulmonary surgery for lung cancer. A literature review. Revista Portuguesa de Pneumologia (English Edition).	Not a systematic review
Looijaard, S.M., Slee-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.	Only included one relevant trial, which had been represented in one of the included reviews
Ni, H.J., Pudasaini, B., Yuan, X.T., Li, H.F., Shi, L. and Yuan, P., 2017. Exercise Training for Patients Pre-and Postsurgically Treated for Non–Small Cell Lung Cancer: A Systematic Review and Meta-analysis. Integrative cancer therapies, 16(1), pp.63-73.	Relevant included trials represented in a more comprehensive recent systematic review
Puts, M.T., Toubasi, S., Andrew, M.K., Ashe, M.C., Ploeg, J., Atkinson, E., Ayala, A.P., Roy, A., Rodríguez Monforte, M., Bergman, H. and McGilton, K., 2017. Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies. Age and ageing, 46(3), pp.383-392.	Did not focus on prehabilitation interventions
Segal, R., Zwaal, C., Green, E., Tomasone, J.R., Loblaw, A. and Petrella, T., 2017. Exercise for people with cancer: a clinical practice guideline. Current Oncology, 24(1), p.40.	Did not focus on prehabilitation interventions
Rooijen, S.J., Engelen, M.A., Scheede-Bergdahl, C., Carli, F., Roumen, R.M., Slooter, G.D. and Schep, G., 2017. Systematic review of exercise training in colorectal cancer patients during treatment. Scandinavian Journal of Medicine & Science in Sports.	Focus was on exercise during chemotherapy rather than exercise before surgery
Boereboom, C., Doleman, B., Lund, J.N. and Williams, J.P., 2016. Systematic review of pre-operative exercise in colorectal cancer patients. Techniques in coloproctology, 20(2), pp.81-89.	Relevant included trials represented in a more comprehensive recent systematic review
Bruns, E.R.J., Heuvel, B., Buskens, C.J., Duijvendijk, P., Festen, S., Wassenaar, E.B., Zaag, E.S., Bemelman, W.A. and Munster, B.C., 2016. The effects of physical prehabilitation in elderly patients undergoing colorectal surgery: a systematic review. Colorectal Disease, 18(8).	Relevant included trials represented in a more recent systematic review
Cabilan, C.J., Hines, S. and Munday, J., 2016. The impact of prehabilitation on postoperative functional status, healthcare utilization, pain, and quality of life: A systematic review. Orthopaedic Nursing, 35(4), pp.224-237.	Relevant included trials represented in a more recent systematic review

Nardi, A.T.D., Real, A.A., Santos, T.D.D., Rocha, R.D.O. and Lenzi, T.L., 2016. Effect of inspiratory muscle training on patients undergoing bariatric surgery: a systematic review. Fisioterapia e Pesquisa, 23(4), pp.448-457.	No relevant outcome measures
Levett, D.Z., Edwards, M., Grocott, M. and Mythen, M., 2016. Preparing the patient for surgery to improve outcomes. Best Practice & Research Clinical Anaesthesiology, 30(2), pp.145-157.	Not a systematic review
Mainini, C., Rebelo, P.F., Bardelli, R., Kopliku, B., Tenconi, S., Costi, S., Tedeschi, C. and Fugazzaro, S., 2016. Perioperative physical exercise interventions for patients undergoing lung cancer surgery: What is the evidence? SAGE open medicine, 4, p.2050312116673855.	Relevant included trials represented in a more comprehensive recent systematic review
Myers, J.N. and Fonda, H., 2016. The impact of fitness on surgical outcomes: the case for prehabilitation. Current sports medicine reports, 15(4), pp.282-289.	Not a systematic review
Pouwels, S., Hageman, D., Gommans, L.N., Willigendael, E.M., Nienhuijs, S.W., Scheltinga, M.R. and Teijink, J.A., 2016. Preoperative exercise therapy in surgical care: a scoping review. Journal of clinical anesthesia, 33, pp.476-490.	Was a scoping review; not a systematic review of RCTs
Sebio Garcia, R., Yáñez Brage, M.I., Giménez Moolhuyzen, E., Granger, C.L. and Denehy, L., 2016. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: a systematic review and meta-analysis. Interactive cardiovascular and thoracic surgery, 23(3), pp.486-497.	Relevant included trials represented in a more recent Cochrane systematic review
Wallen, M.P., Skinner, T.L., Pavey, T.G., Hall, A., Macdonald, G.A. and Coombes, J.S., 2016. Safety, adherence and efficacy of exercise training in solid-organ transplant candidates: A systematic review. Transplantation Reviews, 30(4), pp.218-226.	Relevant included trials represented in a more recent systematic review
Weston, M., Weston, K.L., Prentis, J.M. and Snowden, C.P., 2016. High-intensity interval training (HIT) for effective and time-efficient pre-surgical exercise interventions. Perioperative Medicine, 5(1), p.2.	Not a systematic review
Cabilan, C.J., Hines, S. and Munday, J., 2015. 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.	Relevant included trials represented in a more recent systematic review
Halloway, S., Buchholz, S.W., Wilbur, J. and Schoeny, M.E., 2015. Prehabilitation interventions for older adults: an integrative review. Western journal of nursing research, 37(1), pp.103-123.	Only included studies in orthopaedic surgery
Katsura, M., Kuriyama, A., Takeshima, T., Fukuhara, S. and Furukawa, T.A., 2015. Preoperative inspiratory muscle training for postoperative pulmonary complications in adults undergoing cardiac and major abdominal surgery. The Cochrane Library.	Relevant included trials represented in a more recent systematic review
Mans, C.M., Reeve, J.C. and Elkins, M.R., 2015. Postoperative outcomes following preoperative inspiratory muscle training in patients undergoing cardiothoracic or upper abdominal surgery: a systematic review and meta analysis. Clinical rehabilitation, 29(5), pp.426-438.	Relevant included trials represented in a more recent systematic review
Pouwels, S., Fiddelaers, J., Teijink, J.A., ter Woorst, J.F., Siebenga, J. and Smeenk, F.W., 2015. Preoperative exercise therapy in lung surgery patients: A systematic review. Respiratory medicine, 109(12), pp.1495-1504.	Relevant included trials represented in a more recent systematic review
Pouwels, S., Willigendael, E.M., van Sambeek, M.R.H.M., Nienhuijs, S.W., Cuypers, P.W.M. and Teijink, J.A.W., 2015. 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.	Of the 5 included studies, 1 was represented in a more recent review, 1 reported non-controlled data, and 3 were of patients not awaiting surgery

Silver, J.K., 2015, February. Cancer prehabilitation and its role in improving health outcomes and reducing health care costs. In Seminars in oncology nursing (Vol. 31, No. 1, pp. 13-30). WB Saunders.	Not a systematic review
Crandall, K., Maguire, R., Campbell, A. and Kearney, N., 2014. Exercise intervention for patients surgically treated for Non-Small Cell Lung Cancer (NSCLC): a systematic review. Surgical oncology, 23(1), pp.17-30.	Relevant included trials represented in a more recent systematic review
Pouwels, S., Stokmans, R.A., Willigendael, E.M., Nienhuijs, S.W., Rosman, C., van Ramshorst, B. and Teijink, J.A., 2014. Preoperative exercise therapy for elective major abdominal surgery: a systematic review. International journal of surgery, 12(2), pp.134-140.	Relevant included trials represented in a more recent systematic review
Rodriguez-Larrad, A., Lascurain-Aguirrebena, I., Abecia-Inchaurregui, L.C. and Seco, J., 2014. Perioperative physiotherapy in patients undergoing lung cancer resection. Interactive cardiovascular and thoracic surgery, 19(2), pp.269-281.	Relevant included trials represented in a more recent systematic review
Santa Mina, D., Clarke, H., Ritvo, P., Leung, Y.W., Matthew, A.G., Katz, J., Trachtenberg, J. and Alibhai, S.M.H., 2014. Effect of total-body prehabilitation on postoperative outcomes: a systematic review and meta-analysis. Physiotherapy, 100(3), pp.196-207.	Relevant included trials represented in a more recent systematic review
Lemanu, D.P., Singh, P.P., MacCormick, A.D., Arroll, B. and Hill, A.G., 2013. Effect of preoperative exercise on cardiorespiratory function and recovery after surgery: a systematic review. World journal of surgery, 37(4), pp.711-720.	Relevant included trials represented in a more recent systematic review
O'Doherty, A.F., West, M., Jack, S. and Grocott, M.P.W., 2013. Preoperative aerobic exercise training in elective intra-cavity surgery: a systematic review. British journal of anaesthesia, 110(5), pp.679-689.	Relevant included trials represented in a more recent systematic review
Schmidt-Hansen, M., Page, R. and Hasler, E., 2013. The effect of preoperative smoking cessation or preoperative pulmonary rehabilitation on outcomes after lung cancer surgery: a systematic review. Clinical lung cancer, 14(2), pp.96-102.	No relevant trials included
Singh, F., Newton, R.U., Galvão, D.A., Spry, N. and Baker, M.K., 2013. A systematic review of pre-surgical exercise intervention studies with cancer patients. Surgical oncology, 22(2), pp.92-104.	Relevant included trials represented in a more recent systematic review
Olsén, M.F. and Anzén, H., 2012. Effects of training interventions prior to thoracic or abdominal surgery: a systematic review. Physical Therapy Reviews, 17(2), pp.124-131.	Relevant included trials represented in a more recent systematic review
Jack, S., West, M. and Grocott, M.P.W., 2011. Perioperative exercise training in elderly subjects. Best practice & research Clinical anaesthesiology, 25(3), pp.461-472.	Not a systematic review
Nagarajan, K., Bennett, A., Agostini, P. and Naidu, B., 2011. Is preoperative physiotherapy/pulmonary rehabilitation beneficial in lung resection patients? Interactive cardiovascular and thoracic surgery, 13(3), pp.300-302.	Relevant included trials represented in a more recent systematic review
Valkenet, K., van de Port, I.G., Dronkers, J.J., de Vries, W.R., Lindeman, E. and Backx, F.J., 2011. The effects of preoperative exercise therapy on postoperative outcome: a systematic review. Clinical rehabilitation, 25(2), pp.99-111.	Relevant included trials represented in a more recent systematic review

Appendix S4. Randomised controlled trials and systematic reviews used in the evidence section of this statement

Systematic review: Cavalheri V, Granger C Preoperative exercise training for patients with non-small cell lung cancer. Cochrane Database Syst Rev 2017; 6: CD012020.

Relevant RCTs included in this review:

Lai Y, Huang J, Yang M, Su J, Liu J, Che G. Seven-day intensive preoperative rehabilitation for elderly patients with lung cancer: a randomized controlled trial. Journal of Surgical Research 2017; 209: 30-6.

Benzo R, Wigle D, Novotny P, et al. Preoperative pulmonary rehabilitation before lung cancer resection: results from two randomized studies. Lung Cancer 2011; 74: 441-5.

Pehlivan E, Turna A, Gurses A, Gurses HN The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. Ann Thorac Cardiovasc Surg 2011; 17: 461-8.

Stefanelli F, Meoli I, Cobuccio R, et al. High-intensity training and cardiopulmonary exercise testing in patients with chronic obstructive pulmonary disease and non-small-cell lung cancer undergoing lobectomy. Eur J Cardiothorac Surg 2013; 44: e260-5.

Morano MT, Araujo AS, Nascimento FB, da Silva GF, Mesquita R, Pinto JS, et al. Preoperative Pulmonary rehabilitation versus chest physical therapy in patients undergoing lung cancer resection: A pilot randomized controlled trial. Archives of Physical Medicine and Rehabilitation 2013; 94: 53-8.

Systematic review: Hijazi Y, Gondal U, Aziz O A systematic review of prehabilitation programs in abdominal cancer surgery. Int J Surg 2017; 39: 156-62.

Relevant RCTs included in this review:

Carli F, Charlebois P, Stein B, et al. Randomized clinical trial of prehabilitation in colorectal surgery. Br J Surg 2010; 97: 1187-97.

Dunne DFJ, Jack S, Jones RP, et al. Randomized clinical trial of prehabilitation before planned liver resection. Br J Surg 2016; 103: 504-12.

Dronkers JJ, Lamberts H, Reutelingsperger IM, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. Clin Rehabil 2010; 24: 614-22.

Kim, DJ, Mayo NE, Carli F, et al. Responsive measures to prehabilitation in patients undergoing bowel resection surgery, Tohoku J Exp Med 2009; 217: 109-15.

Banerjee S, Manley K, Thomas L, et al. Preoperative exercise protocol to aid recovery of radical cystectomy: results of a feasibility study. European Urology 2013; Suppl. 12: 125.

Systematic review: Moran J, Guinan E, McCormick P, et al. The ability of prehabilitation to influence postoperative outcome after intra-abdominal operation: A systematic review and meta-analysis. Surgery 2016; 160: 1189-201.

Relevant RCTs included in this review:

Barbalho-Moulim MC, Miguel GP, Forti EM, Campos FoA, Costa D Effects of preoperative inspiratory muscle training in obese women undergoing open bariatric surgery: respiratory muscle strength, lung volumes, and diaphragmatic excursion. Clinics (Sao Paulo) 2011; 66: 1721-7.

Kulkarni SR, Fletcher E, McConnell AK, Poskitt KR, Whyman MR. Pre-operative inspiratory muscle training preserves postoperative inspiratory muscle strength following major abdominal surgery---A randomised pilot study. Ann R Coll Surg Engl 2010; 92: 700-5.

Soares SM, Nucci LB, da Silva MM, Campacci TC. Pulmonary function and physical performance outcomes with preoperative physical therapy in upper abdominal surgery: A randomized controlled trial. Clin Rehabil 2013; 27: 616-27.

Dronkers J, Veldman A, Hoberg E, van der Waal C, van Meeteren N Prevention of pulmonary complications after upper abdominal surgery by preoperative intensive inspiratory muscle training: a randomized controlled pilot study. Clin Rehabil 2008; 22: 134-42.

Carli F, Charlebois P, Stein B, et al. Randomized clinical trial of prehabilitation in colorectal surgery. Br J Surg 2010; 97: 1187-97.

Dronkers JJ, Lamberts H, Reutelingsperger IM, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. Clin Rehabil 2010; 24: 614-22.

van Adrichem EJ, Meulenbroek RL, Plukker JT, Groen H, van Weert E Comparison of two preoperative inspiratory muscle training programs to prevent pulmonary complications in patients undergoing esophagectomy: a randomized controlled pilot study. Ann Surg Oncol 2014; 21: 2353-60.

Systematic review: Loughney L, West MA, Kemp GJ, Grocott MP, Jack S Exercise intervention in people with cancer undergoing neoadjuvant cancer treatment and surgery: A systematic review. Eur J Surg Oncol 2016; 42: 28-38.

Relevant RCTs included in this review:

Hornsby WE, Douglas PS, West MJ, et al. Safety and efficacy of aerobic training in operable breast cancer patients receiving neoadjuvant chemotherapy: a phase II randomized trial. Acta Oncol 2014; 53: 65-74.

Rao R, Cruz V, Peng Y, et al. Bootcamp during neoadjuvant chemotherapy for breast cancer: a randomized pilot trial. Breast Cancer (Auckl) 2012; 6: 39-46.

Additional individual trials

Barberan-Garcia A, Ubré M, Roca J, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. Ann Surg 2017.

Licker M, Karenovics W, Diaper J, et al. Short-Term Preoperative High-Intensity Interval Training in Patients Awaiting Lung Cancer Surgery: A Randomized Controlled Trial. J Thorac Oncol 2017; 12: 323-33.

Barakat HM, Shahin Y, Khan JA, McCollum PT, Chetter IC Preoperative Supervised Exercise Improves Outcomes After Elective Abdominal Aortic Aneurysm Repair: A Randomized Controlled Trial. Ann Surg 2016; 264: 47-53.

Tew GA, Batterham AB, Colling K, et al. Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair. Br J Surg 2017.

Appendix S5. Intervention details from included trials

Trial	Materials/provider/setting	Delivery/dosage/tailoring	Adherence
Rationale for exercise = to reduce post-operative pulmonary complications by improving pulmonary function			
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 manoeuvers 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).
Dronkers 2008	*Materials*: 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

	Provider: "experienced physical therapist" (one session per week) and unsupervised (five sessions per week) *Setting*: partly home-based	session/week was supervised by the same physical therapist and the other five sessions were unsupervised. The participants were instructed to keep a daily diary during the study and were trained to use an inspiratory threshold-loading device (Threshold IMT®). IMT sessions were initiated at 20% of MIP, and the resistance was increased incrementally to maintain a hard level of perceived exertion. Both study groups also received pre-operative "usual care" consisting of instruction in diaphragmatic breathing, deep inspirations with the aid of incentive spirometer, and coughing and forced expiration techniques.	
Rationale for exercise = to reduce post-operative pulmonary complications by improving pulmonary function and cardiorespiratory fitness			
Lai 2017	*Materials*: NuStep recumbent cross trainer, Voldyne 5000 respiratory training devices *Provider*: physiotherapist *Setting*: Hospital ward and rehabilitation centre	Daily abdominal breathing exercises, expiration exercises and endurance exercise training for one week. For the abdominal exercises, the patients slowly inhaled to their maximum lung capacity through their nose, held their breath for a short period, and then exhaled slowly through their lips with their abdominal muscles tightened: performed for 15 to 20 minutes twice per day. For the expiration exercises, a simple respiratory training device was used. The patients were guided to exhale calmly at the beginning, to then deeply inhale through the suction nozzle of the training device, and to finally exhale slowly after holding their breath for several seconds: performed for 20 minutes 3 times per day. For the endurance exercise training, a NuStep recumbent cross trainer was used. The patients adjusted the resistance gear range according to their own speed and power at first and then increased the resistance range progressively. During the training, the procedure was stopped if the patients had any obvious discomfort, such as shortness of breath, dyspnoea, or exhaustion. The patients were allowed to rest until their condition could withstand subsequent training. This pattern lasted 30 minutes daily.	Not reported
Morano 2013	*Materials*: Treadmill, Threshold IMT® device *Provider*: not reported *Setting*: "teaching hospital"	Five sessions of IMT and treadmill walking exercise per week for four weeks. IMT was performed using the Threshold IMT® device for 10 to 30 minutes per session. Patients started breathing at a resistance that required generation of 20% of their MIP and kept this intensity during the first week. The load was then increased by 5 to 10% each session, to reach a generation of 60% of their MIP at the end of the first month. The walking exercise was done for 10 to 30 minutes per session; 10 minutes for the first week, 20 minutes for the second week, and 30 minutes thereafter. Exercise intensity was based on 80% of the maximum load achieved during a treadmill incremental test. Flexibility, stretching, and balance exercises were also included as part of the warm-up and cool-down section of each exercise session.	All patients completed 5 sessions per week for 4 weeks.

Stefanelli 2013	*Materials*: Bench, mattress pad, wall bars, rowing ergometer, treadmill, cycle ergometer *Provider*: Not reported *Setting*: “outpatient”	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.	Not reported
Benzo 2011 (second study)	*Materials*: Treadmill, NuStep recumbent cross training, arm ergometer, TheraBand, Threshold IMT® or P-Flex valve devices *Provider*: unclear but weekend sessions were unsupervised *Setting*: “Mayo Clinic”	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.
Pehlivan 2011	*Materials*: incentive spirometer, treadmill, heart rate monitor, pulse oximeter *Provider*: physical therapist from the surgery department *Setting*: not reported	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.
Rationale for exercise = to reduce post-operative pulmonary complications and enhance the post-operative recovery of functional capacity			
Soares 2013	*Materials*: Gym space, Threshold IMT® devices	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

	Provider: physical therapist (two sessions per week) and unsupervised (four sessions per week) *Setting*: unclear, but partly home-based	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 cmH_2O 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.	reported full adherence with the home-based respiratory muscle training and walking.
Rationale for exercise = to reduce post-operative complications and enhance the post-operative recovery of functional capacity			
Carli 2010 (cycling/ strengthening group)	*Materials*: stationary cycle, heart rate monitor, "weights" *Provider*: unsupervised exercise *Setting*: McGill University Health Centre	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.	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).
Dronkers 2010	*Materials*: free weights or resistance exercise machines, IMT devices, aerobic exercise machines, heart rate monitors *Provider*: physical therapists (two sessions per week) and unsupervised (daily)	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	The mean number of training sessions was 5.1 ± 1.9. The attendance at training sessions was 97%.

	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.	
Rationale for exercise = to reduce post-operative complications by improving cardiorespiratory fitness			
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.	The mean duration of the prehabilitation programme was 6 ± 2 weeks and during this period patients attended 12 ± 5 supervised exercise training sessions.
Tew 2017	*Materials*: cycle ergometer, heart rate monitor, stethoscope and sphygmomanometer, CPET equipment to determine baseline power output at anaerobic threshold and $\dot{V}O_2$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	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

	Setting: Hospital physiotherapy gym	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.	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).
Licker 2017	*Materials*: cycle ergometer, resistance exercise machines *Provider*: physiotherapists (two to three sessions per week) and unsupervised (four sessions per week) *Setting*: Hospital outpatient clinic	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.	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).
Barakat 2016	*Materials*: cycle ergometer, assorted-weight dumbbells, exercise steps, treadmill *Provider*: unclear *Setting*: Hospital physiotherapy gym	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-raise 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.	Attended 0 classes: n=11 Attended 6-12 classes: n=19 Attended 13-18 classes: n=32 (of which 18 attended all 18 classes)
Dunne 2014	*Materials*: cycle ergometer, CPET equipment to determine VO_2peak *Provider*: "clinicians"	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	18 of 19 exercise-group participants completed 100% of the exercise sessions, with one patient missing two sessions whilst having

	Setting: tertiary hepatobiliary centre	between exercise of moderate (<60% of $\dot{V}O_2$peak) and vigorous (>90% $\dot{V}O_2$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.	emergency colonic stenting for an obstructing primary tumour.
Banerjee 2013	*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	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.	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.
Kim 2009	*Materials*: cycle ergometer, heart rate monitor *Provider*: unsupervised *Setting*: participant's home	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.	The prehabilitation group underwent 3.8 ± 1.2 weeks (27 ± 9 sessions) of pre-operative exercise training. The compliance was 74 ± 16%.
Rationale for exercise = to improve or maintain cardiopulmonary/cardiometabolic health during neoadjuvant chemotherapy			
Hornsby 2014	*Materials*: cycle ergometer, CPET equipment *Provider*: unclear *Setting*: unclear	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	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

		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