CycLing and EducATion (CLEAT): a single centre randomised controlled trial of a cycling and education intervention versus standard physiotherapy care for the treatment of hip osteoarthritis

Statistical Analysis Plan

Trial name:	A pragmatic single-centred randomised controlled trial with economic evaluation, to compare a cycling and educational programme with usual physiotherapy care in the treatment of hip osteoarthritis: CycLing and EducATion (CLEAT)
Trial registration number:	ISRCTN19778222
Protocol title and version number:	A pragmatic, randomised controlled trial with economic evaluation, to compare a cycling and educational programme (CHAIN) with usual physiotherapy care in the treatment of hip osteoarthritis: CycLing and EducATion V4.1
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To be approved and reviewed by:

	Name	**Signature**	**Date**
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List of Abbreviations

Abbreviation	
AE	Adverse Event
AR	Adverse Reaction
CEA	Cost-effectiveness analysis
CHEERs	Consolidated Health Economic Evaluation Reporting
CI	Chief Investigator
CRF	Case Report Form
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
DMEC	Data Monitoring and Ethics Committee
GCP	Good Clinical Practice
HOOS	Hip dysfunction and Osteoarthritis Outcome Score
IB	Investigator Brochure
ICER	Incremental Cost-effectiveness Ratios
ICF	Informed Consent Form
ICH	International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.
ISF	Investigator Site File (This forms part of the TMF)
ISRCTN	International Standard Randomised Controlled Trials
HEAP	Health Economic Analysis Plan
HOOS	Hip Disability and Osteoarthritis Outcome Score
HOOS function score	The “Function, daily living” component score from the HOOS
HOOS sports and recreational activities score	The “Function, sports and recreational activities score” component score from the HOOS
HRA	Health Research Authority
NHS R&D	National Health Service Research & Development
OARSI	Osteoarthritis Research Society International
PAM	Patient Activation Measure
PI	Principal Investigator
PIS	Participant Information Sheet
PSFS	Patient Specific Functional Scale
QALY	Quality adjusted Life Years
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SOP	Standard Operating Procedure
SSI	Site Specific Information
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee
UHD	University Hospitals Dorset NHS Foundation Trust
VAS	Visual Analogue Score
WOMAC	Western Ontario and McMaster Universities Arthritis

Keywords
Osteoarthritis, hip; exercise therapy; group exercise; cycling, patient education

1 Introduction

1.1 Purpose of SAP

This statistical analysis plan (SAP) describes in detail the methods that will be used to analyse the data collected as part of the CLEAT trial. This will form the basis of the final trial publication. The final analysis will follow the SAP to ensure that the analyses are conducted in a scientifically valid manner and to avoid post hoc decisions which may affect the interpretation of the statistical analysis. Any deviations from the SAP will be detailed in the final report.

1.2 SAP Roles and responsibility

Chief Investigator:	**Prof Tom Wainwright** **Email:** twainwright@bournemouth.ac.uk
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1.3 Trial background and rationale (short synopsis)

In the UK, 8.75 million people aged over 45 years (33%) have sought treatment for osteoarthritis, and with increasing levels of obesity and an ageing population, projections show that by 2035 this number could nearly double (Arthritis ResearchUK 2013). Osteoarthritis is a chronic degenerative joint disorder usually associated with ageing, and it is estimated that a quarter of people affected by osteoarthritis have osteoarthritis of the hip (2.12 million people, 8% of the UK population) (Versus Arthritis 2018). Hip osteoarthritis is associated with hip pain, stiffness and limitations to activities of daily living, and is the most common reason for a total hip replacement.

There is no known cure for osteoarthritis, and so non-surgical management for people with symptoms not yet severe enough for surgery mainly focuses on alleviating pain, and maximising function by addressing aspects which can be modified. The National Institute for Health and Care Excellence (NICE) guidelines (National Institute for Health and Care Excellence (NICE) 2014) state that three core treatments should be the first line treatment for patients with osteoarthritis. These are education and advice, exercise (aerobic and local muscle strengthening), and weight loss where appropriate, however there is no specific guidance on type of exercise, dose or intensity.

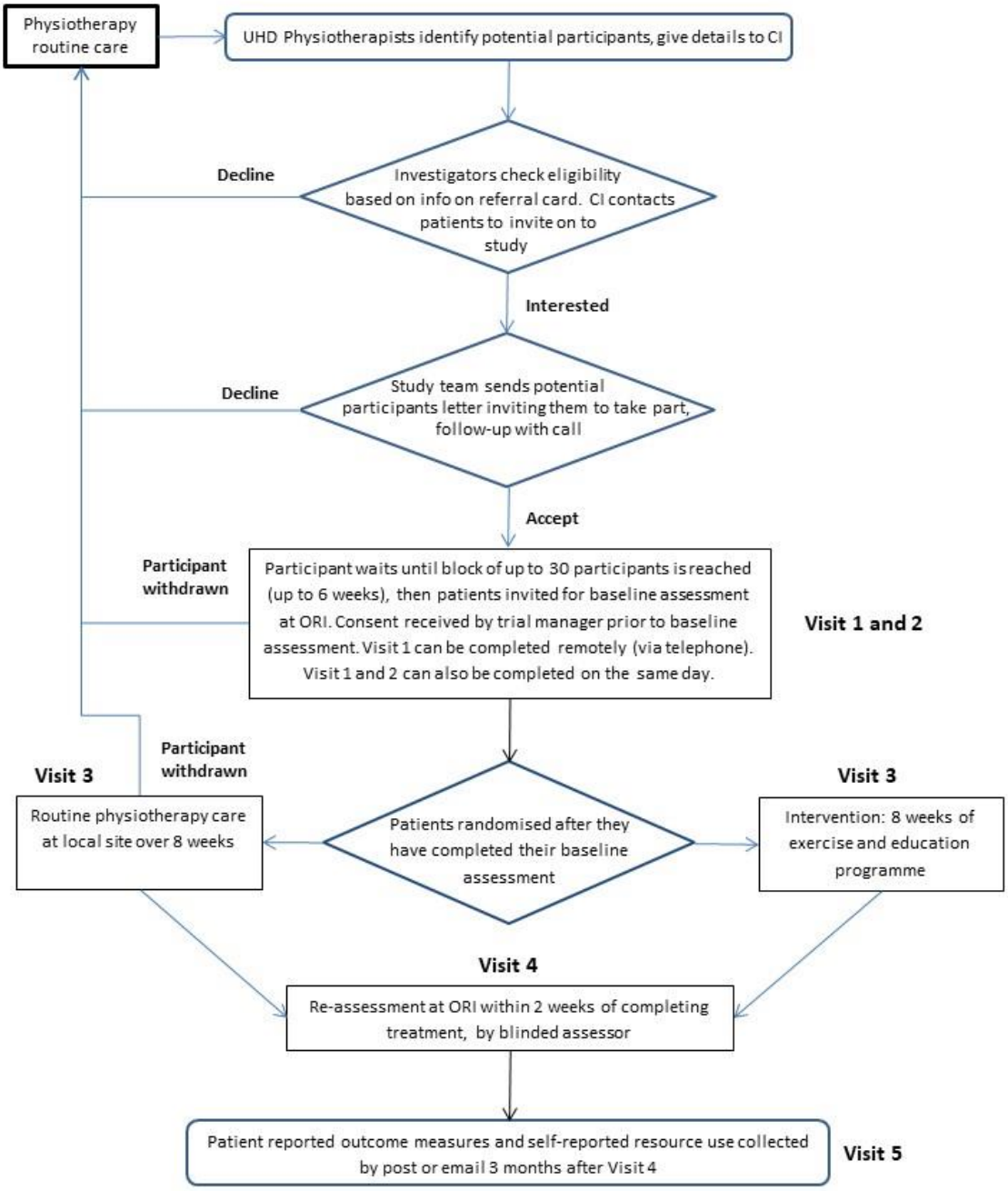
To date, studies have used exercises of low to moderate intensity with low to moderate success, but as yet there is little research on whether increasing the intensity of exercise in a safe way can increase the benefit of the exercise. It is important that appropriate models of prevention and treatment are developed to support and treat osteoarthritis sufferers.

Cycling may be of benefit in comparison to other forms of exercise because it is a health enhancing form of physical activity (Bauman and Rissel 2009) and a non-weight bearing activity that is considered less stressful on the body than impact or other running sports (Rissel et al. 2013). Furthermore, positive relationships between cycling and increased cardiorespiratory fitness, increased functional ability, and disease risk factor profiles have been found (Oja et al. 2011). There is also evidence in longitudinal epidemiological studies that cycling can lead to significant risk reduction for all-cause and cancer mortality, cardiovascular disease, colon and breast cancer, and obesity morbidity in the middle-aged and elderly (Oja et al. 2011).

In addition to the specifics of the cycling activity, the programme has been designed to influence behaviour change and includes components to motivate, increase adherence and prevent drop out of participants. There will be (1) a programme of education, (2) plans for lifestyle changes, (3) involvement of participants in the development of the programme, (4) a group-based cycling class, with (5) a dedicated exercise leader, (6) encouragement to maintain an exercise diary, (7) resources to remove barriers to the uptake of the programme and continued involvement after the programme, and (8) on-going encouragement and support. These components have been designed to increase the likely efficacy of the intervention, by drawing on the evidence and models regarding behaviour change (Michie et al. 2013) addressing participants' needs at individual (personal), group (social), and environmental levels; (King and Sallis 2009; Michie 2008) and focusing on developing participants' capability, motivation, and opportunity (Michie and West 2013).

This study will compare outcome data collected from hip osteoarthritis patients undertaking an eight-week education and cycling programme (CHAIN) with patients who undertake routine physiotherapy care. The aim of the study is to investigate the effectiveness and cost-effectiveness of a cycling and education intervention compared to usual physiotherapy care to manage symptoms of hip osteoarthritis in people 18 years and over.

Trial flow chart



1.4 Objectives

Primary Objective:

To determine whether there is a difference in self-reported function of performing everyday activities (i.e. walking, using the stairs, driving and shopping) between those receiving the cycling and education intervention compared to those with usual physiotherapy care.

Secondary objectives:

1. To determine whether there is a difference in self-reported hip pain between those receiving the cycling and educational intervention compared to those with usual physiotherapy care.
2. To determine whether there is a difference in objectively observed function between those receiving the cycling and education intervention compared to those with usual physiotherapy care.
3. To determine whether there is a difference in quality of life between those receiving the cycling and educational intervention compared to those with usual physiotherapy care.
4. To determine whether there is a difference in resources used and associated costs between those receiving the cycling and educational intervention compared to those with usual physiotherapy care.
5. To estimate the resources used and costs of providing the cycling and education intervention and its cost-effectiveness compared with usual physiotherapy care.
6. To determine whether there is a difference in activation levels (defined as the individual's knowledge, skill and confidence to manage their own health) between those receiving the cycling and educational intervention compared to those with usual physiotherapy care.

1.5 Definition of endpoints

1.5.1 Definition of primary endpoint

The primary endpoint is the score (1-100) from the self-reported "Function, daily living" component from the Hip Disability and Osteoarthritis Outcome Scale (HOOS) at visit 4 (approximately 10 weeks after the baseline assessment).

For the purposes of this document, the "Function, daily living" component score from the HOOS will be termed as 'HOOS function score'.

1.5.2 Definition of secondary endpoints

For the purposes of this document, the HOOS 'function, sports and recreational activities score' will be termed as 'HOOS sports and recreational activities score'.

- Weight, height, BMI, body composition (% body fat), blood pressure, resting heart rate at visit 4
- HOOS function score at visit 5
- HOOS pain component score at visits 4 and 5
- HOOS symptoms component score at visits 4 and 5
- HOOS stiffness component score at visits 4 and 5
- HOOS sports and recreational activities component score at visits 4 and 5
- HOOS Quality of Life component score at visits 4 and 5
- Stair climb test at visit 4
- 30-second chair stand test at visit 4
- 40 metre walk test at visit 4
- Patient Activation Measure (PAM) at visits 4 and 5
- Medication use at visits 4 and 5 (Y/N)
- EQ-5D VAS at visits 4 and 5
- EQ-5D-5L index values at visits 1/2, 4 and 5 used to derive QALYs
- Self-reported resource use at visits 4 and 5

Mechanistic variables to be reported include:

- Range of motion of index and contralateral hips (Flexion, Extension, Abduction, Adduction, Internal Rotation and External Rotation measured in degrees) at visit 4
- Patient-Specific Functional Scale (PSFS) at visits 4 and 5
- Exercise diary at visit 4

1.6 Analysis principles

1.6.1 General principles

All analyses will be reported according to CONSORT 2010 and Southampton Clinical Trials Unit (SCTU) standard operating procedure (SOP) on planning, implementing and reporting statistical analyses (CTU/SOP/5058) and ICH E9 guidelines on Statistical Principles in Clinical Trials.

1.6.2 Model checking

For all regression models applied, the assumptions underlying these models will be checked using appropriate methods such as a residual analysis. If the residual analysis shows any issues with the model then appropriate transformations will be attempted.

2 Design considerations

2.1 Description of trial design

CLEAT is a pragmatic parallel-arm randomised controlled trial comparing an 8-week cycling and education complex intervention, that is underpinned by physiological and behaviour change theory, with routine physiotherapy care reflecting standard practice in the NHS in the UK.

The trial population will be patients who have been diagnosed, using the NICE criteria, with osteoarthritis of the hip. The osteoarthritis will be diagnosed by a clinician reviewing medical history and current symptoms. An x-ray will not be required to confirm the diagnosis (OARSI 2019).

This trial is based at the University Hospitals Dorset NHS Foundation Trust. Patients referred to the Physiotherapy Department at the hospital will be considered for the trial. The trial intervention will be conducted at a local centre, led by instructors with previous experience of delivering spin classes, for all patients in the intervention arm; whilst the control arm, physiotherapy care, will be delivered by the Physiotherapy Department at the University Hospitals Dorset.

2.2 Trial power and sample size

The sample size calculation is based on the primary outcome measure, the physical function score (range 0-100) from the HOOS function scale taken at 10 weeks. This has identical items to the WOMAC function scale, the only difference being a transformation of the scores to a percentage for the HOOS. Mean primary outcome will be compared between the intervention and control arms and will be analysed using baseline function score as a covariate. Thus, the sample size calculation takes into account the correlation between pre-exercise and post-exercise values (Borm et al. 2007).

The literature mostly uses the WOMAC function score, so parameters for the sample size calculation are based on that, though we indicate the equivalent HOOS score where relevant. We will assume a correlation between pre and post exercise outcomes of 0.6 (conservative estimate based on (a) data from our feasibility study and (Wallis et al. 2014) where the lower limits of the 95% confidence interval were 0.75 and 0.69 respectively, and (b) the paper (Bennell et al. 2010) that assumed a value of 0.6 for their sample size calculation). This will reduce required sample size by a factor of 0.64. The intervention is delivered in groups, so to allow for potential clustering effects in the intervention arm of the trial we have inflated the variance of the mean in that arm by a factor of 1.22, assuming a cluster size of 12 and intra-cluster correlation coefficient of 0.02 (Allen et al. 2017). Using a 5% two-sided significance test, an effect size of 5 points on WOMAC (equivalent to 7.4% on HOOS) (average of minimum clinically important difference found previously (Angst et al. 2001; Tubach et al. 2005) and assuming a standard deviation of 13 on WOMAC (equivalent to 19.1 on HOOS) (average taken from previous literature (Angst et al. 2001; Bennell et al. 2014; Ehrich et al. 2000; Tubach et al. 2005) and the feasibility study (Wainwright et al. 2016) a sample size of 102 per arm would be required for 90% power. Allowing for a withdrawal/ incomplete primary outcome data rate of 20% (for example (Hurley et al. 2007) the recruitment target for sample size will be increased to 256 (allowing for 9 clusters of size 15 in the intervention arm). In case there is under

recruitment into the planned cohorts of 30 participants (15 in each arm) we will increase the number of cohorts from 9 to 10. The sample size calculation was partly conducted using NQuery Advisor software.

2.3 Randomisation details

The study will use block randomisation. Each programme in the study will have up to 30 participants (see below) randomised to the intervention: the education and cycling programme, or routine physiotherapy care, with a 1:1 allocation ratio. Randomisation will be performed for each programme using a web-based system. The randomisation process will be performed using an algorithm on the web-based system once up to 30 participants have agreed to take part and will be blinded to the assessors and trial manager. The randomisation allocation for each participant will not be revealed until participants have signed the consent forms and completed their baseline assessments. A delegated member of the study team will then be able to see which treatment arm the participant has been allocated and will arrange their first treatment and post-treatment assessment, at the end of the baseline assessment. Participants will receive this information on a leaflet which also contains the address of their treatment site, contact details and other relevant information.

Screening ID, gender and date of birth data will be attached to each randomisation, to ensure the there is an audit trail to show that the correct participants have been randomised accordingly.

Assessors undertaking assessments at baseline and visit 4 will be blinded to the randomisation, and participants will be educated to ensure that they do not inform the assessors of which treatment arm they participated in. The nature of the intervention means that participants and treatment providers will not be blinded.

Ideally each programme will have 30 patients, 15 randomised to the education and cycling programme, and 15 to routine care. However, if there is a shortfall in recruitment to a programme, the programme can proceed with fewer patients so that patients do not have to wait longer.

2.4 Timing of planned analyses

2.4.1 Interim analyses and early stopping

No interim analyses are planned for CLEAT and there are no details of guidelines for stopping the trial early.

2.4.2 Final analysis

The final trial analysis, as outlined in Section 4 below, will be performed once all trial patients have been recruited, study follow up for these patients has been completed and all data has been cleaned.

3 Statistical considerations

3.1 Definition of analysis populations

3.1.1 Intention-to-treat analysis population

The intention-to-treat analyses will include all randomised participants (subject to data being available) and participants will be analysed in the group they were randomised to.

3.1.2 Per-protocol analysis population

For the primary outcome we will also conduct a per protocol analysis where participants will be excluded from the analysis if (a) there was a protocol violation (including swapping treatment arms) or (b) adherence to exercise was poor (e.g. attendance at less than 87.5% of classes i.e. less than 7 classes) or adherence to physiotherapy was poor in the control arm (e.g. attendance at less than 100% of sessions i.e. participant must attend all physiotherapy sessions).

3.1.3 Safety population

For safety analyses, all patients who received any treatment will be evaluable.

3.2 Analysis software

The data analysis will be conducted using SAS version 9.4 or above, Stata version 17 or above, or R version 4.2 or above.

3.3 Methods for handling data

3.3.1 Withdrawal from trial

All data up until the point of patient withdrawal from the trial will be used in analyses unless the patient withdrew consent and does not wish for the data already collected prior to withdrawal to be used for the trial.

3.3.2 Missing data

It is anticipated that the main analyses will assume data are missing completely at random and therefore we will not use any imputation for the missing values. The analysis method (outlined in Section 4.5 below) does not require complete data, therefore the treatment effect can still be estimated with incomplete data.

A sensitivity analysis using imputed data may be carried out if the percentage of missing data is high. See section 4.7 for more details.

3.3.3 Outliers

No methods will be used to handle outliers in the data.

3.3.4 Assumption checking and alternative methods

The primary endpoint analysis uses multi-level regression modelling. One of the assumptions of this type of modelling is normally distributed residuals. If there are any issues with the model assumptions, then appropriate transformations will be considered. If a suitable transformation cannot be found, then non-parametric analysis will be considered.

3.3.5 Data transformations

Any data transformations which will be considered during the analysis of the data will be due to the statistical models assumption checking described in section 3.3.4 above. No further transformations are planned.

3.4 Definition of key derived variables

3.4.1 Hip Disability and Osteoarthritis Outcome Scale (HOOS)

The Hip Disability and Osteoarthritis Outcome Scale (HOOS) is a 40-item scale to measure the patient-relevant measures of osteoarthritis. It contains the following components:

- Function, daily living (17 items)
- Pain (10 items)
- Symptoms (3 items)
- Stiffness (2 items)
- Function, sports and recreational activities (4 items)
- Quality of life (4 items)

Participants respond to symptom questions in a 5-point frequency response (e.g. never, rarely, sometimes, often, and always), and respond to the severity of symptoms in a 5-point severity response (none, mild, moderate, severe, extreme). The component scores equal the sum of the scores of all items within the corresponding component, where the scores are defined as follows:

- 0 = Never/none
- 1 = Rarely/mild
- 2 = sometimes/moderate
- 3 = often/severe
- 4 = always/extreme

For example, the primary outcome is the HOOS function, daily living score component which has a total of 17 items and a maximum possible component score of 68.

These scores are then converted to a standardised score out of 100 (a percentage) using the following formula:

- 100 – (participant's component score/maximum possible component score)*100

Where a score of 0 indicates extreme symptoms and a score of 100 indicating no symptoms.

For the purposes of this protocol, the HOOS 'function, daily living score' will be termed as 'HOOS function score', and the HOOS 'function, sports and recreational activities score' will be termed as 'HOOS sports and recreational activities score'.

3.4.2 Baseline and demographic characteristic variables

The following baseline and demographic variables will be collected through a self-reported questionnaire:

- **Age (computed from date of birth and date of randomisation)**
- **Gender, one of:**
  - Male
  - Female
  - Other
- **Ethnicity, one of:**
  - White
  - African
  - Caribbean
  - Arab
  - Indian
  - Pakistani
  - Bangladeshi
  - Chinese
  - Mixed/multiple ethnic group
  - Other ethnic group, or
  - Prefer not to say
- **Highest level of education, one of:**
  - None
  - O-level/CSE/GCSE
  - A-level or equivalent
  - Degree or equivalent
  - Doctorate/higher degree
  - Other qualifications, or
  - Don't know
- **Employment status, one of:**
  - Paid/unpaid work full-time
  - Paid/unpaid work part-time
  - Unemployed and currently looking for work
  - Unemployed and not currently looking for work
  - Student
  - Retired
  - Unable to work because of osteoarthritis, or
  - Unable to work for reason other than osteoarthritis
- **Co-morbidities, all that apply:**
  - Musculoskeletal
  - Neurological
  - Cardiovascular
  - Respiratory
  - Dermatological
  - Haematological
  - Endocrine
  - Hepatic
  - Gastrointestinal
  - Urogenital diseases

- **Medication use, all that apply:**
  Analgesia
  - Paracetamol (tablet)
  - Paracetamol (liquid)

  Oral Opioids
  - Co-codamol
  - Codeine (tablet)
  - Codeine (liquid)
  - Tramadol (tablet)
  - Tramadol (liquid)
  - Morphine (tablet)
  - Morphine (liquid)
  - Oxycodone (tablet)
  - Oxycodone (liquid)

  Nonsteroidal Anti-inflammatory
  - Aspirin
  - Ibuprofen (tablet)
  - Ibuprofen (liquid)
  - Diclofenac (tablet)
  - Naproxen (tablet)
  - Naproxen (liquid)
  - Meloxicam
  - Celecoxib
  - Etodolac

  Topical anti-inflammatories
  - Ibuprofen (topical)
  - Diclofenac (topical)

  Neuro (anti-convulsants)
  - Gabapentin (tablet)
  - Gabapentin (liquid)
  - Pregabalin (tablet)
  - Pregabalin (liquid)

  Anti-depressant
  - Amitriptyline (tablet)
  - Amitriptyline (liquid)

Yes/no for all that apply. Present frequencies and group according to categories.

3.4.3 Weight, height, body composition, blood pressure and resting heart rate
The Trial Assessors will complete the baseline anthropometric measurements of height (m) and weight (kg) (SECA measurement scales), and body fat percentage of the participants with an electronic segmental body composition monitor (Tanita MC-780MA Multi Frequency Body Composition Analyser). Resting heart rate and blood pressure will be measured using the Welch Allyn Connex Spot Monitor.

The BMI of the patients will be calculated as the weight (in kg) divided by the square of height (in m).

3.4.4 Functional measures

As recommended by Osteoarthritis Research Society International, the patients' performance based functional measures will be evaluated by the Assessor Physiotherapist with the following:

- 40m Fast Paced Walk Test (recording the time taken to complete the 40m walk to the nearest 0.01 second) Report as speed ($m.s^{-1}$) and use of walking aid (yes/no).
- 30s Chair Stand Test (recording the number of stands completed). Report as number of stands, test adapted (yes/no), test failed (yes/no).
- Stair Climb Test (recording the time taken to complete the test to the nearest 0.01 second). Report number of stairs in test, time taken (s), use of handrail (yes/no) and use of walking aid (yes/no).

3.4.5 Patient Activation Measure (PAM)

The Patient Activation Measure (PAM) is a 13-item scale to measure the degree of activation or self-initiation of the patients. The patients respond to the items in a 4-point Likert scale:

- 1=strongly disagree
- 2=disagree
- 3=agree
- 4=strongly agree
- Not applicable (N/A)

Raw total PAM scores (derived by [raw score]/[number of items answered excepting non-applicable items] * 13) can be transformed to a scale (PAM score) with a theoretical range of 0-100 based on calibration tables, with higher scores indicating higher activation. The PAM scores will be calculated by a third party and be entered into the CLEAT database. Analysis will be done using these entered PAM scores.

3.4.6 Health-related quality of life measures (EQ-5D-5L and EQ-5D VAS)

The health-related quality of life measures (EQ-5D-5L and EQ-5D VAS) will be described and evaluated in a separate Health Economic Analysis Plan (HEAP) and therefore are not described in this document.

3.4.7 Self-reported resource use questionnaire

Primary and secondary health care, analgesia use, social care, and participant and carer-related resource use will be self-reported by the patients and evaluated in a separate Health Economic Analysis Plan (HEAP) and therefore are not described in this document.

3.4.8 Mechanistic Variables

Range of motion

The range of motion at flexion, extension, abduction, adduction, internal rotation and external rotation for index and contralateral hips will be measured in degrees. No group comparisons will be carried out.

Patient-Specific Functional Scale (PSFS)

The Patient-Specific Functional Scale (PSFS) asks the patients if they have any difficulties in carrying out a list of self-identified daily activities. They can choose at most 6 of them and rate the degree of difficulty from 0 to 10, where 0 represents "unable to perform" and 10 represents "able to perform at prior level". No group comparisons of the scores will be carried out.

Activity diary
The patients will complete an activity diary which record the types of exercise they did (with a choice of 17 exercises and an open option of "other"), the date of the exercise, the total duration, and the intensity rated using the Borg Scale (1 to 10 where 1 represents very light activity and 10 represents maximum effort).

Psychological questionnaire and patient feedback on cycling and education intervention
Participants in the cycling and education (CHAIN) group only will complete a questionnaire covering four scales and each scale has four questions based on a rating of 1 to 7.

- Group Identification (1 represents "Fully Disagree" and 7 represents "Fully Agree")
- Social Support (1 represents "Strongly Disagree" and 7 represents "Strongly Agree")
- Education Leader (1 represents "Not at All" and 7 represents " Completely")
- Cycling Leader (1 represents "Not at All" and 7 represents " Completely")

An average score for each scale will be calculated by dividing the total score by 4.

3.5 General principles for reporting and analysis

The following principles will be applied:

- 5% 2-sided level of statistical significance will be used
- 95% level confidence interval (CI) will be produced where defined
- No adjustment for multiplicity will be used
- Descriptive statistics will be presented as appropriate to the nature of the data. For example, continuous variables may be summarised by the number of observations, mean, standard deviation, median (interquartile range if appropriate), minimum, and maximum. Categorical variables may be summarised by frequency counts and percentages for each category.
- For continuous data, the mean, standard deviation, median and IQR will generally be rounded to 1 decimal place more than the accuracy of the original data. Minimum and maximum will be displayed with the same accuracy as the original data.
- Unless otherwise stated, percentages will be presented to 1 decimal place.
- Where results are split by treatment arm, tables may also include a total column.
- The treatment groups will be labelled as "Cycling/educational intervention" and "Usual physiotherapy care"

4 Planned analyses and reporting

4.1 Disposition of the study population

A CONSORT diagram will be produced showing a clear account of all participants who entered the study (see Figure 1).

A summary of analysis populations will be presented in Table 1 and end of study information summarised in Table 2.

4.2 Protocol deviations

Important deviations related to study inclusion or exclusion criteria, conduct of the trial, patient management or patient assessment will be listed by patient in Table 3.

4.3 Baseline and demographic characteristics (ITT population)

Summary statistics will be produced and presented by treatment group for: demographic characteristics, co-morbidities, medication use, HOOS scores, range of motion index hip, 30-second chair stand test, stair climb test, 40 metre walk test, and patient activation measure (PAM) at baseline - see Tables 4 to 7.

4.4 Compliance to study interventions (ITT population)

Summary statistics will be produced and presented by treatment group for compliance to education and cycling and physiotherapy sessions respectively – see Table 8.

4.5 Participant Information at visit 4 and visit 5 (ITT population)

Summary statistics will be produced and presented by treatment group for weight, height, BMI, body composition (% body fat), blood pressure, resting heart rate , HOOS scores, range of motion index, 30-second chair stand test, stair climb test, 40 metre walk test, and patient activation measure (PAM) at visits 4 and 5 – see Tables 9 to 11.

4.6 Withdrawals (ITT population)

Withdrawal information including the primary reasons of discontinuation will be summarised and presented by treatment group – see Table 12.

4.7 Primary endpoint

The ITT population will be used to assess the primary outcome of the difference in the HOOS functional component between baseline and visit 4. The computation of the score is explained in Section 3.4 above. Summary statistics for the HOOS functional component score will be produced and presented by treatment group for the number of participants, mean, SD, median, interquartile range, minimum and maximum at baseline and visit 4. The difference in mean HOOS functional component score between baseline and week 4 will also be presented - see Table 13.

The primary outcome will be compared between trial arms using multi-level regression, controlling for baseline HOOS function component score and cycling group (cluster), see Table 14. The cycling/education intervention will take place in groups of around 15, and so we will treat grouping as a random effect in the analysis. For the usual care arm each participant will be assumed to be in their own group (or cluster) of one. The distribution of the residuals will be

tested against normality, and if the normality assumption is violated then a suitable method will be used instead (e.g., generalised estimating equation).

We will also conduct a per protocol analysis where participants will be excluded from the analysis if (a) there was a protocol violation (including swapping treatment arms) or (b) adherence to exercise was poor (e.g. attendance at less than 87.5% of classes i.e. less than 7 classes) or adherence to physiotherapy was poor in the control arm (e.g. attendance at less than 100% of sessions i.e. participant must attend all physiotherapy sessions) - see Tables 15 and 16.

It is anticipated that the main analyses will assume data are missing completely at random (ie will not use any imputation). To assess the robustness of the result to this assumption, for the analysis of primary outcome (HOOS function component) we will also conduct a sensitivity analysis using a multiple imputation method if 20% or more of the primary endpoint data is missing. All baseline variables significantly associated with HOOS function component score at baseline will be included in the prediction model, and the missing data will be imputed 10 times. If multiple imputation is used, we will also do a complete case analysis.

No subgroup analyses are planned.

4.8 Secondary endpoints

The analysis of the following secondary outcomes will use the same approach as that of the primary outcome, adjusting each outcome for its own baseline. However, where visits 4 and 5 are both included in the model, we will use a repeated measures model with a random effect for patient together with the random effect for cycling group. The fixed effects of treatment group, time, and group-by-time interaction will also be included, and the interaction effect will be used to present the effectiveness of the trial intervention at the different time points.

Continuous variables and binary variables will be analysed with linear and logistic models, respectively HOOS function score at visit 5 (score at visit 4 is primary outcome)

- HOOS pain score at visits 4 and 5
- HOOS symptoms score at visits 4 and 5
- HOOS stiffness score at visits 4 and 5
- HOOS sports and recreational activities score at visits 4 and 5
- HOOS Quality of Life score at visits 4 and 5
- 30-second chair stand test at visit 4
- Stair climb test at visit 4
- 40 metre walk test at visit 4
- Patient Activation Measure (PAM) at visits 4 and 5
- BMI, body composition, blood pressure and resting heart rate at visit 4
- Medication use at visits 4 and 5
- Self-reported resource use at visits 4 and 5

Mechanistic outcomes to be reported include:

- Range of motion of index and contralateral hips (Flexion, Extension, Abduction, Adduction, Internal Rotation and External Rotation measured in degrees) at visit 4
- Patient-Specific Functional Scale (PSFS) at visits 4 and 5
- Exercise diary at visit 4

No subgroup analyses are planned.

See Tables 17 to 55 for shell tables.

4.9 Additional analyses

The health-related quality of life measures (EQ-5D-5L and EQ-5D VAS) will be described and evaluated in a separate Health Economic Analysis Plan (HEAP) and therefore are not described in this document.

4.10 Safety reporting

All safety analyses will be performed on the safety population.

4.10.1 Adverse Events

Adverse events (AE) are defined as any untoward medical occurrence in a participant who has been treated on the study, including occurrences which are not necessarily caused by or related to the treatment. Treatment is defined as having taken part in the intervention or undergone routine physiotherapy treatment for this study.

The only AEs which will be recorded in the participant's medical record and also in their CRF are those for which they sought unplanned advice from a health care professional, i.e. visiting a GP for an acute condition.

A summary of adverse events experienced during the trial will be presented by treatment arm in Tables 56 to 58.

4.10.2 Serious Adverse Events

A Serious adverse event (SAE) is defined as any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

In general osteoarthritis of the hip is a non-life-threatening condition typified by on-going progression of symptoms and deterioration of function. There are no expected SAEs for this study.

Information regarding serious adverse events, including overall assessment, grade, will be summarised in Tables 59 to 60 and a list of all SAEs will also be presented in Table 61.

5 Tables, listings and figures templates

5.1 Disposition of study population

Figure 1 CONSORT Diagram

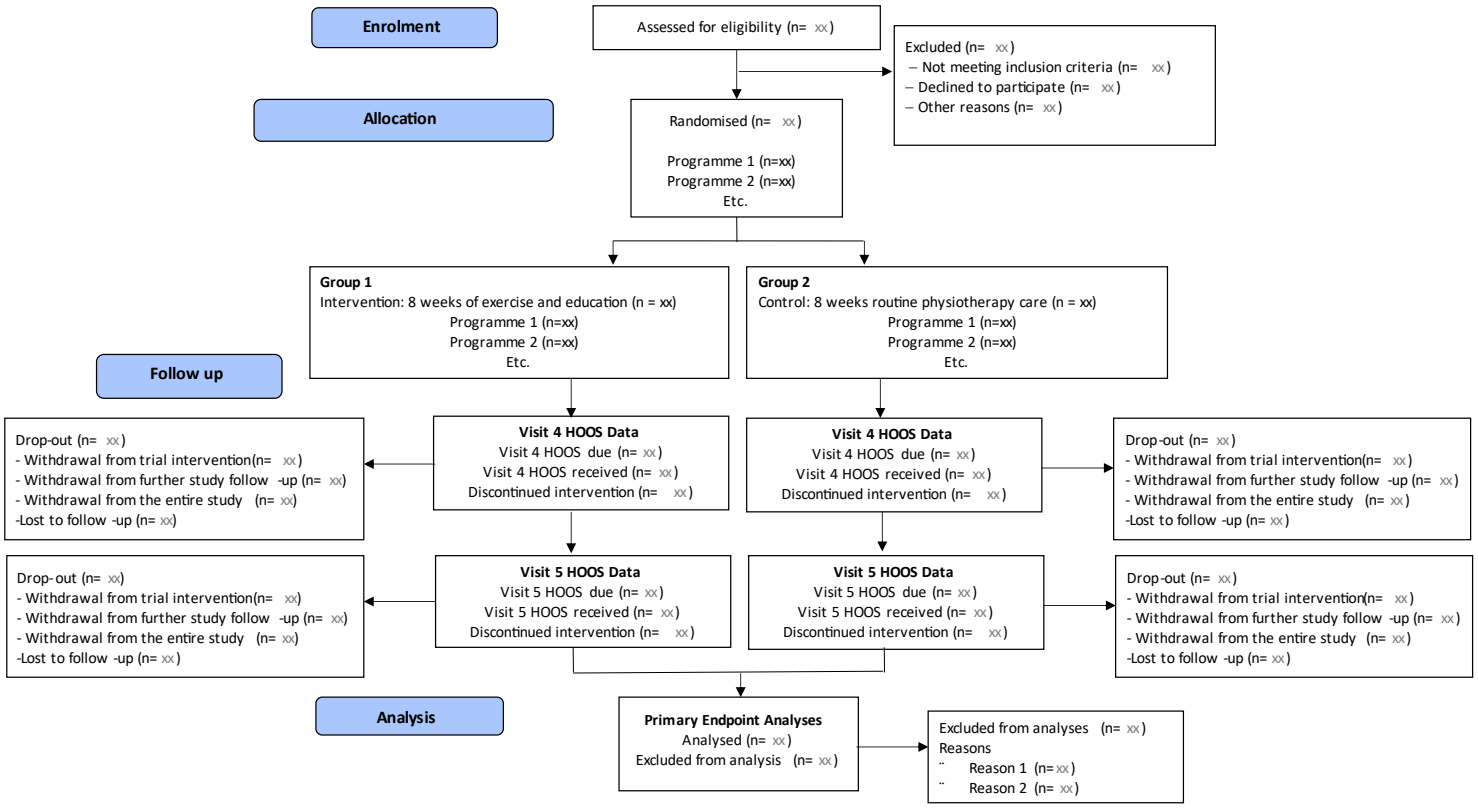


Table 1 Summary of Populations

	Cycling/educational intervention (n=xx)	**Usual physiotherapy care (n=xx)**	**Total (n=xx)**
Included in ITT population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Excluded from ITT population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason 1 etc.	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Included in per protocol population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Excluded from per protocol population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason 1 etc.	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Included in safety population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Excluded from safety population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason 1 etc.	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 2 End of Study Information

	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)	Total (n=xx)
Number of participants completed study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of participants completing visit 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of participants completing visit 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of participants discontinued study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for discontinuation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subject withdrawal			
Etc…	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

5.2 Major Protocol Violations

Table 3 Listing of protocol deviations/violations

Violation	Participant ID (if applicable)	Treatment arm (if applicable)	Comments	Actions
xxxx	xxxx	xxxx	xxxx	xxxx

Programming note: this information comes from the trial management team

5.3 Demographic, Baseline and Medical History Information

Table 4 Baseline and demographic characteristics

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Gender - n(%)		
Male	xxx (xx.x%)	xxx (xx.x%)
Female	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Age		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Ethnicity - n(%)		
White	xxx (xx.x%)	xxx (xx.x%)
African	xxx (xx.x%)	xxx (xx.x%)
Caribbean	xxx (xx.x%)	xxx (xx.x%)
Arab	xxx (xx.x%)	xxx (xx.x%)
Indian	xxx (xx.x%)	xxx (xx.x%)
Pakistani	xxx (xx.x%)	xxx (xx.x%)
Bangladeshi	xxx (xx.x%)	xxx (xx.x%)
Chinese	xxx (xx.x%)	xxx (xx.x%)
Mixed/Multiple ethnic group	xxx (xx.x%)	xxx (xx.x%)
Other ethnic group	xxx (xx.x%)	xxx (xx.x%)
Prefer not to say	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Education level - n (%)		
None	xxx (xx.x%)	xxx (xx.x%)
O-level/CSE/GCSE	xxx (xx.x%)	xxx (xx.x%)
A-level or equivalent	xxx (xx.x%)	xxx (xx.x%)
Degree or equivalent	xxx (xx.x%)	xxx (xx.x%)
Doctorate/Higher Degree	xxx (xx.x%)	xxx (xx.x%)
Other qualification	xxx (xx.x%)	xxx (xx.x%)
Don't know	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Employment status - n(%)		
Paid/unpaid work full-time	xxx (xx.x%)	xxx (xx.x%)
Paid/unpaid work part-time	xxx (xx.x%)	xxx (xx.x%)
Unemployed (currently looking for work)	xxx (xx.x%)	xxx (xx.x%)
Unemployed (not currently looking for work)	xxx (xx.x%)	xxx (xx.x%)
Student	xxx (xx.x%)	xxx (xx.x%)
Retired	xxx (xx.x%)	xxx (xx.x%)
Unable to work (OA)	xxx (xx.x%)	xxx (xx.x%)
Unable to work (not OA)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Height in m		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Weight in kg		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
BMI in kg/m^2		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Body fat %		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Resting heart rate in bpm		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Systolic blood pressure in mmHg		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Diastolic blood pressure in mmHg		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Medication Use		
Analgesia (all)	**xxx (xx.x%)**	**xxx (xx.x%)**
Paracetamol (tablet)	xxx (xx.x%)	xxx (xx.x%)
Paracetamol (liquid)	xxx (xx.x%)	xxx (xx.x%)
Nonsteroidal Anti-inflammatories (all)	**xxx (xx.x%)**	**xxx (xx.x%)**
Aspirin	xxx (xx.x%)	xxx (xx.x%)
Ibuprofen (tablet)	xxx (xx.x%)	xxx (xx.x%)
Ibuprofen (liquid)	xxx (xx.x%)	xxx (xx.x%)
Diclofenac (tablet)	xxx (xx.x%)	xxx (xx.x%)
Naproxen (tablet)	xxx (xx.x%)	xxx (xx.x%)
Naproxen (liquid)	xxx (xx.x%)	xxx (xx.x%)
Meloxicam	xxx (xx.x%)	xxx (xx.x%)
Celecoxib	xxx (xx.x%)	xxx (xx.x%)
Etodolac	xxx (xx.x%)	xxx (xx.x%)
Topical Anti-inflammatories (all)	**xxx (xx.x%)**	**xxx (xx.x%)**
Ibuprofen (topical)	xxx (xx.x%)	xxx (xx.x%)
Diclofenac (topical)	xxx (xx.x%)	xxx (xx.x%)
Oral Opioids (all)	**xxx (xx.x%)**	**xxx (xx.x%)**
Co-codamol	xxx (xx.x%)	xxx (xx.x%)
Codeine (tablet)	xxx (xx.x%)	xxx (xx.x%)
Codeine (liquid)	xxx (xx.x%)	xxx (xx.x%)
Tramadol (tablet)	xxx (xx.x%)	xxx (xx.x%)
Tramadol (liquid)	xxx (xx.x%)	xxx (xx.x%)
Morphine (tablet)	xxx (xx.x%)	xxx (xx.x%)
Morphine (liquid)	xxx (xx.x%)	xxx (xx.x%)
Oxycodone (tablet)	xxx (xx.x%)	xxx (xx.x%)
Oxycodone (liquid)	xxx (xx.x%)	xxx (xx.x%)
Anti-convulsant (all)	**xxx (xx.x%)**	**xxx (xx.x%)**
Gabapentin (tablet)	xxx (xx.x%)	xxx (xx.x%)
Gabapentin (liquid)	xxx (xx.x%)	xxx (xx.x%)
Pregabalin (tablet)	xxx (xx.x%)	xxx (xx.x%)
Pregabalin (liquid)	xxx (xx.x%)	xxx (xx.x%)
Anti-depressant (all)	**xxx (xx.x%)**	**xxx (xx.x%)**
Amitriptyline (tablet)	xxx (xx.x%)	xxx (xx.x%)
Amitriptyline (liquid)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 5 Co-morbidities

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Musculoskeletal disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Neurological disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Cardiovascular disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Respiratory disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Dermatological disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Haematological disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Endocrine disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Hepatic disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Gastrointestinal disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Urogenital disease - n (%)		
Yes	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Number of Co-morbidities – n (%)		
0	xxx (xx.x%)	xxx (xx.x%)
1	xxx (xx.x%)	xxx (xx.x%)
2	xxx (xx.x%)	xxx (xx.x%)
3 or more	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 6 Baseline HOOS scores

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
HOOS function score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS pain score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS symptoms score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS stiffness score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS sports and recreational activities score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS Quality of Life score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 7 Baseline performance based functional measures

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
30-second chair stand test		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Test Adapted n (%)	xxx (xx.x%)	xxx (xx.x%)
Test Failed n (%)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Stair climb test in s		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Use of Handrail n (%)	xxx (xx.x%)	xxx (xx.x%)
Use of Walking Aid n (%)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
40m walk test in m/s		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Use of Walking Aid n (%)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
PAM		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 8 Baseline Mechanistic Variables

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Range of Motion (degrees)		
Flexion (index hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Flexion (contralateral hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Extension (index hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Extension (contralateral hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Abduction (index hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Abduction (contralateral hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Adduction (index hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Adduction (contralateral hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Internal Rotation (index hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF – n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Internal Rotation (contralateral hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
External Rotation (index hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
External Rotation (contralateral hip)		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**
Patient-Specific Functional Scale		
Baseline Total Score		
N	**xxx**	**xxx**
Mean (SD)	**xx.x (xx.x)**	**xx.x (xx.x)**
Median (IQR)	**xx.x (xx.x to xx.x)**	**xx.x (xx.x to xx.x)**
Range	**xx.x to xx.x**	**xx.x to xx.x**
Missing from CRF - n(%)	**xxx (xx.x%)**	**xxx (xx.x%)**

5.4 Compliance to study interventions

Table 9 Intervention compliance

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Attendance of cycling and education sessions N Mean (SD) Median (IQR) Range Missing from CRF - n(%)	 xxx xx.x (xx.x) xx.x (xx.x to xx.x) xx.x to xx.x xxx (xx.x%)	**N/A**
Attendance of physiotherapy sessions N Mean (SD) Median (IQR) Range Missing from CRF - n(%)	**N/A**	 xxx xx.x (xx.x) xx.x (xx.x to xx.x) xx.x to xx.x xxx (xx.x%)

5.5 Participant Information at visit 4 and visit 5

Table 10 Demographic characteristics at visit 4

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Height in m		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Weight in kg		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
BMI in kg/m^2		
N	xxx (xx.x%)	xxx (xx.x%)
Mean (SD)	xxx (xx.x%)	xxx (xx.x%)
Median (IQR)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Body fat %		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Resting heart rate in bpm		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Systolic blood pressure in mmHg		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Diastolic blood pressure in mmHg		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 11 HOOS scores at visit 4 and visit 5

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Visit 4		
HOOS function score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS pain score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS symptoms score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS stiffness score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS sports and recreational activities score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS Quality of Life score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Visit 5		
HOOS function score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS pain score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS symptoms score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS stiffness score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS sports and recreational activities score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
HOOS Quality of Life score		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 12 Performance based functional measures for Visit 4

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
30-second chair stand test		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Test adapted n(%)	xxx (xx.x%)	xxx (xx.x%)
Test Failed n(%)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Stair climb test in s		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Use of Handrail n (%)	xxx (xx.x%)	xxx (xx.x%)
Use of Walking Aid n (%)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
40m walk test in m/s		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Use of Walking Aid n (%)	xxx (xx.x%)	xxx (xx.x%)
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 13: Patient Activation Measure at Visits 4 and 5

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
PAM (visit 4)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
PAM (visit 5)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Table 14 Mechanistic Variables at Visits 4 and 5

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Range of Motion (degrees) at Visit 4		
Flexion (index hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Flexion (contralateral hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Extension (index hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Extension (contralateral hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Abduction (index hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Abduction (contralateral hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Adduction (index hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Adduction (contralateral hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Internal Rotation (index hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF – n(%)	xxx (xx.x%)	xxx (xx.x%)
Internal Rotation (contralateral hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
External Rotation (index hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
External Rotation (contralateral hip)		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)

Variable	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)
Activity Diary		
Activity Diary Visit 4		
Activity Diary Visit 5		
Patient-Specific Functional Scale		
Total Score Visit 4		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Total Score Visit 5		
N	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median (IQR)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x
Missing from CRF - n(%)	xxx (xx.x%)	xxx (xx.x%)
Feedback on Group Intervention at Visit 4		
Group Identification		
N	xxx	
Mean (SD)	xx.x (xx.x)	
Median (IQR)	xx.x (xx.x to xx.x)	
Range	xx.x to xx.x	
Missing from CRF - n(%)	xxx (xx.x%)	
Social Support		
N	xxx	
Mean (SD)	xx.x (xx.x)	
Median (IQR)	xx.x (xx.x to xx.x)	
Range	xx.x to xx.x	
Missing from CRF - n(%)	xxx (xx.x%)	
Education Leadership		
N	xxx	
Mean (SD)	xx.x (xx.x)	
Median (IQR)	xx.x (xx.x to xx.x)	
Range	xx.x to xx.x	
Missing from CRF - n(%)	xxx (xx.x%)	
Cycling Leadership		
N	xxx	
Mean (SD)	xx.x (xx.x)	
Median (IQR)	xx.x (xx.x to xx.x)	
Range	xx.x to xx.x	
Missing from CRF - n(%)	xxx (xx.x%)	

5.6 Withdrawal Information

Table 15 Patient withdrawals

Reason for withdrawal	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)	Total (n=xx)
Primary reason for discontinuation[1] – n (%)			
Withdrew from trial intervention	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Withdrew from further study follow-up	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Withdrew from the entire study and does not want her data used	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

[1] Denominator is the number of patients that discontinued the study

5.7 Primary Outcome Information

Table 16 Summary of HOOS functional component scores

Characteristic	Cycling/educational intervention (n=xx)	Usual physiotherapy care (n=xx)	Total (n=xx)
Mean HOOS functional score at baseline			
N	xx	xx	xx
Mean (SD)*	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median(IQR)*	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
Mean HOOS functional score at visit 4			
N	xx	xx	xx
Mean (SD)*	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median(IQR)*	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
Difference in mean HOOS functional score between baseline and visit 4			
N	xx	xx	xx
Mean (SD)*	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median(IQR)*	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Range	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x

* Note: If mean HOOS functional score at baseline or visit 4 follows normal distribution then the means and SD will be presented. Otherwise, the medians and IQRs will **also** be presented.

Table 17 PRIMARY ENDPOINT MODEL – Multi-level regression results for mean HOOS function component score for Cycling/educational intervention vs. Usual physiotherapy care at visit 4

Characteristic	Statistic		
Regression model results[3]	**n**		
Number of observations read	xxx		
Number of observations used	xxx		
Number of observations not used	xxx		
Solution for Fixed Effects	**Estimate**	**95% CI**	**p-value**
Group - Usual physiotherapy care	0 (Ref)[1]	-	-
Group - Cycling/educational intervention	x.xxx	x.xxx to x.xxx	x.xxx
Intercept	x.xxx	x.xxx to x.xxx	x.xxx
Baseline HOOS function score	x.xxx	x.xxx to x.xxx	x.xxx
Covariance Parameter Estimates (Random effects)	**Estimate**	**95% CI**	**ICC**
Cycling group[2]	x.xxx	x.xxx to x.xxx	x.xxx
Residual	x.xxx	x.xxx to x.xxx	

[1] Reference category.

[2] Cycling group included in the mixed model using a unique identifier for each cycling cohort for the intervention group and a unique group for each participant in the usual care arm

5.8 Per Protocol Analyses[#] on the Primary Outcome

Table 18 Summary of HOOS functional component scores for per-protocol participants

Note: This table will be a copy of Table 16 for the per-protocol participants

Table 19 Multi-level regression results for per-protocol mean HOOS function component score for Cycling/educational intervention vs. Usual physiotherapy care at visit 4

Characteristic	Statistic		
Per-Protocol Analysis			
Regression model results[3]	**n**		
Number of observations read	xxx		
Number of observations used	xxx		
Number of observations not used	xxx		
Solution for Fixed Effects	**Estimate**	**95% CI**	**p-value**
Group - Usual physiotherapy care	0 (Ref)[1]	-	-
Group - Cycling/educational intervention	x.xxx	x.xxx to x.xxx	x.xxx
Intercept	x.xxx	x.xxx to x.xxx	x.xxx
Baseline HOOS function score	x.xxx	x.xxx to x.xxx	x.xxx
Covariance Parameter Estimates (Random effects)	**Estimate**	**95% CI**	**ICC**
Cycling group[2]	x.xxx	x.xxx to x.xxx	x.xxx
Residual	x.xxx	x.xxx to x.xxx	

[#] Per-protocol defined as attendance of at least 7 out of 8 cycling and education classes and 100% attendance to usual physiotherapy care

[1] Reference category.

[2] Cycling group included in the mixed model using a unique identifier to for each cycling group for the intervention group and a unique group for each participant in the usual care arm

[3] Inclusion of multiple-imputed data model dependent on the use of multiple-imputation

Note: If multiple imputation is used tables 16 and 18 will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis.

5.9 Secondary Outcome Information

Table 20 – Multi-level regression results for mean HOOS function component score for Cycling/educational intervention vs. Usual physiotherapy care at visit 4 & 5

Characteristic	Statistic		
Regression model results[3]	**n**		
Number of observations read	xxx		
Number of observations used	xxx		
Number of observations not used	xxx		
Solution for Fixed Effects	**Estimate**	**95% CI**	**p-value**
Group - Usual physiotherapy care	0 (Ref)[1]	-	-
Group - Cycling/educational intervention	x.xxx	x.xxx to x.xxx	x.xxx
Intercept	x.xxx	x.xxx to x.xxx	x.xxx
Baseline HOOS function score	x.xxx	x.xxx to x.xxx	x.xxx
Visit 4	0 (Ref)[1]	-	-
Visit 5	x.xxx	x.xxx to x.xxx	x.xxx
Treatment by visit interaction	x.xxx	x.xxx to x.xxx	x.xxx
Covariance Parameter Estimates (Random effects)	**Estimate**	**95% CI**	**ICC**
Cycling group[2]	x.xxx	x.xxx to x.xxx	x.xxx
Patient	x.xxx	x.xxx to x.xxx	x.xxx
Residual	x.xxx	x.xxx to x.xxx	

[1] Reference category.

[2] Cycling group included in the mixed model using a unique identifier for each cycling cohort for the intervention group and a unique group for each participant in the usual care arm

[3] Inclusion of multiple-imputed data model dependent on the use of multiple-imputation

Note: A sentence or paragraph is needed here to interpret the results of the interaction in the table above i.e. stating the treatment effect at visit 4 and the treatment effect at visit 5 taking into account the interaction.

Note: An extra table for a pre-protocol analysis will be included for this measure if deemed appropriate.

Note: If multiple imputation is used table 16 will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis.

Table 21 Summary of HOOS pain component scores

Note: This table will be a copy of Table 16 for the pain component scores

Table 22 Multi-level regression results for mean HOOS pain component score for Cycling/educational intervention vs. Usual physiotherapy care at visit 4 & 5

Note: This table will be a copy of Table 20 for the pain component score

Note: A sentence or paragraph is needed here to interpret the results of the interaction in the table above i.e. stating the treatment effect at visit 4 and the treatment effect at visit 5 taking into account the interaction.

Note: Extra tables for a pre-protocol analysis will be included for this measure if deemed appropriate.

Note: If multiple imputation is used this table will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis if deemed appropriate.

Tables 23-30 Multi-level regression results for mean HOOS symptoms, stiffness, sports, and quality of life component score for Cycling/educational intervention vs. Usual physiotherapy care at visit 4 & 5

Note: These tables will be a copy of Tables 16 and 20 for the relevant HOOS component score

Note: A sentence or paragraph is needed here to interpret the results of the interaction in the table above i.e. stating the treatment effect at visit 4 and the treatment effect at visit 5 taking into account the interaction.

Note: Extra tables for a per-protocol analyses will be included for these measures are deemed appropriate.

Note: If multiple imputation is used these tables will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis if deemed appropriate.

Tables 31-36 Multi-level regression results for 30-second chair stand, stair climb test, 40 minute walk for Cycling/educational intervention vs. Usual physiotherapy care at visit 4

Note: These tables will be a copy of Tables 16 and 17 for the relevant measure

Note: Extra tables for a per-protocol analyses will be included for these measures are deemed appropriate.

Note: If multiple imputation is used these tables will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis if deemed appropriate.

Tables 37-38 Multi-level regression results for patient activation measure (PAM) for Cycling/educational intervention vs. Usual physiotherapy care at visit 4 & 5

Note: These tables will be a copy of Tables 16 and 20 for the patient activation measure (PAM)

Note: Extra tables for a per-protocol analyses will be included for these measures are deemed appropriate.

Note: If multiple imputation is used these tables will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis if deemed appropriate.

Tables 39-46 Multi-level regression results for BMI, body composition, blood pressure, resting heart rate for Cycling/educational intervention vs. Usual physiotherapy care at visit 4

Note: These tables will be a copy of Tables 16 and 17 for the relevant measure

Note: Extra tables for a per-protocol analyses will be included for these measures are deemed appropriate.

Note: If multiple imputation is used these tables will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis if deemed appropriate.

Tables 47-48 Multi-level regression results for analgesia use for Cycling/educational intervention vs. Usual physiotherapy care at visits 4 & 5

Note: These tables will be a copy of Tables 16 and 20 for the relevant measure

Note: Extra tables for a per-protocol analyses will be included for these measures are deemed appropriate.

Note: If multiple imputation is used these tables will be repeated to present the results of the model using multiple imputation, and separately, using a complete-case analysis if deemed appropriate.

5.10 Safety Reporting

Table 49 Summary of adverse events reported

Characteristic	Cycling/educational intervention (n=xx)		Usual physiotherapy care (n=xx)		Total (n=xxx)	
Adverse events by Grade– n(%)	**Events n**	**Patients n (n%)[2,3]**	**Events n**	**Patients n (n%)[2,3]**	**Events n**	**Patients n (n%)[2,3]**
Grade 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Grade 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Grade 3	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Grade 4	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Grade 5	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
No AE	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Missing from eCRF – n(%)[4]	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Number of AE per patient (for patients with at least one AE) – median (range)	x (x.x to x.x)		x (x.x to x.x)		x (x.x to x.x)	

[2] Denominator is the number of patients randomised.
[3] The worst grade is used when more than one grade is available for a patient.
[4] Denominator is the number of patients randomised with an Adverse event eCRF available.

Table 50: Summary of terms of adverse events

Characteristic	Cycling/educational intervention (n=xx)		Usual physiotherapy care (n=xx)		Total (n=xx)	
	Events n	Patients n (%)	Events n	Patients n (%)	Events n	Patients n (%)
Number of Adverse Events	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Summary of AEs – n(%)[1, 2]						
SOC term 1	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Preferred term 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Preferred term 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
[etc.]						
SOC term2	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Preferred term 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Preferred term 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
[etc.]						

[1] Denominator is the number of patients randomised.

[2] The worst grade is used when more than one grade is available for a patient.

Table 51 Summary of terms of grade 3+ (severe) adverse events

Characteristic	Cycling/educational intervention (n=xx)		Usual physiotherapy care (n=xx)		Total (n=xx)	
	Events n	Patients n (%)	Events n	Patients n (%)	Events n	Patients n (%)
Number of Adverse Events Grade 3 or above	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Summary of AEs – n(%)[1, 2]						
SOC term 1	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Preferred term 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Preferred term 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
[etc.]						
SOC term2	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Preferred term 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Preferred term 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
[etc.]						

[1] Denominator is the number of patients randomised.

[2] The worst grade is used when more than one grade is available for a patient.

Table 52: Summary of serious adverse events (SAEs), serious adverse reactions (SARs) and suspected, unexpected serious adverse reactions (SUSARs)

Characteristic	Treatment (n=xxx)	Control (n=xxx)	Total (n=xxx)
Number of SAE/SAR/SUSAR per patient (for patients with at least one SAE/SAR/SUSAR) – median (range)	x (x.x to x.x)	x (x.x to x.x)	x (x.x to x.x)
CTCAE v4.0 grade – n(%)[2]			
1 – Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Life threatening	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Death related to AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Overall assessment – n(%)[2]			
SUSAR (Suspected Unexpected Serious Adverse Reaction)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SAR (Serious Adverse Reaction)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SAE (Serious Adverse Event)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pending SUSAR	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Why was the event serious – n(%)[2]			
1 – Resulted in death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Life threatening	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Required hospitalisation or prolongation of existing hospitalisation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
6 – Other important medical event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Denominator is the number of patients randomised.

[2] Denominator is the number of SAEs/SARs/SUSARs with non-missing information.

[3] Denominator is the number of SAEs/SARs/SUSAR.

Table 53: Summary of main symptom reported on the SAE form

Characteristic	Cycling/educational intervention (n=xx)		Usual physiotherapy care (n=xx)		Total (n=xx)	
	Events n	Patients n (%)	Events n	Patients n (%)	Events n	Patients n (%)
Number of Serious Adverse Events	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Summary of AEs – n(%)[1, 2]						
SOC term 1	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Preferred term 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Preferred term 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
[etc.]						
SOC term2	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**	**xx**	**xx (xx.x%)**
Preferred term 1	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Preferred term 2	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
[etc.]						

[1] Denominator is the number of patients randomised.
[2] The worst grade is used when more than one grade is available for a patient.

Table 54: List of all SAEs

ID	Arm	PI assessment	CR assessment	Date SAE reported	SOC	Main symptom	Grade[2]	Serious[3]	Action[4]	Causality[5]	Expected ness[6]

[2]CTCAE v5.0

[3]Why was the event serious: 1=Resulted in death, 2=Life-threatening, 3=Required hospitalisation or prolongation of existing hospitalisation, 4=Persistent or significant disability/incapacity, or 5=Congenital anomaly/birth defect.

[4]Action taken due to SAE: 0=None, 1=Dose reduction, 2=Treatment delayed, 3=Treatment reduced & delayed, 4=Treatment stopped

[5]Investigator's Opinion – Causal relationship to SAE: 1 = Definitely, 2 = Probably, 3 = Possibly, 4 = Unlikely, 5 = Not related

[6]Investigator's Opinion – Expectedness: 1 = Expected, 2 = Unexpected

6 References

7 SAP revision history

Version number	Revision history	Author	Date
0.1	Original draft	Sharon Docherty	
0.2	Revision of the original draft	Paul Lee & Geoff Saunders	17-Mar-2023
0.3	Revision of draft 0.2 addition of tables to reflect reporting of data	Sharon Docherty	29-Jun-2023
0.4	Revision of draft 0.3 with additional changes to Tables and numbering	Sharon Docherty	12-Jul-2023
1.0	Clean version for signatures	Sharon Docherty	08-Sep-2023