Eccentric Cycling Rehabilitation after Anterior Cruciate Ligament Reconstruction: a Randomised Controlled Trial of Strength and Biomechanical Outcomes

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Dedicated to Sergio & Elizabeth

I'm so happy I could share this journey with you close by.

Also, to my lovely.

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Abstract

After anterior cruciate ligament reconstruction (ACL-R), persistent strength and biomechanical deviations remain. Reducing these by training may reduce risk of re-injury or osteoarthritis for these patients.

A cross-sectional study investigated biomechanics of ACL-R male patients long-term (~5 years) post surgery. Fifteen ACL-R and fifteen healthy controls were tested in walking and running using motion capture. Deviations were found, primarily between-limbs, and also between groups. Largest deviations were lower knee angles and moments in the affected limb during running. However, these were not found during walking; thus, differences were highlighted by the higher-intensity task. During running, knee abduction moment was lower (more valgus) for the affected compared to unaffected and control limbs. The larger effects in moment show greater clinical potential than knee valgus angle. The ACL-R patients had lower impact foot strike during running than controls. The above results indicate chronic, clinical changes in joint loading.

A randomised controlled intervention trial evaluated progressive eccentric cycling for ACL-R males, compared to concentric controls. This is one of the first trials of eccentric vs. concentric training for ACL-R, matched by rating of perceived exertion. Twenty-six adult males, 12 weeks post hamstring-graft ACL-R trained three times/week for 8 weeks under supervision.

During training the eccentric group limb powers absorbed were higher than those produced by the concentric group, with a lower heart rate. For both groups, pain scores were low, and one of the patient-reported outcomes (IKDC) improved. Hamstring strength increased in the eccentric group by 15%, but this was not seen in the concentric group. For both groups, 60°/s quadriceps strength increased by a similar amount, approximately 28%.

Biomechanically, eccentric training was more effective than matched concentric training at resolving knee ($P = 0.022$, walk) and hip ($P = 0.010$, run) flexion angle deviations in the affected limb. In both groups, knee extension

moments increased, reducing asymmetries. Large knee abduction moment deviations at baseline were not reduced by either programme ($P > 0.05$). At follow-up (~6 months), both groups showed similar return-to-sports progress; several patients passed using one criterion (IKDC), and none passed using a stricter four-criteria method (Univ. Delaware).

Thus it can be concluded that for adult ACL-R males, eccentric cycle training is clinically acceptable, with similar or in some cases better outcomes than concentric cycle training. It improves patient-reported outcomes, strength recovery, biomechanical deviations, and return-to-sports measures.

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Nomenclature

95%CI	95% Confidence Interval
ACL	Anterior Cruciate Ligament
ACL-D	Anterior cruciate ligament-deficient
ACL-R	Anterior cruciate ligament reconstruction
ADL	Activities of daily living
AFF	Affected limb, ACL-R
AIC	Akaike's Information Criterion
ANOVA	Analysis of variance
BL	Baseline
BMI	Body Mass Index
BW	Body Weight
CoG	Centre of Gravity
CON	Concentric cycling ergometry group
CONSORT	CONsolidated Standards Of Reporting Trials
CPM	Continuous passive mobilisation
CTRL	Uninjured controls
DOMS	Delayed Onset Muscle Soreness
DVJ	Drop vertical jump

ECC	Eccentric cycling ergometry group
FED	Flexion-extension difference
FPPA	Frontal Plane Projection Angle
FU	Follow-Up
GRF	Ground Reaction Force
GRS	Global Rating Scale
H/Q	Hamstring-Quadriceps ratio
HR	Heart Rate
IK	Inverse Kinematics
IKDC	International Knee Documentation Committee
IQR	Inter-quartile range
KOOS	Knee injury and Osteoarthritis Outcome Score
LESS	Landing Error Scoring System
LSI	Limb Symmetry Index
LTV	Lean Thigh Volume
MCID	Minimal Clinically Important Differences
MRSS	Melbourne Return to Sports Score
OA	Osteoarthritis
PAR-Q	Patient Activity Readiness Questionnaire
PRO	Patient Reported Outcomes
PWB	Partial Weight Bearing
QAF	Quadriceps Activation Failure
QI	Quadriceps Index
QOL	Quality Of Life

RCT	Randomised controlled trial
ROM	Range of Motion
RPE	Rating of perceived exertion
RTAC	Return To Activity Criteria
RTS	Return-to-sports
SD	Standard deviation
UNAFF	Unaffected limb, ACL-R
VAS	Visual Analogue Scale

Chapter 1

Introduction

1.1 Background

Anterior cruciate ligament (ACL) rupture is one of the most significant soft tissue injuries, in terms of impact on the patient's quality of life (QOL), cost and time to return to activity. They are relatively common, with an estimated average general population incidence of 35 per 100 000 person-years [1, 2]. In the USA, for example, this leads to the estimation of over 200 000 injuries per year [1]. However, the rate may be higher based on a value of 81 from the Swedish national registry [3, 4].

The physiological effect of ACL injury is reduction of stability of the knee, primarily in the anterior movement of the tibia with respect to the femur. Rupture of the ligament also results in a loss of afferent neurological signals from mechanoreceptors in the torn ligament, which alters proprioception of the knee, and general motor function [5]. Possible additional tearing of the meniscus, joint capsule and bone bruising may also affect the stability and signalling of the joint.

ACL reconstruction (ACL-R) surgery is a common treatment for this injury, with around 50% being reconstructed in the Swedish ACL register [2], for example. Surgical reconstruction restores joint stability, and results in several additional effects at the

joint. First, graft placement, tension, and mechanical properties result in altered rolling and gliding movement of the femur with respect to the tibia, changing the cartilage loading of the joint. Second, graft harvesting (hamstring or bone-patellar-tendon-bone) alters the muscle pain, strength, and other properties [6, 7]. Finally, joint effusion and pain result in neural (arthrogenic) inhibition of the knee musculature [8, 9].

Clinically, post-surgical effects are a reduced range of motion (ROM), effusion, reduced quadriceps activation and strength, and reduced knee angles and moments during gait. Over time, reduced use of the quadriceps results in muscle atrophy on the affected side [10]. Secondary effects include reduced control at at the hip and trunk [11, 12, 13, 14], even though these other joints do not tend to show strength deficits [9, 12].

Taken together, over time these effects develop into persistent changes in gait. Several key deviations have been well documented in literature, between-limbs and compared to controls. This is particularly in the female population, where more research has been done in this field due to their higher risk of primary injury. Repetitive, long-term motion with altered loading of the cartilage seems to play a key role in the early development of osteoarthritis seen in these patients [4]. In addition, higher risk movement patterns coupled with reduced responsiveness and control, seem to contribute to the high rate of re-injury in this population.

After ACL-R, standard rehabilitation is long, typically 6-9 months to return-to-sports. Accelerated protocols have shown shorter time periods are possible without being unsafe [15, 16, 17], but a lack of standardisation [18], and mixed results have meant that they have not been widely adopted. Thus, there is potential to optimise rehabilitation outcomes.

As a candidate therapy, eccentric training is well-tolerated by patients, and allows significantly higher joint loading for the same perceived exertion [19]. It also has a unique neuromuscular physiology; the higher force levels have the potential to improve

muscle hypertrophy, joint signalling, stimulate neural circuits [20], and condition tendon [21] and connective tissue. A few early studies have shown strong support for eccentric training for ACL-R early after surgery, particularly with regard to reducing loss of muscle strength and volume. For eccentric cycle training in particular after ACL-R, the one study to date showed good patient outcomes, also at 1-year follow-up.

A study of the literature showed there is very limited research regarding the effect of eccentric training on ACL-R patients at any stage of rehabilitation. In addition, the trial design can be improved. Thus far, only one trial has attempted to match total exercise dose between eccentric training and controls, but the eccentric group still had a higher exposure to resistance training. The other trials have *added* eccentric training to baseline therapy, meaning that the exercise dose has not been matched to controls, and thus evidence of benefit should be understood in light of this. Also, the effect of eccentric training on gait has not yet been investigated.

1.2 Thesis aims and objectives

Aim 1. To compare long-term biomechanical deviations of male ACL-R patients who used standard rehabilitation, with respect to healthy controls.

Objectives:

1. To determine if residual biomechanical deviations exist between ACL-R affected and unaffected limbs, and between ACL-R affected limbs and controls.

2. To investigate if deviations in dynamic knee valgus angle and abduction moment, documented risk measures in females, exist in male participants.

Aim 2. To compare *muscle strength* and *volume* gains between two 8-week rehabilitation programs (eccentric and concentric) during the third phase (~3-6 months) of recovery after ACL-R surgery for young, active males.

Objectives:

1. To determine if the eccentric protocol is more effective than the concentric protocol in improving concentric and eccentric *strength and muscle volume* in the affected limb, in the quadriceps and hamstring muscle groups.

2. To determine if the eccentric protocol is more effective than the concentric protocol in improving concentric and eccentric *strength and volume symmetry* of quadriceps and hamstrings.

Aim 3: To determine if the eccentric exercise protocol is more effective than the concentric exercise protocol in *improving biomechanics* after ACL-R surgery during phase III of rehabilitation.

Objectives:

1. To determine if the eccentric protocol is more effective compared to the concentric protocol in reducing biomechanical deviations during walking and running gait. Particularly, investigate a) hip and knee flexion angles and moments, b) rate of force production at foot-strike, and c) knee valgus angles and abduction moment.

2. To determine if the eccentric protocol is more effective compared to the concentric protocol in improving clinical outcome scores, particularly on functional tests of balance, hopping, and landing.

3. To compare long-term deviations from a cross-sectional trial to biomechanical deviations measured at baseline for the intervention trial.

1.3 Thesis argument and scope

In light of the above, the thesis of this work is for adult ACL-R males, eccentric cycle training is as good, or better than concentric cycle training at improving strength and

reducing biomechanical deviations during the third phase of rehabilitation. In addition, eccentric cycling is safe, and is equivalent or better at improving patient-reported outcomes and return-to-sports. Also, for patients who had returned to sports, it is hypothesised that clinically relevant biomechanical deviations are present long-term after surgery.

The scope of thesis is limited to the study of male patients only, due to their well-documented differences from female patients in primary injury risk, as well as differences in healthy [22] and ACL-R biomechanics. Also, the effect of fatigue on outcome variables was seen to be outside the scope of this work.

This thesis assumes that long-term biomechanical deviations in ACL-R males represent markers of chronic residual risk as compared to healthy normal populations, despite patients having returned to sports. Also, it assumes that the effect of a rehabilitation programme on these deviations during rehabilitation can give an indication of how successful it is at modifying this risk long-term. To match the rehabilitation programme to controls, the assumption was made that self-reported rating of perceived exertion (RPE) was a suitable measure, representative of the patient's experience. However, perception of effort during eccentric exercise may be different from concentric exercise, due to the lower load on the cardio-respiratory system, and higher load on the limb.

1.4 Thesis overview

This thesis is based on two clinical trials. In Chapter 2, a cross-sectional study tests long-term biomechanical deviations in male ACL-R reconstructed patients, ~5 years after surgery, comparing them to healthy control participants. The other is a clinical intervention, using eccentric cycle training for ACL-R rehabilitation in males, as compared to concentric cycle training. In Chapter 3, the clinical results are presented, including strength, patient-reported outcomes. This is followed by biomechanical

outcomes in Chapter 4, and return-to-sports results in Chapter 5. A schematic outline of the content of the thesis is given in Figure 1.1 below, with trials in blue, and chapters in red.

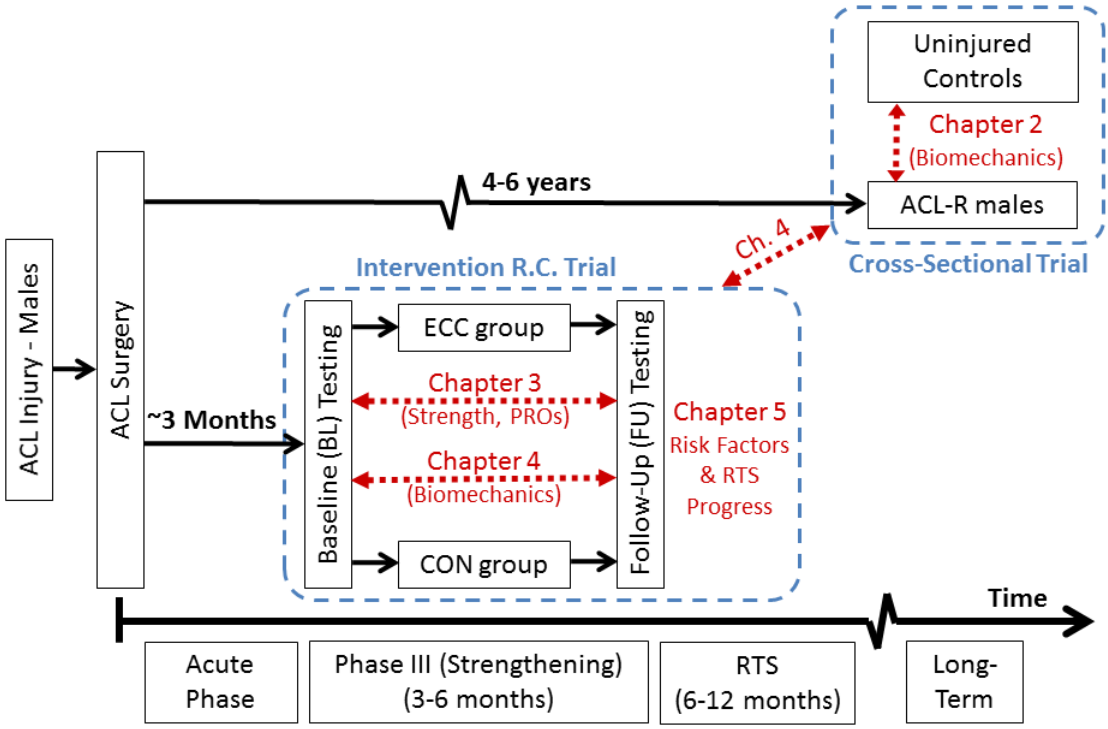

Figure 1.1: Thesis clinical trials and chapters

Chapter 2

Long-term gait deviations in ACL-reconstructed males

2.1 Introduction

Anterior cruciate ligament (ACL) reconstruction is commonly used to restore stability of the knee joint. After surgery, persistent deviations are detected in the patient's biomechanics of gait and other activities [23, 24, 25], resulting in long-term alterations of joint loading. They are suggested to play a role in the increased risk of secondary ACL injury [26, 27]. In addition, changes in knee ab/adduction moment and tibial rotation have been detected; these are suggested to be linked to the high rates of early-onset osteoarthritis (OA) in this population [28, 29, 30], although it is debated whether surgery is protective [31]. The identification of these deviations may further direct physical therapy interventions for these patients.

A greater risk of primary ACL injury among females relative to males has been widely-reported [32], and has been prospectively linked to biomechanical deviations, among other factors [33, 34]. While landing biomechanics stratified by sex has received

more extensive study [35], in gait these have been much less well described for males, as discussed in a recent systematic review by Alentorn-Geli *et al.* [36]. This gap in the literature is also seen for tests after ACL-reconstruction. In a recent review of 18 studies of walking biomechanics after this surgery [23], only one explicitly compared males to females, or was stratified by sex. Two recent studies have started to correct this gap, but many questions remain; one measured sex-specific sagittal-plane variables up to six months after surgery [37], and one focused on long-term changes in knee adduction moment between sexes [30].

To better understand chronic joint loading in males after ACL-reconstruction surgery, a broader study of long-term biomechanical deviations is required. In addition, gait testing is less commonly performed during running, even though it is an activity causing chronic load patterns, with vertical ground reaction forces more than double those during walking. A recent study by Noehren *et al.* [24] did this for females, investigating walking and running kinematic, kinetic and impact variables long-term (mean 5.2 SD 3.2 years) after surgery. The ACL-reconstructed group demonstrated significantly higher average loading rates and peak impact forces in walking and running, as well as smaller hip flexion angles and knee extensor moments, compared to uninjured controls. Interestingly, between-limb differences were not found. These results show that long-term biomechanical deviations persist in females during standard gait tasks, suggesting chronic changes in joint loading.

The objective of this study is thus to address the above gaps, and investigate long-term biomechanics in ACL-reconstructed males during both chronic conditions of walking and running. Our a priori hypothesis was that the affected limbs would demonstrate higher average loading rates and peak impact forces, as well as smaller knee flexion angles and moments, compared to the contralateral limb, and controls. In addition, because of their relevance in the clinical and research literature, several

exploratory variables were added; these include knee abduction moment, frontal-plane knee valgus angle, and maximum loading rate during foot strike.

2.2 Methods

2.2.1 Participants

Thirty male participants were recruited for this study. Participants consisted of 15 individuals who had undergone unilateral hamstring-autograft ACL reconstruction surgery between 4-6 years before testing (the ACL-R group) and 15 individuals who had never injured their ACLs as a control (CTRL) group. This 'long-term' timeframe was bracketed to reduce any potential time effects, and chosen to be clearly longer than the maximum time between injury and surgery. All in the ACL-R group had completed rehabilitation for at least one year and had returned to activities of daily living (ADL). Participants completed questionnaires of surgical history and Tegner [38] physical activity level. Participants were excluded if they previously had any other knee surgery, or knee injury during the previous six months. The study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee, and all participants provided written informed consent to participate in the study.

2.2.2 Test protocol

All participants underwent instrumented gait analysis. Participants were requested to perform straight-line barefoot walking and jogging at self-selected speeds, to allow recording of natural level-ground gait. Each participant completed five valid gait cycles trials for each limb. Trials with partial or dual foot strikes on the force plates were excluded. Foot strike time was taken as the start of the period when the force value rose over 30N for more than 50ms. Gait was tracked using an 8-camera Vicon® system

(Vicon Motion Systems, Oxford, UK), with 16 reflective markers on the pelvis and lower limbs, according to the Vicon Plug-In Gait lower limb marker set. Ground reaction forces were measured using two AMTI® force plates (Watertown, MA, USA). Marker and force plate data were 4th order Butterworth filtered (zero lag) at 150Hz and 30Hz, respectively. Data processing for custom measures was done in MATLAB® (Mathworks, Natick, USA).

2.2.3 Data processing

Impact kinetics were quantified for each participant during the gait analysis. Maximum impact force was taken as the maximum vertical Ground Reaction Force (GRF) during the first 50% of stance for walking, or maximum vertical GRF during stance for running. In addition, overall loading rate, maximum loading rate, and initial impact transient average vertical load rate were calculated for each trial. Forces and load rates were normalised by Body Weight (BW) in newton. Overall vertical loading rate was defined between the points of 20% and 80% of the time between foot strike and 15% of stance phase for walking, or primary impact peak for running, as described by Noehren *et al.* [24]. Initial load rate of the heel strike transient was calculated, if present, i.e. during heel-striking running. If no initial impact peak was detected, i.e. forefoot strike, the average vertical load rate was used as the initial load rate for that trial.

Kinematic and kinetic outcome measures were taken at 15% of stance phase for walking or at initial impact peak for running, as described by Noehren *et al.* [24]. They were the hip and knee flexion angles, hip and knee flexion/extension moments, knee abduction moment, and front view knee valgus as described below. External moments were used, and normalisation was by BW and participant height in metres. Angles were computed using the Cardan angle sequence, referencing the distal to the proximal segment, in the order flexion-varus-rotation.

Frontal plane knee valgus angle during stance was investigated. Femoral and tibial axes were based on hip, knee and ankle joint centres as calculated using the Vicon plug-in gait model (Oxford, UK). This approach highly correlated to the 2-dimensional (2-D) knee valgus angle observed clinically from the front view, used routinely in video analysis of gait or drop vertical jumps [39]. This has been typically used in 2-D studies of knee alignment [40], and is also used for trials of large clinical populations as, for example, in Hewett *et al.* [33]. It has also been referred to as frontal plane projection angle (FPPA) [41].

2.2.4 Statistical analysis

T-tests were performed to detect differences in the average characteristics of participants in the ACL-R and CTRL groups. These included height, body weight, age and Tegner activity level.

Differences in biomechanical variables, between groups and limbs, were evaluated using a linear mixed effects model, fitting using the nlme package in R, Version 3.2.0 [42, 43]. Each variable of interest was analysed in turn. The model allows for a different mean response in (i) CTRL group participants (pooled limbs), (ii) the affected limbs of ACL-R participants (AFF), and (ii) the unaffected limbs of ACL-R participants (UNAFF). The mean response is also allowed to vary by (i) running versus (ii) walking, within each of the three groups.

Mixed effects models were chosen as they allow for the estimation of population-level relationships between predictors and responses (fixed effects) while allowing subjects to have their own unique deviations (random effects) from these. The random effects capture the correlation amongst the (varying numbers) of repeated measurements per participant, and also aim to contain all the subject-specific information lost by not including additional variables in the model. Changing variability of the response was evident in the data, and therefore a number of variance functions was considered, as

Table 2.1: Physical and injury demographics of ACL-R and CTRL groups

	ACL-R group	CTRL group	P[a]
Height (m)	1.80 SD0.07	1.78 SD0.09	0.572
Body Weight (kg)	90.3 SD13.5	85.2 SD13.8	0.308
Age (years)[b]	37.4 SD10.7	28.6 SD6.8	**0.012**
Tegner activity level[b]	6.2 SD2.0	6.5 SD1.4	0.669

[a] P-value between groups. Bold P-values < 0.05.
[b] At time of testing.

well as approaches for including random effects. After comparing the different model fits, for all responses, by the visual inspection of residual diagnostic plots and considering Akaike's Information Criterion values, a model was chosen with a random intercept, which allowed for different variability of the response by gait.

Results are presented as mean ±SD, and statistical significance was accepted when $P < 0.05$. Effect sizes, where discussed, were calculated using Cohen's d [44], where $d = 0.2$–0.5, $d = 0.5$–0.8 and $d \geq 0.8$ indicate small, moderate and large effects, respectively. To account for naturally-occurring limb differences in healthy controls, minimal important clinical differences (MCID) followed those measured by Di Stasi *et al.* [45], with hip and knee flexion values both 3°, knee moments 0.04Nm/kg/m, and hip moments 0.06Nm/kg/m.

2.3 Results

2.3.1 Participant characteristics

Time between injury and surgery for participants in the ACL-R group was an average of 5.3 months (range: 0-36 months). Participants in the ACL-R and CTRL groups were matched for height ($P = 0.572$), body weight ($P = 0.308$) and Tegner activity level ($P = 0.669$), given in Table 2.1. However, the average age in the ACL-R group was larger than in the CTRL group ($P = 0.012$).

Table 2.2: Mean biomechanical variables, compared between limbs in the ACL-R group, and between ACL-R affected and CTRL limbs. Values are mean ±SD.

		AFF	UNAFF	P^a	CTRL	P^b
Self-selected velocity (m/s)	Walk	1.17±0.09	1.17±0.09	0.824	1.16±0.09	0.853
	Run	3.25±0.15	3.31±0.16	0.184	3.38±0.12	**0.015***
Step length (mm)	Walk	642.7±35.5	639.2±35.6	0.465	646.7±34.7	0.760
	Run	705.6±39.6	704.5±40.1	0.891	723.8±36.2	0.201
Step width (mm)	Walk	119.2±29.8	118.7±29.8	0.929	107.3±28.3	0.273
	Run	75.7±28.2	73.3±28.4	0.541	79.7±27.1	0.695
Cadence (steps/min)	Walk	55.6±9.1	55.6±9.1	0.986	55.5±8.5	0.990
	Run	164.1±8.0	162.8±8.0	0.173	162.8±7.8	0.679
Max.Impact force (BW)	Walk	1.07±0.059	1.07±0.059	0.730	1.07±0.058	0.984
	Run	2.39±0.11	2.47±0.11	**0.015***	2.40±0.81	0.873
Overall Loading rate (BW/s)	Walk	7.54±1.43	7.62±1.43	0.604	7.66±1.42	0.826
	Run	27.67±2.32	29.50±2.38	**0.008***	27.5±1.86	0.860
Max. Loading Rate (BW/s)	Walk	51.2±15.5	55.7±15.5	**0.031***	60.4±15.4	0.115
	Run	228.4±49.0	236.8±50.8	0.630	286.6±34.8	**0.001***
Initial Loading Rate (BW/s)	Walk	8.52±1.72	8.62±1.73	0.626	8.56±1.74	0.959
	Run	122.4±30.6	123.0±31.8	0.958	153.3±20.7	**0.003***
Hip Angle (°)	Walk	31.08±4.75	31.45±4.75	0.454	27.4±4.67	**0.039***
	Run	34.77±5.07	35.6±5.10	0.333	33.83±4.79	0.607
Knee Angle (°)	Walk	20.02±4.04	21.0±4.04	0.217	17.82±3.78	0.134
	Run	20.59±4.01	22.56±4.06	**0.010***	20.67±3.70	0.957
Hip Moment (Nm/kg/m)	Walk	-0.022±0.20	-0.131±0.21	**0.001***	-0.063±0.20	0.586
	Run	0.076±0.37	-0.240±0.38	**0.008***	-0.025±0.28	0.406
Knee Moment (Nm/kg/m)	Walk	0.421±0.12	0.449±0.12	0.208	0.401±0.12	0.629
	Run	0.380±0.16	0.530±0.17	**0.001***	0.391±0.13	0.839
Frontal knee valgus angle (°)	Walk	-0.14±4.20	1.01±4.2	**<0.001***	0.46±4.16	0.699
	Run	2.05±4.35	2.82±4.36	0.143	3.26±4.22	0.444
Knee Abd. Mom. (Nm/kg/m)	Walk	0.005±0.14	0.066±0.14	**<0.001***	0.051±0.14	0.373
	Run	0.184±0.22	0.320±0.22	**0.032***	0.397±0.18	**0.007***

* Bold, starred P-values <0.05

[a] P-value, between limbs.

[b] P-value, between ACL-R affected limb and CTRL limbs.

2.3.2 Standard gait metrics

In both walking and running, no differences were found between groups in step length (walk, $P = 0.760$; run, $P = 0.201$), step width (walk, $P = 0.273$; run, $P = 0.695$), and cadence (walk, $P = 0.990$; run, $P = 0.679$) (Table 2.2). Although the mean velocity was not significantly different during walking ($P = 0.853$), there was a small difference in mean velocity between groups during running (CTRL group, 3.38±SD0.12; ACL-R group, 3.28 ±0.15, $P = 0.015$). Between-limbs in the ACL-R group, no differences were found in trial velocity (walk, $P = 0.824$; run, $P = 0.184$), step length (walk, $P = 0.465$; run, $P = 0.891$), step width (walk, $P = 0.929$; run, $P = 0.541$), and cadence (walk, $P = 0.986$; run, $P = 0.173$).

2.3.3 Between-group comparison: kinetics, kinematics, and impact

For the ACL-R affected limb compared to CTRL group during running, lower values were found in both maximum load rate (ACL-R limb: 228 SD49.0 BW/s, CTRL group: 286.6 SD34.8 BW/s, $P = 0.001$) and initial load rate (ACL-R group: 122.4 SD30.62 BW/s, CTRL group: 153.25 SD20.71 BW/s, $P = 0.003$) (Table 2.2). During walking, hip angles were significantly higher for the ACL-R affected limb (31.08° SD4.75°) compared to CTRL group (27.4° SD4.67°, $P = 0.039$). During running, knee abduction moment for the ACL-R affected limb (0.184 SD0.218 Nm/kg/m) was lower than the CTRL group (0.397 SD0.180 Nm/kg/m, $P = 0.007$), but this was not seen during walking ($P = 0.373$).

No differences were found between ACL-R affected limbs and CTRL group in the other variables. These were impact force (walk, $P = 0.984$; run, $P = 0.873$), average loading rate (walk, $P = 0.826$; run, $P = 0.860$), knee angle (walk, $P = 0.134$; run, $P = 0.957$), hip moment (walk, $P = 0.586$; run, $P = 0.406$), knee moment (walk, $P = 0.629$; run, $P = 0.839$) and frontal knee valgus angle (walk, $P = 0.699$; run, $P = 0.444$).

2.3.4 ACL-R Between-limb kinetics, kinematics, and impact

During running the affected limb (AFF) had a significantly lower maximum force (AFF: 2.39 SD0.11 BW, UNAFF: 2.47 SD0.11 BW, $P = 0.015$) and significantly lower overall load rate (AFF: 27.67 SD2.32 BW/s, UNAFF: 29.50 SD2.38 BW/s, $P = 0.008$) compared to the unaffected limb (UNAFF) in Table 2.2. During walking, however, there were no significant differences in these variables (maximum force, $P = 0.730$; average load rate, $P = 0.604$). In contrast, a lower maximum load rate on the affected limb was found in the unaffected limb during walking (AFF: 51.2 SD15.5 BW/s, UNAFF: 55.7 SD15.5 BW/s, $P = 0.031$), but not during running ($P = 0.630$). No significant differences were found in initial load rate (walk, $P = 0.626$; run $P = 0.958$).

During running, the knee angle (AFF: 20.59° SD4.01°, UNAFF: 22.56° SD4.06°, $P = 0.010$) and knee moment (AFF: 0.380 SD0.161 Nm/kg/m, UNAFF: 0.530 SD0.165 Nm/kg/m, $P = 0.001$) were both significantly lower in the affected compared to the unaffected limbs. During walking, knee angle ($P = 0.217$) and knee moment ($P = 0.208$) were not significantly different between limbs. In the affected compared to unaffected limbs, hip extensor moments were significantly reduced during both walking (AFF: -0.022 SD0.204 Nm/kg/m, UNAFF: -0.131 SD0.205 Nm/kg/m, $P = 0.001$) and running (AFF: 0.076 SD0.366 Nm/kg/m, UNAFF: -0.240 SD0.377 Nm/kg/m, $P = 0.008$), but hip angles did not differ between limbs in both walking ($P = 0.454$) and running ($P = 0.333$). Knee valgus angles during walking at the time point of interest were lower for the affected limbs (AFF: -0.138 SD4.20°, UNAFF: 1.01 SD1.07°, $P < 0.001$), but not during running ($P = 0.143$). In the affected limbs, knee abduction moment was significantly lower in both walking (AFF: 0.0046 SD0.140 Nm/kg/m; UNAFF: 0.0661 SD0.140 Nm/kg/m, $P < 0.001$) and running (AFF: 0.184 SD0.218 Nm/kg/m; UNAFF: 0.320 SD0.224 Nm/kg/m, $P = 0.032$).

To inspect variables over the whole stance phase, ensemble average data for walk and run gait for the three limb types (affected ACL-R, unaffected ACL-R, and control)

were plotted and compared. Output variables were vertical ground reaction forces (GRF) in Figure 2.1, hip and knee angles in Figure 2.2, and normalised moments in Figure 2.3.

2.4 Discussion

This study sought to identify and describe biomechanical deviations in males long-term after ACL reconstruction, as has been previously done for females. In this study, contrary to our hypothesis, the initial and maximum loading rates were lower in the ACL-R affected limbs as compared to controls. In addition, no kinematic differences were found, except for hip angle during walking, where the ACL-R affected limbs had a higher hip angle. Also, when comparing the affected limb to the unaffected limb in ACL-R participants, running had a lower impact force, loading rate, knee angle and knee moment, and walking had a lower maximum loading rate. Hip moment in the affected limb was reduced (closer to zero) during both walking and running. Several of these findings were contrary to our a priori hypothesis, and have not previously been shown for this population.

This study demonstrates long-term alterations in impact dynamics for this population. These have been associated with increased risk of osteoarthritis [46], particularly during repetitive tasks such as walking or running. Another lower limb pathology, tibial stress fractures, has also shown altered footstrike loading rates, where meta-analysis [47] has shown that rate of impact is a better predictor than impact force alone. In our study of ACL reconstruction, we used several impact variables to investigate this further, similar to those presented for females by Noehren *et al.* [24]. We found that during running, the unaffected limb supported a higher peak GRF than the affected. Higher GRF on the unaffected limb correlates with the strategy seen long-term after surgery during drop landing tasks [48]. This may suggest lower strength of the affected limb, although this

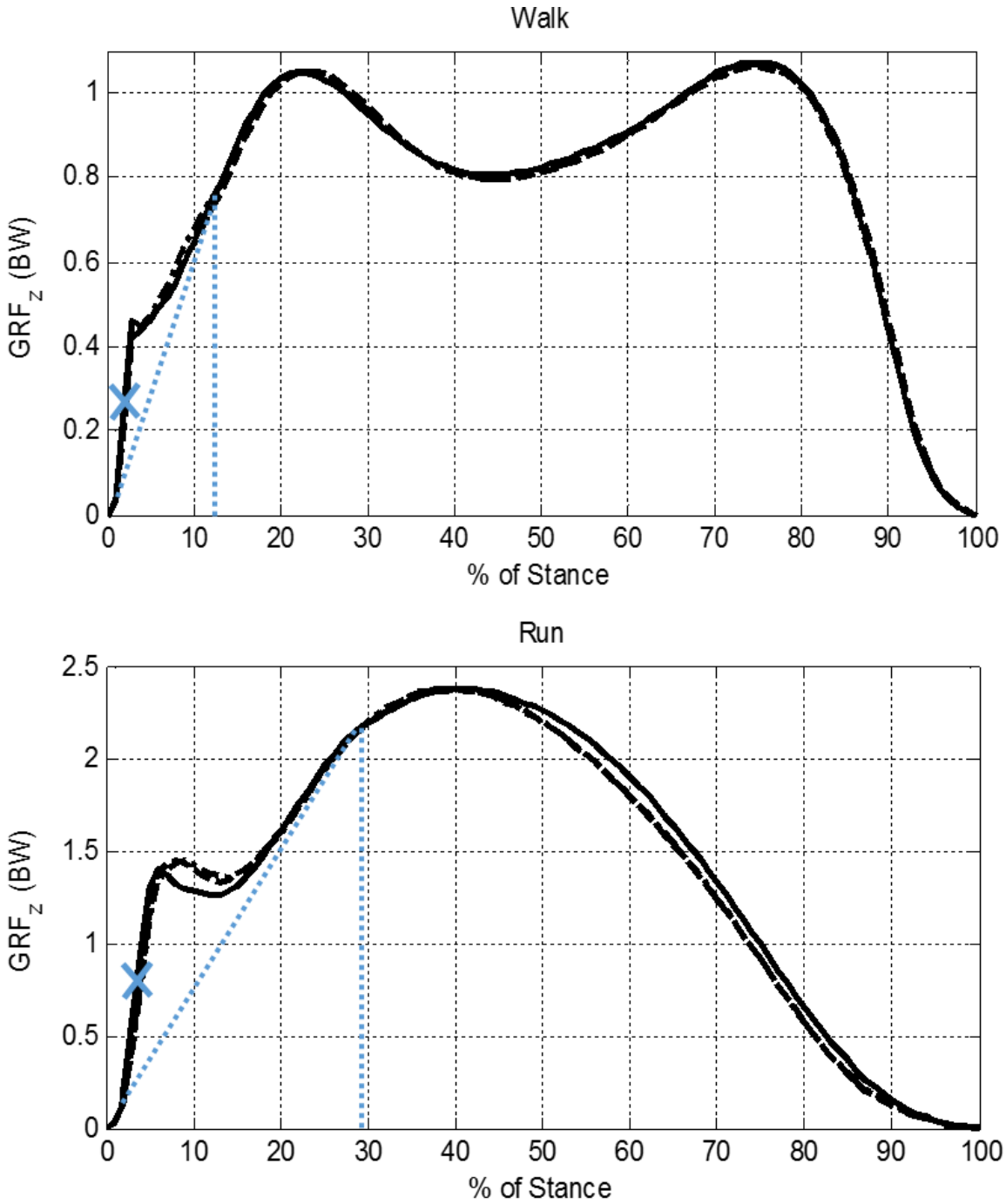

Figure 2.1: Walk and run vertical GRF profiles. Dashed (–) line: ACL-R affected limb, Dash-Dot (-.): ACL-R unaffected limb, Solid line: Control (both limbs). Dotted vertical lines indicate approximate % stance of interest, dotted slopes indicate average rate, and X indicates approximate point of maximum rate. Initial load rate not shown.

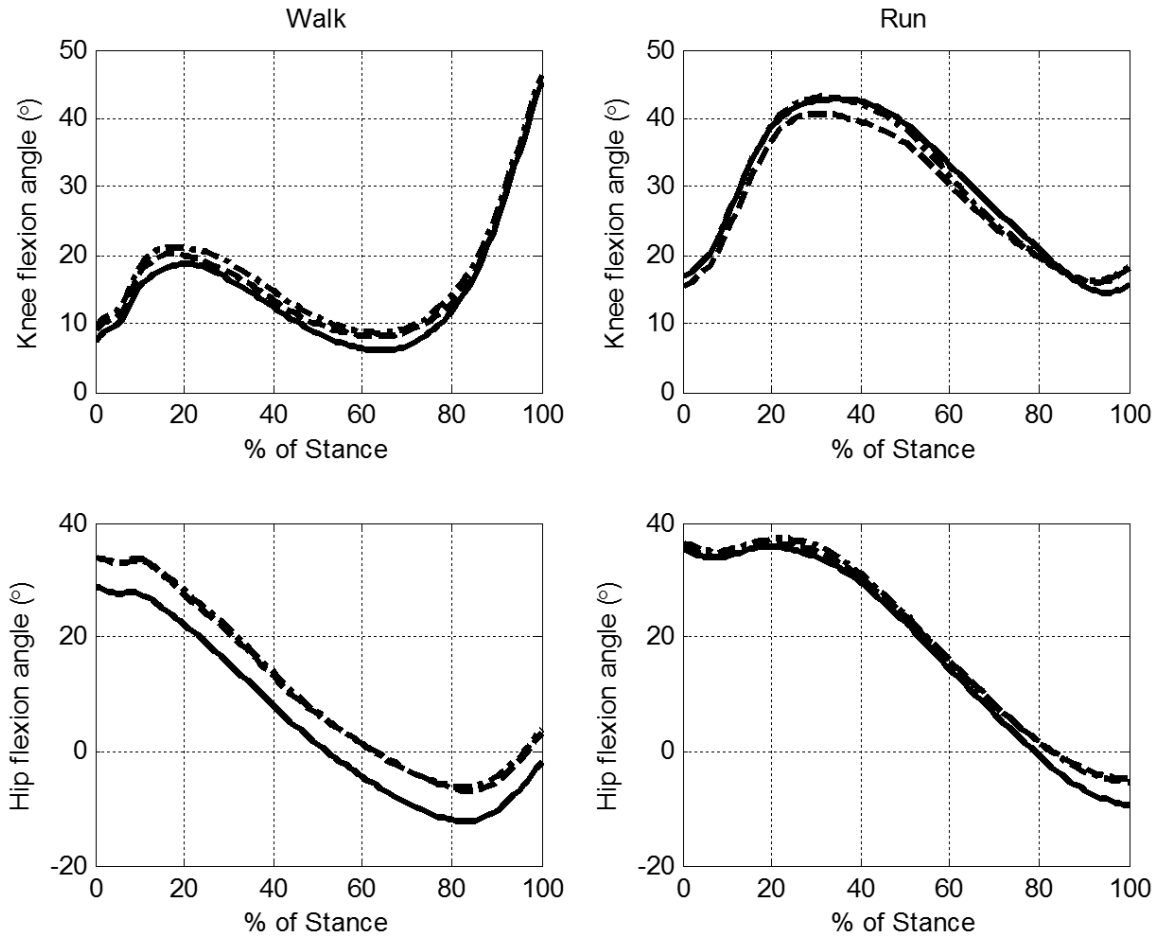

Figure 2.2: Ensemble average of hip and knee saggital plane angles in stance phase of gait, during walking and running. Dashed (–) line: ACL-R affected limb, dash-dot (-.) ACL-R unaffected limb, solid line: both limbs of CTRL group. Hip and knee flexion is positive.

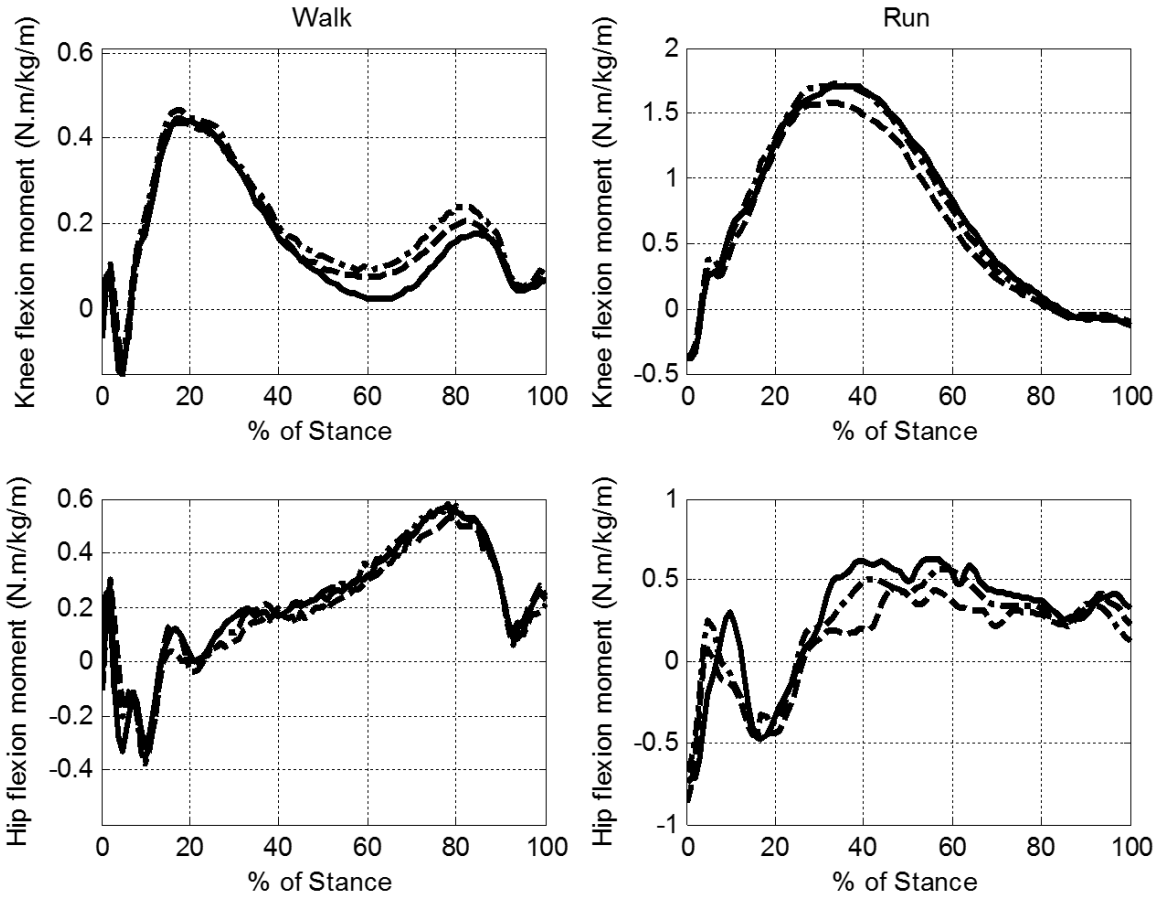

Figure 2.3: Normalised ensemble average of hip and knee saggital moments in stance phase of gait, during walking and running. Dashed (–) line: ACL-R affected limb, dash-dot (-.) line: ACL-R unaffected limb, solid line: both limbs of control participants. Hip and knee extension moments are positive.

was not tested in this study. Long-term strength deficits have been widely reported at different follow-up times, generally with limb symmetry indexes in the range 87-99% [49]. This difference was not seen during walking, but this could be because it is a less demanding task, requiring less strength.

Focusing on the impact transient at foot strike, we found a very much lower maximum and initial load rate in the ACL-R group, compared to the CTRL group during running (both Cohen's $d > 2$, large effect size), indicating a foot strike with much softer initial impact for the ACL-R group. This finding is the opposite to the finding by Noehren *et al.* [24], but aligns with impact rates found during drop landing by Paterno *et al.* [48]. In Figure 2.1 during running, a smoother transition for the ACL-R group can also be seen after the initial impact peak.

Investigating kinematic and kinetic variables between groups, we found ACL-R participants had a higher average hip angle than CTRL participants during walking, by about 4°. This finding was observed over the whole stance phase of the gait cycle (Figure 2.2), and is clinically significant (>MCID = 3°). As compared to the curves given by Noehren et al. [24] for females, this constant difference is also seen in both walk and run, but *opposite* to the findings here, i.e. the ACL-R group had a more extended hip over the gait cycle than the CTRL group. This may be a biomechanical difference between sexes, but it would need to be verified by a study comparing them directly.

As in [24], we found no significant differences between groups in knee angle during stance in either walk or run condition. This pose of increased hip angle, without increased knee angle, suggests that the ACL-R participants were not walking with a more flexed leg overall. Also, these differences in hip and knee angles were not associated with a significant change in moments at these joints. An explanation for this combination of variables would be that the ACL-R group walked with a more anteriorly-tilted pelvis, the reference in calculating the hip angle. Further, the lack

of difference in moments suggests that the trunk lean does not differ in this group, although this cannot be confirmed because no upper body model was used in this study.

Between limbs in the ACL-R group in running, the knee angle is significantly smaller on the affected side ($d = 0.49$), but this is not above the minimum clinically important difference (3°). In addition, the knee moment is strongly reduced ($d = 0.88$, large effect size), and is clinically relevant (>MCID). This indicates quadriceps avoidance on the affected side, or possible increased hamstring activity. This effect is not seen during walking, but the loads exerted are less than half of those during running, which may mask these differences.

Asymmetries in hip moments were also measured, and were clinically relevant during both walk and running gait. From Figure 2.3, in both conditions the phase of gait of interest (approx. 15% stance) is during a period of higher variability for the calculated moment. However, for the period from 30-70% of stance, the differences in limbs are more consistent (lowest – affected limbs, highest – control limbs). It would be useful to quantify these differences later in the stance phase to complement the metric used here. Interestingly, the differences in hip moments were not associated with differences in hip angles in either gait condition. This suggests that unquantified pelvis and upper body movement differences may be contributing to the differences in hip moment.

Knee valgus angle and knee abduction moment are not often reported during gait, even though these risk factors are widely-reported and clinically relevant [26, 33, 50]. We extended the analysis to include these variables, because of demonstrated deviations in other biomechanical studies [23]. For the knee abduction moment, clinically significant lower values (reduced varus moment) were seen for the affected limb as compared to the unaffected limb in both walking and running (walk; $d = 1.7$, run; $d = 2.45$, both large effect sizes). Similarly, a large effect size moment deviation was also seen for the

ACL-R group as compared to the CTRL group ($d = 2.82$). This biomechanical deviation during weight acceptance (reduced varus moment, increased valgus effect) is the same as seen in the literature prospectively for females during a Drop Vertical Jump (DVJ) task [33]. In the study, the biomechanical deviation was shown to be a risk factor for ACL injury. This suggests that ACL-reconstructed males may share this risk factor during gait tasks, and warrants further prospective investigation.

For the frontal plane knee valgus angle at maximum GRF, a reduction was seen for the affected limb compared to unaffected during walking (1.1° more valgus, $d = 1$, large effect size), and no difference was observed in running or between groups. This walking result is the same as was seen by Gokeler *et al.* [23] in two studies reviewed. However, this small measured difference may be difficult to observe clinically without either video analysis or motion capture, limiting its usefulness in this setting.

It would be convenient to use the easily observable frontal knee valgus angle to estimate knee abduction moment, a much more costly variable to measure. However, in this study, correlation was low (0.233) between these variables for all participants. This observation is supported by recent literature [41]. Despite this, the measure of knee valgus used above, inspired by clinical observation from the front view, is recommended as a relevant variable during gait.

In conclusion, long-term residual biomechanical deviations were found for males between ACL-R and CTRL groups, and between-limbs in the ACL-R group. This helps to characterise chronic joint loading patterns for this population separately from females, as they have been shown to have different ACL-R biomechanics. The ACL-R group had lower initial and maximal impact rates during running, suggesting a reduced impact foot strike pattern. Asymmetries were also present between limbs in the ACL-R group, noticeably reduced knee angles and moments during running in the affected as compared to the uninjured side, suggesting reduced use of the quadriceps muscles. Knee abduction moment and front view knee valgus angle at maximum GRF showed

large valgus effects for the affected limbs compared to unaffected and control limbs for both walking and running. Overall, the observed biomechanical deviations indicate altered joint loading patterns, which contribute to understanding the long-term changes to males after this surgery. Clinicians should be aware of these persistent effects after ACL reconstruction and follow specific rehabilitation programs to try to reduce them.

Chapter 3

A Randomised Controlled Trial of isokinetic eccentric cycling for ACL-R rehabilitation

3.1 Introduction

Injury of the anterior cruciate ligament (ACL) and subsequent surgical reconstruction is common in sporting populations. It is one of the most costly acute sports injuries, in terms of incidence, cost per patient, and lost play time. Rehabilitation after anterior cruciate ligament reconstruction (ACL-R) is typically long and time-consuming, and despite extensive research effort, remains stubbornly so. In addition, risk of osteoarthritis (OA) and re-injury remain a concern. For OA, a recent systematic review has shown the rate of development to be 16.4% of patients without meniscectomy [51], which is lower than previously thought. Two-year re-injury rates remain between 0-24% for the ipsilateral limb (0-15% for the contralateral limb) [52].

Thus rehabilitation needs optimising in terms of both outcomes and cost, particularly among sub-elite and amateur athletes; elite athletes tend to have the resources for more

rapid return-to-sports, with reports of approximately half the typical time. For amateur athletes, more tailored programmes, better progress tracking and more patient-friendly protocols will help to boost compliance, while reducing costs.

Eccentric training offers a possible improvement to standard rehabilitation, due to its potential for higher musculo-skeletal loads for the same perceived exertion. In healthy adults, a meta-analysis seems to show better strength and muscle volume gains than concentric training [53], although the *intensity* was higher in the eccentric group in most of the studies, making direct comparison difficult. For ACL-R, adding eccentric training to standard rehabilitation in the early phases has been shown to be effective compared to standard concentric rehabilitation alone [54, 55, 56]. The current randomised controlled trial (RCT) uses it during phase III of rehabilitation (~3-6 months) to compare its effectiveness for strengthening and improvement of biomechanics. These outcomes have been shown to indicate injury risk in certain populations, [32, 57], and have been targeted in injury prevention efforts [58].

This chapter reports on strength, pain, and patient-reported outcomes of a RCT of eccentric training to achieve these goals in male patients. Following this, the effects of this eccentric program on biomechanical deviations are investigated in detail in Chapter 4. These are compared to long-term deviations from a cross-sectional trial in a separate cohort in Chapter 2. Finally, the potential of this eccentric programme to improve performance on functional tasks and return-to-sports are investigated in Chapter 5.

3.2 Literature review

The first part of this review covers standard, neuromuscular, and eccentric ACL-R rehabilitation types. The second section discusses ACL-R clinical, patient-reported, and strength outcome measures to monitor its success.

3.2.1 ACL-R Rehabilitation programmes

The purpose of ACL-R rehabilitation is to restore structure and function, while reducing the risks of associated chronic or acute injury, within acceptable time and cost. A typical programme timeline starts with goals of range of motion (ROM) and weight-bearing recovery during the first few weeks, progressing to strengthening and proprioception training up to 3 months, increasing use of exercise and drills up to 6 months, then return-to-sports training from 6-12 months. Progress is adapted depending on the patient's individual response, goals, and compliance to the programme [59].

3.2.1.1 Standard rehabilitation

Current clinical protocols target initial resolution of pain and effusion, restoration of range of motion, and retention of thigh muscular strength. Later stages generally focus on strengthening of hamstrings and quadriceps to pre-injury levels (or at least to the point of symmetry within 10% of the contralateral limb). The primary mode is usually low velocity isotonic exercises, with equal concentric and eccentric contraction phases. These are generally with weights or elastic bands of open- or closed-chain type, and completed during a home-based programme. As part of this, concentric cycling (ergometer or outdoor) is often recommended as a component. It is discussed in more detail in Section 3.2.1.3 below.

Progression is approximately time-based, guided by functional tests before introducing new training types. Some examples of well-documented clinical recommendations are given in the protocol by Werstine [60], Adams *et al.* [61], and the training course given by [62]. However, significant unexplained risk factors remain despite strength-based programs, prompting the recent trend toward interventions which target neuromotor aspects as well, especially in mid- to late-stage programmes. These are discussed further in Section 3.2.1.2 below.

The evidence base for ACL rehabilitation is growing, but significant unanswered questions remain in the literature. Wright *et al.* conducted a systematic review of studies in two parts [17, 63], including 54 studies of level 1 or 2 evidence, noting that the methodological quality of studies is often mixed. Similarly, in 2010 van Grinsven *et al.* [16] also conducted a systematic review of the evidence base, finding 32 rehabilitation programmes, randomised controlled trials, and reviews, and compiling these into a recommended protocol. They too emphasize that gaps exist in the evidence base, and that high-quality studies with standardised outcomes are often lacking. To achieve a full evidence-based protocol for clinical use, they say

> .. we added evidence, with lower level and methodological quality, from soundly based protocols and available background literature ... to the high level evidence... . Without the added information ..., we would not have been able to develop a continuous rehabilitation protocol, leaving the orthopedic surgeon and physiotherapist with gaps in scientific evidence ...

Thus, this intervention trial aims to add to this evidence base, regarding the safety and efficacy of eccentric vs. concentric training.

3.2.1.2 Neuromuscular programmes

In ACL rehabilitation, the inclusion of exercises targeting neural (proprioceptive) and vestibular training is becoming more common in clinical practice, over and above strength training [64]. This is partly due to the poor correlation of strength to other outcomes such as patient satisfaction [65].

There is epidemiological evidence that neuromuscular training for ACL injury prevention reduces the primary ACL injury risk [4, 66], particularly for young, female athletes [67], and improved risk reduction with higher compliance [27]. From a meta-analysis of 12 studies, Sugimoto *et al.* [68] calculated a relative risk reduction (RRR) of 73.4% for non-contact ACL injuries, and 43.8% for ACL injuries in general. However, the

number needed to treat (NNT) values of 108 and 120, respectively implies that many athletes need to participate to prevent one ACL injury. Programmes with a variety of types of training were emphasised, as these had the strongest RRR. It would seem to follow that these programmes would aid recovery and reduce risk of re-injury after ACL-R as well. In males, similar data is scarce, and not conclusive [69].

Examples of preventive programmes in use are given by Pappas *et al.* [70], such as the FIFA 11+ warm up programme used to reduce injuries in soccer. These often include balance exercises, which start with various levels of challenge progressing to functional activities (e.g. ball catching) on unstable surfaces. Later stages often use explosive hopping and bounding exercises, also known as plyometrics, which are discussed further in Section 3.2.1.4 below. They are evaluated on power and landing technique. Landing is an important phase of movement to investigate as it is typically when ACL injuries occur [71]. It is primarily a phase of eccentric muscle activity (contraction during lengthening), and requires control, balance and appropriate response to unexpected perturbations.

However, the evidence for these types of ACL injury prevention programmes has sometimes been questioned. For males in particular, a review of these programmes by Alentorn-Geli *et al.* [36], found that the evidence of reduced risk is scarce and not conclusive. Supporting this, van Grinsven *et al.* [16] reviewed several clinical trials evaluating the effectiveness of these programmes, also showing the benefits to be mixed. In order to make these programmes worthwhile, it is important that better screening of high-risk patients is developed, and programmes are optimised to reduce their cost.

While modification of risk is difficult to show directly in this population, the effect of neuromuscular training on clinical outcome measures is well-documented. Risberg *et al.* compared neuromuscular training to strength training pre-operatively, at 6 months, 1-year, and 2-years after surgery [72, 73]. The neuromuscular training group had a better global function visual analogue score (VAS) at 6-months and 1 year (no

difference at 2-years), improved Cincinnati score at 6-months, and improved Pain Scores at 1-year as compared to strength training. Interestingly, no differences were found in isokinetic strength profiles at any time points. In another trial, of proprioceptive training compared to strength training, Liu-Ambrose *et al.* [74] found that concentric quadriceps and eccentric hamstring strengths of the injured limb increased more in the proprioceptive training group than in the strength group. This example demonstrates how important the neural component is in strength outcomes for these patients.

There have also been several studies using neuromuscular training to modify biomechanical variables. Paterno *et al.* [75] improved single-limb stability in young female athletes after 6-weeks of neuromuscular training. In another study, the *Talent Jump System*, a training programme, reduced muscle reaction times after 6 weeks, 12-36 months after surgery [76]. Another trial by Liu *et al.* [77] used a knee extension-limiting brace to improve motor learning showing that a greater knee angle is learned after 4 weeks of wearing the brace, which was partially retained after its removal.

Novel training programmes focusing on the neural system only, have shown the potential impact of this type of training on ACL-R rehabilitation. For example, simple gait retraining using natural frequency audio cues [78] improved kinematics and concentric and eccentric energetics in one study. In another, Fitzgerald *et al.* [79] used random perturbations in a movable ground surface to train reaction to unexpected input in addition to standard rehabilitation. The group that received the perturbation training enhanced the probability of return to high-level activity. This type of perturbation-enhanced training has also been shown to normalise ACL agonist muscle activity patterns during gait [80], has been used to improve anterior cruciate ligament-deficient (ACL-D) gait [45, 81, 82].

These concepts are now more common in clinically-recommended protocols. In a clinical commentary, Di Stasi *et al.* [83] recommend neuromuscular training to target ACL re-injury. In a recent ACL-R rehabilitation protocol, Bishop [62] emphasizes

restoring neuromuscular control by stabilisation of knee from above and below (ankle and hip) during phase V (Advanced Activity Phase, 12-20 weeks).

Based on this evidence, both neuromuscular and strength training is recommended, using combined training modalities where possible to improve training efficiency. The unique neurophysiology of eccentric training [84], coupled with strengthening effects, has the potential to apply neural and muscular training simultaneously.

3.2.1.3 Concentric ergometer cycling

Concentric cycling (on an ergometer or outdoors) is well-recommended as a component of standard rehabilitation. However, in general, ACL-R rehabilitation programmes do not provide guidelines for frequency, intensity, duration, or specific indications for its use (for e.g., [61]). Advantages of ergometer cycling for ACL-R rehabilitation include:

- safe application of cyclical, constrained, alternating training targeting each lower limb independently, which can be seen to be functional, closed chain type.
- continuous progression from no weight-bearing (continuous passive mobilisation) to partial weight-bearing (PWB), to full weight-bearing using standing cycling.
- partial body weight support training at low cost, and suitable for home use
- some ROM targeting is possible by adjustment of cycle setup, including seat height.

Early stage limitations of ergometer cycling include possible ROM limitations. Later stage limitations include the focus primarily on the sagittal plane of motion, lack of task-specific gait patterning and training, and difficulty in providing training forces higher than body weight.

Concentric cycling was used as a control intervention in this study, and is a viable option for several reasons. First, it is a safe, commonly used modality for ACL-R, and

is recommended in an extensive review of the literature by van Grinsven *et al.* [16], which allows cycling ergometry as early as 3 weeks post-surgery. However, the review provides no specific dosage or intensity guidelines, except that pain and discomfort should be monitored.

Secondly, concentric ergometer cycling is possible using the same studio and ergometer as for the eccentric study programme. This means that the training context is identical between programmes, greatly reducing the chance of bias due to awareness by the participants of which programme they performed. This was borne out by experience in this trial, in that almost no questions were posed by participants regarding the nature of their programme.

Finally, use of concentric cycling at the same rating of perceived exertion (RPE) as eccentric cycling ensured that the perceived exercise dose was matched, in contrast to some trials where eccentric exercises have been added to a standard programme that is given to all participants. Also, perceived exertion seems to play an important role in adherence to an exercise programme, which means that results of this trial are more likely to represent results found in clinical practice.

3.2.1.4 Eccentric rehabilitation

Eccentric training seems to be beneficial for the following reasons. Firstly, maximal eccentric muscle contractions can produce two to three times the force production of a typical isometric or concentric muscle contraction [85]. Also, for the same perceived exertion, eccentric muscle contractions have long been understood to have lower metabolic (or oxygen) cost than concentric muscle contractions [86]. A systematic review and meta-analysis has shown that in healthy adults, eccentric training provides higher strength and muscle volume gains than concentric training [53]. However, the review also showed that most trials were not matched for *intensity*, which makes interpretation difficult. For bone, joint, muscle and tendon, benefits of higher mechanostimulation are

possible, while maintaining the comfort (and presumably, compliance), of the patients. This may promote ligamentisation and/or reinnervation of the ACL graft. For tendons, the higher forces in eccentric training improve mechanical properties [87]. A stiffer tendon is seen to improve sensory feedback from muscle spindles and Golgi tendon organs, resulting in better proprioception of the joint.

Secondly, eccentric training may have superior neural benefits. It may be a practical way to overcome arthrogenic inhibition, a key factor slowing rehabilitation efforts [88], which can be quantified by measuring quadriceps activation failure (QAF). In the study, eccentric training was better than electrical stimulation or concentric training at reducing QAF [89], and this was associated with significantly greater quadriceps strength.

Neural effects of eccentric training seem to have benefits at different levels. Increased cortical activity has been shown during eccentric as compared to concentric exercise[84], and in a cat model, perturbations due to eccentric training were found to be predominantly central, rather than peripheral [90]. At the spinal level, it has been documented that eccentric cross-exercise of the uninjured lower limb can increase strength of the injured limb by neural spill-over [91, 92].

In performance and injury-prevention exercise programmes, the benefits of including specific eccentric work is well-documented (see for e.g. Pull and Ranson [93]). This can be seen in plyometrics, especially, which include a rapid eccentric landing phase followed by a shortening concentric phase. There is extensive evidence for plyometrics in the performance literature [94], and recently this has been extended to ACL-R rehabilitation [16, 62, 73, 95]. However, it is more suited to late-stage rehabilitation once sufficient baseline strength has been recovered, as there is a risk of poor technique and aggravation of the injury during landing. This has meant that early- or mid-stage rehabilitation using eccentric training for the ACL-reconstructed limb has traditionally been contraindicated.

Eccentric cycle training offers an alternative which is safer and more controlled than plyometrics. Recent evidence suggests that early, progressive, eccentric cycling can be safely added for ACL-R rehabilitation to increase muscle volume and strength, compared to standard rehabilitation [54]. In this trial, Gerber *et al.* added a progressive, eccentric-based rehabilitation programme to a standard concentric programme starting three weeks after surgery. They found that the muscle volume changes in the quadriceps and gluteus maximus muscles greatly exceeded those changes in the control group using standard rehabilitation only. The structural changes were noted in both the involved and uninvolved limbs, and these benefits were still significant in a 1-year follow up study [96]. While the trial did try to match control participants by perceived exertion, a stated limitation of this trial was that the eccentric group performed a larger volume of training than the control group, meaning that the benefits may be overstated.

Two studies investigated the effects of a 12-week maximal eccentric training of male ACL-R bone-patellar tendon-bone (BPTB) participants, approximately 9 months after surgery. Only the affected limb was trained in both cases. In the first [97], 5 patients were trained, and showed a 25% increase in the affected limb strength. However, no control participants were trained for comparison. Gait changes were seen from pre- to post-training, but were not different from control gait, and stated methodological challenges make interpretation difficult. In the second trial, 9 patients were trained using the same programme [98]. Outcome measures were isometric and eccentric torque production, distal and proximal quadriceps cross-sectional areas, and quadriceps muscle electromyography. Increases of eccentric strength (at 30°/s) were found in the affected limb of +12% and +28% at 6- and 12-weeks, respectively. At 12-weeks, isometric strength gains were +20%. Increase in muscle cross-sectional area in the distal quadriceps at 12-weeks was 11.5%, mainly in the *vastus medialis* muscle. At the mid-thigh and proximal quadriceps locations, cross sectional area increased by +8.9%

and +9.6%, respectively, primarily in *vastus intermedius*, *vastus lateralis,* and *rectus femoris.* These results, while encouraging, were also not compared to a control group.

The above studies have resulted in increased interest on the potential of eccentric cycle training during ACL-R. In a clinical review, Lepley and Palmieri-Smith [56] support the use of eccentric exercise for ACL rehabilitation. In a review of practices to strengthen quadriceps after ACL reconstruction, Gokeler *et al.* [99] conclude that *eccentric training may be most effective to restore quadriceps strength*. However, both these reviews are based on a very limited number of studies, meaning that while promising, further study is needed.

Following this, a more recent trial [89] compared five groups: 6-weeks of eccentric training, neuromuscular electrical stimulation, combined therapy, standard therapy and controls, and with follow-up testing at return-to-sports (RTS). Results showed that eccentric training was better than neuromuscular stimulation at reducing quadriceps activation failure, and better at restoring quadriceps strength. However, in a biomechanical study of the same groups [100], the eccentric-only group did not show greater restoration of symmetry in knee moment and angle during landing, compared to the other groups, with the greatest restoration of symmetry seen in the combined therapy group. Limitations to the above study were the stated lack of patient randomisation, and a lack of matching between groups, comparing a) *eccentric + standard of care* to b) *standard of care only*.

3.2.1.5 Progressive eccentric isokinetic cycling

Based on the evidence provided above, and the success of a similar programme by Gerber *et al.* [54, 96], eccentric isokinetic cycle ergometry based on RPE progression is proposed as a clinical intervention for ACL-R. As a control intervention, isokinetic concentric cycle ergometry is used. Based on clinical experience in our studio, during the last phase of the training, standing training can be added for both modes of training,

to progress to full weight bearing, and allow more natural, whole-body movements. In contrast to the above studies, this programme will be applied during the strengthening phase of rehabilitation, starting approximately 3 months after surgery. In terms of training frequency, one study comparing eccentric exercise 3x per week vs. 5x per week didn't show significant differences in Lysholm scores [92]. Thus, 3x per week is to be used in this study.

To track the progress and outcomes of the above intervention as compared to controls, the following section of this literature review covers the outcome measures. A comprehensive range of clinical and biomechanical measures was used, to better understand the effects of the training.

3.2.2 ACL-R rehabilitation outcomes

To track progress of the programmes described above, a wide variety of measures have been used, with limited consensus on what constitutes successful rehabilitation [101]. This chapter covers a range of commonly-used clinical measures. In Chapter 4 biomechanical measures are covered, and RTS and risk measures are covered in Chapter 5.

3.2.2.1 Clinical outcomes

In this study, acute-stage clinical outcomes were primarily used for screening of patients entering the study. They include dynamic stability, effusion, joint laxity and stability (pivot-shift / A-P laxity tests), ROM, and pain.

3.2.2.2 Patient reported outcomes

Patient reported outcome (PRO) questionnaires are key to evaluating the patient's view of rehabilitation progress; a review of commonly-used measures of knee function is given in [102] and [103]. The patient's perspective is an important dimension which

has been shown not to be correlated with functional outcomes, meaning that testing of both is recommended [104]. From the above reviews, well-used questionnaires designed for ACL injuries, that had been developed for patient self-administration were selected. This selection is also supported in a review by Johnson and Smith [105].

The Knee injury and Osteoarthritis Outcome Score (KOOS) was developed and validated for knee injury and OA, including patients after ACL surgery [106]. It consists of 5 sub-scales; pain, other symptoms, function in daily living (KOOS-ADL), function in sport and recreation (Sport/Recreation) and knee related quality of life (KOOS-QOL). The past week is taken into consideration when answering the questions. Standardized answer options are given (5 Likert boxes) and each question is scored from 0 to 4. A normalized score (100 indicating no symptoms and 0 indicating extreme symptoms) is calculated for each sub-scale. KOOS construct validity has been determined in comparison with SF-36 and expected correlations were found [106]. Moderate to high correlations were found when comparing to the Lysholm knee scoring scale [106]. In addition, the Swedish ACL-R register [107] uses the KOOS PRO, giving reference values from a very large cohort.

The International Knee Documentation Committee (IKDC) subjective rating score evaluates patient perspective to evaluate the knee function. It uses three categories of questions: symptoms, sports activities and function, with each potential answer given a number of points. Shaw *et al.* [108] and Higgins *et al.* [109] investigated various measures of validity of the score, concluding that the IKDC has sufficient internal consistency, and displays construct, concurrent and criterion validity and reliability. Regarding the use of the IKDC specifically to evaluating rehabilitation after ACL-R surgery, Collins *et al.* [102] performed a clinical and research review, corroborating the usefulness of this metric.

However, the IKDC scoring system has its limitations. Hambly and Griva [110] compared it to the KOOS for use after ACL-R, concluding that although the IKDC

outperformed KOOS, they recommended that KOOS sub-scales of a) function in sports/recreation and b) knee-related quality of life be included as they are not fully represented by IKDC. KOOS also shows greater validity long term after surgery [102], with more emphasis on OA risk. Thus both IKDC and KOOS were considered in the current study. IKDC gives a global score of knee outcomes, and sub-scores for the KOOS give more detail on underlying patient-reported areas.

The SF-36 is a multi-purpose, short-form health survey with 36 questions, often used in orthopaedic populations [111]. It yields an 8-scale profile of functional health and well-being scores, as well as physical and mental health summary measures [112]. The SF-36 Health Survey Update reported the reliability of the eight-scale profile of scores and the mental and physical health summary measures, estimated using both internal consistency and test-retest methods. In most cases, published reliability statistics have exceeded the minimum standard of 0.70 recommended for measures used in group comparisons in more than 25 studies [113]; most have exceeded 0.80 [114]. Studies of validity generally support the intended meaning of high and low SF-36 scores as documented in the original user's manuals [114, 115].

3.2.2.3 Strength and thigh volume

Biomechanically, to reduce excessive anterior tibial movement, compensation from a deficient ACL results in a reduced quadriceps activation, and altered hamstring activation patterns. This has been seen in ACL-D knees, where a recent meta-analysis showed a 3-fold greater decrease in quadriceps strength than in the hamstrings [116]. While ACL-R surgery reduces this movement at joint level, biomechanical habits often mean that this pattern becomes ingrained.

Strength deficits are widely reported after ACL-R w.r.t. the contralateral limb and healthy normals, and these are often used as a primary outcome. These are seen to be due to a combination of reduced neural drive (central activation failure and/or

arthrogenic inhibition)[117], and muscle atrophy from reduced activity of the muscles during the acute phase of rehabilitation. A recent clinical review showed that average side-to-side strength asymmetry at 6-months of 23%±8%, while at 12-months it was 14%±6% [118], showing that the common guideline of <10% asymmetry is often not met by this point. In the review, functional strength outcomes at 6- and 12-months using a hop test were 11%±7% and 1.3%±2%, respectively. Strength deficits seem to vary by donor site; a recent meta-analysis by Xergia *et al.* [119] showed greater extensor strength deficit exists in patients using BPTB autograft and a flexor strength deficit exists in patients with hamstring-tendon autografts, 12 months post-operatively. Similar conclusions were also found in a recent meta-analysis of functional measures by Abrams *et al.* [120].

To quantify strength deficits, concentric, isokinetic open-chain dynamometry has been extensively used. Typically maximum concentric torque and hamstring/quadriceps ratio are reported for several speeds. Eccentric isokinetic strength testing was not found to be commonly reported, but is included here due to the mode-specific interest of the two training groups. Thigh circumference deficits have also been reported in both ACL-R and ACL-D [121], and are often also measured as a general indication of muscle recovery, particularly w.r.t. the loss of larger, fast-twitch fibres, which tend to atrophy faster than slow-twitch fibres.

Isokinetic tests are good at identifying problem areas, but are not recommended to predict functional performance [122]. For functional strength in this population, single-repetition-maximum weight lifting (1RM) is not typically used, but repetitions-to-fatigue are used as a safer proxy, using the correlation between the two measures [123]. In this trial both isokinetic tests, and squat repetitions-to-failure are used, with the latter discussed as part of the functional evaluation in Chapter 5.

Apart from the strength effects at the knee, other muscular effects have also been found after ACL-R. These include strength deficits at the hip and ankle [9], reduced explosive strength [124], and increased variability in maximum force generation.

3.2.2.4 Other outcome measures

This chapter focuses on the clinical outcomes of the randomised controlled trial. Biomechanical and functional outcomes are discussed further in Chapters 4 and 5.

3.3 Trial aims and objectives

The aim of this randomised controlled trial is to evaluate the safety and effectiveness of eccentric training to improve clinical outcomes in ACL-R rehabilitation, as compared to concentric training in exactly the same setting, at the same perceived dose. The *a priori* hypothesis is that eccentric training is safe, and is more effective than concentric training at improving outcomes than concentric training. The objectives are to determine if during the third phase of rehabilitation, the eccentric exercise protocol is more effective compared to the concentric exercise protocol in improving the following in this population:

1. increased concentric and eccentric strength (quadriceps and hamstring) and lean thigh volume in both the affected (AFF) and unaffected (UNAFF) limbs.

2. improved symmetry between AFF and UNAFF limbs for concentric and eccentric strength in quadriceps and hamstrings, and lean thigh volume

3. improved PROs, as measured by the IKDC, KOOS, and SF-36 questionnaires

3.4 Methods

The following section describes the methods used in this randomised controlled intervention trial (Class I device, phase-II trial). The trial was registered on the pan-African clinical trials registry (registration number: PACTR201602001449365), and the South African National Health Research Ethics Council registry (NHREC registration #: 4344).

3.4.1 Participants

Twenty-six male patients (18-40 years of age), who had undergone ACL-R surgery within the past 3-4 months, were recruited for this randomised controlled intervention study. Only males were included for the following reasons. The ACL primary injury rate (per exposure) is 2-4 times higher for females than in males for matched sports and age groups, as shown by meta-analyses [4, 32]. The incidence rates calculated (in *tears-per-1000-exposures*) for females and males, respectively, for soccer were 0.32 and 0.12, and for basketball were 0.20 and 0.21. Despite their lower risk, males however typically undergo more ACL-R surgeries (e.g. in the Swedish registry [107]) due to their higher number of exposures. Some of the risk factors contributing to the difference between sexes that have been determined thus far are biomechanical in nature [125], suggesting that trials of biomechanics should be stratified by sex. While it is still not common, two recent studies that have done this post ACL-R, have confirmed biomechanical differences [37, 126]. No ethnicity or social demographics factors have been seen in the literature, and were not included as requirements. Genetic and anatomical risk factors were beyond the scope of this study, and were not assessed. The study was approved by the UCT Human Research Ethics Committee (HREC# 578-2014), and all participants gave written informed consent for the trial (Appendix A).

3.4.1.1 Injury status

All participants had sustained a unilateral primary ACL injury, without other ligament tears. Proportions of contact and non-contact injuries are shown in Table 3.1 below; sports at the time of injury included rugby, soccer, squash, grappling, and motocross, among others.

3.4.1.2 Surgical procedure

All participants had undergone unilateral single-bundle ACL-R surgery performed by one of two surgeons. Both surgeons use the same surgical technique, and all patients received *semitendinosis* or *semitendinosis*/*gracilis* hamstring grafts, except for 1 patient in the ECC group who received an allograft. The femoral tunnel position is deep in the footprint in the femoral notch, and the tibial tunnel position is in the anteriomedial part of the footprint. Grafts were secured with an Arthrex® (Naples, Florida) Tightrope® and Graftbolt®. For tightening, firm hand tension is used at approximately 20 degrees of knee flexion. BPTB grafts were excluded because both surgeons more commonly performed hamstring-graft ACL-Rs, and biomechanics have been shown to differ between hamstring- and patellar tendon grafts [127, 128, 129, 130]. Time between injury and surgery for the two groups is shown in Table 3.1. Revision surgeries were included, but only if they were using the same surgical technique, and excluding grafts taken from the contralateral limb.

3.4.1.3 Surgical history and screening

A lower limb surgical history and pre-injury Tegner activity scale [38] was recorded for each patient. Patients had not had other lower-limb surgeries except for partial meniscectomy or meniscus repair, and were free of symptoms in the uninvolved leg affecting activities of daily living (ADL). Additional exclusion criteria were:

- Moderate or Severe pain in the involved knee during ADL using the Visual Analogue Scale (VAS). VAS Categories: mild, < 30 mm, moderate, 31-69mm, severe, > 70 mm.
- A corticosteroid injection in either knee since the ACL-R surgery.
- Current (last 1 week) pain or anti-inflammatory medication use
- Deep vein thrombosis, rheumatoid arthritis, gout or other rheumatological pathology in either limb.
- Tegner activity level [38] < 4.
- Body Mass Index (BMI) > 30 kg$\cdot$m^2
- An answer of *Yes* for any question in the Physical Activity Readiness Questionnaire (PAR-Q) (Appendix J).

For screening, the phases of rehabilitation are only approximately time-based. An examination by the surgeon or a physiotherapist was used to confirm that the participant had reached the goals of Phase II, and was ready to proceed to Phase III of rehabilitation (approx. 10-16 weeks post surgery). They are [59]:

- No Swelling - mild swelling as assessed by the clinician was accepted
- Full active knee hyperextension, and flexion to $>110°$
- Full squat
- Good balance and control
- Unrestricted walking

3.4.1.4 Randomised group assignment and blinding

The 26 participants were randomly assigned to one of two groups, the eccentric cycling ergometry group (ECC) or concentric cycling ergometry group (CON), according to the order in which they gave written informed consent. The order of assignment was defined before the first recruitment in groups of 12 at a time to reduce differences between groups, by the sequence which concealed slips of paper were withdrawn from a bowl. While single blinding was not completely possible, patients were not told whether their programme was the intervention or active control, and the type of programme was not discussed with patients. Also, patients typically trained independently, so they could not easily compare their programme to that of others. Investigator blinding was not possible, due to resource constraints.

3.4.1.5 Rehabilitation before intervention

Rehabilitation before surgery was not recorded, but was not typical in these groups. Rehabilitation after surgery and before recruitment was not prescribed, and was according to the surgeon and/or physiotherapist's recommendations. Standard isometric and isotonic home exercise programmes were typically reported for an average of 5.8 weeks in these groups. In addition, in this stage some patients used Continuous Passive Mobilisation (ECC group: n = 4, CON group: n = 1) and early-stage eccentric training (ECC group: n = 4, CON group: n = 5). The goals for this rehabilitation was completion of Phase II, according to the screening criteria given above, which deemed them fit to proceed to phase III of rehabilitation.

3.4.2 Intervention

3.4.2.1 Grucox rehabilitation cycle and studio

The cycle ergometer used for the intervention was the Grucox Rehabilitation Cycle (Grucox Medical, Cape Town, South Africa), and all training was done in a training studio with 12 isokinetic cycles (Figure 3.1). The cycle is driven by a motor controlled by a small industrial automation system. Eccentric work is done by resisting the driven pedals, with the aim of stopping the pedals. For concentric work, the participant exerts a force in the direction of the driven pedals. The cycle also allows for continuous passive mobilisation (CPM), where the participant effortlessly allows the driven pedals to move their lower limbs, and this was used for warm-up and cool-down in the program. The pedalling speed (rpm) is set using a user-friendly touch screen, and it is governed and constant for the session. The screen dynamically displays real-time and trend levels of power output (Watt) for the AFF and UNAFF limbs, giving biofeedback to the participant.

During familiarisation, the patients were given technique instructions, commonly used at the studio, but no coaching was provided. They include:

- knees and feet pointing straight ahead
- smooth application of force
- keeping the lumbar spine straight and pelvis stable
- during standing, keeping a straight body posture, and minimising vertical movement of the trunk

3.4.2.2 Eccentric (ECC) and concentric (CON) interventions

Participants were required to attend three supervised cycle ergometry exercise sessions per week over a period of 8 weeks. Three times per week is a typical dose which allows

Figure 3.1: Eccentric cycle training studio. ©Grucox Medical

sufficient recovery between sessions, according to ACSM guidelines [131]. During each exercise session, participants performed a 26-minute exercise protocol (Appendix C) focusing on either eccentric or concentric work, depending on their intervention group. After a warm-up, all participants cycled for 10 minutes in each of the forward and reverse directions, followed by a warm-down in the form of CPM so as to reduce the risk of injury. ECC group participants were instructed to try and slow down the pedals in either the forward or reverse direction, while CON group participants pushed in the direction of pedal movement.

Participants were positioned on the ergometer (Figure 3.2), with the seat height adjusted allowing for approximately 10 degrees of knee flexion when the leg is fully extended, minimizing the possibility of injury to the knee by training at the limit of ROM. The intensity level of the exercise session was based on their Borg Rating of

Figure 3.2: Eccentric rehabilitation cycle. ©Grucox Medical

Perceived Exertion scale using the previous session as a reference (RPE, Appendix D).

The pedalling speeds are described in Section 3.4.2.4 below.

3.4.2.3 Monitoring

Each session was monitored by a trained physical therapist to ensure the patient's safety, and the following information was recorded in the testing sheet (Appendix E). Participants were required to complete a minimum of 80% of the exercise sessions to be included in the study.

Limb-specific power After each exercise session, average power (Watt) calculated by the ergometer for each limb was recorded from the values reported on the screen. If clear asymmetries were noted between limbs, the patient was made aware of this, and encouraged to focus on the less active limb.

Heart rate During each exercise session at 5 and 20 minutes from the start, heart rate (HR) was measured by counting beats for 15s, using the pulse on the wrist.

Perceived exertion and pain At the same time points (5 and 20min), RPE was recorded by asking the patient to subjectively score their training experience. A VAS scale was used to assess pain level, as well as description of the pain location and type if present. This was to determine if pain was contributing to alterations in biomechanics, as well as to give an indication of potentially unsafe situations for the patient. If moderate or severe pain was experienced during the 8 weeks, a single session was performed with a reduced torque (and associated RPE) level. The subsequent session was returned to the prescribed RPE level; if the moderate or severe pain returned, the participant was recommended to leave the trial, and the reason reported.

Other training During the intervention, participants were asked to report on any other physical activity/rehabilitation. This was categorised by type (*upper body*/core, *cardiovascular*, or *lower limb*), and intensity (*none*, *low*, *medium*, *high*). They were also asked about medication usage or feedback from therapists, as these may affect the results of the intervention.

Patient safety Patient safety and comfort took precedence over progression according to the programme given above. If an injury was sustained during the intervention, the physiotherapist or biokineticist attending performed a diagnostic evaluation to assess the injury. If the injury was due to training too hard, the intensity was reduced, and the RPE change noted. Rest was prescribed as appropriate to see if the injury resolved.

3.4.2.4 Progression

The first session was familiarization at an *extremely light* intensity (RPE = 7), which confirmed no exacerbation of pain or effusion from the ergometry. If these were not present, the participant progressed to a *hard* intensity (RPE = 15) over the 8 weeks according to prescribed intensities in Appendix D, and shown as the target reference line in Figure 3.4 below.

Speed was progressed according to norms of the training studio, starting from 25-35rpm, and progressing to approximately 55rpm over the 8-week period, as comfortable for the participant. Pedalling torque was then adjusted by the participant to achieve the target RPE value.

Participants were allowed to hold the handlebars during the training. Cleated shoes were available if preferred although they were seldom used. Participants were instructed not to use the cleated shoes for pulling training (hamstring-specific work). During weeks 7 and 8, participants were encouraged to alternate 30s standing intervals with 30s sitting as they could tolerate, and it was recorded if they did.

3.4.3 Baseline and follow-up testing

The following data were collected at baseline (BL) and follow-up (FU) testing time points. FU testing was performed 3 to 10 days after the last training session, to allow recovery [132].

3.4.3.1 Patient questionnaires

Participants completed the IKDC (Appendix G), KOOS (Appendix H), and the SF-36 (Appendix I) surveys at baseline and follow-up testing. The first two questionnaires are specific to knee health, and the third reflects the patient's mental and physical general health, used in assessing and comparing the self-reported health of the ECC group and CON group at BL and FU.

3.4.3.2 Lean thigh volume

In order to model the individuals' lean leg volume in both legs, the sub-gluteal, mid-thigh and above-knee circumferences of both legs were recorded, as well as the anterior mid-thigh skin-fold measurement, to calculate the lean thigh volume (LTV). The test was performed by the same investigator throughout the study. This technique for estimating LTV assumes the upper section of the lower limb has the shape of a truncated cone. The technique was adapted from the technique described by Katch and Katch [133] and has been validated against LTV assessed by magnetic resonance imaging [134]. Outcome variables were LTV of the AFF and UNAFF limbs at BL and FU.

3.4.3.3 Isokinetic strength assessment

Knee strength was measured for both limbs using a Biodex Isokinetic Dynamometer (Biodex Medical Systems Inc., Shirley, NY) at both 60°/s and 120°/s. Measurements were taken for concentric contractions of the quadriceps (extension) and hamstrings (flexion) muscle groups through full knee extension and flexion ROM. In addition, these tests were done for eccentric contractions through 85% extension and 90% flexion ROM to resist extension (hamstrings) and resist flexion (quadriceps). The eccentric test ROM was limited due to the reduced maximum torque capacity at the extremes. For all testing, dynamometer seat orientation was 90° with seat back reclined to 10°. Alignment of the lateral femoral condyle in the sagittal plane corresponded with the

axis of the rotation of the dynamometer. Participants were securely strapped to ensure other body segments were adequately stabilised so that they may not unintentionally skew the results.

At the start of the test session, several warm-up repetitions were given, before a maximal trial of seven reps was performed at 60°/sec, and seven at 120°/sec, with a rest of 30s between speeds. This were completed on both legs, with set up remaining the same. Standardisation was enhanced by performing a gravity correction (weighing the leg via gravity without an exertional force applied by the leg) and standardising arm positions during all testing. A comfort stop button was available to stop the test if patients felt uncomfortable.

A familiarisation trial took place within a week before the actual testing day to minimize the learning effect of equipment use. The participant was able to familiarize himself with the equipment, concentric and eccentric testing, as well as the speed used in the current protocol. The seat setup and range of motion for the participant was recorded so that setup and testing was smoothly executed on the day of testing.

3.4.3.4 Pain monitoring

For gait, functional, and strength tests, pain was recorded for the participants using a visual analogue scale (VAS) of between 0 and 100mm.

3.4.4 Data and statistical processing

Data reduction

KOOS, IKDC and SF-36 questionnaires were scored using standard templates, and sub-scores calculated for BL and change from BL to FU. Lean thigh volume estimates were calculated using the methods described above, and limb symmetry indexes (LSI)

were calculated by

$$LSI = \frac{V_{affected}}{V_{unaffected}} \times 100\%$$

where V represents the net volume of the thigh (excluding skin-fold layer) between above-knee and sub-gluteal circumference points.

Concentric and eccentric maximum torques for each of the four isokinetic test conditions were extracted, normalised by body weight. Torque LSI values (%) were calculated the same way as thigh volume LSI above.

Statistical processing

For KOOS, IKDC, SF-36, strength and LTV outcome measures, statistical processing was done in *R*, Version 3.2.0 [43]. BL means are given, and change between BL and FU calculated. Group-wise changes are given as median and 95% confidence intervals (95%CI). 95%CI's which are positive and don't cross zero are described as evidence of a change in the score. To compare changes between groups from BL to FU, these data are tested for statistical significance using the two-tailed Mann-Whitney-U test, with a threshold of $P < 0.05$.

3.5 Results

The flowchart of the trial, according to the consolidated standards of reporting trials (CONSORT) reporting guidelines [135] is given in Figure3.3. Twenty-two of the twenty-six patients randomised into ECC group or CON group were analysed. Patient and injury profile of the analysed patients in each of the two groups, is given in Table 3.1.

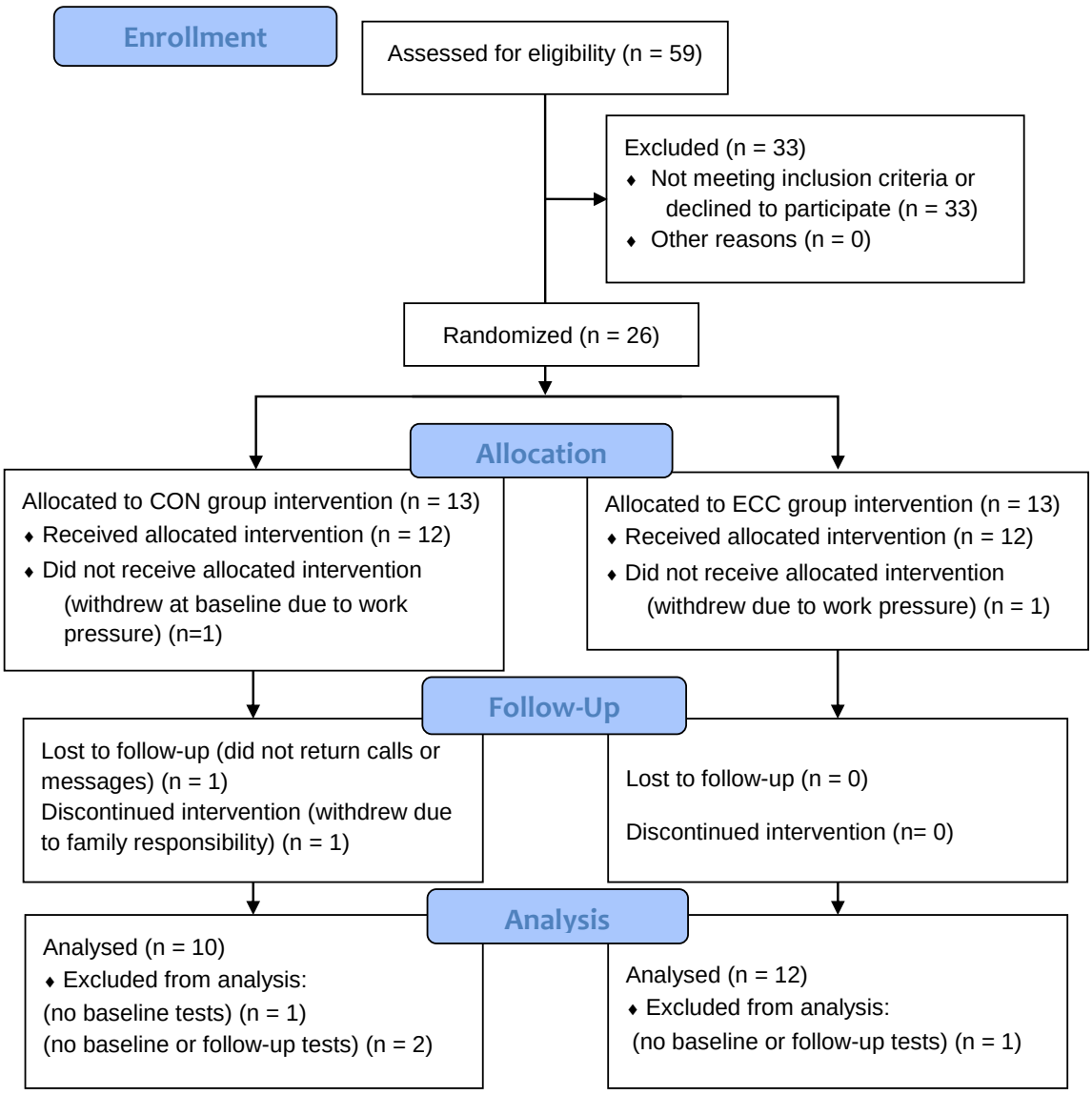

Figure 3.3: CONSORT flow chart of the study

3.5.1 Clinical observations

3.5.1.1 RPE and speed progression

Progression of weekly-averaged RPE between groups is given in Figure 3.4. The target RPE progression is also shown for reference. Speed progression was approximately linear, and similar between groups, from 25rpm in week 1, to 55rpm in week 8. On

Table 3.1: Patient characteristics by group (mean ±SD, unless noted)

	ECC (n = 12)	CON (n = 10)	*P*
Age at surgery	25.8 ±6.4 years	25.2 ±6.0 years	0.843
Height at BL	1752 ±62.5mm	1792 ±60.6mm	0.234
Weight at BL	74.7 ±13.2kg	79.4 ±9.2kg	0.254
Pre-injury Tegner score	6.4 ±1.7	6.6 ±2.1	0.893
% Non-contact ACL injury	33% of patients	80% of patients	N/A
Median injury-surgery months (range)	3.0 mo. (0.3-12)	2.0 mo. (0-120)	0.666
Dominant limb affected	50%	90%	N/A
% Partial meniscectomy	8%	50%	N/A
% Meniscus repair	33%	10%	N/A

average, the ECC group started at a slightly higher speed, but this difference (approx. 3rpm) disappeared by week 3.

3.5.1.2 Training limb session power

Session average power reported for each week in the AFF limb and UNAFF limb for the ECC group and CON group, is reported in Figure 3.5. Output power was normalised by body weight (BW) in kg.

3.5.1.3 Recorded pain and measured heart rate

Numbers of reports of pain, grouped by severity, are reported by group in Table 3.2. No reports of *Moderate* or *Severe* category pain was reported in either group. No trend was observed over the training period, and the difference between incidence of pain between groups was small. Measured HR, averaged for each week, is also given in Table 3.2 below.

3.5.1.4 Adverse events/training interruptions

For all patients, adverse events and interruptions were as follows:

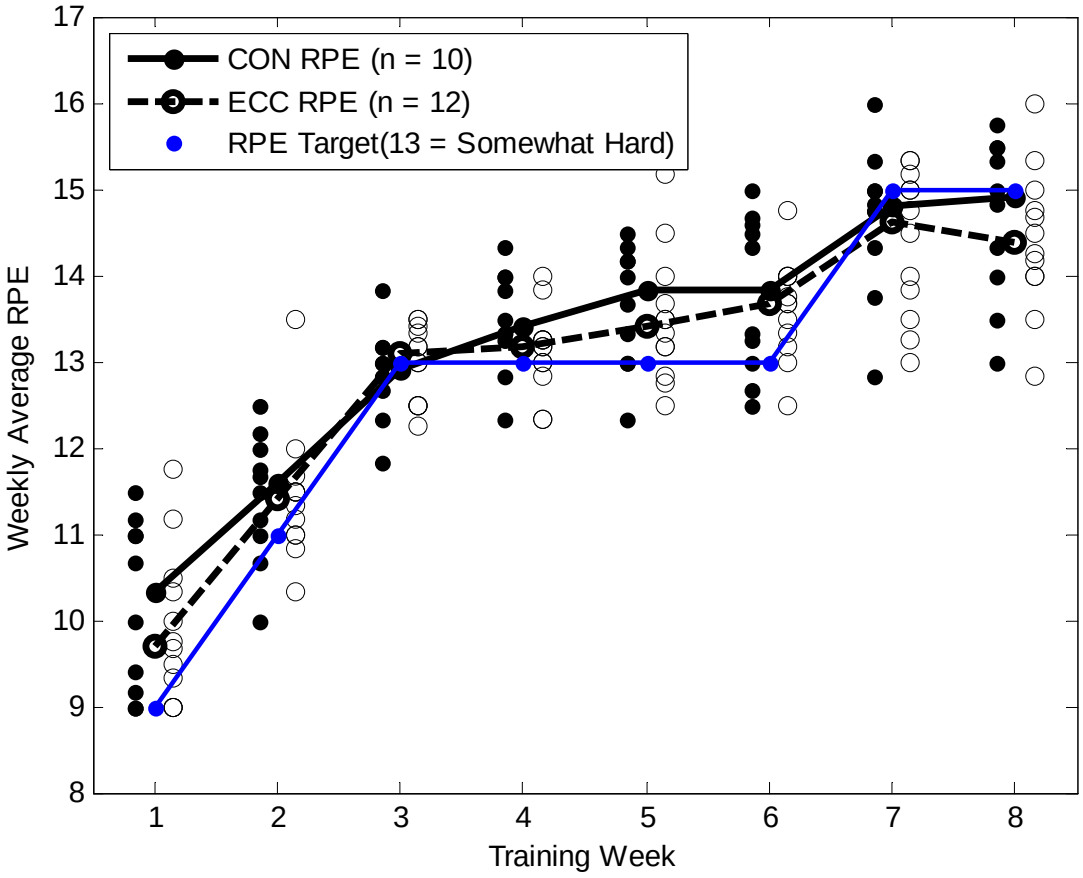

Figure 3.4: Weekly ECC group and CON group RPE progression w.r.t. RPE target. Circles represent ECC group patient values, dots represent CON group patient values.

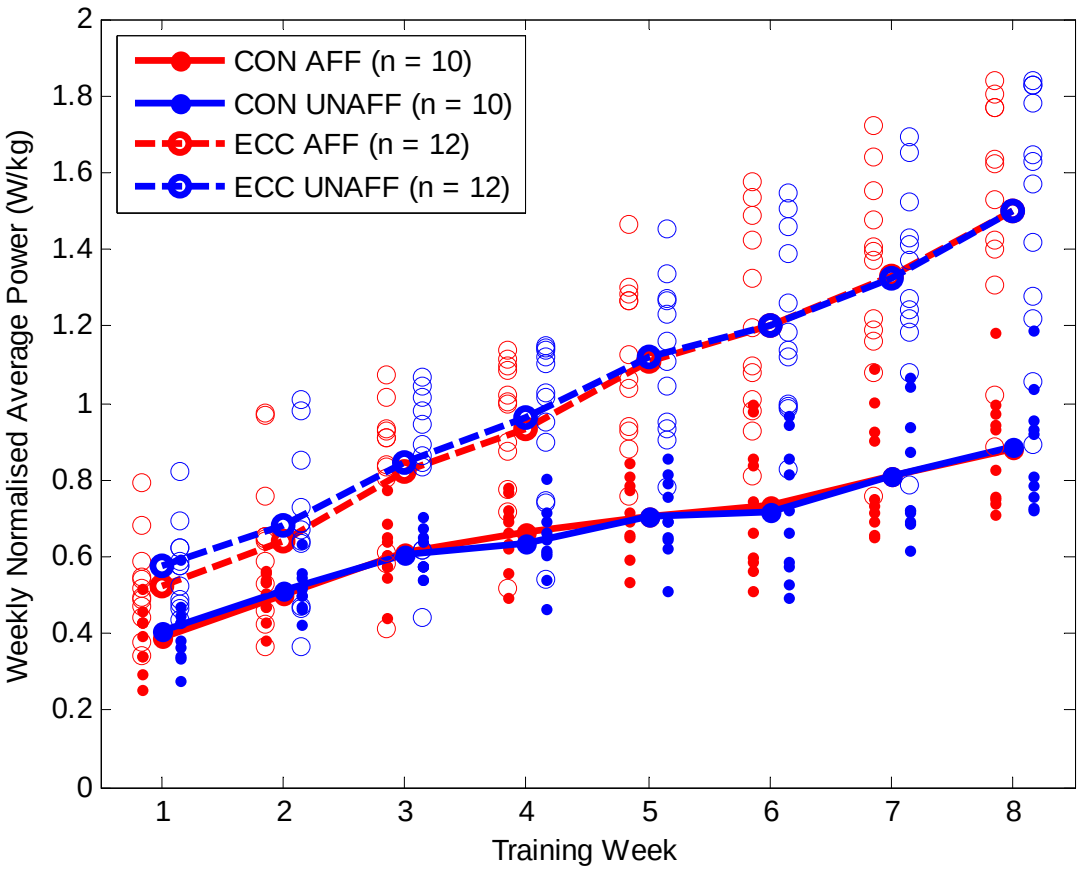

Figure 3.5: Weekly power progression for ECC group and CON group, by AFF or UNAFF limb. Circles represent ECC group patient values, dots represent CON group patient values. Red - AFF limbs, blue - UNAFF limbs.

- one patient in the CON group experienced foot pain in week 7. He was referred to a physiotherapist for treatment, and was given rest and rehabilitation exercises for three weeks, after which he returned to the program, with no further adverse effects.

- one patient in the ECC group experienced effusion at week 7. He was referred to a physiotherapist, who treated him with rest for two weeks, after which he returned to the program with no further adverse effects.

- three patients in the ECC group took a 1-week break for work reasons, after which they returned to the program.

Table 3.2: Weekly measured HR in bpm±SD, and pain reported during training

			Training Week								total
			1	2	3	4	5	6	7	8	
	Heart Rate (bpm)	ECC	90.2 ±15.5	92.5 ±14.7	95.1 ±17.4	96.0 ±16.1	101.3 ±13.8	103.4 ±17.8	109.0 ±13.4	112.5 ±15.4	100.0 ±15.5
		CON	104.2 ±17.6	115.3 ±14.6	122.8 ±14.7	125.9 ±19.0	129.1 ±17.9	128.5 ±17.8	137.3 ±13.8	138.8 ±17.6	125.2 ±16.6
Pain category[a]	None	ECC	9	10	12	11	10	11	10	8	84%
		CON	8	7	8	7	6	9	10	9	80%
	Mild	ECC	3	2	0	1	2	1	2	3	16%
		CON	2	3	2	3	4	1	0	1	20%
	Mod.	ECC	0	0	0	0	0	0	0	0	0%
		CON	0	0	0	0	0	0	0	0	0%
	Severe	ECC	0	0	0	0	0	0	0	0	0%
		CON	0	0	0	0	0	0	0	0	0%

[a] None: 0-9mm, mild: 10-39mm, moderate: 40-69mm, severe: 70-100mm

- two patients (one ECC group, one CON group) took a 2-week break for work/ personal reasons during the program.

3.5.1.5 Other activity, medication use

Physical activity outside the intervention was not controlled, although most patients considered the programme to be their primary lower-limb strengthening. From the patients' self-report of their other physical activity, overall dose of other activity in the categories of *a) cardiovascular*, *b) upper body/core*, or *c) home programme (lower limb)* was rated as *none*, *light*, *moderate*, or *heavy*, and scored from 0, 1, 2 or 3, respectively. The three activity scores were added, and total score > 1 was categorised as having done other physical activity. Using this, 8/12 ECC group patients, and 8/10 CON group patients performed other training. *Moderate* or *heavy* lower limb activity was performed by 2/12 ECC group and 1/10 CON patients (Table 3.3). This higher proportion of control participants that performed other activity could be seen to have biased the

trial in favour of controls. Medication use was tracked for the patients, and none used anti-inflammatory or cortico-steroidal drugs during training.

Table 3.3: Other training performed by patients

		ECC (n = 12)	CON (n = 10)
All other training (inc. lower limb)		8	8
Lower limb training	*light*	1	4
	moderate	1	2
	heavy	0	0

3.5.2 Patient reported outcomes

Patient reported outcomes are given in Table 3.4. For example, at BL, the IKDC score was 72.7 (95%CI: 64.4, 78.3) and 66.1 (95%CI: 59.2, 73.2) for the ECC group and CON group, respectively. Change in IKDC from BL to FU was +7.6 (95%CI: -2.3, 17.2) and +10.3 (95%CI: -3.5, 21.9) for the ECC group and CON group, respectively ($P = 0.821$). IKDC Score and male age-matched percentiles are first given; evidence for a change was only seen for the percentile, by +5% in both groups. No changes, and no differences between groups were seen for KOOS Pain, Symptoms, ADL, Sport/Recreation, and QOL sub-scores ($P > 0.05$). In addition, no changes, and no differences between groups were seen for both SF-36 mental (MCS) and physical (PCS) summary scores ($P > 0.05$).

3.5.3 Clinical, muscle volume, and strength tests

3.5.3.1 Body mass and skin-fold thickness

Changes in body weight from training are given in Table 3.5. The CON group average change in body weight was -1.1% (95%CI: -3.5 0.5), and the ECC group average change in weight was +0.8% (95%CI: -1.3 2.7), but evidence for difference between groups

Table 3.4: Patient Reported Outcomes for ECC group and CON group.

		Values at BL			change BL to FU		
		ECC	CON	P^a	ECC	CON	P^b
IKDC	Score	72.7 (64.4 78.3)	66.1 (59.2 73.2)	0.635	+7.6 (-2.3 17.2)	+10.3 (-3.5 21.9)	0.821
	Percentile	15 (10 20)	15 (10 20)	-	**+5 (0 20)**[*]	**+5 (0 20)**[*]	-
KOOS	Pain	88.9 (81.9 94.4)	84.7 (77.8 91.7)	0.465	+2.8 (-5.6 11.1)	+5.6 (-2.8 13.9)	0.466
	Symptoms	78.6 (71.4 89.3)	80.4 (71.4 92.9)	0.790	+3.6 (-7.1 17.9)	+0.0 (-10.7 14.3)	0.529
	ADL	96.8 (92.6 99.3)	94.1 (89.7 97.1)	0.286	0.0 (-2.9 2.9)	+1.5 (-1.5 5.9)	0.205
	Sport/Rec.	70.0 (60.0 80.0)	63.8 (50.0 75.0)	0.404	+5.0 (-5.0 20.0)	+10.0 (-5.0 25.0)	0.572
	QOL	50.0 (37.5 62.5)	43.8 (31.2 56.3)	0.527	+6.25 (-12.5 25.0)	+12.5 (-6.25 25.0)	0.738
SF-36	PCS	52.9 (49.2 54.6)	48.3 (40.5 52.9)	0.123	+2.0 (-1.3 5.5)	+2.8 (-2.8 8.5)	0.644
	MCS	51.5 (43.0 57.0)	53.6 (49.2 57.9)	0.575	+0.7 (-5.1 7.5)	-0.2 (-5.1 5.9)	0.974

[*] Bold, starred values represent evidence for a change BL to FU.
[a] Difference between ECC group and CON group at baseline.
[b] Difference between ECC group and CON group changes from BL to FU.

Table 3.5: Lean thigh volume, skin-fold thickness, and BW % change BL to FU.

		% Change BL to FU		
		ECC	CON	P^a
Lean thigh volume	AFF	+2.8% (-2.3 7.8)	+3.1% (-3.2 10.2)	0.722
	UNAFF	+2.0% (-2.3 11.0)	−2.0% (-6.7 3.8)	0.418
	LSI	+0.9% (-3.8 4.0)	**+4.4% (0.9 7.9)**[*]	0.180
Skin-fold thickness	AFF	+2.7% (-10.0 13.9)	**−12.5% (-25.5 -0.2)**[*]	0.092
	UNAFF	+0.5% (-9.8 10.7)	**−10.8% (-20.3 -2.4)**[*]	0.123
Body mass	-	+0.8% (-1.3 2.7)	−1.1% (-3.5 0.5)	0.140

[*] Bold, starred values are evidence for a change BL to FU.
[a] Test of difference between changes in ECC group and CON group

was not found ($P = 0.140$). In the CON group, skin-fold thickness decreased in AFF limb by -12.5% (95%CI: -25.5 -0.2) and in UNAFF limb by -10.8% (95%CI: -20.3 -2.4), while in the ECC group, no changes in skin-fold thicknesses were seen. No evidence was found of differences between the groups for either limb (AFF: $P = 0.092$, UNAFF: $P = 0.123$).

3.5.3.2 Lean thigh volume

No evidence was found for changes in lean thigh volume for AFF or UNAFF limb for the ECC group and CON group, or for differences between them (AFF: $P = 0.722$, UNAFF: $P = 0.418$). Lean thigh volume LSI, however, in the CON group increased, by +4.4% (95%CI: 0.9 7.9), while no evidence was found for change in the ECC group, or for differences between groups ($P = 0.180$).

3.5.3.3 Strength

Maximum isokinetic torque results for the AFF limb are provided in Table 3.6, and LSI in Table 3.7. Both of these are for the four test types, namely the concentric strength test and the eccentric strength test, each at 60°/s and 120°/s isokinetic speed. For every test, flexion and extension results are organised by agonist muscle group,

i.e. quadriceps and hamstrings. Hamstring-quadriceps (H/Q) ratios are presented in Chapter 5. Group-wise ECC group and CON group strength results at BL are first given, followed by change between BL and FU for each group. Median and 95% confidence intervals (95%CI) are given for all values.

For example, during the concentric test, maximum extension (quadriceps) torque at 60°/s speed for the ECC group was 144.8N.m/kg (95%CI: 118.3, 174.8), and for the CON group was 166.0N.m/kg (95%CI: 131.0, 196.1). From BL to FU, change in the ECC group was +27.5% (95%CI: 18.2, 37.4), while in the CON group it was +28.3% (95%CI: 13.4, 40.9). Comparing the changes in ECC group to CON group gave a *P*-value of 0.456, accepting the null hypothesis that there was no evidence of difference between groups for this test.

3.5.3.4 Functional tests

Functional testing, including the single-leg and triple crossover hops for distance, Y-balance test, drop vertical jump, and single-leg squats-to-fatigue were performed, at BL and FU. These results are reported separately in Chapter 5.

3.6 Discussion

A common clinical reason for the use of eccentric over concentric training is for enhanced mechanical stimulus to the joint tissues, muscles and mechanoreceptors, for the same level of perceived exertion. From the results presented above, for the same level of perceived exertion, the ECC group in this trial did cycle with higher training forces, as can be seen from comparing average powers absorbed to those generated by the CON group. Also, both groups had very similar AFF limb compared to UNAFF limb average session powers throughout the programme, which means that patients were successfully able to produce symmetrical power output. In terms of recalibrating force

Table 3.6: AFF limb strength measures at BL, and group-wise changes BL to FU.

			Values at BL (N.m/kg)		% Change BL to FU		
			ECC	CON	ECC	CON	P^a
Concentric Maximum Isokinetic Torque	Quadriceps	60°/s	144.8 (118.3 174.8)	166.0 (131.0 196.1)	**+27.5%* (18.2 37.4)**	**+28.3%* (13.4 40.9)**	0.974
		120°/s	129.3 (114.4 162.2)	154.4 (114.7 178.7)	**+17.4%* (6.5 32.1)**	**+24.5%* (10.6 43.8)**	0.582
	Hamstrings	60°/s	90.2 (75.7 112.6)	105.9 (86.9 130.7)	**+15.4%* (6.8 34.1)**	+7.6% (-9.3 17.1)	0.180
		120°/s	83.7 (71.5 98.3)	90.0 (73.1 103.0)	**+7.6%* (1.7 32.6)**	+13.3% (-3.2 22.7)	0.628
Eccentric Maximum Isokinetic Torque	Quadriceps	60°/s	188.9 (152.6 213.7)	195.4 (155.9 220.3)	**+24.0%* (9.3 41.0)**	**+20.5%* (13.0 26.4)**	0.923
		120°/s	203.9 (166.3 232.2)	206.0 (155.0 243.5)	**+17.5%* (8.7 31.1)**	**+25.0%* (10.5 39.5)**	0.582
	Hamstrings	60°/s	131.6 (111.6 152.9)	141.2 (112.4 155.7)	+14.9% (-5.2 29.7)	**+15.5%* (4.1 25.6)**	0.974
		120°/s	138.4 (118.6 162.8)	148.7 (118.4 169.7)	**+14.1%* (1.9 25.2)**	**+11.4%* (3.3 20.5)**	0.497

* Bold, starred values represent evidence for a change BL to FU.

[a] Test of difference between ECC group and CON group changes BL to FU.

Table 3.7: Isokinetic strength limb symmetry (% deficit).

			AFF limb % deficit at BL		Change in % deficit BL to FU		
			ECC	CON	ECC	CON	P^a
Concentric Strength Symmetry	Quadriceps	60°/s	-41.4% (-28.9 -50.8)	-32.7% (-20.5 -47.6)	**+12.3%*** **(4.3 20.1)**	**+17.2%*** **(6.6 28.9)**	0.418
		120°/s	-37.8% (-18.3 -46.2)	-23.6% (-10.2 -44.9)	**+10.3%*** **(0.8 19.4)**	**+16.2%*** **(5.2 24.1)**	0.539
	Hamstrings	60°/s	-24.5% (-14.1 -39.1)	-24.6% (-6.7 -32.9)	+7.8% (-3.3 18.5)	+4.3% (-7.9 16.9)	0.628
		120°/s	-26.3% (-14.4 -36.8)	-24.6% (-16.0 -32.4)	+5.0% (-4.7 18.4)	+10.4% (-5.3 18.2)	0.456
Eccentric Strength Symmetry	Quadriceps	60°/s	-25.5% (-11.5 -40.1)	-18.1% (-6.5 -38.9)	+3.6% (-7.5 18.7)	+5.9% (-3.1 20.3)	0.497
		120°/s	-33.1% (-14.1 -45.0)	-22.4% (-9.9 -41.2)	**+8.0%*** **(-0.7 16.9)**	**+12.4%*** **(2.7 32.3)**	0.497
	Hamstrings	60°/s	-17.8% (-8.4 -27.9)	-15.9% (-2.0 -28.1)	+5.6% (-10.7 18.4)	+7.8% (-2.0 15.7)	0.674
		120°/s	-18.8% (-7.9 -29.8)	-17.3% (-6.1 -28.4)	+3.8% (-6.4 12.9)	+3.7% (-2.3 17.5)	0.821

* Bold values represent evidence for a change BL to FU.

[a] Test of difference between ECC group and CON group changes BL to FU.

signals experienced through the body, equal forces may have a positive effect on symmetry throughout. These patients probably achieved this symmetry with conscious effort to focus on AFF limb, as that limb would be functioning at a higher relative fraction of maximum voluntary contraction than the UNAFF limb. This is informed by the per-stroke and trend feedback on the screen, as well as the session averages from the previous session.

In addition, the ECC group had a lower HR than the CON group for the same RPE, and speed progression. This is in line with reports from other studies. The speeds that were used were well-tolerated by patients; while they are lower than typical cadences used in cycling, this achieves a higher limb load for the same power output.

Regarding the strength results obtained, quadriceps strength for both ECC group and CON group during concentric testing increased. Statistical testing did not show evidence for differences between the groups. For the hamstring muscle group, evidence of increased strength was only seen for the ECC group only, in both 60°/s and 120°/s speeds.

This lack of difference between the groups in quadriceps strength increase does not support the stated hypothesis that the ECC group would increase quadriceps strength more than the CON group. During eccentric quadriceps training, any activity in the antagonist hamstring groups is concentric in nature. Also, as discussed, the joint forces are about 80% higher for the eccentric training. Thus, it is likely that hamstring activity would likely be higher, to stabilise the joint. Thus, the observed increase in concentric hamstring strength in the ECC group would follow from this increased concentric activity.

During eccentric testing, quadriceps and hamstring torque increases across speeds and ECC group and CON group, with no evidence for difference between groups. By inspection, the means and 95%CI were similar. From the above concentric and eccentric torques for the ECC group and CON group, there were no apparent mode-specific

strength changes, i.e. the CON group did not do better on the concentric test, neither did the ECC group do better than on the eccentric strength test.

Looking at strength symmetry between AFF and UNAFF limbs (using LSI), quadriceps concentric strength symmetry improved in both groups, with no difference between groups ($P > 0.05$). In the eccentric test, symmetry only improved at the higher test speed (120°/s), but not at the lower speed. For the hamstrings, symmetry did not change for either the ECC or CON group, in either concentric or eccentric test. Coupled with the finding that concentric hamstring strength increased in the ECC group, implies a parallel increase in UNAFF limb hamstring strength, to maintain the same asymmetry. However, the UNAFF limb was not analysed separately in this study.

Interestingly, PROs did not improve from BL to FU for either the ECC group or CON group, in any of the questionnaires and sub-scores, except for the IKDC percentiles. This is an unexpected result, as it is commonly assumed that patient-reported function would improve over 8-weeks of training. This time period is a typical minimum to see functional gains, and it may be that at follow-up directly after the programme, patients have not fully become aware of the benefit in their everyday lives, i.e. their recall of the last few weeks as required, also includes a time period of lower function.

The progression of the intervention was well-tolerated and acceptable. This can be seen from the actual RPE as compared to the target RPE (Fig. 3.4). In the early and middle stages of the programme, both ECC and CON group patients tended to train harder than the target RPE. This, as well as the observations of safety discussed below suggest that the target RPE in the first part of the programme could be raised. A limitation of this trial was that because of the demonstrated differences in heart rate and limb loads between groups, the perception of exertion was sometimes variable, as it is a subjective, global measure. However, the use of RPE is clinically motivated, as patient compliance to a programme is likely to be linked to the patient's perception of how intense/difficult it is.

Both isokinetic eccentric and concentric intervention programmes were low-risk, and acceptable for patients. There were few numbers of patients that dropped out or were lost to follow-up in either of the groups. Regarding pain, there were very few reports of delayed onset muscle soreness (DOMS) or pain during training. Also, numbers of adverse events were low.

Regarding design of the trial, despite promising results other in other studies available, only one of them used a matched RPE. In this trial, this was also used. The use of concentric cycling as an active control was convenient, safe, and well-tolerated by patients, and allowed an exertion- and environment-matched trial. Blinding/placebo in rehabilitation trials is difficult, but this approach is a close approximation to a single-blinded design.

This chapter discusses clinical results for young, moderately active males after ACL-R. This is a valid population, as more ACL-R surgeries are performed on males, despite their much lower incidence rate than females. Older patients were excluded, due to their much lower number of these surgeries. Moderately active patients tend not to have the resources of intensive physiotherapy available to elite athletes, but the importance of return-to-sports for these patients is still high. In addition, for amateur athletes, work and other daily pressures mean that time available is limited, and rehabilitation may be adversely impacted. Thus, a time-effective rehabilitation programme is of high value to this population.

While patient weight gain or loss was not a stated outcome of this trial, body weight was reported as part of patient characteristics, and thigh skin-fold thickness measured for calculation of LTV. The difference in metabolic load between eccentric and concentric training has been well documented for almost a century (see review in [136], for e.g.). Thus, it would make sense that those patients training eccentrically would have a lower metabolic (and energy) use on average than those training concentrically. This may be confounded by gains in muscle mass. The changes in average body weight

of the groups, though small, are in line with this rationale. From skin-fold thickness, a measure of thigh adipose layer, evidence of a reduction in thickness in the concentric group is also in line with this. A study with weight changes as its primary goal would be a valuable contribution to the clinical application of eccentric exercise; a search of the literature found no trials in any population group that investigated this theme.

Limitations to this trial are that it is a clinical study with a wide range of outcomes, meaning that it could be seen as a clinical pilot study. Thus, the statistical threshold of $P < 0.05$ of an individual outcome needs to be interpreted with this in mind. The benefit, however, from this wider range of outcomes, is a better ability to narrow down possible underlying causes of the differences observed. Another limitation is that no control group was recruited without ACL-R, which would help to explain changes in terms of the injury. However, the use of the contralateral limb as a control is a common practice, even though it is not able to detect central/spinal neural effects.

An additional limitation to this trial is that no long-term FU, or mid-intervention tests were used, primarily due to cost of testing. This means that washout effects, or compound benefits triggered by the intervention, are not detectable. Thus the results presented can be seen to be only the primary effect of the intervention, and not secondary, long-term effects.

3.7 Conclusion

This randomised controlled trial of an eccentric intervention for male ACL-R patients sought to quantify clinical effects as compared to concentric controls. This is one of the first studies to use this matched design in a population of ACL-R patients, and the first during this phase of rehabilitation. The eccentric programme was well-received by patients, with notable increases in quadriceps strength, and some increase in hamstring strength.

In the AFF limb, the 8-week programme resulted in similar quadriceps strength increases for both ECC group and CON group. Hamstring strength increased in the ECC group, but not in the CON group. Concentric or eccentric mode-specific strength improvements were not observed from concentric or eccentric training.

In conclusion, the eccentric training programme can be recommended for rehabilitation of ACL-R male patients, as evaluated by typical clinical outcome measures. Indications are that the programme is low-risk and effective, and that RPE target intensity can be raised in the first part of the programme. Biomechanical and functional return-to-sports outcome measures which were collected in parallel, are presented in Chapters 4 and 5.

Chapter 4

Biomechanical effects of eccentric cycling in ACL-R rehabilitation

4.1 Introduction

Biomechanical deviations are between-limb or between-group differences in kinematics and kinetics during standardised tasks, commonly investigated during activities such as walking or running gait. While some of these may be due to natural variation between people (or limb dominance), certain patterns can be identified as being correlated to the effects of injury or disease. These deviations can thus be used clinically as markers of altered neuromuscular function and/or joint loading. In anterior cruciate ligament reconstruction (ACL-R), short-term changes in biomechanics may indicate risk of re-injury, and long-term chronic changes in repetitive activity may play a key part in the development of osteoarthritis (OA).

Biomechanical deviations are common after ACL-R, and the degree to which an intervention is able to rehabilitate them can be quantified using standardised testing. In the randomised controlled trial (RCT) covered in this chapter, it is argued that eccentric training is low-risk, and is more effective than (or at least as good as) concentric

training in doing this. Walk and run gait testing are used to quantify the changes in biomechanical deviations, compared to active ACL-R controls performing concentric training in a carefully matched design. This study is new in the field - no other studies were found on the biomechanical effects of eccentric cycling, and few studies have investigated biomechanical effects of any type of eccentric training.

In this chapter, kinematics, kinetics, and impact outcomes are presented. The question of risks associated with return-to-sports is addressed in Chapter 5.

4.2 Literature review

After ACL-R, biomechanical deviations have been widely reported. In a review of the literature, Pappas *et al.* [70] discusses the large increase in number of biomechanical studies over the past 20 years, and the level-III evidence base which has been formed. A similar level of evidence was found by Gokeler *et al.* [23] in a systematic review of 22 studies, which demonstrated quality of level IIIa grade. In both of these reviews, deviations were found in sagittal, frontal and transverse planes, some of which normalise over time, and some of which remain in the long-term.

While these deviations are associated with muscular strength deficits after surgery, recovery of strength is not enough to eliminate them. This indicates that lingering neuromuscular control deviations may be contributing to residual risk in this population. Thus, reduction of these biomechanical deviations as a specific goal could help to reduce OA or re-injury risk. This has not yet been shown prospectively, but a systematic review by Padua and Distefano [25] of pre-injury interventions to modify sagittal plane biomechanics as a preventative measure found that these were correlated with reduced first-time ACL injury risk. This indicates possible usefulness in rehabilitation as well.

This literature review focuses on gait testing to assess the impact of the eccentric intervention on biomechanical deviations during repetitive, everyday tasks of walking

and running. While some of these deviations may indicate risk of re-injury, this chapter more specifically focuses on the risk of chronic conditions such as OA. ACL-R has been seen to age a knee significantly [28], and improved understanding of biomechanical deviations is key to addressing this risk.

4.2.1 Gait kinematics and kinetics

Gait conditions for this study were walking and running at self-selected speeds, similar to those used in Chapter 2, allowing for a comparison between studies. Walking and running are long-term, repetitive motions, and thus are more likely linked to chronic disease such as OA. For re-injury risk and return-to-sports assessment, the same participants were also tested during drop vertical jump (DVJ) and other functional tasks; those results are presented in Chapter 5.

4.2.1.1 Sagittal plane joint angles and moments

Sagittal plane knee and hip angles and moments are the most commonly reported biomechanical gait variables after ACL-R. Generally, biomechanical strategies are used by ACL-R patients to alter these variables, initially because of pain, effusion, or apprehension after the surgery, or patterns developed while ACL-deficient (ACL-D). Over time, the reduction of muscle forces in the quadriceps results in atrophy and weakness of the muscles due to disuse, which tends to result in an ingrained pattern of long-term reduction in knee moments and angles. As markers of this effect, they have been shown to indicate ACL-injury risk. For example, in 2010, Paterno *et al.* showed that sagittal plane moments predicted ACL re-injury risk [137].

To address this, rehabilitation protocols are required which target this systemic biomechanical effect; in this study, eccentric training is trialled as it combines strength training with cyclical, whole-body, weight-bearing activity. In numerous studies, much work has been done to increase strength of the quadriceps in ACL-R patients. How-

ever, while strength symmetry may be achieved through these methods, this may be addressing only one part of the picture; persistent gait deviations may lead to the strength asymmetry redeveloping over time due to differences in muscle use. This effect seems to be a gap in the literature.

As markers of rehabilitation progress, sagittal plane knee and hip angles and moments have been widely reported. Very recently, Kaur *et al.* [138] performed a thorough meta-analysis on 27 studies for knee angles and moments, ordering results by time after surgery. For peak knee flexion angle in walking, there were clear deviations from the contralateral limb, reducing to approximately zero by about ten months after surgery. Interestingly, no overall differences from control participants were found during walking ($P = 0.26$), but were found for running in two studies ($P = 0.05$). In stair ascent and descent, no differences were found from control limbs or participants, although there were few studies found. Regarding knee flexion moments, during walking, stair ascent and descent, strong evidence was found for deviation from the contralateral limb and healthy controls, although there didn't seem to be an effect based on time after surgery. In running, limited evidence was found, but only compared to a control group.

In 2010, another systematic review by Hart *et al.* [139] found large effect sizes in sagittal plane moments during walking, running, stair ascent and descent compared to control limbs and groups. Knee angles were not reviewed in this study. This review was six years before the meta-analysis discussed above, and the difference in the number of articles is clear, indicating that there is a trend toward more studies in this area. At that point there was also some controversy regarding the presence or absence of *quadriceps avoidance* gait (discussed further below), but recent additional studies seem to have shifted away from this concept toward quantifying the moment directly.

This was followed by a further recent systematic review by similar authors in 2015 [140]. The review divides studies by time after surgery, and shows that <6 months after surgery, affected limb knee angles and moments were actually *greater*

than healthy controls. Following the early period (>6 months), individuals walk with *equal or lower* knee flexion angles and moments compared to healthy controls and contralateral knees. This latter finding is consistent with previous systematic reviews [139, 141] that reported lower peak knee flexion angles and moments in individuals after ACL-R compared with healthy controls.

Comparing the effect sizes in the above two systematic reviews [138, 140], it seems that deviations in moments are greater than deviations in angles, and those in running more than walking. This aligns well with the findings of Chapter 2. While moments are much more difficult to observe clinically, requiring 3-D motion analysis, they may be more sensitive and specific than more commonly measured angles. Also, this motivates collection of running data from patients wherever possible.

Regarding sagittal plane deviations by graft type, there is limited data in the literature. Webster *et al.* [127] showed that BPTB-graft ACL-Rs had lower knee flexion angle and moment (horizontal and vertical hop) compared to contralateral limbs, or hamstring grafts. In a subsequent study, they showed that in gait, knee flexion moment at mid-stance was lower for BPTB than hamstring grafts, while the opposite was found at terminal stance [130].

Generally, the above deviations have been measured in cross section, but some studies have followed them in time. Di Stasi *et al.* [37] measured flexion-extension moments and angles in sex-specific ACL-R groups, before and after a preoperative strengthening and neuromuscular programme. The patients were followed up 6-months after the operation. Kinetic and kinematic knee and hip asymmetries remained in both men and women; in women, the benefits of the training were reversed, i.e. deviations *increased* at 6-months compared to post-operative testing. This may be because the surgery came *after* the training, and emphasizes the need for optimisating the timing of training. In another study, deviations were tracked from 10 months to 3 years after surgery (no intervention) [142]. In the sagittal plane, knee angles and moments remained

relatively unchanged, except for a reduction in knee flexion at terminal stance, for which the clinical relevance is unclear.

This deviation at terminal stance highlights the need to carefully select how knee flexion angle is described. Most commonly, maximum values near mid-stance are reported. Values at initial or terminal stance are much less common; an alternative is the use of the flexion/extension difference (FED) which did show correlation to isokinetic strength in one study[10], but this has not always been shown to be useful [121].

Based on the above literature, use of flexion angles and moments hold promise in tracking patient progress and the effectiveness of interventions. An example of this compared expert clinician evaluation with automatic estimation of progress towards return-to-sports (RTS) using an instrumented knee brace [143, 144], showing good correlation between the two methods. Braces have also been used therapeutically to target the knee angle directly, by the use of extension-limiting braces [77], with some success. However, this focus on knee angle and moment may be overly simplistic, as deviations at the knee can be caused by a range of biomechanical strategies, at the hip, trunk, knee and foot. This interaction of effects at different joints seems to be a gap in the literature describing the strategy used by the ACL-R patient to reduce sagittal knee moments and/or angles. This study attempts to address this somewhat, by collecting and analysing a wide range of variables, but further work is needed in this area.

4.2.1.2 Quadriceps avoidance

One of the early concepts regarding gait modifications from ACL injury was *quadriceps avoidance,* a term introduced by Berchuck *et al.* in 1990 [145]. It was defined as a complete lack of external extension moment during mid-stance, removing the anterior component of the quadriceps tendon force, which has been shown to be greatest for

angles near full extension. According to this definition, in their study of patients after ACL injury, 75% showed quadriceps avoidance. Subsequent studies have varied in their findings, one finding it after ACL-R [146] and meniscectomy [147], one not finding it in ACL-R patients [148], and one not finding it in ACL-R at 3 months [149]. In all the above, it was only studied during walking, most likely because the knee extension moments and angles are much greater during jogging or stair ascent/descent, and complete avoidance of knee extension moment would be highly unlikely.

Despite its simplicity and indication of a clear change in gait, quadriceps avoidance hasn't been found consistently, causing perhaps unnecessary controversy. Also, there is still a lack of clear clinical utility of the concept, and the term may be misleading because it doesn't distinguish between a lack of moment due to co-contraction, and true avoidance of the quadriceps muscle group (discussed further in [149]). Thus it is recommended that during walking the values of maximum and minimum knee extension moment be reported instead; this gives more detailed information, and allows more consistent comparison across studies. In this study, it is reported for reference only.

4.2.1.3 Knee and hip ab/adduction angles and moments

Excessive knee valgus angle is a well-recognised marker of ACL risk, and has been used in clinical practice, during both static and dynamic evaluations (see e.g. [59]). It is typically evaluated either during single support tasks such as running, cutting, hopping or single leg squatting, or during double support high load tasks such as the DVJ. This has been particularly the case for risk assessment of female patients using 2D video. However, during 3D gait analysis, it has been reported less often, with the meta-analysis of Kaur *et al.* only finding 3 studies that reported it, with moderate evidence of no significant difference from controls [138]. This is surprising, as knee medio-lateral control is commonly observed and targeted clinically, and poor

medio-lateral control has been shown in ACL-R patients even >10 months after surgery [150].

Knee abduction moment is more costly to evaluate than knee valgus angle, requiring 3D motion capture and inverse kinematics, but recent evidence seems to show that it is a better indicator of risk than knee valgus angle alone. For example, in females these moments have been used prospectively to predict primary ACL injury in females with 73% specificity and 78% sensitivity [33]. In healthy patients, knee abduction moment has been associated with OA disease progression [151, 152, 153].

In the meta-analysis discussed above by Kaur *et al.* [138], moderate and strong evidence was found for significantly lower peak adduction moments compared to controls and contralateral limbs, respectively. In stair ascent and descent, lower adduction moments were found compared to the contralateral limb, but no difference was found w.r.t. control participants. In the other meta-analysis of knee abduction moments and angles by Hart *et al.* [140], moderate to strong evidence was found for no difference from ACL-R limbs compared to the contralateral limb, or control participants. However, a sensitivity analysis of graft type revealed strong evidence of lower peak knee adduction angles (i.e. less varus) in hamstring-tendon patients 6 – 12 months post ACL-R compared to healthy controls, but no evidence in those with a patellar-tendon graft. The authors cautiously propose that hamstring-tendon ACL-R may increase the risk of lateral post-traumatic knee OA. Similarly, other studies have shown that hamstring-graft ACL-R patients have a lower varus angle [129] and adduction moment [30] than controls or BPTB patients. Thus, in the current study, which only uses hamstring-tendon grafts, this is an important outcome measure to monitor.

Interestingly, no studies reporting knee abduction moment during running were found; it is felt that this is a clear gap in the literature. This is especially since in the long-term study in Chapter 2, effect sizes of knee abduction moment were much larger in running than in walking compared to contralateral limb (running: $d = 0.62$

vs. walking: $d = 0.44$), and compared to healthy controls (running: $d = 1.1$ vs. walking: $d = 0.33$). This may make diagnostic evaluation easier, due to a higher signal-to-noise ratio.

Regarding normalisation of these knee abduction moments over time, only studies by Hooper *et al.* [154] (6 months to 12 months) and Webster *et al.* [142] (10 months to 3.3 years) measured at more than one time point. The former found no differences compared to the contralateral limb, but in all test conditions (walking, upstairs, and downstairs), the knee varus moment increased (decreased valgus) from 6 to 12 months. In the second study, the varus moment also increased over time in both limbs (decreased valgus), and there was a between-limb difference, but over time the difference did not change.

Some attempts have been made to 'treat' deficits such as high-risk knee abduction moment in a DVJ using neuromuscular training. Myer *et al.* [155] trained participants which had been sorted by 'high-risk' and 'low-risk' knee abduction moment groups for 7 weeks. The 'high-risk' group decreased their knee abduction moment by 13%, while those in the 'low-risk' group saw no change in knee abduction moment. The training volume was insufficient, however, to re-classify this group as 'low-risk'.

4.2.1.4 Tibial rotation

Tibial rotation is becoming more well-recognised as a biomechanical measure of knee joint health. It has been challenging to measure, possibly because a) marker placement results in variable static values, b) a clear definition of zero rotation is not agreed upon, and c) cross-talk artifacts between this and other knee angles may be present. This may be the cause of high variability, and no clear results being found in studies such as Georgulis *et al.* [121]. However, this may be changing; in the meta-analysis of Kaur *et al.* [138], in walking there was strong evidence for less internal rotation of the

ACL-R knee as compared to the contralateral. Also, there was strong evidence for lack of difference in peak external rotation angle as compared to control participants.

In these studies, the size of the tibial rotation differences tends to be relatively large. For two of the studies reporting internal rotation, mean differences were 5.1°. For a the one longitudinal study, values were 3.6° and 2.1°, at 10 months and 3.3 years, respectively [142]. Webster and Feller [156] also showed a reduction of internal tibial rotation from ACL-R during drop landings, in over 60% of cases the difference was greater than 5°. These large angular deviations (>MCID = 3°) may have greater clinical usefulness as markers of rehabilitation status, and warrant further study.

4.2.1.5 Upper body (trunk) angles

The trunk constitutes approximately 60% of the body mass - current clinical concepts are that trunk angle deviations and poor trunk control can be the source of deviations in the lower limbs, and injury risk [26, 157, 158]. One key study has found evidence that ACL injury risk can be prospectively predicted by several measures of trunk proprioception and responsiveness, particularly in the lateral direction [34]. Also, simulation studies have described the mechanistic link between the trunk and lower limb dynamics [159].

Post ACL-R, very little information is available on alterations in trunk control. An important contribution to this was a study which showed that in ACL-R females there was greater ipsilateral trunk lean at initial contact (approx. 2°), forward lean during stance (approx. 3.5°), and higher errors on a trunk stability test with both limbs [12]. However, this has not been repeated for males. Additional work has been done during drop vertical jump [160] and cutting [11] tasks in females. However, in both of these studies, trunk angles during stance were assessed in 2D using video analysis only.

Despite this lack of clear data, biomechanical strategies for quadriceps avoidance can involve forward [161] and lateral trunk leaning. The above studies prompted an exploratory investigation of trunk angles for male patients in this study. Because

of differing trunk morphologies, absolute values of trunk angle were less of interest than changes in angle due to training, and comparisons between trunk angles during different stance limbs.

4.2.1.6 Step length and width

Despite limited reporting in the literature, to thoroughly address the question of biomechanical deviations, step length and width are helpful low-cost general measures. One meta-analysis showed no difference in step length [141], but the choice to analyse the 12 month values from Knoll *et al.* [146] is questioned. In that study, reduced step lengths and width were reported at 6 weeks in both males (~100mm shorter and ~13mm narrower than control limbs or group) and females (~70mm shorter and ~20mm narrower than control limbs or group), and this difference normalised by the four-month test point. Another study by Gao and Zheng also showed lower mean step lengths for ACL-R [162]. Thus step length and width are included in the analysis here, normalised by patient height.

4.2.2 Foot-strike and impact effects

Apart from the maximum Ground Reaction Force (GRF) time point of the gait cycle, impact effects around foot strike are of interest. This early stance phase involves high rate of force from the impact with the ground, and rapid eccentric contractions of the quadriceps muscles at the knee. Joint angles and velocities at foot-strike in preparation for landing can be seen as feed-forward control, as this phase is very rapid, and happens faster than most (polysynaptic) reflex arcs. As yet, deviations in this phase have been shown in certain populations, but have not been clearly linked to ACL-R risk.

Initial contact knee and foot angles

One of the clinical effects of ACL-R is limited extension range of motion, especially during the first few months after surgery. This tends to result in an increased knee flexion angle at initial contact, reducing knee angular excursion. This pattern may remain even once the extension ROM has normalised. It has been shown (reproduced in [152]) that the anterior-posterior location of the thickest cartilage on the medial femoral condyle was associated with the angle of knee flexion at heel-strike. However, a recent systematic review by Gokeler *et al.* [23] failed to find any clear trend in these variables in six studies. For this study, it was felt that this didn't warrant statistical testing of this variable, and that qualitative discussion of the knee flexion angle ensemble average at foot strike would be sufficient.

Rate of force development and initial impact peak

Rate of force development during the heel strike transient has been associated with increased subchondral bone stiffening and cartilage degeneration. Recently, this has prompted investigation of these variables in ACL-R females long-term after surgery [24]. Higher initial impact peak and initial impact load rate were found in ACL-R females, in both walking and running, but no differences were found between limbs. This was also found by Co *et al.* in 1993 [163], the only other study that was found reporting these variables for ACL-R. The study in Chapter 2 of this thesis also found these deviations in males, prompting the inclusion of these variables in the current study, to evaluate the effectiveness of the intervention to modify them.

4.2.3 Conclusion

This literature review has covered the use of biomechanical deviations as markers of neuromuscular changes in ACL-R patients. In the following sections, the randomised

controlled trial of eccentric cycle training is described, with respect to biomechanical measures during gait.

4.3 Trial aims and objectives

The aim of this randomised controlled trial is to improve biomechanics in ACL-R rehabilitation using eccentric training, as compared to concentric training, using matched equipment, studio setting, and perceived exertion dose. The *a priori* hypothesis is that eccentric training is more effective than concentric training at increasing knee and hip angles and moments during gait, and reducing biomechanical asymmetries.

The trial objectives are to determine if during the third phase of ACL-R rehabilitation, the eccentric exercise protocol is more effective compared to the concentric exercise protocol to improve the following:

1. Increase sagittal plane knee and hip angles and moments,
2. Reduce sagittal plane asymmetries in the above variables,
3. Reduce biomechanical deviations in knee valgus and knee abduction moment,
4. Reduce biomechanical deviations in impact dynamics using force plate measures following foot strike.

A further (exploratory) objective is to explore the effect of eccentric training in reducing biomechanical deviations in trunk kinematics.

4.4 Methods

To measure ACL-R biomechanics 3-D motion capture, the gold standard method, was used in walking and running gait. In total, 26 male participants aged 18-40 were recruited for this study, approximately 3 months after surgery. They were tested using

at the UCT biomechanics laboratory before and after the isokinetic cycling training intervention. This is part of a broader testing protocol which is described in more detail in Chapters 3 and 5. The study was approved by the UCT Human Research Ethics Committee (HREC# 578-2014), and all participants gave written informed consent for the trial (Appendix A).

4.4.1 Intervention

The intervention protocol, randomisation, and recruitment of patients is described in Chapter 3. Briefly, patients trained for 26 minutes 3 times per week for 8 weeks. Training was done on a powered isokinetic cycle ergometer (Grucox Medical, Cape Town, South Africa), in either eccentric mode resisting the pedal motion (ECC group), or concentric mode in the direction of the pedal motion (CON group), depending on their randomly-assigned group. Training intensity was progressed by target rating of perceived exertion (RPE, Appendix D) in both groups for each training week (Figure 3.4).

4.4.2 Gait testing

Participants were required to walk along the runway at a self-selected, moderate walking speed. The test was then repeated running; participants were asked to run the length of the runway at comfortable self-selected speed. They were asked to repeat the walk or run trial until at least 5 strikes were attained with each foot. For either of these tests, the approximate speed was monitored, and the participant guided if the speed differed noticeably from his average. All data in this study were adjusted to walk or run average speed by the regression model, to address velocity as a possible confounding variable.

Outcome variables include the knee and hip joint angles and moments, and upper body angles during gait. In addition, several GRF impact variables were calculated.

The surgically involved limb (AFF) at follow-up (FU) was compared to baseline (BL) measurements, and between-limb differences compared AFF limb to uninvolved limb (UNAFF) as a control for each group.

Kinematic/kinetic data

Three-dimensional marker data was recorded using an 8-camera Vicon motion capture system (Oxford Metrics, Oxford, UK) at 250Hz. Ground reaction force (GRF) data was recorded using two AMTI® (AMTI, Watertown, MA, USA) force plates at 1000Hz mounted in the walkway, hidden from the participant. Data handling from C3D to MATLAB® (Mathworks, Natick, MA, USA) was performed by extending the MOtoNMS package in SimTK [164].

Vicon's Plug-In Gait full-body marker set was used, which allowed for the calculation of joint centres and angles of rotation as well as the calculation of joint moments by inverse kinematics (IK). It comprised of the Plug-In Gait 16-marker lower body marker set (modified Helen Hayes) as shown in Figure 4.1, as well as an upper body model consisting of four additional trunk markers and a headband of four markers. Trunk markers were the spinous process of the 7th cervical vertebra (C7), the spinous process of the 10th thoracic vertebra (T10), the jugular notch where clavicles meet the sternum (CLAV), and at the xiphoid process of the sternum (STRN). Thus 24 reflective markers were used in total, which also allowed an estimate of the whole-body centre of gravity (CoG, not used).

To ensure the consistency of the data, all markers were placed by the same trained investigator to remove inter-rater placement error. Also, to reduce variability due to thigh and tibial marker placements, during static calibration the thigh and shank axis systems were rotated to align with anterior/posterior and medio/lateral axes of the foot. This is as described in the Vicon user manual [165].

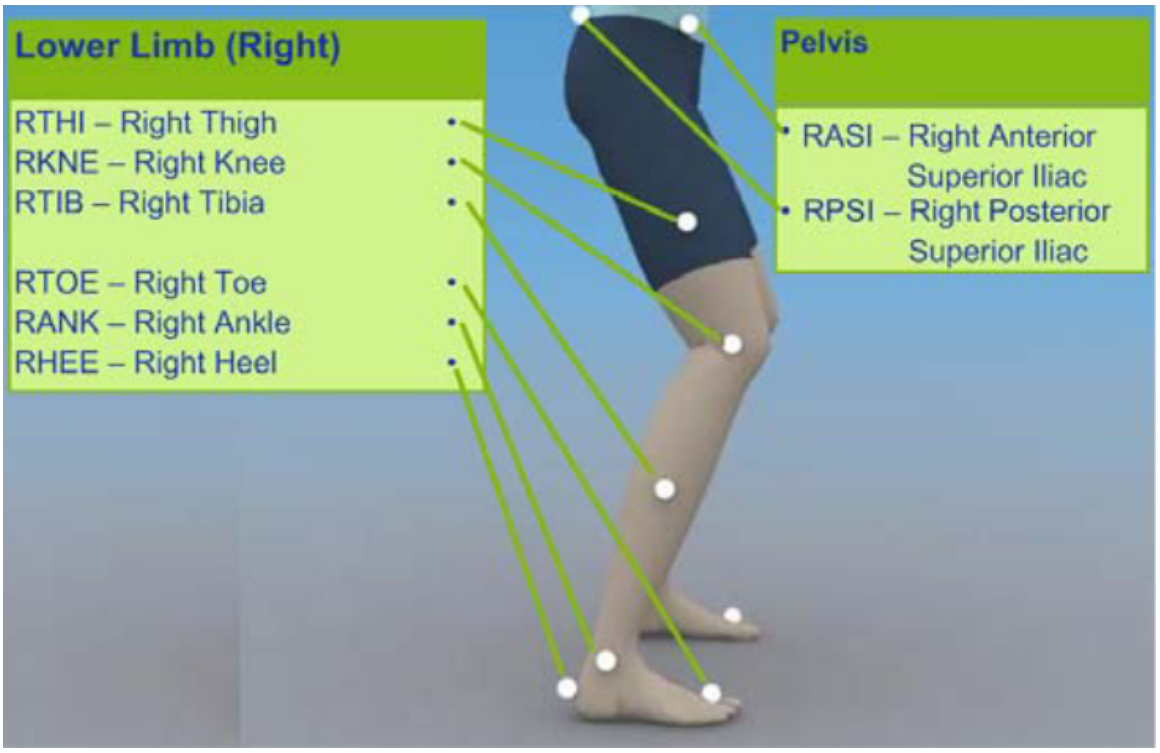

Figure 4.1: Plug-in Gait lower body marker set (right hand side shown, left hand symmetrical). ©Vicon (from Nexus user manual)

During post-processing, marker and GRF data were filtered at 100Hz using a Butterworth zero-lag fourth order filter. This filter frequency is higher than usual, which was chosen to allow investigation of higher-frequency effects, and avoid damping the maximum rate of force development (discussed further in [166]).

Foot-strikes were defined as a GRF of over 30N. Kinematic and kinetic outcome variables were hip and knee flexion angles, hip and knee flexion/extension moments, knee abduction moment, knee valgus angle, knee tibial rotation angle and trunk angles at maximum GRF for each trial. External moments were used, and normalisation was by body weight (BW) and participant height in metres. Angles were computed using the Cardan angle sequence, referencing the distal to the proximal segment, in the order flexion-varus-rotation.

Due to cross-talk in X and Y axes of the femoral axis system, frontal plane projected knee valgus angle during stance was used instead of the built-in variable, as was

done in Chapter 2. Femoral and tibial axes were based on hip, knee and ankle joint centres as calculated using the Vicon plug-in gait model (Oxford, UK). This is the 2-dimensional (2-D) knee valgus angle observed clinically from the front view, used routinely in video analysis of gait or drop vertical jumps. This has been typically used in 2-D studies of knee alignment [40], and is also used for trials of large clinical populations as, for example, in Hewett *et al.* [167]. It has also been referred to as frontal plane projection angle (FPPA) [41].

Impact kinetics were quantified for each participant during the gait analysis from force plate data, using custom MATLAB® code. Maximum vertical GRF was detected during the first 50% of stance for walking, or maximum during stance for running. In addition, maximum loading rate (BW/s), initial impact transient peak force (BW), and initial load rate (BW/s) were calculated for each trial. Forces and load rates were normalised by BW in Newton. Initial loading rate was defined between the points of 20% and 80% of the time between foot strike and 15% of stance phase for walking, or primary impact peak for running, as described by Noehren *et al.* [24], and also used in Chapter 2. Initial load rate of the heel strike transient was calculated during heel-striking running; for forefoot strike (no initial impact peak), the primary vertical GRF peak was used.

For future analysis, EMG was also recorded during the gait analysis. The EMG signal was taken from the following muscles: *Vastus Medialis*, *Vastus Lateralis*, *Semi-tendinosis* and *Biceps Femoris* on both the involved and uninvolved legs. The measured signals were transmitted using a telemetry system (Noraxon GT 2000), which was placed in a halter strapped to the participants' back.

Pain monitoring

Before and after each functional test, including gait analysis, a visual analogue scale (VAS) was used to assess pain level, as well as description of the pain location and

type. This was to determine if pain was contributing to alterations in biomechanics, as well as to give an indication of potentially unsafe situations for the patient.

4.4.3 Statistical analysis

Average characteristics of participants in the ECC group and CON group were given previously, in Section 3.5. These included height, body weight, age and Tegner activity level before the injury. Mann-Whitney U tests were performed to detect differences in groups, due to their non-normal distributions.

Differences in biomechanical variables, between groups (AFF limbs) and asymmetries between-limbs (AFF - UNAFF), were evaluated using a linear mixed effects regression model, fitting using the *nlme* package in R, Version 3.1-128 [42, 43]. Each variable of interest was analysed in turn for either of the walk or run conditions. The model allows for a different mean response in (i) pooled ECC+CON group participants at BL, (ii) change BL to FU of ECC group, and (iii) change BL to FU of CON group. The mean response is also allowed to vary by AFF limb versus UNAFF limb, within each of the three groups.

Mixed effects models were chosen as they allow for the estimation of population-level relationships between response variables, and group and limb predictors (fixed effects) while allowing participants to have their own unique deviations from these (random effects). The aim of using random effects is to capture the correlation amongst the (sometimes varying numbers) of valid repeated measurements per participant, and contain all the subject-specific information not accounted for by the model. Several different model fits were compared for all response variables, and evaluated by the visual inspection of residual diagnostic plots (residual scatter and q-q) and considering Akaike's Information Criterion (AIC) values. A model was chosen with a random intercept, and interactions between limb and group included in the prediction, as well as self-selected gait velocity as a possible confounder. To check validity of including velocity

as a fixed effect, models were statistically compared with- and without the velocity term using Likelihood Ratio ANOVA. For 77% of the cases, $P < 0.05$ (mostly < 0.001), which justified using this model structure.

Results are presented as mean and 95% confidence intervals (95%CI), adjusted to mean velocity for walk or run condition. ANOVA null hypothesis testing was used to compare a model with a pooled BL, which captures the design of the experiment, to one with separate groups at BL. This generally resulted in $P > 0.05$, justifying the selection of the pooled-BL model; in cases where $P < 0.05$ at BL (primarily in trunk variables), mean values were reported, but further statistical testing was not performed. Null hypothesis testing was also used to compare BL-to-FU changes between ECC group and CON group, and asymmetry between groups at FU.

A large number of outcome variables were tested. To control the effect of multiple testing resulting in false discoveries, the false discovery rate (FDR) was used as described by Hochberg and Benjamini [168], restricting false discovery to 10% of tests. To check the results of this, it was confirmed that null hypotheses that were rejected all had $P < 0.05$.

Effect sizes, where discussed, were calculated using Cohen's d [44]; $d = 0.2 - 0.5$, $d = 0.5 - 0.8$ and $d \geq 0.8$ indicate *small*, *moderate* and *large* effects, respectively. Minimal clinically important differences (MCID) were not available for many variables in the literature, but Di Stasi *et al.* [45] used hip and knee flexion values of 3°, knee moments at 0.04Nm/kg/m, and hip moments at 0.06Nm/kg/m, which were used here. These values are similar to those given by Webster *et al.* [142], but the latter did not normalise by body height, meaning the values could not be used directly.

4.5 Results

Results of BL and FU testing are given in the following sections. First, stance phase kinematic and kinetic ensemble average curves are presented for the knee and hip variables during walking and running, for visual inspection. This is followed by regression model results at maximum GRF for the same variables, impact variables, and upper body variables.

4.5.1 Stance phase kinetics and kinematics

For the stance phase of walking or running gait, ensemble average curves are given for the eight limb conditions (group x limb x BL/FU). AFF limbs are in *red*, UNAFF limbs in *blue*; dashed lines are at BL, solid lines at FU. Plots are given for vertical GRF (Fig. 4.2), knee flexion angle (Fig. 4.3) and moment (Fig. 4.4), hip flexion angle (Fig. 4.5), knee valgus angle (Fig. 4.6), knee abduction moment (Fig. 4.7), and knee tibial rotation angle (Fig. 4.8). In the first two figures, vertical dotted lines indicate the maximum GRF time point of interest in walk or run, and Figure 4.3 gives example points of interest for the AFF limb knee angle in each group at BL or FU, showing that the change in the ECC group mean increased more than in CON group mean.

4.5.2 Knee and hip biomechanics

Knee and hip biomechanical response variables were estimated by the regression mixed effects models. Mean values at BL for the AFF limb, and change to FU for each of the groups are given in Table 4.1, for both walk and run gait conditions. For example, during walking at BL, knee flexion angle (both groups) is 26.4° (95%CI: 25.0, 27.8). Statistically comparing this *pooled BL* model with a model using separate groups at BL, shows no evidence of significant difference between groups ($P = 0.714$). At FU, ECC group knee flexion angle increased, by +3.5° (95%CI: 2.1, 4.9), while the CON

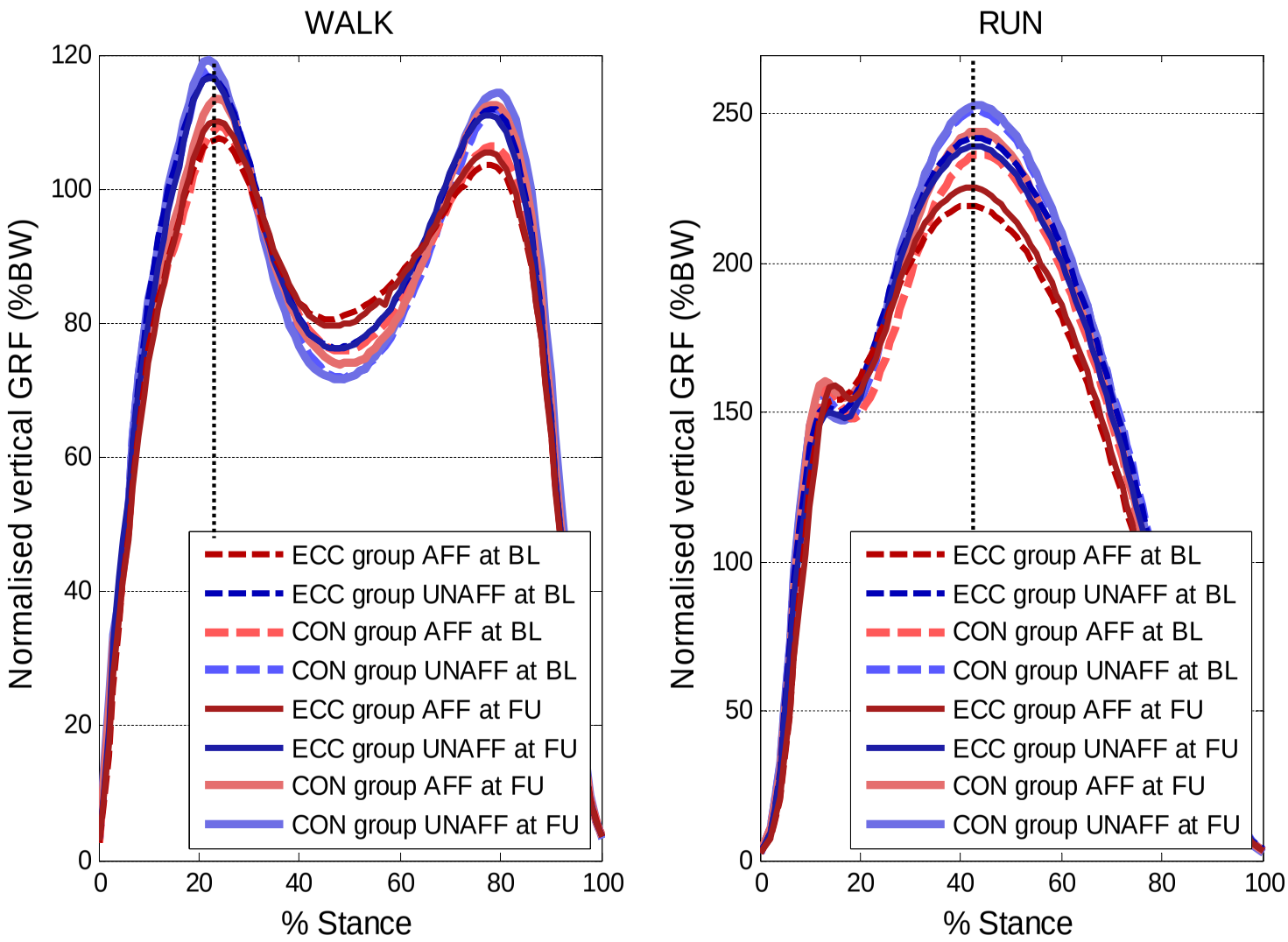

Figure 4.2: Vertical GRF stance phase profiles. Red - AFF limbs, blue - UNAFF limbs. Dashed line - BL, solid line - FU. Dark red/blue - ECC group, light red/blue - CON group. A and B are ECC and CON group GRF at BL, C and D are at FU. Vertical dotted lines indicate approximate maximum GRF.

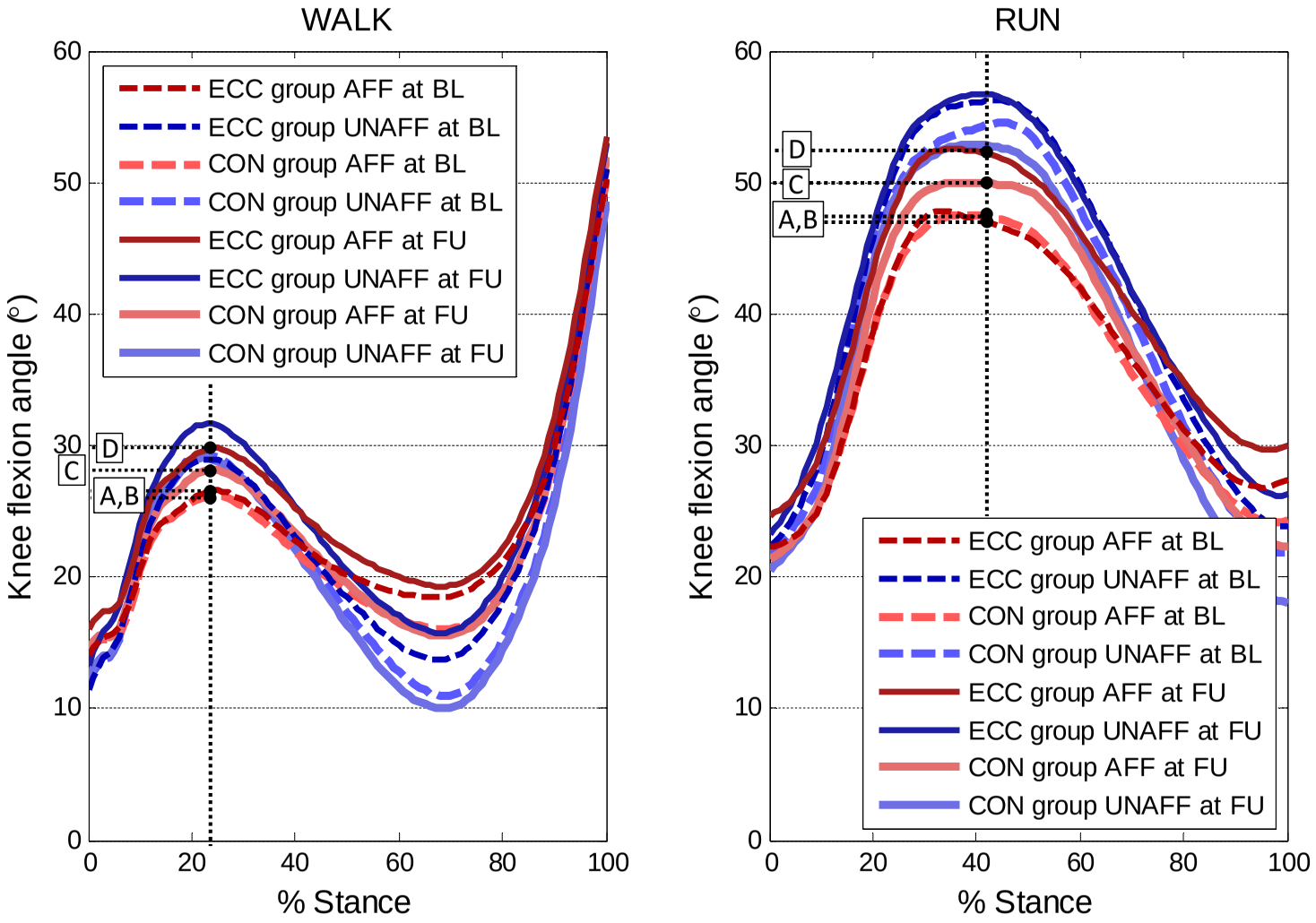

Figure 4.3: Knee flexion angle ensemble averages during stance. For AFF limb, points A and B are ECC group and CON group at BL, points C and D are CON group and ECC group at FU, respectively. Vertical dotted lines indicate approximate maximum GRF.

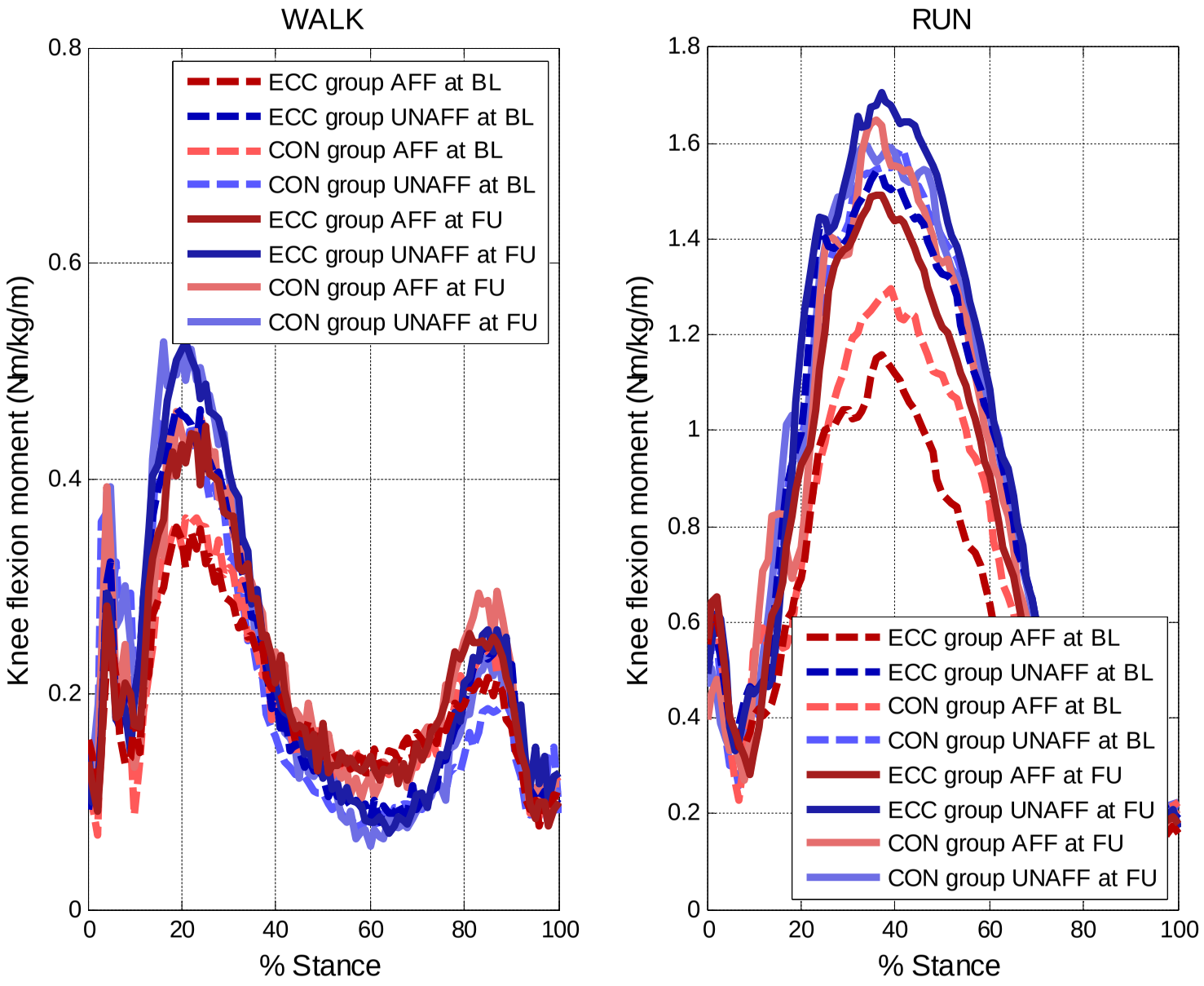

Figure 4.4: Knee flexion moment ensemble averages during stance

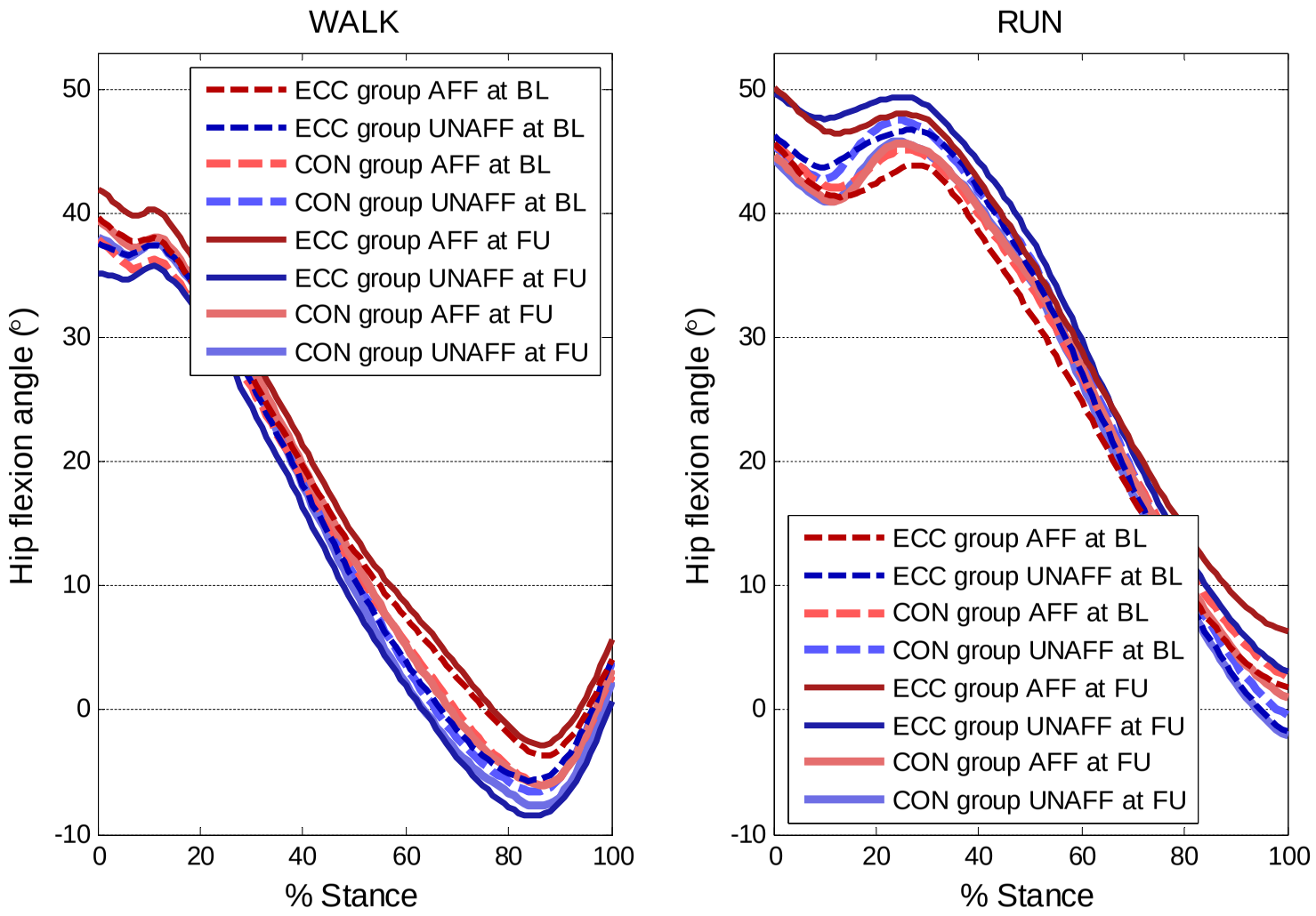

Figure 4.5: Hip flexion angle ensemble averages during stance

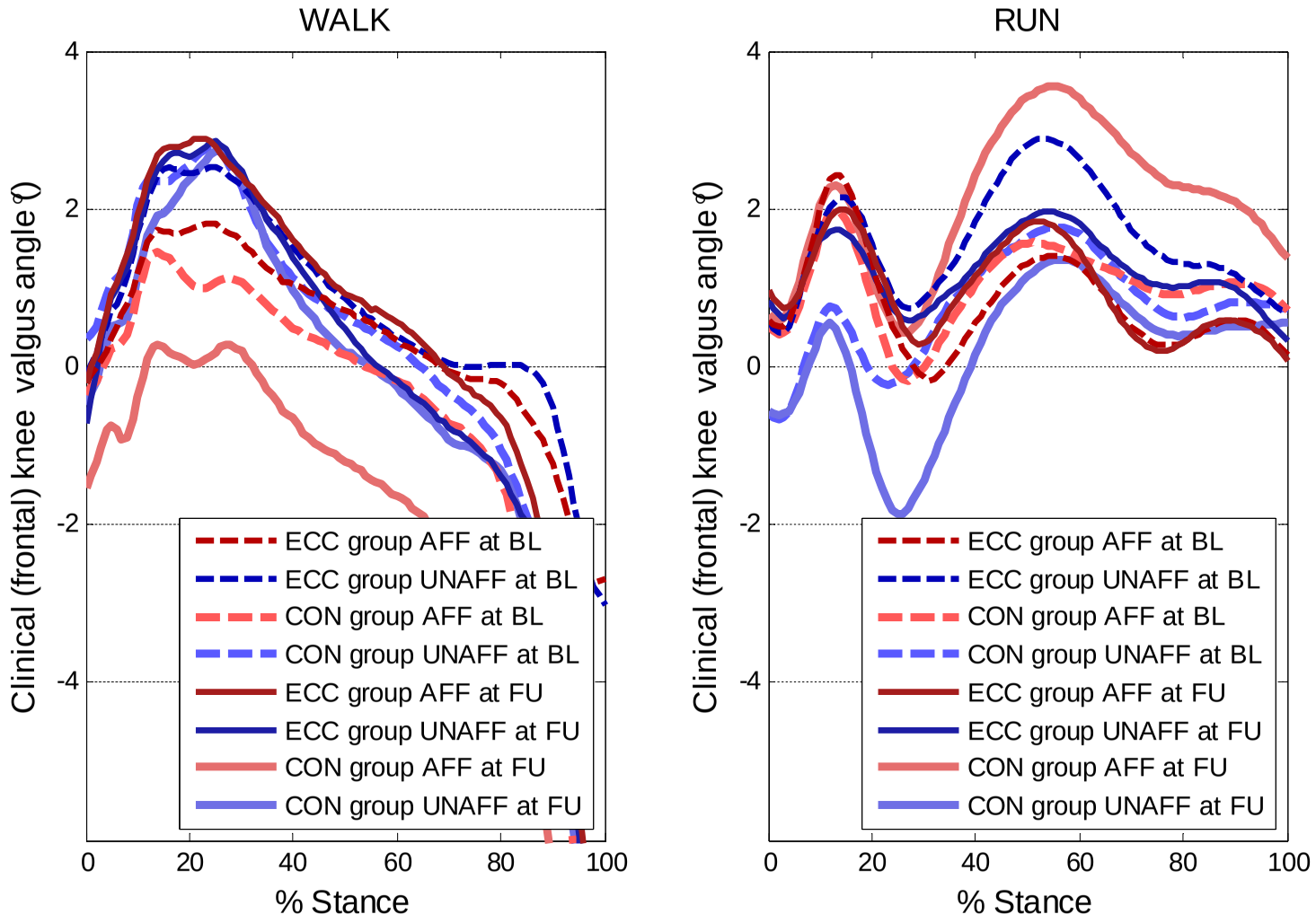

Figure 4.6: Knee valgus angle ensemble averages during stance

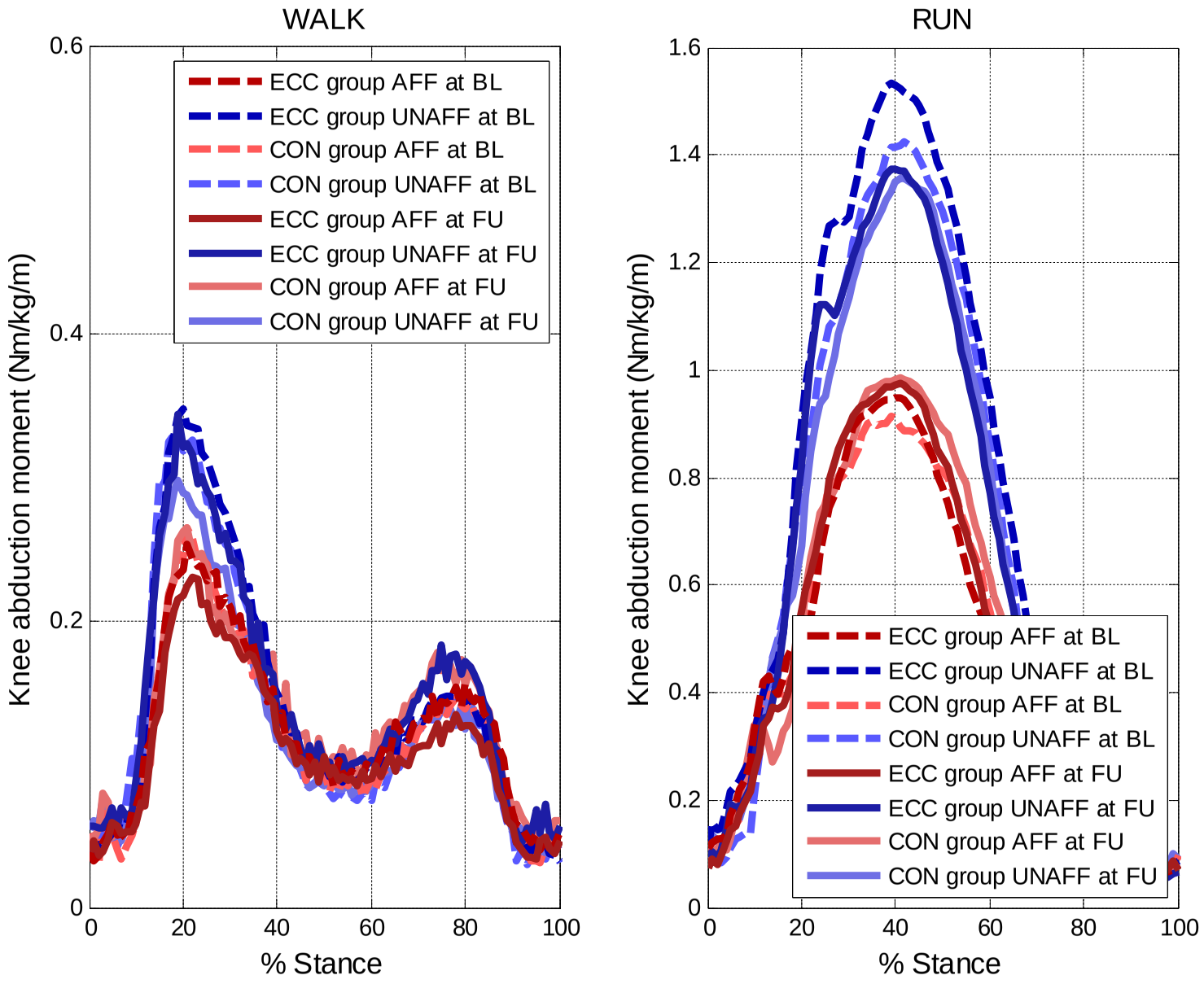

Figure 4.7: Knee abduction moment ensemble averages during stance

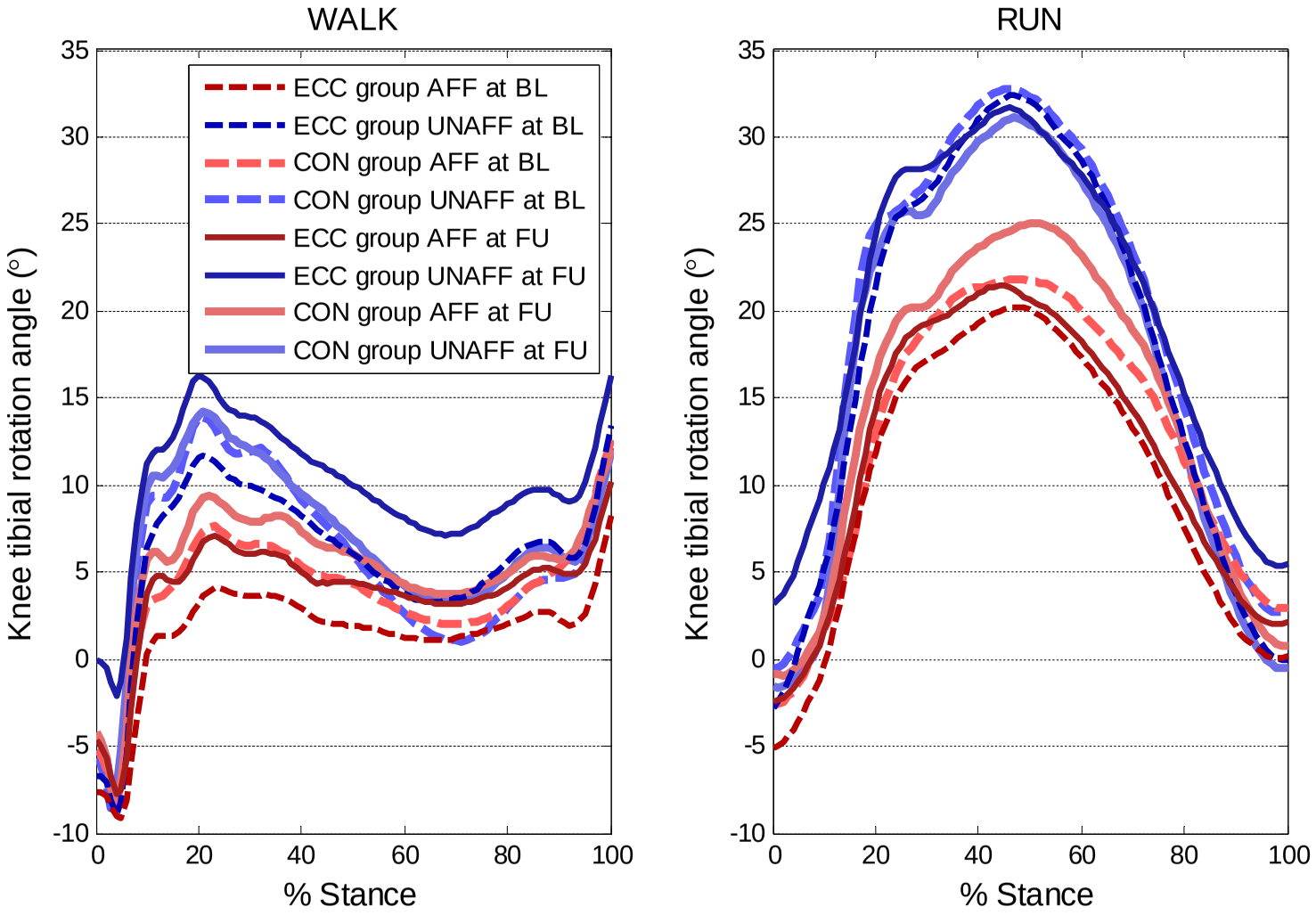

Figure 4.8: Knee tibial rotation ensemble averages during stance

group mean changed by +1.4° (95%CI: -0.1, 2.8). Statistical testing found evidence for a difference in response between groups ($P = 0.022$). This was repeated for hip flexion angle, knee and hip flexion moments, knee frontal plane valgus angle, knee abduction moment, and knee tibial rotation angle.

Comparing changes from BL to FU, evidence was found for a between-group difference in change in knee flexion angle during walking ($P = 0.022$), hip angle during running ($P = 0.010$), knee valgus during walking ($P = 0.021$) and running ($P = 0.008$). No evidence was found for between-groups difference for changes in knee flexion angle during running, knee flexion moment (walk/run), hip moment (walk/run), knee abduction moment (walk/run), or knee tibial rotation (walk/run). Using the model-comparison analysis of variance (ANOVA) described above to test for difference between groups at BL, evidence was only found for difference in knee flexion moment ($P = 0.034$) and hip moment ($P = 0.006$) during walking, but not for any of the other knee or hip variables.

Between-limb symmetry at BL and for each group at FU, as well as results of statistical testing between groups at FU are given in Table 4.7. For example, for knee flexion angle, asymmetry of -2.6° (95%CI: -3.7, -1.6) at BL was shown, with ECC group at FU showing asymmetry of -1.6° (95%CI: -3.0, -0.2). For the CON group, no evidence of asymmetry was found, with between-limb mean differences of -1.0° (95%CI: -2.6, 0.6). Statistical testing of asymmetry at FU between groups showed no difference ($P = 0.582$). Across all knee and hip variables, asymmetries at BL were found (both walk and run) for knee and hip flexion angles, knee valgus and tibial rotation angles, and knee flexion and abduction moments, but not in hip flexion moment. At FU, asymmetries for each of the groups is given in the same table, with statistical test results for differences between groups. Evidence for ECC group being more symmetrical at FU than CON group was found for knee valgus angle during walking ($P = 0.027$) and running ($P < 0.001$). This is also evident from the stance phase curves shown in

Figure 4.6. In contrast, the CON group was more symmetrical at FU than ECC group for tibial rotation angle during running ($P < 0.001$).

4.5.3 Quadriceps avoidance

The number of patients exhibiting quadriceps avoidance during walking are given in Table 4.3 below.

4.5.4 Trunk kinematics

Thorax kinematics, and spine kinematics (thorax w.r.t. pelvis) response variables are given in Table 4.4 for walk and run gait conditions. For example, mean thorax flexion angle during walking at BL during AFF limb stance was 4.8° (95%CI: 3.4, 6.3). At BL, no evidence was found for a difference between groups ($P = 0.510$). At FU, ECC group decreased (trunk backward), by -0.7° (95%CI: -1.2, -0.1), and CON group decreased by -1.4° (95%CI: -2.0, -0.8). Statistical testing found no evidence for a difference in response between groups ($P = 0.061$). Checking other angles at BL, a difference between groups was found for thorax lateral angles during walking/running (both $P < 0.001$) and spine angles during running ($P = 0.019$), and for these variables, no further statistical testing was performed. Comparing changes from BL to FU, change in ECC group was 1.7° more forward leaning than the CON group for thorax flexion angle during running ($P < 0.001$).

Symmetry of trunk angles during UNAFF and AFF limb stance at BL and FU, as well as results of statistical testing between groups at FU are given in Table 4.5. For example, for trunk flexion angle, asymmetry of 0.5° (95%CI: 0.1, 1.0) at BL was shown during walking. At FU, no evidence of asymmetry was found in the ECC group or CON group, with means of 0.2° (95%CI: -0.4, 0.8) and 0.1° (95%CI: -0.5, 0.8), respectively. Statistical testing of asymmetry at FU between groups showed no difference ($P = 0.905$). For trunk variables, asymmetries at BL were found (both walk and run) for flexion

Table 4.1: AFF limb changes (BL to FU) of knee and hip variables

		at BL		change BL to FU		
			P^a	ECC	CON	P^b
Knee flexion angle (°)	Walk	26.4° (25.0 27.8)	0.714	**+3.5° (2.1 4.9)**	+1.4° (-0.1 2.8)	**0.022***
	Run	46.5° (43.2 49.8)	0.191	**+4.6° (3.4 5.8)**	**+3.2° (1.9 4.4)**	0.082
Knee flexion moment (N·m/kg/m)	Walk	0.35 (0.30 0.40)	0.034	**+0.08 (0.03 0.12)**	**+0.07 (0.02 0.12)**	0.859
	Run	0.98 (0.68 1.29)	0.314	**+0.33 (0.20 0.46)**	**+0.33 (0.19 0.47)**	0.988
Hip angle (°)	Walk	30.9° (27.1 34.7)	0.308	**+2.85° (1.58 4.13)**	+1.0° (-0.33 2.42)	0.039
	Run	29.9° (26.6 33.2)	0.648	**+3.22° (2.07 4.4)**	+1.1° (-0.1 2.4)	**0.010***
Hip moment (N·m/kg/m)	Walk	0.20 (0.12 0.28)	**0.006***	+0.00 (-0.10 0.09)	-0.03 (-0.13 0.08)	§
	Run	0.07 (-0.44 0.58)	0.104	-0.16 (-0.39 0.07)	**-0.26 (-0.51 -0.01)**	0.530
Knee valgus angle (°)	Walk	1.7° (0.0 3.3)	0.168	+0.4° (-0.4 1.3)	**-1.0° (-1.9 0.0)**	**0.021***
	Run	0.94° (-1.6 3.5)	0.423	+0.6° (-0.3 1.4)	**+2.1° (1.2 3.1)**	**0.008***
Knee abduction moment (N·m/kg/m)	Walk	0.24 (0.20 0.28)	0.204	-0.02 (-0.05 0.02)	+0.00 (-0.03 0.05)	0.342
	Run	0.65 (0.40 0.90)	0.938	+0.08 (-0.02 0.17)	+0.07 (-0.03 0.18)	0.958
Knee Tibial Rotation (°)	Walk	5.5° (2.5 8.4)	0.387	**+2.9° (0.9 4.9)**	**+3.2° (1.1 5.4)**	0.801
	Run	12.9° (7.5 18.3)	0.754	+1.4° (-0.6 3.3)	**+3.7° (1.6 5.8)**	0.088

Bold values indicate evidence for group mean change.

[a] Difference in ECC vs. CON group AFF limbs at BL.

[b] Difference in change in ECC vs. CON group AFF limbs, BL to FU. Bold, starred P-values are significant (FDR=10%).

[§] Differences found between groups at BL, P-value not applicable.

Table 4.2: Knee and hip AFF-UNAFF limb asymmetry

		limb difference at BL	mean limb difference at FU		
			ECC	CON	P^a
Knee angle (°)	Walk	**-2.6° (-3.7 -1.6)**	**-1.6° (-3.0 -0.2)**	-1.0° (-2.6 0.6)	0.582
	Run	**-7.6° (-8.6 -6.7)**	**-4.2° (-5.5 -2.9)**	**-2.6° (-4.0 -1.2)**	0.106
Knee moment (N·m/kg/m)	Walk	**-0.12 (-0.16 -0.08)**	**-0.09 (-0.14 -0.04)**	**-0.06 (-0.11 -0.01)**	0.463
	Run	**-0.30 (-0.40 -0.20)**	**-0.16 (-0.30 -0.01)**	-0.03 (-0.18 0.13)	0.224
Hip angle (°)	Walk	**-1.6° (-2.6 -0.6)**	**-2.7° (-4.0 -1.3)**	-0.6° (-2.1 0.9)	0.042
	Run	**-2.2° (-3.1 -1.3)**	-0.9° (-2.2 0.4)	+0.2° (-1.1 1.6)	0.229
Hip moment (N·m/kg/m)	Walk	0.05 (-0.03 0.13)	0.06 (-0.05 0.16)	-0.01 (-0.13 0.10)	§
	Run	0.16 (-0.02 0.34)	**0.30 (0.05 0.56)**	0.11 (-0.16 0.38)	0.314
Knee valgus angle (°)	Walk	**-0.7° (-1.4 0.0)**	-0.4° (-1.3 0.5)	**-1.9° (-2.9 -0.9)**	0.027
	Run	**-1.2° (-1.8 -0.5)**	**-1.1° (-2.1 -0.2)**	**+2.3° (1.3 3.3)**	**<0.001***
Knee abduction moment (N·m/kg/m)	Walk	**-0.10 (-0.13 -0.07)**	**-0.09 (-0.13 -0.05)**	**-0.04 (-0.09 0.00)**	0.090
	Run	**-0.54 (-0.61 -0.47)**	**-0.42 (-0.53 -0.32)**	**-0.42 (-0.53 -0.31)**	0.989
Tibial Rotation **(°)**	Walk	**-6.8° (-8.4 -5.2)**	**-8.0° (-10.1 -5.8)**	**-5.0° (-7.3 -2.6)**	0.061
	Run	**-10.9° (-12.4 -9.4)**	**-12.1° (-14.3 -10.0)**	**-5.8° (-8.1 -3.5)**	**<0.001**

Bold values indicate evidence for asymmetry.

[a] Difference in ECC vs. CON group asymmetry at FU. Bold, starred P-values are significant (FDR=10%).

[§] Differences found between groups at BL, P-value not applicable.

Table 4.3: Numbers of patients exhibiting quadriceps avoidance gait during walking

	ECC (n = 12)		CON (n = 10)	
	BL	FU	BL	FU
AFF	7	5	3	3
UNAFF	7	7	8	7

angles, but not in thorax lateral angles. At FU, statistical test results for differences in asymmetry between groups was only found differences in the spine flexion angle ($P = 0.002$).

4.5.5 Impact dynamics

Impact dynamics variables at BL of the AFF limb are given in Table 4.6 below for walk and run conditions. For example, maximum impact force during walking at BL (pooled) during AFF limb stance was 1.11BW (95%CI: 1.07, 1.14). Statistically comparing models as described above, shows no evidence for a difference between groups ($P = 0.811$). At FU, the ECC group had no evidence of change in group mean +0.0BW (95%CI: -0.02, 0.03), and CON group mean increased, by +0.02BW (95%CI: -0.01, 0.05). Statistical testing found no evidence for a difference between groups ($P = 0.286$). Checking all impact variables at BL, a difference between groups was only found for maximum impact rate during running ($P = 0.014$). Comparing BL to FU, the change in ECC group was higher than the CON group for peak vertical GRF ($P = 0.003$) and initial impact rate ($P = 0.015$) during running. During walking, however, no evidence was found for change between groups for any variables.

Symmetry of impact variables at BL and FU, as well as results of statistical testing between groups at FU are given in Table 4.7. For example, for peak vertical GRF, asymmetry of -0.09BW (95%CI: -0.11, -0.07) at BL was shown during walking. At FU, the ECC group and CON group showed asymmetry of -0.05BW (95%CI: -0.08, -0.02) and -0.05BW (95%CI: -0.08, -0.02), respectively. Statistical testing of asymmetry at FU

Table 4.4: AFF limb changes (BL to FU) of upper body angles

		at BL		Change BL to FU		
		AFF limb	P^a	ECC	CON	P^b
Thorax flexion angle (absolute, + forward lean)	Walk	4.8° (3.4 6.3)	0.510	**-0.7° (-1.2 -0.1)**	**-1.4° (-2.0 -0.8)**	0.061
	Run	13.4° (11.7 15.0)	0.048	**+0.9° (0.3 1.5)**	**-0.8° (-1.5 -0.2)**	**<0.001***
Spine flexion angle (thorax w.r.t. pelvis, + forward)	Walk	-3.7° (-6.1 -1.4)	0.976	**-1.8° (-2.7 -0.9)**	**-1.1° (-2.1 -0.2)**	0.270
	Run	-2.9° (-5.7 -0.1)	**0.019***	-0.5° (-1.3 0.3)	-0.1° (-1.0 0.7)	§
Thorax angle, Y (absolute)	Walk	-2.3° (-2.7 -1.9)	**<0.001***	+0.4° (-0.2 0.9)	+0.2° (-0.4 0.8)	§
	Run	-4.9° (-5.6 -4.3)	**<0.001***	+0.5° (-0.1 1.0)	-0.4° (-1.0 0.2)	§
Spine angle, Y (thorax w.r.t. pelvis)	Walk	5.6° (3.9 7.4)	0.088	-1.4° (-4.2 1.4)	-0.1° (-3.1 2.9)	0.472
	Run	7.8° (6.9 8.6)	0.167	-0.4° (-1.2 0.4)	0.0° (-0.9 0.8)	0.458

Bold values indicate evidence for group mean change.

[a] Difference between CON to ECC AFF limbs at BL.

[b] Difference in change in CON and ECC group AFF limbs, BL to FU. Bold, starred P-values are significant (FDR=10%).

§ Differences found between groups at BL, P-value not applicable.

Table 4.5: Asymmetry in upper body angles, AFF vs. UNAFF limb stance.

		difference at BL	difference at FU		
			ECC	CON	P^a
Thorax flexion Angle (absolute, + forward lean)	Walk	**0.5° (0.1 1.0)**	0.2° (-0.4 0.8)	0.1° (-0.5 0.8)	0.905
	Run	**0.5° (0.1 1.0)**	**0.9° (0.2 1.6)**	0.1° (-0.6 0.8)	0.133
Spine Flexion Angle (thorax w.r.t. pelvis, + forward)	Walk	-0.1° (-0.8 0.6)	0.7° (-0.2 1.7)	**-1.5° (-2.6 -0.4)**	**0.002***
	Run	**-1.7° (-2.3 -1.1)**	-0.2° (-1.1 0.7)	**-1.7° (-2.6 -0.7)**	§
Thorax Angle, Y (absolute)	Walk	-0.2° (-0.7 0.2)	**0.6° (0.0 1.2)**	-0.1° (-0.7 0.6)	§
	Run	-0.3° (-0.6 0.1)	0.3° (-0.3 0.8)	**-0.7° (-1.3 -0.1)**	§
Spine Angle, Y	Walk	**-2.5° (-4.8 -0.2)**	**-3.3° (-6.4 -0.2)**	-1.2° (-4.7 2.2)	0.382
	Run	**-1.4° (-2.0 -0.8)**	**-2.0° (-2.9 -1.1)**	**-2.3° (-3.3 -1.4)**	0.563

Bold values indicate evidence for asymmetry.

[a] Difference in ECC vs. CON group asymmetry at FU. Bold, starred P-values are significant (FDR=10%).

§ Difference found between groups at BL, P-value not applicable.

showed no difference between groups ($P = 0.897$). For these variables, asymmetries at BL were found (both walk and run) for step length, peak GRF and initial impact rate, but not in maximum impact rate, or initial impact peak. At FU, asymmetries for each of the groups is given in the same table, with statistical test results for differences between groups. Evidence for ECC group being more symmetrical at FU than CON group was found for initial impact rate during walking ($P = 0.025$). The CON group was more symmetrical at FU than ECC group for step length ($P = 0.002$) and initial impact rate during running ($P = 0.016$).

4.6 Discussion

This study argues that eccentric training is beneficial for ACL-R male patients in reducing biomechanical deviations. From the data presented above, this is supported in the sagittal plane, as compared to the concentric training controls. In the frontal and transverse planes, some benefits were shown, but were not larger than in controls. The following sections discuss the individual variables presented, and discuss them in light of the long-term results obtained in Chapter 2.

4.6.1 Knee and hip biomechanics

From BL to FU, the ECC group saw increases in knee flexion angle, hip flexion angle, and knee flexion moment. This can be seen from the ensemble average curves (Figures 4.3, 4.4, and 4.5), as well as in Table 4.1. From the literature, these three variables tend to be lower in ACL-R AFF limbs compared to the contralateral limb or healthy controls (e.g. [138]). Thus, the evidence is that the eccentric intervention programme was beneficial to the patients in correcting these sagittal-plane variables. In walking, the increase in knee flexion angle of the ECC group was greater than in the CON group ($P = 0.022$), the latter which had evidence for no change. The ensemble average

Table 4.6: AFF limb changes (BL to FU) in step length, width, and impact variables

		at BL		change BL to FU		
		value	P^a	ECC	CON	P^b
Step length (mm/m HT)	Run	704.2 (689.1 719.4)	0.089	-8.8 (-19.2 1.6)	+5.7 (-5.6 17.0)	0.045
Step width (mm/m HT)	Run	55.5 (46.9 64.1)	0.073	+5.7 (-1.5 13.0)	+0.1 (-7.8 8.0)	0.267
Peak vertical GRF (BW)	Walk	1.11 (1.07 1.14)	0.811	+0.00 (-0.02 0.03)	+0.02 (-0.01 0.05)	0.286
	Run	2.30 (2.20 2.41)	0.153	+0.01 (-0.03 0.05)	**+0.10 (0.05 0.14)**	**0.003***
Initial Impact Rate (BW/s)	Walk	9.1 (8.3 9.8)	0.387	**-0.6 (-1.1 0.0)**	**-0.8 (-1.4 -0.2)**	0.483
	Run	69.7 (62.4 77.0)	0.157	-3.1 (-7.7 1.6)	+4.8 (-0.3 9.9)	**0.015***
Initial Impact Peak (BW)	Walk	N/A	-	N/A	N/A	-
	Run	1.81 (1.71 1.91)	0.888	-0.04 (-0.12 0.03)	+0.06 (-0.02 0.14)	0.045
Maximum Impact Rate (BW/s)	Walk	23.2 (20.5 25.9)	0.245	-2.3 (-4.9 0.3)	+1.1 (-1.7 4.0)	0.056
	Run	120.2 (108.7 131.8)	**0.014**	-6.6 (-14.0 0.9)	+3.9 (-4.2 12.0)	0.044

Bold values indicate evidence for group mean change.

[a] Difference in ECC group and CON group AFF limbs at BL.

[b] Difference in change in ECC vs. CON group AFF limbs, BL to FU. Bold, starred P-values are significant (FDR=10%).

Table 4.7: Asymmetry in step length, width, and impact measures between limbs. Bold values represent evidence for asymmetry.

		difference at BL	difference at FU		
			ECC	CON	P^a
Step length (mm/m HT)	Run	**23.6 (15.6 31.6)**	**23.0 (11.5 34.5)**	-3.3 (-15.5 8.9)	**0.002***
Step width (mm/m HT)	Run	1.1 (-4.5 6.7)	**8.2 (0.1 16.2)**	7.0 (-1.6 15.6)	0.848
Peak vertical GRF (BW)	Walk	**-0.09 (-0.11 -0.07)**	**-0.05 (-0.08 -0.02)**	**-0.05 (-0.08 -0.02)**	0.897
	Run	**-0.18 (-0.21 -0.15)**	**-0.10 (-0.14 -0.05)**	**-0.12 (-0.16 -0.07)**	0.535
Initial Impact Rate (BW/s)	Walk	**-0.6 (-1.0 -0.2)**	-0.1 (-0.6 0.48)	**-1.0 (-1.6 -0.4)**	**0.025***
	Run	**-6.5 (-10.1 -3.0)**	**-6.8 (-12.0 -1.7)**	2.4 (-3.0 7.9)	**0.016***
Initial Impact Peak (BW)	Walk	N/A	N/A	N/A	-
	Run	-0.02 (-0.1 0.05)	0.0 (-0.1 0.1)	**0.1 (0.0 0.2)**	0.110
Maximum Impact Rate (BW/s)	Walk	-0.8 (-2.9 1.3)	**-4.0 (-6.8 -1.1)**	-1.7 (-4.8 1.3)	0.294
	Run	-4.8 (-10.5 1.0)	-5.9 (-14.2 2.4)	6.4 (-2.4 15.2)	0.045

Bold values indicate evidence for asymmetry.

[a] Difference in ECC vs. CON group asymmetry at FU. Bold, starred P-values are significant (FDR=10%).

curves show this across the stance phase, and a similar trend during running (Figure 4.3). From this figure, while it wasn't tested statistically, there seems to be evidence of a persistent lack of full extension in the AFF limbs of both groups in walking and running. By inspection, it can be seen that during the late stance (push-off) phase while walking, the participants failed to straighten the AFF knee as much as the UNAFF knee. This can also be seen in the knee flexion moment ensemble average during walking; late stage moment is noticeably higher than in the UNAFF limb, and does not resolve after training. Even though these participants had regained full extension of the knee, this may indicate a residual effect of the limited ROM from early-stage rehabilitation.

Hip flexion angle had similar flexion angle effects during running; the increase in the ECC group was greater than the CON group ($P = 0.010$), the latter which had evidence for no change. For knee moments, there was no evidence of a difference between groups. Thus, the eccentric programme can be seen to be more effective than the concentric programme at correcting deficits in knee and hip flexion angles, while being equivalent at correcting deficits in knee flexion moment.

For the knee abduction moment, no evidence was seen of changes in either group, and no evidence was found for difference between groups. By inspection, this is the case across the whole stance phase (Figure 4.7). Thus, knee abduction moment seems to be insensitive to either type of training. While unexpected, this result can be explained by the fact that the cycle training was in the sagittal plane, and no specific training was done in the frontal plane of motion. This is a disadvantage of using this type of training - it seems that neuromuscular control in this plane was not improved.

Knee valgus angle showed difference between groups in both walk and run, but the effect was the opposite in each case. In walking, ECC group increased more than CON group ($P = 0.021$, $d = 0.47$), and in running, CON group increased more than ECC group ($P = 0.008$, $d = 0.90$). While increased varus angle (reduced valgus) is seen

to reduce risk during drop vertical jumping tasks (double support task), no clinical evidence is available for risk during walking or running.

For hip moment, there were no clear patterns of changes, and no difference between groups. For (internal) tibial rotation angle, both groups showed an increase. This is compared to literature, in four studies during walking [138]. Because the contralateral control had higher values in UNAFF limb than in AFF limb ($P<0.001$), the training can be seen to be normalising tibial rotation in both ECC and CON groups.

Regarding between-limb symmetry, at BL for knee flexion angles, moderate effects ($d=0.76$) are seen in walking, and large effects in running ($>6°$, $d=2.4$). All other variables also showed *moderate* or *large* effect size BL asymmetries (except knee valgus in walking). At FU, knee valgus angle was more symmetrical in the ECC group than the CON group, across the whole stance phase (Figure 4.6). For all other knee and hip biomechanical variables, mean asymmetry was lower or equal for CON group than for the ECC group. Also, for both groups, asymmetries reduced from BL to FU. Thus, concentric training can be seen to have been more effective than the eccentric programme at reducing asymmetries. However, increased asymmetries may also be caused by a parallel change in reference UNAFF limbs. Upon inspection, this is the case for ECC group in knee flexion angle, hip angle, and knee moment, taking into account greater mean changes in ECC group AFF limbs than in CON group AFF limbs.

The investigation into quadriceps avoidance showed a very small decrease in patient numbers from BL to FU. By inspection, there was no discernible pattern of this result. Based on this, quadriceps avoidance was present, but was not a useful concept to distinguish between groups, and these exercise programmes did not result in a noticeable change. Thus, it is not recommended as a useful clinical measure for this context.

4.6.2 Comparison with long-term study, and meta-analysis

The above *rehabilitation* BL results (~3 months post surgery) are compared to the *long-term* results (4-5 years) obtained in the cross-sectional study presented in Chapter 2. In both studies, the population pools are similar; both recruited males in a comparable age group (18-40 as compared to 18-60 years old), with ACL-R performed by the same two surgeons. Control participants were healthy normals in the *long-term* study, and concentric ACL-R controls in the *rehabilitation* study. Where possible, these two studies are compared to the recent *meta-analysis* by Kaur *et al.* [138] in the following paragraphs.

Knee flexion angle

For knee angle in walking, statistical testing showed no differences between ACL-R and healthy controls in the *long-term* study ($P = 0.134$) or the *meta-analysis* ($P = 0.26$ for overall effect). In running, no evidence was found of a difference to healthy controls in the *long-term* study ($P = 0.957$), while the *meta-analysis* showed an overall effect of lower knee angle in ACL-R ($P = 0.05$, $d = -0.49$), but this is based on only two studies, one at 3.3 months, and one at 5 years after surgery.

Looking at between-limb knee angle differences during walking, the *long-term* study showed no evidence of asymmetries ($P = 0.214$), while in the *rehabilitation* study at BL there was strong evidence for difference of -7.6° (95%CI: -8.6, -6.7), $d = 2.4$. This effect size is larger than in the *meta-analysis*, where the overall effect was $d = -0.61$, starting from a similar value of $d = -2.0$ for 2 weeks after surgery, and decreasing to around $d = 0$ for long-term studies later than 2 years after surgery. Thus these data agree well on the effect sizes at the start of rehabilitation, and the reduction of asymmetries in the long-term.

Inspecting the hip and knee ensemble average curves in the two studies over the stance phase during walk and run, the shapes correspond well. However, there is

a noticeable static offset, with values for the *long-term* study being lower than the *rehabilitation* study BL values. This could be from variations between ACL-R groups, or from measurement differences; a different investigator placed reflective markers in each study. These differences, comparing absolute values between studies, are not unusual in terms of the differences seen in studies in the *meta-analysis*.

Knee flexion moment

Considering plots of stance-phase knee flexion moments between the *long-term* study (Chapter 2, Figure 2.3) and this *rehabilitation* study (Figure 4.3), very similar results were observed compared to each other in shape and amplitude. In walk, peak AFF limb values were 0.42N.m/kg/m compared to 0.35N.m/kg/m, respectively. Comparing these to the *meta-analysis*, this was a common range of values: 12 out of 19 studies reported knee moment in the range [0.3; 0.5] N.m/kg/m. Compared to healthy controls, no differences were found in the *long-term* study in walking ($P = 0.629$). Even though the *meta-analysis* showed an overall difference compared to controls ($P < 0.001$, $d = -0.43$), this was made up of 7 out of 10 studies that did not show a difference and the effect size is small, so this result is not surprising. In running, the *long-term* study showed no differences from controls ($P = 0.839$), which agreed with the overall effect of the meta-analysis ($P = 0.06$, d = -0.48), although this was made up of only 2 studies, one of which showed a large difference, and one which did not show any.

Between-limbs, the *long-term* study showed no difference in knee flexion moment during walking ($P = 0.208$), and during running, a *large* effect size difference was found of -0.15N.m/kg/m ($P = 0.001$, $d = -0.91$). In the *rehabilitation* study, differences at BL were found for walking and running, both with $d = -0.9$, a very similar, large effect size. In the *meta-analysis*, during walking the overall effect size found is $d = -0.36$ ($P < 0.001$), with a range of [-0.90, 0.06], so the findings of the *long-term* study and *rehabilitation* study at BL were at the upper end of this range. Thus, it seems that the

long-term study suggests that asymmetries in knee moment resolve over the long term during walking, but not in running.

Knee abduction moment, valgus angle, tibial rotation

For knee abduction moments, between-group comparisons to healthy controls showed no difference in the *long-term* study during walking ($P = 0.373$), and large effect size during running ($d = -1.16$). While the overall effect in the *meta-analysis* did show evidence of difference ($P = 0.05$), the effect was small ($d = -0.22$).

Between-limbs deviations in the *rehabilitation* study at BL were large during walking ($d = -1.0$), and during running were 0.54N.m/kg/m, a very clinically large result, with a large effect size ($d = 2.3$). In the *long-term* study these were small during walking ($d = -0.44$), and moderate during running ($d = -0.62$), both giving evidence that these differences resolve over time. In the *meta-analysis*, evidence was found for a small overall effect during walking ($d = -0.25$, $P = 0.04$), but there was no visible trend over time. The very large BL deviation in the *rehabilitation* study is a approximately -40%, a similar percentage deficit found in the *long-term* study. Interestingly, the *meta-analysis* did not find any studies comparing knee abduction moment during running.

In the knee valgus angle, the two studies resulted in similar values, but small differences make conclusions difficult. In the *long-term* study, the ACL-R values were lower (more valgus) compared to control or contralateral, by about 0.7° in both walk and run. In this *rehabilitation* study, values of the ACL-R limb were 0.5°-1.5° lower (more valgus) than contralateral at BL, but this wasn't consistently the case at FU, possibly due to different effects of training type.

Tibial rotation was not reported in the *long-term* study. In this *rehabilitation* study at BL, a between-limbs internal rotation deviation of -6.8° was found during walking ($d = -1.28$), and 10.9° during running ($d = -2.2$). These were larger than those found

in the *meta-analysis*, which had an overall effect of $d = -0.74$ ($P < 0.001$, range -0.46, -1.03).

4.6.3 Impact dynamics

During running, for both peak vertical GRF and initial impact rate, statistical tests of changes BL to FU show that the CON group rises more than the ECC group. These can be seen in the vertical GRF curve for the AFF limb in Figure 4.2 above. Because at BL these variables are lower for the AFF limb compared to UNAFF limb, it may be expected that concentric training promotes symmetry better than eccentric training. From Table 4.7 above this is seen for initial impact rate during running, but not for peak vertical GRF, because the values for UNAFF limb drop at the same time. While reference values are not available for these variables, lower values were seen in control participants compared to ACL-R participants in the long-term study for females [24]. This is seen to be beneficial due to reduced impact transient on the heel, which has been associated with tibial stress fractures in runners [169].

From step length asymmetry, UNAFF limb step (i.e. during AFF limb stance) is longer at BL. In the ECC group this does not change at FU, while symmetry is restored in CON group ($P = 0.002$). This would make sense in light of the higher impact results seen for UNAFF limb, as a longer step length for the same running speed, would tend to promote heel-strike, and an associated higher impact.

During walking, there was no evidence for change in impact variables for either group, and statistical tests between ECC group and CON group yielded no evidence of difference between groups. Walking is a lower-impact activity, without an initial impact peak; thus statistical testing of these variables during walking has less power to demonstrate differences in ACL-R individuals.

A limitation in this study of impact dynamics, especially for maximum impact rate, is that the filtering frequency would affect the values obtained. This makes comparison

to values obtained in other studies difficult. An investigation of this effect has not been seen in the literature, but it would seem that *relative* sizes using the same methods would still show differences between limb groups, even if *absolute* values are difficult to compare.

Comparison to long-term impact results

As discussed above for knee and hip variables, these impact variables can be compared to those recorded during the *long-term* study presented in Chapter 2.

During walking, at BL the *rehabilitation* study mean initial rate for the AFF limb was 9.1BW/s (95%CI: 8.3, 9.8). This 95%CI includes the values for AFF limb *long-term* after surgery, 8.52BW/s, and for healthy controls, 8.56BW/s, which suggests that the values are relatively stable. At FU, values for both ECC group and CON group dropped to very similar mean values (8.5 and 8.3BW/s), showing that the training had the effect of bringing both groups closer to mean values seen in healthy normal controls. For UNAFF limb at BL, this *rehabilitation* study mean can be calculated to be 9.7BW/s compared to the *long-term* values of 8.62BW/s, and values for healthy control of 8.56BW/s. At FU, mean values for ECC group UNAFF limb was 8.6BW/s and CON group was 9.3BW/s. Thus, the eccentric training program was more successful at normalising UNAFF limb to long-term and healthy normal values.

For running, at BL the *rehabilitation* study had initial rate values for AFF limb of 69.7BW/s (95%CI: 62.4, 77.0), while for the *long-term* study, AFF limb mean values were higher, at 122.4BW/s. The same was seen for UNAFF limbs (75.2BW/s vs. 123.0BW/s). In healthy control participants in the *long-term* study, values were 25% higher (153.3 vs. 122.4BW/s, $P = 0.003$). Thus, it may seem that rehabilitation raises this variable towards *long-term* and healthy normal values. This would support the CON group over the ECC group, which raised this value from BL to FU. However, when comparing this result to a similar long-term study in females [24], in that study healthy controls had

lower mean values than ACL-R (65.8 vs. 82.8BW/s, $P = 0.01$). This confounding this conclusions that can be drawn from this variable during running.

Comparing peak vertical GRF values between the studies, this *rehabilitation* study had BL mean values during walking and running of 1.11BW and 2.30BW, respectively, only changing at FU in the CON group during running, by +0.10BW ($P = 0.003$). In the *long-term* study, AFF limb mean values were 1.07 and 2.39BW, and healthy controls had similar mean values (1.07 and 2.40BW).

For peak GRF between-limbs, the *rehabilitation* study had BL differences of -0.09 and -0.18BW, which reduced to approximately half for both groups at FU (no evidence for difference between groups). The *long-term* study showed mean between-limb differences of 0.0BW ($P = 0.730$) and -0.08BW ($P = 0.015$) during walking and running. Thus, in general, AFF limb values changed toward the *long-term* and healthy control values during running in the CON group, while in the ECC group, this difference remained. Between-limb values at FU showed the training was successful in restoring symmetry for both ECC group and CON group to *long-term* values.

The maximum impact rate was reported in both trials. While this is an easy value to calculate from the vertical GRF, it differed by large amounts, making comparison difficult. Walk and run values at BL in the *rehabilitation* trial were 23.2 and 120.2BW/s, respectively, while in the long-term trial they were 51.2 and 228BW/s. These differences may be from a different filter frequency used between trials, group differences, or the difference between barefoot (long-term) and shod (rehabilitation) trial conditions. In summary, this variable is not recommended as a stable comparison, and the initial impact rate should be used instead.

4.6.4 Trunk biomechanics

Trunk angle for running was 8.6° more forward leaning than walking. At FU, for both walk and run conditions, the direction of change was the same (ECC group further

forward than CON group), but a difference was only seen in running, by 1.8°. Between-limbs at BL, participants leaned 0.5° forward in both walk and run during stance on the AFF limb compared to UNAFF limb. Forward leaning is typically seen to favour the hip musculature over the knee, so this result makes sense in light of the relative knee weakness in the AFF limb. At FU, asymmetries were no longer observed, except for a difference for ECC group during running of 0.9°. After training, both groups walked with a reduced spine flexion (straighter back), with no difference between groups.

For the thorax lateral lean, statistical testing showed a difference between groups at BL, likely due to different self-selected pose. Thus, the assumption of a pooled BL was not valid, and the remaining statistical tests were not performed. Lateral spine angle did not show evidence of a change in either walk or run, and no difference was found between groups.

From the above data, trunk kinematics can give a more complete picture of the strategies and adaptations, but pose, and small angular differences may make interpretation difficult. It is likely that trunk data would be more useful in an explanatory model, to attribute sagittal or frontal plane movement strategies in these patients to change lower limb moments.

4.6.5 Study limitations

Limitations in this study included lack of a uninjured control group that participated in the intervention study. ACL injury may result in specific differences in response to eccentric or concentric training as compared to the response of healthy individuals. However, the primary question was the clinical comparison of eccentric with concentric training using a matched studio, equipment, and perceived exertion.

An additional limitation is the single follow-up test period, which does not quantify the long-term effect of the training, and whether the observed changes are maintained, or are subject to compounding or wash-out effects. While other physical activity

performed voluntarily by the patients has been previously reported in Chapter 3, and was not found to be very different between groups, the above data were not adjusted for this effect. In addition, no analysis was done to quantify the effect of dominant vs. non-dominant limbs in this study.

This study investigates biomechanical and impact variables, but a further limitation is that it does not include a study of neuromuscular control effects using EMG. Further work may explain some of the differences by investigating passive vs. active control of the joint, for instance.

4.7 Conclusion

The *a priori* hypothesis of this study that biomechanical deviations can be effectively reduced by eccentric training as compared to concentric training, particularly for knee and hip flexion angle and moment, knee abduction moment and valgus angle, and tibial rotation angle, and impact measures. These have previously been established to differ from the contralateral limb and controls in general, and remain long-term after surgery in males, as demonstrated in the study in Chapter 2, indicating chronic changes in joint loading. No *a priori* hypotheses were proposed for trunk angles, but these were reported as possible explanatory variables.

In the sagittal plane, this study showed greater mean increases in knee and hip flexion angles for the ECC group for walking (moderate effect size) and running (large effect size) compared to the CON group. Statistical testing showed that these differed between groups in knee flexion angle during walking, and hip angle during running. Thus, partial evidence for this hypothesis was found. For the similar hypothesis regarding knee and hip sagittal plane moments, knee moments increased for both groups in both walking and running, but no evidence was found for a difference between groups. Hip moments did not show evidence for a change from BL to FU, or a difference between

groups. In this population, quadriceps avoidance was present, but it did not provide a useful clinical metric for this population.

Sagittal plane asymmetries in the hip and knee angles and moments showed no differences between ECC group and CON group at FU. However, at this point mean asymmetries for these variables were larger for the ECC group than the CON group. This is seen to be from a greater effect of the eccentric training on the UNAFF limb, because it has been shown above that the eccentric programme had an equal or larger effect on the AFF limb toward the UNAFF limb values.

In the frontal and transverse planes, change in knee valgus angle was different in the ECC group compared to the CON group in both walk and run, but the effect size was small in both cases, meaning that the clinical potential is limited. The knee abduction moment did not show any change from BL to FU, or difference between groups. Knee tibial rotation increased in both groups, which seems to indicate a change in the rotational control at the knee; further study is required to clarify this.

Asymmetries in the frontal and transverse planes showed large effect sizes in knee abduction moment at BL, giving evidence of deviations in medio-lateral control for these patients. At FU, both groups still had asymmetries, with CON group being smaller than ECC group during walk and run, but there was no evidence for a difference between group changes. Thus, this type of training was not effective in reducing this deviation, and this is a key limitation of this type of training. In knee valgus, mean asymmetries for ECC group were smaller than the CON group, which was seen to be beneficial. However, during running, CON group had larger positive asymmetry, meaning that concentric was more effective than eccentric training at promoting a positive valgus angle in the AFF limb. Knee tibial rotation asymmetry during running for the CON group was around half that of the ECC group at FU, which favours controls.

In the exploratory analysis of trunk data presented, the ECC group ended with a more forward trunk than the CON group during running. Other results were mixed and

inconclusive, made difficult by differences between the two groups at BL, particularly for the lateral thorax angle.

Looking at impact at foot-strike, results showed a reduced impact in the AFF limb for the ECC group as compared to the CON group. Peak GRF asymmetry remained in both groups, and initial impact asymmetry results were mixed.

In summary, the cycle training, which was in the sagittal plane, had the largest effect on sagittal-plane kinematics, with the (higher-torque) ECC group programme having a greater effect than the (lower-torque) CON group programme. Asymmetries were reduced in both programmes, but follow-up asymmetry remained higher in the ECC group than the CON group, likely due to a greater parallel effect on the UNAFF (reference) limb. In sagittal plane kinetics, knee moments increased for both groups, reducing asymmetries, and hip moments showed no changes, and no consistent change in asymmetry. In other planes, comparing groups, changes were either neutral or mixed, with no clear biomechanical benefit to one group over the other. Asymmetries were also mixed in the direction and size of effect, except for knee tibial rotation, where the CON group was more symmetrical at FU than the ECC group.

Thus, the eccentric cycle training programme can be recommended for reduction of biomechanical deviations in the sagittal plane. In the frontal plane, reduction of knee abduction moment asymmetries were not different between the intervention or control group. In general, no detrimental biomechanical effects were observed for these patients in either of the groups tested. These findings support the argument that the intervention is clinically effective and safe for the ACL-R male population during this phase of rehabilitation.

Chapter 5

ACL-R eccentric vs. concentric cycling: the effect on patient risk and return-to-sports

A key clinical task is return-to-sports (RTS) clearance, to evaluate when the patient's risk is acceptably low to recommend that the person is ready to return to sporting activity. There are a wide variety of clinical criteria after anterior cruciate ligament (ACL) injury, based primarily on expert opinion which combines subjective and objective measures. At present there is a lack of clinically-relevant objective tools, standardisation and even clear definitions of terms used in return-to-sports (RTS) [18]. This is primarily because of a lack of evidence to show a test to be directly indicative of risk. This randomised controlled trial (RCT) aims to contribute to this knowledge by evaluating eccentric training for anterior cruciate ligament reconstruction (ACL-R) using several RTS criteria which are available.

5.1 Literature review

This literature review covers the testing and criteria used at follow-up (FU) testing (~6 months), to assess the safety and effectiveness of the eccentric cycling programme. These results are compared to baseline (BL) values, published values, and similar testing from active control (concentric) participants. The focus is on evaluation of risk and RTS readiness - this review summarises the available evidence at this time. Further literature for patient-reported outcomes (PROs), strength, and gait biomechanics has been discussed in detail in Chapters 2, 3, and 4.

5.1.1 Consensus outcomes

With respect to successful rehabilitation outcomes, a recent review by Lynch *et al.* [101] interviewed over 1700 clinical professionals in various related fields to identify consensus indicators of a *successful ACL-R surgical outcome* (recommended by >80% of clinicians). In order from highest consensus, the six that were identified are:

- absence of knee joint giving way
- return to sport (participation)
- symmetrical quadriceps muscle strength (structure and function)
- the absence of knee joint effusion
- symmetrical hamstrings muscle strength (structure and function)
- PROs with clearly defined thresholds for success (activity and participation).

Other non-consensus criteria (<80%) identified in this review were: functional tests (75.4% agree), negative pivot-shift (77.8% agree), laxity <3 mm (72.9% agree), and absence of radiographic osteoarthritis (36.5% agree). In the discussion, despite a lack of consensus, functional testing was defended as a standardised, low-cost method of

simulating on-field performance. The lack of predictive power of common clinical tests may be the reason for their lower consensus status. For pivot shift and laxity, it was discussed that these have not been successfully correlated with functional performance after injury. Thus, the authors question why they are still used in the literature and clinical practice as important measures of successful outcome after ACL injury [101]. The lack of consensus around radiographic osteoarthritis (OA) was explained due to the relatively short time-frame (1-2 years) in question, compared to the common time frame for the development of OA in ACL-R patients.

Despite this relatively strong support for objective, criteria-based RTS, it is not common in practice, even in the research environment. This can be seen by results of a systematic review (level IV evidence) by Barber-Westin and Noyes [170], where only 13% of research studies (35 of 264) reported objective criteria for RTS. In another systematic review by Harris *et al.* [171], a similar result was found; only 10% of studies (5 of 49) reported objective criteria for RTS.

Objective measures are likely to become more common as they are validated, standardised, and shown to be clinically cost-effective, and the underlying risk factors are better understood. In the short term, this requires systematic review of published group means and criteria-based data, with correlations to highlight associations between them. While data in registries such as the Swedish ACL Register can give valuable data on the rates of revision surgery [172], and contralateral injury [173], there are very limited objective outcome measures reported at present. In the longer term, larger prospective studies will be needed to better answer these questions.

5.1.2 Patient reported outcomes

Patient reported outcomes are questionnaire instruments used to quantify the patient experience. Further details relating to choice of PRO questionnaires in this study are

given in the literature review in Section 3.2.2.2. The following literature are specifically related to the use of PROs to assess patient RTS readiness.

In the study discussed above by Lynch *et al.* [101], the use of PROs was found to be a consensus outcome. The study further performed a breakdown of PRO instruments, asking clinicians which instruments they thought were important, and not important. The Knee injury and Osteoarthritis Outcome Score (KOOS) and International Knee Documentation Committee (IKDC) questionnaires were among the highest-recommended. The study also recorded scores used by clinicians to categorise successful outcomes. For IKDC, median threshold and inter-quartile range (IQR) was 90 (IQR: 80, 90), and for KOOS they were 85 (IQR: 80, 90). The Global Rating Scale (GRS) and KOS-ADLS had similar recommended median threshold scores of 90 (IQR 90, 90) and 90 (IQR: 80, 90), respectively.

In the Swedish national ACL register, KOOS was used. Pre-operative, and post-operative mean values are given for 1, 2, and 5-year follow up [107]. At 1-year, they are: Symptoms, 78.2±17.6, Pain, 85.0±15.4, ADL, 91.8±12.9, Sport/Recreation, 65.3±27.4, Quality of Life (QOL), 60.2±24.2. In a clinical review of PROs at RTS by Lepley [118], gives self-reported deficits at 6 months post-reconstruction using a range of questionnaires from 8% to 24%, with a mean of 14%. For IKDC in particular, the average deficit was 19.3% (5 studies), and the one study that focused on hamstring-grafts only (34 patients), had a deficit of 25%.

While the above studies give indicative thresholds and references values for comparison, they are difficult to use for analysis. No stratification was performed by age or gender, and they lack detailed description of patient percentiles or minimal clinically important differences. Also, threshold values have not been correlated to risk. This means that it is difficult to evaluate the status of a patient or group, or comment on clinical change due to an intervention.

The only PROs that have been used for RTS were the GRS and KOS-ADLS, in RTS evaluation as part of the University of Delaware's return-to-activity criteria [61, 174, 175, 176], and in clinical protocols [177]. While they were not recorded directly in this trial, they could be approximated after-the fact, using a method discussed in Section 5.2.1 below. An addition, a method which predicted RTS using the IKDC was found by Logerstedt *et al.* [175], which found that scores below the 15th percentile of the age- and gender-specific data were good at predicting passing the return-to-activity criteria (RTAC). Thus, the approximation of the University of Delaware criteria, and IKDC 15th percentile cutoff are used as criteria to evaluate RTS for the patient groups involved in this study.

5.1.3 Strength metrics

Symmetrical quadriceps and hamstrings strength and size are consensus outcome measures of successful rehabilitation (see Section 5.1.1 above), and are commonly quantified measures in assessing RTS, as the quadriceps index (QI) and hamstring index. However, the consensus threshold of limb symmetry index (LSI) >90% [101] is based primarily on clinical experience, and not prospective RTS or injury-risk data, and direct evidence of correlation with either of these is scarce. This has been shown in a recent systematic review by Undheim *et al.* [178], with the authors also highlighting the need for standardised protocols to allow consistency of research. In the one prospective study available, Myer *et al.* [179] tested females for strength before injury, and found no difference in quadriceps or hamstring strength between subsequent ACL injury and matched female controls. This suggests that strength is not a predictor of ACL injury in females. An additional finding was a difference in hamstring strength compared to matched male controls, suggesting that this may partially explain the higher ACL injury risk in females.

Abrams *et al.* [120] performed a systematic review of strength measures after ACL-R. Isokinetic knee extension and flexion peak torque LSI values were by far the most commonly reported. At 6-months, hamstring-graft ACL-R patients had extension LSI of 77±SD14 and flexion LSI of 84±SD11 at 60°/s (10 studies each). At 120°/s, the second speed used here, there were unfortunately no studies of hamstring-grafts only, which limits direct comparison. At 180°/s, the values were extension LSI of 89±SD8 and flexion LSI of 86±SD4. These provide good starting values, but the study doesn't provide detail on how the average and SD was calculated, only saying that *descriptive statistics* were used. Shortcomings in this review were that no attempt was made to evaluate studies on quality or risk of bias, or scale the results on numbers of participants.

The other strength measure which is widely used is the hamstring-quadriceps (H/Q) ratio, to assess the balance of strength around the joint. One use of the H/Q ratio in calculating risk was a nomogram developed by Myer *et al.* for female patients [180], where the inverse, the Q/H ratio is used. Values between 0.6 (0 points) and 3.0 (20 points) are shown, which increase the total points, which is scaled against a *probability of high knee load* scale. While this method is clinician-friendly and would be helpful in developing RTS criteria, it was developed specifically for young females, including risk factors such as *tibia length*, a maturational factor. Thus it was not utilised here, as the risk model would be very different for adult males.

A systematic review of healthy normal H/Q ratios for different isokinetic speeds, stratified by sex, was performed by Myer *et al.* [179]. It found that H/Q ratio increases with isokinetic speed for males, but not for females. For the current study, using the raw values for the trials of healthy males at 60°/s and 120°/s, target normal values are calculated in Section 5.2.2 below. In this study, mean and 95%CI of the measured H/Q ratio will be compared to these calculated healthy normal target values from literature.

Strength correlated to other metrics

In the absence of risk models, correlation of strength measures to patient-reported, biomechanical, and functional outcomes helps to understand clinical similarities and differences between these outcomes. An early study of correlation of PROs, quadriceps strength and function was performed by Wilk *et al.* [181], using data from a group of 50 male and female patients. It showed a positive correlation between isokinetic quadriceps strength and hop tests (at 180°/s, 300°/s, 450°/s, $P<0.01$, $r = 0.41$-0.69), with the strongest correlation at the lowest speed. Correlations were also found for knee extensor peak torque and PROs, but only at the slowest speed of 180°/s ($P = 0.01$, $r = 0.71$). Interestingly, no correlations were found for hamstring peak torque with hop testing or PROs.

PROs are a potential screening tool for strength, where the former can more easily be applied in a clinical setting. Zwolski *et al.* [182] correlated low vs. high IKDC scores at RTS to isokinetic quadriceps strength and QI. They found that an IKDC score >94.8 predicted QI>90% with high sensitivity (0.813) and moderate specificity (0.493).

In jumping and landing biomechanics, which have been seen to be associated with re-injury risk, strength deficits seem to play a role. In a longitudinal study at 12 months post-surgery [161], landing biomechanics had still not normalised, and it was shown that weakness played an important role in these alterations. In other studies, quadriceps strength has been correlated with single leg landing dynamics [183], reduced strength with reduced knee valgus control in young females [184], strength with landing error score (LESS) [185], and quadriceps strength with landing symmetry [186] and movement patterns [187] during a counter-movement jump. However, the use of correlations does not necessarily imply clinical usefulness, with some researchers claiming that predicting strength from hop tests is not viable [188].

From the above results, it is still recommended that strength and strength symmetry still be used where possible. This is particularly important for predictive studies, where

risk of subsequent injury is an outcome measure. In this study, strength, PRO, and functional tests are all used to give a comprehensive evaluation of these patients' rehabilitation.

5.1.4 Functional testing

Functional testing uses standardised tasks to test whole-body motions. Symmetry is an important concept used in evaluating these tasks, either in distance, height, or time taken to perform a task. Most commonly, these involve jumping and hopping tasks; a wide range of tests and outcome measures have been found in the literature, as described in Abrams *et al.* [120]. In another recent systematic review, it was shown that there is limited and conflicting evidence regarding the reliability, agreement, construct validity, criterion validity and responsiveness of eight commonly-used performance tests [189]. For the tests used in the current study, the review only covers single hop for distance and triple crossover hop tests in detail. The above shortcomings limit the conclusions that can be drawn from results of the following tests.

Drop vertical jump test

Of the functional tests to evaluate RTS, the drop vertical jump (DVJ) is a key test that has shown clinical usefulness in evaluating ACL injury risk and the effect of training, particularly in female patients [190, 191]. However, double-limb tasks may mask differences clinically, as additional strategies of unloading the limb are possible [13], meaning that it is probably best combined with other single-limb tests. It safely applies a higher Ground Reaction Force (GRF) than during gait or hop testing, and simultaneous testing of both limbs allows convenient evaluation of differences. Using 3-D motion capture and force plates, the reliability and validity of outcome variables has been shown [192]. These include knee abduction moment and angle, GRF, knee and hip flexion angle.

While prospective data is limited, in female athletes excessive knee abduction moment from the DVJ test has been shown to predict ACL injury with a sensitivity of 78% and specificity of 73% [33]. In another study to predict re-injury in ACL-R patients [137], a logistic regression model of four variables predicted second injury with excellent sensitivity of 92%, and specificity of 88%. However, a recent systematic review has shown that knee abduction moment in females to be consistently higher than males in many weight-bearing tasks [193]. This may be associated with females' higher injury risk, and suggests that high knee abduction moment deviations may be less important for males.

Comparing ACL-R affected limbs to controls and the contralateral limb after RTS in females, lower GRF and GRF loading rates, as well as lower take-off GRF production have been shown [48]. This was also found by Paterno *et al.* [194], which additionally found no difference between sexes. Schmitt *et al.* [186] showed that ACL-R patients with lower quadriceps strength had impaired landing biomechanics as compared to controls, while those with higher strength had no difference from controls.

To reduce the cost of the above 3-D methods for clinical application, several approaches have been used. Multiplanar 2-D video methods have been used to measure knee valgus movement and flexion angle for young females [180, 195, 196], during development of a risk assessment tool. Another method correlated frontal-plane measures to knee abduction moment using 3-D motion capture, obtaining 'favourable' correlations ($r > 0.59$). However, despite the authors recommending these be included in large-scale studies, this less-than-ideal correlation can mean that the predictive power of these measures is very low, and remains to be demonstrated. To improve on this, it has recently been shown that a single depth camera (Microsoft Kinect®) could give more accurate results for a similar cost [197]. In addition to these kinematic methods, methods using clinical evaluation of landing errors have been developed, as discussed below.

Landing error scoring system

As a clinical alternative to 3-D motion capture, the Landing Error Scoring System (LESS) has been developed. It uses multi-planar sagittal and frontal plane video recordings to score errors using 17 criteria. Its validity and interrater reliability have been shown in a large cohort (2691 participants) of healthy military recruits [198]. This study did not investigate subsequent ACL injury, but it did show that using this tool, females had poorer landing biomechanics than males, suggesting agreement with the generally higher risk of ACL injury in females.

Chimera and Warren [199] provide a clinical review of the LESS to predict sports injury in general. They describe a factor analysis that was performed on the large cohort described above, which showed that females tend to have higher errors in the frontal plane, while males had higher errors in the sagittal plane.

The LESS has also been used to evaluate ACL-R cohorts. In terms of predicting ACL injury, a recent review showed that, thus far, one study has showed predictive power one did not [199]. Bell *et al.* [160] showed that ACL-R participants had higher LESS scores than controls (+1.1 errors, $P = 0.04$), and particularly high difference in the criterion for trunk flexion ($P = 0.002$). Kuenze *et al.* [185] performed a similar study, finding that the ACL-R group had 3.2 errors more than the control group ($P = 0.002$). Maximal voluntary isometric contraction was also measured, and found to be correlated with a lower LESS score, but only in the injured limb (r = -0.455, $P = 0.03$).

For faster clinical evaluation, Chimera and Warren [199] describe a 10-item *real-time* version utilising four jumps, the LESS-RT, but this only has one small reliability study available thus far. An even shorter test with 5 items, which they called the *iLESS*, also only has a single study and also requires further validation. In a similar approach, an 'abridged LESS' has been used as part of the Melbourne RTS score (MRSS, discussed below). It only contains 5 elements of the 17 in the full LESS described above, and is scored during the test, not using video recordings. This may seem attractive, but

despite literature searches, no evidence could be found for its development. Another concern is that the items used, while similar to the LESS items, are not used verbatim, reducing validity. Also, on further inspection of data for individual items in Kuenze *et al.* [185], the 5 selected do not seem to align with the most common errors, or noticeable differences from controls. Thus, while results for the 'abridged LESS' is reported here, these were done only for the purposes of calculating the MRSS. This lack of evidence means that it (and the MRSS) do not allow clear conclusions to be drawn from this data.

Hop tests

Hop tests are the most commonly used clinical functional criteria for RTS. Abrams *et al.* [120] performed a systematic review of the literature, which gives normative data for different types of tests. The single-leg hop for distance was the most commonly reported, with around 30 studies; at 6, 9 and 12 months, values reported were 87±6, 90±2, and 92±2, respectively. The cross-over hop, triple hop, and 6-meter timed hop had about half as many reported studies. For the cross-over hop test, values at 6, 9, and 12 months were 90±4, 91±3, and 92±3, respectively. However, similar caution is recommended for these numbers for reasons described in Section 5.1.3 above, because the methodology in this systematic review is not well documented, resulting in a risk of bias.

Star excursion balance test

The star excursion balance test is recommended by several clinical protocols [58, 176, 200] and recently reviewed by Chimera and Warren [199]. It does not yet have a strong evidence base, or norms developed for ACL-R patients. However, a promising recent study used Y-balance anterior asymmetry >4cm at 12 weeks to identify those who failed single-hop LSI >90 at 6 months with a sensitivity of 96% [201]. Prior to this,

studies show less clear outcomes. In 2013, De la Hunt *et al.* [202] compared test results between-limbs of ACL-R female athletes, showing strongest effect size differences in the posterio-lateral and posterio-medial directions. In 2012, a review article on its use in various pathologies only found one cross-sectional trial of anterior cruciate ligament-deficient (ACL-D) patients [203]. The test was used here as a low-cost, easy-to-implement balance test that is part of the MRSS (see below), but these results should be used with caution in light of the above lack of evidence.

Squat-to-fatigue testing

Several attempts have been made to quantify closed kinetic chain functional strength of the knee for clinical use, as compared to open kinetic chain measured by the isokinetic dynamometer. In the MRSS used below, a squat-to-fatigue test is prescribed. However, the motivation for its inclusion was not explained, and thus should be used with caution, as discussed further below.

5.1.5 Combined RTS scores

University of Delaware criteria

In 2000, Fitzgerald *et al.* [204] developed RTS criteria for non-operative treatment of ACL injuries. These criteria, often known as the University of Delaware return-to-activity criteria (RTAC), involve passing all four testing domains - 2 PROs (KOS-ADLS and global rating score), a set of hop tests, and QI >90%. Interestingly, hamstring index was determined not to be necessary. These criteria (also known as SKIPP) have been subsequently used in ACL-R patients in large studies [83, 205], and have been recommended as part of a clinical protocol [61]. They were used here as described below in Section 5.2.4, as the only set of criteria that were found to have a pre-determined cut-off point, indicating readiness for RTS.

Melbourne Return-To-Sports Score

In an attempt to integrate clinician assessment, PROs, and functional testing, the Melbourne Return-to-Sports Score (MRSS) has been proposed. It has been shown that in a study of 94 patients, those who returned to sports had significantly higher MRSS [206]. The PRO used is the IKDC, which has been discussed above. Functional testing, which forms 50% of the final MRSS, implements the DVJ, two hop tests, Y-balance and a squat-to-fatigue test.

5.2 Methods

The methods used in this chapter for PROs and strength testing have been previously described in Chapters 3 and 4; only the additional methods used here are described below. Outcome measures are those linked to patient risk and progress towards RTS.

5.2.1 Patient reported outcomes

Full PROs for this randomised controlled trial, IKDC, KOOS, and SF-36, have been reported in Chapter 3, at BL and FU for each of the groups. However, RTS or risk thresholds in these outcome variables are not common in the literature.

The KOS-ADLS >90 has been used as a RTS criterion by several researchers, as described in the literature review above. While this metric was not captured directly, the content of the KOS-ADLS questionnaire overlaps closely with 8 items found in the KOOS activities of daily living (KOOS-ADL) and KOOS-Symptoms subscores. The former has 6 Likert levels, and the latter 5, but the scoring methodology is the same. Thus, a substitute calculation of KOS-ADL was performed, to give an indication of the number of patients that would pass that criterion.

Similarly for the Global Rating Scale (GRS), this was extracted from the last two questions of the IKDC questionnaire. The one asks the patient to rate their pre-injury

knee function out of 10, and the other asks them for their current estimate of their knee function, also out of 10. The score for current function was divided by the pre-injury score, and values >90 were considered above the threshold for RTS for this criterion.

The IKDC questionnaire score was utilised in two ways. It formed 25 points of the MRSS, described in Section 5.2.4 below. In addition, patient scores were compared to age-specific healthy thresholds using the rationale of Logerstedt *et al.* [175], which found that scores below the 15th percentile of the age- and gender-specific data provided by the IKDC were good at predicting passing the RTAC. For the male patients in this study, values were 89.7 for 18-24 year olds, 86.2 for 25-34 year olds, and 85.1 for 35-50 year olds. The number of patients that were above these values are used as a stand-alone RTS criterion.

5.2.2 Strength and thigh volume

Using the consensus criteria in Section 5.1.1above, hamstring and quadriceps *function* was measured by isokinetic strength testing. Full details have been reported in Chapter 3 at BL and FU for each of the groups. Here, the number of patients above the consensus threshold of LSI >90 are reported, to see how many had successful rehabilitation by this criterion. In addition, the median score is reported, i.e. the LSI threshold which 50% of patients in each group would pass. Hamstring and quadriceps combined *structure* was measured, using lean thigh volume - without imaging data, it was not possible to separate these results into hamstring or quadriceps muscle groups.

H/Q ratios were calculated by dividing hamstring by quadriceps peak concentric torques for the 60°/s and 120°/s conditions. Based on the regression model developed in Chapter 3, the 95%CI of the mean H/Q for the affected (AFF) and unaffected (UNAFF) limbs were calculated. Target H/Q ratios for healthy males were calculated from the studies reviewed in Hewett *et al.* [207] where the ten studies that reported 60°/s results for males were averaged (952 total males from 10 studies) to give a value of 57.2% as

a target; at 120°/s, 5 studies reported results (185 male patients), giving an average H/Q ratio of 51.9%.

5.2.3 Functional testing

Functional testing was done using common hop, jump, and balance clinical tests to evaluate readiness for RTS. These tests also form part of the MRSS, described below in Section 5.2.4. Tests were performed by the principal biomechanist performing this study. However, he is not a clinical practitioner in these tests, which may limit the interpretation of results.

For the single-leg hop test and triple crossover hop test, they were performed twice with each limb, after a warm-up test. The average of these hop distances was taken, and the LSI calculated. For the single hop test, patients placed their hands on their hips, and for the triple hop, their hands were free. Errors were discarded, and the test performed again until two successful distances were obtained with each limb.

For the Y-balance (star excursion) test, the toe of the test limb was centred on the intersection of the Y. Maximum reach with the toe of the contralateral limb in the anterior, postero-lateral (45°), and postero-medial (45°) directions were taken, and averaged for each limb, and the LSI calculated as above. For the squat-to-fatigue test, single-leg squats were performed at a rate of 2s down, 2s up, to a point of 90° knee flexion angle, until the patient gave up or lost balance.

For the DVJ test, patients were positioned on a 31cm-high box, with feet 35cm apart. They drop jumped 3-5 times and performed a maximal vertical jump for height in a single motion. They were visually graded by the same investigator for the abridged LESS, using 5 subjective measures, each with a score out of 5 points. Note that during this test, for review and potential further study, motion capture data was also collected, as described in Section 4.4.2.

Using a regression model for scores obtained for these individual elements as described in Chapter 3, mean values at BL and FU, with 95%CIs for the mean were calculated, and differences between eccentric (ECC) group and CON group statistically tested for differences. Statistical significance was set at $P < 0.05$.

5.2.4 Combined RTS scores

The following combined scores from literature were used to evaluate RTS readiness of the patients. While neither of them have been validated for predictive capability, they represent efforts towards standardisation of patient testing.

University of Delaware criteria

The combined University of Delaware RTAC as defined above in Section 5.1.5 were used with the data from this trial. QI was used from Section 5.2.2, 'KOS-ADL' and 'GRS' from Section 5.2.1, and hop test LSI from two tests in Section 5.2.3. Patients who passed >90 on all criteria were defined as a *Pass* at the FU time point.

Melbourne Return-To-Sports Score

The Melbourne Return-to-Sports Score (MRSS) is a combined tool to assess the participant's functional capacity and symmetry by one score, and is not sports-specific. It is a 100-point score, made up of 25-points for the IKDC subjective knee evaluation (described above), 25-points for a clinical examination, and the remaining 50 points made up of clinical functional testing. The clinical exam is performed by the physiotherapist or surgeon, and involves 5 standard evaluations of 5 points each, which are

- Presence of Effusion (5 points)
- Lachman's test (5 points) and Pivot Shift test (5 points)

- Flexion (5 points) range of motion, and extension (5 points) range of motion using the prone hang test

The functional testing consists of:

- Star Excursion (or 'Y') Balance Test LSI (10 points)
- Single Hop Test for distance LSI (5 points),
- Triple Crossover Hop Test for distance LSI (5 points),
- abridged Landing Error Scoring System (LESS): Jump-Land-Rebound Score (25 points), also known as the Drop Vertical Jump (DVJ) test,
- Single Leg Squats to Fatigue LSI (90° knee flexion) (5 points)

The above tests are commonly used individually in physiotherapy practices to evaluate different functional aspects in a clinical setting with little requirement for expensive equipment. The scoring of LSI values has different points allocations for dominant vs. non-dominant limbs. Further information on scoring is published online [208]. Outcome metrics are an overall score (/100), as well as sub-scores of surgeon's and patient's score of function, as well as specific tests to highlight relevant functional aspects.

5.3 Results

The results presented below are a RTS evaluation of the patients in the ECC group and CON group at BL and FU testing points (~6 month after surgery). They use criteria-based evaluation where possible, as described above, and provide average values for group comparison purposes.

Table 5.1: Median PRO scores, with number (%) of patients passing respective thresholds at BL and FU

	BL Median		BL > Ref.[a]		FU Median		FU > Ref.[a]	
	ECC	CON	ECC	CON	ECC	CON	ECC	CON
'KOS-ADL'[b]	88.5	87.0	6 (50%)	2 (20%)	88.5	87.5	6 (50%)	4 (40%)
'GRS'[b]	65.0	65.0	1 (8%)	2 (20%)	75.0	70.0	5 (42%)	3 (30%)
IKDC	73.0	65.5	0 (0%)	0 (0%)	81.0	78.2	3 (25%)	2 (20%)

[a] References: LSI>90 for KOS-ADL and GRS, >15th percentile male age-specific healthy IKDC
[b] As defined in methods section

5.3.1 Patient reported outcomes

PROs for which reference values were determined, median values and number of patients passing threshold for BL and FU conditions are given in Table 5.1. For the 'KOS-ADL' as defined above, median values at BL were 88.5 and 87.0 for the ECC group and CON group, respectively, and 88.5 and 87.5 at FU. At BL, six patients in the ECC group and two in the CON group passed, and at FU, six of the ECC group and four of the CON group passed.

For the 'GRS' as defined above in Section 5.2.4, median values at BL were 65.0 and 65.0 for ECC group and CON group, respectively, and 75.0 and 70.0 at FU. At BL, one in the ECC group and two patients in the CON group passed the threshold, and at FU, five and three patients in each of the ECC group and CON group passed, respectively.

For the IKDC criterion (15th percentile male age-specific healthy scores given above), no patients passed at BL, and three and two patients in each of the ECC group and CON group passed at FU, respectively. Median values were 73.0 and 65.5 for the ECC group and CON group at BL, respectively, and at FU they were 81.0 and 78.2.

5.3.2 Strength, H/Q ratio

Numbers of patients passing LTV and strength LSI >90 at BL and FU are given in Table 5.2. At BL, 83% of ECC group and 90% of the CON group passed the LTV criterion, while at FU they were 83% and 100%. For the Quadriceps test at 60°/s (QI), at BL 0% passed in both groups, while at FU 25% passed in the ECC group, and 40% in the CON group. For the hamstrings test at 60°/s, at BL 17% of ECC group patients passed, and 20% of CON group patients, while at FU they were 33% and 20%, respectively. For other strength test results, refer to Table 5.2.

H/Q ratios are provided in Table 5.3. For example, at BL, the AFF limb had a ratio of 63.2 (95%CI: 52.1, 74.3) and 67.2 (95%CI: 52.3, 82.9) in the ECC group and CON group, respectively. At FU, the ratios were 59.2 (95%CI: 50.9, 68.4) in the ECC group, and 52.8 (95%CI: 44.9, 71.7) in the CON group. The 95%CI ranges of these ratios all contain the 60°/s target of 57.2. The 95%CI ranges were found not to include the target value at 60°/s for the UNAFF limb in the ECC group at BL and FU, as well as for the AFF limb at 120°/s at FU.

5.3.3 Functional tests

Functional test mean estimates and 95%CI at BL, and change BL to FU, are given in Table 5.4. For the single leg hop, values at BL for the ECC group and CON group were 80.5 (95%CI: 65.1, 92.7) and 82.7 (95%CI: 61.1, 90.9), respectively, and from BL to FU these values changed by +6.9 (95%CI: -6.3, 22.3) in the ECC group, and +8.4 (95%CI: -2.0, 21.5) in the CON group. The 95%CI of both of these span zero, meaning that this data does not provide evidence for change in either of the group scores. Statistical testing between groups at BL showed no difference between them ($P = 0.539$). Also, no difference was found between group changes BL to FU ($P = 0.456$). Similar results are presented for the triple hop LSI, Y-balance LSI, Squat-to-fatigue LSI, and DVJ (*abridged LESS*) scores. No evidence was found between groups at BL, nor in difference

Table 5.2: Numbers (%) of patients passing RTS threshold LSI >90 at BL and FU

			LSI >90 at BL		LSI >90 at FU	
			ECC	CON	ECC	CON
Concentric strength LSI	Quadriceps	60°/s (QI)	0 (0%)	0 (0%)	3 (25%)	4 (40%)
		120°/s	2 (17%)	2 (20%)	3 (25%)	7 (70%)
	Hamstrings	60°/s	2 (17%)	2 (20%)	4 (33%)	2 (20%)
		120°/s	2 (17%)	1 (10%)	3 (25%)	3 (30%)
Eccentric strength LSI	Quadriceps	60°/s	2 (17%)	3 (30%)	4 (33%)	6 (60%)
		120°/s	2 (17%)	2 (20%)	3 (25%)	4 (40%)
	Hamstrings	60°/s	4 (33%)	3 (30%)	5 (42%)	4 (40%)
		120°/s	5 (42%)	3 (30%)	6 (50%)	4 (40%)
LTV LSI			10 (83%)	9 (90%)	10 (83%)	10 (100%)
Hop tests	single leg hop		2 (17%)	2 (20%)	4 (33%)	6 (60%)
	triple crossover hop		3 (25%)	3 (30%)	7 (58%)	5 (50%)
	both above tests		2 (17%)	1 (10%)	4 (33%)	3 (30%)

Table 5.3: H/Q isokinetic strength ratios in AFF and UNAFF limbs at BL and FU.

			at BL		at FU	
			ECC	CON	ECC	CON
H/Q ratio	60°/s (target: 57.2%)	AFF	**63.2*** **(52.1 74.3)**	**67.2*** **(52.3 82.9)**	**59.2*** **(50.9 68.4)**	**52.8*** **(44.9 71.7)**
		UNAFF	50.7 (46.3 54.3)	**52.8*** **(45.9 63.1)**	50.8 (46.5 56.4)	**52.7*** **(45.9 60.2)**
	120°/s (target: 51.9%)	AFF	**62.8*** **(50.4 76.7)**	**61.1*** **(47.5 80.8)**	61.3 (52.9 70.1)	**53.7*** **(42.0 65.5)**
		UNAFF	**56.3*** **(50.3 60.9)**	**57.2*** **(50.0 64.5)**	**57.1*** **(51.8 61.4)**	**55.2*** **(49.5 61.9)**

* Bold, starred values contain target in 95%CI

between changes BL to FU (all $P > 0.05$). No evidence was found for change in any of the variables (95%CI span zero) except for the Y-balance LSI in the ECC group, which increased by +3.6 (95%CI: 0.5, 7.1).

For the functional hop tests used in RTS evaluation, the number of patients LSI >90 threshold at BL and FU are given in Table 5.2. At BL for the single leg hop test, 17% of ECC group patients and 20% of CON group patients passed. At FU, 33% of ECC group patients and 60% of CON group patients passed this test. For the triple crossover hop test, at BL 25% of the ECC group and 30% of the CON group passed, while at FU 58% and 50% of the ECC group and CON group passed, respectively. Determining the patients that passed both hop tests, at BL 17% of the ECC group and 10% of the CON group passed, while at FU there were 33% and 30% that passed, respectively, an increase of 2 patients in each group.

5.3.4 University of Delaware combined criteria

The number of patients passing all four criteria (QI, both hop tests, KOS-ADL and GRS >90%) were determined. At BL, no patients passed all criteria, and the best performance was one patient that passed 3/4 criteria in the ECC group, and one patient that passed 2/4 criteria in the CON group. At FU, no patients passed all criteria in either group; two ECC group patients and three CON group patients passed 3/4 criteria.

5.3.5 Melbourne Return-To-Sports Score

Using the MRSS sub-scores, the functional score /25 was calculated (Table 5.4). At BL, scores were 27.2 (95%CI: 20.5, 35.0) in the ECC group and 31.5 (95%CI: 24.0, 36.0) in the CON group. From BL to FU, group means changed by +7.0 (95%CI: -2.0, 16.0) in the ECC group, and +6.0 (95%CI: 0.0, 14.0) in the CON group. Statistical testing

Table 5.4: Change BL to FU of functional test results.

	at BL			Change BL to FU		
	ECC	CON	P^a	ECC	CON	P^b
Single leg hop LSI	80.5 (65.1 92.7)	82.7 (61.1 90.9)	0.539	+6.9 (-6.3 22.3)	+8.4 (-2.0 21.5)	0.456
Triple hop LSI	77.4 (59.4 90.9)	86.6 (79.2 91.8)	0.456	+11.1 (-6.0 23.8)	+5.1 (-2.3 13.8)	0.418
Y-Balance LSI	94.2 (88.6 96.5)	95.7 (91.1 101.1)	0.381	**+3.6*(0.5 7.1)**	+3.4 (-2.9 9.0)	0.872
Squat-to-fatigue LSI	74.8 (45.3 106.7)	71.0 (47.3 95.6)	0.792	+1.1 (-26.6 38.8)	+26.3 (-5.6 50.0)	0.203
DVJ score	12.5 (7.5 17.5)	15.0 (10.0 20.0)	0.456	+5.0 (-5.0 10.0)	+5.0 (-5.0 10.0)	0.753
MRSS functional score (/50)	27.2 (20.5 35.0)	31.5 (24.0 36.0	0.447	+7.0 (-2.0 16.0)	**+6.0*(0.0 14.0)**	0.921
MRSS (/100)	67.4 (57.4 78.6)	70.3 (61.5 78.5)	0.674	+10.4 (-3.3 22.4)	+7.7 (-2.3 20.6)	0.923

* Bold, starred values show evidence for a group change BL to FU
[a] Difference between ECC group and CON group AFF limbs at BL.
[b] Difference in change in ECC group and CON group AFF limbs from BL to FU.

at BL between groups, and between groups BL to FU, showed no difference between groups ($P > 0.05$).

Combining the MRSS functional score with the IKDC (/25) and clinical (/25) scores, yields the MRSS total values (/100). At BL, patients had scores of 67.4 (95%CI: 57.4, 78.6) in the ECC group and 70.3 (95%CI: 61.5, 78.5) in the CON group. From BL to FU, group mean scores changed by +10.4 (95%CI: -3.3, 22.4) in the ECC group, and +7.7 (95%CI: -2.3, 20.6) in the CON group. Statistical testing at BL between groups, and between groups BL to FU, showed no difference between groups ($P > 0.05$).

5.4 Discussion

The use of quantitative, objective clinical RTS criteria helps to systematically evaluate effectiveness of a training programme from the perspective of individual patient progress. At present, a combination of measures is required to measure enough rehabilitation dimensions, until further research improves evidence for tailored screening measures. While this combined approach is more costly, it is necessary to be collected to drive this process retrospectively, until prospective studies can be carried out, and move away from the time-based guidelines which are commonly used in practice.

The above data show progress in the ECC group and CON group on RTS dimensions including PROs, strength testing, and functional tests. In general, the finding was that there was no consistent difference between groups in progress towards RTS.

Examining the H/Q ratios, for the AFF limb at 60°/s, the ECC group mean most closely matched the target value at FU. The CON group, however, overshot this target, because increases in quadriceps strength were not matched by increases in hamstring strength. For the higher 120°/s speed, the AFF limb ECC group 95%CI was above the target at FU, while the CON group contained the target value. In general, values above the target are seen to be lower-risk for the ACL (strong hamstrings w.r.t. quadriceps).

For this test, the width of the 95%CI was large, showing variability in response between patients. For the UNAFF limb, values in both ECC group and CON group remained similar from BL to FU, showing that the training maintained the ratio of strength appropriately in this limb. Also, the ECC group UNAFF limb at the slower speed didn't contain the target value, implying that more hamstring work would be needed for the amount of quadriceps strengthening from the program.

Using the University of Delaware criteria, no patients in either group passed RTS at the end of the 8-week training programme (approx. 6 months post-surgery). At most, several patients in each group passed 3 out of the 4 criteria.

Regarding the use of the MRSS, no threshold scores were available by the time this study was concluded, except for the IKDC subscale, where normal age-ranges for males (>15th percentile) are available, and are used above. The hop test and Y-balance test are documented in the literature, and can be used as is. The 'abridged LESS' scoring for the DVJ test has not been validated, and this component, while easy to implement, is problematic. It is recommended that the full LESS as published be used instead, based on recorded video footage. The squat-to-fatigue test was performed to calculate the MRSS, and it is an attempt to include a functional strength/endurance component in the scoring without requiring isokinetic strength testing equipment. However, the results of the test varied widely, as can be seen in the high variability of the resulting scores. This may be due to several problems with the test experienced during the trial:

- Technique in squatting can be highly variable, and hip flexion can alter the work performed by the gluteus muscles as opposed to those of the quadriceps.
- Patients goals on the test seem to be variable, and are affected by central motivation, and there were signs of some patients 'giving-up' before reaching fatigue. Also, some patients counted the number of squats, targeting certain symmetry or number goals.

- Near fatigue point, certain patients were challenged by lack of balance. This is not the focus of the test, and is a potential confounder.

Based on the above issues with test implementation, it is recommended that another strength/endurance test be proposed as part of the MRSS, for instance leg press test using a gym machine.

Limitations of this study were: the numbers of patients were calculated for effect on biomechanical deviations using motion capture, and thus this study may be under-powered to answer RTS considerations in sufficient detail. The University of Delaware criterion which was used was tested using only 2 hop tests, and not the prescribed 4 tests, likely making these results less conservative. Also, the University of Delaware PROs (KOS-ADL, GRS) questions were sourced by extracting the relevant questions from the IKDC and KOOS questionnaires; in this process, the two questions which were not addressed by this approach were the 'weakness', and 'limping' items.

5.5 Conclusion

This chapter investigates the effect of eccentric cycle training on RTS for ACL-R males, based on the limited criteria available at this time. It was found that several additional patients passed each of the RTS evaluation criteria from BL to FU. However, using the stricter four combined University of Delaware criteria, no patients in either the ECC group or CON group passed RTS at the FU point (~6-months).

Despite the common use of several of the constituent tests, the MRSS as a whole was found to be lacking in evidence and having methodological issues, and cutoff criteria are not available. Thus, it is not recommended to be used clinically without substantially more data.

Regarding H/Q ratios, the ECC group mean at FU was closer to the target than the CON group, due to the former having better increases in hamstring strength. In

general, both the programmes did not change the risk profiles of either the ECC group or CON group, except for the AFF limb in the ECC group at 120°/s, which indicates additional hamstring strengthening is required to go with the increases in quadriceps strength. Thus adding hamstring strengthening would be recommended to counteract this effect.

Chapter 6

Conclusions

Rehabilitation after anterior cruciate ligament reconstruction (ACL-R) remains persistently time-intensive and costly. In addition, significant risks of re-injury and osteoarthritis remain. The aims of this thesis were first to investigate the biomechanics of male ACL-R male patients long-term after surgery, for possible markers of this risk. Secondly, the aim was to evaluate the use of eccentric cycle training to improve these biomechanical, strength, and other clinical outcomes during the third phase of rehabilitation (~3-6 months), using a randomised controlled trial (RCT).

In summary, it can be concluded that for adult ACL-R males, eccentric cycle training is well-liked by patients, low-risk, and good at promoting strength recovery in quadriceps and hamstrings. It is also effective at reducing sagittal-plane biomechanical deviations, improves patient-reported outcomes, and seems to facilitate return-to-sports. This is using a progressive, clinical exercise programme during the strengthening phase of rehabilitation (~3-6 months). However, most of these benefits were also seen in a group of concentrically-trained controls, matched for level of perceived exertion. The primary exceptions were that the control group did not increase hamstring strength, and had significantly less improvement in sagittal-plane knee and hip angles. A summary of the outcome measures tested, and changes in the AFF limb and symmetry, is given

Table 6.1: Findings of this thesis for AFF limb, and for symmetry. Up arrow (↑) represents a group improvement BL to FU, dash (-) represents no change.

		AFF limb		Symmetry	
		ECC	CON	ECC	CON
Concentric Strength	Quadriceps	↑↑	↑↑	↑	↑
	Hamstrings	↑	-	↑	↑
Eccentric Strength	Quadriceps	↑↑	↑↑	↑	↑
	Hamstrings	↑	↑	-	-
Lean Thigh Volume	-	-	-	-	↑
Biomechanics	Sagittal plane angles	↑↑	↑	↑	↑
	Sagittal plane moments	↑	↑	↑	↑↑
	Knee abduction moment	-	-	↑	↑
	Knee valgus angles	↑	-	↑	-
	Knee tibial rotation	↑	↑↑	-	↑
	Impact	↑	-	↑	↑
	Trunk angles	N/A	N/A	N/A	N/A
Bodyfat	-	-	↑	N/A	N/A
PROs	-	↑	↑	N/A	N/A
Return-To-Sports	-	↑	↑	N/A	N/A

in Table 6.1 below. In addition, from a cross-sectional study of similar cohort long-term after surgery (~5 years), it was found that clinically-relevant biomechanical deviations were still present, despite return-to-sports, suggesting chronic changes in joint loading.

The above conclusions are based on the result of a randomised controlled intervention trial, and a cross-sectional study. Further detail of the findings of each study are given in Sections 6.1 and 6.2 below.

6.1 Long-term biomechanical deviations in ACL-R males

In the cross-sectional trial, walking and running biomechanics of fifteen active ACL-R males long-term (~5 years) after surgery were compared to a group of healthy controls, for chronic changes in joint loading during daily tasks. Findings were that long-term, clinically relevant deviations exist, mostly between-limbs, but also between groups for some variables.

Largest deviations found were reduced knee angles and moments in the affected (AFF) as compared to the unaffected (UNAFF) limb during running. These were not found during walking; this shows the value of running, a higher intensity task, to highlight differences. Knee abduction moment showed valgus effects for the AFF limbs compared to UNAFF and control limbs. The knee valgus angle, however, only showed a difference between-limbs, and only during walking. Also, the AFF limb angle was only 1.1° more valgus than the UNAFF limb, much lower than the defined clinically-important difference of >3°, meaning that the knee abduction moment shows much more promise clinically. Regarding impact dynamics, as a group the ACL-R patients had lower initial and maximal impact rates during running than control participants, suggesting a reduced impact during foot strike.

From these findings, it can be concluded that, for active ACL-R males with typical rehabilitation and return-to-sports (RTS) protocols, deviations in gait biomechanics remain long-term after surgery. These results indicate chronic, clinical changes in joint loading. Running testing highlights deviations which are not noticeable during walking for this population. Knee valgus angle deviations in this population, while present, are small and are not likely to be clinically as useful as knee abduction moment.

6.2 Eccentric intervention

The randomised controlled intervention trial evaluated progressive eccentric cycling for ACL-R males (ECC group), compared to a group of active concentric controls (CON group). Clinical findings were that eccentric cycle training does not cause pain, is low-risk, and very well tolerated in this population of patients. Also, the progressive increase in intensity avoids delayed-onset muscle soreness (DOMS). Compliance to the programme was not an outcome measure, but the approach using matched rating of perceived exertion (RPE) suggests similar compliance can be expected for these ECC group and CON group programmes.

For hamstring strength, the ECC group improved, while no increase was seen for the CON group. Quadriceps strength was found to have improved for both the ECC group and CON group AFF limbs, by a similar amount (~25%). Quadriceps strength asymmetries were effectively reduced by both the ECC group and CON group programmes. No change in hamstring strength asymmetry was seen for either group, suggesting that hamstring strengthening in the UNAFF limb for the ECC group was higher than in the CON group. Interestingly, eccentric training improved strength, but did not result in higher peak torque during the eccentric strength tests, i.e. no mode-specific differences were seen from eccentric vs. concentric training. This corresponds with the literature on this topic (e.g. [209]), that mode-specific strength gains, if any, are not consistently seen with eccentric training.

Contrary to expectations, no evidence was found for the hypothesised lean thigh volume (LTV) gains in either limb of either group. From body weight and skin-fold thickness, evidence was found for loss of body-fat in the CON group, but not in the ECC group. While no hypothesis was made for this outcome, it makes sense in terms of the higher heart-rate seen in the CON group, and concentric cycling having higher oxygen demands. Interestingly, patient reported outcomes (PROs) only improved slightly, and no difference was seen in in PROs between training groups. Improvement was only

seen for the International Knee Documentation Committee (IKDC) percentile, and no change was seen for the raw IKDC score, Knee injury and Osteoarthritis Outcome Score (KOOS) subscales, or SF-36 sub-scales.

Biomechanical findings in the sagittal plane were that the ECC group intervention was more effective than the matched CON group intervention at increasing knee angle in the AFF limb, a common deviation in this phase of rehabilitation. However, at follow-up (FU), asymmetry was more evident in the ECC group than in the CON group, likely because this greater effect was also seen on the UNAFF limb. For hip flexion angle, the ECC group training successfully increased this variable, while in the CON group no evidence was found for a change from baseline (BL) to FU. In sagittal plane kinetics, knee moments increased for both groups, reducing asymmetries, and hip moments showed no changes, and no consistent change in asymmetry. These findings show that the sagittal-plane eccentric training resolved sagittal-plane deviations better than or equal to concentric training.

Biomechanical findings in the frontal and transverse plane were very large asymmetries in knee abduction moment and tibial rotation angle at BL. At FU, no change was seen in AFF limb knee abduction moment in either group, showing that deviations in neuromuscular medio-lateral knee control were not resolved - this appears to be a key limitation of this type of training. Tibial rotation asymmetry was better resolved in CON group than the ECC groups. Over the stance phase, FU knee valgus angle appeared more symmetrical and stable in the ECC group than in the CON group. These findings show that the benefit of eccentric training seen in the sagittal plane is not necessarily seen in the frontal or transverse planes.

From a RTS perspective, no patients in either group passed all four of the University of Delaware RTS criteria; a similar number in either group passed 3 of 4 criteria. Using the IKDC 15th percentile criterion, similar numbers of patients (3 ECC group patients, 2 CON group patients) passed RTS at FU. The Melbourne RTS score (MRSS) did not

show differences between groups, and the lack of evidence for this measure prevented further conclusions from being drawn.

6.3 Clinical and research implications

The above conclusions have significant implications for clinical practice and research, particularly with respect to the use of eccentric training. As has been previously demonstrated, this trial showed that eccentric cycle training applies a higher limb loading dose for the same perceived exertion. This resulted in better hamstrings strength improvement for eccentric training, even though hamstring-specific training was not performed as part of either program. However, this trial shows that the higher load dose does not necessarily result in superior quadriceps strength or lean thigh volume outcomes. This challenges the prevailing view in the literature that eccentric training is overwhelmingly superior to concentric training for strength and patient-reported outcomes.

A possible explanation for the above findings are that this trial for ACL-R used a *matched* design, by submaximal perceived exertion. Other published trials to date have tended to add eccentric training to standard-of-care, meaning that the exercise dose is not directly comparable between groups. In this trial, the use of active control participants with identical studio environment and equipment, lends strength to the above conclusion. Outside the trial, voluntary other training was infrequent, and low intensity; however, it was more frequent in the CON group than in to the ECC group, which may be seen to favour controls.

This is the first randomised controlled trial to investigate the effect of eccentric training on ACL-R gait. For sagittal-plane biomechanical deviations from this surgery, eccentric training can be recommended, particularly to increase knee and hip angles. However, to treat ACL-R deviations in other planes, neither of the cycling programmes

were effective. This suggests that additional training types are needed that target the other (non-sagittal) planes specifically. In the training studio, several additional aspects have been clinically piloted to address this. One is to encourage patients to stand on the cycle as soon as they are comfortable with it, rather than only in week seven, as in this trial. This removes the seat support, thus encouraging more activation of the hip out-of-plane muscles, which are seen to help in frontal-plane control of the knee. An additional suggestion, which has been tried in limited cases, is to loop an elastic band around the thighs, which gently pulls them together. The patient must then activate hip abduction muscles to resist this, training them in the process.

Based on the results of the trial, patients can be recommended eccentric training for ACL-R, but concentric training can also be recommended. It is expected that concentric training using a traditional exercise cycle, or an outdoor cycle at similar pedalling speeds and RPE levels would yield similar improvements in outcomes to the concentric protocol using the rehabilitation cycle of this trial. To communicate the results of this trial with patients, a suggested clinical wording could be: *"For rehabilitation of your knee you can perform concentric or eccentric cycling in a gym. Both strategies are safe. If you choose to do eccentric cycling, at the same perceived level of effort, you will be likely on average to improve your knee and hip flexion angles by 2 degrees more than the concentric cycling, and you will have an improved hamstring strength. These rehabilitation strategies are not likely to improve out of plane movements and loading of your knee joint."*

Regarding the frequency, intensity, and time parameters of the training programme, they were acceptable to these patients in terms of level of commitment. However, this trial did not evaluate relative effectiveness of varying parameters. Regarding intensity, most of the training programme tested here was performed at a perceived exertion of *somewhat hard* or higher. If needed, this dose could be raised a little, especially during the first few weeks of the programme, despite likely higher incidence of DOMS.

Biomechanically, it seems from literature that male response to ACL-R surgery may be different from females. Thus, it is recommended that stratification by sex should be used wherever possible in testing and patient progress tracking. For male patients, the use of knee valgus angle as biomarker does not seem to be as valuable as has been shown for females. In this population, abduction moment deviations are more revealing than valgus angles, even if are harder to observe clinically and more costly to test (requiring 3-D motion capture). Lower-cost methods of estimating knee abduction moment would be helpful in improving progress tracking and screening of these patients. Higher-impact testing, such as drop vertical jumping, running, etc. help to highlight deviations to be expected from sports environments. The emphasis on walk testing should be balanced with safe, higher-intensity tasks such as running, especially in research studies.

RTS testing, while still not common in literature, and not validated for predictive power, remains valuable for low-cost evaluation of progress towards these goals. Multi-criteria testing (such as the University of Delaware's four criteria) are recommended over single-measure (such as IKDC %ile), or combined score (MRSS) approaches, which are at risk of not detecting unbalanced recovery profiles.

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Appendix A

Patient information and informed consent

APPENDIX A: Participant Information Sheet and Informed Consent Form

UCT/MRC Research Unit for Exercise Science & Sports Medicine
Faculty of Health Sciences, University of Cape Town
3rd floor, SSISA, Boundary Road, Newlands
Tel: + 27 21 650 4561

Comparison of two exercise programmes for rehabilitation after Anterior Cruciate Ligament Reconstruction (ACL-R) surgery

PARTICIPANT INFORMATION SHEET

The UCT/MRC Research Unit for Exercise Science and Sports Medicine will be doing a study to try out two exercise programmes starting about three months after Anterior Cruciate Ligament Reconstruction surgery. The study is part of a PhD in Biomedical Engineering.

Why are we doing this study?

Anterior Cruciate Ligament Reconstruction (ACL-R) surgery is a commonly performed surgery in which the torn knee ligament is replaced with a biological substitute. While most patients experience less pain and instability, and improved strength, long-term undesirable changes in movement are observed even several years after the surgery. A strengthening programme focused on increasing thigh strength is commonly used to get back to physical activity. In this study we are planning to investigate the effects of two different strengthening programmes (one called eccentric and one called concentric) during the third stage of rehabilitation, starting approximately three to four months after surgery. The strengthening programmes will be done on a specially designed stationary bike known as the Grucox Rehabilitation Cycle. Studies have shown that both types of exercises lead to improvements in thigh strength, but that compromised movement patterns can still remain long-term after surgery. This study aims to investigate if one of the exercise programmes yields greater improvements in knee function and strength than the other, and evaluate the effect that these programmes have on reducing the changes in movement patterns. Also, calculations from the testing will give information on whether these people use their hip, knee or ankle differently between the leg that was operated and the one that was not.

What are the aims of the study?

Aim 1: Compare thigh muscle strength and size gains of two different 8-week rehabilitation programmes during the third phase (~3 months) after ACL-R surgery for young males.

Aim 2: To determine if the eccentric exercise programme is better than the concentric exercise programme in improving movement quality and readiness to return to sport after ACL-R surgery during the third phase of rehabilitation.

Aim 3. To compare scores obtained on the training bicycle compared to other standard tests.

Aim 4: To describe movement patterns of both types of cycling at the start and end of the exercise programme for this group.

Who can participate in this study?

Thirty-six patients, who have undergone Anterior Cruciate Ligament Reconstruction surgery 3-4 months before, can participate in this study. They must be:

- Male, between 18 and 40 years old
- Are available to start exercising 3-4 months post surgery and continue for 8 weeks
- Were moderately or very active before the injury
- They have completed the first two stages of their rehabilitation and are ready to proceed to the third stage, as checked by a doctor and using a questionnaire.
- Knee range of motion should be good in both directions
- Not overweight (BMI less than 30 $kg.m^{-2}$)
- Not have moderate or severe swelling in their knee
- Not have had ACL-R surgery on the other knee.
- Not have any symptoms in the other leg that limits daily activities
- Not have moderate or severe pain in the involved knee during daily activities
- Have not had an injection in either knee since the ACL-R surgery.
- Not be currently (last 1 week) using pain or anti-inflammatory medication
- Not have any other lower limb injuries or a current Deep Vein Thrombosis
- Not have had any other previous lower limb surgery, except for partial menisectomy
- Not have rheumatoid arthritis or gout in either the involved or uninvolved limbs.

The fact that we have contacted you means that you qualify for the study, based on the information we have checked in your medical record at the surgeon's practice. You will be

required to sign an informed consent form to join. Once you are part of the study, you will be randomly put into one of the two treatment groups, decided by pulling a folded piece of paper from a bowl, i.e. you cannot select either of the two programmes. Each of the groups will undergo 8 weeks of exercise with either of the two programmes. The only differences between the two programmes that we know about are that the eccentric programme has a higher chance of delayed muscle soreness, but we have designed the programme to minimise this risk (see below). It has the benefit that it seems to build muscle faster. Before and after the programme, tests and assessments will be used to see which of the exercise types lead to greater improvements in strength and movement patterns.

What do we want you to do?

The pre and post-intervention assessments and tests

You will be required to complete two testing sessions: one within a week of commencing the exercise programme and one within a week of completing it. Each testing session will be 3 hours. You will also have to attend a training visit (1 hour) 2 to 4 days before your first testing. All the testing will occur at the Sports Science Institute of South Africa, Newlands, Cape Town. Two and four months after the training finishes, you will be asked to come back and be tested again, to check your progress as you continue your rehabilitation.

You will be required to complete a questionnaire of personal details, medical and knee injury history. The start and end assessments include questionnaires about your physical activity (The Tegner Activity Level Scale), global health (The SF-36 Health Survey) and your ability to do certain tasks (International Knee Documentation Committee [IKDC], return-to-sports and constant power cycling assessments). In addition, you will be required to complete 5 other physical assessments.

- In the walking and running tests, we will evaluate your movement patterns by asking to walk and run (approximately ten times each) at a comfortable speed through an area monitored by cameras, while wearing little reflective plastic balls stuck with tape to your legs, waist and upper body. You will also wear electrical sensors taped to various muscles on your legs to detect the electrical activity produced by the muscles, and you will keep wearing them through the other activities.
- During the muscle strength test you will be required to push hard against a bar on the machine (while seated), which will measure the strength of your thigh muscles in both legs in straightening and bending.

- Return-to-sports tests will require you to balance on one leg, jump off a 31cm box several times, hop along a line, and squat on either leg, to evaluate your technique and power in both of your legs.
- Cycling testing involves a test of your cycling technique across a range of speeds and leg pressing forces. The pedals turn, and you will be asked to first go along and then resist them while trying to match a force target on the screen in front of you.
  The muscle volume test is a measurement of muscle size by measuring at various places on both legs with a measuring tape.

The exercise intervention

You will be required to attend three exercise sessions per week over a period of eight weeks. During each exercise session, you will exercise by cycling for 26-minutes focusing on either eccentric work (when a muscle lengthens during a contraction) or concentric work (when a muscle shortens during a contraction). You will turn the pedals both in the forwards and reverse pedaling directions. Either a physiotherapist or biokineticist will supervise you at all times during the session recording various readings including your heart rate, Rating of Perceived Exertion (effort) and a rating on pain if any felt in the affected knee. You will be asked to train at a specific level of effort. This level of effort will gradually progress from very light exercise, to a hard level, as judged by you. If you wish to participate in other sports or rehabilitation exercises during this time, you are permitted to do so, and this will be recorded at each session.

The training bicycle to be used in this study is known as the Grucox Rehabilitation Cycle and is driven by a small motor. The speed and pedaling force level of the cycle are set using a user-friendly touch screen. The screen constantly displays real time progress of your cycling effort (measured in watts), with the speed and your pedaling force shown compared to a reference level. Pedaling is either in the forward or reverse direction while the speed and required pedaling force are selected in accordance with the exercise protocol. All exercise sessions will be conducted at the Sports Science Institute of South Africa.

What are the costs and benefits of participating?

Strengthening exercises of both types (concentric or eccentric) are understood to be beneficial to a person's health and knee function after ACL-R surgery. Assessments before and after the exercise programme give you an objective evaluation on your progress towards your rehabilitation goals. The exercise programme and evaluations will be provided free of any cost to you. You will only be required to pay for transport to the Sports Science Institute,

Newlands for approximately 28 visits during the study, as no reimbursement is available for this.

We will keep you informed about the outcomes of your assessment and the overall scientific findings of the study. These will be summarized and posted/emailed to you. You will receive a report of the changes in your leg strength, movement patterns and evaluation of readiness for sport that we were able to measure before and after the exercise programme.

What are the risks of participating?

Assessment and testing procedure:

Electromyography (EMG):

You may have an allergic reaction to electrodes or the gel used, or may be sensitive to shaving or the use of alcohol on exposed skin. These will be minimised by the use of sterile equipment and availability of soothing lotions after completion of the testing session.

Muscle strength testing:

There is a possible risk of acute muscle strain injury during the testing procedure. This risk will be reduced by the following measures:

(1) You will be screened to ensure you are ready to undergo testing and training,
(2) The testing will be performed at a moderate speed, which reduces the risk of injury
(3) You will be required to exert the desired force and not the machine; therefore the machine will not be able to induce any uncontrolled muscle or joint damage.

In addition, you may experience Delayed Onset Muscle Soreness (DOMS) or stiffness, a normal response to exercise testing, thought to be the result of microscopic strain of the muscle fibres following unaccustomed exercise testing. This will be minimised by correct and sufficient warm up prior to testing and familiarization with the procedure (2 to 4 days prior to baseline testing), which decreases the possibility of injury and DOMS. You will also be given a Comfort Stop button to use during the procedure should you feel unsafe or uncomfortable. Medical personnel will also be available in the event of a medical emergency.

Exercise/Training Programme and cycling testing

You may feel discomfort in your legs during the eight week exercise period. Although the protocol is developed to slowly get you used to the training intensity, with a gradual increase in intensity, delayed onset muscle soreness (DOMS) may still occur, specifically in the eccentric training protocol group. This is however normal for eccentric exercise (when a muscle lengthens during a contraction). This will be minimised by correct and sufficient

warm-up prior to testing and familiarization with the protocol and bike, which decreases the possibility of injury and DOMS. A trained physiotherapist or biokineticist will also be supervising each exercise session in which your Rating of Perceived Exertion (effort) will be monitored. Hence, the intensity of the workload can be accordingly adjusted to ensure the desired level of comfort.

What will be done if you injure yourself during testing or training?

If you injure yourself during testing or training, more seriously than the risks described above, the physiotherapist or biokineticist will perform a diagnostic evaluation on the spot to assess the injury. If the injury was because of training too hard, the intensity will be reduced and recorded. Rest may be prescribed, to see if the injury gets better. If this means that you cannot complete 80% or more of the training sessions, you will be removed from the trial, although you can complete the planned sessions if you want to. If the injury is more serious, you will be referred to one of the attending surgeons for additional clinical evaluations.

What are the ethical considerations?

This study will be performed in accordance with the principles of the Declaration of Helsinki (2013, Fortaleza, Brazil), International Conference on Harmonisation and the European Good Clinical Practice (GCP) guidelines, the South African GCP guidelines, and the laws of South Africa. The study will be covered by the no-fault insurance policy of the University of Cape Town. You will not be included in the study unless you have signed a consent form, after the investigator has provided substantial verbal and written explanation of the study, including risk factors. Participation in the study is entirely voluntary and you have the right to withdraw from the study at any time without stating a reason. The investigator may also withdraw you from the study at any time. All the information collected during the trial will be stored in a computer database in a secure facility, will be kept confidential and will only be used for scientific purposes. Your anonymity will be ensured should the data be published.

This study was granted Ethics approval from the Faculty of Health Sciences (FHS) Human Research Ethics Committee (REC) at the University of Cape Town. If you have any complaints or queries that the investigator has not been able to answer to your satisfaction, you may contact **Prof Marc Blockman** from the FHS REC on telephone number **021 406 6452,** Email: nosi.tywabi@uct.ac.za or at address: Room E52-24, Old Main Building, Groote Schuur Hospital, Observatory, 7925.

What if Something Goes Wrong?

The University of Cape Town (UCT) has insurance cover for the event that research-related injury or harm results from your participation in the trial. The insurer will pay all reasonable medical expenses in accordance with the South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI) in the event of an injury or side effect resulting directly from your participation in the trial. You will not be required to prove fault on the part of the University.

The University will not be liable for any loss, injuries and/or harm that you may sustain where the loss is caused by

- The use of unauthorised medicine or substances during the study
- Any injury that results from you not following the protocol requirements or the instructions that the study doctor may give you
- Any injury that arises from inadequate action or lack of action to deal adequately with a side effect or reaction to the study medication*
- An injury that results from negligence on your part*

[*Researchers must bear in mind that it is unacceptable to impose a burden on participants who may not recognize symptoms or have the ready means to take action.]

"By agreeing to participate in this study, you do not give up your right to claim compensation for injury where you can prove negligence, in separate litigation. In particular, your right to pursue such a claim in a South African court in terms of South African law must be ensured. Note, however, that you will usually be requested to accept that payment made by the University under the SA GCP guideline 4.11 is in full settlement of the claim relating to the medical expenses."

An injury is considered trial-related if, and to the extent that, it is caused by study activities. You must notify the study doctor immediately of any side effects and/or injuries during the trial, whether they are research-related or other related complications.

UCT reserves the right not to provide compensation if, and to the extent that, your injury came about because you chose not to follow the instructions that you were given while you were taking part in the study. Your right in law to claim compensation for injury where you prove negligence is not affected. Copies of these guidelines are available on request.

Contact

Thank you for your time and we look forward to working with you. If you have any questions about this study, please feel free to contact us at:

- Mr Giovanni Milandri, University of Cape Town, (021) 404 7613, MLNGIO001@myuct.ac.za
- Dr. Mike Posthumus, PhD, University of Cape Town, (021) 650 4572, mposthumus@uct.ac.za
- Dr. Sudesh Sivarasu, University of Cape Town (021) 404 7613 Sudesh.sivarasu@uct.ac.za
- Dr. Willem Van Der Merwe, MD, The Sports Science Orthopaedic Clinic, (021) 686 1196, willem@grucox.com

UCT/MRC Research Unit for Exercise Science & Sports Medicine
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Tel: + 27 21 650 4561

Comparison of two exercise programmes for rehabilitation after Anterior Cruciate Ligament Reconstruction (ACL-R) surgery

CONSENT FORM

I, the undersigned, have been fully informed about the UCT/MRC Research Unit for Exercise Science and Sports Medicine within the Department of Human Biology of the University of Cape Town and the Sports Science Orthopaedic Clinic's study on the comparison of two treatment modalities for rehabilitation after Anterior Cruciate Ligament Reconstruction surgery.

I have undergone Anterior Cruciate Ligament Reconstruction surgery and agree to participate in one of two treatment modalities during the third stage of my rehabilitation starting about three months after surgery. I understand that if I am deemed fit to participate in an exercise programme, I will be given a supervised exercise programme to follow for eight weeks and I will be expected to attend three 26-minute exercise sessions for each of the eight weeks. To avoid bias in the study, I understand that none of the investigators will discuss how the specific exercise programme I have been allocated to differs from the other exercise protocol. I understand that the selection process will be random (drawn out of a hat). I understand that the exercise treatment I receive may result in discomfort and pain, but that this is similar to that which is experienced by any individual undergoing exercise, and is a sign of adaptation to the exercise training programme.

I agree to perform all the measurements and assessments prior to starting and after completing the 8-week exercise protocol. It has been explained to me that I will attend a 30 minute familiarization visit to demonstrate the correct use of the equipment, followed by a 3 hour visit in which I will complete an isokinetic strength assessment, a gait analysis assessment, return-to-sports testing, a test on the Grucox exercise bicycle and complete questionnaires about my knee. I will again attend an identical 3-hour visit after I have completed the 8-week exercise protocol. I understand that all the information that will be

collected during the study will be treated with the strictest confidentiality and will only be used for scientific research purposes. I have been informed that participation in the rehabilitation provided in this study, as well as all the assessments will be provided free of charge. I will not be paid for participating in this research trial.

The University of Cape Town (UCT) has an appropriate insurance policy to cover payment for any trial-related injury. I may therefore receive compensation in the event of me sustaining any trial-related injury and/or a significant deterioration in my health. My right in law to claim compensation for injury where you prove negligence is not affected. Copies of these guidelines are available if I should request them.

I agree to participate in the study and I have been informed that I will be free to withdraw from the study at any time if I so wish. I understand that I will receive the overall results of the study. I have read (or where appropriate, have had read to me) and understand the information about this study, and any questions I have asked have been answered to my satisfaction. I agree that research data provided by me or with my permission during the project may be presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

Participant:

Full name	Signature	Date

Investigator:

Full name	Signature	Date

Appendix B

Patient history questionnaire

APPENDIX B: Patient History Questionnaire

PATIENT HISTORY

A. PATIENT DEMOGRAPHICS

1. Age at Time of Surgery: _____ Years

2. Gender: ☐ Male ☐ Female

3. Weight: _____ Kilograms

4. Height: _____ Centimeters

B. MEDICAL HISTORY

1. Have you been diagnosed with one or more Chronic Diseases? ☐ Yes ☐ No

If yes, Please elaborate:

_____

_____

2. Are you currently on any prescription or non-prescription medication? ☐Yes ☐No

If yes, Please elaborate:

_____

_____

C. KNEE HISTORY *(*Involved Knee refers to the operative knee.)*

1. Involved Knee: ☐ Right ☐ Left

3. Pre-operative Duration of Symptoms:_____ Months ☐ Unknown

4. Activity at Onset of Symptoms/Injury: ☐Sports ☐ ADL ☐ Work ☐ Motor Accident

OTHER: (specify) _____ ☐ Unknown

5. Mechanism of Injury:

☐ Non-traumatic gradual onset ☐ Traumatic non-contact onset

☐ Non-traumatic sudden onset ☐ Traumatic contact onset

D. SURGICAL HISTORY:

1. Record any significant surgical procedures of the past ***other than in the involved knee***:

_____

_____

2. Previous Cartilage Procedure in the Involved Knee: ☐ **No Prior Cartilage Procedure**

☐ 0–6 Months ☐ 6–12 Months ☐ >12 Months ☐ >2 Years ☐ >3 Years

3. Comments on Surgical History:

_____

_____

4. Surgical History. *Please indicate the **number** of previous procedures in the **involved knee** (excluding the current total knee replacement):*

Medial Compartment Surgical History:		☐ **No Prior Procedure**	
Medial Femoral Condyle		**Medial Tibial Plateau**	
Debridement	_____	Debridement	_____
Microfracture	_____	Microfracture	_____
Abrasion Arthroplasty/Chondroplasty/Drilling	_____	Abrasion Arthroplasty/Chondroplasty/Drilling	_____
Thermal Tissue Ablation	_____	Thermal Tissue Ablation	_____
Osteochondral Autograft	_____	OTHER:	
Osteochondral Allograft	_____	_____	
Cell Based Cartilage Procedures	_____		
Focal HemiCAP Resurfacing (15/20mm)	_____	**Medial Meniscus**	
OTHER:		Partial Meniscectomy	_____
_____		Meniscal Repair	_____
		Meniscal Allograft	_____
		OTHER:	
		_____	
Lateral Compartment Surgical History:		☐**No Prior Procedure**	
Lateral Femoral Condyle		**Lateral Tibial Plateau**	
Debridement	_____	Debridement	_____
Microfracture	_____	Microfracture	_____
Abrasion Arthroplasty/Chondroplasty/Drilling	_____	Abrasion Arthroplasty/Chondroplasty/Drilling	_____
Thermal Tissue Ablation	_____	Thermal Tissue Ablation	_____
Osteochondral Autograft	_____	OTHER:	
Osteochondral Allograft	_____	_____	
Cell Based Cartilage Procedures	_____		
Focal HemiCAP Resurfacing (15/20mm)	_____	**Lateral Meniscus**	
OTHER:		Partial Meniscectomy	_____
_____		Meniscal Repair	_____
		Meniscal Allograft	_____
		OTHER:	
		_____	
Patellofemoral Joint Surgical History:		☐ **No Prior Procedure**	
Patella		**Trochlea**	
Debridement	_____	Debridement	_____
Microfracture	_____	Microfracture	_____
Abrasion Arthroplasty/Chondroplasty/Drilling	_____	Abrasion Arthroplasty/Chondroplasty/Drilling	_____
Thermal Tissue Ablation	_____	Thermal Tissue Ablation	_____
Osteochondral Autograft	_____	Osteochondral Autograft	_____
Osteochondral Allograft	_____	Osteochondral Allograft	_____
Cell Based Cartilage Procedures	_____	Cell Based Cartilage Procedures	_____
OTHER:		OTHER:	
_____		_____	
Ligament, Tendon, Capsular, Realignment Procedures, etc.:		☐ **No Prior Procedure**	
ACL Reconstruction	_____	Patella Tendon Repair	_____
PCL Reconstruction	_____	Quadriceps Tendon Repair	_____
MCL Reconstruction	_____	PF Medial Imbrication	_____
LCL Reconstruction	_____	PF Lateral Release	_____
Posterolateral Reconstruction	_____	PF Tibial Tubercle Transfer	_____
OTHER:		Trochleoplasty	_____
_____		Patellectomy	_____
		High Tibial Osteotomy	_____

5. Surgical History. *Please indicate the **number** of previous procedures in the **uninvolved knee:***

Medial Compartment Surgical History:	☐ **No Prior Procedure**
Medial Femoral Condyle	**Medial Tibial Plateau**
Debridement _____	Debridement _____
Microfracture _____	Microfracture _____
Abrasion Arthroplasty/Chondroplasty/Drilling _____	Abrasion Arthroplasty/Chondroplasty/Drilling _____
Thermal Tissue Ablation _____	Thermal Tissue Ablation _____
Osteochondral Autograft _____	OTHER:
Osteochondral Allograft _____	_____
Cell Based Cartilage Procedures _____	
Focal HemiCAP Resurfacing (15/20mm) _____	**Medial Meniscus**
OTHER:	Partial Meniscectomy _____
_____	Meniscal Repair _____
	Meniscal Allograft _____
	OTHER:
	_____

Lateral Compartment Surgical History:	☐ **No Prior Procedure**
Lateral Femoral Condyle	**Lateral Tibial Plateau**
Debridement _____	Debridement _____
Microfracture _____	Microfracture _____
Abrasion Arthroplasty/Chondroplasty/Drilling _____	Abrasion Arthroplasty/Chondroplasty/Drilling _____
Thermal Tissue Ablation _____	Thermal Tissue Ablation _____
Osteochondral Autograft _____	OTHER:
Osteochondral Allograft _____	_____
Cell Based Cartilage Procedures _____	
Focal HemiCAP Resurfacing (15/20mm) _____	**Lateral Meniscus**
OTHER:	Partial Meniscectomy _____
_____	Meniscal Repair _____
	Meniscal Allograft _____
	OTHER:
	_____

Patellofemoral Joint Surgical History:	☐ **No Prior Procedure**
Patella	**Trochlea**
Debridement _____	Debridement _____
Microfracture _____	Microfracture _____
Abrasion Arthroplasty/Chondroplasty/Drilling _____	Abrasion Arthroplasty/Chondroplasty/Drilling _____
Thermal Tissue Ablation _____	Thermal Tissue Ablation _____
Osteochondral Autograft _____	Osteochondral Autograft _____
Osteochondral Allograft _____	Osteochondral Allograft _____
Cell Based Cartilage Procedures _____	Cell Based Cartilage Procedures _____
OTHER:	OTHER:
_____	_____

Ligament, Tendon, Capsular, Realignment Procedures, etc.:	☐ **No Prior Procedure**
ACL Reconstruction _____	Patella Tendon Repair _____
PCL Reconstruction _____	Quadriceps Tendon Repair _____
MCL Reconstruction _____	PF Medial Imbrication _____
LCL Reconstruction _____	PF Lateral Release _____
Posterolateral Reconstruction _____	PF Tibial Tubercle Transfer _____
OTHER:	Trochleoplasty _____
_____	Patellectomy _____
	High Tibial Osteotomy _____

A. FOLLOW-UP KNEE EXAMINATION

1. Symptoms of the Involved Knee *("Involved Knee" refers to the operative knee)*

Pain:	☐ None	☐ Mild	☐ Moderate	☐ Severe	☐ Extreme
Swelling:	☐ Yes	☐ No			
Locking:	☐Yes	☐ No			
Giving-way:	☐ Yes	☐ No			

B. POSTOPERATIVE MILESTONES

1. Length of Hospitalization (admission to discharge): _____ **Hours**

2. Time to Ambulation with Support (Crutches etc): _____ **Hours**

3. Time to Ambulation without Support (Crutches etc.): _____ **Days**

3. Time to reach full range of motion (ROM): _____ **Days**

4. Length of Postoperative Rehabilitation _____ **Weeks**

Please explain what this rehabilitation entailed and its duration (Physiotherapy, Biokinetics etc.):_____
_____
_____

5. Time to Return to Work _____ **Weeks**
   ☐ NA - Patient not working prior to surgery

6. Time to Return to Sports _____ **Months**
   ☐ NA - Patient was not seeking to return to sport

G. ADDITIONAL COMMENTS

_____
_____
_____

Patient Signature: _____ **Date:** _____

Investigator Signature: _____ **Date:** _____

Thank you for completing all the questions in this questionnaire.

Appendix C

The 26-minute cycle ergometry protocol

APPENDIX C: The 26-minute Cycle Ergometric Protocol

Eccentric Group (ECC)		Concentric Group (CON)	
Direction of Grucox Bike pedals – Reverse		Direction of Grucox Bike pedals – Reverse	
2 min	Continuous Passive Movement warm-up	2 min	Continuous Passive Movement warm-up
10 min	Eccentric work	10 min	Concentric work
Direction of Grucox Bike pedals – Forwards		Direction of Grucox Bike pedals – Forwards	
2 min	Continuous Passive Movement warm-up	2 min	Continuous Passive Movement warm-up
10 min	Eccentric work	10 min	Concentric work
2 min	Cool down	2 min	Cool down

Appendix D

The Borg Rating of Perceived Exertion scale

APPENDIX D: The Borg Rating of Perceived Exertion Scale

6	No exertion at all
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Appendix E

Testing sheet

Participant Name		Week: _____ Start Date:_____					
		Session 1		Session 2		Session 3	
Preparation and settings	Weight (kg)						
	Seat Height (#)						
	Speed (rpm)						
	Torque (Nm)						
Measures during Session		5 min	20 min	5 min	20 min	5 min	20 min
	RPE						
	HR						
	VAS for Pain						
Power for session (Watt)	Left (max)						
	Left (ave)						
	Right (max)						
	Right (ave)						
	Comments, medication/other physical activity, Pain site/type (mark X for none)						

Appendix F

Ergometry exercise protocol

APPENDIX F: Ergometry exercise protocol

Training week	Exercise session #	Intensity: Rating of Perceived Exertion	Duration (minutes)
1	1	Familiarization – 7 (Extremely light)	20
	2	9 (Very light)	26
	3	9 (Very light)	26
2	4	11 (Light)	26
	5 – 6	11 (Light)	26
3-4	7-12	13 (Somewhat hard)	26
5-6	13 - 18	13 (Somewhat hard)	26
7-8	19 - 24	15 (Hard)	26

Appendix G

IKDC Subjective knee evaluation

IKDC Subjective Knee Evaluation

Your Full Name_____

Today's Date: _____/_____/_____ (Day / Month / Year) Date of Injury: _____/_____/_____ (Day / Month / Year)

SYMPTOMS*:

*Grade symptoms at the highest activity level at which you think you could function without significant symptoms, even if you are not actually performing activities at this level.

1. What is the highest level of activity that you can perform without significant knee pain?

   4❑Very strenuous activities like jumping or pivoting as in basketball or soccer
   3❑Strenuous activities like heavy physical work, skiing or tennis
   2❑Moderate activities like moderate physical work, running or jogging
   1❑Light activities like walking, housework or yard work
   0❑Unable to perform any of the above activities due to knee pain

2. During the past 4 weeks, or since your injury, how often have you had pain?

	10	9	8	7	6	5	4	3	2	1	0	
Never	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	Constant

3. If you have pain, how severe is it?

	10	9	8	7	6	5	4	3	2	1	0	
No pain	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	Worst pain imaginable

4. During the past 4 weeks, or since your injury, how stiff or swollen was your knee?

   4❑Not at all
   3❑Mildly
   2❑Moderately
   1❑Very
   0❑Extremely

5. What is the highest level of activity you can perform without significant swelling in your knee?

   4❑Very strenuous activities like jumping or pivoting as in basketball or soccer
   3❑Strenuous activities like heavy physical work, skiing or tennis
   2❑Moderate activities like moderate physical work, running or jogging
   1❑Light activities like walking, housework, or yard work
   0❑Unable to perform any of the above activities due to knee swelling

6. During the past 4 weeks, or since your injury, did your knee lock or catch?

   0❑Yes 1❑No

7. What is the highest level of activity you can perform without significant giving way in your knee?

   4❑Very strenuous activities like jumping or pivoting as in basketball or soccer
   3❑Strenuous activities like heavy physical work, skiing or tennis
   2❑Moderate activities like moderate physical work, running or jogging
   1❑Light activities like walking, housework or yard work
   0❑Unable to perform any of the above activities due to giving way of the knee

SPORTS ACTIVITIES:

8. What is the highest level of activity you can participate in on a regular basis?

4❑Very strenuous activities like jumping or pivoting as in basketball or soccer
3❑Strenuous activities like heavy physical work, skiing or tennis
2❑Moderate activities like moderate physical work, running or jogging
1❑Light activities like walking, housework or yard work
0❑Unable to perform any of the above activities due to knee

9. How does your knee affect your ability to:

		Not difficult at all	Minimally difficult	Moderately Difficult	Extremely difficult	Unable to do
a.	Go up stairs	4❑	3❑	2❑	1❑	0❑
b.	Go down stairs	4❑	3❑	2❑	1❑	0❑
c.	Kneel on the front of your knee	4❑	3❑	2❑	1❑	0❑
d.	Squat	4❑	3❑	2❑	1❑	0❑
e.	Sit with your knee bent	4❑	3❑	2❑	1❑	0❑
f.	Rise from a chair	4❑	3❑	2❑	1❑	0❑
g.	Run straight ahead	4❑	3❑	2❑	1❑	0❑
h.	Jump and land on your involved leg	4❑	3❑	2❑	1❑	0❑
i.	Stop and start quickly	4❑	3❑	2❑	1❑	0❑

FUNCTION:

10. How would you rate the function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?

FUNCTION PRIOR TO YOUR KNEE INJURY:

Couldn't perform daily activities	0 ❑	1 ❑	2 ❑	3 ❑	4 ❑	5 ❑	6 ❑	7 ❑	8 ❑	9 ❑	10 ❑	No limitation in daily activities

CURRENT FUNCTION OF YOUR KNEE:

Cannot perform daily activities	0 ❑	1 ❑	2 ❑	3 ❑	4 ❑	5 ❑	6 ❑	7 ❑	8 ❑	9 ❑	10 ❑	No limitation in daily activities

Appendix H

KOOS questionnaire

Knee Injury and Osteoarthritis Outcome Score (KOOS)

INSTRUCTIONS:

This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to do your usual activities. Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

SYMPTOMS:

These questions should be answered thinking of your knee symptoms during the **last week**.

S1. Do you have swelling in your knee?

Never	Rarely	Sometime	Often	Always
□	□	□	□	□

S2. Do you feel grinding; hear clicking or any other type of noise when your knee moves?

Never	Rarely	Sometime	Often	Always
□	□	□	□	□

S3. Does your knee catch or hang up when moving?

Never	Rarely	Sometime	Often	Always
□	□	□	□	□

S4. Can you straighten your knee fully?

Always	Often	Sometime	Rarely	Never
□	□	□	□	□

S5. Can you bend your knee fully?

Always	Often	Sometime	Rarely	Never
□	□	□	□	□

STIFFNESS:

The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

PAIN:

P1. How often do you experience knee pain?

Never	Monthly	Weekly	Daily	Always
□	□	□	□	□

What amount of knee pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your knee

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P3. Straightening knee fully

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P4. Bending knee fully

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P5. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P6. Going up or down stairs

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P7. At night while in bed

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P8. Sitting or lying

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

P9. Standing upright

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

FUNCTION, DAILY LIVING:

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1. Descending stairs

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A2. Ascending stairs

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A3. Rising from sitting

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A4. Standing

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A5. Bending to floor/pick up an object

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A6. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A7. Getting in/out of car

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A8. Going shopping

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A9. Putting on socks/stockings

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A10. Rising from bed

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A11. Taking off socks/stockings

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A12. Lying in bed (turning over, maintaining knee position)

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A13. Getting in/out of bath

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A14. Sitting

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A15. Getting on/off toilet

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A16. Heavy domestic duties: moving heavy boxes, scrubbing floors, etc.

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

A17. Light domestic duties (cooking, dusting, etc.)

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

FUNCTION, SPORTS AND RECREATIONAL ACTIVITIES:

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

SP1. Squatting

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

SP2. Running

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

SP3. Jumping

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

SP4. Twisting/pivoting on your injured knee

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

SP5. Kneeling

None	Mild	Moderate	Severe	Extreme
□	□	□	□	□

QUALITY OF LIFE:

Q1. How often are you aware of your knee problem?

Never	Monthly	Weekly	Daily	Constantly
□	□	□	□	□

Q2. Have you modified your lifestyle to avoid potentially damaging activities to your knee?

Not at all	Mildly	Moderately	Severely	Totally
□	□	□	□	□

Q3. How much are you troubled with lack of confidence in your knee?

Not at all	Mildly	Moderately	Severely	Extremely
□	□	□	□	□

Q4. In general, how much difficulty do you have with your knee?

Not at all	Mild	Moderate	Severe	Extreme
□	□	□	□	□

Thank you for completing all the questions in this questionnaire.

Appendix I

SF-36 Health survey

SF-36 Health Survey

This survey asks for your views about your health. Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor
□	□	□	□	□

2. Compared to *one year ago*, how would you rate your health in general *now*?

Much Better Now	Somewhat Better Now	About the Same	Somewhat Worse	Much Worse
□	□	□	□	□

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes. Limited a Lot	Yes. Limited a little	No. Not limited at all
Vigorous Activities: running, lifting heavy objects, participating in strenuous sports……	□	□	□
Moderate Activities: moving a table, pushing a vacuum cleaner, bowling or playing golf……..	□	□	□
Lifting or carrying groceries…….……..	□	□	□
Climbing several flights of stairs……..	□	□	□
Climbing one flight of stairs……..	□	□	□
Bending, kneeling or stooping…….	□	□	□
Walking more than one kilometre……	□	□	□

Walking several hundred metres…….	□	□	□
Walking one hundred metres……...	□	□	□
Bathing or dressing yourself……	□	□	□

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Cut down on the amount of time you spent on work or other activities……..	□	□	□	□	□
Accomplished less than you would like.....	□	□	□	□	□
Were limited in the kind of work or other activities…….....	□	□	□	□	□
Had difficulty performing the work or other activities (for example, it took extra effort)...	□	□	□	□	□

5. During the past 4 years, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Cut down on the amount of time you	□	□	□	□	□

spent on work or other activities……..

Accomplished less than you would like…… □ □ □ □ □

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

7. How much bodily pain have you had during the past 4 weeks?

None	Very Mild	Mild	Moderate	Severe	Very Severe
□	□	□	□	□	□

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside and home and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?	□	□	□	□	□
Have you been very nervous?	□	□	□	□	□
Have you felt so down in the dumps that nothing could cheer you up? …….	□	□	□	□	□
Have you felt calm and peaceful? ……	□	□	□	□	□
Do you have a lot of energy? ……	□	□	□	□	□
Have you felt downhearted and	□	□	□	□	□

depressed? ……..……..

Did you feel worn out? ……...	□	□	□	□	□
Have you been happy? ……..	□	□	□	□	□
Did you feel tired? ……..	□	□	□	□	□

10. During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
□	□	□	□	□

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
I seem to get sick a little easier than other people……..	□	□	□	□	□
I am as healthy as anybody I know.	□	□	□	□	□
I expect my health to get worse….	□	□	□	□	□
My health is excellent……..	□	□	□	□	□

Thank you for completing all the questions in this questionnaire.

Appendix J

Physical Activity Readiness Questionnaire (PAR-Q)

Physical Activity Readiness Questionnaire (PAR-Q)

Name			Date
DOB:	Age:	Home Phone:	Work Phone:

Regular exercise is associated with many health benefits, yet any change of activity may increase the risk of injury. This questionnaire identifies whether you are at risk.
Please read each question carefully and answer every question honestly:

Yes	No	1) Has a physician ever said you have a heart condition and you should only do physical activity recommended by a physician?
Yes	No	2) When you do physical activity, do you feel pain in your chest?
Yes	No	3) When you were not doing physical activity, have you had chest pain in the past month?
Yes	No	4) Do you ever lose consciousness or do you lose your balance because of dizziness?
Yes	No	5) Do you have a joint or bone problem that may be made worse by a change in your physical activity?
Yes	No	6) Is a physician currently prescribing medications for your blood pressure or heart condition?
Yes	No	7) Are you pregnant?
Yes	No	8) Do you have insulin dependent diabetes?
Yes	No	9) Are you 69 years of age or older?
Yes	No	10) Do you know of any other reason you should not exercise or increase your physical activity?

If you answered **yes** to any of the above questions, you need to consult your doctor BEFORE you can participate in this experiment. If you honestly answered **no** to all questions, you can be reasonably positive that you are not at an increased risk by participating in this study. If your health changes so you then answer **yes** to any of the above questions, seek guidance from a physician.

Participant Signature	Date

Thank you for completing all the questions in this questionnaire.