STUDY PROTOCOL

PROTOCOL TITLE: A multi-centre randomised controlled trial of standard care versus an accelerated care pathway after cardiac surgery (FARSTER-care).

PROTOCOL SHORT TITLE: FARSTER-care

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STUDY SUMMARY

TITLE	A multi-centre randomised controlled trial of standard care versus an accelerated care pathway after cardiac surgery (FARSTER-care).
ACRONYM	FARSTER-care
Protocol Version **Date** **IRAS** **ISRCTN** **FUNDER**	Version 2.0 23/09/2024 334434 12204742 NIHR Health Technology Assessment Programme: NIHR152069
Methodology	Multi-centre, two arm, parallel group, open RCT, including a health economic analysis.
Study Duration	48 months
Study Centres	At least 16 hospital sites across the United Kingdom.
Objective	To determine whether, following cardiac surgery with sternotomy, early specialist outpatient review carried out at three weeks after hospital discharge followed by commencement of cardiac rehabilitation from four weeks will lead to improved patient outcomes and is cost effective compared to standard care, where outpatient review is typically six weeks after hospital discharge followed by commencement of cardiac rehabilitation from eight weeks.
Number of Subjects/Patients	Using a 1:1 randomisation ratio, 588 patients will be randomised, stratified by centre, to intervention arm or a control (standard care) arm.
Main Inclusion Criteria	Adults aged ≥18 years undergoing elective and urgent cardiac surgery who are having a full median sternotomy.
Statistical Methodology and Analysis	For the analysis of the full trial (assuming continuation), participant flow will be presented using a CONSORT diagram. Analyses will be conducted on an intention-to-treat basis unless otherwise stated. Baseline and outcome data will be summarised by group and overall. Incremental Shuttle Walk Test (ISWT) distance will be analysed via mixed-effects repeated-measures linear regression, including sites and participant as random effects. Randomised treatment group and clinically important participant-level covariates including gender, age and Body Mass Index (BMI) will be included as fixed-effects. The secondary outcomes will be analysed using appropriate regression techniques based on the type of data controlling for the same covariates as included in the analysis of the primary outcome. Complier Average Casual Effect (CACE) analysis using two-stage least-squares instrumental variable regression will be carried out to assess the treatment effect in participants whose actual timing of Cardiac Rehabilitation (CR) commencing complied with the timing which

	was allocated. Remote patient review and home-based CR are now common practice but the impact of these on clinical outcomes, Patient Reported Outcome Measures (PROMs) and Quality of Life (QoL) are unknown. Baseline and outcome data will be summarised descriptively by group, stratified by whether patients received face-to-face or remote review, and home or centre-based CR. Full analyses will be detailed in the trial's Statistical Analysis Plan (SAP), which will be reviewed and approved by the trial steering and data monitoring committees and finalised prior to the end of data collection.

PROTOCOL VERSION HISTORY LOG

Version	Date	Editor(s)	Comments
0.1	26/06/2023	Jessica Goodliffe	Set-up document and drafted protocol
0.2	01/09/2023	Jude Watson, Grace O'Carroll	Review comments
0.3	12/09/2023	YTU trial team	Review comments
0.4	27/09/2023	Sebastian Hinde, Alex Mitchell	Additional health economic and statistics section included
0.5	11/10/2023	YTU trial team	Review comments
1.0	12/10/2023	YTU trial team	Finalised document
1.1	26/02/2024	Grace O'Carroll	Patient incentive wording
2.0	23/09/2024	Jessica Goodliffe	Addition of inclusion criteria around ISWT completion and updated previous inclusion criteria to include patients who will receive CR as part of clinical pathway. Other updates to reflect trial procedures including reconfirmation of consent, duration of CR, timing of NSAE/SAE reporting, protocol deviations relating to appointment timings, and completion of questionnaires. Updated home-based CR protocol. Updated data collection and storage at YTU, recruiting and CR sites.

ABBREVIATIONS

AE	Adverse Event
CABG	Coronary Artery Bypasses Grafting
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials statement
CR	Cardiac Rehabilitation
CRF	Case Report form
DMC	Data Monitoring Committee
EQ-5D-5L	EuroQol 5 Dimensions 5 Levels
GAD-7	Generalized Anxiety Disorder Scale
GCP	Good Clinical Practice
ISWT	Incremental Shuttle Walk Test
NHS	National Health Service
NIHR	National Institute for Health Research
NSAE	Non-Serious Adverse Event
HRA	Health Research Authority
PAG	Patient Advisory Group
PIS	Patient Information Sheet
PROM-CR	Patient Reported Outcome Measure - Cardiac Rehabilitation
PSS	Personal Social Services
QoL	Quality of Life
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RN	Research Nurse
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SP	Sternal Precautions
TMG	Trial Management Group
TSC	Trial Steering Committee
YTU	York Trials Unit

CONTENTS

1. BACKGROUND AND RATIONALE

In the UK, cardiac surgery has steadily increased since 2010, with 36,166 surgeries being performed in 2016 [1]. In a survey we conducted in May/June 2017, 35 of the 42 UK cardiac centres responded, and confirmed this it is current practice that, following cardiac surgery, patients attend their first outpatient review approximately six weeks after hospital discharge, where recovery is assessed and fitness to commence Cardiac Rehabilitation (CR) is determined; CR is then started from eight weeks [2].

The standard access for cardiac surgery is through a median sternotomy [3,4,5,6], following which patients are required to refrain from upper body exercises, lifting of heavy objects and usual strenuous activities for 12 weeks [7,8,9,10]. These restrictions, called "Sternal Precautions" (SP), are intended to aid healing of the cut breastbone. CR, which has significant short- and long-term benefits after cardiac surgery [11,12], is therefore delayed. Current time frames for outpatient review and CR are not evidence-based and may prolong recovery after cardiac surgery and be placing unnecessary limitations on patient activity.

1.1 First postoperative outpatient review

The long interval before outpatient review and CR extends the period of vulnerability and inactivity for patients, with patients often seeking medical attention for surgery-related complications during this period [13,14,15]. In a prospective observational study, we found that 38.9% of patients reported surgery-related complications and sought further medical help during this six-week period (15.3% required readmission), and 44.4% would like an earlier review [2].

Early contact with patients has been associated with reduction in hospital readmissions [16]. Non-randomised studies have also shown lower 30-day adverse outcomes with early review, for cardiac and other surgical patients [16, 17].

1.2 Outpatient exercise-based cardiac rehabilitation

In current UK best practice, cardiac surgery patients commence CR around eight weeks from referral; however, 45% of programmes do not meet these standards with wait times over

eleven weeks after hospital discharge [18]. Current guidelines for activity and exercise after median sternotomy have been described as restrictive, conflicting, sometimes arbitrary, frequently anecdotal, and occasionally based on expert opinion [8]. The delay in starting CR can mitigate the benefits of CR [19], contribute to physical deconditioning, and hinder the ability of CR to facilitate timely recovery of fitness and physical activity status [20]. LaPier et al reported functional limitation following sternotomy [21] and related this to surgeon-dictated SP [20]. Furthermore, the delay in starting CR can prolong the recovery process, increase dependence on family and/or carers and can cause frustration. This may contribute to anxiety and depression that is reported in patients recovering after Coronary Artery Bypass Graft (CABG) [22]. According to the 2013 UK national audit of CR, late CR commencement contributes to a substantial number of heart surgery patients declining to participate in CR [23].

Early initiation and progressive physical exercise after cardiac surgery have well known benefits [24, 25] and prolonged restrictions of physical activities appear detrimental to patient health and wellbeing. A small observational study noted that functional recovery to pre-surgery levels was achievable at two months with physical therapy [26]. A Randomised Control Trial (RCT) which compared the effectiveness and safety of CR from two weeks post sternotomy with that of standard care, concluded that with 'appropriate precautions' CR can be started from two weeks post-sternotomy, although this conclusion was made cautiously due to limitations within the trial [27, 28]. The timing of CR impacts functional recovery and level of physical fitness after cardiac surgery [29,30,31,32]. Improvement in post sternotomy symptoms [33] is also associated with physical activity. The British Associate for Cardiovascular Prevention and Rehabilitation (BACPR) standards and core components [34] and National Certification Programme (NCP) for CR [35] recommend early commencement of CR which is monitored by National Audit of Cardiac Rehabilitation (NACR) 2018 [18], showing that early rehabilitation is a performance standard for all programmes in patients following coronary artery stents or post-heart attack conservative pathways [18].

There are variations in types of exercises permitted, limits for weight of objects that can be lifted, guidelines for activities, and timeline for resumption of driving. Parker et al [36] demonstrated that the force elicited on the breastbone by coughing far exceeded lifting above the recommended limit. Adams and colleagues [8] investigated forces associated with

32 activities of daily living and reported that the majority not restricted by SP, such as opening and closing doors, generated forces greater than the weight limit allowed. While SP may help to support bone healing, the optimal nature and duration are unclear especially since sternal bone healing occurs by five weeks [9]. Our observational study (FORCAST6) showed that the incidence of postoperative complications is highest in the first week after hospital discharge and declines to lowest levels by four weeks [2]. The logic for the timing of early CR is associated with this area of postoperative stability and will therefore commence at five weeks after surgery (four weeks after hospital discharge).

In summary, published data is lacking about the appropriate timing of postoperative review and CR following cardiac surgery. The dominant role of SP as a deterrent to early CR after cardiac surgery has been questioned [9,10]. Cahalin and associates [10] identified major setbacks with current SP practice to include: lack of supporting evidence, variation between institutions, lack of universally accepted definition, and the functional limitations they engender. A similar experience was reported in Europe [37] and Australia [38]. These inconsistencies create a dilemma for patients, their families, and healthcare professionals alike. Nevertheless, SP continues to inform conventional practice and recommendations of The British Heart Foundation (BHF) [7].

Our feasibility study established that bringing forward outpatient review and CR, in order to facilitate recovery, physical fitness and Quality of Life (QoL) was acceptable to patients and that a full scale RCT was feasible [39]. This RCT aims to provide robust evidence to underpin a post-cardiac surgery care pathway that facilitate fast, clinically efficient, and cost-effective recovery, with improved patient outcomes.

2. AIM AND OBJECTIVES

2.1 Aim

To determine whether, following cardiac surgery with sternotomy, early specialist outpatient review carried out at three weeks after hospital discharge followed by commencement of CR from four weeks, leads to improved outcomes and is cost effective compared to standard care, where the outpatient review is six weeks after hospital discharge followed by commencement of CR from eight weeks.

2.2 Objectives

i. To undertake a randomised parallel group comparison to determine the effects of early CR on physical functional capacity using the using incremental shuttle walk test (ISWT) at six months post-randomisation (primary outcome).

ii. To undertake an eight-month internal pilot to obtain robust estimates of recruitment and retention ensuring trial viability.

iii. To undertake a randomised parallel group comparison to determine the effects of early CR on outcomes related to physical health and psychological health at six- and twelve-months post-randomisation.

iv. To conduct a detailed economic evaluation to assess the cost-effectiveness of early CR.

3. STUDY DESIGN

The study design has been informed by the results of a feasibility study (FARSTER) [39], which demonstrated that it would be acceptable and feasible to undertake a full-scale trial, subject to some modifications to maximise recruitment. The objectives of FARSTER-care will be addressed using a multi-centre, two arm, parallel group, open RCT, including an internal pilot study and embedded health economic analysis. The trial will recruit 588 cardiac surgery participants who have had a sternotomy at UK centres over 24 months and will randomise participants 1:1 to the FARSTER-care (intervention) or standard care (control) arms.

Participants in the intervention arm will have specialist outpatient review at three weeks after hospital discharge, followed by commencement of CR from four weeks. Participants in the standard care arm will receive standard post-sternotomy cardiac surgery care which includes specialist outpatient review at six weeks after hospital discharge, followed by commencement of CR from eight weeks.

At the start and end of CR, and again at six months post-randomisation, participants will undergo fitness testing using the ISWT during face-to-face appointments. Clinical data will be recorded at baseline and appointments up to six months post-randomisation. Participants will be asked to self-report outcome data by completing questionnaires from baseline up to

twelve months post-randomisation. The study flow chart (Figure 1) and study assessment schedule (Figure 2) detail the study timelines.

3.1 Internal Pilot Study

The first eight months of recruitment will constitute an internal pilot phase, after which progress will be assessed against pre-specified criteria using a traffic light system (red/amber/green) (Table 1). The outcome of the pilot study will enable a confirmation of whether the trial is feasible and determine progression to the main trial. The criteria assessed relate to the recruitment of sites and participants, deliverability of the intervention, and rate of follow-up for the primary outcome. The recruitment rates and number of sites open are based on the projected recruitment targets for the 24-month recruitment period. Results will be compared against the study's recruitment assumptions and progression targets, and continuation of the trial or relevant modifications will be decided by the Trial Steering Committee (TSC) and the funding body.

Table 1. Internal pilot progression criteria.

	Red	**Amber**	**Green**
Recruitment rate/site/month	<1	1-1.9	≥2
Number of sites opened	<5	5-7	≥8
Collection of ISWT at the post-CR timepoint	<60%	60-84%	≥85%
Adherence with intervention pathway (difference between average time between surgery and CR between the two groups in weeks)	<2	2-3	3+

The actions taken for the progression criteria are outlined below:

- **Green**: continue the trial.
- **Amber**: review procedures to identify underlying problems, and put in place strategies to address these, review after an interval and if recruitment trajectory does not indicate that full recruitment will occur within scheduled recruitment period, discuss next steps with TSC and funder.
- **Red**: terminate the trial unless we can confidently identify successful strategies or rapidly resolve the problem.

3.2 Outcomes

Primary outcome

The primary outcome is the difference in ISWT (meters walked) between the treatment groups at six months post-randomisation. The ISWT is a functional capacity test used to measure physical fitness and is widely used in CR programmes in the UK [40]. Participants will be asked to perform this test before their CR commences (pre-CR time point), once CR finishes (post-CR time point) and at the six-month time point.

Secondary outcomes

Secondary outcomes will be collected at baseline, pre-CR, post-CR, six- and twelve- months post-randomisation (see Figure 2: Study assessment schedule). The secondary outcomes include:

- Physical health
    - **Heart rate**: Measured in beats per minute using a pulse oximeter.
    - **Blood pressure**: Systolic and diastolic blood pressure measured following standard site procedure and recorded in mmHg.
    - **Oxygen saturation**: Measured using a pulse oximeter showing the percentage of oxygen in the blood.
- Patient outcomes
    - **Patient Reported Outcome Measure - Cardiac Rehabilitation (PROM-CR)***:* A patient-reported questionnaire designed and validated for cardiac rehabilitation which asks a patient how much their heart condition has impacted their life over the preceding two weeks in relation to physical, social and lifestyle, emotional and care aspects [41].
- Psychological health
    - **Generalized Anxiety Disorder Scale (GAD-7**): The GAD-7 is a seven-item self-administered patient questionnaire used as a screening tool and severity measure for generalised anxiety disorder [42].

- Quality of life
    - **EQ-5D-5L**: The EQ-5D-5L is a validated generic patient-reported outcome measure [43, 44]. The descriptive system has five health domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with five response options for each domain (no problems, slight problems, moderate problems, severe problems, and extreme problems). In addition, it has a health status Visual Analogue Scale (VAS) which measures self-rated health with endpoints ranging from 'the best health you can imagine' to 'the worst health you can imagine'.
- National Health Service (NHS) resource use
    - **NHS resource use questionnaire:** Patient reported NHS and Personal Social Services (PSS) resource use will be collected using bespoke questionnaire.
- Complications
    - These will be collected in the documentation at baseline and six months, and throughout the trial in the form of adverse events.
- CR uptake
    - This will be recorded in the CR session logs.

4. STUDY POPULATION

4.1 Target population

Inclusion

- Adults (aged ≥18 years).
- Patients undergoing elective or urgent cardiac surgery through a sternotomy and will be receiving CR, as part of the standard clinical pathway.
- Patients capable of giving informed consent.
- Patients capable of completing, and willing to complete, the ISWT.

Patients who are taking part in other research studies can still enter the trial as long as the first study does not include an intervention or element that may affect the FARSTER-care trial outcomes or would be overly burdensome for patients.

Exclusion

- Patients with postoperative sternal wound complications such as sternal instability.
- Patients with postoperative complications requiring further specialised care, such as stroke rehabilitation or regular dialysis.

These postoperative complications would interfere with their ability to undertake exercise-based CR or require long periods of treatment so it would not be possible to randomise patients with these complications in the times set out in the study.

4.2 Study sites

The trial will recruit cardiac surgery participants from NHS Cardiothoracic Surgery Units within the UK and linked third party community exercise partners commissioned by the NHS. A record of all study sites will be maintained by the trial management team and held in the trial master file.

5. PARTICIPANT RECRUITMENT

5.1 Identification and consent of potential participants

All patients aged 18 years and over who are undergoing planned (elective or urgent) cardiac surgery with a sternotomy will be screened by the research team at the recruiting NHS sites. Prospective participants will be given the Patient Information Sheet (PIS) in clinic or at hospital admission by a Research Nurse (RN), who will also explain the research.

5.2 Consent process

Patients who are interested in taking part in the trial can be approached for informed consent pre- or post-surgery. Patients who consent pre-surgery will be asked to reconfirm their

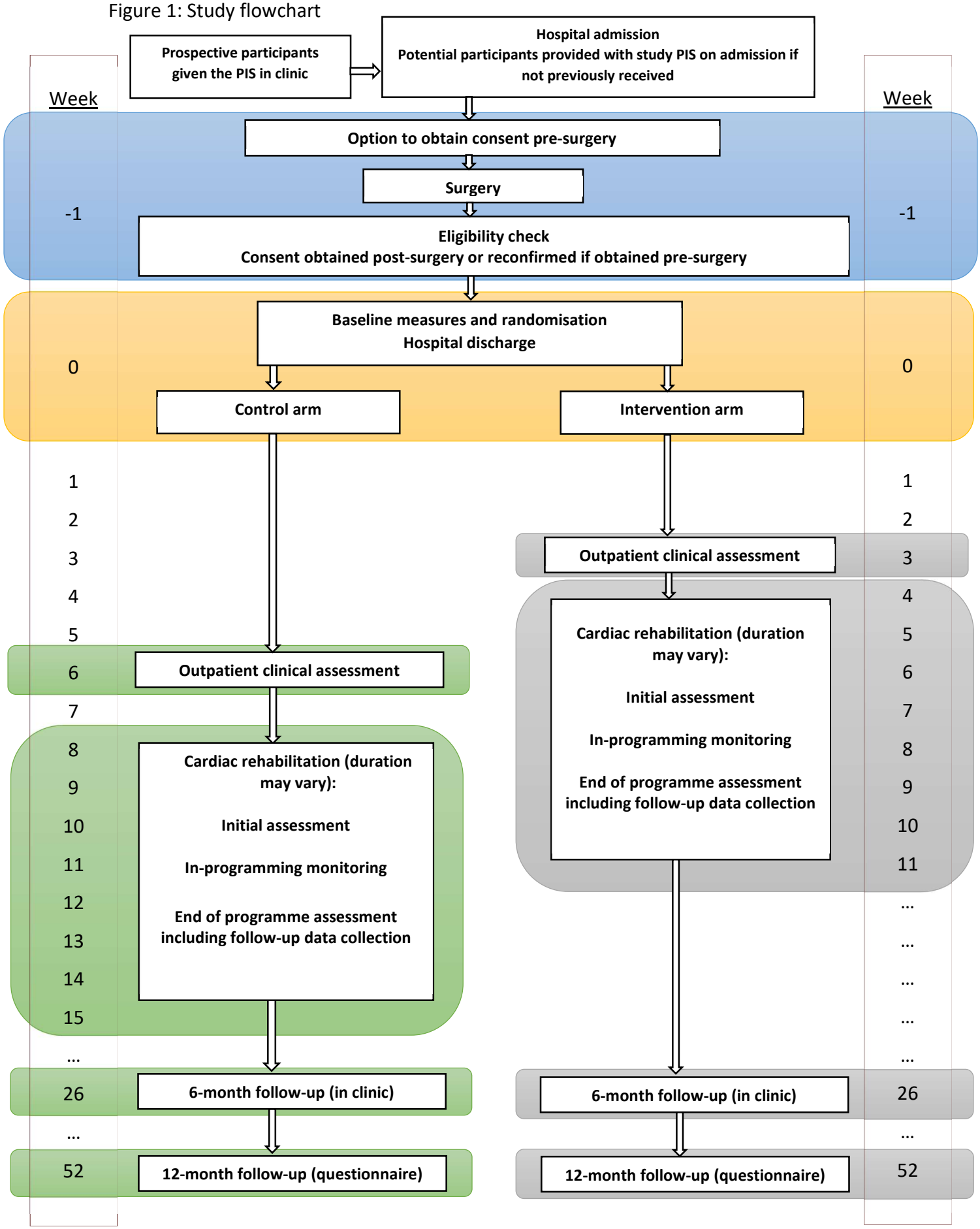
consent post-surgery. The RN will obtain written informed consent according to Good Clinical Practice (GCP) guidelines. Specific consent will be sought to enable the sharing of identifiable data with York Trials Unit (YTU) as part of the study to facilitate the collection of outcome data. Those who develop complications that will exclude them from the study can be excluded after consenting. Basic data will be collected for those not willing to provide informed consent. The patient pathway is outline in Figure 1.

All patients will undergo surgery as normal and receive standard in-hospital postoperative care.

5.2 Screening for eligibility

Following their surgery, patient eligibility will be confirmed by the clinical team. An *Eligibility Screening Checklist* will be completed and for those patients deemed ineligible, reasons for their ineligibility (including not willing to provide consent) will be recorded anonymously. Screening for complications that would render a patient ineligible can be done anytime during the hospital stay, before randomisation. Patients will be screened against the inclusion and exclusion criteria in Section 4.1.

Figure 1: Study flowchart



6. BASELINE DATA COLLECTION

Prior to randomisation all consenting patients will undergo baseline assessment, including a questionnaire and clinical assessments. The *Participant Baseline Questionnaire* will include patient demographics, and questionnaires related to the secondary outcomes. An appropriately trained member of the research team at the site will carry out baseline assessments. Data will be recorded in the *Clinician Baseline Form.*

7. RANDOMISATION

Following the completion of all baseline measures, the research team at the site will arrange randomisation. Consenting participants will be randomised 1:1 to the FARSTER-care (intervention arm) or standard care (control arm) group using block randomisation stratified by site. The allocation schedule will be generated by a trial statistician not otherwise involved in the recruitment or randomisation of patients, and implemented via a central, web-based randomisation system designed and managed by the YTU. Sites will be provided access to the randomisation system which will automatically send the research team at the site and the trial team at YTU the treatment allocation. The research team can then inform the participant of their allocation.

Intervention arm: Participants will have a post-operative outpatient specialist review three weeks after hospital discharge, followed by commencement of CR from four weeks.

Control arm: Participants will have a post-operative outpatient specialist review six weeks after hospital discharge, followed by commencement of CR from eight weeks.

All appointments will be made as near as possible to the timescales defined in this protocol. The RN at each site will ensure that the patient's outpatient review appointment and CR are arranged at the correct timings. This information will be conveyed to the YTU.

Appointments that are not arranged within 10 days (before or after) of the stated timepoint will constitute a protocol deviation. If a participant does not attend an arranged appointment,

then this will not constitute a protocol deviation, although the relevant information should be recorded.

8. POSTOPERATIVE OUTPATIENT SPECIALIST REVIEW

A specialist clinical staff member at the recruitment site will perform a face-to-face or remote (with telephone or video call) outpatient review. Postoperative history, medication review and clinical assessment, including for sternal stability, will be done and patients certified fit for CR. This review will take place three weeks after hospital discharge from surgery in the FARSTER-care group, and six weeks in the standard care group. Data will be recorded in the *Outpatient Review Form.*

Participants considered unfit for CR will be given a further review appointment for approximately one week later, the reason(s) documented and the relevant pages of their *Outpatient Review Form*. If following this further review, the participant is deemed fit, they will start their CR. If the participant fails this second review, they will be given another review appointment for two weeks later, the reason(s) documented and the relevant pages of their *Outpatient Review Form*. If following this third review, the participant is deemed fit, they will start their CR. If they fail, they will be deemed unfit for CR and not take part in CR as part of the study but will continue to be monitored as per usual practice. However, they will be sent all participant questionnaires stated in the PIS to complete by trial team at YTU.

9. INITIAL CARDIAC REHABILITATION APPOINTMENT (PRE-CR TIMEPOINT)

Participants referred for CR will be offered a comprehensive programme including an assessment carried out at their initial cardiac rehabilitation appointment, prior to starting their programme in line with the recruiting sites' policies. The initial appointment will take place as near as possible to four weeks post-hospital discharge in the FARSTER-care group and as near as possible to eight weeks post-hospital discharge in the standard care group.

This appointment will be a face-to-face appointment where the participant will perform the ISWT and will be provided with advice on cardiac risk factor reduction. This will typically include information on medication, diet, exercise, and physical activity as well as psychosocial wellbeing and smoking cessation. Participants will be offered further education sessions on

cardiac risk factor reduction during the programme. These would be delivered by specialist CR staff. Referral to other healthcare professionals such as specialist counsellors, pharmacists and dieticians may also be considered if necessary. Unless contraindicated, referral to the exercise component of the CR programme will be made. Following this initial assessment, participants will be enrolled in exercise programmes. Data from the initial CR appointment will be recorded in the *Clinician Pre-CR Form.* If a participant does not attend this appointment, they will be sent another appointment.

During this appointment, participants will be asked to complete PROM-CR, EQ-5D-5L, GAD-7 and resource use questions (*Participant Pre-rehabilitation [control or intervention] Questionnaire*). If required, the trial team at YTU may send this questionnaire to the participant, either electronically or by post.

10. CARDIAC REHABILATION SESSIONS

Participants who have been certified fit for CR will be offered a comprehensive programme organised by the recruiting site. As this is a pragmatic trial, CR exercises will be performed either at designated centres, in patient's homes or a combination of both (hybrid), according to the usual practice of the recruiting centre and the participant's preference.

The participants and the CR team will keep records of attendance and participation in the exercise sessions, including whether the session was centre-based or home-based. Each session will be recorded in either the *Participant Exercise Session Form* or the *Clinician Exercise Session Form,* depending on whether the participant or a member of the CR team are completing the form.

Centre-based CR:

Exercise training will be performed in a gym-like environment with other patients (these are general CR sessions so could include patients not in the trial). Interval circuit training is the most commonly prescribed form of exercise with each individual exercise programme tailored to patients' specific needs and fitness level. The following equipment may be used: heart rate monitors, treadmill, static bikes, and hand weights (alternative/ additional equipment can also be used if required).

Home-based CR:

Home-based CR may be completed instead of centre-based CR and will be undertaken in line with standard clinical practice at each site. This will include remote monitoring by CR professionals and measures for safe home exercising. Participants will be made aware of adverse signs and symptoms and when to stop exercising or call for help [45]. Pulse oximeters may be provided to participants by sites for use during home exercise sessions. Home exercise programmes may be provided to patients using software such as Physiotec (https://physiotec.ca) or the myHeart App (https://mymhealth.com/myheart). Any home-based CR will follow the local CR delivery team pathway.

Hybrid-CR delivery:

CR delivery teams may be able to support patients who wish to have a combination of centre- and home-based CR to ensure continuity and progression through the CR programme. After their exercise testing and prescription, the patients would agree a programme with the CR team. With fore-planning, this will easily be achieved, but when a sudden change in circumstances impose the need for an unplanned switch from one mode to the other, then this will be accommodated as much as possible by the local CR delivery team.

11. CARDIAC REHABILITATION PROGRAMME COMPLETION *(*POST-CR TIMEPOINT)

Following completion of the CR programme, at around 16 weeks post-hospital discharge for control arm and twelve weeks post-hospital discharge for intervention arm, all study participants will attend an appointment and have a repeat ISWT with data recorded in the participant's *Clinician Post-CR Form*. A discharge letter will be sent to patients' General Practitioner (GP) summarising their treatment. If a participant does not attend this appointment, they will be sent another appointment.

During this appointment, participants will complete PROM-CR, EQ-5D-5L and GAD-7 questions (*Participant Post-rehabilitation [control or intervention] Questionnaire).* If required, the trial team at YTU may send this questionnaire to the participant, either electronically or by post.

12. SIX MONTH FOLLOW-UP

About six months (26 weeks) after randomisation, all study participants will attend clinic to have an end-of-study consultation with a member of the research and/or the CR team. All study participants will undergo a final ISWT at this visit. Postoperative history including hospital attendance after discharge, clinical examination including sternal stability, and measurement of vital signs will be undertaken (see Figure 2: Study assessment schedule). Medical records will be checked for hospital readmissions and Accident & Emergency department attendance for surgery-related complications. Clinical data will be recorded on the *Clinician 6-month (Final) Form.* If a participant does not attend this appointment, they will be sent another appointment.

During this appointment, participants will complete PROM-CR, EQ-5D-5L, GAD-7 and resource use questions (*Participant 6-month Questionnaire*). If required, the trial team at YTU may send this questionnaire to the participant, either electronically or by post.

13. TWELVE MONTH FOLLOW UP

About twelve months (52 weeks) after randomisation, all study participants will be invited to complete EQ-5D-5L, GAD-7, and NHS resource use, costs, and time off work questions (*Participant 12-month Questionnaire*). The trial team at YTU will manage the follow-up at this timepoint. Participants can opt to complete the questionnaire electronically, by post or by telephone.

Figure 2: Study assessment schedule

	Baseline		Post-randomisation					
	Pre-surgery	**Post-surgery**	**Outpt. review**	**Pre-CR**	**CR**	**Post-CR**	**6m FU**	**12m FU**
Screening for eligibility		X						
Consent	X	X						
Baseline data collection		X						
Randomisation		X						
Clinical assessment		X*	X*				X	
ISWT				X*		X*	X	
PROM-CR				X		X	X	
EQ-5D-5L		X		X		X	X	X
GAD-7		X		X		X	X	X
CR assessments				X*		X*		
Vital signs – heart rate, blood pressure, oxygen saturation		X*	X*	X*		X*	X	
CR session logs					X			
Resource use questions				X			X	X
Adverse event monitoring			X*	X		X	X	X

**part of normal patient pathway*

14. LEVEL OF BLINDING

By the nature of the timing of the study treatments used within this study, blinding of the participants and clinicians is not possible and procedure for un-blinding is not necessary.

15. SAFETY MEASUREMENTS

15.1 Definitions

An Adverse Event (AE) in this trial is any untoward medical occurrence in a participant to whom a trial intervention or procedure has been delivered, including occurrences which are not necessarily caused by or related to that intervention or procedure.

An AE can therefore be any unfavourable and unintended sign (including abnormal laboratory results), symptom or disease temporally associated with the use of the trial intervention, whether considered to be related to the trial intervention or not.

Examples of Non-Serious Adverse Events (NSAE) related to participation in this study would be:

- Atrial fibrillation (irregular fast heartbeat causing palpitations);
- Sternal pain;
- Undue fatigue or exhaustion.

A Serious Adverse Event (SAE) would be regarded as an event which:

- resulted in death;
- is/was life threatening and/or required hospitalisation (unplanned or prolonged);
- resulted in persistent or significant disability or incapacity;
- resulted in surgical or medical intervention to prevent the above;
- is otherwise considered medically significant by clinical members of the study team.

Study participants will undergo clinical assessment after discharge following cardiac surgery and be certified fit for CR by the clinical team. Before commencing exercise-based CR they will undergo an ISWT, and CR will be tailored to their fitness levels. Exercise will be supervised for centre-based programmes and remotely monitored for home-based programmes. Participants undergoing home-based CR will be contacted by the CR team throughout the rehab period to ensure correct safety measures are in place. At completion of CR, they would have another assessment, including the ISWT, and an exit consultation. These measures would reduce the risk and enable early detection of sternal complications and enable early detection of possible complications. Any suspicion of the following complications during CR or follow-up would warrant urgent medical consultation:

Sternal pain: Delayed sternal healing by forces or pressure not severe enough to disrupt healing contributes to severe pain associated with tenderness along the sternotomy. This may be confused with muscular or sternal wire pain, and paraesthesia which are more common. This would be recorded as an AE which was related to study treatment but expected.

Sternal instability: This is abnormal movement between the surgically divided sternum due to delayed healing or non-union. This complication is rare. This would be considered an SAE.

Any study participant who complains of sternal wound pain or a feeling of "sternal click" will be seen urgently by the surgical staff, examined, and investigated appropriately. All NSAE/SAEs will be recorded. Participants who suffer adverse events with causality linked to sternal instability will be given appropriate treatment, or surgery if required.

15.2 Collecting, recording and reporting of NSAE/SAEs

NSAE/SAEs will be collected, recorded and reported for participants from the point of randomisation up to and including the twelve-month follow-up. Information about NSAE/SAEs, whether volunteered by the patient, discovered by the clinical team questioning or identified through physical examination, or recorded in the medical notes, will be collected and recorded on the NS*AE/SAE Report Form.* The YTU should be informed of NSAE/SAEs within the timeframes specified in the trial procedures.

When a participant has completed their twelve-month follow-up, it should be checked whether there have been any unrecorded NSAE/SAEs for the participant before they exit the trial. Any unresolved NSAE/SAEs should be followed up for one month after the participant has exited the trial.

Adverse events that are deemed related to participation in this study and all SAEs will be reported to the Chief Investigator (CI). Any SAEs deemed as 'related and unexpected' to study intervention will be reported to the Sponsor, Research Ethics Committee (REC), DMC and TSC.

Ongoing review of all AEs will take place during monthly Trial Management Group (TMG) meetings, discussed with the Patient Advisory Group (PAG), DMC and TSC and reported to the Sponsor and REC in line with their guidelines.

15.3 Safety monitoring plan

The RNs, CR staff and clinicians will record all NSAE/SAEs directly observed or reported by the trial participant from randomisation up to the final twelve month follow-up. In addition, sites should follow their own local procedures for the reporting of any adverse events linked to clinical care.

16. COMPLAINT HANDLING

The PIS will provide participants with contact details of the Sponsor in case of complaint. If there is negligent harm during the trial, when the NHS site owes a duty of care to the person harmed, NHS Indemnity covers NHS staff and medical academic staff with honorary contracts only when the trial has been approved by the Research and Development (R&D) department. NHS indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm.

17. DATA MANAGEMENT

17.1 Data collection

Table 2 outlines the data collection. Data collection will be carried out by appropriately trained members of the research team in each participating site using calibrated site equipment following standard site procedures. Data collection may take place at recruiting or CR sites. Recruiting sites will recruit participants and may also complete CR onsite, or alternatively, they may refer to CR sites.

For recruiting sites, all data collected will be entered onto a secure online Research Electronic Data Capture (REDCap) interface, which will be designed and developed for this study. Site staff will enter the data collected (Table 2) onto the REDCap database. Paper

copies of the Case Report Forms (CRFs) can be used. If a paper copy is used by the clinical team at the site, then the clinical team at the site is responsible for inputting this data into REDCap. Participants will have the option to complete questionnaires electronically on REDCap or on paper. Where paper CRFs or questionnaires are completed, they are deemed to be the source data.

For CR sites, the data collected (Table 2) will be collected on paper CRFs and questionnaires. These will be posted to YTU, using pre-paid envelopes, where the data will be entered onto the REDCap database.

The trial team at YTU will manage the participant-reported data collection (participant questionnaires) at the twelve-month timepoint. To maximise the data collection at this timepoint, participants will have the option to complete the questionnaire electronically, by post or by telephone. Participants completing the questionnaire electronically or by post will be recontacted at two, four and five weeks after the initial contact was made. Of these, participants opting for email questionnaires will instead be contacted by post at four weeks. The contact attempt at five weeks will be by telephone for all these participants. Participants who opt to complete the questionnaire by telephone will be contacted up to three times, which can be repeated 2 weeks later if necessary. If a participant cannot be contacted by telephone, a questionnaire may be posted to them. All questionnaires sent in the post will include a pre-paid envelope for the participant to return the questionnaire to YTU.

YTU will also manage the participant-reported data collection at the Pre- and Post-CR timepoints for participants who do not attend CR (if they are not deemed as fit for CR following the Outpatient Review or if they withdraw from CR by completing a Change of Status). As and when required, YTU may also send questionnaires to participants at other timepoints to support clinical teams.

To promote attendance at the six-month follow-up, during which visit the primary outcome measure is collected, participants will be sent a newsletter to optimise their engagement with the trial. Participants will also be offered £10 for completing their six-month follow-up, to cover for any travel costs. To enhance response rates of the twelve-month follow-up which consists of a participant questionnaire, participants will be sent a postcard thanking

them for their ongoing participation and support of their trial. YTU will coordinate the distribution of these documents.

Table 2. Data collection

Visit	**Timepoint**	**Completed by**	**Site responsible**	**CRF capturing data**
Eligibility	Prior to hospital discharge at week 0	Specialist clinical staff	Recruiting site	Eligibility Screening Checklist
Baseline	Prior to hospital discharge at week 0	Specialist clinical staff/RN	Recruiting site	Clinician Baseline Form
		Participant	Recruiting site	Participant Baseline Questionnaire
Outpatient review	6 weeks (control) or 3 weeks (intervention)	Specialist clinical staff	Recruiting site	Outpatient Review Form
Initial CR appointment	8 weeks (control) or 4 weeks (intervention)	Specialist CR staff	Recruiting or CR site	Clinician Pre-CR Form
		Participant	Recruiting or CR site	Participant Pre-rehab Questionnaire (control/ intervention)
CR sessions	One or two times a week between 8 to 16 weeks (control) or 4 to 12 weeks (intervention)	Participant OR Specialist CR staff	Recruiting or CR site	Participant Exercise Session Form or Clinician Exercise Session Form
CR programme completion	16 weeks (control) or 12 weeks (intervention)	Specialist CR staff	Recruiting or CR site	Clinician Post-CR Form
		Participant	Recruiting or CR site	Participant Post-rehab Questionnaire (control/ intervention)
6-month follow-up	26 weeks	Specialist clinical staff/specialist CR staff/RN	Recruiting or CR site	Clinician 6-month (final) Form
		Participant	Recruiting or CR site	Participant 6-month Questionnaire
12-month follow-up	52 weeks	Participant	YTU	Participant 12-month Questionnaire

All information collected over the course of the study will be kept strictly confidential. Participant's name, personal addresses, postcodes, NHS ID numbers and other contact details of consenting participants will be collected on the REDCap database, for the

purposes of assisting in follow-ups during the study. Participant data collected will all be pseudo-anonymised using a unique ID number and all related documents will use this ID number throughout the trial. Sites will be provided with a list of ID numbers and the research team at sites are responsible for allocating participants an ID number. Enrolment logs, which include patient-identifiable details, will be maintained at sites. A screening log will be used to capture information on the patients screened providing data on screening date, whether they were eligible or not (with reason) and if consented or not (with reason). This log will not contain any patient-identifiable details.

17.2 Data storage

All work will be conducted following the University of York's data protection policy which is publicly available (University of York, 2017) [46]. Each site and YTU will hold data according to Good Clinical Practice guidelines, the Caldicott principles, the current Data Protection Act (2018) [47] and the General Data Protection Regulation (May 2018) [48].

Data, including patient-identifiable information, will be stored on the REDCap database, which is encrypted and password-protected. Access to the database will be restricted to delegated members of the site research team and the YTU trial team.

Electronic or scanned copies of documents used to collect trial data may be stored on the NHS or the University of York servers, which are accessed through password-protected computers. Patient-identifiable information may be stored on NHS servers (such as consent forms and enrolment logs), however no patient-identifiable information will be stored on university servers. Sensitive data that will be transferred between sites and/or computers will be transferred via encrypted methods, such as secure email.

Paper documents used to collect trial data will be stored at sites and YTU, and these will be retained in a secure location that is kept locked when not in use, for the duration of the trial. Paper CRFs and questionnaires may be returned to YTU from sites, by post using pre-paid envelopes. There will be no patient-identifiable information included in these CRFs and questionnaires.

The University of York has a backup procedure as part of the University's Disaster Recovery process for central IT systems, allowing data to be restored in the event of a catastrophic failure. Backups are made on central file stores, and the backup service takes periodic copies of data on the file stores, meaning they can be restored to that point in time if needed.

17.3 Data quality assurance

Data collected as part of this research includes questionnaires, clinical assessments, and information from medical records. If data are found to be missing from participant completed questionnaires, or if data clarification or follow-up is required, participants will be contacted by either a RN or YTU research team member in an attempt to collect the data required. Therefore, participants will be asked for full contact details at baseline (including mobile phone number and email addresses) to enable this to occur.

Every attempt will be made to ensure the data are accurate, complete and reliable:

- The RNs and lead CR staff will be trained in collecting and reporting valid functional outcome measures (clinical assessments).
- Care will be taken to ensure participants are given clear instructions when completing the questionnaires and these will be checked for missing data by the clinic team before the participant leaves clinic.
- A source data form will be completed by each site to ensure suitable procedures are being followed to gather and store data.

18. SAMPLE SIZE AND STATISTICAL/ECONOMIC METHODS

18.1 Determination of sample size

In our external pilot trial, FARSTER, the mean and standard deviation (SD) of the ISWT pre-CR for the standard care group was 356.1m (174.2m) [39]. A study of CR participants found a minimum clinically important difference of 70m (95% CI 51.5–88.5) [49]. This study included a very comparable population of patients to FARSTER, with a similar mean pre-CR

ISWT of 390.8m (SD 173.1m). We shall conservatively power the trial to detect an Minimum Clinically Important Difference (MCID) of 52, which is the lower bound of the 95% CI for the MCID estimate. Assuming a SD of 174, this equates to a standardised effect size of 0.3. With 90% power, 5% two-sided significance, and 20% attrition (based on FARSTER), 588 patients will need to be recruited and randomised.

18.2 Statistical and analytical plans

For the analysis of the full trial (assuming continuation from the internal pilot trial), participant flow will be presented using a CONSORT diagram. Analyses will be conducted on an intention-to-treat basis unless otherwise stated. Baseline and outcome data will be summarised by group and overall. The ISWT distance will be analysed via mixed-effects repeated-measures linear regression, including site and participant as random effects. Randomised treatment group and clinically important participant-level covariates including gender, age and BMI will be included as fixed effects. CACE analysis using two-stage least-squares instrumental variable regression will be carried out to assess the treatment effect in participants whose actual timing of CR commencing complied with the timing which was allocated.

The secondary outcomes will be analysed using appropriate regression techniques based on the type of data controlling for the same covariates as included in the analysis of the primary outcome, plus baseline value of the outcomes where available.

Remote patient review and home-based CR are now common practice but the impact of these on clinical outcomes, PROMs and QoL are unknown. Details on intervention delivery and adherence will be presented, and baseline and outcome data will be summarised descriptively by group, stratified by whether patients received face-to-face or remote review, and home or centre-based CR.

Full analyses will be detailed in the trial's statistical analysis plan (SAP), which will be reviewed and approved by the trial steering and data monitoring committees and finalised prior to the end of data collection.

18.3 Health economics analysis

To inform objective four of the study to 'To conduct a detailed economic evaluation to assess the cost-effectiveness of early CR' we will conduct a number of analyses, consisting of the secondary outcome data collected in the trial (primarily EQ-5D-5L and resource use questionnaires alongside CR uptake) and the updating of an existing decision analytical model. These analyses will be considered in two parts: a within-trial analysis; and an extrapolated, model-based analysis.

The within-trial analysis will explore the costs and health outcomes associated with the interventions during the one-year trial follow-up period. This will take an NHS and PSS perspective, with costs estimated by applying published estimates of unit cost interactions to the frequency of NHS resource use reported through the participant questionnaires. Health outcomes will be estimated using the EQ-5D-5L generic health outcome questionnaire and used to inform estimates of quality adjusted life-years (QALYs) using the latest standardised UK value set. Additional economic metrics around out of pocket payments by the participants and the impact on employment will also be considered. Missing data will be described and imputed where appropriate using multiple imputation. In addition to summarising the total mean cost and QALYs for both arms during the within trial period, regression analysis will be used to explore the relationship between different variables. Stratification of results by clinically relevant characteristics including age, sex, and Index of Multiple Deprivation (IMD) status will also be explored. All within-trial analyses will apply methods consistent with the statistical analysis plan.

The extrapolated, model- based analysis will explore the potential longer-term cost-effectiveness of the two treatment approaches, an important consideration as the benefits of successful CR are expected to impact health outcomes and associated NHS resource use beyond the one-year trial follow-up. This model-based analysis will draw evidence from the FARSTER-care trial results, primarily the level of engagement with CR in the two arms, and the wider literature to interrogate whether the findings of the within-trial clinical and economic analyses are consistent with the longer-term cost-effectiveness implications, building on existing modelling analyses conducted by this team [50]. The existing model will be updated through a review of the latest effectiveness evidence, exploring whether the

Cochrane systematic review and meta-analysis that inform the original analysis remain up to date. Extensive uncertainty analysis will be conducted including one way and probabilistic sensitivity analysis to consider the sources and impact of uncertainty, commenting on the potential value of future research to resolve it.

Both the within-trial and extrapolated analyses will additionally explore the implications of the early and standard CR pathways stratified by socio-economic factors. For the within-trial analysis this is expected to consist of stratification of the comparative analyses by patient IMD, estimated for their residential area using lower-layer super output areas. The extrapolated analysis will similarly stratify patients by IMD, consistent with the existing decision model, additionally exploring the potential to conduct a distributional cost-effectiveness analysis (DCEA) if relevant.

19. DEFINITION OF END OF STUDY

End of study will be defined as the date at which the last participant has completed the study processes (i.e. completion of final data collection). The Sponsor, or delegated individual in the study team must notify the National Institute of Health Research (NIHR) and Health Research Authority (HRA) of the end of a clinical trial within 90 days of its completion.

20. ETHICAL CONSIDERATIONS

20.1 Informed consent

Written informed consent will be obtained from all participants prior to entry to the study.

The consenting process will be conducted by a RN according to GCP guidelines in the patient's normal clinical care setting. Verbal consent will also be made available.

All prospective participants will be provided with a detailed PIS and provided the opportunity to ask any questions regarding the study. We will also emphasise that participants are free to withdraw from the study at any time without any explanation and

doing so will not affect their treatment or care in any way. Participants will be advised that a letter will be sent to their GP informing them of their involvement in the study.

20.2 Ethical Review

This protocol and the associated informed consent documents will be submitted to the required regulatory authorities (e.g. REC and HRA) for review and approval.

20.3 Confidentiality of data and patient records

The research team at the York Trials Unit and all participating sites will comply will all aspects of the Data Protection Act (2018) [47] and the General Data Protection Regulation (2018) [488]. All staff involved in the research will have up-to-date training relevant to this study, such as GCP training.

All information collected during the study will be kept strictly confidential. Information will be held securely on paper and electronically at the YTU and participant sites, including appropriate storage, restricted access, and disposal arrangements of patient personal and clinical details. Participants will not be identified in the results of the study. Data will be archived for a minimum period of ten years following the end of the study. Personal data will be processed under Article 6 (1) (e) (Processing necessary for the performance of a task carried out in the public interest) and Special Category data under Article 9 (2) (j) (Processing necessary for ... scientific ... research purposes) of the General Data Protection Regulation (2018).

20.4 Potential risks and benefits

There are no foreseen areas for clinical concern and there were no concerns based on AEs and SAEs experiences in the feasibility study. In the context of lack of robust evidence to determine the best time frames for post-operative review and CR, risks are not increased through participation in the study.

Individual participants may not benefit directly from this research. A PIS has been developed with the involvement of patients and gives a balanced account of the possible benefits and any known risks. It states explicitly that future treatment will not be affected if the patient decides not to enter the trial or withdraw their consent.

All participants will be closely monitored so postoperative complications can be identified early and managed. This would reduce attendance at Accident and Emergency departments and hospital readmissions. Early commencement of graded and supervised exercise could potentially result in reduced muscle wasting, joint stiffness, and physical deconditioning, early return to usual fitness levels, improved post-sternotomy symptoms and improved cardiac function.

Risks and burdens to patients have been considered during the study design process. Burdens include questionnaires, and some clinical assessments/tests which are not part of the normal patient pathway. In the unlikely event that, new information arises during the trial that may affect participants' willingness to take part, this will be reviewed by the TSC to assess the need for any additions to the PIS and whether patient re-consent is required.

21. TRIAL OVERSIGHT

21.1 Project management

The YTU is responsible for project management. The day-to-day management of the trial will be the responsibility of the trial coordinators, supported by other relevant members of trials unit staff (senior managers, trial support officer, trial statistician, data manager, and administrative staff).

21.2 Trial Management Group (TMG)

The TMG is responsible for overseeing the day-to-day running and management of the trial. Led by the Chief Investigator, it will include members of YTU (senior researchers, trial manager, trial coordinators, trial support officer, statistician, and health economist), and

other lead investigators. The TMG will meet monthly or according to the needs of the study (via teleconference and/or face-to-face at least once a year).

21.3 Trial Steering Committee (TSC) and Data Monitoring Committee (DMC)

The TSC and DMC comprise of independent members including a Chair who is an expert in the area, a statistician, one other independent person from a relevant discipline/ profession, and a member of the PAG along with the Principal Investigator and the Trial Manger. Other study collaborators may also attend the meeting at the discretion of the Chair. The role of these committees will include the review of all SAEs, and the AEs which are thought to be treatment related and unexpected. They will also play a role during the stop-start criteria following the pilot phase. The committees will meet annually or more often, as appropriate.

22. PATIENT AND PUBLIC INVOLVEMENT

Patient and public involvement will play an integral role in this study. These volunteers will form a PAG and hold meetings with RNs, CR staff and sites' Principal Investigators during the study to discuss any challenges encountered and how to overcome them. The group will act as an important source of reference and the research progress will be discussed with the members. Their role will include:

- assist with the development of study documentation ensuring material is clear to the lay public;
- identify barriers to participation and comment on possible ways to reduce those barriers;
- assist in developing recruitment strategies;

Towards completion of the study, the role of the group will include:

- identifying appropriate pathways for dissemination;
- contributing to the writing of the lay summary.

23. COMPLIANCE AND WITHDRAWAL

23.1 Participant compliance

Attendance at each of the CR sessions will be recorded. Also, the proportion of follow-up completed will be reported.

23.2 Loss to follow-up

Attrition from follow-up is problem encountered in many studies and one that can lead to selection bias [51]. Where required, the RN will work collaboratively with the direct care team and may contact participants by telephone regarding missing questionnaires and/ or appointments. The trial team at the YTU may also contact the participants regarding outstanding patient-reported questionnaires.

23.3 Withdrawal/ dropout of participants

Participants may withdraw from the study at any time without influencing their future care or treatment. Withdrawal may refer to the following situations:

i. Withdrawal from intervention - Where a participant wishes to withdraw from the intervention (proposed pathway) but is prepared to complete the follow-up questionnaires.

ii. Withdrawal from follow-up - Where a participant wishes to withdraw from completing the follow-up questionnaires.

iii. Full withdrawal - Where a participant wishes to withdraw from both the study AND from completing any follow-up questionnaires.

The staff at the sites will be aware of the difference in these situations and will inform YTU in the case of any withdrawal.

24. PUBLICATIONS AND DISSEMINATION

We will discuss our study findings with study participants, the PAG, and at a meeting of local GPs. We will present the study results at the annual conferences of The Society for Cardiothoracic Surgery of Great Britain and Ireland, The British Association for Cardiovascular Prevention and Rehabilitation, and The European Association for Cardiothoracic Surgery.

The study will be registered on the International Standard Randomised Controlled Trial Number (ISRCTN) database so that the study hypothesis, design, and methodology are easily accessible online. The study would be written up and submitted for publication in cardiothoracic, cardiac rehabilitation journals and to journals with wide readerships such as The British Medical Journal.

25. RETENTION OF TRIAL DOCUMENTS

All study documentation including records for all participants (all CRFs) as well as REC records and other regulatory documentation will be retained by the YTU and only accessible by the research team. We will use a web portal, called REDCap, to consent, randomise and complete data collection on patients in the trial, this will be username and password protected. Data transferred to the University of York via REDCap will be held securely on the cloud-hosted REDCap server. Access to the study interface will be restricted to named authorised individuals granted user rights by a REDCap administrator at YTU.

Data entered onto a database will be stored on a private network protected by a firewall at the YTU, University of York. Access to the database is restricted to trial staff. All paper records will be securely archived by the YTU in a separate storage facility within the University of York initially and then at an approved off-site location and will be destroyed after ten years. The trial database will be securely archived for at least ten years on the YTU computer network with restricted access to YTU staff. Access to the archived data will be restricted to YTU staff and named individuals but will be retrievable at the request of the sponsor or investigators.

Transfer of paper documents from study sites to YTU will be the responsibility of the Trial Coordinator. After at least ten years, paper documents will be shredded and disposed of as confidential material.

REFERENCES

1. Grant, S. W., Kendall, S., Goodwin, A. T., Cooper, G., Trivedi, U., Page, R., & Jenkins, D. P. (2021). Trends and outcomes for cardiac surgery in the United Kingdom from 2002 to 2016. *JTCVS open*, *7*, 259-269.
2. Ngaage DL, Gooseman M, Bulliment K, et al. Is six weeks too long for first planned postoperative review after cardiac surgery? FORCAST6. Br J Cardiol 2019;26
3. Braimbridge MV. Median Sternotomy. Lancet (1965) 1(7385):585.
4. Fischer H. [Evaluation of medial sternotomy as an approach to the heart]. Zentralbl Chir 1956; 81(40):2099-101.
5. Gerbode F, Braimbridge MV, Melrose DG. Median sternotomy for open cardiac surgery during total heart-lung by-pass. AMA Arch Surg 1958;76(5):821-3; discussion 823-4.
6. Lillehei CW, Cardozo RH. Use of median sternotomy with femoral artery cannulation in open cardiac surgery. Surg Gynecol Obstet 1959;108(6):706-14.
7. British Heart Foundation. Cardiac rehabilitation. Available at www.bhf.org.uk/publications. Accessed November 26, 2017.
8. Adams J, Cline MJ, Hubbard M, McCullough T, Hartman J. A new paradigm for post-cardiac event resistance exercise guidelines. Am J Cardiol 2006; 97(2):281-6.
9. Brocki BC, Thorup CB, Andreasen JJ. Precautions related to midline sternotomy in cardiac surgery: a review of mechanical stress factors leading to sternal complications. Eur J Cardiovasc Nurs 2010; 9(2):77-84.
10. Cahalin LP, Lapier TK, Shaw DK. Sternal Precautions: Is It Time for Change? Precautions versus Restrictions - A Review of Literature and Recommendations for Revision. Cardiopulm Phys Ther J 2011; 22(1):5-15.
11. Anderson L, Thompson DR, Oldridge N, Zwisler AD, Rees K, Martin N, Taylor RS. Exercise-based cardiac rehabilitation for coronary heart disease (Review). Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD001800. DOI: 10.1002/14651858.CD001800.pub3.
12. Pack QR, Goel K, Lahr BD, Greason KL, Squires RW, Lopez-Jimenez F, Zhang Z, Thomas RJ. Participation in cardiac rehabilitation and survival after coronary artery bypass graft surgery a community-based study. Circulation. 2013; 128:590-7.
13. Shroyer AL, Coombs LP, Peterson ED, Eiken MC, DeLong ER, Chen A, Ferguson TB., Jr, Grover FL, Edwards FH. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. Ann Thor Surg 2003; 75(6): 1856-64; discussion 1864-5.
14. Fox JP, Suter LG, Wang K, Wang Y, Krumholz HM, Ross JS. Hospital-based, acute care use among patients within 30 days of discharge after coronary artery bypass surgery. Ann Thorac Surg 2013; 96(1):96-104
15. Hannan EL1, Zhong Y, Lahey SJ, Culliford AT, Gold JP, Smith CR, Higgins RS, Jordan D, Wechsler A.. 30-day readmissions after coronary artery bypass graft surgery in New York State JACC Cardiovasc Interv. 2011; May;4(5):569-76.
16. Hall MH, Esposito RA, Pekmezaris R, Lesser M, Moravick D, Jahn L, Blenderman R, Akerman M, Nouryan CN, Hartman AR. Cardiac surgery nurse practitioner home visits prevent coronary artery bypass graft readmissions. Ann Thorac Surg. 2014; May;97(5):1488-93; discussion 1493-5

17. Saunders RS, Fernandes-Taylor S, Rathouz PJ, Saha S, Wiseman JT, Havlena J, Matsumura J, Kent KC. Outpatient follow-up versus 30-day readmission among general and vascular surgery patients: a case for redesigning transitional care. Surgery. 2014; Oct;156(4):949-56
18. Doherty P, Petre C, Onion N, Harrison A, Dale V, Fell J, Cardy K, Tang L. The National Audit of Cardiac Rehabilitation. Annual Statistical Report (London: The British Heart Foundation, 2017; p66-67 https://www.bhf.org.uk/informationsupport/publications/statistics/national-audit-of-cardiac-rehabilitation-annual-statistical-report-2017
19. Marzolini S, Blanchard C, Alter DA, Grace SL, Oh PI. Delays in Referral and Enrolment Are Associated With Mitigated Benefits of Cardiac Rehabilitation After Coronary Artery Bypass Surgery. Circ Cardiovasc Qual Outcomes. 2015; Nov;8(6):608-20
20. LaPier TK. Functional status of patients during subacute recovery from coronary artery bypass surgery. Heart Lung 2007; 36(2):114-24
21. LaPier TK. Functional status during immediate recovery after hospitalization for coronary heart disease. J Cardiopulm Rehabil 2003;23(3):203-7.
22. Tully PJ, Baker RA. Depression, anxiety, and cardiac morbidity outcomes after coronary artery bypass surgery: a contemporary and practical review**.** J Geriatric Cardiol 2012; 9: 197−208.
23. Doherty P, Petre C, Onion N, Harrison A, Dale V, Fell J, Cardy K, Tang L. The National Audit of Cardiac Rehabilitation. Annual Statistical Report (London: The British Heart Foundation, 2017; p66-67 https://www.bhf.org.uk/informationsupport/publications/statistics/national-audit-of-cardiac-rehabilitation-annual-statistical-report-2017
24. Eder B, Hofmann P, von Duvillard SP, Brandt D, Schmid JP, Pokan R, et al. Early 4- week cardiac rehabilitation exercise training in elderly patients after heart surgery. J Cardiopulm Rehabil Prev 2010;30(2):85-92.
25. Ungerman-deMent P, Bemis A, Siebens A. Exercise program for patients after cardiac surgery. Arch Phys Med Rehabil 1986;67(7):463-6
26. LaPier TK. Indicators of functional deficits after coronary artery bypass surgery. J Cardiopulm Rehabil Prev 2007;27(3):161-5.
27. Ennis S, Lobley G, Worrall S, Powell R, Kimani P, Khan AJ et al. Early initiation of post-sternotomy cardiac rehabilitation exercise training (SCAR): study protocol for a randomised controlled trial and economic evaluation. BMJ Open 2018; 8:e019748.
28. Ennis S, Lobley G, Worrall S, Evans B, Kimani PK, Khan A, Powell R, Banerjee P, Barker T, McGregor G. Effectiveness and Safety of Early Initiation of Poststernotomy Cardiac Rehabilitation Exercise Training: The SCAR Randomized Clinical Trial. JAMA Cardiol. 2022 Aug 1;7(8):817-824. doi: 10.1001/jamacardio.2022.1651. PMID: 35731506; PMCID: PMC9218928. 33.
29. Fell J, Dale V, Doherty P. Does the timing of cardiac rehabilitation impact fitness outcomes? An observational analysis. Open Heart 2016;3:e000369.
30. Johnson DA, Sacrinty MT, Gomadam PS, Mehta HJ, Brady MM, Douglas CJ, Paladenech CC, Robinson KC. Effect of early enrollment on outcomes in cardiac rehabilitation. Am J Cardiol. 2014; Dec 15;114(12):1908-11.

31. Pack QR, Mansour M, Barboza JS, Hibner BA, Mahan MG, Ehrman JK, Vanzant MA, Schairer JR, Keteyian SJ. An early appointment to outpatient cardiac rehabilitation at hospital discharge improves attendance at orientation: a randomized, single-blind, controlled trial. Circulation. 2013; Jan 22;127(3):349-55
32. Collins ZC, Suskin N, Aggarwal S, Grace SL. Cardiac rehabilitation wait times and relation to patient outcomes. Eur J Phys Rehabil Med. 2015 Jun;51(3):301-9.
33. Zimmerman L, Barnason S, Schulz P, Nieveen J, Miller C, Hertzog M, et al. The effects of a symptom management intervention on symptom evaluation, physical functioning, and physical activity for women after coronary artery bypass surgery. J Cardiovasc Nurs 2007;22(6):493-500.
34. BACPR. Standards and Core Components for Cardiovascular Disease Prevention and Rehabilitation. 2017. Available from: http://www.bacpr.com
35. http://www.cardiacrehabilitation.org.uk/NCP-CR.htm
36. Parker R, Adams JL, Ogola G, McBrayer D, Hubbard JM, McCullough TL, et al. Current activity guidelines for CABG patients are too restrictive: comparison of the forces exerted on the median sternotomy during a cough vs. lifting activities combined with valsalva maneuver. Thorac Cardiovasc Surg 2008;56(4):190-4.
37. Westerdahl E, Moller M. Physiotherapy-supervised mobilization and exercise following cardiac surgery: a national questionnaire survey in Sweden. J Cardiothorac Surg 2010; 5:67.
38. Tuyl LJ, Mackney JH, Johnston CL. Management of sternal precautions following median sternotomy by physical therapists in Australia: a web-based survey. Phys Ther 2012; 92(1):83-97.
39. Ngaage D, Mitchell N, Dean A et al, A randomised controlled, feasibility study to establish the acceptability of early outpatient review and early cardiac rehabilitation compared to standard practice after cardiac surgery and viability of a future large-scale trial (FARSTER). *Pilot and Feasibility Studies* **9**, 79 (2023).
40. Grove T. Incremental shuttle walk test in cardiac rehabilitation. British Journal of Cardiac Nursing. 2013 Jan;8(1):31-7.
41. Cowie A, Hair M, Kerr E, McKay J, Allan L, Thomson P (2019) Validity and testretest reliability of a patient-reported outcome measure for an outpatient cardiac rehabilitation programme. British Journal of Cardiac Nursing 14(8):1–13. https://doi.org/10.12968/bjca.2018.0039
42. Spitzer RL, Kroenke K, Williams JB, et al; A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May 22;166(10):1092-7.
43. EuroQoL. EQ-5D-5L. Available at https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/. Accessed October 11, 2024.
44. Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A. Measuring health-related quality of life in rheumatoid arthritis: Validity, responsiveness and reliability of EuroQol (EQ-5D). Br J Rheumatol. 1997; 36 (5):551-9.
45. BACPR_EPG_CV19_Supplement. Available at: https://www.bacpr.org/__data/assets/pdf_file/0025/38662/BACPR_EPG_CV19_Supplement__FINAL.pdf Accessed August13th, 2002.

46. University of York, Data Protection Legislation https://www.york.ac.uk/records-management/dp/
47. Data Protection Act, UK Government http://www.legislation.gov.uk/ukpga/2018/12/contents/enacted
48. Information Commissioner's Office https://ico.org.uk/for-organisations/guide-tothe-general-data-protection-regulation-gdpr/
49. Houchen-Wolloff L, Boyce S, Singh S. The minimum clinically important improvement in the incremental shuttle walk test following cardiac rehabilitation. Eur J Prev Cardiol. 2015 Aug;22(8):972-8. doi: 10.1177/2047487314540840. Epub 2014 Jun 23. PMID: 24958737.
50. Hinde S, Harrison A, Bojke L, Doherty P. Quantifying the impact of delayed delivery of cardiac rehabilitation on patients' health, Eur J Preventive Cardiol, 2020;27(16):1775–81, https://doi.org/10.1177/2047487320912625
51. Torgerson D, Torgerson C. Designing randomised trials in health, education and the social sciences: An introduction. London: Palgrave Macmillan; 2008.