Statistical Analysis plan (SAP):

Patellar tendinopathy - The role of restitution time in exercise- based treatment: A Randomized controlled trial (the TEREX trial)

Table of Contents

1. Administrative information

1.1 Trial registration

ClinicalTrials.gov – Trial registration identifier: NCT05731037
Ethical Committee of Regional Copenhagen: H-22031880

1.2 SAP Version and Date

Version 1.0
Date: 27-09-2024

1.3 Protocol version

The SAP document has been written based on information contained in the TEREX trial study protocol version 3, dated 08 August 2024.

1.4 SAP revision history

Protocol version	Updated SAP version no.	Section number changed	Description of and reason for change	Date changed

1.5 SAP contributors - roles and responsibility

The below listed persons contributed equally to SAP development and AA drafted the SAP:
Anne-Sofie Agergaard (AA), Department of Physical and Occupational Therapy/ Institute of Sports Medicine Copenhagen, Bispebjerg Frederiksberg University Hospital.

Rene B. Svensson*,* Senior researcher, PhD, Institute of Sports Medicine Copenhagen, Bispebjerg Frederiksberg University Hospital

S. Peter Magnusson, Professor, B.Sc., DMSc, Department of Physical and Occupational Therapy / Institute of Sports Medicine Copenhagen, Bispebjerg Frederiksberg University Hospital, Faculty of Health & Medical Sciences, University of Copenhagen.

2. Introduction

2.2 Background and rational

Tendons play an essential role in transmitting force from muscle to bone and are thus designed to resist considerable loads during locomotion. Yet, repetitive use often results in overuse injuries, such as tendinopathy. Loading based treatment is currently the preferred treatment for tendinopathy, although the optimal loading configuration and time of loading remains unknown.

We have previously shown that, both high and moderate loading regimes yielded similar improvements in all outcome measures in the short term. Importantly, the improvements were maintained in the long term (12 months), however, most of the patients, unfortunately, did not reach normal function even after one year, and the reason for this incomplete recovery remains an enigma. This has prompted questions that relate to whether other exercising variables may improve the treatment of tendinopathy patients. Specifically, the present project aims to answer whether the restitution duration impact the outcome and ability to fully recover from tendinopathy.

2.3 Objectives

Research hypothesis

We hypothesize that greater restitution from loading (1 exercise day per week) will yield a greater positive clinical outcome, and tissue structure and function in patients with patellar tendinopathy compared to less restitution (3 exercise days per week), when impact activities are restricted in both groups.

Study objectives

The primary objectives of this trial is to assess if greater restitution from loading (1 exercise day per week) vs. less restitution (3 exercise days per week) during exercise-based treatment will yield a greater change in Victorian Institute of Sports Assessment –patella (VISA-P) score from baseline to 12 weeks, in patients with chronic (symptoms > 3 month) patellar tendinopathy.

S*econdary* objectives are:

To asses if greater restitution from loading (1 exercise day per week) vs. less restitution (3 exercise days per week) during exercise-based treatment will yield a greater change on the following outcomes:

- Change in patient-evaluated symptoms, physical function, sports participation, or patient-evaluated improvement and treatment satisfaction
- Change in muscle and tendon function
- Change in patellar tendon structure and vascularization.

Other objectives (exploratory) of this study include:

- Investigate the feasibility of using Magnetic resonance imaging (MRI) with Blood Oxygenation Level Dependent (BOLD) imaging for mapping of brain structure, function and metabolism changes in chronic tendinopathy patients and for assessment of possible differences between patients that respond and those that do not respond to loading-based treatment.
- Test the feasibility and response to individualized treatment protocols focused on extended duration of the rehabilitation program combined with activity modification and load management after the 12-week intervention.
- Investigate the effect of add-on treatment with corticosteroid (injection and 4 weeks of continued training) in a cohort of patients not responding to the initial 12-weeks loading-based treatment or patients that after week 20, 24, 28, 32, 36 or 40 respond that they have not achieved their Patient Acceptable Symptom State (PASS), have pain (NRS>2) during daily life activity, and who wish to receive a corticosteroid injection.

3. Study Methods

3.1 Trial design

This study is a prospective, randomized, controlled, open label, superiority trial with a two-group parallel design and primary endpoint after 12 weeks. The study has two phases; The first phase includes the main trial in which a 12-week intervention period will be undertaken to test the hypotheses in patients with chronic patellar tendinopathy (symptoms > 3 months). Treatment allocation is a 1:1 ratio. Patients are randomized to training with either short or extended restitution from loading. At 12 weeks, a smaller group of patients (5 responding and 5 not-responding to the 12-week intervention period) will be offered to participate in sub-study 1. In this explorative cross-sectional study, the feasibility of mapping brain structure, function and metabolism using MRI BOLD imaging in chronic patellar tendinopathy patients will be assessed. The second phase in the main study includes the follow-up from 12 week to the secondary endpoint at 52 weeks after baseline. During this period the participants will be monitored via questionnaires for treatment satisfaction and improvements at 4-week intervals. What treatment and the duration of treatment patients will receive in this phase is based on the concept of personalized medicine. A smaller group of the 52 patients from the main study is expected to be included in sub-study two.

Sub study two is designed as an observational cohort study. In this sub study, patients reporting no self-evaluated improvement after 12 weeks of loading-based treatment will be asked to be part of a group receiving corticosteroid injection treatment followed by continued exercise-based treatment and avoidance of impact loading. The cohort will further include patients that after week 20, 24, 28, 32, 36 or 40 respond that they have not achieved their Patient Acceptable Symptom State (PASS), have pain (NRS>2) during daily life activities, and who wish to receive a

corticosteroid injection. At the end of the corticosteroid-related treatment, patients will be offered the standard phase-two intervention and will continue to be monitored every 4 weeks until the same secondary endpoint as in the main study.

3.2 Blinding

It is not possible to blind an exercise intervention and therefore this trial will be carried out as an "open-label" trial where neither the patients, nor the physiotherapists providing the intervention will be blinded to treatment allocation. All patient-reported outcomes will be obtained electronically and blinded for members of the research team using REDCap. Furthermore, outcome assessors will be blinded to treatment allocation where possible and patients are requested not to disclose their allocation when outcomes are assessed. In addition, all baseline measurements will be collected before treatment allocation, and all data analyzed blinded. To test the blinding efficacy, the outcome assessors are asked what treatment strategy they think a patient has received after assessments.

3.3 Randomization

After baseline assessments, participants will be randomized to one of the two intervention groups:

A) Short restitution group (SR). This constitutes the currently accepted rehabilitation program of patellar tendinopathy with resistance training, three training session per week and is therefore considered the control group.
B) Extended restitution group (ER): Greater restitution from loading (1 exercise day per week)

Randomization procedure is performed using a computer-generated block randomization (block size is randomized to either 4 or 6) procedure. The allocation ratio is 1:1 and stratified for the following baseline factors:

- Sex (male, female)
- Symptom duration (3-8, 9-24 months)

Senior researcher Rene B. Svensson developed the randomization scheme for allocation of participants to the two groups in REDCap and will not be involved in the screening and inclusion process.

3.4 Sample size

The main study is powered based on previous data, a within-subject standard deviation of the primary outcome (VISA-P) of 12.8 after 12 weeks is expected[2]. A sample size analysis reveals that each group should contain n=18 to detect a 13 points difference[3] (minimal clinically important

difference) on VISA-P score[3] with an alpha level of 0.05 and a power/beta level of 0.80. To account for a 20% dropout rate and an estimated compliance rate of 75% (percentage of participants completing >80% of intervention) based on previous data[2], a total of 26 participants will be recruited for each group to ensure sufficient numbers for both intention-to-treat and per-protocol analysis.

Sub-study 1 is an explorative cross-sectional study investigating the feasibility of mapping brain structure. Therefore, number of participants is based on feasibility and will include 5 patients responding and 5 not-responding to the 12-week intervention period in the main study. Participation in sub-study 1 will not influence how the patients progress in phase two of the main study or if they be enrolled in sub-study 2.

Number of participants included in sub-study 2 will be based on how many patients from the main study, that rate themselves 'not improved' (dichotomized as described in sub-study one) in symptoms after 12 weeks and how many patients who have not achieved Patient Acceptable Symptom State (PASS) after week 20, 24, 28, 32, 36 and 40, and agree to participate. Based on data from a previous study[1] this is expected to be approximately 20% corresponding to 11 patients from the main study

3.5 Framework

This is a superiority trial.

3.6 Statistical Interim Analyses and Stopping Guidance

No statistical interim analysis has been planned. and there is no guidance for stopping the trial.

The primary investigator has the right to terminate this study at any time. Reasons may include the following, but are not restricted to:

- The incidence of events in this or other studies that indicate a potential health hazard to participants.
- Unsatisfactory participant enrolment.

3.7 Timing of final analysis

The main analysis of the trial will be prepared for the SR/ER comparison when trial participants have reached 12 weeks follow-up and data for the primary and secondary outcomes have been received and cleaned (anticipated to be October 2024).

3.8 Timing of outcome assessment

		STUDY PERIOD												
	Enrolment	**Allocation**	**Post-allocation**											**Close-out**
TIMEPOINT	***February 2023 – July 2024***	***February 2023 – July 2024***	***0 wk***	***12 wk***	***16 wk***	***20 wk***	***24 wk***	***28 wk***	***32 wk***	***36 wk***	***40 wk***	***44 wk***	***48 wk***	***February 2024- July 2026 (52-week follow-up)***
			Phase 1 intervention 12 wk		***Phase 2 Individualized Intervention between wk 12 and 52 + intervention sub-study 2***									
ENROLMENT														
Eligibility screen	X													
Informed consent	X													
Allocation		X												
INTERVENTIONS														
High Rest Group			—	—										
Low Rest Group			—	—										
Individualized					—	—	—	—	—	—	—	—		
Injection add on						—	—	—	—	—	—			
ASSESSMENT (Main Study)														
Diagnosis	X													
Questionaries			X	X	X	X	X	X	X	X	X	X	X	X
Functional test			X	X										X
Imaging			X	X										X
ASSESSMENT (Sub-study one)														
MRI brain				X										
ASSESSMENT (Sub-study two)														
Ultrasound*					▨	▨	▨	▨	▨	▨	▨	▨	▨	

Figure. Schedule of enrolment, intervention and assessment. *outcome assessment will vary within the time span, depending of inclusion timepoint in sub-study two.

The visit windows are as follows:

- Pre-exam will be done no more than 4 weeks before randomization.
- Baseline assessment will be taken no more than 7 days before intervention.

- The 12-week assessment will be taken no more than 3-4 days after intervention.
- The monthly follow-up (week 16- 48) can be taken up to 7 days after the scheduled date.
- 52-week follow-up can be taken within +/- 14 days of the scheduled date.

4. Outcomes

4.1 Primary Outcome and endpoint

The primary outcome of this study is the change in Victorian Institute of Sports Assessment – patella (VISA-P) from baseline to 12-week follow-up.

4.2 Secondary outcomes

The following outcome are assessed as secondary outcomes:

- Change from baseline in VISA-P at week 16 and 52.
- Change from baseline in truncated VISA-P (questions 2-6) at week 12, 16 and 52.
- Change from baseline in pain rating on numeric rating scale (NRS) during preferred sport, rest and daily activities at week 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52.
- Change in Self-reported improvement from baseline on a GROC scale at week 12, 16, 52.
- Change from pre-injury level in number of sports participation hours per week (training and competition), type of sport and intensity at baseline and week 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52.
- Change from baseline level in number of sports participation hours per week (training and competition), type of sport and intensity at week 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52.
- Patient Acceptable Symptom State (PASS) at week 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52.
- Registration of care-seeking behavior and treatment received in the period after last follow-up at week 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52.
- Change from baseline in pain during SLDS test at week 12 and 52.
- Change from baseline in maximal muscle strength at week 12 and 52.
- Chang from baseline in tendon thickness and neovascularization at week 12 and 52.
- Change from baseline in microvascular blood flow at week 12 and 52
- Change from baseline in jump height at week 12 and 52.

In addition change from 12 to 52 weeks will be analyzed as explorative outcomes.

4.3 Other outcomes

Only for patients participating in sub-study one:

- If it is feasible to map brain structure, function and metabolism changes in patient with chronic patellar tendinopathy using MRI.

- Assess if Patient Acceptable Symptom State (PASS) is correlated with brain structure, function and metabolism MRI findings.

Only for patients participating in sub-study two:

- Number of injections received from week 12-52
- Change from 1. injection in tendon thickness and neovascularization at week 4 and 8 after the injection.
- Change from 1 injection in self-evaluated PASS and improvement at week 4 and 8 after the injection.

5. Data Management

All variables used in the database will be checked for missing values, outliers and inconsistencies. Missing outcome values will be handled by imputation in the mixed linear model. Outliers will be defined by Grubb's test. Inconsistencies will be carefully evaluated on an individual basis based on the context and a decision on how to resolve them will be made by the SAP contributors. The number and nature of any inconsistencies and how they were resolved will be registered.

6. Trial Population

6.1 Participant flow

A CONSORT participant flow diagram will be drawn following the CONSORT standards (see Shell Figure, Appendix 10.1).

The flow diagram will be used to summarize the number of participants who were:

- Assessed for eligibility at screening
- Ineligible at screening*
- Eligible but not randomized*
- Received the randomized allocation
- Did not receive the randomized allocation*
- Lost to follow-up at week 12*
- Withdrawals at week 12*
- Discontinued the intervention*
- Randomized and included in the primary analysis
- Randomized and excluded from the primary analysis*

*reasons will be provided.

6.2 Baseline patient characteristics

Baseline demographics and characteristics will be described in terms of age (y), height (cm), weight (kg), Body mass index, Symptom duration (mo), Sport participation (h/wk), NRS score (pain during activity), and Unilateral/ bilateral injury (n) and presented in a table (Shell table 10.2). Continuous data will be described in terms of mean and standard deviation whereas categorical data will be presented in terms of numbers and percentages.

6.3 Intention-To-Treat population

The Intention-To-Treat (ITT) population consist of all randomized participants irrespective of whether the participants actually received study intervention or the participant's compliance with the study protocol, in the treatment group to which the participant was assigned at randomization (Intention-To-Treat principle). A participant will be considered randomized as soon as a treatment is assigned according to the allocation sequence.

6.4 Per protocol Population

The per protocol (PP) population consists of all participants in the ITT population who did not have any major protocol deviations.

The following are pre-defined major protocol violations with a direct bearing on the primary outcome:

- Not adherent to the allocated intervention (see below for definition of satisfactory adherence)
- Initiation of other exercise programs/treatments than the one the participants are allocated to during the main trial phase (week 1-12).
- Surgery to the lower extremity during trial participation
- Significant injury to the lower extremity during trial participation
- Failure to perform primary endpoint assessment, i.e. VISA-P questionnaire not assessed at week 12
- The 12-week assessment not completed within the specified time window.

The number (and percentage) of patients with major protocol deviations will be summarized by treatment group with details of type of deviation provided. The number of randomized participants in each group will be used as the denominator to calculate the percentages.

6.5 Satisfactory adherence

Compliance with the prescribed exercise protocol and activity modification will be tracked using a training diary. Participants will be asked to record the number of sessions and load of the treatment exercises completed and whether they performed running, jumping or other activities outside of the intervention.

Adherence is assessed based on the percent of the scheduled number of training sessions that was performed. A training session is considered performed, if an exercise activity is registered at a given date, even if the repetitions, sets or exercises are only partly recorded. The number of scheduled training sessions is predefined in the trial protocol and is 36 sessions for 12 weeks for the SR group, and 12 sessions for 12 weeks for the ER group.

The patient will be defined as 'compliant' with the treatment if they have performed at least 80% of the prescribed exercise sessions (29/36 for the SR group and 10/12 for the ER group) and have complied with the load-reduction (not performing intense running or jumping outside of the intervention protocol) for at least 10 of the 12 weeks.

Descriptive statistics on the percent compliance (Mean, SD) will be summarized by intervention group. Also, the number and % of participants receiving at least 80% of the prescribed treatment and complied with the load-reduction for at least 10 of the 12 weeks will be presented by treatment group.

7. Statistical Analysis

7.1 General considerations

All data will be checked for normal distribution by quantile-quantile plots (QQ-plots). For data with parametrically distributed residuals, continuous data will be presented as mean and standard deviation and categorical data will be presented by numbers and percentages. In case of non-normally distributed residuals, continuous data will be presented as median, interquartile range, and range and categorical data by numbers and percentages.

This study will apply the principle of *intention-to-treat* in the main statistical analysis and a compliance based (≥80%) *per-protocol* subgroup analysis.

The results of the main analysis of the trial (baseline to 12 week) will be presented in table format (see table 10.3, 10.4, 10.5, and 10.6).

7.2 Analysis of primary outcome

The analysis of the primary outcome will examine if ER will yield a superior change in VISA-P score compared to SR following a 12-week rehabilitation protocol. We will use a mixed-linear model with two independent variables: Time (baseline and 12 weeks) and group (ER and SR). The primary analyzed outcome is the interaction term, which describes if the change over time differs between groups.

7.3 Analysis of secondary outcomes

Secondary continuous outcome variables will be analyzed using the same mixed model as described for analysis of the primary outcome.
Further, analysis will be carried out using the mixed model with additional timepoints as indicated in section 4.

An exploratory analysis of the predictive value of baseline parameters will be performed by multiple regression to analyze if baseline values (tendon thickness, Power Doppler area, gender, BMI, age, pain during activity, Sport participation) for the whole population and on group level influence the outcome at 12 week.

Correlations between structural and clinical outcome will be performed as exploratory analyses. Pearson's correlation will be applied for parametric data and Spearmann's rho for non-parametric.

Unpaired t-tests will be used to analyze if baseline values (tendon thickness, Power Doppler area gender, BMI, pain during preferred sport, activity level and self-reported satisfaction) differ for those participant who have; injection/no injection, a high/low VISA-P score at 52 week, returned/ not returned to sport at week 20 and 52, respectively.

Finaly, we will divide participants into two groups (those who have returned to impact training or not, based on progression steps in the phase-two intervention program) and correlations with satisfaction and pain will be performed as an exploratory analysis. Pearson's correlation will be applied for parametric data and Spearmann's rho for non-parametric.

If there are no group differences or interaction effects for a given outcome, groups will be collapsed and analyzed using a mixed model with only time as a variable.

7.4 Analysis of Sub study 1 – Functional MRI

Analysis of brain structure, function and metabolism from MRI will be performed in an explorative manner and will be presented in text or presented as table depending on data.

7.5 Statistical software

The analysis will be performed in the statistical software SAS (SAS Institute inc., Cary, NC, USA) and graphs will be created in GraphPad PRISM (GraphPad Software).

7.6 Harms

Analyses of adverse events (AEs) will be performed on the ITT Population (see section 6.3).
AEs will be categorized according to type of AE and assessed for relationship with the trial treatment. The number and percentage of related AEs will be presented for each treatment arm. Deaths and AEs leading to discontinuation of study treatment will be listed. No formal statistical testing will be undertaken.
The AEs will be presented in text or presented as table depending on data.

8. Deviations from the protocol

The following details in this SAP represents deviations from trial protocol version 3.

Header in protocol	**Change**	**Reason**
8.3 Other outcomes	Registration of pain rating on numeric rating scale (NRS) during injection was not performed.	This outcome was deemed unimportant.

9. Reference

1. Agergaard AS, Svensson RB, Malmgaard-Clausen NM, et al. Clinical Outcomes, Structure, and Function Improve With Both Heavy and Moderate Loads in the Treatment of Patellar Tendinopathy: A Randomized Clinical Trial. *American Journal of Sports Medicine*. 2021;49(4):982-993.

2. Agergaard AS, Svensson RB, Malmgaard-Clausen NM, et al. Clinical Outcomes, Structure, and Function Improve With Both Heavy and Moderate Loads in the Treatment of Patellar Tendinopathy: A Randomized Clinical Trial. *Am J Sports Med*. 2021;49(4):982-993.

3. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Responsiveness of the VISA-P scale for patellar tendinopathy in athletes. *Br J Sports Med*. 2014;48(6):453-457.

10. Appendix

10.1 Shell Figure CONSORT

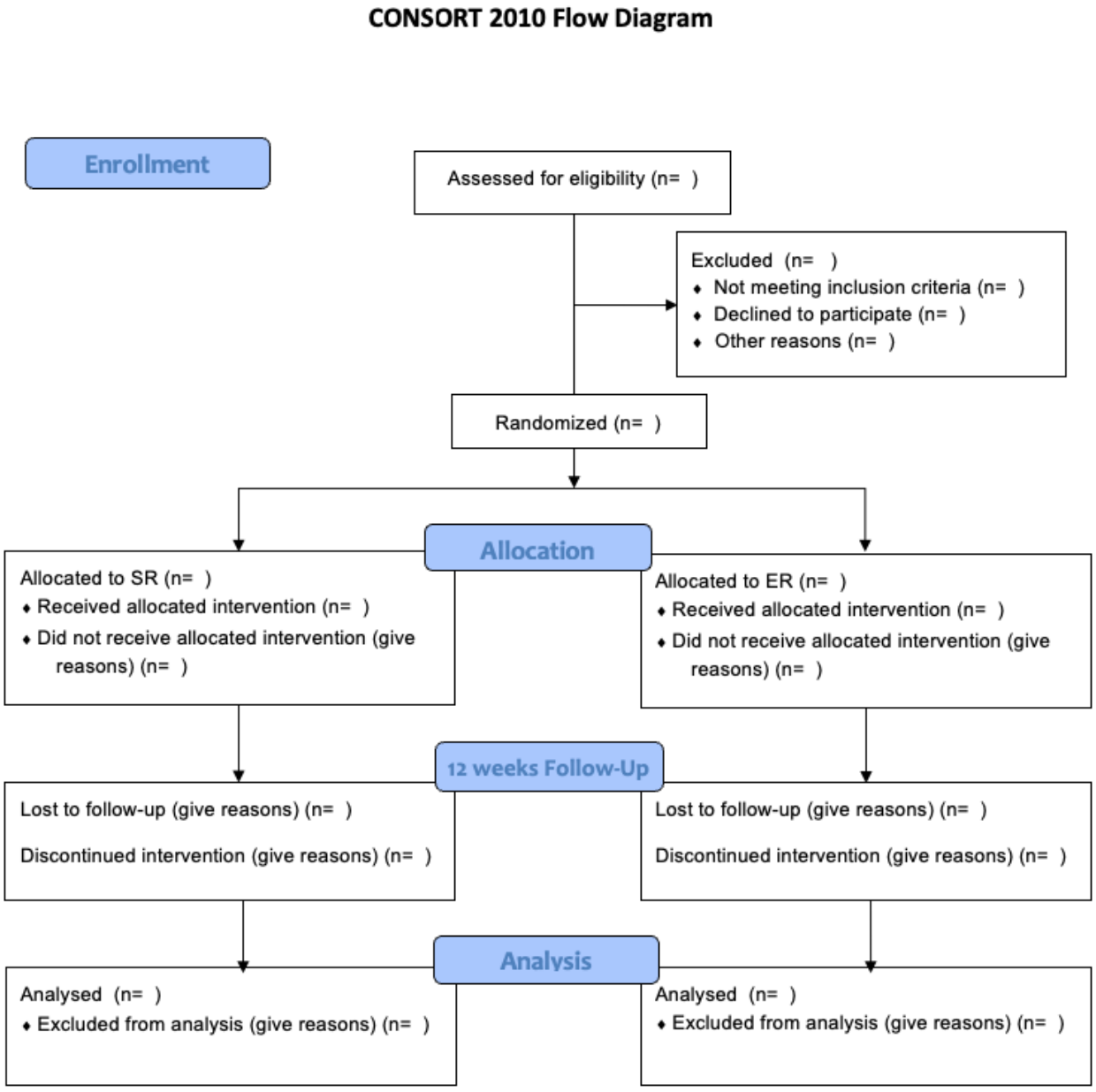

Figure XX: CONSORT (Consolidated Standards of Reporting Trials) flowchart for the primary outcome of the Victorian Institute of Sport Assessment–Patella (VISA-P). SR, Short restitution group; ER, Extended restitution group

10.2 Shell table- Baseline results

Baseline demographics will be described in terms of age, height, weight, BMI, symptom duration, Sport participation, pain during activity, and Unilateral or bilateral injury.
Continuous data will be described in terms of mean and standard deviation unless otherwise noted.

TABLE X. Baselines characteristics

Variable	**SR** (n=xx)	**ER**(n=xx)
Age, y	xx ± xx (xx-xx)	xx ± xx (xx-xx)
Height, cm	xx ± xx	xx ± xx
Weight, kgkg	xx ± xx	xx ± xx
Body mass index	xx ± xx	xx ± xx
Symptom duration, mo	xx ± xx (x-x)	xx ± xx (x-x)
Sport participation, h/wk	xx ± xx (x-x)	xx ± xx (x-x)
NRS score (pain during activity)	xx ± xx (x -x)	xx ± xx (x -x)
Unilateral/bilateral injury, n	xx ± xx	xx ± xx

Values are expressed as mean ± SD (range) unless otherwise noted.
There were/ were no differences between groups for any parameters at baseline. SR, Short restitution group; ER, Extended restitution group; NRS, numeric rating scale.

10.3 Shell table - Clinical results

Data from the clinical results which include the primary outcome VISA-P questionnaire and secondary outcome single-leg decline squat, pain during activity, muscle strength and jump hight..
Data will be presented as means and standard error with 95% confidence interval for change scores and as means and standard error with 95% confidence intervals and P-values for between group. All significant results will be marked with * p-value < 0.05, ** p-value < 0.01 and *** p<0.0001.

TABLE x : Clinical Results

			P Value		
	SR (n=xx)	**ER** (n=xx)	Group	Time	Group x Time
VISA-P, Point					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
VISA-P truncated, Point					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
SLDS, NRS					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
Pain during activity, NRS					

Running					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)		x.xxx	
Preferred sport					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
Daily activity					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
Rest					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
CMJ					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
Leg press (intervention)					
0 to 6 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
0 to 12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
Knee extension (intervention)					
0 to 6 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
0 to 6weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
Satisfaction with function (5-points Likert scale)					
Daily activity					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
Sport and physical activity					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			

Values are presented as least mean±SEM (95% CI). Mixed effect model was performed for all analysis with time and group as main factors. Alpha level set at P <0.05. SR, Short restitution group; ER, Extended restitution group; VISA-P, Victorian Institute of Sports Assessment- Patella; SLDS, single-leg decline squat NRS, numeric rating scale, CMJ, countermovement jump.

10.4 Shell table – Ultrasonography findings

Data from ultrasonographic imaging includes Power Doppler area, microvascular blood flow, and tendon thickness. Data will be presented as means and standard error with 95% confidence

interval for change scores and as means and standard error with 95% confidence intervals and P-values for between group. All significant results will be marked with * p-value < 0.05, ** p-value < 0.01 and *** p<0.0001.

TABLE x : Ultrasonography findings

			P- Value		
	SR (n=xx)	**ER** (n=xx)	Group	Time	Group x Time
Power Doppler area, mm^2					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
B-flow area, mm^2					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
Tendon Thickness, mm					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			

Values are presented as least mean±SEM (95% CI). Mixed effect model was performed for all analysis with time and group as main factors. Alpha level set at P <0.05. SR, Short restitution group; ER, Extended restitution group; B-flow, microvascular blood flow.

10.5 Shell table – Functional results

Data from Functional testing includes muscle strength, counter movement jump height on 2 leg and injured site. Data will be presented as means and standard error with 95% confidence interval for change scores and as means and standard error with 95% confidence intervals and P-values for between group. All significant results will be marked with * p-value < 0.05, ** p-value < 0.01 and *** p<0.0001.

TABLE x : Functional results

			P- Value		
	SR (n=xx)	**ER** (n=xx)	Group	Time	Group x Time
Muscle strength, n*m					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
CMJ height, cm					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			
CMJ height injured site, cm					
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)			

Values are presented as least mean±SEM (95% CI). Mixed effect model was performed for all analysis with time and group as main factors. Alpha level set at P <0.05. SR, Short restitution group; ER, Extended restitution group; CMJ, Counter movement jump.

10.6 Shell table – Sport participation

Data on sport participation includes self-reported recall data on sport participation before injury, and self-reported data from baseline and 12 week follow-up. Data will be presented as means and standard error with 95% confidence interval for change scores and as means and standard error with 95% confidence intervals and P-values for between group. All significant results will be marked with * p-value < 0.05, ** p-value < 0.01 and *** p<0.0001.

TABLE x : Sports participation (h/wk)

			P- Value		
	SR (n=xx)	**ER** (n=xx)	Group	Time	Group x Time
Before injury	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
0 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
12 weeks	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
Δ before injury to 0 wk	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx
Δ before injury to 12 wk	xx ± xx (xx, xx)	xx ± xx (xx, xx)	x.xxx	x.xxx	x.xxx

Values are presented as least mean±SEM (95% CI). Mixed effect model was performed for all analysis with time and group as main factors. Alpha level set at P <0.05. SR, Short restitution group; ER, Extended restitution group; Δ, change in time interval.