BMJ Open

Prehabilitation in elective patients undergoing cardiac surgery: a randomised control trial (THE PrEPS TRIAL) – a study protocol

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To cite: Akowuah E, Mathias A, Bardgett M, *et al*. Prehabilitation in elective patients undergoing cardiac surgery: a randomised control trial (THE PrEPS TRIAL) – a study protocol. *BMJ Open* 2023;**13**:e065992. doi:10.1136/bmjopen-2022-065992

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065992).

Received 23 June 2022
Accepted 09 December 2022

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ABSTRACT

Introduction Prehabilitation prior to surgery has been shown to reduce postoperative complications, reduce length of hospital stay and improve quality of life after cancer and limb reconstruction surgery. However, there are minimal data on the impact of prehabilitation in patients undergoing cardiac surgery, despite the fact these patients are generally older and have more comorbidities and frailty. This trial will assess the feasibility and impact of a prehabilitation intervention consisting of exercise and inspiratory muscle training on preoperative functional exercise capacity in adult patients awaiting elective cardiac surgery, and determine any impact on clinical outcomes after surgery.

Methods and analysis PrEPS is a randomised controlled single-centre trial recruiting 180 participants undergoing elective cardiac surgery. Participants will be randomised in a 1:1 ratio to standard presurgical care or standard care plus a prehabilitation intervention. The primary outcome will be change in functional exercise capacity measured as change in the 6 min walk test distance from baseline. Secondary outcomes will evaluate the impact of prehabilitation on preoperative and postoperative outcomes including; respiratory function, health-related quality of life, anxiety and depression, frailty, and postoperative complications and resource use. This trial will evaluate if a prehabilitation intervention can improve preoperative physical function, inspiratory muscle function, frailty and quality of life prior to surgery in elective patients awaiting cardiac surgery, and impact postoperative outcomes.

Ethics and dissemination A favourable opinion was given by the Sheffield Research Ethics Committee in 2019. Trial findings will be disseminated to patients, clinicians, commissioning groups and through peer-reviewed publication.

Trial registration number ISRCTN13860094.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Largest pragmatic trial combining exercise and inspiratory muscle training for the first time in this population.
⇒ Will establish if a prehab intervention is feasible and if it is effective in improving overall functional exercise capacity prior to surgery.
⇒ Robust assessment of fidelity of the intervention and compliance.
⇒ Important accelerometer substudy to explore change in activity levels and qualitative sub study to explore views and experiences of patients and staff.
⇒ Limited to single centre but will provide critical safety data essential for wider implementation.

INTRODUCTION

Over 35 000 patients undergo cardiac surgery every year in the UK alone.[1] Over the last decade, the average age of these patients has increased worldwide, as has the prevalence of patients with multiple comorbidities having cardiac surgery.[2] This has the potential to increase mortality, morbidity and resource use resulting from increasing rates of postoperative complications and associated prolonged use of hospital resources.

Prehabilitation programmes are fast becoming a method of being pro-active prior to surgery with the aim of reducing postoperative complications and mortality, giving patients themselves a method of managing their fitness presurgery; ultimately with the aim of speeding up recovery and return to normal function after surgery. A BMJ editorial in September 2017[3] highlighted the urgent need to recognise that the drive to improve outcomes after surgery must include optimising patients' health prior to surgery with evidence-based prehabilitation programmes. It recognised that programmes would have to be tailored for patients and specific interventions.

In cardiac surgery, however, there have been few trials investigating the impact of

prehabilitation. Primarily, concerns around safety due to delaying intervention to allow prehabilitation to occur and the impact of exercise as part of the intervention has contributed to a lack of trial data. This is despite evidence that exercise interventions can improve cardiovascular function and fitness; an important predictor of mortality in older patients.[4] Poor cardiovascular fitness is known to be associated with higher all-cause mortality.[5]

In patients awaiting cardiac surgery, the concern has been that severe coronary and valvular lesions, for example, severe aortic stenosis, cause symptoms with exercise and may precipitate complications. Furthermore patients are frequently told by their clinicians not to exercise while they wait for surgery. Moreover, severe aortic stenosis, left main stem stenosis, unstable angina, aortic aneurysms and other cardiac condition are all contraindicated in most exercise and rehabilitation protocols currently used in the UK.[6]

There is emerging evidence that patients with severe cardiac conditions can undergo exercise safely. The 6 min walk test (6MWT) was shown to be safe in a feasibility study of 244 patients with chronic lung or heart disease with no instances of adverse events (AEs).[7] A trial in which low-risk patients awaiting electives coronary artery bypass surgery underwent high-intensity treadmill training reported no significant adverse effects.[8] However, neither of these trials included patients with severe cardiac conditions awaiting surgical intervention. A recent trial in patients with large abdominal aortic aneurysms awaiting repair has showed that even high-intensity interval training appeared to be safe and beneficial.[9] These data have suggested that exercising patients awaiting cardiac surgery may be safe, therefore, stimulating further interest in the role of exercise based prehabilitation prior to cardiac surgery.

Inspiratory muscle training (IMT) has the most evidence for improving outcomes after thoracic and cardiac surgery. This is most commonly achieved using inspiratory threshold-loading devices (threshold-IMT), which increase respiratory muscle strength and endurance, in turn improving respiratory volume and sputum clearance,[10] thereby reducing postoperative pulmonary complications (PPCs). In cardiac surgery, preoperative IMT has been shown to reduce PPCs and have a modest effect on postoperative length of stay in high-risk patients with pre-existing chronic obstructive pulmonary disorder after surgery.[11] This finding has been confirmed in a number of systematic reviews and meta-analyses.[12–14] A large multicentre trial funded by the National Institute for Health and Care Research (The INSPIRE Trial) to provide definitive evidence of benefit of IMT is currently ongoing.

To date, no randomised control trial (RCT) has combined IMT with exercise in a prehabilitation intervention to determine the impact in patients undergoing cardiac surgery.

A trial is urgently needed to determine if patients with severe cardiac conditions can undergo prehabilitation safely prior to cardiac surgery. This was corroborated by a priority setting exercise conducted by The James Lind Alliance in the UK in 2019, to identify the top 10 research priorities for adult cardiac surgery research. In this Delphi style, consensus exercise involving nearly 1000 patients and stakeholders, research to determine if prehabilitation benefited patients prior to cardiac surgery was the fourth most important of the ten priority research areas.[15]

The PrEPs trial will evaluate if a prehabilitation intervention consisting of exercise and IMT in patients awaiting elective cardiac surgery can improve preoperative physical function, inspiratory muscle function, frailty and quality of life prior to surgery. Other assessments include the impact of the intervention on postoperative clinical outcomes, speed of return to normal activity, patients' recovery from surgery and quality of life after surgery.

METHODS/ANALYSIS

Trial design

A single-centre prospective, parallel group randomised controlled trial will be conducted to compare the effect of a prehabilitation intervention on functional, physical and clinical outcomes compared with standard care. Participants will be randomly allocated 1:1 to either standard care or the intervention. Participants allocated to standard care will receive routine preoperative advice only. Participants allocated to the intervention will receive routine preoperative advice and a prehabilitation intervention consisting of supervised cardiac exercise sessions, high intensity IMT and a home exercise programme.

Participants will be followed up at routine clinical appointments prior to surgery, during surgical admission, and at 6 and 12 weeks following index surgery (figure 1). After the intervention period, all participants will continue with the site's standard preoperative and postoperative care.

Objectives

The primary objective is to assess the impact of a preoperative rehabilitation intervention (prehabilitation) on preoperative functional exercise capacity (measured by change in the 6MWT) from baseline in patients awaiting cardiac surgery.

The secondary objectives are to evaluate the impact of prehabilitation on outcomes including; respiratory function (measured by maximal inspiratory pressure (MIP)), health-related quality of life (measured by the EuroQol 5 Dimension scale questionnaire) (EQ-5D-5L), anxiety and depression (measured by the Hospital Anxiety and Depression Scale (HADS) and frailty (measured by grip strength) after the prehabilitation intervention.

The tertiary objectives are to evaluate the impact of prehabilitation on postoperative complication rates, including length of hospital stay, PPCs and health-related quality of life up to 12 weeks after surgery.

Two substudies will also explore: the use of activity monitors to measure change in objectively measured physical activity from baseline to postintervention, and

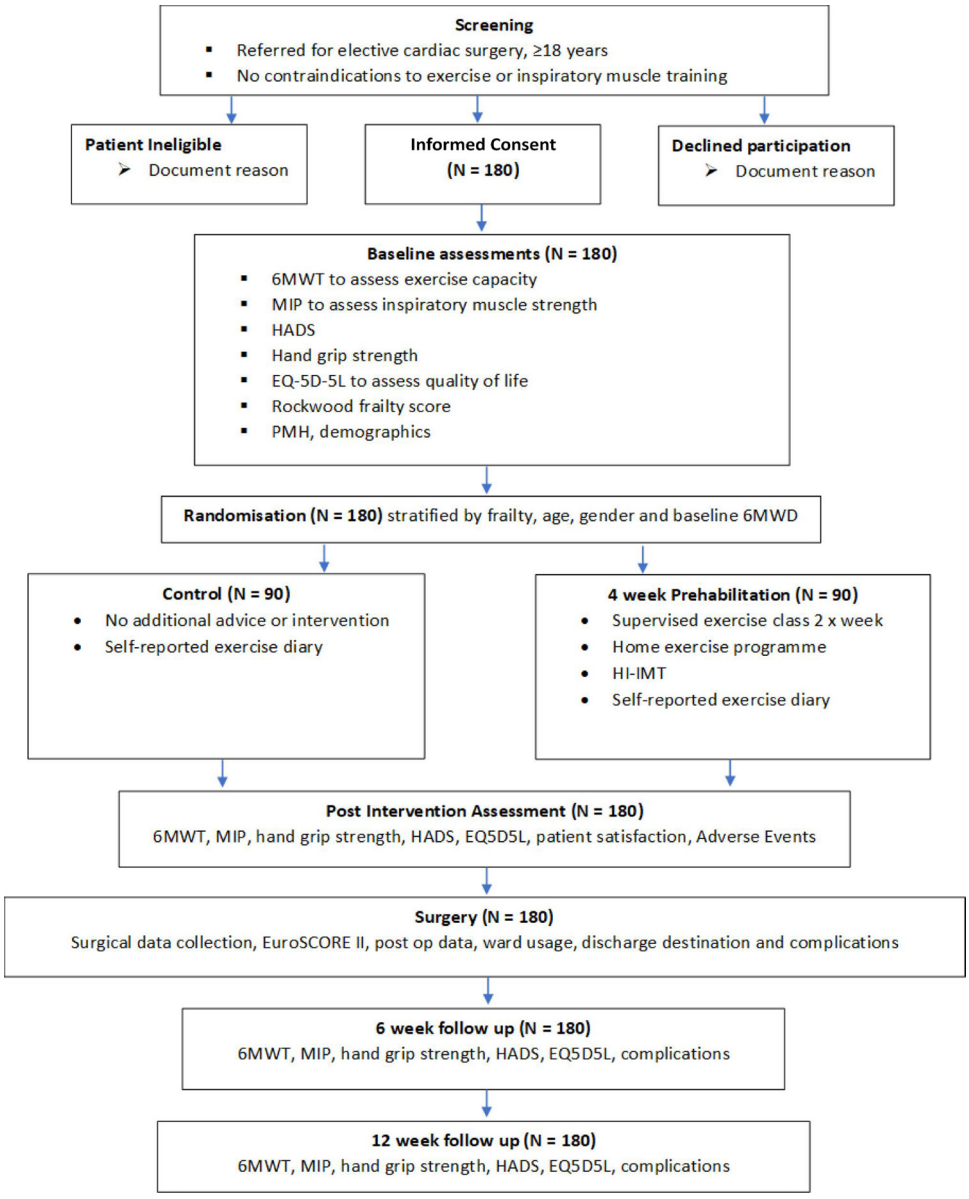

Figure 1 CONSORT diagram to show research activity in the PrEPS trial—this consort diagram depicts the stages throughout the trial from screening, randomisation, intervention and through the various follow-up stages. A summary of which assessments are conducted is provided at each stage.

the experiences of prehabilitation prior to elective cardiac surgery through the opinions of trial participants and the healthcare professionals responsible for prehabilitation delivery.

Eligibility

Patients aged 18 and over listed for elective cardiac surgery under the care of the participating surgeons will be screened for eligibility.

Box 1 describes the exclusion criteria in detail specific to the trial.

Recruitment

Adults listed for elective cardiac surgery will be screened by the clinical team and given a patient information sheet and letter of invitation prior to their routine clinic appointment. Eligibility will be confirmed by a clinician at the time of listing for surgery. Written informed consent (see online supplemental material consent form v4.0) will be obtained before any trial procedures are performed.

Baseline data collection

Baseline assessments will be performed after consent and prior to randomisation. Women of childbearing potential will perform a pregnancy test to confirm pregnancy status before undertaking any further research activity. The baseline assessments will consist of the 6MWT, MIP, EQ5D5L questionnaire, activity monitoring (optional), HADS, Rockwood frailty score (nine-point Clinical Frailty Scale) and hand grip strength. Participants' medical notes will be used to collect a full medical history, gender, height and weight, and date of birth/age. Participants consenting to take part in the 7-day activity monitoring substudy will be

Box 1 Exclusion criteria

Exclusion criteria.
Unstable angina/indication for urgent surgery.
Malignant arrhythmias.
Currently participating in another interventional clinical trial.
Known pregnancy.
Contraindications to known cardiac rehabilitations:
⇒ Acute systemic illness or fever.
⇒ Uncontrolled atrial or ventricular arrhythmias.
⇒ Uncontrolled sinus tachycardia (heart rate>120 bpm).
⇒ Aortic stenosis with presyncope/syncope.
⇒ Acute pericarditis or myocarditis.
⇒ Uncompensated Heart Failure.
⇒ Third degree (complete) atrioventricular block without pacemaker.
⇒ Recent embolism.
⇒ Severe musculoskeletal conditions that would prohibit exercise.
Contraindications to inspiratory muscle training:
⇒ History of spontaneous pneumothorax/incomplete recovery following traumatic pneumothorax.
⇒ Asthma patients who suffer from frequent, severe exacerbations.
⇒ Recently perforated ear drum (within last 3 months).
⇒ Large bullae.

provided with an accelerometer, instructions on it use, and options for returning the accelerometer.

Randomisation

Participants will be randomised in a 1:1 ratio to either the control arm (standard care only), or the intervention arm (standard care plus the prehabilitation intervention) using a 24-hour, central, secure, web-based system (SealedEnvelope). Randomisation will be performed using a minimisation scheme that takes into account Rockwood frailty score, 6MWD, age and gender to balance baseline physical fitness between the arms. It will not be possible to conceal the allocation of treatment from the participant, or the team delivering the intervention and measuring the primary outcome. The surgeons performing the participants' cardiac surgery will not be informed of the allocation, however, they will not be officially blinded.

Outcome measures

The primary outcome will be changed in exercise capacity measured by the 6MWT from baseline to presurgical assessment. This is a self-paced 6 min walk recording the distance walked in metres around a 25 m standardised track.

This outcome was chosen because preoperative 6MWT distance is associated with moderate or severe complications after both non-cardiac surgery[16] and cardiac surgery.[17] It has also been validated as an indicator of recovery in patients undergoing cardiac surgery.[18]

All participants will receive standardised instruction and support.[19] A pulse oximeter will be attached to the participant during the walk for continuous monitoring of oxygen saturations and heart rate (HR). The test will be performed twice at baseline to account for a learning effect; the distance achieved on the two walks will be recorded and the highest value used for baseline measurement. The 6MWT will be repeated once at 6 and 12 weeks following index surgery to assess the postoperative impact of prehabilitation.

Table 1 Secondary outcome measures

Secondary outcomes	Measurement
Change in Inspiratory muscle strength	Maximal inspiratory pressure
Frailty	Hand Grip strength
Quality of life	EQ-5D-5L
Anxiety and depression	Hospital Anxiety and Depression Scale

The secondary outcome measures in table 1 will be collected at baseline, presurgical assessment, 6 and 12 weeks following index surgery.

MIP is used to measure inspiratory muscle strength and will be measured using a hand-held electronic transducer (POWERbreath KH2 (HaB, UK), according to guidelines set out in the American Thoracic Society/European Respiratory Society statement of 2002.[20]

Hand grip strength will be used as an objective measurement of frailty. Participants will be asked to grip a dynamometer (Jamar hydraulic hand dynamometer) as hard as they can using their dominant hand while being seated. The highest grip strength of three attempts will be recorded.

Two patient reported questionnaires will be collected; the EQ-5D-5L general health questionnaire[21] consists of five domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a standard vertical 20 cm EuroQol Visual Analogue Scale on a scale of 0–100 measuring current health-related quality of life. The health state of each participant will be measured before and after the intervention period and postsurgery to determine any change in their health (gain or loss). The HADS self-reported questionnaire consists of 14 questions (7 for anxiety and 7 for depression) rated on a Likert-type scale from 0 to 3[22]and will be used to evaluate participants' mood.

In addition, surgical and postoperative data will be collected from participants' medical notes including: duration of operation, cardiopulmonary bypass times, time onintensive care unit and discharge information. Pulmonary and cardiac complications will be documented as outlined in table 2.

Substudies

Accelerometer substudy

Participants in both trial arms will be invited to take part in an accelerometer substudy. We anticipate that 50%–60% of the trial cohort will take part in the substudy, however, this trial is ongoing, and therefore, these data are not yet available. Participants will wear an activity monitor on their non-dominant wrist for a continuous period of

Table 2 Pulmonary cardiac complications

Postoperative cardiac surgery complications	
Renal failure/acute kidney injury, tracheostomy, delirium, transient ischemic attack, stroke, new atrial fibrillation, RBC transfusion, blood product transfusion, cardiac arrest, myocardial infarction, all-cause mortality, infection (in-hospital only), or sepsis (6-week and 12-week follow-up only)	
Pulmonary complications	
Grade 1	▶ New-onset purulent sputum or change in character of chronic sputum ▶ Fever with no focus outside of the lungs ▶ New rise in C reactive protein or white blood cell count, positive blood culture ▶ Atelectasis radiological finding or abnormal lung findings requiring non-invasive intervention ▶ Hypoxaemia ▶ Administration of additional postoperative antibiotics ▶ Transtracheal aspirate
Grade 2	▶ Pleural effusion needing drainage ▶ Lung infection ▶ Pneumothorax ▶ Postoperative reintubation ▶ Clinically significant atelectasis requiring tracheobronchial suction
Grade 3	▶ Ventilatory failure with postoperative ventilator dependence >8 hours ▶ Reintubation with a subsequent period of ventilation >48 hours

Table 3 Participant initial assessments to gauge physical fitness

Subjective assessment	
1	General well-being
2	Recent health issues and medical history
3	Fitness and activity levels
4	Anxiety levels
5	Social circumstances and support
Objective Assessment	
1	HR and Blood Pressure measurements
2	ECG if indicated
3	Respiratory function (rate, breathing pattern and auscultation with stethoscope)
4	Musculoskeletal system (joint range and muscle strength)
5	Other physical problems

HR, heart rate.

7 days at baseline and after the intervention period. Data collected will be processed using the GGIR package in R[23] to explore change in activity levels (including time spent in moderate to vigorous physical activity (MVPA), light physical activity and sedentary behaviour), change in MVPA and between the control and intervention group. The correlation between 7-day activity monitor data and patient reported activity diaries preintervention and postintervention will also be explored.

Qualitative substudy

Participants in both arms will be offered the opportunity to take part in a focus group exploring their experiences of the taking part in the PrEPS trial. Written informed consent (see online supplemental material qualitative consent v2.0) will be obtained for each participant. Participants within the intervention and control arms of the trial will attend separate focus groups which will take place after the 12-week postoperative assessment to avoid interference with 12-week patient-reported outcomes.

Focus groups will also take place with HCPs involved in the delivery of prehabilitation to explore their experiences of delivering the intervention as part of the PrEPS trial.

Focus group recordings will be transcribed verbatim and analysed using a deductive thematic analysis.[24] Themes will be mapped against theoretical constructs of normalisation process theory to highlight relationships and overlap between themes.[25]

Standard care

Participants randomised to the standard care group will continue with routine preoperative care, consisting of specialist nurse review, meeting the surgeon and anaesthetist, and receiving information regarding preparation for surgery. Participants will be provided with a patient diary and asked to document any form of exercise that they carry out independently as well as healthcare visit details to aid collection of AEs.

Prehabilitation intervention

Participants randomised to the intervention group will receive standard care and a hospital-based prehabilitation intervention consisting of an initial fitness assessment, a supervised exercise programme twice a week for 4 weeks, an unsupervised home exercise programme consisting of up to 45 min of prescribed daily exercise and high intensity-IIMT (HI-IMT) involving twice daily training for a duration of 4 weeks.

Initial assessment

At the first cardiac prehabilitation visit, participants will be assessed by a cardiac rehab specialist physiotherapist and nurse to gauge their physical fitness. This involves a subjective and objective assessment; table 3 details these assessments.

Participants will also be seen by a respiratory physiotherapist and instructed on how to carry out HI-IMT. Participants will be given their own device (a POWERbreathe medic plus (HaB)) and an instruction leaflet/diary to use at home.

Supervised exercise programme

The maximum HR and target HR will be calculated for each participant. Exercise intensity will be individually prescribed using the combined results of the initial fitness assessment and the baseline 6MWT. The physiotherapist will discuss the principles of the prescribed exercise with the participant and any precautions they should take to mitigate injury and illness. Participants will be encouraged to achieve a predicted target HR of 60%–75% max

Table 4	Stages of cardiac prehabilitation programme
Stage 1	15 min warm up consisting of preparatory stretches
Stage 2	Up to 25 min of cardiovascular exercise and resistance-based training with active recovery
Stage 3	15 min cool down period including maintenance stretches

and a moderate BORG score (12 or 13) during their cardiovascular exercise with actual figure achieved being recorded.

The cardiac prehabilitation exercise sessions will consist of three stages listed in table 4.

Home exercise programme

Participants will be asked to perform up to 45 min of exercise at home (unsupervised) up to seven times a week during the 4-week intervention period. This exercise will be tailored to the individual participant's ability based on their physical fitness assessment and their baseline 6MWT results. Progress will be discussed with the participant once a week during the prehabilitation classes. As this is unsupervised, the intensity will be lower than that prescribed for the supervised classes. Participants will be set achievable targets and have their exercise progressed if they have managed comfortably during the week as measured by their self-reported Borg scores and diaries.

High intensity-inspiratory muscle training

Participants will be asked to perform HI-IMT twice a day for 4 weeks at home starting from their first supervised exercise session. Using their device, participants will be asked to breathe in as forcefully as possible before slowly breathing out six times, then rest, before performing another set of six breaths. There will be six sets of six breaths in each HI-IMT training session. The resting time between the sets starts at 60 s and decreases by 15 s after each set, ending with a rest period of 5 s before the final set.

The device will be set at 50% of their MIP. Participants will be shown how to increase or decrease the resistance on their device to train with a difficulty level of 'somewhat hard', which is equivalent to a Borg score of 12–13. This will be highlighted in the instruction booklet/diary. Participants will have their HI-IMT technique checked once a week during their prehabilitation classes to ensure they are training effectively.

End of intervention

The end of the intervention is the final prehabilitation class. On completion of the 4-week intervention period, participants will be encouraged to continue with home exercise and IMT independently until their day of surgery and document any activity in their patient diary.

Fidelity of the intervention

The five domains of the treatment fidelity framework, provided by the National Institutes of Health's Behavioural Change Consort will be assessed to ensure fidelity of the prehabilitation intervention throughout the trial.[26] Table 5 details these domains.

In addition to the above, self-monitoring data will be collected via exercise diaries.

Assessment of compliance

Self-reported patient diaries and prehabilitation attendance records will be used to measure adherence to the intervention. Adherence was defined as completing 50% of the supervised exercise classes (four out of eight sessions) in-line with documented adherence rates to cardiac rehabilitation.[27–29] Exercise diaries will capture the physical activity completion for the unsupervised component.

Patient and public involvement

Patients and members of the public were involved in identifying prehabilitation in this population as a research priority and in the design of the trial. Cardiac rehabilitation patients were consulted in the development of the prehabilitation intervention and relevant trial documentation. A patient representative is a member of the Trial Oversight Committee (TOC) to ensure patient and public involvement (PPI) input throughout the entirety of the trial. Findings will also be disseminated to participants and relevant patient groups.

End of trial

The end of the clinical trial is defined as the 12-week follow-up of the last participant. Data queries will be addressed for a period of up to 3 months following this. Participants may choose to withdraw from the trial at any time. Clinicians may also choose to withdraw participants at any time for reasons including non-compliance, AEs and pregnancy.

Table 5	Five domains of the treatment fidelity framework in line with assessments to record fidelity
1	Study design issues will ensure the 'treatment dose' in each condition is fixed
2	Monitoring and improving the intervention will involve standardising the process by providing interventionists with a protocol
3	Fidelity of intervention delivery will involve a single observation of an exercise class to ensure delivery is per-protocol. A checklist will then be completed at 6 monthly intervals to ensure consistency in delivery
4	Receipt of treatment by patients (did they understand how to undergo the exercises)
5	Enactment of treatment skills by patients (eg, did they engage in a home exercise programme) will be assessed during focus groups conducted within the qualitative substudy

Safety reporting

The safety of delivering a prehabilitation intervention a key outcome of the trial. Although there is now some evidence of a low risk to patient safety from studies where physical activity has been assessed in patients with cardiac and/or pulmonary conditions, there is no such evidence in patients with severe cardiac conditions awaiting cardiac surgery.

To mitigate any safety concerns of participants, clinician and other stakeholders, the trial is designed so that the most intensive exercise intervention will be carried out within a hospital setting. Lower intensity exercise will be prescribed at home after assessment each week by the trial team.

AEs and SAEs will be collected and monitored throughout the trial. Due to the nature of the study, population identified expected AEs, including angina, breathlessness, light-headedness, arrhythmia and fatigue.

The relationship between the intervention (prehabilitation) and the occurrence of each AE will be assessed and categorised by the chief investigator (or delegate). Serious events that are unexpected and related, will be reported to the REC committee within 15 days of notification.

It is crucial that safety is monitored throughout the trial so that any findings may be used in future trials, particularly when considering if this practice can be circulated across the wider community and out of hospitals settings.

STATISTICAL ANALYSIS

Primary and secondary outcomes will be analysed following the intention-to-treat principle, with patients analysed according to randomisation regardless of whether they actually received or adhered to the allocated treatment. Per-protocol and as-treated analyses may be conducted as sensitivity and exploratory analyses. A full statistical analysis plan will be developed and agreed with the TOC before data collection is completed. Data will be analysed at the end of the study; no interim outcome analyses are planned.

The primary analysis testing the impact of the cardiac prehabilitation programme on preoperative functional exercise capacity (measured by 6MWD) will be based on a linear mixed-effects model accounting for baseline randomisation factors, except for baseline 6MWD, which is explicitly incorporated in the model to calculate change from baseline. The model will account for intrapatient correlation using a random intercept model. Subgroup analyses conducted for the primary outcome will be prespecified in the analysis plan. All continuous secondary outcomes will be analysed using the same approach as used for the primary outcome. All non-continuous data will be analysed in the same way, but with a generalised linear model using the appropriate distributional assumptions and link function. Descriptive analysis will be used to explore outcomes related to the feasibility of the trial. Analyses will be conducted using R statistical software.

Sample size

The sample size is based on detecting a significant improvement in 6MWD after the prehabilitation programme compared with the 6MWD at baseline. We have assumed a minimal clinically important difference in 6MWD of 25 m with an SD of 56.5 m for preoperative participants.[30] Based on detecting a medium effect size of 0.44, 164 participants (82 in each group) will provide 80% power to detect a difference of 25 m in the 6MWD. Adjusting for 10% missing data, 180 participants will be recruited for the trial.

Data

Data will be entered at site onto an electronic case report form for each participant. The database will be hosted by Sealed Envelope who abide by the general data protection regulations (GDPR) and are responsible for the security of the data contained within the database.

Data will be used according to the provision of GDPR, and applicable new regulations, and individuals will not be identifiable through any reports or publications that result from the trial. Quality control measures will ensure that all data are reliable and have been processed accurately at every stage of the study. Source data validations will be undertaken by the trial management staff to optimise data quality for key data including primary/secondary outcome variables and SAE data.

Trial Oversight Committee

An independent TOC will monitor data completion rates and safety reporting throughout the duration of the trial. Data collected in the trial will be used to support other research in the future, and may be shared anonymously with other researchers.

ETHICS AND DISSEMINATION

The PrEPS trial was granted a favourable opinion by the Yorkshire and Humber, Sheffield Research Ethics Committee on the 25 October 2019 (19/YH/0317). Trial findings will be disseminated to patients using patient focused literature, visual aids and animated films via patient charities including Heart Valve Voice and the British Heart Foundation national PPI group. Dissemination to clinicians and professional stakeholders like commissioners will be through peer-reviewed publication and conferences. Any changes to the protocol will be communicated to all relevant parties as per the HREC requirements.

DISCUSSION

Prehabilitation in cardiac surgery has lagged behind that for other specialties, especially cancer surgery, abdominal general surgery and limb reconstruction surgery in the UK.[31] This is despite the fact that large numbers of patients undergo cardiac surgery in the UK every year (around 35 000). Moreover, cardiac surgery patients in particular stand to benefit from a prehabilitation

interventions because they tend to be older, mean age 67 years and increasing[1] and have a higher comorbid burden (average Charlson score 2.1 vs 1.7) (GIRFT Programme National Specialty Report). In particular, they suffer from high levels of obesity, diabetes, coexisting lung disease and reduced mobility. The chronic nature of most cardiac conditions prior to reaching the point of surgical intervention and the fact that the cardiac disease process itself usually limits physical activity, means that patients awaiting cardiac surgery usually exhibit a high prevalence of frailty and loss of muscle mass and function, a condition usually referred to as sarcopenia.[32–34]

In 2019, our group published a review of 483 publications, of which 10 (including 4 metanalysis and 6 RCTs) represented the best evidence to answer the clinical question 'does prehabilitation improve outcomes in cardiac surgical patients?'.[35] The RCTs were limited by small sample sizes (the smallest had a sample size of 15) and no trial combined physical activity and IMT (the 2 interventions with the largest evidence base of impact for outcomes) as components in the intervention. A subsequent systematic review which explored associations between objectively measured physical activity during the prehabilitation period and health-related outcomes across surgery types reported significant beneficial associations.[36]

The significant benefit of prehabilitation in other therapeutic areas and the scarcity of high-quality evidence in cardiac surgery patients identifies an urgent need to provide further data in this area.

Anticipated impact

This will be the largest ever RCT investigating the impact of a prehabilitation intervention composed of exercise and IMT in patients with severe cardiac disease awaiting elective cardiac surgery. The findings will establish if such an intervention is feasible and if it is effective in improving overall functional exercise capacity prior to surgery. It will also indicate if there are any impacts on clinical outcome after surgery.

TRIAL STATUS

The PrEPS trial opened to recruitment in November 2019, just prior to the start of the global pandemic. The restrictions imposed by the COVID-19 pandemic has had a significant impact on recruitment, elective cardiac surgery and the ability to deliver the prehabilitation intervention. Despite these challenges PrEPS continues to recruit patients and is projected complete follow-up data collection by early 2023.

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Acknowledgements We would like to thank HRUK for their funding and on-going support of the PrEPS trial with an extension to ensure this clinically important trial is seen through to completion.The successful delivery of PrEPS would not have been possible without the support from the cardiac surgeons at the James Cook University Hospital (Simon Kendall, Andrew Goodwin, Andrew Owens, Ralph White, Mazzy Kanani and Danai Karamanou), Newcastle CTU and the cardiac research and rehab delivery teams (Jon Pritchard, Jess Wigham, Carmen Neave, Karen Ainsworth, Lyn Whitehouse, Louise Sarginson and Fiona Bowe).

Contributors All authors meet the criteria for authorship stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (ICMJE). EA: devised the clinical question, applied for funding, chief investigator with overall responsibility for the trial, reviewed and contributed to all areas of the manuscript. AM: trial manager with day to day responsibility for delivery of the trial, drafted all areas of the manuscript and contributed to all areas. MB: senior trial manager, author of the trial protocol, governance oversite, contributed to all areas of manuscript. SH: contributed specifically to the Qualitative substudy and Intervention Design and Delivery sections within the manuscript. ASK: general oversight of the Statistical Analysis section of the manuscript and overall review of whole manuscript. KL: contributed specifically to the Qualitative subtudy section within the manuscript. EO: statistical oversight and contributed specifically to the Statistical Analysis. JT: contributed specifically to the Qualitative substudy section within the manuscript9. JW: drafted and contributed specifically to the Statistical Analysis and accelerometer substudy sections of the manuscript. PW: contributed specifically to the Qualitative substudy section within the manuscript. HCH: coapplicant, protocol author, general overview and contribution to all areas within manuscript. RHM: coapplicant, protocol author, general overview and contribution to all areas within manuscript. Several reviews of the manuscript took place prior to a final draft with all authors reviewing the final draft once complete prior to submission. All authors are informed of any revisions that may need to take place following editorial review and confirm these changes are acceptable prior to resubmission.

Funding The PrEPS trial is funded by Heart Research UK (RG2671/18/20) and Research Capacity Funding from South Tees NFH.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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and relevant contact details to be entered

CONSENT FORM

Prehabilitation in Elective Patients Undergoing Cardiac Surgery (PrEPS)

Name of Researcher: [Recruiting Centre PI to be entered]

Participant Identification Number for this trial: __ __ __ __ __

Please INITIAL the box where you agree. Please note that statement 9 is optional:

1. I confirm that I have read the information sheet dated …….. (version ……..) for the above trial. I have has the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from Newcastle Clinical Trials Unit, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records ☐

4. I understand that anonymised information about me relevant to the trial will be held on a secure database, which is hosted on an external server and will be transferred to individuals within the research team including members at Newcastle and Durham University for analysis. All data will be anonymised using a participant identification number and stored securely on restricted servers for a period of 7 years after the end of the trial. Any publications resulting from this trial will not include any personal identifiable information ☐

5. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers ☐

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and relevant contact details to be entered

6. I agree to my General Practitioner being informed of my participation in the trial, including any necessary exchange of information about me between my GP and the research team. ☐

7. I understand that if I lose the capacity to decide about my healthcare changes during the trial, ☐

   I will not be asked to undertake any further trial activity, however routinely collected information relevant to the trial may be collected.

8. I agree to take part in the above trial. ☐

Optional:

9. I have been offered the opportunity to take part in the trials activity monitor sub study. I have been provided with information and understand what this entails. I agree to take part in the sub study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

When completed: 1 for participant; 1 for researcher site file; 1 to be kept in medical notes

PrEPS: Consent Form V4.0 1st July 2021 IRAS: 265113, REC 19/YH/0317

South Tees Hospitals NHS
NHS Foundation Trust

QUALITATIVE CONSENT FORM

Prehabilitation in Elective Patients Undergoing Cardiac Surgery (PrEPS)

Name of Researcher: *Mr Enoch Akowuah*

Participation is entirely optional, and non-participance will have no detrimental affects upon your ongoing care/participation in the primary clinical trial. You are free to withdraw yourself from the sub-study at any point, without any detrimental impact.

Please read the following statements, initial the boxes next to them and sign below.

• I have read the patient/HCP information sheet dated …….. ((Version……) and understand what the PrEPS sub-study entails.	
• I consent to my details being passed to and being contacted by the qualitative research team.	
• I consent to participate in a focus group.	
• I consent to being audio recorded during a focus group.	
• I understand that if participating in an online focus group my email address may be visible to other participants	
• I consent to the audio of my conversation at said focus group being passed to a professional transcription service.	
• I am aware that I may withdraw myself from this sub-study at any time up to and during the focus group and any data already collected will remain in the study.	
• I consent to the data generated being anonymised and published for academic purposes.	

Print name of participant:	Print name of person taking consent:
Signature of participant:	Signature of person taking consent:
Date:	