

**NEUROMUSCULAR CONTROL AND KNEE FUNCTION  
AFTER ANTERIOR CRUCIATE LIGAMENT  
RECONSTRUCTION**

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For my wife Zuzana and my sons Thomas and Henry

## Abstract

Knee functional outcomes after anterior cruciate ligament reconstruction (ACLR) are variable, particularly amongst recreational athletes. Functional performance tests and self-reported measures of knee function are used clinically to quantify knee function after ACLR. Although these tests provide some indication of gross-motor function, they do not accurately quantify neuromuscular control. Sub-optimal neuromuscular control may be associated with poor knee function and, in turn, to altered knee joint loading and knee osteoarthritis.

Despite years of ACLR research, knowledge of the relationship between neuromuscular control and knee function is limited mostly to bivariate analyses. These analyses do not account for participant characteristics such as age, sex, body mass index, the presence of chondral and meniscal injuries, greater anterior knee joint laxity or the participation limitations experienced by individuals. Knowledge of these associations is necessary to help explain the variability in knee functional outcomes following ACLR. Therefore, the aim of the research reported in this thesis was to investigate the cross-sectional associations between clinical tests of knee joint function and i) sports participation, ii) participant characteristics and iii) neuromuscular control following ACLR.

To address this broad aim, four studies were conducted using a cross-sectional, observational study design. Sixty-six participants (23 women, median age 28.4, range 19-39) at an average of 18 months (SD 3 months) following ACLR with an ipsilateral hamstring graft, and 41 matched control participants (16 women, median age 25.8, range 18-39) were recruited. The inter-session reliability and standard error of measurement of variables were determined with 26 control participants (8 women, median age 24.7, range 19-37).

In Study 1, the knee function of ACLR and control participants was assessed using a battery of self-reported and functional performance (hop) tests. Compared to control participants, ACLR participants demonstrated significant limitations in self-reported knee function and functional performance and significantly more ACLR participants failed the battery of functional tests. In a multivariate logistic regression model, older

age, higher BMI and greater anterior knee joint laxity were significant predictors of failing the battery of knee functional tests.

In Study 2, the quadriceps force control and thigh muscle activation strategies of ACLR and control participants were assessed using a novel, sub-maximal intensity, open kinetic chain force-matching task. Participants used quadriceps force to match a moving target torque that was displayed on a screen. ACLR participants demonstrated significantly greater target matching error, indicative of less-accurate quadriceps force production and higher levels of quadriceps activation and hamstring coactivation. In a multivariate linear regression model, less-accurate quadriceps force production was associated with greater vastus lateralis activation, lower lateral hamstring coactivation, female sex, older age at the time of testing, greater anterior knee joint laxity and meniscal surgery at the time of ACLR. Together these variables explained 42% of the variance in quadriceps force control in the ACLR group.

In Study 3, the trunk and lower limb biomechanics of ACLR and control participants were compared in the landing phase of a novel forward hopping task which involved a dynamic take-off. Hop distance and take-off velocity were standardised to minimise variability in task performance between individuals. Significantly smaller knee flexion excursion, peak knee extensor moments and peak trunk flexion angles were observed in the ACLR group. In a multivariate linear regression model, greater anterior knee joint laxity, higher vastus medialis activation, lower medial hamstring coactivation and lower quadriceps strength relative to body mass accounted for 54% of the variance in knee flexion excursion in the ACLR group.

Study 4 addressed the main aim of the thesis by investigating the multivariate associations between knee joint function, participant characteristics and neuromuscular control. Less-accurate quadriceps force production, greater lateral hamstring coactivation during the force matching task and female sex were significant predictors of failing the functional test battery. In the closed kinetic chain, smaller knee flexion excursion, smaller peak knee extensor moment and greater anterior knee joint laxity were significant predictors of failing the test battery. Prospective studies are now needed to determine whether the biomechanical and neuromuscular variables identified by this research are predictive of long-term knee function and knee osteoarthritis.

## **Declaration**

This is to certify that:

- i. the thesis comprises only my original work towards the PhD except where indicated in the Preface,
- ii. due acknowledgement has been made in the text to all other material used,
- iii. the thesis is fewer than 100,000 words in length, exclusive of tables, figures, bibliographies and appendices
- iv. all research procedures reported in this thesis were approved by the Human Research Ethics Committee, The University of Melbourne.

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## Publications and conference papers

The following publications and conference papers have arisen directly from the work reported in this thesis:

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## Abbreviations

ACL	Anterior cruciate ligament
ACLD	Anterior cruciate ligament deficient
ACLR	Anterior cruciate ligament reconstruction
ACL-RSI	Anterior cruciate ligament return to sport after injury scale
ADL	Activities of daily living
ASIS	Anterior superior iliac spine
AUC	Area under the curve
BMI	Body mass index
C3D	Co-ordinate 3D file
CHESM	Centre for Health, Exercise and Sports Medicine
CI	Confidence interval
CKRS	Cincinnati knee rating scale
EEG	Electroencephalogram
EMG	Electromyography
GRF	Ground reaction force
Hz	Hertz
ICC	Intraclass correlation coefficient
ICF	International Classification of Functioning, Disability and Health
IKDC	International Knee Documentation Committee Score
IQR	Interquartile range
kg	Kilogram
KOOS	Knee Osteoarthritis Outcome Score

LSI	Limb symmetry index
MDC	Minimal detectable change
MOCP	Monophasic oral contraceptive pill
MVIC	Maximum voluntary isometric contraction
N	Newtons
Nm	Newton metres
OA	Osteoarthritis
OR	Odds ratio
RMS	Root mean square
RMSE	Root mean square error
RR	Risk ratio
SD	Standard deviation
SE	Standard error
SEM	Standard error of measurement
STGT	Semitendinosus tendon gracilis tendon



# Chapter 1

## Introduction and thesis overview

### 1.1 Overview of thesis

The research reported in this thesis was conducted at the Centre for Health, Exercise and Sports Medicine (CHESM) movement laboratory at the University Of Melbourne between March 2011 and September 2013. The overall aim of the research was to investigate the cross-sectional associations between clinical tests of knee joint function and i) sports participation, ii) participant characteristics, iii) neuromuscular variables and iv) biomechanical variables following anterior cruciate ligament reconstruction (ACLR). Throughout this thesis, the term knee joint function refers to activity limitations, assessed using self-reported knee function questionnaires and functional performance tests. The term neuromuscular variable refers to muscle activation strategies and the term biomechanical variable refers to kinematics (i.e., movement) and kinetics (i.e., ground reaction forces, joint moments and muscle forces). Collectively, neuromuscular and biomechanical variables are referred to as measures of neuromuscular control.

To achieve the aims listed above, four separate cross-sectional observational studies were conducted involving 66 individuals with ACLR and 41 physically-active control participants. Novel methods were developed to assess sub-maximal neuromuscular control using both open and closed kinetic chain activities. The data analysis procedures described in this thesis were developed specifically for the research and built upon the methodology of previous investigations. Pilot and reliability testing were used to inform the development of the testing protocol and data analysis procedures. An overview of the structure of the thesis follows:

**Chapter one** is an overview of the thesis and introduction to the problem. **Chapter two** is a review of the literature related to the thesis. Literature pertaining to the assessment of knee functional outcomes and biomechanical and neuromuscular variables derived from open and closed kinetic chain tasks was synthesised, critically appraised and

discussed. The findings of this literature review were used to inform the four cross-sectional observational studies that comprise the research undertaken for the thesis.

**Chapter three** is the first of four observational studies included in this thesis. In this study, the self-reported knee function and functional performance of participants with ACLR was compared to a group of uninjured participants. The associations between knee function, sports participation and participant characteristics were then investigated.

**Chapter four** describes the assessment of open kinetic chain neuromuscular control following ACLR. The accuracy of quadriceps force and thigh muscle activation strategies of participants with ACLR and control participants were assessed using a sub-maximal force-matching task. The task was piloted and developed by the PhD candidate specifically for this research. As a foundation to the study presented in this chapter, a group of ACLR and control participants were compared using the force-matching task (Telianidis *et al.*, 2014). The study reported in this chapter extends on the work by Telianidis *et al.* (2014), by exploring the relationships between quadriceps force control, level of sports participation and participant characteristics in a larger group of participants.

**Chapter five** describes the investigation of closed kinetic chain neuromuscular control following ACLR. The trunk and lower limb kinematics and kinetics of ACLR and control participants were assessed using a standardised single leg landing task. The multivariate associations between knee flexion excursion, level of sports participation and participant characteristics and preparatory muscle activation were then observed in the ACLR group.

**Chapter six** addresses the primary aim of the thesis. Drawing on the findings of the previous three studies, the associations between knee joint function (assessed in Chapter 3) and i) sports participation, ii) participant characteristics, iii) neuromuscular variables and iv) biomechanical variables derived from open and closed kinetic chain testing (assessed in Chapters 4 and 5) were investigated. **Chapter seven** summarizes the findings of the four studies, and presents a synopsis of the clinical implications of the research reported in the thesis.

## 1.2 Introduction

The anterior cruciate ligament (ACL) of the knee is an intracapsular, extrasynovial ligament consisting of dense, non-parallel collagenous tissue (Danylchuk, 1978; Yasuda *et al.*, 2011). The ACL consists of anteromedial and posterolateral bundles that originate from a wide origin on the anterior intercondylar eminence of the tibia and insert on the posteromedial aspect of the lateral femoral condyle (Georgoulis *et al.*, 2010; Yasuda *et al.*, 2011). These anatomical characteristics give the ACL considerable strength, whilst permitting a large range of physiological movement and limiting anterior tibial translation, internal tibial rotation and valgus movements (Butler, 1980).

While providing mechanical stability to the knee joint, the ACL also has a neurosensory role. Mechanoreceptors located within the ACL provide the central nervous system with information about the magnitude of stress and strain within the knee joint (Ageberg & Fridén, 2008; Johansson *et al.*, 1991; Solomonow & Krogsgaard, 2001). Through repeated experience, individuals use this sensory feedback to refine dynamic restraints and optimise the performance of functional tasks (Bryant *et al.*, 2009b; Swanik *et al.*, 2004). Subtle adjustments to the timing and magnitude of muscle contractions allow individuals to optimise movement patterns and protect the knee from injury during high load activity (Ageberg & Fridén, 2008; Blackburn *et al.*, 2013; Bryant *et al.*, 2008b; Ingersoll *et al.*, 2008).

Despite its neurosensory protective mechanisms and its strength, the ACL is the most frequently injured of the knee ligaments (Johnson, 1983; Miyasaka *et al.*, 1991). ACL rupture is common in young, active individuals participating in pivoting, cutting, jumping and landing sports (Desai *et al.*, 2014; Järvelä *et al.*, 2002; Micheo *et al.*, 2010). The worldwide annual population incidence of ACL rupture is estimated to be between 0.01 and 0.05% (8 to 52 per 100,000 people) in the general population and between 0.15 and 3.37% (152 to 3672 per 100,000 people) among professional athletes (Moses *et al.*, 2012). Anterior cruciate ligament rupture is commonly associated with injury to the chondral surfaces or fibro-cartilaginous menisci of the knee (Ahldén *et al.*, 2012; Borchers *et al.*, 2011; Lind *et al.*, 2009; Maletis *et al.*, 2013). An analysis of 16,192 ACLR surgeries performed in North America over a six year period identified

chondral and meniscal injuries in 25% and 61% of ACLR surgeries respectively (Maletis *et al.*, 2013).

In most cases, ACL rupture results in knee joint instability and significant knee functional limitations (Pinczewski *et al.*, 2002). Following ACL injury, patients are presented with the options of conservative or surgical management. Although good self-reported knee function can be achieved with either management approach (Frobell *et al.*, 2010), ACL reconstruction (ACLR) is commonly recommended to individuals who experience recurrent episodes of giving way in their knee, or who wish to return to pivoting sports (Feller & Webster, 2013). The incidence of osteoarthritis (OA) is high following ACLR regardless of whether a conservative or surgical approach is used (Lohmander *et al.*, 2004).

ACLR involves drilling bone tunnels in the tibia and femur and using those tunnels to attach a graft within the knee joint as a substitute for the native ACL (Noh *et al.*, 2013). A number of graft choices are available for ACLR, including patella tendon, single bundle or double bundle hamstring tendon, allografts and synthetic grafts (Feller & Webster, 2003; Hemmerich *et al.*, 2011; Machotka, 2010; Maletis *et al.*, 2013; Pinczewski *et al.*, 2007; Song *et al.*, 2014; Yasuda *et al.*, 2011). The four-strand hamstring and gracilis tendon (STGT) graft harvested from the ipsilateral limb has become the most widely used ACL graft in recent years amongst recreational athletes (Andernord *et al.*, 2014; Kvist *et al.*, 2014; Lind *et al.*, 2009).

The primary goal of ACLR is to restore the mechanical stability of the knee joint and facilitate the safe return to pivoting, cutting and jumping sports (Yasuda *et al.*, 2011). Following surgery, an extensive program of rehabilitation is required to achieve *functional* knee stability; that is, to optimise movement patterns and eliminate episodes of the knee giving way during demanding functional tasks (Barber-Westin & Noyes, 2011a; Wilk *et al.*, 2012). The objective of rehabilitation after ACLR is to improve knee joint function by addressing modifiable impairments, such as reduced range of movement (Risberg *et al.*, 1999c), knee effusion (Lentz *et al.*, 2009) and neuromuscular impairments such as strength deficits and mal-adaptive movement patterns (Ageberg, 2002; Eitzen *et al.*, 2010; Risberg & Holm, 2009). That said, knee functional outcomes after ACLR are variable; i.e., not all patients achieve a high level of function (de Jong *et*



*al.*, 2007; Myer *et al.*, 2012; Thomeé *et al.*, 2012). Hence, the identification of factors that are associated with knee functional limitations following ACLR may help clinicians identify patients who may benefit from additional rehabilitation and contribute to the development and refinement of existing rehabilitation protocols (Myer *et al.*, 2012).

Many previous investigations have utilised maximal intensity tasks such as strength testing (Petschnig, 1998; Schmitt *et al.*, 2012; Xergia *et al.*, 2014) and maximal hopping tests (Bryant *et al.*, 2009b) to examine the association between neuromuscular impairments and knee function. However, few studies have investigated the association between neuromuscular impairments and knee function using sub-maximal intensity tasks. Although strength and maximal functional performance are important determinants of knee function after ACLR (Myer *et al.*, 2006; Myer *et al.*, 2008), the ability to control sub-maximal force in both open and closed kinetic chain movements may also be associated with knee functional outcomes after ACLR.

The associations between knee joint function and participant characteristics, such as age, sex, body mass index and concomitant injuries, have been evaluated using large, population-based investigations (Barenius *et al.*, 2013; Cox *et al.*, 2014; Inacio *et al.*, 2014; Røtterud *et al.*, 2013). However, to the author's knowledge, no previous investigations have directly examined the multivariate associations between knee joint function, participant characteristics and neuromuscular control, whilst accounting for current sports participation. Therefore, the overall aim of the research presented in this thesis was to quantify the associations between knee joint function and i) sports participation, ii) participant characteristics, iii) neuromuscular variables and iv) biomechanical variables following ACLR.

## Chapter 2

### Literature review

#### 2.1 Chapter Overview

In the last 20 years there has been a rapid growth in the volume of published research on neuromuscular control and knee functional outcomes following ACLR (Pappas *et al.*, 2013). To inform the development of the studies included in this thesis, it was necessary to understand the neuromuscular adaptations and knee functional limitations that occur following ACLR, by critically appraising this literature. Hence, this review of the literature is organised in the following sections:

- 2.2 Knee function following ACLR
- 2.3 Non-neuromuscular factors associated with knee function after ACLR
- 2.4 Open kinetic chain neuromuscular adaptations after ACLR
- 2.5 Closed kinetic chain neuromuscular adaptations after ACLR
- 2.6 The relationship between neuromuscular control and knee joint function.

A vast number of investigations have assessed knee function and neuromuscular responses following ACLR; hence, it was necessary to carefully define the population of interest. The aim of the research reported in this thesis was to investigate the associations between clinical tests of knee joint function and i) sports participation, ii) participant characteristics, iii) neuromuscular variables and iv) biomechanical variables following anterior cruciate ligament reconstruction (ACLR). Differences in knee function, sports participation, rehabilitation and concomitant knee injuries may exist between older and younger patients following ACLR, particularly between children, adolescents and adults (Barendrecht *et al.*, 2011; Desai *et al.*, 2014; Hartigan *et al.*, 2012; Kaeding *et al.*, 2010); therefore, this literature review focused on individuals with ACLR aged 18 years and older.

## **2.2 Knee function following ACLR**

### **2.2.1 Overview**

The aim of ACLR is to restore knee joint function and facilitate a safe return to activities of daily living, work and sport (Myer *et al.*, 2006; Myer *et al.*, 2008). Previously, time since surgery has been used to determine readiness to return to unrestricted activities following ACLR (Barber-Westin & Noyes, 2011a). However, it is increasingly recognised that time from surgery is a poor predictor of knee joint function and sports participation (Myer *et al.*, 2012). A growing body of research demonstrates that knee functional criteria, rather than time, should be used to guide rehabilitation decisions after ACLR (Barber-Westin & Noyes, 2011b; Di Stasi *et al.*, 2013; Hartigan *et al.*, 2010; Hartigan *et al.*, 2012; Myer *et al.*, 2012; Thomeé *et al.*, 2011).

Despite the restoration of mechanical knee joint stability, knee functional outcomes after ACLR are variable, particularly amongst recreational athletes (Lentz *et al.*, 2009; Logerstedt *et al.*, 2012b). Poor knee joint function following ACLR may prevent individuals from achieving their previous or desired level of sports participation (Nyland *et al.*, 2013). Asymmetrical functional performance is also associated with the development of knee osteoarthritis (Pinczewski *et al.*, 2007) and a greater risk of further ACL injury (Paterno *et al.*, 2010; Webster *et al.*, 2014a). Knee function is a broad construct (Reiman & Manske, 2011) and the factors that may associate with knee function after ACLR are numerous (Ageberg *et al.*, 2010; Bryant *et al.*, 2008b; Chmielewski *et al.*, 2011; Desai *et al.*, 2014; Inacio *et al.*, 2014; Lentz *et al.*, 2009; Sofu *et al.*, 2014). Hence, prior to investigating the relationship between neuromuscular control and knee function after ACLR, it was necessary to review the literature in the following sub-sections to determine:

- 2.2.2 How knee function is assessed following ACLR
- 2.2.3 Knee functional limitations experienced by individuals following ACLR
- 2.2.4 The association between self-reported knee function and functional performance
- 2.2.5 Non-neuromuscular factors associated with knee function after ACLR (participant characteristics, concomitant injuries and psychological factors)

### **2.2.2 How knee function is assessed following ACLR**

Knee function following ACLR can be assessed using self-reported measures (i.e., questionnaires; (Collins *et al.*, 2011), or functional performance measures such as jumping and hopping tests (Gustavsson *et al.*, 2006). Self-reported knee function questionnaires and functional performance tests assess different aspects of knee function, and neither can act as a proxy for the other (Fitzgerald *et al.*, 2001; Reinke *et al.*, 2011). A comprehensive evaluation of knee function should therefore include both self-reported knee function and measures of functional performance (Reiman & Manske, 2011).

### **2.2.3 Knee functional limitations experienced by individuals following ACLR**

#### *Assessing self-reported knee function following ACLR*

Knee functional questionnaires provide clinicians with a summary of a patient's perspectives on their current knee function, and allow researchers and clinicians to assess changes in knee function over time, in a standardised manner (Hartigan *et al.*, 2010; Reinke *et al.*, 2011). Self-report knee function questionnaires quantify symptom-related activity limitations and limitations during occupational tasks or activities of daily living (Hambly & Griva, 2010; Irrgang *et al.*, 2001; Noyes *et al.*, 1989). Prior to selecting a self-reported knee function questionnaire, it is necessary to understand their purpose, intended populations, clinimetric properties and limitations.

The questionnaires most commonly used to assess knee function following ACLR are the Knee Osteoarthritis Outcome Score (KOOS) (Roos *et al.*, 1998), the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation form (Irrgang *et al.*, 2001), the Lysholm scale (Lysholm & Gillquist, 1982) and the Cincinnati Knee Rating Scale (CKRS) (Noyes *et al.*, 1991). The clinimetric properties of these measures have been extensively investigated and each measure has demonstrated good internal consistency, test-retest reliability, content validity and construct validity (Barber-Westin *et al.*, 1999; Collins *et al.*, 2011; Comins *et al.*, 2008; Hambly & Griva, 2010; Wang *et al.*, 2010). The purpose, intended populations, administration and clinimetric properties of these questionnaires is summarised in Table 2.1.

**Table 2.1** Summary of four self-reported questionnaires used to assess knee function following ACLR; the Knee Osteoarthritis Outcome Score (KOOS), the International Knee Documentation Committee Score (IKDC) Subjective Knee Evaluation form, the Lysholm scale and the subjective components of the Cincinnati Knee Rating Scale (CKRS).

	<b>KOOS</b> (Roos <i>et al.</i> , 1998)	<b>IKDC</b> (Irrgang <i>et al.</i> , 2001)	<b>Lysholm scale</b> (Lysholm & Gillquist, 1982)	<b>CKRS*</b> (Noyes <i>et al.</i> , 1991)
<b>Purpose</b>	To investigate the short and long-term consequences of knee injury	To assess knee-related activity limitations in activities of daily living and sport	To evaluate symptoms and knee functional limitations after knee injury	To assess knee-related activity limitations in activities of daily living and sport
<b>Intended populations</b>	Patients with knee injuries and/or osteoarthritis	Patients with ACL injury, meniscal or chondral pathology, patellofemoral pain	Patients with knee ligament injuries – particularly with symptoms of instability	Patients with knee injury, particularly ACL injury, or following ACLR
<b>Domains or sub-scales</b>	42 items across 5 sub-scales: 1. Pain 2. Knee symptoms 3. Knee function in activities of daily living 4. Knee function in sports and recreation 5. Knee-related quality of life	18 items across 3 sub-scales: 1. Symptoms (pain, stiffness, swelling, locking/catching giving way) 2. Knee function in sports and activities of daily living 3. Overall rating of current and pre-injury knee function	8 items in a single scale: Limping, support, knee locking, knee instability, knee pain, swelling, stair climbing and squatting	10 items across 3 sub-scales: 1. Knee functional limitations due to: • Pain • Swelling • Giving way 2. Knee function in activities of daily living 3. Knee function in sport
<b>Scoring</b>	Scores converted to percentage, where 100% = no limitation	Score range from 0-100 points, where 100 points = no limitation.	Score range from 0-100 points, where 100 points = no limitation. Scores are categorized as excellent (95–100), good (84–94), fair (65–83), and poor ( $\leq 64$ ) (Lysholm & Gillquist, 1982; Noyes <i>et al.</i> , 1991).	
<b>Validity and reliability</b>	Good test-retest reliability and internal consistency, no floor or ceiling effects for knee injuries and knee OA (Roos <i>et al.</i> , 1998)	Good test-retest reliability and internal consistency, no floor or ceiling effects for knee injuries (Collins <i>et al.</i> , 2011)	Adequate test-retest reliability, unacceptable ceiling effects for limp, support, locking and instability items (Briggs <i>et al.</i> , 2006)	Good test-retest reliability, good content validity, no floor or ceiling effects at 24 months following ACLR (Barber-Westin <i>et al.</i> , 1999)
<b>Comments</b>	Broader scope and purpose. A total score has not been validated	Highly correlated with CKRS ( $r = 0.88 - 0.95$ ) (Agel & LaPrade, 2009)	May be most suitable for meniscal or chondral injuries (Briggs <i>et al.</i> , 2006)	Provides the most specific assessment of activity limitations following ACL injury and ACLR

The four self-reported knee function questionnaires presented in Table 2.1 appear to assess knee function in a similar way, and all demonstrate adequate face validity (Collins *et al.*, 2011). However, before selecting a self-reported knee function questionnaire for research purposes, differences in the design, administration and intended populations of each instrument should be carefully considered (Agel & LaPrade, 2009).

The KOOS has been used extensively over the last 15 years to quantify self-reported knee function after ACLR (Hjermundrud *et al.*, 2010; Inacio *et al.*, 2014; Kvist *et al.*, 2005; Möller *et al.*, 2009; Risberg *et al.*, 1999a; Ruiz *et al.*, 2002). The extensive use of the KOOS can be attributed to its broader scope and purpose. The KOOS assesses knee pain, symptoms and knee function in activities of daily living, sports and recreation and knee-related quality of life using five separate sub-scales which are reported separately (Roos *et al.*, 1998). One disadvantage of the KOOS is that a total score has not been validated (Collins *et al.*, 2011).

The Lysholm scale and the IKDC are commonly used to assess functional limitations after ACLR; however, these questionnaires are less specific to ACL injury and ACLR (Risberg *et al.*, 1999b; Wang *et al.*, 2010; Wright, 2009). The Lysholm scale emphasizes knee stability and symptoms of knee locking; hence, it is less ACLR-specific and may be more appropriate for assessing chondral or meniscal injuries, or knee function following ACL injury and/or meniscal or chondral injuries (Briggs *et al.*, 2006). Concern has been raised about potential ceiling effects for the Lysholm scale after ACLR and a lack of sensitivity for detecting neuromuscular impairments and change in knee function over time (Andrade *et al.*, 2002; Bollen *et al.*, 1991; Risberg *et al.*, 1999b). The IKDC, although versatile and having age and gender-specific normative data, is a more general knee questionnaire, which is less specific to the activity limitations experienced by individuals following ACLR who may participate in high-level functional activities (Collins *et al.*, 2011; Wang *et al.*, 2010).

Of the four self-reported knee questionnaires listed above, the CKRS arguably provides the most specific assessment of knee-related activity limitations after ACLR, in that it focusses exclusively on knee joint function and functional limitations as they relate to symptoms (Agel & LaPrade, 2009). The CKRS assesses knee limitations related to

symptoms, knee function in activities of daily living and knee function in sports (Noyes *et al.*, 1991). The sports sub-scale focuses on tasks that are known to stress the ACL, such as pivoting, jumping and landing (Barber-Westin *et al.*, 1999; Noyes *et al.*, 1991). Hence the CKRS is commonly used for concurrent assessments of self-reported knee function, functional performance and biomechanics, where assessment of the symptoms of osteoarthritis and quality of life is not assessed, or assessed separately (Bryant *et al.*, 2008b; Bryant *et al.*, 2009b; Eitzen *et al.*, 2010; Risberg *et al.*, 1999c; Risberg *et al.*, 2007).

In a well-powered, prospective investigation involving 120 individuals with ACLR of both genders, Risberg *et al.* (1999b) reported significant improvements in self-reported knee function between three, six, 12 and 24 month post-operative time points. Self-reported knee function was quantified using the IKDC, Lysholm scale and CKRS; however, of the three questionnaires, only the CKRS demonstrated significant changes between each follow up. The authors concluded that the CKRS was the most sensitive to change over time of the three questionnaires.

The original CKRS also included measures of knee joint instability, radiographic findings and the results of functional performance tests (Barber-Westin *et al.*, 1999). However, previous authors who have used the CKRS have elected to report knee joint instability and radiographic findings separately, as these are measures of impairment, not knee function (Bryant *et al.*, 2009b; Eitzen *et al.*, 2009; Hopper *et al.*, 2002; Reiman & Manske, 2011; Risberg *et al.*, 1999c). Furthermore, previous authors have recommended that functional performance measures are reported separately from self-reported knee function, rather than being combined in a single continuous score (Risberg *et al.*, 1999b). Hence, consistent with these previous investigations, the CKRS scores referred to in this literature review are comprised of only the self-reported components of the original CKRS; that is, the symptoms, activities of daily living and sports sub-scales.

### *Self-reported knee function following ACLR*

Numerous studies have assessed the self-reported knee function of patients following ACLR. However, fewer studies have reported the scores for individual questions within these measures. The studies that have reported this data have found that the self-reported knee function of individuals following ACLR during activities of daily living is comparable to that of uninjured subjects at greater than 12 months following surgery (Noyes & Barber-Westin, 1997; Seto *et al.*, 1988). However, jumping, landing, twisting, cutting and pivoting activities, typical of sports such as soccer, basketball and handball, are challenging for many individuals following ACLR (Feller & Webster, 2013; Zaffagnini *et al.*, 2014) and progressively greater knee limitations become apparent as activity intensity increases (Noyes *et al.*, 1989).

Table 2.2 provides a summary of 23 investigations that have assessed self-reported knee function after primary ACLR with a hamstring tendon graft, using the KOOS, the IKDC, the CKRS or the Lysholm scale. Despite an average time since ACLR of over two years (27.1 months), the average self-reported knee function score for all measures was 84.5% and the weighted averages for each questionnaire ranged from 93.5% for the Lysholm score to 84% for the IKDC. The minimum clinically important difference (MCID) for these knee function questionnaires after ACLR is not known (Collins *et al.*, 2011; Risberg *et al.*, 1999b). However, scores below 85% are typically considered unacceptable in terms of general knee function after ACLR, regardless of the knee function scale used (Arderm *et al.*, 2011b; Logerstedt *et al.*, 2012a; Lustosa *et al.*; Williams *et al.*, 2005b), and a minimum of 90% on at least two self-reported knee function scales is recommended prior to return to sport (Di Stasi *et al.*, 2013; Hartigan *et al.*, 2010). The definition of unacceptable knee function should therefore be population specific, and should consider the lifestyle, occupation and level of sporting activity of individuals (Reiman & Manske, 2011).



**Table 2.2** Summary of investigations that have assessed self-reported knee function following ACLR with a hamstring autograft from the ipsilateral limb, using either the Knee Osteoarthritis Outcome Score (KOOS), the International Knee Documentation Committee Score (IKDC) Subjective Knee Evaluation form, the Lysholm scale or the subjective components of the Cincinnati Knee Rating Scale (CKRS)

Study	Participants	Time since ACLR (months)	Questionnaire	Self-reported knee function (%)	
				Mean $\pm$ SD	Weighted mean
<b>Knee Osteoarthritis Outcome Score</b>					
Zaffagnini <i>et al.</i> (2014)	21 men	3	KOOS <sub>ADL</sub> KOOS <sub>SPORT</sub>	84.4 $\pm$ 15.5 81.2 $\pm$ 17.0	91.3%
		6	KOOS <sub>ADL</sub> KOOS <sub>SPORT</sub>	96.9 $\pm$ 8.6 98.3 $\pm$ 8.7	
		12	KOOS <sub>ADL</sub> KOOS <sub>SPORT</sub>	98.3 $\pm$ 6.5 98.6 $\pm$ 6.2	
Delahunt <i>et al.</i> (2012a)	14 women	34.8 $\pm$ 33.6	KOOS <sub>ADL</sub> KOOS <sub>SPORT</sub>	98.1 $\pm$ 4.4 81.1 $\pm$ 15.8	
Ageburg <i>et al.</i> (2009)	16 (4 women)	36 (24-60)	KOOS <sub>ADL</sub> KOOS <sub>SPORT</sub>	95.0 $\pm$ 9.6 77.0 $\pm$ 22.1	
<b>International Knee Documentation Committee Score</b>					
Vermesan <i>et al.</i> (2014)	23 (7 women)	12 (11-13)	IKDC	95.7 $\pm$ 2.6	84.0%
	48 (6 women)	12 (11-13)	IKDC	92.7 $\pm$ 3.6	
Jang <i>et al.</i> (2014)	51 men (RTS group)	33 $\pm$ 7	IKDC	90.7 $\pm$ 8.7	
	16 men (non-RTS group)	37 $\pm$ 7	IKDC	87.7 $\pm$ 7.8	
Delahunt <i>et al.</i> (2012a)	14 women	34.8 $\pm$ 33.6	IKDC	88.2 $\pm$ 11.8	
Leys <i>et al.</i> (2012)	51 (24 women)	180	IKDC	90.0 $\pm$ 11.8	
Kim <i>et al.</i> (2012)	39 men	32 $\pm$ 6	IKDC	81.1 $\pm$ 10.5	
Lam <i>et al.</i> (2011)	10 men	10 $\pm$ 4	IKDC	92.1 $\pm$ 10.1	
Aglietti <i>et al.</i> (2004)	120 (14 women)	4 12 24	IKDC IKDC IKDC	72 83 85	
<b>Lysholm score</b>					
Jang <i>et al.</i> (2014)	51 men (RTS group)	33 $\pm$ 7	Lysholm score	93.9 $\pm$ 6.9	93.5%
	16 men (non-RTS group)	37 $\pm$ 7	Lysholm score	90.5 $\pm$ 8.4	
Leys <i>et al.</i> (2012)	51 (24 women)	180	Lysholm score	93.0 $\pm$ 10.0	
Kim <i>et al.</i> (2012)	39 men	32 $\pm$ 6	Lysholm score	88.7 $\pm$ 10.5	
Lam <i>et al.</i> (2011)	10 men	10 $\pm$ 4	Lysholm score	97.4 $\pm$ 4.0	
Misonoo <i>et al.</i> (2011)	22 (11 women)	12.3 $\pm$ 2.7	Lysholm score	93.1 $\pm$ 3.5	

Study	Participants	Time since ACLR (months)	Questionnaire	Self-reported knee function (%)	
				Mean $\pm$ SD	Weighted mean
Misonoo <i>et al.</i> (2011)	12 men	24 (24-26)	Lysholm score	92 †	
Holm <i>et al.</i> (2010)	29 (14 women)	128 $\pm$ 5	Lysholm score	86.1 $\pm$ 15.1	
Chouliaras <i>et al.</i> (2009); Georgoulis <i>et al.</i> (2007)	11 men	12 $\pm$ 2.2	Lysholm score	92 †	
Lidén <i>et al.</i> (2007)	37 (11 women)	84	Lysholm score	90 †	
Logan <i>et al.</i> (2004)	10 men	NR (9-18)	Lysholm score	98 †	
Pinczewski <i>et al.</i> (2002)	90 (43 women)	24 60	Lysholm score	95 † 95 †	
Corry <i>et al.</i> (2002)	61 (43 women)	24	Lysholm score	90 (10) †	
<b>Cincinnati Knee Rating Scale</b>					
Vermesan <i>et al.</i> (2014)	23 (7 women)	12 (11-13)	CKRS	96.1 $\pm$ 2.9	88.9%
	48 (6 women)	12 (11-13)	CKRS	92.5 $\pm$ 4.6	
Holm <i>et al.</i> (2010)	29 (14 women)	128 $\pm$ 5	CKRS	87.8 $\pm$ 12.3	
Bryant <i>et al.</i> (2009b)	13 men	14 $\pm$ 5	CKRS	87.5 $\pm$ 11.8	
Feller and Webster (2003)	33 (10 women)	12	CKRS	87.7 $\pm$ 12.0	
		24		91.9 $\pm$ 9.3	
		36		93.7 $\pm$ 9.0	
Buelow <i>et al.</i> (2002)	30 (12 women)	26.6	CKRS	86.0 $\pm$ 8.5	
	30 (13 women)	27.1	CKRS	87.0 $\pm$ 8.9	
Hopper <i>et al.</i> (2002)	19 (6 women)	12	CKRS	82.1	
Aune <i>et al.</i> (2001)	37 (16 women)	12	CKRS	87.1 $\pm$ 10.5	
		18		87.8 $\pm$ 18.0	
Wilk (1994)	50 (21 women)	6 (4.8-6.9)	CKRS	86.6 $\pm$ 23.1	

Values are means  $\pm$  standard deviations (ranges). Where no error measurement is presented this data was not provided in the study; † = median (interquartile range) and weighted medians; SD = standard deviation; NR = not reported; RTS = return to sport

Collectively, these investigations demonstrate that many individuals continue to experience self-reported knee functional limitations following ACLR, and that these limitations do not necessarily resolve with time. Inspection of the standard deviations of knee function scores provided in Table 2.2 reveals considerable variability in self-reported knee function. This variability is further highlighted by the seven investigations that provided the range of self-reported knee function scores. Within these investigations, some individuals rated their knee function at 100% (Lidén *et al.*, 2007; Logan *et al.*, 2004; Pinczewski *et al.*, 2002; Wilk, 1994); whereas other individuals rated their knee function as low as 50% (Lidén *et al.*, 2007).

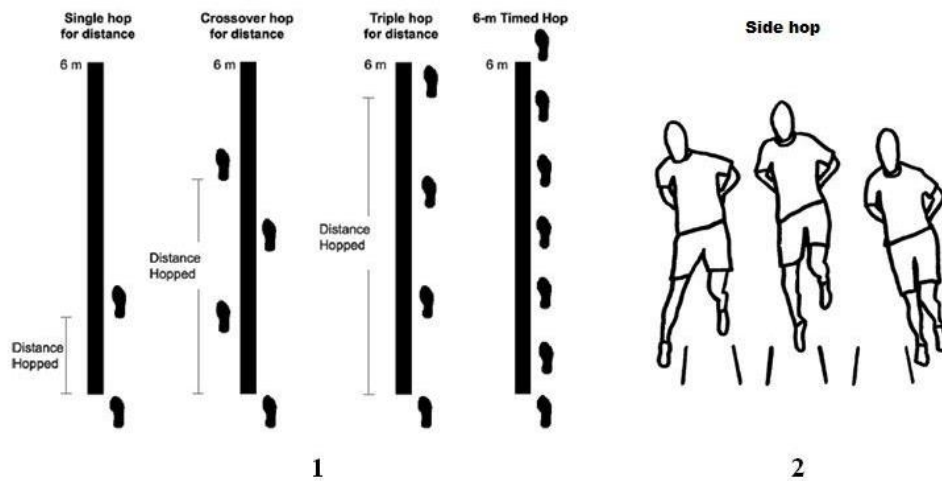
#### *Assessing functional performance following ACLR*

Self-reported knee function measures provide insight into the patient's perspective on their knee function; however, they do not provide an objective measurement of current knee function (Logerstedt *et al.*, 2012a). Hence, in addition to quantifying self-reported activity limitations following ACLR, testing routines typically also include measures of functional performance (Abrams *et al.*, 2014). Evaluation of functional performance may involve sports-specific tests such as jumping (Delahunt *et al.*, 2012c), landing (Decker *et al.*, 2002), sidestepping or cutting (Miranda *et al.*, 2013), agility or running (Jang *et al.*, 2014) and single leg hopping tests (Gustavsson *et al.*, 2006).

Functional performance tests are typically chosen to replicate specific demands of sport, such as muscular power, strength, endurance and postural control (Clark, 2001). A recent systematic review of 88 primary investigations found that single leg hop tests are the most commonly used functional performance test after ACLR (Abrams *et al.*, 2014). Furthermore, single leg hop tests have been found to be more sensitive than double leg functional performance tests (e.g. jumping), in detecting functional deficits after ACLR (Myer *et al.*, 2011b). Hence, this review of the literature focused on investigations that have used hop tests to assess function performance after ACLR.

Hop tests are simple to administer and functionally demanding; hence, these tests are commonly used to assess both knee function and readiness to return to sport following ACLR, without the need for population-specific normative data (Barber-Westin & Noyes, 2011a; Fitzgerald *et al.*, 2001; Hopper *et al.*, 2008). Hop tests involve either the

maximum distance hopped or the maximum number of hops completed in a designated time on the involved (i.e., ACLR) leg (Gustavsson *et al.*, 2006). Distance-based hop tests include the single hop for distance, crossover hop for distance, triple hop for distance and 6 metre timed hop (Abrams *et al.*, 2014). The side hop, which assesses the maximum number of hops side-to-side between two lines placed 40 centimetres apart, is an example of a time-based hop test (Gustavsson *et al.*, 2006). An overview of these hop tests is provided in Figure 2.1.



**Figure 2.1** Example of single leg hop tests commonly used to assess functional performance after ACLR; 1 from (Grindem, 2011), and 2 from (Gustavsson *et al.*, 2006).

The distance hopped, or number of hops performed on the involved leg, may be influenced by differences in height, motivation and sporting experience between individuals (Reiman & Manske, 2011; Reinke *et al.*, 2011). To account for this variability, functional performance tests are commonly expressed as an index of the uninvolved side; that is, a limb symmetry index (LSI; (Narducci *et al.*, 2011). A LSI is calculated by dividing the performance measured for the involved leg by the performance of the uninvolved (i.e., contralateral) leg and multiplying the result by 100 (Noyes *et al.*, 1991).

Hop tests are reliable in ACLR and uninjured control populations both as absolute measures (i.e. distance or number of hops; (Augustsson *et al.*, 2006; Brosky Jr *et al.*, 1999; Gustavsson *et al.*, 2006; Kramer *et al.*, 1992; Munro & Herrington, 2011) or when expressed as a LSI (Hopper *et al.*, 2002; Kramer *et al.*, 1992; Paterno & Greenberger, 1996; Reid *et al.*, 2007). The reliability of hop tests has been demonstrated at four months (Reid *et al.*, 2007) seven months (Brosky Jr *et al.*, 1999; Paterno & Greenberger, 1996) and twelve months following ACLR (Hopper *et al.*, 2002). For example, with a sample of 42 men and women, Reid *et al.* (2007) reported intraclass correlation coefficients ( $ICC_{2,1}$ ) of 0.92 for the hop for distance test (95% CI 0.87-0.97) and 0.84 for the crossover hop test (95% CI 0.74-0.94) at four months following ACLR.

The validity of single leg hop tests has also been evaluated extensively after ACLR (Hamilton *et al.*, 2008; Logerstedt *et al.*, 2012c; Reid *et al.*, 2007; Reinke *et al.*, 2011). Individually, hop tests demonstrate variable levels of sensitivity and specificity. For example, Logerstedt *et al.* (2012a), in a well-designed investigation involving 79 men and women following ACLR, used univariate logistic regression to assess whether hop LSI's assessed at six months following surgery were predictive of IKDC scores at the 12 month post-operative time-point. Collectively, the hop LSI's demonstrated good sensitivity and specificity. For example, a sensitivity of 0.88 was observed for the crossover hop test (95% CI 0.66 – 0.97) and a specificity of 0.72 (95% CI 0.60 – 0.81) was observed for the hop for distance test. However, the hop for distance test demonstrated a sensitivity of 0.53 (95% CI 0.31 – 0.74). Hence, individual hop tests, used in isolation, may not be sensitive enough to detect knee functional limitations for all individuals following ACLR.

To increase the sensitivity of functional performance tests after ACLR, previous authors have used batteries of three to five hop tests (Di Stasi *et al.*, 2013; Gustavsson *et al.*, 2006; Hartigan *et al.*, 2010; Thomeé *et al.*, 2012). Rather than report an average LSI, individuals are dichotomised according to whether they do, or do not achieve a pre-determined LSI on each test (Gustavsson *et al.*, 2006). Gustavsson *et al.* (2006) at 6 months following ACLR and Thomeé *et al.* (2012) at 24 months following ACLR, reported that a battery of single leg hop tests was more sensitive in discriminating between the performance of the involved and uninvolved legs than any single hop test

used in isolation. The inclusion of hop tests that involve muscular endurance, such as the side hop test, has been found to further increase the sensitivity of functional performance test batteries (Augustsson *et al.*, 2004; Gustavsson *et al.*, 2006).

Previous investigations that have used batteries of hop tests to assess knee function after ACLR have used 90% LSI on each of the tests as a criterion for passing the test battery (Di Stasi *et al.*, 2013; Gustavsson *et al.*, 2006; Hartigan *et al.*, 2010; Logerstedt *et al.*, 2012a). However, in each of these investigations, the purpose of assessing a battery of hop tests has been to assess readiness for return to sport. Furthermore, each of these investigations included individuals who planned to return to higher levels of sport. For the general ACLR population, particularly for individuals who plan to return to lower levels of sport, fewer individuals may achieve 90% or more LSI on all tests. For example, (Thomeé *et al.*, 2012) reported that approximately 50% of their participants were unable to achieve greater than 90% LSI on the side hop test at 12 months post ACLR, despite being involved in high level sport (median Tegner score 8).

The use of a lower cut-off (e.g. 85% LSI) to assess general knee joint function may help to improve the specificity of the testing battery, by reducing the number of otherwise well-functioning individuals who are inappropriately classified as having unacceptable knee function (Holsgaard-Larsen *et al.*, 2014). Indeed, several previous investigations have used a cut-off of 85% LSI to dichotomise participants as having acceptable or unacceptable knee function (Ardern *et al.*, 2011b; de Jong *et al.*, 2007; Hohmann *et al.*, 2011; Holsgaard-Larsen *et al.*, 2014; Hopper *et al.*, 2008; Noyes *et al.*, 1991; Wilk, 1994; Williams *et al.*, 2005b). However, the use of a lower cut-off LSI may reduce the sensitivity of the hop testing battery (Thomeé *et al.*, 2012). Hence, a higher cut-off value (i.e. > 90%) has been recommended for determining the ability of individuals to return to sport (Thomeé *et al.*, 2011).

Moreover, when selecting a cut-off score to determine whether individuals pass or fail a battery of functional performance tests, it is important to consider the goals and sporting experience of individuals, as well as the clinimetric properties of individual hop tests. Reid *et al.* (2007), calculated the minimal detectable change (MDC) at the individual level of the hop for distance, crossover hop, triple hop and six metre timed hop tests in a group of 42 recreational athletes with ACLR. The MDC (90% confidence level) for the

crossover hop, triple hop and six metre timed hop tests was greater than 10% (range  $\pm$  10.02 to  $\pm$  12.96%). Hence, if a LSI of 95% was recorded, the true LSI may vary be between 85 and 105% (Reid *et al.*, 2007).

When interpreting LSI's from hop tests after ACLR, it is important to consider that the contralateral limb may not be a stable denominator. Over the course of ACL injury, reconstruction and rehabilitation, the contralateral leg may also undergo neuromuscular adaptations that are associated with worse biomechanics and/or functional performance (Hiemstra *et al.*, 2007; Paterno *et al.*, 2007). Such adaptations may not only reduce the size of the LSI, but contribute to the increased risk of contralateral ACL injury (Paterno *et al.*, 2010). Indeed, recent evidence suggests that individuals with ACLR have up to 15 times greater risk (risk ratio = 15.2;  $p = 0.0002$ ) of either ipsilateral or contralateral ACL injury than uninjured individuals (Paterno *et al.*, 2012).

#### *Functional performance after ACLR*

Despite these limitations, the performance of the uninvolved leg still offers the most convenient and participant-specific comparison of functional performance (Holsgaard-Larsen *et al.*, 2014; Thomeé *et al.*, 2011). The use of a battery of functional performance tests may help to account for inter-subject and inter-limb variability in functional performance. Hence, to inform the selection of functional performance tests for the studies included in this thesis, a summary of previous case control and cross-sectional investigations that have used a battery of hop tests (i.e., three or more tests) to assess knee joint function following ACL is provided in Tables 2.3 and 2.4.

**Table 2.3** Summary of case control studies that have assessed functional performance after ACLR with a hamstring graft, using batteries of at least three functional performance tests, with emphasis on single leg tasks

Methods				Findings					
Study	Participants	Time since ACLR (months)	Functional performance test	ACLR groups			Uninjured control groups		
				Involved limb	Uninvolved limb	Limb symmetry index (%)	Involved limb	Uninvolved limb	Limb symmetry index (%)
Holsgaard-Larsen <i>et al.</i> (2014)	23 recreational male athletes 25 matched controls	27 ± 7	Hop for distance (cm) Single leg jump (cm) Double leg jump (cm)	152 ± 33 13 ± 5 NR	162 ± 29 14 ± 4 NR	93 ± 9* † 92 ± 22 NR	175 ± 27 16 ± 5 NR	171 ± 25 16 ± 4 NR	98 ± 7 101 ± 18 NR
Xergia and Pappas (2013) ‡	22 recreational male athletes 22 matched controls	7 ± 0.9	Hop for distance (cm) Triple hop for distance (cm) Crossover hop (cm)	120 ± 32 325 ± 88 312 ± 86	146 ± 30 400 ± 88 372 ± 88	82 † 81 † 84 †	161 ± 18 480 ± 69 414 ± 54	158 ± 17 476 ± 66 415 ± 60	102 101 100
Myer <i>et al.</i> (2011b)	10 recreational male athletes (10 matched controls)	12	Hop for distance (cm) Triple hop for distance (cm) Crossover hop (cm) 6 metre timed hop (sec)	185 513 469 2.4	197 542 499 2.4	93 † 94 † 94 † 100 †	199 547 497 2.4	194 539 504 2.5	103 101 92 96
	10 recreational female athletes (10 matched controls)		Hop for distance (cm) Triple hop for distance (cm) Crossover hop (cm) 6 metre timed hop (sec)	158 434 398 2.6	172 486 434 2.5	92 † 89 † 92 † 104 †	170 485 424 2.5	168 434 439 2.5	101 111 97 100
Gustavsson <i>et al.</i> (2006)	35 recreational athletes (10 women) 15 matched controls	6 ± 0	Hop for distance (cm) Drop hop for distance (cm) Side hop (number) Square hop (number)	128 ± 28 256 ± 56 39 ± 16 49 ± 17	148 ± 23 297 ± 48 49 ± 13 57 ± 12	86* † 86* † 80* † 86*	151 ± 16 304 ± 34 50 ± 13 62 ± 7	157 312 54 66	96 97 93 94

Values are means ± standard deviation, if provided in the study; limb symmetry index = performance on the involved limb/performance on the uninjured limb\*100 (Noyes *et al.*, 1991). LSIs calculated manually for (Gustavsson *et al.*, 2006), (Myer *et al.*, 2011b) and (Xergia & Pappas, 2013)

For statistically significant differences between limbs, \* =  $p < 0.05$ ; For statistically significant differences between ACLR and control groups, † =  $p < 0.05$

For all control groups, the involved limb was the dominant limb except for (Myer *et al.*, 2011b); cm = centimetres; sec = seconds; NR = not reported

‡ Includes some subjects with bone-patella-bone autografts; † No between limbs statistical comparisons were provided



**Table 2.4** Summary of cross-sectional studies that have assessed functional performance after ACLR with a hamstring graft, using batteries of at least three functional performance tests, with emphasis on single leg tasks

Methods				Findings				
Study	Participants	Time since ACLR (months)	Functional performance test	Involved limb	Uninvolved limb	Limb symmetry index (%)	95% CI of LSI	Percentage of participants with < 85% LSI
Thomeé <i>et al.</i> (2012) <sup>‡</sup>	82 higher-level recreational athletes (26 women)	6	Hop for distance (cm)	128	146	86 ± 12 <sup>*</sup>	(83 – 89)	40
			Side hop (number)	36	46	78 ± 21 <sup>*</sup>	(73 – 83)	58
			Double leg jump (cm)	13.5	17	77 ± 16 <sup>*</sup>	(74 – 80)	62
		12	Hop for distance (cm)	139	147	94 ± 9 <sup>*</sup>	(92 – 96)	14
			Side hop (number)	42	47	89 ± 19 <sup>*</sup>	(85 – 93)	33
			Double leg jump (cm)	15	17	88 ± 12	(85 – 91)	55
24	Hop for distance (cm)	139	146	95 ± 8 <sup>*</sup>	(93 – 97)	5		
	Side hop (number)	44	48	92 ± 14 <sup>*</sup>	(89 – 95)	24		
	Double leg jump (cm)	16	17	92 ± 13	(89 – 95)	28		
Hartigan <i>et al.</i> (2010) <sup>§</sup>	22 ACLR (5 women)	6	Hop for distance (cm)	-	-	93 (range 73 – 108) <sup>†</sup>		32
			Crossover hop (cm)	-	-	95 (range 77 – 112) <sup>†</sup>		23
			6 metre timed hop (sec)	-	-	95 (range 82 – 109) <sup>†</sup>		9
			Triple hop for distance (cm)	-	-	98 (range 81 – 101) <sup>†</sup>		9
		12	Hop for distance (cm)	-	-	98 (range 85 – 108) <sup>†</sup>		9
			Crossover hop (cm)	-	-	98 (range 73 – 111) <sup>†</sup>		5
Reid <i>et al.</i> (2007)	42 recreational athletes (19 women)	5	Hop for distance (cm)	149 ± 29	167 ± 25	89 ± 9 <sup>*</sup>	(86 – 92)	NR
			Crossover hop (cm)	377 ± 88	431 ± 89	88 ± 10 <sup>*</sup>	(85 – 91)	NR
			Triple hop for distance (cm)	420 ± 88	480 ± 99	87 ± 10 <sup>*</sup>	(84 – 90)	NR
			6 metre timed hop (sec)	2.4 ± 0.6	2.1 ± 0.4	90 ± 9 <sup>*</sup>	(87 – 93)	NR
de Jong <i>et al.</i> (2007)	103 recreationally active ACLR men	6	6 metre timed hop (sec)	-	-	85 ± 13 <sup>†</sup>	(82 – 88)	44
			6 metre backwards timed hop (sec)	-	-	80 ± 16 <sup>†</sup>	(77 – 83)	38
			Crossover hop (cm)	-	-	83 ± 14 <sup>†</sup>	(80 – 86)	4

	91 of original sample	9	6 metre timed hop (sec) 6 metre backwards timed hop (sec) Crossover hop (cm)	- - -	- - -	89 ± 14 <sup>†</sup> 87 ± 15 <sup>†</sup> 89 ± 11 <sup>†</sup>	(86 – 92) (84 – 90) (87 – 91)	50 41 30
	48 of original sample	12	6 metre timed hop (sec) 6 metre backwards timed hop (sec) Crossover hop (cm)	- - -	- - -	95 ± 10 <sup>†</sup> 91 ± 13 <sup>†</sup> 93 ± 9 <sup>†</sup>	(92 – 98) (87 – 95) (90 – 96)	47 30 12
Williams <i>et al.</i> (2005b)	10 higher-level recreational athletes (3 women)	6.2 ± 1.9	Hop for distance (cm) Crossover hop (cm) Triple hop for distance (cm) 6 metre timed hop (sec)	- - - -	- - - -	95 ± 5 <sup>†</sup> 95 ± 5 <sup>†</sup> 95 ± 6 <sup>†</sup> 101 ± 5 <sup>†</sup>	(92 – 98) (92 – 98) (91 – 99) (98 – 104)	NR NR NR NR
Hopper <i>et al.</i> (2002) <sup>¥</sup>	19 recreational athletes (6 women)	12 ± 1.4	Crossover hop (cm) Stair hop (cm) 6 metre timed hop (sec) Vertical hop (sec)	400 ± 100 8.5 ± 2.8 2.3 ± 0.6 0.34 ± 0.06	440 ± 90 7.9 ± 1.9 2.2 ± 0.5 0.38 ± 0.04	91 ± 13 <sup>*</sup> 96 ± 10 <sup>*</sup> 95 ± 11 <sup>*</sup> 89 ± 10 <sup>*</sup>	(85 – 97) (92 – 100) (90 – 100) (85 – 93)	NR NR NR NR
Brosky Jr <i>et al.</i> (1999)	15 recreationally active ACLR men	29 ± 8.9	Hop for distance (cm) Vertical hop (cm) 6 metre timed hop (sec)	173 ± 19 41 ± 8 1.62 ± 0.21	174 ± 21 40 ± 7 1.63 ± 0.22	99 98 99	- - -	NR NR NR
Wilk (1994)	50 recreational athletes (16 women)	32	Hop for distance (cm) Crossover hop (cm) 6 metre timed hop (sec)	51 ± 12 162 ± 40 2.7 ± 0.7	60 ± 10 188 ± 36 2.4 ± 0.4	84 <sup>*</sup> 86 <sup>*</sup> 88 <sup>*</sup>	- - -	47 44 26

Values are means ± standard deviation (SD) if provided in the study; 95% confidence intervals have been calculated for each limb symmetry index (LSI) using the formula  $\text{mean} \pm 1.96 * \text{standard error (SE)}$ , where  $\text{SE} = \text{SD}/\sqrt{n}$  (Petrie, 2006).

Wilk (1994), Brosky Jr *et al.*, (1999) and Hartigan *et al.*, (2010) did not provide SDs; therefore, no confidence intervals have been calculated for these studies

Limb symmetry index = performance on the involved limb/performance on the uninvolved limb\*100 (Noyes *et al.*, 1991); cm = centimetres; sec = seconds; NR = not reported; \* =  $p < 0.05$  (statistically significant differences between limbs)

¥ Includes some subjects with bone-patella-bone autografts; † No between limbs statistical comparisons were provided

Four investigations identified by this literature review compared the knee function of ACLR and uninjured control participants using a battery of three or more functional performance tests (Gustavsson *et al.*, 2006; Holsgaard-Larsen *et al.*, 2014; Myer *et al.*, 2011b; Xergia & Pappas, 2013). Inspection of the average LSI's of these tests reveals significantly lower LSI's for the ACLR groups for all but two tests; the square hop (Gustavsson *et al.*, 2006) and the single leg jump (Holsgaard-Larsen *et al.*, 2014). The weighted means of the LSIs for the ACLR and control groups were 87.6% and 99% respectively. Of these four investigations, Myer *et al.* (2011b) reported the highest average LSI's for ACLR participants (range 89–104%). No significant between limb differences were reported for uninjured control groups.

In the Myer *et al.* (2011b) investigation, all participants were involved in Level I or II sports at the time of testing. Level I sports include jumping, side-stepping and pivoting (e.g. soccer, basketball and handball) and level II sports include lateral movements (e.g. sidestepping or cutting) but less pivoting than Level I sports (e.g. Alpine skiing and racquet sports). Level III sports do not include jumping or pivoting components and level IV indicates no sports participation (Hefti *et al.*, 1993). Participants in the investigations by Hartigan *et al.* (2010) and Thomeé *et al.* (2012) were also involved in Level I or II sports. In the Hartigan *et al.* (2010) investigation, despite hop LSI's of 93% and above at 6 months following ACLR and 98% and above at 12 months following ACLR, the ranges of LSIs (73 to 112%) indicate considerable inter-subject variability in hop performance within the group.

Likewise, even though Thomeé *et al.* (2012) reported LSIs of 88% and above at the 12 and 24 month time-points, the standard deviations of the LSI's reported within the study ranged from 9 to 19%. Hence, it is expected that a number of individuals in these investigations scored well below 85% LSI – the lower limit of what is considered an acceptable LSI in the literature (Ardern *et al.*, 2011b; de Jong *et al.*, 2007; Hohmann *et al.*, 2011; Holsgaard-Larsen *et al.*, 2014; Hopper *et al.*, 2008; Noyes *et al.*, 1991; Wilk, 1994; Williams *et al.*, 2005b).

This expectation is confirmed by inspecting the proportion of individuals who scored less than 85% LSI on each of the functional performance tests. Four of the eight cross-sectional investigations identified by this literature review reported this data. At the six

month post-operative time-point, between 9 and 62% of participants scored below 85% LSI. Surprisingly though, 9% of participants in the Hartigan *et al.* (2010) study and 14% of participants in the Thomeé *et al.* (2012) study scored less than 85% LSI for the hop for distance test at 12 months after ACLR. The weighted mean for the LSIs reported in cross-sectional studies was 88.8%. These findings are concerning, considering that many individuals have returned to sport by 12 months following ACLR. A LSI < 90% on the hop for distance test at 12 months following ACLR has been associated with a higher rate of knee osteoarthritis at 10 years following ACLR (Pinczewski *et al.*, 2007) and could predispose individuals to further ACL injury (Paterno *et al.*, 2010; Webster *et al.*, 2014a).

Collectively, the findings of these investigations confirm that significant deficits in functional performance can persist for years after ACLR. Although average LSI's are higher for individuals that have returned to higher levels of sport, considerable inter-subject variability exists within ACLR groups in both absolute and relative functional performance. This variability provides further justification for the routine use of batteries of functional performance tests and consideration of the proportion of individuals who achieve predetermined criteria for passing functional test batteries, rather than reporting only single tests and average LSI's.

#### **2.2.4 The relationship between self-reported knee function and functional performance following ACLR**

Correlations between self-reported measures and functional performance tests range from weak (Neeb *et al.*, 1997; Reinke *et al.*, 2011) to moderate (Andrade *et al.*, 2002; Logerstedt *et al.*, 2012a; Reid *et al.*, 2007). Hence, self-reported measures and functional performance tests assess different aspects of knee function, and neither can act as a proxy for the other (Fitzgerald *et al.*, 2001; Reinke *et al.*, 2011).

However, a single measure of knee joint function which includes both self-reported knee function and functional performance is sometimes necessary in research, particularly when investigating the associations between knee function and larger numbers of predictor variables (Bryant *et al.*, 2008b; Risberg *et al.*, 1999c; Schmitt *et al.*, 2012). Although it is possible to conduct several separate multivariate analyses (Lentz *et al.*, 2009; Røtterud *et al.*, 2013), clearer comparisons between the strength of

association of each predictor variable and knee function may be made if a single measure of function is used (Bryant *et al.*, 2008b; Harrell, 2001; Petrie, 2006). A summary measure of self-reported knee function and functional performance may also be useful clinically, to give an overall impression of knee function and provide motivation to patients and clinicians (Thomeé *et al.*, 2011). Throughout this thesis, 'knee function' will be operationally defined as a single measure representing both self-reported knee function (questionnaires) and functional performance (task-based) data.

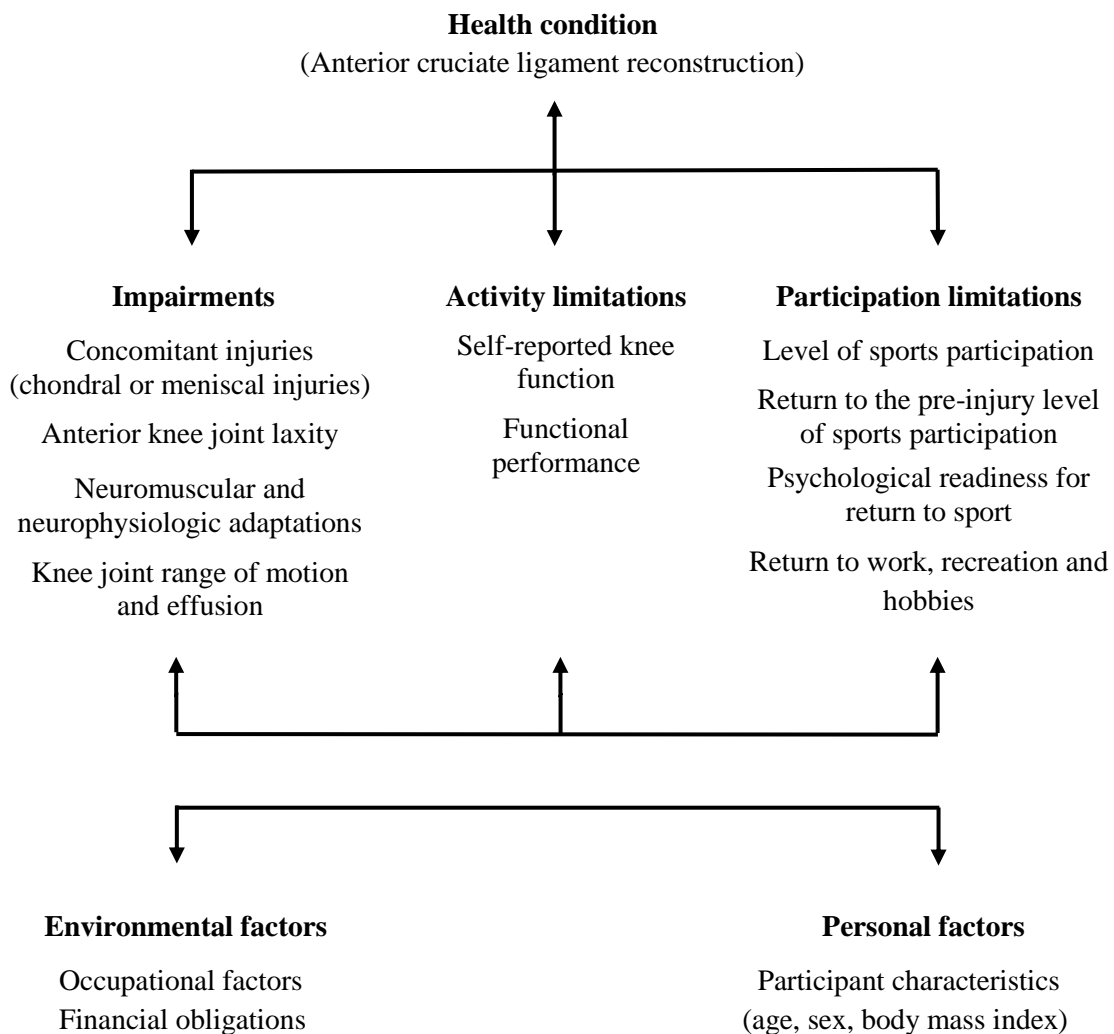
The total IKDC and CKRS scores provide a convenient method of summarising self-reported knee limitations, impairments (i.e., knee joint laxity and clinical assessment of range and quality of movement) and functional performance (i.e., hop test LSIs; (Barber-Westin *et al.*, 1999; Irrgang *et al.*, 1998). However, knee impairments and knee function are different constructs (Reiman & Manske, 2011) and many previous authors have chosen to assess these constructs separately (Holm *et al.*, 2010; Lentz *et al.*, 2009; Lohmander *et al.*, 2004; Risberg *et al.*, 1999c). Considering the low to moderate correlations previously observed between self-reported knee function scores and hop test LSI's, it may be inappropriate to combine these data into a single continuous score.

An alternative to creating a single continuous measure of overall knee function is to categorise individuals as passing or failing a battery of knee function tests (Di Stasi *et al.*, 2013; Hartigan *et al.*, 2012; Thomeé *et al.*, 2012). By defining knee function as a dichotomous variable, individuals who score above a pre-determined percentage on a battery of self-reported knee function questionnaires and functional performance tests are categorized as having unacceptable knee joint function. Although some accuracy and statistical power is lost by creating a dichotomous measure from continuous data (Altman & Royston, 2006), the pitfalls of using an average LSI are avoided and a single dependent variable can be used for statistical analyses or clinical decision making.

The following section reviews the literature to determine the variables related to sports participation and the participant characteristics associated with knee joint function after ACLR. Particular emphasis is placed on studies that included both self-reported and functional performance tests as independent variables, or used batteries of functional tests to assess overall knee function.

### 2.2.5 Non-neuromuscular predictors of knee function following ACLR

The International Classification of Functioning, Disability and Health (ICF), proposed by the World Health Organization (World Health Organization, 2001), provides a framework for summarising the factors that may relate to, or predict, knee function after ACLR (Jette, 2006). Using the ICF framework, variables of interest after ACLR can be classified as impairments or clinical findings, activity limitations, participation limitations or contextual (environmental and personal) factors that are specific to the population of interest (Reiman & Manske, 2011). The ICF framework and examples of variables relevant to ACLR are summarised in Figure 2.2.



**Figure 2.2** The International Classification of Functioning, Disability and Health (ICF), adapted from (Jette, 2006), with examples of variables relevant to ACLR. Bold lettering indicates ICF terminology

Greater anterior knee joint laxity, concomitant injuries to the chondral surfaces or the menisci of the knee, reduced knee joint range of motion and knee joint effusion are examples of clinical findings and impairments (Keays, 2007; Lentz *et al.*, 2009). Activity limitations include limitations in activities of daily living, occupation or sport, i.e., self-reported knee function, and limitations in functional performance (Reiman & Manske, 2011). Participation restrictions include reduced physical activity levels and the failure to return to the pre-injury level of sports participation (Lentz *et al.*, 2012; Spindler *et al.*, 2011). Contextual factors may include an individual's occupation, whether they are supporting themselves financially throughout their rehabilitation or receiving support from a third party together with the interests of coaches, supporters or therapists (Daruwalla *et al.*, 2014; Janssen *et al.*, 2012a).

Each of the impairments, activity limitations and contextual factors described above may influence the association between other factors and knee function. Hence, multivariate analyses; such as linear or logistic regression techniques, are necessary to determine how factors are associated with knee function and how important individual factors are in the context of each other (Spindler *et al.*, 2011). A summary of the factors that may be associated with knee function following ACLR follows.

### **2.2.6 Sports participation**

#### *Level of sport and physical activity*

Physical activity and level of sporting activity are important variables to account for when assessing knee joint function following ACLR (Brophy *et al.*, 2014; Marx, 2003; Spindler *et al.*, 2011). The current level of sport may influence the quantity and quality of training performed by participants, which, in turn, may influence knee function (Risberg *et al.*, 2007). Level I or II recreational athletes with ACLR may expose their knee to a greater variety of activities; hence, they may be more aware of certain activity limitations (Noyes *et al.*, 1989). Patients following ACLR who regularly perform hopping or landing activities as a part of their sport may demonstrate better functional performance than patients who do not regularly perform these activities (Renstrom *et*

*al.*, 2008). Therefore, level of sport may influence the relationship between other variables and knee function in multivariate analyses.

Physical activity participation can be assessed using validated physical activity questionnaires such as the Tegner activity scale (Tegner & Lysholm, 1985) or the Marx activity scale (Marx, 2003). Level of sports participation is commonly reported in the eligibility criteria of ACLR studies (Logerstedt *et al.*, 2012c; Myer *et al.*, 2011b). Large, ACL registry-based studies include all possible patients at all levels of sport (Andernord *et al.*, 2014; Barenius *et al.*, 2013; Hjermundrud *et al.*, 2010). However, to the author's knowledge, no previous ACL registry study has specifically assessed whether lower levels of sport are associated with worse knee function. Smaller ACLR studies often exclude Level III and IV athletes, in order to yield a more homogenous sample (Delahunt *et al.*, 2012b; Eitzen *et al.*, 2009; Gokeler *et al.*, 2010; Hartigan *et al.*, 2012; Moksnes & Risberg, 2009). Hence, the relationship between level of sports participation and knee function after ACLR is not clear.

#### *Return to the pre-injury level of sport*

Return to the pre-injury level of sport is the goal of many individuals following ACLR (Barber-Westin *et al.* 2012); however, return to sports rates following ACLR are low amongst recreational athletes (Czuppon *et al.*, 2014). Arden *et al.* (2011a), conducted a systematic review of 48 studies, which included 5770 participants. In that study, the authors reported that 63% of individuals had returned to their pre-injury level of sport at an average of over 3 years since ACLR. However, only 33% had returned to their pre-injury level of sport at 12 months following ACLR (Arden *et al.*, 2011b).

Evidence for an association between return to sport and knee function is mixed (Czuppon *et al.*, 2014). Using multivariate analyses, Lentz *et al.* (2012) reported finding a strong relationship between self-reported knee function (IKDC score) and return to sport status. Conversely, Arden *et al.* (2011b) reported finding no difference in return to sport outcomes between competitive athletes with normal and abnormal IKDC scores. However, in the same study, athletes who scored < 85% hopping LSI were less likely to have returned to sport.



The inconsistency in the literature relative to the association between knee function and having returned to the pre-injury level of sport may be related to variability in contextual factors (see Figure 2.2). For example, the specific demands of the pre-injury sport, expectations of sporting teams, parents or external funders, or occupational considerations may also influence whether an individual returns to their pre-injury level of sport (Czuppon *et al.*, 2014; Daruwalla *et al.*, 2014; Mueller *et al.*, 2014). Moreover, some individuals may have failed to return to the same level of sport because of reasons other than knee function, such as confidence, fear of re-injury, or social and/or work-related reasons (Ardern *et al.*, 2011a; Czuppon *et al.*, 2014; Daruwalla *et al.*, 2014; Noyes *et al.*, 1991).

#### *Psychological responses to returning to sport*

There is a growing body of literature investigating the influence of psychological factors on the resumption of sporting activities after ACLR (Ardern *et al.*, 2012; Chmielewski *et al.*, 2011; Kvist *et al.*, 2005; Langford *et al.*, 2009; Lentz *et al.*, 2009; Tripp *et al.*, 2011). Many individuals experience ongoing psychological responses related to the resumption of sport, including fearfulness, lack of confidence and thoughts of re-injury (Kvist *et al.*, 2005; Langford *et al.*, 2009). However, the association between these psychological responses and knee joint function following ACLR is still unclear.

Webster *et al.* (2008) developed and validated a questionnaire to quantify psychological responses to the resumption of sport; the Anterior Cruciate Ligament Return to Sport after Injury (ACL-RSI) scale. The ACL-RSI scale evaluates a range of psychological factors thought to be barriers to successfully returning to sport, including fear of re-injury and reduced knee-related confidence. Webster *et al.* (2008) found that individuals who were yet to return to sport after ACLR had a significantly greater psychological response to the resumption of sport than individuals who had successfully returned to sport. However, the relationship between ACL-RSI score and knee joint function was not investigated. Chmielewski *et al.* (2011) reported no relationship between psychological factors and self-reported knee joint function; however, to the author's knowledge, no previous study has investigated whether the psychological response to returning to sport is significantly associated with functional performance following ACLR.

### 2.2.7 Participant characteristics

#### *Age*

Older age at the time of ACLR has been associated with a range of non-neuromuscular factors that may affect knee functional outcomes, such as a greater risk of meniscal and chondral injuries (Desai *et al.*, 2014; Takeda *et al.*, 2011; Tandogan *et al.*, 2004), post traumatic OA (Blagojevic *et al.*, 2010) and reduced physical activity levels (Dunn *et al.*, 2010). Many previous investigations have included age in regression models when investigating factors associated with knee function after ACLR; however, the relative association between age and knee joint function is seldom reported. Hartigan *et al.* (2012) used logistic regression analysis to determine whether demographic and neuromuscular factors were associated with passing a functional test battery, designed to assess readiness to return to sport. In this study, age alone predicted 73% of those who failed the functional test battery, and older age was associated with greater odds of failing one or more of the functional tests.

#### *Sex*

Some investigations have reported that women have lower levels of self-reported knee function than men following ACLR (Ageberg *et al.*, 2010; Barenius *et al.*, 2013; Lindström *et al.*, 2013; Ott *et al.*, 2003). For example, Ageberg *et al.* (2010) conducted a large investigation using data from 10,164 patients with ACLR, with predominately hamstring grafts, derived from the Swedish national knee register. The authors observed that women had significantly worse self-reported knee function than men on four of the five KOOS sub-scales at one and two years following ACLR. Female patients also reported significantly less improvement in self-reported knee function between 12 and 24 months following surgery. However, the differences between men and women in this study were relatively small, ranging from 1.4 to 4.4%. The minimum clinically significant difference of the KOOS is not known (Collins *et al.*, 2011) so it is unclear whether these differences are clinically significant. A recent meta-analysis of 13 studies found only small and clinically insignificant differences in self-reported knee function between male and female ACLR participants (Ryan *et al.*, 2014).

Evidence for the relationship between gender and functional performance after ACLR is equivocal. Some studies have found no difference in absolute or relative measures of functional performance between men and women after ACLR (Gustavsson *et al.*, 2006; Noyes *et al.*, 1991). Conversely, Lindström *et al.* (2013) found significant differences in functional performance between men and women at 12 months after ACLR with a hamstring graft using a battery of hop tests. Although statistically significant differences in hop LSI were identified in this study, both men and women improved significantly in the 12 months following ACLR, and the LSIs for women were still greater than 85%. Hence, although differences may be observed in self-reported knee function and functional performance between men and women, these differences may not be clinically important. However, the findings of these studies provide some justification to include sex as a candidate predictor of knee function in multivariate analyses.

#### *Body mass index*

Few investigations have directly assessed the relationship between BMI and knee joint function. Individuals following ACLR with a higher body mass index (BMI), who participate in pivoting and landing sports may expose their knee to greater compressive forces than individuals with lower BMI (Bowers *et al.*, 2005). Greater compressive forces may, in turn, be associated with greater pain-related limitations to functional performance during more demanding activities (Keays *et al.*, 2010; Robbins *et al.*, 2011). Greater BMI after ACLR has been associated with a greater risk of meniscal and chondral injury (Bowers *et al.*, 2005) and onset and progression of osteoarthritis (Cox *et al.*, 2014; Keays *et al.*, 2010; Takeda *et al.*, 2011). However, in the first one to two years following ACLR, prior to the development of osteoarthritis, BMI may not be associated with worse knee function. In a prospective study involving 83 patients at six months following ACLR (28 women) who regularly participated in Level I or II sports, Logerstedt *et al.* (2012c) reported no association between BMI and IKDC score.

Conversely, Spindler *et al.* (2011) and Kowalchuk *et al.* (2009) found that greater BMI was associated with worse self-reported knee function. Spindler *et al.* (2011), in a large prospective study of 378 patients following ACLR, found that greater BMI at the time of ACLR was predictive of worse IKDC and KOOS scores at six years following ACLR. Kowalchuk *et al.* (2009), in another large study of 402 ACLR subjects (193

women), at an average of 6.3 years following ACLR, found that greater BMI was associated with 2.9 times the odds of scoring below the age and gender-specific IKDC score (i.e., having below average knee function). Given that BMI is associated with a greater risk of osteoarthritis (Øiestad *et al.*, 2011), the presence of symptomatic knee osteoarthritis within these groups may have influenced the strength of these associations. Nonetheless, these findings indicate that BMI should be accounted for when assessing knee function following ACLR, particularly at longer post-operative time points and when including individuals with lower levels of sports participation (Kowalchuk *et al.*, 2009; Spindler *et al.*, 2011).

### **2.2.8 Impairments and clinical findings**

Numerous impairments are observed after ACLR, including knee joint effusion (Lentz *et al.*, 2009), reduced knee joint range of motion (Leys *et al.*, 2012) and neuromuscular deficits (Ingersoll *et al.*, 2008). Many of these impairments are modifiable, particularly in the early perioperative phase of rehabilitation (Feller & Webster, 2003; Janssen *et al.*, 2012b). However, concomitant chondral or meniscal injuries and greater anterior knee joint laxity are largely unmodifiable. These findings are common (Borchers *et al.*, 2011), and may be associated with knee osteoarthritis (Barenus *et al.*, 2014) and worse knee function (Potter *et al.*, 2011). Therefore, it is important to understand their relationship to knee joint function.

#### *Concomitant chondral or meniscal injuries*

Much of the understanding of the relationship between concomitant chondral and meniscal injuries and knee joint function after ACLR has been obtained by analysing data in ACLR registries in Scandinavia and North America (Andernord *et al.*, 2014; Barenus *et al.*, 2013; Chhadia *et al.*, 2011; Desai *et al.*, 2014; Hjermundrud *et al.*, 2010; Kvist *et al.*, 2014; Lind *et al.*, 2009; Maletis *et al.*, 2013; Røtterud *et al.*, 2013). ACLR registries contain data on surgical techniques, graft types, knee function and a range of demographic variables.

Case-control studies have found no differences in self-reported knee function between individuals with or without full thickness chondral injuries or meniscal injury/surgery at the time of ACLR (Ahldén *et al.*, 2012; Hjermundrud *et al.*, 2010). However,

multivariate analyses reveal that both chondral and meniscal injuries are associated with worse self-reported knee function, in both the early postoperative period (i.e., 2 months; Barenius *et al.*, 2013) and at later time-points (i.e. 6 years; Cox *et al.*, 2014; Kowalchuk *et al.*, 2009). Chondral and meniscal injuries were associated with worse self-reported knee joint function in eight of the 12 studies identified by this literature review. No study investigated the relationship between chondral or meniscal injury and functional performance. These studies are summarized in Tables 2.5 and 2.6.

**Table 2.5** Multivariate associations between concomitant chondral injuries and knee function after unilateral primary ACLR

Study	Participants (age at follow up)	Time since ACLR (months)	Assessment of chondral injury	Association with knee function
Inacio <i>et al.</i> (2014)	<ul style="list-style-type: none"> <li>• 430 patients (32% female)</li> <li>• Median age 25.9 years</li> </ul>	< 1	Binary	Chondral injuries were not associated with KOOS
Cox <i>et al.</i> (2014)	<ul style="list-style-type: none"> <li>• 1307 patients (44% female)</li> <li>• Includes 356 allografts (25%)</li> <li>• Median age 29 years</li> </ul>	72	Modified Outerbridge classification	Grade III or IV chondral injuries were significantly associated with worse IKDC and KOOS scores ( $p < 0.01$ )
Rotterud <i>et al.</i> (2013)	<ul style="list-style-type: none"> <li>• 8476 patients (48% female)</li> <li>• Includes 126 revision surgeries (1.5%) 76% hamstring grafts</li> <li>• Age <math>30.4 \pm 10.6</math> years</li> </ul>	$25.2 \pm 2.4$	ICRS classification	Grade III or IV chondral injuries were significantly associated with worse KOOS scores ( $p < 0.01$ )
Barenius <i>et al.</i> (2013)	<ul style="list-style-type: none"> <li>• 3556 patients (49% female)</li> <li>• 87% hamstring grafts</li> <li>• 55% aged 18- 34 years</li> </ul>	2	Binary	Chondral injuries were significantly associated with worse knee function (< 80% on KOOS <sub>SPORT</sub> , < 91% on KOOS <sub>ADL</sub> ), RR = 0.80 ( $p < 0.01$ )
Spindler <i>et al.</i> (2011)	<ul style="list-style-type: none"> <li>• 378 patients (46% female)</li> <li>• 48% hamstring grafts, 16% allografts</li> <li>• Median age 32 years</li> </ul>	80.4 †	Modified Outerbridge classification	Grade III or IV chondral injuries were not associated with KOOS <sub>SPORT/REC</sub> or IKDC scores
Kowalchuk <i>et al.</i> (2009)	<ul style="list-style-type: none"> <li>• 402 patients (48% female)</li> <li>• Includes allografts (% NR)</li> <li>• Age 29 years</li> </ul>	6.3 years (range 2-15)	Modified Outerbridge classification	Grade III or IV chondral injuries were associated with 2.6 times greater odds of having an IKDC score below the population average ( $p < 0.02$ )

Values are means  $\pm$  standard deviation, if provided in the study; NR = not reported; † = median

ICRS = International Cartilage Repair Society: Graded as 0 (normal), I = nearly normal (superficial lesions, soft indentations) II = abnormal (lesions extending down to 50% of cartilage depth), III = severely abnormal (lesions extending down 50% of cartilage depth) or IV = severely abnormal (osteochondral lesions extending just through the sub-chondral bone) (Røtterud *et al.*, 2013). Modified Outerbridge classification: Graded as 0 = normal, I = softening and fibrillation, II = superficial changes, III = deep changes and no exposed bone and IV = exposed bone (Borchers *et al.*, 2011); IKDC = International Knee Documentation Committee Subjective Score (Irrgang *et al.*, 2001); KOOS<sub>SPORT/REC</sub> = Knee Osteoarthritis Outcome Score, Sports and recreation sub-scale (Roos *et al.*, 1998).

**Table 2.6** Multivariate associations between concomitant meniscal injuries and knee function after unilateral primary ACLR

Study	Participants (age at follow up)	Time since ACLR (months)	Assessment of concomitant injury	Association with knee function
Inacio <i>et al.</i> (2014)	<ul style="list-style-type: none"> <li>• 430 patients (32% female)</li> <li>• Median age 25.9 years</li> </ul>	< 1	Injury of either meniscus at the time of ACLR	10 point increase in KOOS <sub>SPORT/REC</sub> was associated with a 9% lower likelihood of having a medial meniscal tear ( $p < 0.05$ )
Cox <i>et al.</i> (2014)	<ul style="list-style-type: none"> <li>• 1307 patients (44% female)</li> <li>• Includes 356 allografts (25%)</li> <li>• Median age 29 years</li> </ul>	72	Injury or repair of either meniscus at the time of ACLR	Medial and lateral meniscus injury or repair at the time of ACLR was significantly associated with worse IKDC and KOOS scores ( $p < 0.01$ )
Rotterud <i>et al.</i> (2013)	<ul style="list-style-type: none"> <li>• 8476 patients (48% female)</li> <li>• Includes 126 revision surgeries (1.5%) 76% hamstring grafts</li> <li>• Age <math>30.4 \pm 10.6</math> years</li> </ul>	$25.2 \pm 2.4$	Injury of either meniscus at the time of ACLR	No significant association with KOOS
Barenius <i>et al.</i> (2013)	<ul style="list-style-type: none"> <li>• 3556 patients (49% female)</li> <li>• 87% hamstring grafts</li> <li>• 55% aged 18- 34 years</li> </ul>	2	Injury of either meniscus at the time of ACLR	Meniscal injuries were significantly associated with worse knee function ( $< 80\%$ on KOOS <sub>SPORT/REC</sub> , $< 91\%$ on KOOS <sub>ADL</sub> ) <ul style="list-style-type: none"> <li>• Medial meniscus injury: RR = 1.23 (<math>p &lt; 0.01</math>)</li> <li>• Lateral meniscus injury: RR = 1.27 (<math>p &lt; 0.01</math>)</li> </ul>
Spindler <i>et al.</i> (2011)	<ul style="list-style-type: none"> <li>• 378 patients (46% female)</li> <li>• 48% hamstring grafts, 16% allografts</li> <li>• Median age 32 years</li> </ul>	$80.4^\dagger$	Injury or repair of either meniscus at the time of ACLR	Lateral (but not medial) meniscus surgery at the time of ACLR associated with worse KOOS <sub>SPORT/REC</sub> scores ( $p = 0.02$ )
Kowalchuk <i>et al.</i> (2009)	<ul style="list-style-type: none"> <li>• 402 patients (48% female)</li> <li>• Includes allografts (% NR)</li> <li>• Age 29 years</li> </ul>	6.3 years (range 2-15)	Surgery to either meniscus at the time of ACLR	Meniscal surgery at the time of ACLR was not associated with worse IKDC scores.

Values are means  $\pm$  standard deviation, if provided in the study; NR = not reported;  $\dagger$  = median

IKDC = International Knee Documentation Committee Subjective Score (Irrgang *et al.*, 2001); KOOS<sub>SPORT/REC</sub> = Knee Osteoarthritis Outcome Score, Sports and recreation sub-scale (Roos *et al.*, 1998).

### *Anterior knee joint laxity*

Anterior displacement of the tibia on the femur is commonly quantified after ACLR using the KT-1000 arthrometer (Daniel *et al.*, 1985). The measurement of anterior/posterior knee joint laxity (or A/P laxity) with the KT-1000 arthrometer have been found to be reliable, with ICCs reported in the literature ranging from 0.91 to 0.97 (Brosky Jr *et al.*, 1999; Robnett *et al.*, 1995; Sernert *et al.*, 2001). A KT-1000 side-to-side difference greater than 3mm is commonly used by researchers to define ACL rupture or as exclusion criteria for ACLR participants (Barenius *et al.*, 2013; Bjornaraa, 2011; Grindem, 2011; Xergia & Pappas, 2013). However, some individuals have been found to demonstrate good knee joint function following ACLR despite having greater than 3 mm side-to-side differences in knee laxity (Kocher *et al.*, 2004; Lentz *et al.*, 2009; Moksnes & Risberg, 2009). Therefore, when assessing multivariate predictors of knee function after ACL, it may be pertinent to include individuals regardless of knee laxity measurements, and include anterior knee laxity as a covariate (Lentz *et al.*, 2009).

Numerous investigations have reported a lack of association between anterior knee joint laxity and self-reported knee function at the univariate level (Hyder *et al.*, 1997; Lentz *et al.*, 2009; Lorbach *et al.*, 2011; Risberg *et al.*, 1999c; Sernert *et al.*, 1999). Likewise, correlations between hop tests and anterior knee laxity are generally low (Lentz *et al.*, 2009; Lindström *et al.*, 2013; Medeni *et al.*, 2014). However, Risberg *et al.* (1999c), found that greater anterior knee joint laxity was associated with worse self-reported knee function (CKRS) at 2 years after ACLR, but only in a multivariate analysis that included knee symptoms and quadriceps strength. In that study, anterior knee joint laxity increased significantly between 3 months and 2 years following surgery. Anterior knee laxity has recently been found to be higher in female patients following ACLR at the time of ovulation (Bell *et al.*, 2014). Hence, anterior knee joint laxity may confound the relationship between other impairments and knee function, particularly at later post-operative time points.



### **2.2.9 Summary of knee function following ACLR**

Following ACLR, individuals experience knee-related limitations in a broad range of functional activities, and considerable variability in knee functional outcomes exists within groups of patients. Age, sex, BMI, sports participation, psychological factors and concomitant chondral and meniscal injuries are associated with knee joint function in various degrees within multivariate analyses. Functional performance testing and self-reported measures of knee function are reliable and valid methods of quantifying gross motor function after ACLR. However, these measures do not accurately quantify neuromuscular control. The following two sections of this literature review focus on the assessment of neuromuscular control after ACLR, in both the open and closed kinetic chain.

## **2.3 Open kinetic chain neuromuscular adaptations following ACLR**

### **2.3.1 Overview**

The production of refined movement is a cyclic process which involves constant input from the sensory system, higher-level processing within the central nervous system, and feedback of the quality of motor output (Sjölander *et al.*, 2002). Any disease or injury which affects these processes has the potential to affect neuromuscular control and affect the quality of movement (Ingersoll *et al.*, 2008).

The ACL and the fibrous capsule of the knee joint contain mechanoreceptors which provide feedback to the central nervous system about joint position and loading (Adachi *et al.*, 2002). This sensory feedback is augmented by input from muscle spindles, which are sensory neurones within the muscle cell that regulate muscle force output (Johansson *et al.*, 1991; Sjölander *et al.*, 2002). Impulses from these sensory neurones communicate directly with descending motor pathways (Sjölander *et al.*, 2002). This feedback process is modulated by the central nervous system and feedback from other sensory systems such as the visual and vestibular systems (Mendiguchia *et al.*, 2011). Hence, sensory input from mechanoreceptors can directly influence the quality of movement produced by muscles (Sjölander *et al.*, 2002).

Rupture of the ACL results in a loss of mechanoreceptor feedback from the ACL. Although mechanoreceptors have been identified within ACL graft tissue, they are significantly fewer in number than those found in the native ACL (Dragoo *et al.*, 2014). The reduction in sensory input from the knee joint after ACLR, and the need to avoid episodes of instability, result in changes to central nervous system processing and motor output (Baumeister *et al.*, 2008; Kapreli *et al.*, 2009; Valeriani *et al.*, 1996). Hence, ACL injury with or without ACLR may be considered not only a mechanical dysfunction, but a neurophysiologic dysfunction (Kapreli *et al.*, 2009; Valeriani *et al.*, 1996; Valeriani *et al.*, 1999).

The neurophysiologic adaptations associated with ACLR may lead to a range of neuromuscular adaptations, including muscle weakness (Bryant *et al.*, 2008b; Snyder Mackler, 1995), muscle atrophy (Nomura *et al.*, 2014; Williams *et al.*, 2005a) and altered muscle activation strategies (Bryant *et al.*, 2009a; Lustosa *et al.*; Nyland *et al.*, 2010). Neuromuscular adaptations may persist long after ACLR and the period of rehabilitation (Bryant *et al.*, 2009b). For example, deficits in postural control have been observed up to 20 years following ACLR (Stensdotter *et al.*, 2013).

A muscle group that is particularly affected by the neurophysiologic sequelae of ACL injury and ACLR is the quadriceps (Palmieri Smith *et al.*, 2008). Deficits in quadriceps strength of up to 18% compared to the uninvolved side have been reported between five and 15 years after ACLR (Ingersoll *et al.*, 2008). Importantly, the neurophysiological mechanisms underpinning quadriceps strength deficits may also result in contralateral strength impairments (Hiemstra *et al.*, 2007; Konishi *et al.*, 2003).

### **2.3.2 Maximal versus sub-maximal assessments**

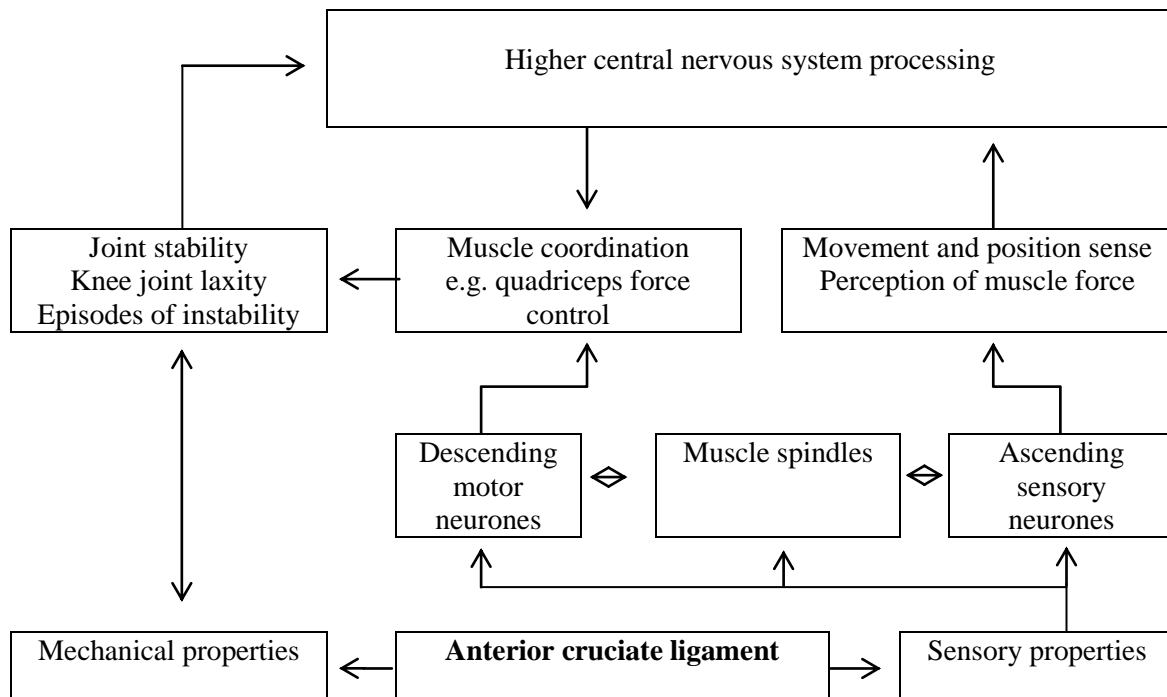
Quadriceps strength deficits are clinically important after ACLR. Preoperative quadriceps strength deficits are associated with worse self-reported knee function at 6 months (Logerstedt *et al.*, 2012c) and 2 years (Eitzen *et al.*, 2009) after ACLR. Quadriceps weakness is associated with a higher risk of developing knee osteoarthritis (Keays *et al.*, 2010; Segal, 2010). Furthermore, quadriceps weakness may affect the quality of functional movement. Individuals with weak quadriceps following ACLR demonstrate smaller knee flexion angles during walking compared to individuals with

strong quadriceps (Lewek *et al.*, 2002). Lower quadriceps strength has previously been associated with greater peak trunk flexion angles and decreased peak knee flexion moments in stair climbing and single leg landing tasks (Hall *et al.*, 2012; Oberländer *et al.*, 2012a).

Despite the clinical importance of quadriceps strength after ACLR, the majority of activities of daily living, and many sporting activities, require only sub-maximal intensities of muscle contraction performed efficiently (Pandy & Andriacchi, 2010). For example, during moderate speed walking (~1.49 m/s) and running (~2.65 m/s), quadriceps forces have been estimated to range from ≈10-30% and ≈25-80% of their predicted maximal isometric forces, respectively (Besier *et al.*, 2009). Therefore, in addition to the assessment of quadriceps maximal strength after ACLR, it may be relevant to assess the quality of quadriceps force production at sub-maximal intensities.

Muscle force control is a term used to describe the variability and accuracy of the force produced by muscles (Hortobágyi *et al.*, 2004; Tracy & Enoka, 2002). Individuals following ACLR have previously been found to have more variable (Bryant *et al.*, 2009a) and less-accurate (Telianidis *et al.*, 2014) quadriceps force production compared to healthy individuals during open kinetic chain tasks. Less-accurate quadriceps force production may be associated with the quality of movement observed during functional tasks. Impaired submaximal quadriceps force control is associated with greater hamstring muscle coactivation (Perraton *et al.*, 2013; Telianidis *et al.*, 2014). Greater hamstring coactivation may contribute to increased compressive forces within the tibiofemoral joint and contribute to the onset or progression of knee osteoarthritis (Tsai *et al.*, 2012). However, these hypotheses are yet to be investigated.

In summary, the ability of individuals following ACLR to dynamically stabilise their knee joint during functional activities is determined not only by the mechanical properties of the ACL graft and knee joint, but by an interactive process of biofeedback involving the peripheral and central nervous systems. These processes may influence the quality of movement and muscle coordination observed after ACLR, particularly of the quadriceps (Bryant *et al.*, 2009a; Madhavan & Shields, 2011; Yosmaoglu *et al.*, 2011). A summary of these mechanisms and nervous system pathways is provided in Figure 2.3.



**Figure 2.3.** Summary of the possible mechanisms by which the mechanical and sensory properties of the anterior cruciate ligament (ACL) contribute to dynamic knee joint stability following ACLR. Adapted from (Sjölander *et al.*, 2002).

### 2.3.3 Assessment of quadriceps force control

Quadriceps force control can be assessed using either open or closed kinetic chain tasks (Mikkelsen *et al.*, 2000). Closed kinetic chain tasks, for example single leg squat (Madhavan & Shields, 2011) or leg press (Yosmaoglu *et al.*, 2011), involve movement of the proximal joints over the foot. The magnitude of force production can be assessed using a load cell or force plate (Yosmaoglu *et al.*, 2011). Closed kinetic chain tasks may more closely resemble functional activities (Augustsson & Thomeé, 2000). However, a disadvantage of closed kinetic chain testing is that aberrations in force output cannot be attributed to a single muscle group.

Open kinetic chain tasks involve movement of the leg on stationary proximal segments and can be performed while sitting on an isokinetic dynamometer (Krishnan & Williams, 2011; Williams *et al.*, 2005b). Although these tasks do not replicate functional movements, the force output generated during the task is derived from a single muscle group (i.e., the hamstrings or quadriceps). Thus, impairments in the

quality of force output can be more directly attributed to one or both of these muscle groups (Augustsson & Thomeé, 2000; Bryant *et al.*, 2009a).

Four previous investigations have used open kinetic chain testing to assess quadriceps force control deficits after ACLR (Baumeister *et al.*, 2011; Bryant *et al.*, 2009a; Telianidis *et al.*, 2014; Williams *et al.*, 2005b). Broadly, the tasks used to assess quadriceps force control in these studies can be categorised as maximal (Bryant *et al.*, 2009a) or submaximal effort tasks (Baumeister *et al.*, 2011; Telianidis *et al.*, 2014; Williams *et al.*, 2005b). For example, Bryant *et al.* (2009a) assessed the force variability of *maximal* isokinetic quadriceps contractions by measuring the mean instantaneous frequency of the quadriceps isokinetic torque data.

Conversely, Baumeister *et al.* (2011) assessed the accuracy of *sub-maximal* quadriceps force output. In this study, a target torque was displayed on a computer screen as visual biofeedback. The target torque represented 50% of the participant's previously determined maximum voluntary contraction. The accuracy of quadriceps force control was quantified by determining the average difference between the target torque and the participant's quadriceps torque during a three minute trial.

Open kinetic chain assessments are normally conducted in seated testing position, with the thigh stabilised (Baumeister *et al.*, 2011; Bryant *et al.*, 2009a). However, Williams *et al.* (2005b) developed a target matching protocol that used a seated testing position without thigh stabilisation. Participants were seated on a small platform so that their body weight was supported on their ischial tuberosities. As a foundation for the PhD research reported in this thesis, Telianidis *et al.* (2014) used a similar target matching protocol to assess quadriceps force control after ACLR. In both the Williams *et al.* (2005b) and the Telianidis *et al.* (2014) studies, the lack of stabilisation through the thigh was proposed to increase the difficulty of the target matching task and increase the need for recruitment of trunk and gluteal muscles in order to control quadriceps forces.

The assessment of quadriceps force control is an emerging area of research. Therefore it was necessary to carefully define the parameters used by previous authors in their testing protocols. The parameters of established open kinetic chain quadriceps force matching protocols are summarised in Figure 2.4.

	Maximal intensity	Sub-maximal intensity
Type of contraction <sup>1</sup>	Isometric Isokinetic	Isometric Isotonic
Target force	Not applicable	Static Variable
Testing position	Seated with thigh support	Seated with thigh support Seated with elevated thigh
Other considerations	Testing angle Speed of isokinetic testing	Testing angle Pattern of varying force Frequency of varying force
Outcome variable	Force variability	Force variability Force accuracy
Data analysis <sup>2</sup>	Maximum frequency Mean instantaneous frequency	Absolute mean error Error relative to contralateral side Coefficient of variation Root mean square error

**Figure 2.4** Parameters of open kinetic chain quadriceps force control assessment

A key difference between maximal and sub-maximal intensity quadriceps force control tasks is that higher involuntary force variability observed in maximal intensity testing may not be perceptible to the participant. However, the loss of accuracy observed during sub-maximal target matching task may be noticeable to the participant, particularly if visual feedback is provided on a screen (Krishnan *et al.*, 2011). Hence, the accuracy of quadriceps force production during sub-maximal target matching tasks may involve greater input from higher neurological centres in the brain that are known to be affected by ACL injury and ACLR (Baumeister *et al.*, 2011; Kapreli *et al.*, 2009). A summary of the studies that have assessed sub-maximal quadriceps force control after ACLR using open kinetic chain testing protocols is provided in Table 2.7.

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<sup>1</sup> Maximal isokinetic (Bryant *et al.*, 2009a), maximal isometric (Pua *et al.*, 2010), isometric 50% of maximum voluntary isometric contraction (MVIC) (Hortobágyi *et al.*, 2004; Manini, 2005; Seynnes, 2005), isotonic between 0-30 ° knee flexion (Williams *et al.*, 2004), isometric with constantly varying force (5-30% MVIC) (Telianidis *et al.*, 2014), seated with elevated thigh (Telianidis *et al.*, 2014; Williams *et al.*, 2005b).

<sup>2</sup> Maximum frequency (Tsepis *et al.*, 2004), mean instantaneous frequency (Bryant *et al.*, 2009a), absolute mean error (Baumeister *et al.*, 2011; Hortobágyi *et al.*, 2004), error relative to contralateral side (Williams *et al.*, 2005b), coefficient of variation = [standard deviation/mean]\*100 (Krishnan & Williams, 2010; Seynnes, 2005), root mean square error (Telianidis *et al.*, 2014).

**Table 2.7** Summary of studies that have assessed sub-maximal quadriceps force control after ACLR in the open kinetic chain

Study	Participants	Time since ACLR (months)	Testing protocol	Data analysis methods	Findings
Baumeister <i>et al.</i> (2011)	9 recreationally active patients with ACLR (2 women) No concomitant injuries, mean age 25 ± 5 years 9 matched/uninjured controls (2 women)	12 ± 4.7	<b>Position:</b> Seated on dynamometer, 110 ° hip flexion, 90 ° knee flexion. Stabilisation of thigh: NR <b>Practice trials:</b> Familiarisation trials conducted 1 week before session <b>Test:</b> Static isometric knee extension, 50% MVIC, no visual feedback, 3 minutes with and without visual feedback.	<b>Data processing:</b> Average difference in error between 1) visual feedback and 2) no visual feedback <b>Reliability:</b> Not assessed <b>Validity:</b> Not assessed	No significant differences between the ACLR and control groups for any of the four trials ( $p = 0.86$ )
Williams <i>et al.</i> (2005b)	10 recreational athletes with ACLR (3 women) No concomitant injuries. Returned to Level I or II sports, mean age 19 ± 4 years	Pre-operative  6.2 ± 1.9	<b>Position:</b> Seated on dynamometer with thigh elevated and unsupported, 90 ° hip flexion, 90 ° knee flexion. <b>Practice trials:</b> 25 practice trials each leg <b>Test:</b> Static isometric multidirectional force reproduction task, approximately 15 Newtons, 1 second, 18 trials.	<b>Data processing:</b> Specificity of muscle action derived from EMG assessment. No assessment of torque error <b>Reliability:</b> Not assessed <b>Validity:</b> Not assessed	Quadriceps specificity equal to uninvolved side. Hamstring and gracilis specificity still impaired – not significantly different to pre-operative assessment
Telianidis <i>et al.</i> (2014)	28 recreationally active patients with ACLR (9 women) Concomitant meniscal and chondral injuries, mean age 27 ± 5 years. 29 uninjured controls (14 women)	17 ± 2	<b>Position:</b> Seated on dynamometer with thigh elevated and unsupported, 90 ° hip flexion, 60 ° knee flexion. <b>Practice trials:</b> 3 practice trials of 1 minute duration; <b>Test:</b> Dynamic isometric force reproduction task with involved limb; reproduction of constantly varying target torque (5-30% MVIC) with visual feedback for one minute.	<b>Data processing:</b> Average root mean square error (RMSE) of quadriceps torque in the 1 minute trial <b>Reliability:</b> Excellent test-retest reliability: ICC( 3, k ) = 0.91. <b>Validity:</b> Not assessed	ACLR group demonstrated 23% higher RMSE, indicative of worse quadriceps force control ( $p = 0.03$ )

Values are means ± standard deviation; NR= not reported; MVIC = maximum voluntary isometric contraction; EMG = electromyography

The study by Baumeister *et al.* (2011) found no difference in quadriceps force control between ACLR and control groups. However, this study involved only nine individuals with ACLR. Although a power calculation was performed to justify this sample size, the primary outcome variable for the study was cortical activation, assessed with electroencephalogram (EEG). Hence, it is possible that the lack of significant difference in quadriceps accuracy was a result of type II error (Petrie, 2006). Alternatively, the lack of significant difference may have been related to between-subject variability in the intensity of quadriceps force production, considering that no visual feedback was provided during the trials.

The study by Williams *et al.* (2005b) assessed the specificity of individual thigh and leg muscle activation using EMG, but did not assess the accuracy of torque output. Thus, the results cannot be compared directly to those of Baumeister *et al.* (2011) or Telianidis *et al.* (2014). The study used a multidirectional target matching protocol that engaged multiple muscle groups, including the quadriceps, hamstrings, hip flexors, abductors and adductors. Consequently, even if side-to-side differences in quadriceps torque accuracy were reported, they could not be attributed only to the quadriceps. The Williams *et al.* (2005b) study also used a relatively low intensity of contraction (approximately 1.5 kilograms of force), rather than normalising the target torque to the participant's MVIC. These methods allowed multiple trials to be completed without inducing fatigue, a known confounder of neuromuscular assessments (McLean & Samorezov, 2009). However, the relatively low intensity of contraction may not be generalisable to sporting activities and most activities of daily living (see Section 2.4.1).

The Baumeister *et al.* (2011) and Williams *et al.* (2005b) studies did not include individuals with concomitant chondral and meniscal injuries following ACLR. Although this may have increased the homogeneity of their samples, it may also reduce the external generalizability of the findings. Concomitant chondral and meniscal injuries are highly prevalent (Maletis *et al.*, 2013; Wyatt *et al.*, 2014); hence, the inclusion of these individuals may make the findings more generalisable to the wider ACLR population.

To address this issue, Telianidis *et al.* (2014) did not exclude individuals with concomitant chondral and meniscal injuries and recruited a larger sample (28 ACLR



and 29 uninjured control participants). Individuals following ACLR with side-to-side differences in anterior knee joint laxity greater than 3 mm were also included (mean  $3.3 \pm 1.6$  mm), with 14 (50%) of the participants having greater than 3 mm side-to-side difference in anterior knee laxity. In this study, the authors found a large (23%) and significant ( $p = 0.03$ ) difference in quadriceps force output between ACLR and control participants; that is, the ACLR group demonstrated less-accurate quadriceps force production. The work in this thesis extends on this pilot investigation by exploring the relationships between the accuracy of quadriceps force output and participant characteristics, concomitant chondral and meniscal injuries and anterior knee joint laxity. The following section of this literature review relates to the potential mechanisms of impairments in quadriceps force accuracy after ACLR.

#### **2.3.4 Mechanisms of quadriceps force control deficits**

In addition to assessing quadriceps force accuracy, Telianidis *et al.* (2014) also attempted to clarify the neuromuscular mechanisms of quadriceps force control impairments. Bivariate correlations were used to assess the strength of associations between quadriceps force control and the average root mean square (RMS) EMG values derived from the individual quadriceps and hamstring muscles during the target matching test. In this study, quadriceps force control was associated with a greater magnitude of hamstring coactivation. It was speculated that greater hamstring coactivation may have been a secondary adaptation that helped individuals control quadriceps force output.

However, it is also possible that the hamstring coactivation and impairments in quadriceps force accuracy that were observed in this study were related to changes in the central nervous system. In this respect, several previous authors have proposed that adaptations within the central nervous system after ACLR may lead to a loss of normal movement variability, which may place individuals at a higher risk of ACL graft rupture or overuse injury or impaired neuromuscular control (Baumeister *et al.*, 2008; Baumeister *et al.*, 2011; Hamill *et al.*, 2012; Littmann *et al.*, 2012; Stergiou & Decker, 2011).

Baumeister *et al.* (2011) also investigated factors associated with quadriceps force control by performing concurrent assessments of neuromuscular (i.e., individual quadriceps muscle EMG) and central nervous system adaptations during quadriceps force control testing. However, this study was not sufficiently powered to investigate the correlations between quadriceps force control neuromuscular/central nervous system adaptations. Hence, to the author's knowledge, the study by Telianidis *et al.* (2014) is the only study to have investigated the potential neuromuscular mechanisms contributing to open kinetic chain quadriceps force control impairments.

Other investigations using closed kinetic chain force control protocols (Madhavan & Shields, 2011) and maximal intensity protocols (Bryant *et al.*, 2009a) have found similar relationships between muscle activation strategies and quadriceps force control impairments. Bryant *et al.* (2009a) reported significantly higher mean instantaneous frequency of quadriceps force output (i.e., greater involuntary force variability) at a mean of 16 ( $\pm$  6) months following ACLR, compared to a group of uninjured control participants (percentage difference 15.4,  $p = 0.001$ ). Bivariate correlations within the ACLR group ( $n = 25$ , 11 women), revealed a moderate positive correlation between hamstring coactivation and quadriceps force variability. The authors speculated that greater hamstring coactivation may have contributed to the quadriceps force variability that was observed. However, no multivariate analyses were performed, so it is unclear whether this relationship was influenced by the presence of concomitant chondral or meniscal injuries, knee joint laxity, quadriceps strength or participant characteristics such as age or sex or (Tracy & Enoka, 2002).

### **2.3.5 Summary of open kinetic chain adaptations following ACLR**

The current literature provides some evidence that quadriceps force control may be impaired after ACLR, and that less-accurate quadriceps force output is associated with altered muscle activation strategies. However, the small number of studies and the lack of multivariate analyses within these studies mean that the mechanisms of impaired quadriceps force control following ACLR are still unclear. Small sample sizes together with the exclusion of patients with concomitant chondral/meniscal injuries and anterior knee laxity may limit the potential for the findings of these studies to be generalized to the wider ACLR population.

## 2.4 Closed kinetic chain neuromuscular adaptations after ACLR

### 2.4.1 Overview

ACL rupture is associated with severe knee symptoms and limitations, including episodes of the knee giving way and difficulty in sports and activities of daily living (Eastlack, 1999; Fitzgerald *et al.*, 2000). For most people with ACL deficient (ACLD) knees, compensatory movement patterns and altered muscle activation strategies develop soon following ACL rupture, either as a response to pain and/or instability or to allow improved knee function (Bryant *et al.*, 2009a; Georgoulis *et al.*, 2003; Goerger *et al.*, 2014; Rudolph *et al.*, 2001). In order to avoid episodes of knee instability and optimise knee joint function, higher functioning people with ACLD knees make biomechanical (i.e., kinematic and kinetic; Andriacchi & Dyrby, 2005) or neuromuscular adaptations (i.e., altered muscle activation strategies (Andriacchi & Dyrby, 2005; Chmielewski *et al.*, 2005). Knowledge of the biomechanical and neuromuscular adaptations associated with ACL rupture may be helpful in interpreting adaptations that may persist following ACLR (Bryant *et al.*, 2009b; Swanik *et al.*, 2004). Hence, a discussion of these adaptations follows.

People who compensate poorly after ACL rupture have been termed non-copers (Rudolph *et al.*, 1998). During functional, closed kinetic chain activities such as walking, non-copers demonstrate smaller knee flexion angles, smaller knee extensor moments and greater hamstring and gastrocnemius coactivation compared to uninjured people (Klyne *et al.*, 2012; Rudolph *et al.*, 2001; Rudolph *et al.*, 1998). These changes are thought to reflect an unsophisticated or crude adaptation to the anterior and rotary instability that is associated with ACLD.

People who compensate successfully for ACLD, also known as copers, demonstrate more sophisticated movement patterns and muscle activation strategies than non-copers (Bryant *et al.*, 2009b; Klyne *et al.*, 2012; Rudolph *et al.*, 1998). For example, copers activate their hamstrings and gastrocnemius earlier following weight acceptance in walking (Klyne *et al.*, 2012; Rudolph *et al.*, 1998) and activate their quadriceps earlier prior to ground contact in single leg landing tasks (Bryant *et al.*, 2009b). These strategies reduce excessive anterior tibial translation and internal tibial rotation

movement (Boeth *et al.*, 2013), which may otherwise predispose these individuals to experiencing episodes of knee joint instability (Rudolph *et al.*, 2001; Shelburne *et al.*, 2005).

The force produced by reflexive muscle activity does not occur quickly enough to stabilise the knee joint during dynamic functional tasks and prevent knee instability (Bryant *et al.*, 2009b; McNair *et al.*, 1992; Ristanis *et al.*, 2011; Steele & Brown, 1999; Swanik *et al.*, 1999). Instead, it has been proposed that ACLD copers develop successful, feed-forward, or preparatory muscle activation strategies (Bryant *et al.*, 2008b; Rudolph *et al.*, 2001; Swanik *et al.*, 2004). These preparatory muscle activation strategies may be augmented by biomechanical adaptations such as smaller knee flexion excursion (i.e. the difference between minimum and peak knee flexion angle; (Rudolph *et al.*, 1998) and smaller peak knee extensor moments (Oberländer *et al.*, 2012b). Conversely, ACLD non-copers demonstrate a strategy of generalized muscle coactivation (Chmielewski *et al.*, 2005; Takeda *et al.*, 2014), which may increase knee joint stability, at the cost of movement efficiency and knee joint function (Eastlack, 1999). Greater thigh muscle coactivation may also be associated with longer term structural changes in the knee joint (Tsai *et al.*, 2012).

Neuromuscular adaptations can persist following ACLR, despite the restoration of mechanical knee stability.<sup>3</sup> For example, significantly smaller peak knee flexion angles have been observed in the landing phase of the hop for distance test (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010) and in the stance phase of walking (Shi *et al.*, 2010). These adaptations are believed to be indicative of neuroplastic changes in the higher motor centres (Baumeister *et al.*, 2008; Kapreli *et al.*, 2009). In the short term following ACLR, lower knee flexion range of movement and greater thigh muscle coactivation may help to minimise strain on the ACL graft, whilst still allowing individuals to walk and perform most activities of daily living (Bryant *et al.*, 2008b; Fitzgerald *et al.*, 2000; Laughlin *et al.*, 2011; Swanik *et al.*, 2004). However, in the long term, and particularly

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<sup>3</sup> (Bell *et al.*, 2014; Breen *et al.*, 2014; Delahunt *et al.*, 2012c; Di Stasi *et al.*, 2013; Ernst *et al.*, 2000; Frank *et al.*, 2014; Gao & Zheng, 2010; Goerger *et al.*, 2014; Gokeler *et al.*, 2010; Hall *et al.*, 2012; Kuenze *et al.*, 2014; Lewek *et al.*, 2002; Miranda *et al.*, 2013; Misonoo *et al.*, 2011; Morrissey *et al.*, 2004; Nyland *et al.*, 2010; Oberländer *et al.*, 2012a; Orishimo *et al.*, 2010; Ortiz *et al.*, 2011; Paterno *et al.*, 2010; Scanlan *et al.*, 2010; Tashman *et al.*, 2004; Tashman & Araki, 2013).

following return to higher-intensity functional activities, these adaptations may be considered maladaptive, considering the potential impact on sporting performance (Nyland *et al.*, 2013) and knee joint loading (Chaudhari *et al.*, 2008; Tsai *et al.*, 2012).

#### **2.4.2 Assessment of closed kinetic chain neuromuscular adaptations following ACLR**

The dynamic functional tasks that have been used in previous investigations to assess closed kinetic chain neuromuscular adaptations after ACLR are numerous (Ingersoll *et al.*, 2008). In summary these tasks can be categorised as locomotion, e.g. walking, jogging or running (Di Stasi *et al.*, 2013; Kuenze *et al.*, 2014; Tashman *et al.*, 2004), sports-specific, e.g. kicking or cutting (Breen *et al.*, 2014; Cordeiro *et al.*, 2014), or isolated tasks, e.g. hopping (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010; Xergia & Pappas, 2013).

Isolated closed kinetic chain tasks such as hopping, jumping and landing and squatting assess specific aspects of knee function. For example, the landing phase of hop tests assesses coordination of movement patterns (Xergia & Pappas, 2013), muscle activation strategies (Gokeler *et al.*, 2010) and dynamic postural stability (Oberländer *et al.*, 2012a). Single leg hopping and landing tasks place higher loads on the tibiofemoral joint and ACL than locomotion tasks and double leg landing tasks (Laughlin *et al.*, 2011; Sell, 2006). At longer post-operative time-points, for example greater than 12 months, neuromuscular adaptations may become less apparent in low demand activities such as squatting (Neitzel *et al.*, 2002), but persist during high demand activities such as single leg landings (Vairo *et al.*, 2008). Hence, single leg landing tasks are commonly used to assess neuromuscular responses after ACLR (Bryant *et al.*, 2009b; Miranda *et al.*, 2013; Oberländer *et al.*, 2012a; Vairo *et al.*, 2008; Xergia & Pappas, 2013).

Single leg hopping and landing tasks involve hopping a standardised (Oberländer *et al.*, 2012a) or maximal distance (Xergia & Pappas, 2013), or dropping from a standardised height and landing on the involved limb (i.e., a drop landing (Vairo *et al.*, 2008). Hopping and drop landing tasks can be linear (i.e., performed in a straight line), or can involve multidirectional components. For example, Delahunt *et al.* (2012b) assessed the landing biomechanics of patients with ACLR using a diagonal hopping task, and

Miranda *et al.* (2013) assessed similar variables after ACLR using a jump-cut manoeuvre. Ultimately, the selection of a single leg hopping or landing task for biomechanical research will depend on the functional abilities of the participant and the variables of interest (Tashman *et al.*, 2007). Examples of functional tasks that can be used to assess neuromuscular control after ACLR are provided in Figure 2.5.

<b>Locomotion</b> <sup>4</sup>	<b>Sports-specific tasks</b> <sup>5</sup>	<b>Isolated tasks</b> <sup>6</sup>
Walking Jogging Running Stair ascent/descent Pivoting during locomotion	Cutting or sidestepping Stop jumps Kicking	Hopping (time or distance based, maximal or sub-maximal) Drop landing/jump Vertical jump Counter-movement jumps (linear or multidirectional) Squatting*

**Figure 2.5** Examples of functional closed kinetic chain tasks that can be used to assess neuromuscular adaptations after ACLR

Specific parameters of single leg hopping and landing tasks, such as hop distance or height, may be easier to standardise than sports-specific tasks. The intensity or difficulty of hopping tasks and drop landings can be manipulated by increasing or decreasing the distance hopped or the height of the drop (Ali *et al.*, 2012). These parameters can also be normalised to each participant’s anthropometry (e.g. leg length or height; Gribble *et al.* (2012). Standardisation of some aspects of these tasks may reduce variability in the

<sup>4</sup> **Locomotion tasks:** Walking (Butler *et al.*, 2009; Gao & Zheng, 2010; Georgoulis *et al.*, 2003; Gokeler *et al.*, 2003; Hall *et al.*, 2012; Lustosa *et al.*; Moraiti *et al.*, 2009; Morrissey *et al.*, 2004; Scanlan *et al.*, 2010; Scanlan *et al.*, 2013; Timoney *et al.*, 1993; Webster & Feller, 2011; Zabala *et al.*, 2013), Jogging (Kuenze *et al.*, 2014), Running (Patras *et al.*, 2009; Tashman *et al.*, 2007), Stair ascent/decent (Gao *et al.*; Georgoulis *et al.*, 2007; Hall *et al.*, 2012; Morrissey *et al.*, 2004; Ristanis *et al.*, 2003; Zabala *et al.*, 2013), Pivoting during locomotion (Chouliaras *et al.*, 2009; Georgoulis *et al.*, 2007; Lam *et al.*, 2011; Ristanis *et al.*, 2003; Webster *et al.*; Zampeli *et al.*, 2012)

<sup>5</sup> **Sports-specific tasks:** Cutting or sidestepping (Breen *et al.*, 2014; Misonoo *et al.*, 2011), Shuttle running (Breen *et al.*, 2014), Kicking (Cordeiro *et al.*, 2014), Stop jumps (Nyland *et al.*, 2010)

<sup>6</sup> **Isolated tasks:** Hopping (Bryant *et al.*, 2009b; Gokeler *et al.*, 2010; Nyland *et al.*, 2014; Oberländer *et al.*, 2012a; Orishimo *et al.*, 2010; Ortiz *et al.*, 2011; Roos *et al.*, 2013; Webster & Feller, 2012; Xergia & Pappas, 2013; Xergia *et al.*, 2014), Drop landing (Decker *et al.*, 2002; Misonoo *et al.*, 2011; Tsai *et al.*, 2012; Vairo *et al.*, 2008; Webster & Feller, 2012) Drop jump (Bates *et al.*, 2013; Breen *et al.*, 2014; Delahunt *et al.*, 2012c; Gokeler *et al.*, 2014b; Paterno *et al.*, 2010), Jump landing (Bell *et al.*, 2014; Delahunt *et al.*, 2012b), Single leg vertical jump (Ernst *et al.*, 2000; Pairo de Fontenay *et al.*, 2014), Double leg countermovement jump (Gokeler *et al.*, 2014b), Multidirectional countermovement hop (Bjornaraa, 2011; Miranda *et al.*, 2013), Squatting (Castanharo *et al.*, 2011; Clark *et al.*, 2014; Neitzel *et al.*, 2002; Webster *et al.*, 2014b)

quality of performance between individuals, which may confound comparisons between groups of individuals. For example, upper limb movement can be used to improve dynamic balance after landing; hence, landing tasks are commonly performed with the participant's arms folded over their chest or on their hips (Gokeler *et al.*, 2010).

Locomotor and sports-specific tasks have external validity (Donnelly *et al.*, 2012); however, the performance of sports-specific tasks such as cutting and kicking may be influenced by the participant's experience or skill in performing that task (Sigward & Powers, 2006). For example, individuals with a higher frequency of sports participation have been found to use greater gluteus maximus and lower vastus medialis activation during a counter-movement jump task compared to individuals with less frequent sports participation (Nyland *et al.*, 2013). Consequently, studies that have used sports-specific tasks such as cutting to assess neuromuscular control after ACLR typically recruit highly homogenous samples of participants (e.g. athletes from the same sport), at a similar level of competition (Cordeiro *et al.*, 2014), or with high levels of knee function (Breen *et al.*, 2014). Whilst important knowledge about neuromuscular responses after ACLR in these populations has been generated from these investigations, the findings may not be generalisable to the wider ACLR population.

### **2.4.3 Kinematic and kinetic adaptations after ACLR in single leg landing tasks**

The most commonly used method to assess lower limb kinematics after ACLR is three dimensional movement analysis (Hart *et al.*, 2010), which uses multiple cameras to track the position of reflective markers that are attached to the skin overlying important anatomical landmarks (McGinley *et al.*, 2009). Such analyses can yield a large number of variables, including peak joint angles in the sagittal, frontal or transverse planes, or joint angles at a specific time-point; such as, knee flexion angle at the time of peak vertical ground reaction force (Podraza & White, 2010).

In general, studies using multidirectional landing or pivoting tasks involve higher-functioning individuals with ACLR, at later post-operative time-points, who have returned to multidirectional sports (Miranda *et al.*, 2013; Delahunt *et al.*, 2012b). Although multidirectional landing tasks assess biomechanical parameters that are highly-relevant to sport and knee joint function (Dempsey *et al.*, 2009), linear landing

tasks may still elucidate kinematic adaptations in higher-functioning individuals; adaptations which may have implications for sporting performance and joint health (Breen *et al.*, 2014; Gokeler *et al.*, 2010; Xergia & Pappas, 2013).

The decision to use a linear task may be partly based on safety; multidirectional and unanticipated landing tasks result in greater valgus and internal rotation forces within the knee compared to linear tasks (McLean *et al.*, 2010) and these forces may increase the risk of ACL graft rupture for some participants (Paterno *et al.*, 2010). It was anticipated that some of the participants recruited for this PhD research would have lower levels of knee function and/or would not have returned to multidirectional sports. Hence, in order to inform the selection of a task for Study 3 of this thesis, this section focusses on investigations of the kinematics and kinetics in the landing phase of linear and anticipated single leg landing tasks. Only tasks involving a static landing and stabilisation phase were included (i.e., hopping and drop landing tasks) so that variables could be more easily compared between these tasks. A summary of the trunk, hip, knee and ankle kinematic variables reported within these investigations is presented in Table 2.8.



**Table 2.8** Summary of trunk, hip, knee and ankle kinematics of individuals following ACLR in the landing phase of single leg landing tasks (hop and drop landings) compared to the uninvolved limb or an uninjured control group

Study	Participants	Time since ACLR (months)	Description of single leg landing task	Data acquisition, processing and clinimetric properties	Findings		
					Variable	Involved limb	Comparison limb
Xergia & Pappas (2013) <sup>‡</sup>	22 recreationally active male patients with ACLR No concomitant injuries. Mean age 29 ± 11 years	7 ± 1	Single hop for distance: <ul style="list-style-type: none"> <li>• Free movement of arms</li> <li>• Wearing own sports shoes</li> <li>• 2-3 practice trials for each leg</li> <li>• 3 successful trials analysed</li> </ul>	3D motion analysis, 8 camera Vicon system (100Hz, 6 Hz Woltring filter) Reliability: Not assessed	<u>Peak joint angles</u> Hip flexion (°) 57.9 ± 17.8 Knee flexion (°) 47.0 ± 16.9 Ankle DF (°) 21.4 ± 9.0	Uninvolved 55.2 ± 12.6 54.6 ± 20.6* 26.1 ± 12.8*	<b>Summary:</b> Significantly less peak knee flexion and ankle dorsiflexion angles
Webster (2012)	15 recreationally active male patients with ACLR, concomitant injuries NR Excluded patients with knee laxity > 3mm Mean age 27 ± 6 years  11 uninjured control participants Mean age 23 ± 3 years	67 ± 8	30 cm drop landing: <ul style="list-style-type: none"> <li>• Hands on hips, no footwear</li> <li>• 3 practice trials</li> <li>• 5 successful trials analysed for each leg</li> </ul>	3D motion analysis, 10 camera Vicon system (100Hz, filter NR) Reliability: Not assessed	<u>Joint excursions</u> Hip flexion (°) 19.9 Knee flexion (°) 44.4 Ankle DF (°) 36.1 <u>Peak joint angles</u> Knee adduction (°) 3.9 Knee IR (°) 21.1	Matched 22.8 49.7 37.2 3.1 24.3	<b>Summary:</b> No significant differences compared to uninvolved limb
Gokeler <i>et al.</i> (2010) <sup>‡</sup>	9 recreational athletes with ACLR (3 women) Level I or II sports only No concomitant injuries Mean age 28 ± 10 years	27 ± 2	Single hop for distance: <ul style="list-style-type: none"> <li>• Hands behind back</li> <li>• Wearing own sports shoes</li> <li>• 5-10 practice trials for each leg</li> <li>• 3 successful trials analysed</li> </ul>	3D motion analysis with two camera OPTOTRAK system (150 Hz). Average of 3 trials used for analysis Reliability: Not assessed	<u>Joint excursions</u> Hip flexion (°) 13.7 ± 7.0 Knee flexion (°) 31.3 ± 7.3 Ankle DF (°) 13.3 ± 11.0	Uninvolved 18.8 ± 6.2 42.3 ± 5.1* 5.7 ± 2.1	<b>Summary:</b> Significantly less knee flexion excursion compared to uninvolved limb

Deneweth <i>et al.</i> (2010)	11 recreationally active patients with ACLR (3 women) Level I or II sports only No concomitant injuries. Mean age 29 ± 13 years	4.4 ± 1	30 cm hop forwards over 4cm obstacle: <ul style="list-style-type: none"> <li>• Upper limb not standardised</li> <li>• Footwear not reported</li> <li>• Practice trials not reported</li> <li>• 3 successful trials analysed</li> </ul>	3D motion analysis using RSA. Average of 3 trials used for analysis Reliability: Not assessed but previously reported	<u>Peak joint angles</u> Knee flexion (°) 38.9 ± 10.9 Knee adduction (°) 1.3 ± 1.9 Knee IR (°) 4.8 ± 6.3	Uninvolved 47.7 ± 8.1* 0.9 ± 2.3 9.8 ± 5.7*
					<b>Summary:</b> Significantly less peak knee flexion and internal tibial rotation angle compared to uninvolved limb	
Nyland <i>et al.</i> (2010)	70 recreational athletes with ACLR (35 women) All levels of sport Included concomitant chondral and meniscal injuries and knee laxity > 3mm Mean age NR	64 ± 3	Maximum vertical countermovement jump with single leg landing: <ul style="list-style-type: none"> <li>• Free movement of arms</li> <li>• Wearing own sports shoes</li> <li>• 3 practice trials for each leg</li> <li>• 3 successful trials analysed</li> </ul>	2D motion analysis with single camera SIMI motion software (60 Hz). Average of 3 trials used for analysis Reliability: Not assessed	<u>Peak joint angles</u> <i>Males</i> Hip flexion (°) 56.7 Knee flexion (°) 56.8 Ankle DF (°) 20.6 <i>Females</i> Hip flexion (°) 50.3 Knee flexion (°) 50.8 Ankle DF (°) 19.7	Uninvolved 56.9 57.5 20.6 51.0 52.4 20.4
					<b>Summary:</b> No significant differences compared to uninvolved limb	
Orishimo <i>et al.</i> (2010) <sup>‡</sup>	13 recreationally active patients with ACLR (4 women) Concomitant injuries NR Mean age 33 ± 10 years	Range 4-12 months	Single hop for distance: <ul style="list-style-type: none"> <li>• Free movement of arms</li> <li>• Wearing own sports shoes</li> <li>• 3 practice trials for each leg</li> <li>• 3 successful trials analysed</li> </ul>	3D motion analysis, 5 camera Qtrac system (60Hz, 10 Hz Butterworth filter) Reliability: Not assessed	<u>Joint excursions</u> Hip flexion (°) 10.5 ± 5.0 Knee flexion (°) 35.7 ± 8.2 Ankle DF (°) 22.3 ± 13.2	Uninvolved 12.3 ± 4.9 43.3 ± 12.3* 25.0 ± 7.5
					<b>Summary:</b> Significantly less knee flexion excursion compared to uninvolved limb	
Vairo <i>et al.</i> (2008)	14 recreationally active patients with ACLR (9 women), no concomitant injuries mean age 23 ± 4 years. 14 matched and uninjured control participants	21 ± 11	30 cm drop landing: <ul style="list-style-type: none"> <li>• Hands on hips, no footwear</li> <li>• 3 practice trials</li> <li>• 3 successful trials analysed</li> </ul>	3D motion analysis, 6 camera Peak Motus System (120Hz, 6 Hz Butterworth filter) Reliability: Not assessed	<u>Joint angles at peak vertical GRF</u> Hip flexion (°) 31.7 ± 8.8 Knee flexion (°) 37.0 ± 9.8 Ankle DF (°) -3.3 ± 6.2	Matched 24.2 ± 6.0* 27.8 ± 7.5* 1.9 ± 5.9*
					<b>Summary:</b> Significantly greater hip and knee flexion and ankle DF angles at peak GRF compared to matched control group	

Webster <i>et al.</i> (2004)	10 recreationally active patients with ACLR (1 woman) Hamstring graft group only	27 ± 7	1. Horizontal hop: distance standardised to leg length 2. 15 cm drop landing: <ul style="list-style-type: none"> <li>• Hands on hips, no footwear</li> <li>• 3 practice trials</li> <li>• 6 successful trials</li> </ul>	3D motion analysis, 6 camera Vicon system (50Hz, 20 Hz Woltring filter) Reliability: Not assessed	<u>Peak joint angles</u> <i>Horizontal hop</i> Knee flexion (°) <i>Vertical hop</i> Knee flexion (°)	52.5 ± 4.5 52.5 ± 5	Uninvolved 52 ± 4.5 52 ± 5
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Values are means ± standard deviation if reported in study ; ° = degrees; RSA = radiostereophotogrammetric analysis; NR= not reported; 3D = three dimensional; 2D = two dimensional; Hz = Hertz; DF = dorsiflexion; IR = internal tibial rotation; cm = centimetres; GRF = ground reaction force; For statistically significant differences between limbs, \* =  $p < 0.05$ ; For statistically significant differences between ACLR and control groups, § =  $p < 0.05$ ; Joint excursions = difference between minimum and maximum joint angle during the landing phase (initial ground contact until time-point defined by authors)  
Uninvolved = the uninvolved or contralateral limb of the ACLR group. Matched = the matched limb of an uninjured control group  
¥ Includes subjects with bone-patella-bone autografts

Of the eight investigations that were reviewed, two used a matched control group and the remainder reported the side-to-side difference in lower limb kinematics. Regardless of whether a comparison to the uninvolved limb or an uninjured control group was made, there was a trend for participants with ACLR to land with smaller knee flexion angles on their involved side. The exception to this was the investigation by Vairo *et al.* (2008), in which significantly higher peak knee flexion angles were observed at the point of peak vertical GRF compared to a matched control group. However, five of the remaining studies reported significantly smaller peak knee flexion angles or smaller knee flexion excursion on the ACLR limb compared to the uninvolved or matched control limb (Deneweth *et al.*, 2010; Gokeler *et al.*, 2010; Nyland *et al.*, 2010; Orishimo *et al.*, 2010; Xergia & Pappas, 2013).

Lower knee flexion range of movement is consistently observed after ACLR during single leg landing tasks, regardless of whether the uninvolved leg or a matched control is used for comparison. However, the kinematics of the hip, ankle and secondary planes of movement of the knee appear to be more variable between groups of participants with ACLR. For example, smaller hip flexion excursion or peak hip flexion angles were observed for three studies (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010; Webster *et al.*, 2012b) and greater hip flexion angles were observed for two studies (Vairo *et al.*, 2008; Xergia & Pappas, 2013). It is possible that these kinematic adaptations are quite variable within ACLR groups and are associated with other factors apart from the demands of the task, such as sex (Miranda *et al.*, 2013) or the level of sports participation of individuals (Nyland *et al.*, 2013).

Smaller knee flexion excursion in single leg landings has previously been associated with greater peak vertical ground reaction force (Miranda *et al.*, 2013). Hence, smaller knee flexion excursion contributes to greater impact forces within the knee. Conversely, greater hip flexion angles could be seen as a knee joint-sparing adaptation, as greater forces may be transferred through the posterior chain of muscles (i.e., hamstrings, gluteal muscles and trunk extensors), and less force transferred through the knee joint and knee extensor mechanism (Shimokochi *et al.*, 2013; Shultz *et al.*, 2009; Stearns & Powers, 2014). This proposition is supported by the findings of Tsai & Powers (2013), who asked a group of individuals with ACLR to deliberately increase

their hip and knee flexion angles during a drop landing. Using an EMG-driven musculoskeletal model, the authors reported finding lower tibio-femoral forces when hip and knee flexion angles increased.

In straight-line hopping tasks, the momentum associated with forward movement of the body, combined with the challenge to an individual's dynamic balance, may make it more difficult for individuals to reduce knee joint loading by increasing hip flexion angles (Ernst *et al.*, 2000). Oberlander *et al.* (2012b) analysed the peak trunk flexion angles of a group of individuals at six and 12 months after ACLR surgery. Based on their findings, the authors speculated that individual following ACLR may compensate for lower limb strength and kinematic deficits by increasing their peak trunk flexion after landing. This strategy may allow ACLR individuals to reduce knee joint loading, at the cost of dynamic stability (Oberländer *et al.*, 2012a). Hence, in straight-line landing tasks, peak trunk flexion angle, rather than peak hip flexion angle, may be more closely associated with successful task performance.

Inspection of the standard deviations of the joint excursions and peak joint angles reported in Table 2.8 reveals that there is considerable variability in these variables within ACLR groups. For example, Xergia & Pappas (2013) reported an average peak knee flexion angle of  $47.0^{\circ}$  with a standard deviation of  $16.9^{\circ}$ . Hence, an individual at the upper limit of the standard deviation had a peak knee flexion angle of  $63.9^{\circ}$ , and an individual at the lower limit had a peak knee flexion angle of  $30.1^{\circ}$ . However, this variability may be related to the relatively small sample sizes for the studies, since smaller sample sizes are associated with larger standard deviations. With the exception of Nyland *et al.* (2010) who included 70 individuals following ACLR in their study, the size of the ACLR groups range from nine (Gokeler *et al.*, 2010) to 22 (Xergia & Pappas, 2013).

Moreover, the kinematic deficits observed during functional movements appear to be task-dependent (Tashman *et al.*, 2007). Despite including only linear, single leg landing tasks in this literature review, considerable variability was observed in the peak joint angles and the relative increase or decrease of joint excursion reported in studies. This variability makes it difficult to generalize between studies that have used different tasks. However, a consistent finding amongst the studies was that knee flexion range of

movement for the involved (ACLR) side is smaller following ACLR in single leg landing tasks. Lower knee flexion movement during landing tasks is associated with altered/greater ACL and knee joint forces (Laughlin *et al.*, 2011; Tsai & Powers, 2013), and altered knee joint loading may be associated with the onset or progression of knee osteoarthritis (Hunt & Bennell, 2010; Scanlan *et al.*, 2013). The assessment of kinetics (i.e., ground reaction forces and joint moments), particularly sagittal plane kinetics, provides a starting point for understanding these forces. Therefore, the following section of this literature review focuses on the kinetic adaptations observed during these tasks. A summary of the kinetic adaptations observed during hop landings and single leg drop landings after ACLR is provided in Table 2.9.

**Table 2.9** Summary of the trunk, hip, knee and ankle kinetics of individuals following ACLR in the landing phase of single leg landing tasks (hop and drop landings) compared to the uninvolved limb or an uninjured control group.

Study	Participants	Time since ACLR (months)	Description of single leg landing task	Data acquisition, processing and clinimetric properties	Findings		
					Variable	Involved limb	Comparison limb
Holsgaard-Larsen <i>et al.</i> (2014)	23 recreationally active male patients with ACLR Concomitant injuries and knee laxity NR Mean age 29 ± 11 years 25 matched and uninjured control participants	27 ± 7	Unilateral vertical jump <ul style="list-style-type: none"> <li>• Hands on hips</li> <li>• No footwear</li> <li>• Practice trials NR</li> <li>• 3 maximum effort trials performed</li> </ul>	3D motion analysis, 6 camera Vicon system, AMTI force plate (1000 Hz, 6 Hz Woltring filter) Reliability: Good to moderate; CV 3-14%	Average joint moment Knee extensor (Nm.kg)	1.58 ± 0.41	Uninvolved 1.70 ± 0.36* Matched 1.73 ± 0.35*
					<b>Summary:</b> Smaller average knee extensor moment on ACLR limb, not statistically significant		
Oberlander <i>et al.</i> (2012b)	10 recreational athletes with ACLR (females NR) Level I or II sports only No concomitant injuries Mean age 28 ± 10 years	12	Single horizontal hop, 0.75 times body height: <ul style="list-style-type: none"> <li>• Hands on hips</li> <li>• Wearing own sports shoes</li> <li>• 5 trials performed</li> </ul>	3D motion analysis, 12 camera Vicon system 200 Hz, Kistler force plate sampling at 1000Hz, filtering NR Reliability: Not assessed	Peak joint moments (Nm.kg)		Matched
					Hip extensor Knee extensor Ankle plantarflexor	2.5 2.5 1.2	2.6* 3.0* 0.9*
<b>Summary:</b> Significantly smaller peak hip and knee extensor moments and significantly higher plantarflexor moments on ACLR limb compared to matched limb of control group							
Gokeler <i>et al.</i> (2010) <sup>‡</sup>	9 recreational athletes with ACLR (3 women) Level I or II sports only No concomitant injuries Mean age 28 ± 10 years	27 ± 1.5	Single hop for distance: <ul style="list-style-type: none"> <li>• Hands behind back</li> <li>• Wearing own sports shoes</li> <li>• 5-10 practice trials</li> <li>• 3 maximum effort trials performed</li> </ul>	3D motion analysis with two camera OPTOTRAK, brand of force plate NR (750 Hz, filter NR) Average of 3 trials used for analysis Reliability: Not assessed	Peak joint moments (Nm/BW/LL)		Uninvolved
					Hip extensor Knee extensor Ankle plantarflexor Ground reaction force Peak vertical (N/BW)	0.29 ± 0.08 0.17 ± 0.05 0.14 ± 0.03 2.24 ± 0.36	0.25 ± 0.07 0.30 ± 0.03* 0.12 ± 0.03 2.17 ± 0.23
<b>Summary:</b> Significantly smaller peak knee extensor moment on ACLR limb, no significant difference in hip/ankle moments or vertical GRF							

Nyland <i>et al.</i> (2010) <sup>¥</sup>	70 recreational athletes with ACLR (35 women) All levels of sport Included concomitant chondral and meniscal injuries and knee laxity > 3mm Mean age NR	64 ± 3.2	Maximum vertical countermovement jump with single leg landing: • Free movement of arms, own sports shoes • 3 practice trials	Quattro force plate system (500 Hz) Average of 3 trials used for analysis Reliability: Not assessed	<u>Ground reaction force</u> <i>Males</i> Peak vertical (% BW) 27.6 <i>Females</i> Peak vertical (% BW) 23.2 <b>Summary:</b> No significant differences in peak vertical GRF compared to uninvolved limb	Uninvolved 28.5 23.4
Orishimo <i>et al.</i> (2010) <sup>¥</sup>	13 recreationally active patients with ACLR (4 women) Concomitant injuries NR Mean age 33 ± 10 years	Range 4-12 months	Single hop for distance: • Free movement of arms, own sports shoes • 3 practice trials • 3 successful trials	3D motion analysis, 5 camera Qtrac system Kistler force plate sampling at 1200Hz, filtering NR Reliability: Not assessed	<u>Peak joint moments</u> (Nm/kg) Hip extensor 5.5 ± 3.8 Knee extensor 3.3 ± 1.7 Ankle plantarflexor 1.8 ± 0.9 <u>Peak vertical GRF</u> (N/BW) 4.2 ± 1.5 <b>Summary:</b> No significant differences in peak vertical GRF or peak sagittal plane joint moments compared to uninvolved limb	Uninvolved 5.3 ± 2.1 3.5 ± 1.1 1.3 ± 0.7 4.7 ± 1.3
Vairo <i>et al.</i> (2008)	14 recreationally active patients with ACLR (9 women) No concomitant injuries. Mean age 23 ± 4 years  14 matched and uninjured control participants (9 women) Mean age 23 ± 4 years	21 ± 11	30 cm drop landing: • Hands on hips • No footwear • 3 practice trials • 3 successful trials	3D motion analysis, 6 camera Peak Motus System, Kistler force plate sampling at 1200Hz, filtered with 100Hz Butterworth filter Reliability: Not assessed	<u>Peak hip extensor moment</u> (Nm/kg) 0.24 ± 0.06  <u>Peak vertical GRF</u> (N/BW) 3.72 ± 0.51 <b>Summary:</b> Significantly lower peak vertical GRF on ACLR limb compared to both uninvolved and matched limb of control group. No significant difference between groups in peak extensor moment	Uninvolved 0.27 ± 0.07 Matched 0.28 ± 0.09 Uninvolved 4.19 ± 0.94* Matched 5.11 ± 1.07*
Ernst <i>et al.</i> (2000) <sup>¥</sup>	20 recreationally active patients with ACLR (6 women)	10 ± 2	Landing from maximum vertical jump:	3D motion analysis, 6 camera Vicon system 60 Hz, Kistler force plate	<u>Peak knee extensor moment</u> (Nm/kg) 1.30 ± 0.59	Uninvolved 2.09 ± 0.49* Matched



	Concomitant injuries NR, knee laxity > 3mm Mean age 24 ± 4 years 20 matched and uninjured control participants		<ul style="list-style-type: none"> <li>• Free movement of arms, bare feet</li> <li>• 3 trials performed</li> </ul>	sampling at 1200Hz, filtering NR. Reliability: Knee extensor moment ICC [3,1] = 0.94			0.91 ± 0.45*
<b>Summary:</b> Significantly smaller peak knee extensor moment on ACLR limb compared to both uninjured and matched limb of control group							

Values are means ± standard deviation if reported in study; Nm.kg = Newton metres multiplied by body weight in kilograms; Nm/BW/LL = joint moments (Nm) normalised to body weight (BW) and leg length (LL), N/BW = Newtons divided by body weight in kg (Gokeler *et al.*, 2010); AMTI = Advanced Mechanical Technology, Inc; CV = coefficient of variability; NR= not reported; 3D = three dimensional; 2D = two dimensional; Hz = Hertz; DF = dorsiflexion; IR = internal tibial rotation; cm = centimetres; GRF = ground reaction force; Uninvolved = the uninjured or contralateral limb of the ACLR group. Matched = the matched limb of an uninjured control group

\* =  $p < 0.05$  for statistically significant differences between limbs or groups; ¥ Includes subjects with bone-patella-bone autografts

Four of the studies included in Tables 2.8 and 2.9 reported peak vertical GRF in single leg landing tasks with participants with ACLR (Gokeler *et al.*, 2010; Nyland *et al.*, 2010; Orishimo *et al.*, 2010; Vairo *et al.*, 2008); however, only one study reported significant differences between the ACLR limb and a matched and control limb (Vairo *et al.*, 2008). It is possible that ACLR individuals compensated for the increased vertical GRF associated with reduced knee flexion movement using other adaptations within the kinetic chain, such as increased trunk flexion angle (Ernst *et al.*, 2000).

The largest absolute differences in kinetic variables between people with ACLR and uninjured individuals and between the limbs of people with ACLR were observed for knee extensor moments. In general, peak knee extensor moments during landing tasks were lower than those observed on uninvolved or matched control limbs. Holsgaard-Larsen *et al.* (2014) reported that knee extensor moments of an ACLR group were 7% and 9.5% lower than the uninvolved limb and matched limb of a control group respectively. Factors that may contribute to reduced knee extensor moments include a reduction in the magnitude of GRF and reduced knee flexion excursion, via a reduction in the knee extension moment arm (Orishimo *et al.*, 2010).

#### **2.4.4 Summary of kinematic and kinetic adaptations following ACLR**

Lower knee flexion range of movement and knee extensor moments were observed in most studies, whilst hip and ankle kinematic and kinetic adaptations were more variable and task dependent. The previous investigations that have analysed kinematic and kinetic variables during hopping and drop landing tasks are limited by small sample sizes which increase the risk of type II error. Furthermore, only two studies evaluated the reliability of their variables (Ernst *et al.*, 2000; Holsgaard-Larsen *et al.*, 2014) and no study reported the standard error of measurement. Knowledge of these clinimetric properties is important so that differences in variables can be interpreted with respect to their repeatability and variability.

Analysing the biomechanics of single leg landing tasks can provide insight into adaptations that may underlie knee functional limitations, injury risk and the development of osteoarthritis after ACLR (Hewett *et al.*, 2013; Laughlin *et al.*, 2011; Zampeli *et al.*, 2012). However, the use of maximal effort hop tests for such analyses

may be problematic if hop distance is not accounted for in statistical analyses, potentially resulting in significant variability between individuals in the performance of these tasks (see Table 2.3). Greater horizontal hop distances are associated with significantly higher knee flexion angles in landing in uninjured individuals (Ali *et al.*, 2012). However, reduced knee motion is a hallmark of patients following ACLR; hence, individuals following ACLR who hop further may demonstrate smaller knee flexion angles than individuals who may not be able to, or want to, hop as far. The previous studies that have assessed knee flexion angles during the hop for distance test have not been sufficiently powered to include hop distance as a covariate (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010; Webster *et al.*, 2004a; Xergia & Pappas, 2013).

Finally, the use of small sample sizes has precluded the investigation of the mechanisms of neuromuscular adaptations in previous investigations. Most of the reviewed studies involved both male and female patients with ACLR, and some studies included individuals with concomitant chondral and meniscal injuries and anterior knee joint laxity (see Tables 2.4 and 2.5). However, no investigation was sufficiently powered to conduct a multivariate analysis to determine whether these participant characteristics were associated with neuromuscular adaptations.

#### **2.4.5 Mechanisms of kinematic and kinetic adaptations following ACLR**

Of the variables included in the reviewed studies, knee flexion excursion or peak knee flexion angle are arguably the most simple to measure in clinical practice (Myer *et al.*, 2010) and importantly, are modifiable (Milner *et al.*, 2012; Stearns & Powers, 2014). Previous authors have recommended that individuals following ACLR increase their knee flexion angles during landing tasks, in order to reduce knee joint loading and ACL graft injury risk (Cowling *et al.*, 2003; Gokeler *et al.*, 2014a; Tsai & Powers, 2013). However, before the recommendation to increase knee flexion angles is adopted in the wider ACLR population, greater understanding of the factors that are associated with deficits in knee flexion excursion is needed. One potentially modifiable factor that may be associated with knee flexion excursion is the magnitude or timing of muscle activation prior to ground contact (Shultz *et al.*, 2009).

In landing tasks, preparatory muscle activity is defined as muscle activation that occurs prior to initial ground contact (Bryant *et al.*, 2009b). Preparatory muscle activity is thought to help individuals with ACLR to stabilise their knee during demanding functional activities such as single leg landing tasks (Bryant *et al.*, 2009b). By activating lower limb muscles, particularly the quadriceps and hamstrings, prior to initial ground contact, individuals following ACLR increase the musculotendinous stiffness within their limb; thus, protecting their knee joint and ACL graft from injury (Bryant *et al.*, 2008b; Bryant *et al.*, 2009b; Swanik *et al.*, 2004).

In contrast, reactive muscle activity occurs after initial ground contact (Vairo *et al.*, 2008). Reactive muscle activity may be more difficult to assess in single leg landing tasks using surface EMG, due to the artefact that is produced by the impact of ground contact and movement of overlying skin (Fagenbaum & Darling, 2003). Furthermore, the functional relevance of reactive muscle activity after ACL injury and ACLR is less clear (Bryant *et al.*, 2009b; Swanik *et al.*, 1999; Swanik *et al.*, 2004). Reactive muscle activity may occur too slowly to protect the knee joint during high-demand functional tasks (Bryant *et al.*, 2009b). The increased electromechanical delay of the hamstrings, observed after ACLR with a hamstring graft, may contribute to this inefficiency (Ristanis *et al.*, 2011). Hence, this literature review focuses on the association between preparatory, rather than reactive muscle activation strategies.

Despite the potential relationship between preparatory muscle activation and knee flexion angles after ACLR, few previous studies have directly investigated these associations. Gokeler *et al.* (2010) assessed the timing of lower limb muscles in a group of nine recreational athletes, six months following ACLR. In this investigation, significantly earlier onset times were observed for the ACLR limb compared to the uninvolved limb for all muscles, except vastus medialis ( $p = 0.10$ ). Kinematic variables were also assessed, including knee flexion excursion (see Table 2.8). However, the small sample size precluded investigation of the association between preparatory muscle activation and knee flexion excursion. Likewise, Nyland *et al.* (2010) and Vairo *et al.* (2008) conducted concurrent assessments of kinematics and preparatory muscle activation strategies, but did not analyse the relationship between these variables.

The relationship between preparatory muscle activation and knee flexion excursion may be influenced by differences in body-weight normalised strength (Krishnan & Williams, 2011; Otzel *et al.*, 2014). However, this association has not been investigated in an ACLR population. Shultz *et al.* (2009) used multivariate regression analyses to investigate whether quadriceps and hamstring strength and the magnitude of quadriceps and hamstring preparatory activation predicted knee flexion excursion in a group of 78 uninjured individuals. In this investigation, thigh muscle activation and body-weight normalised strength values were poor predictors of knee flexion excursion. However, individuals following ACLR demonstrate significantly smaller knee flexion excursion than uninjured control subjects (see Table 2.8). Hence, these multivariate associations may be worthy of investigation in an ACLR population.

## **2.5 Associations between neuromuscular control and knee joint function following ACLR**

Laboratory-based assessments of neuromuscular control may help to explain the variability observed in clinically-assessed knee joint function (Hewett *et al.*, 2013). Knowledge of the associations between neuromuscular control and knee joint function following ACLR is important because neuromuscular control is modifiable and is a major focus of rehabilitation programs (Hartigan *et al.*, 2012; Lentz *et al.*, 2009). Greater understanding of the functional relevance of these variables may inform the development of more effective rehabilitation following ACLR (Hartigan *et al.*, 2012).

In the first section of this literature review, knee functional outcomes after ACLR were found to be variable and associated with a range of participant characteristics. These participant characteristics may, in turn, influence the association between neuromuscular control and knee joint function. However, these associations cannot be accounted for when considering only bivariate relationships (e.g. univariate logistic regression; (Logerstedt *et al.*, 2012a) or correlations between continuous variables (Risberg *et al.*, 1999c; Xergia *et al.*, 2014).

Multivariate regression analyses provide a method for evaluating the cross-sectional associations between a dependent variable and multiple predictor variables (Harrell, 2001). This approach facilitates better understanding of the complex relationship

between sports participation, participant characteristics and knee joint function (Lentz *et al.*, 2009). Studies using multivariate regression analyses require larger samples of participants than studies that using bivariate analyses in order to achieve acceptable levels of statistical power (Mason & Perreault Jr, 1991). Furthermore, the assessment of neuromuscular control in laboratory settings is time consuming (Myer *et al.*, 2011a) which makes it difficult to recruit the numbers of participants needed to conduct multivariate analyses.

Lentz *et al.* (2009) used linear regression to determine neuromuscular and non-neuromuscular predictors of IKDC score after ACLR in a group of 58 patients with mixed graft types. In this study, lower pain intensity, more symmetrical isokinetic quadriceps strength, less knee flexion range of motion deficit and lower fear of movement (Tampa Scale for Kinesiophobia) were associated with better self-reported knee function and knee joint effusion was associated with asymmetrical hop for distance performance at 12 months following ACLR.

Although Lentz *et al.* (2009) included a range of demographic, neuromuscular (quadriceps strength) and psychological factors (fear of movement) in their analysis, they excluded individuals with greater than grade I chondral injuries. Individuals with lower levels of sports participation (Tegner score < 5) were also excluded. The exclusion of these individuals may mean that the findings of this study cannot be generalized to these groups of patients.

However, the study by Lentz *et al.* (2009) was notable because it included measures of impairment, psychological factors and neuromuscular factors (quadriceps strength) as candidate predictors of both self-reported knee function and functional performance (hop for distance LSI). Similar analyses are needed to determine whether quadriceps force control deficits (see Table 2.7) and the neuromuscular adaptations observed during landing tasks (see Tables 2.8 and 2.9) are associated with knee function. These analyses are needed because neuromuscular adaptations are commonly targeted in rehabilitation programs (Hartigan *et al.*, 2009; Myer *et al.*, 2008; Risberg *et al.*, 2007), yet the relationship between these impairments and knee function is still unclear.

Amongst ACLD patients, greater variability of quadriceps force production during maximal contractions has been associated with deficits in single leg hop performance in multivariate analyses (Pua *et al.*, 2014). However, to the author's knowledge, no previous studies have investigated the multivariate associations between sub-maximal quadriceps force control impairments and knee joint function after ACLR. Likewise, to the author's knowledge, no previous study has assessed the relationship between biomechanical and/or neuromuscular adaptations in single leg landing tasks and knee joint function. Biomechanical and neuromuscular variables assessed during walking can differentiate people who pass or fail batteries of knee function tests six months after ACLR (Di Stasi *et al.*, 2013). However similar analyses have not been conducted using multivariate analyses and variables derived from single leg landing and hopping tasks, or at later post-operative time points, e.g. greater than 12 months.

Following ACLR, in order to stabilise the knee during demanding functional activities, some individuals rely on a greater magnitude of hamstrings and quadriceps muscle coactivation (Tsai *et al.*, 2012). Greater hamstring coactivation may offer some crude protection for the knee joint from episodes of instability during functional tasks (Rudolph *et al.*, 1998). However excessive hamstring coactivation may also increase knee joint loading (Bryant *et al.*, 2010; Palmieri-Smith *et al.*, 2009; Tsai *et al.*, 2012), and be associated with less-effective responses to external perturbations (Madhavan & Shields, 2011) and lower levels of self-reported knee function (Lustosa *et al.*, 2011).

In addition to altered muscle activation strategies, individuals following ACLR also demonstrate kinematic and kinetic adaptations in single leg landing tasks, such as smaller knee flexion excursion, greater peak trunk flexion angles and smaller peak knee extensor moments (see Table 2.9). In a prospective study with a multivariate analysis, Hartigan *et al.* (2012) demonstrated that pre-operative quadriceps weakness (LSI) and reduced knee extensor moments in walking predicted whether individuals would pass or fail a battery of knee function tests. However, such analyses have not been performed using more demanding tasks to assess neuromuscular control following ACLR. Analysis of single leg landing tasks may elucidate biomechanical adaptations that may be less-apparent during lower intensity tasks such as walking.

## 2.6 Summary

This review of the literature provides evidence that 1) knee functional outcomes after ACLR are variable and 2) participant characteristics such as age, sex, BMI, concomitant chondral and/or meniscal injuries and anterior knee joint laxity may help to explain this variability and potentially predict knee functional outcomes in clinical settings. The level of sports participation, having returned to the pre-injury level of sport and the psychological response to returning to sport may influence the association between knee joint function and participant characteristics. Collectively, these variables may influence the relationship between knee function and neuromuscular control.

Previous investigations have provided important foundational knowledge about the neuromuscular adaptations that exist following ACLR. However, the majority of previous studies have been limited by their use of small and homogenous samples of participants, who may or may not be representative of the wider ACLR population. Furthermore, few studies have reported the reliability and/or standard error of measurement of variables. Given the variability in these variables within ACLR groups (see Tables 2.7–2.9), knowledge of the reliability and measurement error of each variable is essential in the interpretation of the size of group differences.

Neuromuscular control assessed in the open kinetic chain and in functional single leg landing tasks continues to be impaired after ACLR, despite the restoration of mechanical knee joint stability. Impairments are observed regardless of whether the uninvolved side or a matched control group is used for comparison. The aim of ACLR rehabilitation is to improve strength, neuromuscular control and movement patterns in order to optimise knee joint function and facilitate a safe and successful return to sport (Hartigan *et al.*, 2009; Myer *et al.*, 2008; Risberg *et al.*, 2007). Hence, greater knowledge of the associations between neuromuscular adaptations and knee joint function after ACLR will inform the development of more effective rehabilitation programs that take into account sports participation and individual patient characteristics.

Multivariate statistical analyses and larger, more representative samples of ACLR participants are needed to understand these associations and the patient sub-groups for



whom these associations are most relevant. However, few studies have directly investigated the associations between neuromuscular control and knee function after ACLR. Therefore the overall aim of the research presented within the proceeding chapters of this thesis is to determine the strength of the associations between biomechanical and neuromuscular variables derived from open and closed kinetic chain testing and knee function following ACLR.

## ***Chapter 3***

### **Study 1**

#### **Knee joint function after anterior cruciate ligament reconstruction: Association with sports participation and participant characteristics**

### **3.1 Chapter Overview**

The study reported in this chapter utilised self-reported and functional performance measures to determine the functional limitations of a group of ACLR and matched control participants. A test battery was developed that summarised self-reported knee function and functional performance. The associations between knee joint function (pass vs fail), sports participation and participant characteristics were then investigated.

### **3.2 Introduction**

Following anterior cruciate ligament reconstruction (ACLR), many individuals do not achieve the level of knee function needed to safely return to their pre-injury level of sport, particularly if the sport involves pivoting or landing (Myer *et al.*, 2012; Thomeé *et al.*, 2012). Knee functional limitations after ACLR are associated with changes in lifestyle and physical activity habits which can impact significantly on an individual's quality of life and overall health (Chmielewski *et al.*, 2011; Dunn *et al.*, 2010; Kvist *et al.*, 2005; Spindler *et al.*, 2011). Therefore, a comprehensive analysis of the factors associated with knee function after ACLR is warranted.

To quantify knee function after ACLR, and take into account patient perspectives, testing routines typically include self-reported and physical performance measures of knee function (see Section 2.2) (Abrams *et al.*, 2014; Thomeé *et al.*, 2012; Trulsson *et al.*, 2010; Xergia & Pappas, 2013). A range of questionnaires have been developed to assess self-reported knee function (see Section 2.2.3). Of these questionnaires, the Cincinnati Knee Rating Scale (CKRS) has been used most frequently in studies using

biomechanical evaluations (Bryant *et al.*, 2009a; Bryant *et al.*, 2009b; McNair *et al.*, 1992; Risberg *et al.*, 1999c; Risberg *et al.*, 2007). The CKRS has been found to have good content, construct and item-discriminant validity and have minimal ceiling and floor effects (Barber-Westin *et al.*, 1999).

Evaluation of functional performance after ACLR typically includes sports-specific tests such as jumping (Delahunt *et al.*, 2012c), sidestepping (Miranda *et al.*, 2013) and single leg hop tests (Gustavsson *et al.*, 2006) measured quantitatively (e.g. distance or number of jumps/hops) and expressed relative to the uninjured side (Narducci *et al.*, 2011), i.e. a limb symmetry index (LSI). Recently, in an attempt to develop more-sensitive measures of knee function, a number of authors have chosen to combine self-reported questionnaires and functional performance tests in a test battery (Di Stasi *et al.*, 2013; Fitzgerald *et al.*, 2000; Hartigan *et al.*, 2012). This approach may be useful clinically, when determining readiness for return to sport (Barber-Westin & Noyes, 2011b) and in research, when exploring the multivariate relationships between knee joint function and groups of predictor variables (see Sections 2.2.3 and 2.2.4).

Numerous investigations have explored the relationships between knee joint function and participant characteristics following ACLR (see Section 2.2.6). However few studies have accounted for sports participation and the psychological response to returning to sport in their analyses. Furthermore, few studies have quantified knee joint function using both self-reported knee function questionnaires and functional performance tests. Greater understanding of the relationship between knee joint function, sports participation and participant characteristics will help identify sub-groups of individuals following ACLR who may require further or more specialized rehabilitation.

### **3.3 Aims**

Based on this rationale, the current literature (see Sections 2.2 and 2.3) and the overall aims of the study, the specific aims of the research reported in this chapter were to:

1. Compare the self-reported knee function and functional performance of ACLR and control participants

2. Develop a battery of knee functional assessments and use this test battery to compare the knee function (pass vs fail) of ACLR (n = 66) and control (n = 41) participants
3. In the ACLR group, determine the cross-sectional associations between knee joint function (i.e., the dichotomous pass/fail variable) and sports participation (level of sport, whether participants have returned to their pre-injury level of sport, and the psychological impact of returning to sport)
4. In the ACLR group, determine the cross-sectional associations between knee function (pass vs fail) and participant characteristics (age, sex, BMI, chondral injury or meniscal surgery at the time of ACLR and anterior knee joint laxity)

### **3.4 Hypotheses**

Based on the current literature (cited below and summarised in Sections 2.2 and 2.3) the following hypotheses were proposed:

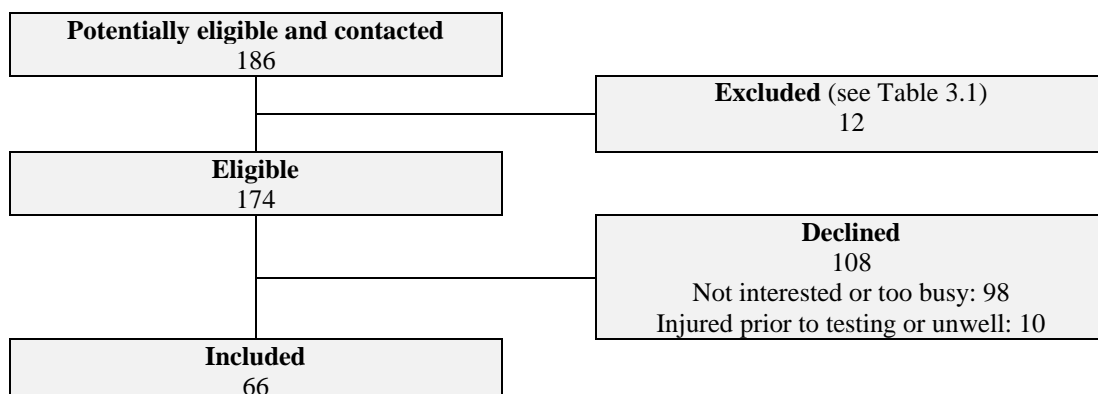
1. Compared to healthy control participants, ACLR participants would demonstrate significantly lower self-reported knee function (Bryant *et al.*, 2009a) and significantly impaired functional performance (Gustavsson *et al.*, 2006)
2. Compared to healthy control participants, a significantly greater proportion of ACLR participants would fail a battery of knee functional tests (Hartigan *et al.*, 2010; Thomeé *et al.*, 2012)
3. In the ACLR group, the following variables would be significantly associated with failing a battery of knee functional tests:
  - a) Lack of level I or II sports participation (Spindler *et al.*, 2011)
  - b) Not having returned to the pre-injury level of sports participation at the time of testing (Ardern *et al.*, 2011b; Lentz *et al.*, 2012)
  - c) A greater psychological response to returning to sport (Ardern *et al.*, 2011b)
4. In the ACLR group, the following variables would be significantly associated with worse knee joint function, (i.e., greater odds of failing a battery of four knee functional assessments):
  - a) Older age at the time of testing (Hartigan *et al.*, 2012)

- b) Female sex (Ageberg *et al.*, 2010)
- c) Higher BMI (Kowalchuk *et al.*, 2009)
- d) Grade III or IV chondral injury at the time of ACLR, determined by Outerbridge grade III or IV (Cox *et al.*, 2014; Røtterud *et al.*, 2013)
- e) Meniscal injury or surgery (e.g. debridement, repair, partial meniscectomy) at the time of ACLR (Cox *et al.*, 2014)
- f) Greater anterior knee joint laxity (Risberg *et al.*, 1999c)

### 3.5 Methods

#### 3.5.1 Participants

A group of ACLR participants (n = 66) were recruited through two Melbourne-based orthopaedic surgeons who specialise in ACLR surgery. The ACLR group were an average of 18 months post-surgery and a median of three months from injury to surgery. Patients fulfilling the eligibility criteria (Table 1) were contacted by letter inviting them to participate in the study. A plain language statement was included with the letter. After two weeks, patients were contacted by phone and invited to attend an initial screening session to confirm their eligibility. A group of healthy, recreationally-active men and women (n = 41) with no history of knee injury and no other abnormalities affecting their function were recruited as control participants. Control participants were recruited from the university and local sporting clubs using convenience sampling. The recruitment process for ACLR participants is summarised in Figure 3.1.



**Figure 3.1.** The process of recruitment of ACLR participants

The control group were matched to the ACLR group for their level of physical activity, level of sporting participation and the proportion of men and women. Patients and control participants who fulfilled the eligibility criteria and provided informed written consent were invited to attend a separate testing session in the movement laboratory at the Centre for Health, Exercise and Sports Medicine (CHESM) at the University of Melbourne. Ethical approval for the study was provided by the University of Melbourne’s Behavioural and Social Sciences Human Ethics sub-committee (ethics ID 1136167, see Appendix 1). Eligibility criteria for the study are presented in Table 3.1

**Table 3.1.** Eligibility criteria for ACLR and control groups

	<b>Inclusion criteria</b>	<b>Exclusion criteria</b>
ACLR group	Age: 18-50 years Ability to understand English Unilateral ACLR with an ipsilateral semitendinosus/gracilis auto-graft, 12-24 months prior to date of testing Successful ACLR as determined by clinical examination by orthopaedic surgeon, i.e. stable knee with trace or no effusion (Reid <i>et al.</i> , 2007) Recreationally active, i.e. regularly participating in sport at least 50 hours a year (Hefti <i>et al.</i> , 1993)	Revision ACLR Knee surgery since ACL reconstruction History of injury or surgery in contralateral knee Grade III collateral ligament, PCL injury or fracture at the time of ACL injury Clinical instability: Positive pivot shift test (Kocher <i>et al.</i> , 2004) or symptoms of knee instability (e.g. clicking, catching) during activities of daily living, hopping, jumping or plyometric activity (Grindem, 2011) Musculoskeletal, cardiovascular or neurological conditions influencing walking, sports activity or daily function
Control group	Age: 18-50 years Ability to understand English Recreationally active, i.e. regularly participating in sport at least 50 hours a year (Hefti <i>et al.</i> , 1993)	History of injury or surgery in either knee Pain or other symptoms during activities of daily living, hopping, jumping or plyometric activity (Grindem, 2011) Musculoskeletal, cardiovascular or neurological conditions influencing walking, sports activity or daily function

### 3.5.2 Sample size

The number of participants recruited was based on measuring clinically-significant differences in functional performance between the ACLR and control groups (Aim 1). Gustavsson *et al.* (2005) reported a 22% difference in side hop performance between ACLR and control participants (effect size 0.63). With 80% power and an alpha level of

5%, at least 41 participants per group were required to detect at least a 22% difference in this variable (Faul, 2007).

The maximum number of predictor variables in the logistic regression analysis was determined using the formula  $N = 10 k / p$ , where  $N$  = the number of ACLR participants to be recruited,  $k$  = the number of predictor variables and  $p$  = the smallest of the proportions of positive (pass) or negative (fail) cases (Peduzzi *et al.*, 1996). Using this formula, a sample of 60 ACLR participants was required to provide sufficient power to include three predictor variables in a multivariate regression model (see Section 3.5.8). To account for the potential inability of some ACLR participants with compromised knee function to perform the more demanding functional tasks, an additional six ACLR participants (10% of sample) were recruited, bringing the final number of ACLR participants to 66. This ensured that a minimum of 60 ACLR participants completed all assessments.

### **3.5.3 Surgical procedure and rehabilitation protocol**

All participants had a primary arthroscopic ACLR performed by one of two experienced orthopaedic surgeons at least 12 months and no more than 24 months prior to the date of the testing session. A 12-24 month window was used because knee functional outcomes and neuromuscular control changes significantly from the early perioperative period to 24 months following ACLR (Hopper *et al.*, 2008; Risberg *et al.*, 1999c; Thomeé *et al.*, 2012; Zaffagnini *et al.*, 2014). A four-strand hamstring and gracilis tendon (STGT) autograft was harvested from the involved (ipsilateral) limb. A transtibial tunnel drilling technique (Rahr-Wagner *et al.*, 2013) was used and tunnels were located on the anatomical footprint of the native ACL. An EndoButton (Acufex, Smith & Nephew, Andover, MA) was used for fixation of the graft to the lateral femoral condyle and an absorbable interference screw (RCI, Smith & Nephew) was used for tibial fixation. The graft was tensioned with the knee in full extension.

Although rehabilitation was not standardised, all participants were encouraged to follow a similar post-operative protocol, including early weight-bearing and quadriceps activation and range of motion exercises. Participants were referred to physiotherapy for

ongoing rehabilitation of range of motion, muscle strength and sports-specific rehabilitation.

#### **3.5.4 Overview of experimental protocol**

All data were collected within a single testing session in the CHESM movement laboratory at the University of Melbourne by the same researcher. Pilot testing was conducted with 15 healthy volunteers to ensure data were collected in a rigorous and standardised manner (see Appendix 2). Prior to physical testing, participants completed questionnaires in a separate room (see Section 3.5.5). Participants were instructed to take their time and answer each question as honestly and accurately as possible (Bent *et al.*, 2009).

Following completion of the questionnaires, participants were interviewed to confirm their understanding of each question and to assess for any inconsistencies or missing data (Noyes *et al.*, 1989). Participants were instructed to avoid heavy or unaccustomed exercise for three days prior to the testing session (e.g. heavy weight training, plyometrics or unaccustomed running) so that the results of physical testing were not adversely influenced by the effects of neuromuscular fatigue (Boham, 2008; Coventry *et al.*, 2006).

#### **3.5.5 Self-reported measures**

##### *Participant characteristics*

Demographic variables for ACLR and control groups were collected using a questionnaire. There was no significant difference in the proportion of women and men between the ACLR and control groups ( $p = 0.82$ ). Despite efforts to match the groups for demographic and anthropometric characteristics, the ACLR group were an average of 2.6 years older ( $p = 0.03$ ) and had an average BMI that was  $1.3 \text{ kg/m}^2$  higher than control participants ( $p = 0.03$ ; see Table 3.2). Furthermore, significantly more control participants were tested on their dominant leg ( $p = 0.02$ , see Section 3.5.6). Hence, age at the time of testing, BMI and limb dominance were included as candidate predictors of knee joint function (see Section 3.6.4).



Physical activity level was assessed using the Tegner Activity Scale, an ordinal self-reported scale that rates the ability to perform physical activities from zero to 10 (Tegner & Lysholm, 1985). A score of 10 indicates participation in elite (national level) sport and a score of zero indicates sick leave or disability pension because of knee problems. Levels 5-10 correspond to participation in competitive sport at recreational or elite level. The Tegner Activity Scale has acceptable reliability and validity following ACL injury and ACLR (Briggs *et al.*, 2006). There was no significant difference in Tegner Activity Scale scores between the ACLR and control groups ( $p = 0.88$ ; see Table 3.2).

Level of sports participation was assessed within the demographics questionnaire. Participants were asked '*What competitive sport are you currently participating in (over the past month)?*'. Based on their response to this question, participants were categorized as 1) currently participating in level I and II sports (involving any type of jumping, sidestepping and pivoting; see Section 2.2.3)  $\geq 50$  hours per year, or 2) not currently participating in level I and II sports (Hefti *et al.*, 1993; Moksnes & Risberg, 2009). Forty-six (69%) of the ACLR group were involved in level I or II sports (i.e., sports involving any type of jumping, sidestepping and pivoting) at the time of testing. These participants were involved in football codes ( $n = 15$ ), basketball ( $n = 12$ ), netball ( $n = 4$ ), snow sports ( $n = 3$ ), martial arts ( $n = 3$ ), tennis ( $n = 3$ ), gymnastics ( $n = 3$ ) and field hockey ( $n = 3$ ). There was no significant difference in the proportion of participants involved in Level I or II sports at the time of testing between the ACLR and control groups ( $p = 0.87$ ; see Table 3.2).

The mechanism of ACL injury (contact or non-contact) was determined by asking ACLR participants the question '*At the exact time of your injury was another player/person involved?* Forty-three (66%) ACLR participants had a non-contact ACL injury mechanism. The ACLR group were also asked '*Since your surgery, have you returned to a level of sporting activity that was the same as before (yes or no?)*'. This question sought to determine whether participants had returned to their pre-injury level of sports participation. Only 30% of the ACLR group reported having returned to their pre-injury level of sport at the time of testing (see Table 3.2).

### *Pain during testing*

Pain during or after hopping, jumping or plyometric activity was an exclusion criterion for the study; therefore, it was not anticipated that participants would report pain during testing. However, pain has been shown to influence functional assessments, particularly self-reported function (Eccleston & Crombez, 1999; Lentz *et al.*, 2009; Reiman & Manske, 2011). Therefore, it was considered important to assess the severity and intensity of any pain that occurred during testing. The presence of pain was assessed subjectively after the completion of each functional performance test. Participants were asked whether they experienced any knee pain (yes or no). If a participant answered yes, they were asked to record the pain intensity on a 100 millimetre visual analogue scale from 0 (no pain) to 100 (extreme pain).

### *Menstrual cycle and monophasic oral contraceptive pill use*

A questionnaire was used to assess current menstrual status and monophasic oral contraceptive pill (MOCP) use in both the ACLR and control groups (see Appendix 3). Fluctuations in estrogen through the normal menstrual cycle may influence anterior knee joint laxity (Deie *et al.*, 2002) and musclotendinous stiffness, particularly in the ovulatory and mid-luteal phases, corresponding to weeks three and four of the menstrual cycle (Bryant *et al.*, 2011; Eiling *et al.*, 2007). Use of the MOCP (e.g. Organon, Femodene) results in more stable estrogen levels through the menstrual cycle, similar to those seen in days 1-14 of the cycle (Cammarata & Dhaher, 2008). For this reason it is important to establish whether female participants have a normal menstrual cycle, the point of their cycle at the time of testing and whether they currently use the MOCP. There was no significant difference between the ACLR and control groups in the proportion of women who were taking the MOCP at the time of testing ( $p = 0.61$ ).

### *The psychological response to returning to sport (ACLR group only)*

The psychological response to returning to sport was assessed using the Anterior Cruciate Ligament Return to Sport after Injury Scale (ACL-RSI; Webster *et al.*, 2008). This 12-item scale assesses confidence, emotions, risk appraisal and fear of re-injury associated with sport (see Appendix 4). An example of a question is ‘*Are you confident that you could play your sport without concern for your knee?*’. Each

question is completed by placing a mark on a 100 millimetre visual analogue scale which ranges from 'extremely' to 'not at all'. The scores out of 100 for the 12 items are averaged to calculate an overall score. Higher scores (closer to 100) represent a more positive psychological response to returning to sport. The ACL-RSI has been shown to have good reliability (Chronbach's alpha = 0.92) and can differentiate people who have or have not returned to their previous level of sports participation (Webster *et al.*, 2008). The mean ACL-RSI score in the ACLR group was 57 (100 represents a more positive psychological response to sports participation after ACLR).

#### *Assessment of self-reported knee function*

The Cincinnati Knee Rating Scale (CKRS) was used to evaluate self-reported knee function (Noyes *et al.*, 1991). The CKRS is an ACL-specific, self-administered questionnaire that has acceptable reliability, good content/construct validity and item-discriminant validity (Barber-Westin *et al.*, 1999; Wang *et al.*, 2010). The CKRS includes three sub-scales that evaluate activity limitations related to symptoms, activities of daily living (ADLs) and sport (see Appendix 5). The scores of the three sub-scales were summed and converted to a percentage.

### **3.5.6 Objective measures**

#### *Physical characteristics*

Body weight (kilograms), height (metres) and leg length (greater trochanter to floor) were recorded at the start of the physical testing. Body mass index ( $\text{kg/m}^2$ ) was calculated using the formula body weight in kilograms divided by height in metres squared (Spicer *et al.*, 2001). Limb dominance was defined by asking participants 'Which leg would you kick a football with?' (Brown *et al.*, 2009). Participants were then asked to confirm their answer by demonstrating a kicking action (Greenberger & Paterno, 1995). This method of determining limb dominance is the most widely used in the literature and was chosen to allow comparison to other investigations to be made. Other methods of determining the dominant limb include the limb with the largest horizontal hop distance (van der Harst *et al.*, 2007) and the preferred leg for a single leg landing (Wang *et al.*, 2012). As the definition of the dominant limb was to be used throughout Studies 1-4, which included measurements of horizontal hop distance (Study

1) and landing biomechanics (Study 3), these definitions of limb dominance may have biased the findings and were therefore not used.

For functional performance testing, the right limb of the control group was defined as the involved limb and compared to the involved (reconstructed) limb of the ACLR group. The same definition of the involved limb was used throughout Studies 1-4. The right limb was used in Studies 2 and 3 for streamlining of data collection because of the large volume of data collected and the technically-demanding nature of the testing session. It was anticipated that the majority of control participants would be right leg dominant, according to the definition of their preferred leg for kicking (Petschnig, 1998). Previous investigations using the same definition of limb dominance have found no significant differences between the dominant and non-dominant limbs of ACLR (Petschnig, 1998) and control participants (Greenberger & Paterno, 1995) in functional performance tests. However, to account for the possible influence of limb dominance on functional performance, additional analyses were performed (see Section 3.6.1).

#### *Clinical impairments and surgical findings (ACLR group)*

Anterior displacement of the tibia on the femur was recorded for both knees using the KT-1000 arthrometer (MEDmetric Corp., SanDiego, California). With the participant supine and the knee positioned in 30 degrees of knee flexion 30 pounds of anteriorly-directed force was applied and the inter-limb difference was calculated in millimetres (Neeb *et al.*, 1997). The KT-1000 arthrometer is a valid and reliable method of quantifying knee joint laxity after ACLR, with ICCs reported in the literature ranging from 0.91 to 0.97 (Brosky Jr *et al.*, 1999; Robnett *et al.*, 1995).

KT-1000 side-to-side difference greater than 3mm is commonly used to define ACL rupture or as exclusion criteria for ACLR participants (Barenius *et al.*, 2013; Bjornaraa, 2011; Grindem, 2011; Xergia & Pappas, 2013). However, considering that some individuals following ACLR have good knee function despite greater than 3mm side-to-side differences in knee laxity (Ageberg *et al.*, 2005; Lentz *et al.*, 2009; Moksnes & Risberg, 2009), knee laxity was not an exclusion criterion for this study, and was instead included as a candidate predictor of knee function in the regression analysis (see Section 3.5.8). The average side-to-side difference in anterior knee laxity for all ACLR

participants was 2.3 mm (SD = 2.4 mm, range -1.9 to 6.1 mm). Within the ACLR group there were no significant differences in anterior knee joint laxity between female participants who were or were not taking the MOCP.

An audit of surgical records was performed during the initial screening session. The location, number and grade of any chondral injuries were noted. Chondral injuries were graded according to the Outerbridge classification system as grade I - softening and fibrillation, Grade II - superficial changes, grade III - deep changes and no exposed bone or grade IV - exposed bone (Borchers *et al.*, 2011). The intra-rater and inter-rater reliability of the Outerbridge classification system have been found to be moderate to good, with Kappa coefficients of 0.52 and 0.80 respectively (Cameron *et al.*, 2003).

Seven participants (11%) had grade III or IV chondral injuries; one participant had grade III femoral trochlear and medial femoral condyle defects, two participants had grade III medial femoral condyle defects, one participant had a grade III lateral femoral condyle defect, one participant had grade III lateral femoral and grade III tibial plateau defects, one participant had a grade IV lateral femoral condyle defect and one participant had a grade IV medial femoral condyle defect.

Any additional surgical procedures were recorded (e.g. meniscal repair, partial meniscectomy or chondral repair). Any meniscal injuries that were stable and therefore not repaired were noted. Twenty-one (32%) participants had meniscal injuries that required meniscectomy or repair at the time of ACLR. Nine of these participants had surgery to both menisci. A further 12 participants had minor meniscal injuries but did not receive surgical intervention. Ten partial meniscectomies (medial = 6, lateral = 4) and 11 meniscal repairs (medial = 9, lateral = 2) were performed. Participant characteristics for ACLR and control groups are presented in Table 3.2.

**Table 3.2** Participant characteristics of ACLR and control groups, with between-group differences (95% confidence intervals) and statistical comparisons

Continuous variables	ACLR (n = 66)		Control (n =41)		Difference (95% CI)	p value
	Mean	SD	Mean	SD		
Age at testing (years) †	28.4	6.2	25.8	5.3	2.6 (0.2 to 4.9)	0.03 *
Height (metres)	1.75	0.1	1.74	0.08	0.02 (-0.02 to 0.05)	0.39
Weight (kilograms)	78.1	14.7	72.5	11.1	5.6 (0.6 to 10.6)	0.03 *
BMI (kg/m <sup>2</sup> ) †	25.3	3.3	24.0	2.6	1.3 (0.1 to 2.5)	0.03 *
Tegner Activity Scale (/10)	5.9	1.8	6.0	2.0	0.1 (-0.8 to 0.7)	0.88
Time since surgery (months)	18	3	-	-	-	-
Time from injury to surgery (months) †	3	4	-	-	-	-
Anterior knee joint laxity (millimetres)	2.3	2.4	-	-	-	-
ACL-RSI (/100)	57	18	-	-	-	-
Categorical (binary data)	n	%	n	%		
Sex (female)	23	35	16	39	4% (-20% to 10%)	0.82
MOCP use	16	70	11	69	1% (-27% to 31%)	0.61
Tested on dominant limb	32	48	30	73	25% (5% to 42%)	0.02*
Level I or II sports at time of testing	46	69	28	68	2% (-16% to 20%)	0.87
Level I or II sports prior to injury	66	100	-	-	-	-
Returned to pre-injury level of sport	20	30	-	-	-	-
Grade III or IV chondral injury	6	9	-	-	-	-
Partial menisectomy or meniscal repair at the time of ACLR (either meniscus)	21	32	-	-	-	-

Difference in means with standard deviation (SD) for continuous data, difference in proportions for categorical data, CI = 95% confidence interval;

† Median (interquartile range), age and BMI compared with independent samples Mann-Whitney U tests

Chi-square ( $\chi^2$ ) tests were used to compare categorical variables

MOCP = monophasic oral contraceptive pill; BMI = body mass index, n = number of participants; SD = standard deviation

ACL-RSI = Anterior cruciate ligament return to sport after injury scale (Webster *et al.*, 2008). ACL-RSI data (n= 66) are derived from the pooling of five imputations of the dataset;

\*  $p < 0.05$

### *Functional performance measures*

Three single leg hop tests were used to assess functional performance; the hop for distance, triple crossover hop for distance (crossover hop) and the side hop test (Gustavsson *et al.*, 2006; Trulsson *et al.*, 2010). The tests were selected based on their reliability and their potential to assess various aspects of neuromuscular control and physical performance, such as muscular strength, power, dynamic balance and knee-related confidence (Ardern *et al.*, 2011b; Bryant *et al.*, 2008a; Morrissey *et al.*, 2004; Reid *et al.*, 2007).

Previous authors have recommended the use of four single leg hop tests, to increase the sensitivity in detecting knee functional limitations (Di Stasi *et al.*, 2013; Hartigan *et al.*, 2010; Hartigan *et al.*, 2012). However, due to the length of the testing session and the risk of participant fatigue, three hop tests were used. A sensitivity of 0.91 has been reported for a similar battery of three hop tests in a group of patients six months after ACLR (Gustavsson *et al.*, 2006).

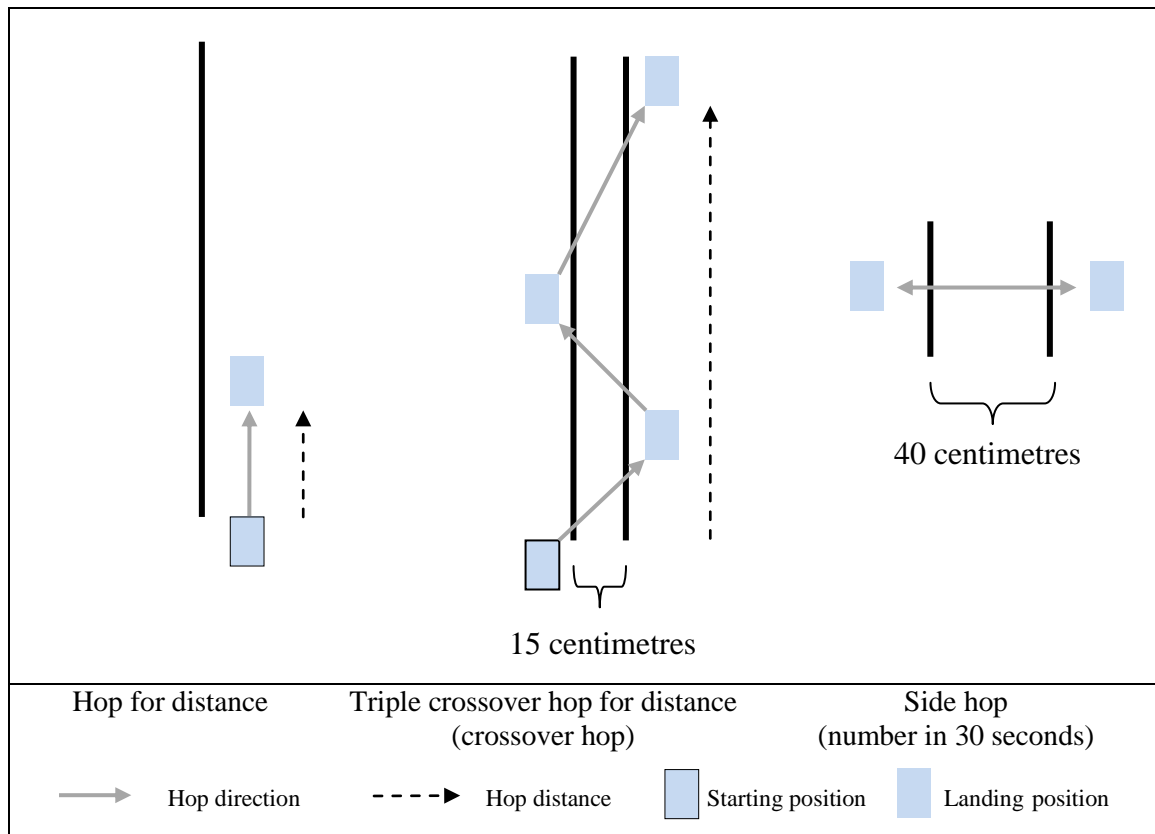
The hop tests were performed in the same order as listed above and were preceded by a standardised warm up involving squats, toe raises and jumps (Augustsson *et al.*, 2004). Participants wore their own athletic shoes and were instructed to keep their hands behind their back throughout the tests (Gustavsson *et al.*, 2006). The uninvolved limb of ACLR participants and left limb of control participants was tested first. Strong standardised verbal encouragement was provided during the testing to ensure a maximum effort was given (Gustavsson *et al.*, 2006). A descriptive of the three hop tests and the rationale for their use follows:

- (a) *Hop for distance* (Kramer *et al.*, 1992): Participants were instructed to stand on one leg with their toes behind a line of white tape. After performing three warm-up trials at a sub-maximal intensity, participants were asked to hop as far forward as they could, land on the same leg and maintain balance for three seconds. Extra hops or use of the contralateral leg after landing was not allowed. Countermovement and free swing of the contralateral limb were allowed. The distance hopped was measured to the nearest centimetre using a tape measure fixed to the floor. The distance was recorded for all attempts and the best of three attempts was used for the

analysis. If the third attempt was the largest (i.e. participants were improving), additional attempts were performed until no improvement was made. A maximum of eight hops were allowed on each limb to ensure the maximum distance was achieved and up to thirty seconds rest was provided between each hop to minimise the effect of fatigue on performance (Reid *et al.*, 2007).

- (b) *Triple crossover hop for distance (crossover hop; Noyes et al., 1991)*: Two parallel lines were marked on the ground with white tape 15 centimetres apart, perpendicular to the start line. Participants were instructed to stand behind the start line on their involved leg. Up to three practice trials were performed. The test involved three sequential countermovement hops with each hop crossing both parallel lines. The testing procedure was otherwise identical to the hop for distance. For a trial to be successful participants had to balance for three seconds after landing the third hop without any extra hops or using their arms or contralateral limb.
- (c) *Side hop (Gustavsson et al., 2006)*: Two parallel lines were marked on the ground 40cm apart and participants stood on one leg with the lateral border of their foot beside one of the lines. Participants hopped from side-to-side over both pieces of tape as many times as possible in 30 seconds. If any part of the foot touched the tape or the contralateral foot made contact with the ground an error was recorded by the examiner, but the test was allowed to continue. The number of successful hops was recorded and the number of errors was subtracted from the final score for that limb. At least three minutes rest was provided between limbs to reduce the influence of fatigue on performance of the task. The side hop task was selected because it demands muscular endurance and significant control over valgus and varus knee loads (Ortiz *et al.*, 2011). The three hop tests are summarised in Figure 3.2.





**Figure 3.2** Single leg hop tests: Maximum distance (hop for distance and triple crossover hop for distance (crossover hop) tests) measured in centimetres and maximum number of side hops in 30 seconds (side hop test)

### 3.5.7 Data analysis

#### *Participant characteristics*

Based on their response to the question ‘*Since your surgery, have you returned to a level of sporting activity that was the same as before (yes or no?)*’, ACLR participants were classified as 1) having returned to their pre-injury level of sport, or 2) not returned to the pre-injury level of sport (Ardern *et al.*, 2011b). Considering the large number of variables it was not possible to include multiple variables to describe the MOCP and menstrual cycle data. Hence, participants were classified as either currently using the MOCP or not using the MOCP (Clark *et al.*, 2010; Eiling *et al.*, 2007).

Chondral injuries and meniscal injuries requiring surgery were considered binary variables. Chondral injuries were categorised as grades 1-2, or grades 3-4 according to

the Outerbridge classification (Borchers *et al.*, 2011). Participants with more than one cartilage lesion were grouped according to the largest lesion (Røtterud *et al.*, 2013). Participants who had surgical intervention to either meniscus during ACLR (e.g. meniscal debridement, partial meniscectomy or meniscal repair) were classified as having meniscal surgery.

#### *Self-reported knee function*

The points from each of the symptoms, ADL and sports sub-scales of the CKRS were summed and converted to a percentage that represented overall self-reported knee function (Barber-Westin *et al.*, 1999). A score of 100% represented a normal knee with no functional limitations. The individual sub-scale scores and scores of the individual CKRS questions were also reported to determine the components of self-reported function that were most limited (see Appendix 7).

#### *Functional performance*

A limb symmetry index (LSI) was calculated for each of the three hop tests. For the maximum hop tests (hop for distance and crossover hop), the distance hopped on the involved limb was divided by the distance hopped on the contralateral limb and the result multiplied by 100 to calculate a percentage (Noyes *et al.*, 1991). For the side hop, the number of successful hops on the involved limb were divided by the number of successful hops on the contralateral side and multiplied by 100 (Gustavsson *et al.*, 2006). In addition to calculating a LSI, hop distance (in centimetres) standardised to participant's height (in metres) and the number of side hops were reported (Gustavsson *et al.*, 2006; Hopper *et al.*, 2008). The standardised hop distance and number of side hops were included as a measure of absolute performance on each limb.

#### *Overall knee function*

The CKRS percentage scores and LSIs for the three hop tests were combined to calculate an overall measure of knee joint function (pass vs fail). Participants were dichotomised according to whether they achieved at least 85% for the CKRS and at least 85% LSI for all three hop tests (Ardern *et al.*, 2011b; Noyes *et al.*, 1991; Wilk, 1994). The use of 85% as the cut-off score is consistent with that of previous

investigations; using similar groups of ACLR participants (see Section 2.2.3). The cut-off of 85% LSI on the hop tests also exceeds the minimal detectable change (MDC, 90% confidence level) for the hop for distance (8.09%) and crossover hop tests (12.25%) at the individual level after ACLR (Reid *et al.*, 2007).

Previous authors who have used functional test batteries to assess readiness for return to sport have recommended including two self-reported knee function questionnaires (Di Stasi *et al.*, 2013; Hartigan *et al.*, 2010; Hartigan *et al.*, 2012). Based on the literature, the CKRS and IKDC were deemed to be the most appropriate questionnaires for this study (see Section 2.2.3). However, the IKDC and CKRS have been found to be highly correlated after ACLR ( $r = 0.88$  to  $0.95$ ,  $p < 0.01$ ); hence, only the CKRS was included in this study and in the functional test battery.

### **3.5.8 Statistical analyses**

#### *ACLR and control group comparisons*

Normality and equality of variance were assessed with Shapiro-Wilk and Levene Median tests respectively. Histograms were inspected for normality and skewness. Means, standard deviations and ranges were calculated for normally distributed continuous variables. Normally distributed data were compared using two-tailed independent t-tests and confidence intervals (CI) were provided for the difference in means (Portney & Watkins, 2008). Frequencies with percentages were used to describe categorical variables.

The CKRS scores in the ACLR group and the LSIs of the three hop tests in both groups were positively skewed; hence, the median, range and IQR were reported and data were compared using Mann-Whitney U tests. The ninety-five percent confidence interval (CI) of the difference in median was also calculated (Petrie, 2006). Box and whisker plots were used to demonstrate the range of hop test scores within both groups. Chi-square ( $\chi^2$ ) analyses were used to compare the proportion of participants who passed or failed the functional test battery, the proportion of men and women, participants tested on their dominant and non-dominant limbs, participants competing in level I or II and level III or IV sports and female participants who were and were not using the MOCP within the ACLR and control groups.

Bivariate correlations of the three hop test LSIs and CKRS scores were calculated to determine the suitability of combining these functional assessments into a binary score (Gustavsson *et al.*, 2006). Firstly, the linearity of each correlation was assessed with scattergraphs. Secondly, Pearson product moment correlation coefficients were used to assess the strength of associations (Mason & Perreault Jr, 1991; Osborne & Waters, 2002). The strength of relationships was categorised as very strong when  $r > 0.75$ , strong when  $r = 0.75$  to  $0.51$ , moderate when  $r = 0.50$  to  $0.25$  and weak/no relationship when  $r < 0.25$  (Portney & Watkins, 2008).

#### *Predictors of knee joint function (pass vs fail) in the ACLR group*

Binary logistic regression analysis was used to determine predictors of overall knee joint function (i.e., whether ACLR participants scored less than 85% on either the CKRS or any one of the three hop tests). Based on the literature review reported in Chapter 2 (see Section 2.3), the following variables were candidate predictors of knee function in the multivariate model:

- a) Sports participation (Aim 3): Current participation in level I or II sport (binary variable), having returned to the pre-injury level of sport at the time of testing (binary variable), the psychological response to returning to sport (ACL-RSI; continuous variable)
- b) Participant characteristics (Aim 4): Age at the time of testing (in whole years), sex, BMI, limb dominance (binary variable), grade III or IV chondral injury at time of ACLR (binary variable), meniscal surgery at the time of ACLR i.e. partial meniscectomy or meniscal repair (binary variable) and anterior knee joint laxity (continuous variable).

#### *Bivariate relationships between candidate predictor variables*

The linearity and strength of the bivariate correlations between continuous predictor variables were assessed with scattergraphs and Pearson product moment correlation coefficients (Mason & Perreault Jr, 1991; Osborne & Waters, 2002). For bivariate relationships that involved binary variables, odds ratios with 95% CIs were calculated. Predictor variables were deemed to be significantly related if the 95% CI of the odds ratio did not include one, or  $p < 0.05$  (Grimmer *et al.*, 2000). When continuous predictor

variables were highly correlated ( $r > 0.75$ ), or when relationships between binary and/or continuous predictor variables were statistically significant, subject matter expertise and the clinimetric properties of variables (including clinical utility) were used to determine which variable was excluded from the analysis (Harrell, 2001). The presence of outliers was assessed with box plots and scattergraphs to help interpret the effect of these scores on the regression analysis; however, no outlying scores were removed (Osborne & Waters, 2002).

#### *Bivariate relationships between candidate predictors and knee joint function.*

The selection of predictor variables for the regression model was determined by a combination of subject matter expertise, previous literature, the clinimetric properties of variables and consideration of the strength and statistical significance of relationships between each variable and knee function (Harrell, 2001). As knee joint function was a binary variable (pass vs fail), odds ratios were calculated between knee function and each candidate predictor variable. A maximum of three predictor variables were included in the model according to the power calculation outlined in Section 3.5.2.

#### *Missing data*

In the ACLR group, ACL-RSI data were missing for four (6%) of the 66 participants. The four participants failed to complete the questionnaire within the testing session and did not return the questionnaire when contacted. Missing data may result in a reduction in statistical power and a subsequent decrease of the precision of estimates (Sterne *et al.*, 2009). Rather than exclude these participants from the analysis and incur a loss of power and precision, multiple imputation was used to impute the missing questionnaire data (Schafer & Graham, 2002).

Multiple imputation is a form of regression analysis that uses all available data to predict missing values, based on multiple iterations of the dataset (Schafer, 1999). Loss of data in predictor variables does not introduce bias to regression analyses if the data are missing completely at random (Rubin, 1976). Hence, this assumption was tested using Little's Chi-square ( $\chi^2$ ) statistic (Little, 1988). After confirming that data were indeed missing completely at random, five imputations of the dataset were performed with 100 iterations (Allison, 2000; Schafer, 1999). CKRS scores and hop LSIs were

included in the imputation model, as standard errors and regression coefficients may be biased by omitting outcome variables from multiple imputation models (Moons *et al.*, 2006).

#### *Logistic regression analysis*

A maximum of three predictor variables identified from the bivariate analyses were entered into a binary logistic regression model. The Nagelkerke  $R^2$  value was calculated to estimate the amount of variation in knee joint function that was explained by the predictor variables (Heijne *et al.*, 2009). To further evaluate the discriminative accuracy of the regression model, the area under the receiver operator curve (AUC) value was calculated. The AUC is a measure of goodness of fit based on the simultaneous measurement of sensitivity and specificity for all possible cut-off points (Hanley & McNeil, 1982).

Odds ratios with 95% confidence intervals were calculated for the three predictor variables to determine the odds of failing the functional test battery (i.e. scoring < 85% on one or more functional measures). Odds ratios were scaled by their respective IQR ( $OR^{IQR}$ ); hence, the interpretation of the odds ratio was the average difference in the dependent variable (log odds) between the 25<sup>th</sup> and 75<sup>th</sup> percentile of the predictor variable (Harrell, 2001).

#### *Evaluation of logistic regression model*

The linearity, homoscedasticity and normality of the standardised residuals of the model were assessed using scattergraphs, normal probability plots and histograms (Osborne & Waters, 2002). Tolerance and variance inflation factors were calculated to assess the model for multicollinearity (Mason & Perreault Jr, 1991; O'Brien, 2007). An *a priori* alpha level of 0.05 was used to determine statistical significance. All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 21.0 (Armonk, NY: IBM Corp).

## 3.6 Results

### 3.6.1 Self-reported knee function

The median CKRS score for the ACLR group (88.6%) was significantly lower than that of the control group (100%;  $p < 0.001$ ). The sports sub-scale revealed the greatest self-reported functional limitations in the ACLR group (22% deficit,  $p < 0.001$ ). Analysis of the individual items within the sports sub-scale revealed that 65% of the ACLR group reported knee limitations or guarding related to hard twists, cuts and pivots and that the average score for hard twisting/cutting/pivoting was 30% lower than that of controls (see Appendix 7).

The ADL sub-scale scores for the ACLR group (walking, squatting, kneeling and negotiating stairs) were 17% lower than that of healthy controls (18% difference,  $p < 0.001$ ). Of those four activities, stair negotiation was the most limited; 50% of participants reported some limitations or guarding with ascending or descending stairs (see Appendix 7). Of the three CKRS sub-scales, the symptoms sub-scale revealed the least limitations (10% difference, 95% CI 5.5 to 14.5%). A significant proportion (47%) of the ACLR group reported having knee pain with strenuous work or sports ( $p < 0.001$ ; see Appendix 7). The median CKRS % scores and sub-scale scores are presented in Table 3.3.

**Table 3.3** The self-reported knee function (Cincinnati Knee Rating Scale and sub-scale scores) of ACLR and control participants including between-group differences in medians and 95% confidence intervals

Knee function measures	ACLR (n = 66)			Control (n = 41)	Difference (95% CI)	p value*
	Median	IQR	Range	Median		
CKRS (%)	88.6	14.3	42.9 -100.0	100	11 (9 to 14)	< 0.001*
Symptoms sub-scale (/20)	18	4	6 - 20	20	10 (6 to 15)	< 0.001*
ADL sub-scale (/6)	5	1	4 - 6	6	17 (8 to 25)	< 0.001*
Sports sub-scale (/9)	7	2	2 - 9	9	22 (17 to 27)	< 0.001*

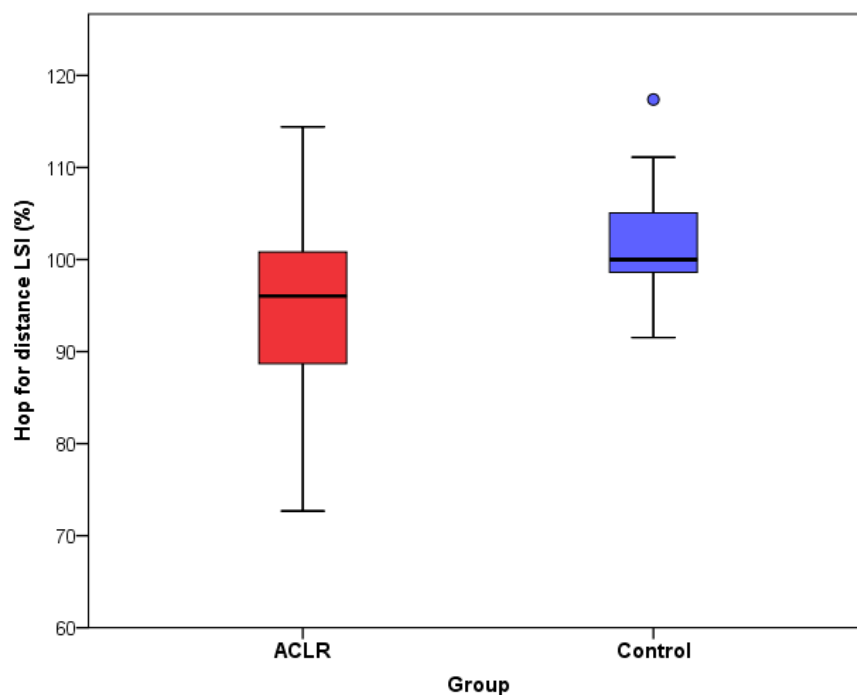
CKRS = Cincinnati Knee Rating Scale; ADL = activities of daily living; IQR = interquartile range; CI = confidence interval; median and interquartile range (IQR); difference in medians with 95% confidence interval (CI); \*  $p < 0.01$  (independent samples Mann-Whitney U test); ranges were 0 for the control group; percentage differences are provided for sub-scales.

### 3.6.2 Functional performance

The three hop tests revealed significant limitations in functional performance within the ACLR group and considerable variability in both the absolute performance on the involved limb and the ratio of performance compared to the uninvolved side.

#### *Hop for distance*

When hop distance was standardised to height, the ACLR group hopped 9.9 cm (14%) less than the control group on their involved limb (95% CI 4.3 to 15.5cm;  $p < 0.01$ ). Although the median LSI for the hop for distance test in the ACLR group was 96%, compared to 100% in the control group, the IQR (12.4%) and range (72.7% to 114.4%) indicate considerable variability in LSI within the ACLR group. Indeed, 12 ACLR participants (18%) scored less than 85% LSI on this test. The median and range of LSI scores for the hop for distance test are presented in Figure 3.3.

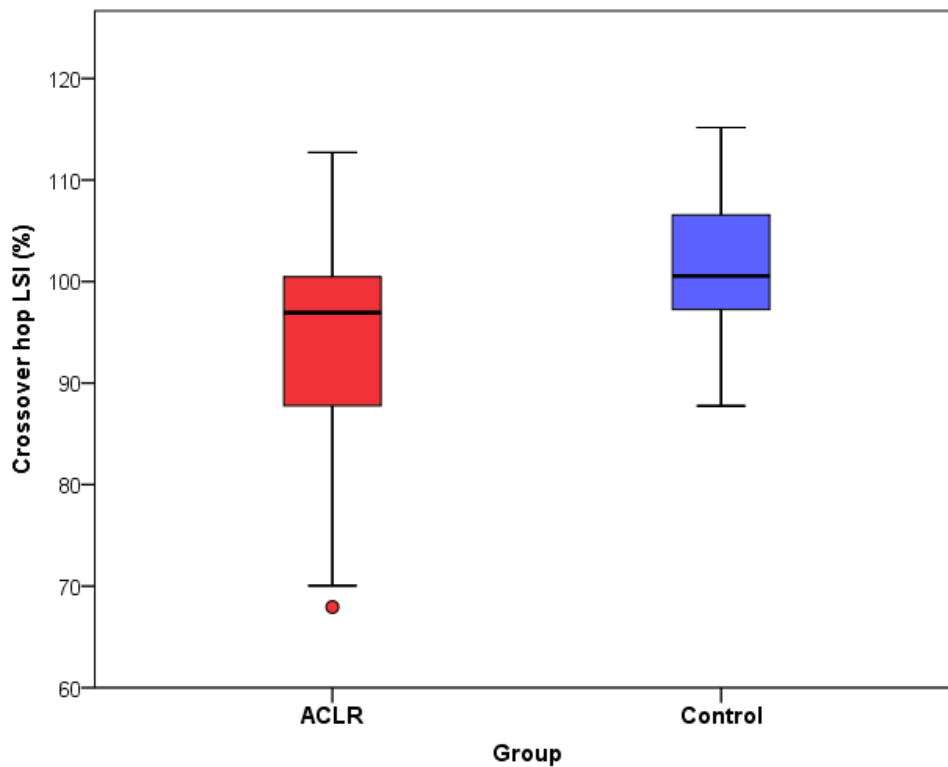


**Figure 3.3** Box and whisker plot of the hop for distance limb symmetry index (LSI) of the ACLR and control groups. The thick central line represents the median LSI, the upper and lower limits of each box represent the 75<sup>th</sup> and 25<sup>th</sup> percentiles, the upper and lower limits of each whisker represent the maximum and minimum scores respectively. An outlying score in the control group is represented as a circle.



### Crossover hop test

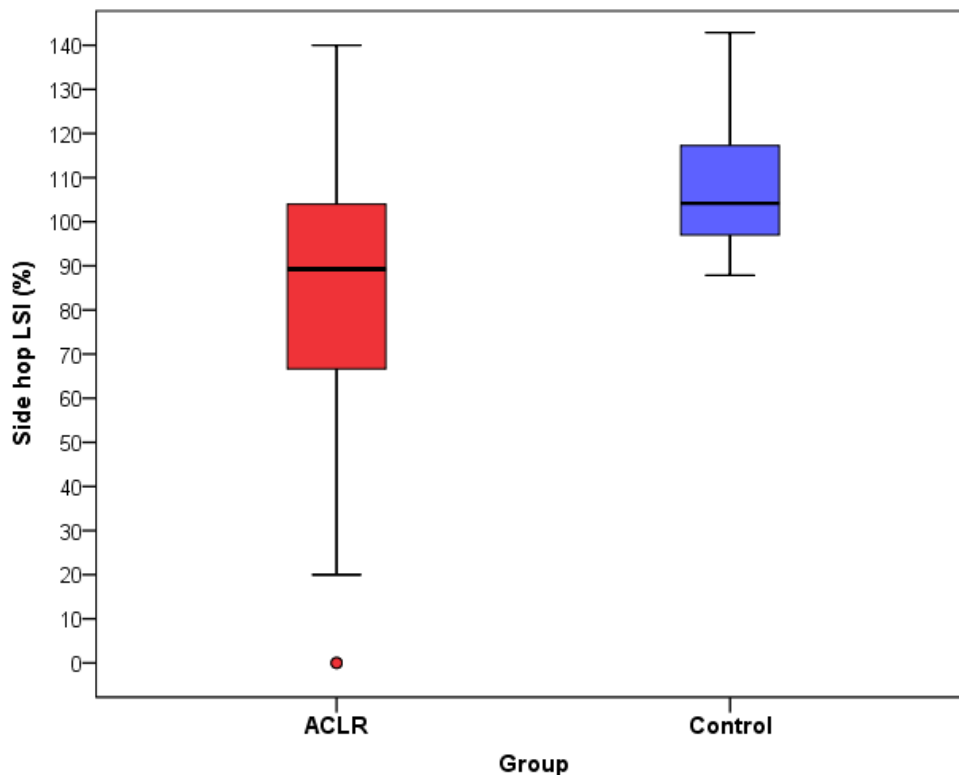
A similar pattern was found for the crossover hop test. Although the median LSI for the hop for distance test was 96.9% in the ACLR group, 13 ACLR participants (20%) scored less than 85% LSI. When hop distance was standardised to height, the ACLR group hopped 15.0cm (7%) less than the control group on their involved limb (95% CI - 5.1 to 35.0); however, this difference was not statistically significant ( $p = 0.14$ ). The median and range of LSI scores for the crossover hop test are presented in Figure 3.4.



**Figure 3.4** Box and whisker plot of the crossover hop (triple crossover hop for distance) limb symmetry index (LSI) of the ACLR and control groups. The thick central line represents the median LSI, the upper and lower limits of each box represent the 75<sup>th</sup> and 25<sup>th</sup> percentiles, the upper and lower limits of each whisker represent the maximum and minimum scores respectively. An outlying score in the ACLR group is represented as a circle.

### Side hop test

The side hop had the lowest median LSI of the three hop tests (89.3%) and had the greatest variability of performance within the ACLR group (IQR 38%, range 0.0 to 140.0%). However, only two ACLR participants scored the minimal possible score of 0% LSI. Both participants were unable to perform the side hop test on their involved limb, due to a lack of confidence rather than pain. The range of side hops performed on the involved limb was similar for the ACLR (range 0 to 65) and control group (range 10-66); however, the ACLR group performed an average of seven fewer hops on their involved limb than the control group ( $p = 0.02$ ) and 25 ACLR participants (38%) scored less than 85% LSI. The median and range of LSI scores for the side hop test are presented in Figure 3.5.



**Figure 3.5** Box and whisker plot of the side hop limb symmetry index (LSI) of the ACLR and control groups. The thick central line represents the median LSI, the upper and lower limits of each box represent the 75<sup>th</sup> and 25<sup>th</sup> percentiles, the upper and lower limits of each whisker represent the maximum and minimum scores respectively. Two outlying scores in the ACLR group are represented as a single circle (0% LSI)

*Overall knee joint function*

A significantly greater proportion of ACLR participants failed the functional test battery compared to healthy control participants ( $p < 0.01$ ). Thirty-three ACLR participants scored below 85% on at least one of the measures (see Table 3.4). Twenty-one of the 33 ACLR participants failed more than one test; ten participants (30%) failed two tests, six participants (18%) failed three tests and five participants (16%) failed all four tests. The side hop test had the lowest pass rate of the four measures; only 41 ACLR participants (62%) achieved a LSI of 85% or more.

**Table 3.4** Number and proportion of ACLR and healthy control participants who scored less than 85% on the Cincinnati Knee Rating Scale (self-reported function) and the three hop tests and the proportion who failed the test battery.

Group	Self-reported function < 85%	Hop for distance LSI < 85%	Crossover hop LSI < 85%	Side hop LSI < 85%	Failed the test battery
ACLR	20 (30%)	12 (18%)	13 (20%)	25 (38%)	33 (50%)
Control	0	0	0	0	0
<i>p</i> value *	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

\* Chi-square ( $\chi^2$ ) analyses

The bivariate correlations between the LSIs and self-reported knee function scores are presented in Table 3.5. Moderate to strong relationships were observed between the hop tests; whereas, only moderate relationships were observed between self-reported knee function and the functional performance tests ( $r = 0.30$  to  $r = 0.38$ ).

**Table 3.5** Bivariate relationships between limb symmetry indices (LSIs) of hop tests and self-reported knee function scores (Cincinnati Knee Rating Scale) in the ACLR group. Values are Pearson product moment correlation coefficients

Variable	Hop for distance LSI	Crossover hop LSI	Side hop LSI
Crossover hop LSI	0.72**	-	-
Side hop LSI	0.60**	0.65**	-
Self-reported function	0.30*	0.38**	0.30**

Self-reported function = Cincinnati Knee Rating Scale percentage score; LSI = limb symmetry index  
 Values are Pearson product moment correlation coefficients; \*\*  $p < 0.01$

### 3.6.3 Predictors of knee joint function in the ACLR group (pass vs fail)

#### *Bivariate relationships between candidate predictor variables*

Significant positive relationships were found between age at the time of testing and grade III or IV chondral injury ( $p = 0.01$ ) and between sex and BMI ( $p = 0.03$ ). A significant positive relationship was also observed between level I or II sports participation and having returned to the pre-injury level of sport at the time of testing ( $p = 0.03$ ). Despite these significant relationships, it was considered important to evaluate the relationships between these variables and knee function prior to excluding either of these variables. No significant bivariate relationships were found between other candidate predictor variables.

#### *Bivariate relationships between candidate predictors and knee joint function.*

A significant relationship was found between knee joint function (pass vs fail) and anterior knee joint laxity ( $p = 0.005$ ); hence, anterior knee laxity was included in the logistic regression model. No significant relationships were found between knee function and sex ( $p = 0.18$ ), limb dominance ( $p = 0.60$ ), level I or II sports participation ( $p = 0.29$ ), having returned to the pre-injury level of sports participation at the time of testing ( $p = 0.59$ ), ACL-RSI ( $p = 0.31$ ), grade III or IV chondral injury ( $p = 0.40$ ) or meniscal surgery at the time of ACLR ( $p = 0.79$ ). Hence, these variables were not included in the regression model.

The relationship between age at the time of testing and knee function trended towards significance ( $p = 0.06$ ). As grade III or IV chondral injury was significantly associated with age at the time of testing, and a relatively small proportion of ACLR participants had grade III or IV chondral injuries ( $n = 7$ , 11%), age at the time of testing was included and grade III or IV chondral injury was not included in the model.

Body mass index was not significantly associated with knee function ( $p = 0.35$ ). However, higher BMI has previously been associated with lower levels of knee function (Kowalchuk *et al.*, 2009; Spindler *et al.*, 2011), is modifiable, and is associated with a greater risk of knee osteoarthritis (Øiestad *et al.*, 2011). Hence, irrespective of statistical

significance and based on subject-matter knowledge and previous literature, BMI was the final variable included in the regression model.

### *Predictors of knee joint function in the ACLR group*

Anterior knee joint laxity, age at the time of testing and BMI explained 33% of the variance in knee function (Nagelkerke  $R^2 = 0.33$ ;  $p < 0.05$ , AUC = 0.78;  $p < 0.001$ ). Anterior knee joint laxity was inversely associated with knee function. An interquartile increase in anterior knee joint laxity (3.3 mm) was associated with 5.5 times greater odds of failing the knee function test battery (95% CI 1.93 to 15.85). Likewise, older age at the time of testing (IQR OR 2.4) and greater BMI (IQR OR 2.1) were significantly associated with greater odds of failing. The interquartile-scaled odds ratios and  $p$  values for anterior knee joint laxity, age at the time of testing and BMI are summarised in Table 3.6.

**Table 3.6.** Predictors of failing the battery of knee functional tests in the ACLR group, with interquartile range odds ratios and  $p$  values (logistic regression model). The model was powered to include a maximum of three predictor variables.

<b>Predictor variables</b>	<b>Median of variable (25<sup>th</sup> and 75<sup>th</sup> percentiles)</b>	<b>Odds ratio (95% CI)</b>	<b><math>p</math> value</b>
Age at time of testing (years)	27.1 (23.8, 32.0)	2.4 (1.1, 5.5)	0.04*
BMI (kg/m <sup>2</sup> )	24.9 (23.1, 26.8)	2.1 (1.0, 4.2)	0.045*
Anterior knee joint laxity (mm)	2.62 (0.7, 4.0)	5.5 (1.9, 15.9)	0.002**

Odds ratios represent the odds of failing the battery of knee function tests (i.e. scoring < 85% on any one of the CKRS or three single leg hop tests). For continuous variables, odds ratios represent the difference in odds of failing for individuals at the 75<sup>th</sup> and the 25<sup>th</sup> percentile of the predictor variable. For example, participants at the 75<sup>th</sup> percentile of age (32.0 years) would have 2.4 times greater odds of failing than participants at the 25<sup>th</sup> percentile of age (23.8 years)

BMI = body mass index (kg/m<sup>2</sup>); anterior knee joint laxity = KT-1000 side-to-side difference in mm.

\*  $p < 0.05$ ; \*\*  $p < 0.01$

### *Evaluation of regression model*

Tolerance and variance inflation factors were within acceptable limits indicating that collinearity between variables was acceptable (Mason & Perreault Jr, 1991; O'Brien, 2007). Standardised residuals demonstrated normality, linearity and homoscedasticity and models were deemed to be valid in terms of these assumptions (Osborne et al. 2002). Little's  $\chi^2$  test confirmed that the four missing ACL-RSI data were missing

completely at random ( $p = 0.82$ ); satisfying this assumption of multiple imputation. However, ACL-RSI score was not included in the logistic regression model; hence, sensitivity analyses were not necessary and were not performed (Little, 1988).

## **3.7 Discussion**

### **3.7.1 Overview**

The main findings of this study were that 1) ACLR participants continued to demonstrate significant limitations in self-reported knee function and functional performance at an average of 18 months following surgery and 2) greater anterior knee joint laxity, older age and higher BMI were significant predictors of failing a battery of knee functional tests. This study has added new knowledge to the field of ACLR research by quantifying the strength of the associations between knee joint function and both sports participation and participant characteristics. The findings of this study will also inform the development and interpretation of studies 2-4 of this thesis. A detailed discussion of the findings of the study follows.

### **3.7.2 ACLR and control group comparisons**

#### *Self-reported knee function*

In support of hypothesis 1, ACLR participants demonstrated significantly worse CKRS scores than control participants, indicative of greater self-reported activity limitations. The median CKRS score of the ACLR group (88.6%) is within the range of CKRS scores reported in previous investigations that have involved similar groups of individuals, at similar time-points following ACLR (see Section 2.2.3). However the range (42.9 to 100%) and IQR (14.3) of the CKRS in the ACLR group indicates that a considerable number of ACLR participants scored below the level (85%) that is considered acceptable in the literature (Ardern *et al.*, 2011b; Hopper *et al.*, 2008; Lustosa *et al.*) and below the level recommended prior to return to any level of sport (Fitzgerald *et al.*, 2001; Logerstedt *et al.*, 2012a; Thomeé *et al.*, 2011). Indeed, 20 ACLR participants, or 30% of the group scored below 85% on the CKRS. Although the minimal detectable change of the CKRS is not known (Agel & LaPrade, 2009), CKRS

scores below 85% are commonly described indicative of poor knee function in the literature (see Section 2.2.4).

Collectively, the findings of this study, and those of previous investigations (see Section 2.2.3), demonstrate that self-reported knee function after ACLR is variable. The median CKRS score (88.6%) in this study is comparable to the weighted average of the CKRS reported in the literature (88.9%; see Section 2.2.3). Given that the goal of ACLR is to allow patients to return to their pre-injury level of knee function, and considering that all participants were participating in either recreational or competitive sport at the time of testing, including contact sports, and the group were an average of 18 months post ACLR, a median CKRS score of 88.6% could be considered low.

#### *Functional performance*

Supporting hypothesis 1, the ACLR group demonstrated significantly worse functional performance compared to the control group for all variables (LSI's and absolute performance on the involved limb), except for crossover hop distance. The lack of significant finding for this test may be attributed to the considerable variability in crossover hop distance within both groups (see Figure 3.4).

The median LSI's observed for the hop for distance test (96.0%, IQR 12.4%) and crossover hop test (96.9%, IQR 12.7%) are comparable to previously published data of similar groups of patients (see Section 2.2.3). At the group level, the performance of these hop tests is acceptable, being above the criterion for passing the battery of functional tests (85%) and above the minimum LSI of 90% that is commonly recommended for recreational athletes to achieve prior to returning to competitive sport (Di Stasi *et al.*, 2013; Gustavsson *et al.*, 2006; Logerstedt *et al.*, 2012b; Thomeé *et al.*, 2011). However, the IQRs of both the hop for distance test (12.4%) and the crossover hop test (12.7%) suggest that many ACLR participants scored well below these criteria.

The side hop was reported by participants to be the most demanding of the three hop tests. The median (89.3%) and IQR (38.0%) of the side hop LSI confirm that this test was challenging for some participants; whereas some participants scored greater than 100% LSI. Similar to the findings for the hop for distance and crossover hop tests, a large range of side hop LSIs were observed in the ACLR group (range 0 – 140%). In

contrast, no participant in the control group scored less than 85% for the side hop. The limb asymmetry revealed by this test may predispose some individuals with ACLR to injury if they are accompanied by neuromuscular asymmetries (Paterno *et al.*, 2010). Moreover, limb asymmetries during landing task are predictive of ACL graft or contralateral ACL rupture (Paterno *et al.*, 2010).

Gustavsson *et al.* (2006) reported a mean LSI of 72% for the side hop test amongst a group of 35 ACLR participants who were an average of 6 months post-surgery. In a group of 82 participants with similar characteristics to the current study, (Thoméé *et al.*, 2012) reported a LSI of 78% at 6 months and 89% at 12 months after ACLR. In a younger and more active group of participations (range 18-35 years, Tegner score range 5-9) who had participated in an accelerated rehabilitation program for at least four months, (Ageberg *et al.*, 2008) reported a LSI of 97% for the side hop test. The difference in LSI between these studies may be related not only to the time since ACLR, but to variability in the physical activity levels and experience in performing hopping tests of participants.

The variability observed within the ACLR group for the functional performance variables demonstrates an important limitation of the LSI; that is, the uninvolved limb may not be normal. Recent evidence suggests that individuals following ACLR have up to 15 times greater risk (risk ratio (RR) = 15.2;  $p = 0.0002$ ) of either ipsilateral *or* contralateral ACL injury than uninjured individuals (Paterno *et al.*, 2012). Hence, the contralateral leg may also demonstrate neuromuscular adaptations that not only increase the risk of contralateral ACL injury (Paterno *et al.*, 2010; Paterno *et al.*, 2014), but reduce the size of the asymmetry of the involved limb (Hewett *et al.*, 2013; Reid *et al.*, 2007).

Hop distance (standardised to the participant's height), and the number of side hops performed on the involved limb, were also reported in this study to provide a more complete understanding of functional performance limitations in the ACLR group (Gustavsson *et al.*, 2006). Although the uninvolved limb is the most convenient and valid comparison of functional performance for the individual (Reid *et al.*, 2007), it is possible that some participants may also demonstrate impairments on their uninvolved limb, for reasons unrelated to the ACLR or their neuromuscular system. For example,



differences in motivation, confidence and experience in performing hopping tasks may result in sub-optimal performance on the uninvolved limb, resulting in a normal LSI, despite impaired functional performance on the involved limb (Reid *et al.*, 2007). By reporting both absolute and relative measures of functional performance it was possible to determine whether there were differences in absolute hop performance between the groups.

The ACLR group demonstrated lower absolute hopping performance on two out of three tests compared to the control group; hop for distance (standardised to height) and the number of side hops performed on the involved limb were significantly lower for the ACLR group. These differences could be attributed to the larger proportion of control participants who were tested on their dominant limb; however, if this were the case, asymmetrical LSIs may also be expected in the control group. The LSIs for the control group ranged from 100 to 104%. This discussion highlights the inherent limitations in presenting functional performance data as either absolute data or as a LSI. Considering these limitations and the variability in the measures of knee function reported in this study, it may be possible to increase the sensitivity of individual knee function measures by reporting the proportion of individuals who meet criteria for successful knee function (Gustavsson *et al.*, 2006; Hartigan *et al.*, 2010).

#### *Overall knee joint function*

In support of hypothesis 2, a significantly greater proportion of ACLR participants failed the battery of functional tests compared to healthy control participants by scoring < 85% on one of the four functional measures. The side hop test had the lowest pass rate of the four measures with only 41 ACLR participants (62%) achieving a LSI of 85% or greater. These findings are concerning, given that side-to-side asymmetry in functional performance tests has been associated with knee osteoarthritis (Pinczewski *et al.*, 2007) and asymmetrical biomechanics may be associated with a greater risk of ACL graft re-injury or contralateral ACL injury (Paterno *et al.*, 2010).

The proportion of ACLR participants in this study who failed the battery of functional tests is surprising when the average time since surgery (18 months) is considered. Return to unrestricted sporting activity is typically recommended by 8-12 months and as

early as six months post-surgery (Kvist *et al.*, 2005). Considering that all control participants passed the test battery, the finding that 50% of the ACLR group failed at least one test and 32% of the ACLR group failed more than one test indicates that many ACLR participants had significant knee functional limitations. Although sensitivity and specificity were not calculated, these findings also indicate that the choice of 85% as a cut-off score for the test battery allowed the battery to be sensitive enough to detect functional limitations in the ACLR group and specific enough that no control participant was classified with unacceptable knee joint function (Gustavsson *et al.*, 2006; Holsgaard-Larsen *et al.*, 2014; Logerstedt *et al.*, 2012b).

Previous authors have proposed that achieving at least 90% LSI on a minimum of three single leg hop tests and two self-reported knee function measures is the minimum acceptable standard for athletes who wish to return to sport after ACLR (Di Stasi *et al.*, 2013; Fitzgerald *et al.*, 2001; Logerstedt *et al.*, 2012b). The cut-off of 85% to define passing or failing the test battery was chosen because it was anticipated that the functional level of the ACLR group would be relatively low compared to the levels reported in comparable studies (see Section 2.2.3). This concern was confirmed by the finding that only 41 (62%) of ACLR participants achieved 85% or more LSI on the side hop test and only 46 (70%) scored greater than 85% on the CKRS.

The relatively weak correlations found between self-reported knee function and hop LSIs ( $r = 0.30$  to  $r = 0.38$ ) provide further evidence that these variables assess different aspects of knee joint function, and neither can act as a proxy for the other (Neeb *et al.*, 1997; Reinke *et al.*, 2011). This finding also highlights a major limitation of combining self-reported and functional performance measures into a single continuous measure of function (see Section 2.2.4). Although some accuracy and statistical power is lost by creating a dichotomous measure (Altman & Royston, 2006), these methods allow individuals with clinically-important functional limitations in any one of the self-reported or functional performance tests to be identified, rather than this information being lost in an average score (de Jong *et al.*, 2007; Hopper *et al.*, 2008; Thomeé *et al.*, 2012).

### **3.7.3 Predictors of knee joint function in the ACLR group (pass vs fail)**

#### *Sports participation*

Contrary to hypotheses 3a, 3b and 3c, participation in level I or II sport, having returned to the pre-injury level of sport and the psychological response to returning to sport were not significantly associated with knee joint function. The finding that having returned to the pre-injury level of sport was not significantly associated with knee function is similar to the finding of (Ardern *et al.*, 2011b), who reported no difference in return to sport outcomes between competitive athletes with normal and abnormal self-reported function. However, in that study, athletes who scored < 85% hopping LSI were less likely to have returned to sport. In a multivariate analysis, (Lentz *et al.*, 2012) found a strong relationship between self-reported knee function (IKDC score) and return to sport status. Hence, it was hypothesized that having returned to the pre-injury level of sport would be associated with worse knee function in this study.

The differences in findings between these studies may be attributed to differences in the type of sport and level of competition that participants were aiming to return to. For example, participants who were attempting to return to contact sports may have responded differently to the questions than participants who were returning to level III or IV sports (Webster *et al.*, 2008). The quantity and quality of sports-specific training performed by participants may also be confounding variables. Individuals with ACLR who regularly perform hopping or landing activities as a part of their sport may be expected to demonstrate better functional performance than patients who do not regularly perform these activities. (Renstrom *et al.*, 2008).

It is important to acknowledge the individual circumstances and preferences of individuals with ACLR when considering return to sport outcomes and knee function (Mueller *et al.* 2014). For example, some individuals may have failed to return to the same level of sport because of reasons other than knee function, such as confidence, fear or social and/or work-related reasons. A recent investigation involving U.S. college football athletes found that athletes who were on scholarship returned to play at a significantly higher rate (88%), than those not on scholarships (69%; Daruwalla *et al.*, 2014).

Given the significant effort and financial burden that is associated with ACLR, some patients with ACLR who have good knee function may be satisfied with returning to a lower level of sport rather than risking sustaining another ACL injury (Feller & Webster, 2013). Conversely, other individuals with poor knee function may have returned to their pre-injury level of sport despite functional limitations. The lack of significant association observed between knee function and having returned to the pre-injury level of sport may also be related to variability in individual's perceptions of their progress following ACLR, the specific demands of their pre-injury sport and external factors such as expectations of sporting teams, parents or external funders (Daruwalla *et al.*, 2014).

The significant relationship that was found between level I or II sports participation and having returned to the pre-injury level of sport may be attributed to the fact that all ACLR participants were involved in level I or II sports at the time of ACLR. Both variables were included in the analysis because of the possibility that a participant could have participated in level III sport prior to ACL injury, and had successfully returned to this level of sport.

Although 69% of the ACLR group were participating in level I or II sports at the time of testing in this study, only 30% reported that they had returned to their pre-injury level of sport. This finding may appear contradictory, considering that all ACLR participants were involved in level I or II sport prior to ACL injury. This discrepancy is most likely related to the method of measurement of both variables. The level of sports participation of each participant was assigned based on their current sports participation. For example, those who played competitive basketball at the time of testing were categorised as being involved in level I sport. Having returned to the pre-injury level of sport at the time of testing was determined subjectively by the participant, based on their response to the question '*Since your surgery, have you returned to a level of sporting activity that was the same as before (yes or no?)*'. Hence, some participants may have returned to a level I or II sport at the time of testing, but were yet to participate at the same level or intensity as they were before their ACL injury. Considering that return to the pre-injury level of sport is the goal of many patients

following ACLR (Barber-Westin & Noyes, 2011a), a 30% rate of return to the pre-injury level of sport could be considered low.

The mean ACL-RSI score of 57 indicates that many participants had ongoing psychological responses related to the resumption of sport, including fearfulness, lack of confidence and thoughts of re-injury (Webster *et al.*, 2008). The average ACL-RSI score found in this study is lower than the scores reported in previous investigations with similar populations (Langford *et al.*, 2009; Webster *et al.*, 2008). (Webster *et al.*, 2008) reported that individuals who were yet to return to sport had significantly lower ACL-RSI scores. Hence, the relatively low ACL-RSI scores in this study may be related to the low proportion of participants who had returned to sport.

A more positive psychological response to the return to sport (higher ACL-RSI score) has previously been observed for individuals who have returned to competitive sport after ACLR (Ardern *et al.*, 2011b; Ardern *et al.*, 2012; Langford *et al.*, 2009). Furthermore, higher ACL-RSI scores have been found for individuals who demonstrated symmetrical hop tests (Ardern *et al.*, 2011b). However, to the author's knowledge, this is the first study to investigate whether ACL-RSI scores are significantly associated with a battery of functional tests after ACLR, using multivariate analyses. Despite the lack of a significant association found in this study, the potential relationship between knee-related confidence, knee function and return to sport outcomes is an emerging area of ACLR research and the findings of this study provide a foundation for ongoing research in this area (Ardern *et al.*, 2012; Chmielewski *et al.*, 2011).

#### *Participant characteristics*

Supporting hypothesis 4a, older age at the time of testing was associated with worse knee joint function (i.e., greater odds of scoring less than 85% on the CKRS or one or more hop test). Previous investigations investigating factors associated with knee function after ACLR have included age in regression models, but the size of the association has seldom been reported (see Section 2.3.2). Although the bivariate relationship between age at the time of testing and knee function was not significant, an interquartile increase in age (8.2 years) was associated with over twice the odds of

failing the functional test battery. Similar findings were reported by Hartigan *et al.* (2012), who used logistic regression to predict whether individuals passed or failed a functional test battery designed to assess readiness for return to sport after ACLR. In that investigation, a 10 year increase in age was associated with 11 times greater odds of failing the battery of knee functional tests. Collectively, this study and that of Hartigan *et al.* (2012) demonstrate that relatively small differences in age, i.e. less than 10 years, may be important for researchers and clinicians to consider when assessing knee function and interpreting knee functional assessments after ACLR.

Older age at the time of ACLR has been found to be associated with a range of non-neuromuscular factors that may negatively affect knee functional outcomes, such as a greater risk of meniscal and chondral injuries (Desai *et al.*, 2014; Takeda *et al.*, 2011; Tandogan *et al.*, 2004), post traumatic OA (Blagojevic *et al.*, 2010) and reduced physical activity levels (Dunn *et al.*, 2010). Older athletes experience longer healing times and greater muscle atrophy despite a similar quantity and quality of rehabilitation (Richardson *et al.*, 2006; Wondrasch *et al.*, 2013). Given that this study included individuals with grade III and IV chondral injuries, a history of meniscal injury and variable physical activity levels; it is also possible that the interaction of these variables contributed to the significant association between age and knee function (Desai *et al.*, 2014). Older patients following ACLR should therefore be counselled that it may take them longer to achieve similar knee functional outcomes to that of younger patients.

Contrary to hypothesis 4b, female sex was not significantly associated with worse knee function. This finding is consistent with those of a recent meta-analysis that found only small and clinically insignificant differences in self-reported knee function between male and female ACLR participants (Ryan *et al.*, 2014). Similarly, previous investigations have found no difference in absolute or relative measures of functional performance between men and women after ACLR (Gustavsson *et al.*, 2006; Noyes *et al.*, 1991). Conversely, other studies have found that women have lower levels of self-reported knee function after ACLR (Ageberg *et al.*, 2010; Ott *et al.*, 2003) and functional performance (Lindström *et al.*, 2013) after ACLR compared to men. Further analysis of these studies reveals that the differences in self-reported function between

the genders in these studies were relatively small and may not be clinically significant (see Section 2.3.2).

Although BMI was not associated with knee function in the bivariate analysis, it was included in the logistic regression model because 1) higher BMI has previously been associated with lower levels of knee function (Kowalchuk *et al.*, 2009; Spindler *et al.*, 2011), 2) BMI is modifiable and 3) higher BMI is associated with a greater risk of knee osteoarthritis (Øiestad *et al.*, 2011). Supporting hypothesis 4c, higher BMI was associated with worse knee joint function in the multivariate analysis. Individuals with ACLR who have a higher BMI and who participate in pivoting and landing sports may expose their knee to greater compressive forces than individuals with a lower BMI (Bowers *et al.*, 2005; Tsai *et al.*, 2012). Greater compressive forces may, in turn, be associated with greater pain-related limitations to functional performance during more demanding activities (Keays *et al.*, 2010).

Indeed, analysis of the individual items of the symptoms sub-scale of the CKRS revealed that a significant proportion (47%) of ACLR participants reported knee pain during strenuous activities such as pivoting and landing (see Appendix 7). Although it was not investigated in this study, the significantly higher BMI of the ACLR group may have contributed to this finding. Higher BMI after ACLR has been found to be associated with a greater risk of meniscal and chondral injury (Bowers *et al.*, 2005) which, in turn, may hasten the onset or progression of OA (Keays *et al.*, 2010; Takeda *et al.*, 2011). The implication of this finding is that higher BMI and the potential interaction between BMI and structural impairments should be considered routinely when assessing knee function and planning rehabilitation after ACLR.

Chondral injuries have previously been associated with worse self-reported function and worse functional performance in similar samples of individuals following ACLR (Cox *et al.*, 2014; Heijne *et al.*, 2009; Potter *et al.*, 2011; Røtterud *et al.*, 2013). However, contrary to hypothesis 4d, grade III or IV chondral injury at the time of ACLR was not significantly related to knee function in this study. The small number of participants in this study with grade III or IV chondral injuries (n = 7, 11%) may have contributed to this non-significant relationship (Harrell, 2001). Chondral injuries may be more strongly associated with knee functional outcomes in the longer term, i.e. greater than

18 months following ACLR (Potter *et al.*, 2011; Røtterud *et al.*, 2013; Shelbourne & Tinker, 2000).

Contrary to hypothesis 4e, meniscal surgery at the time of ACLR was not significantly associated with worse knee joint function. This finding is consistent with some previous studies (Inacio *et al.*, 2014; Røtterud *et al.*, 2013) and contrary to other studies (Cox *et al.*, 2014; Spindler *et al.*, 2011). The lack of significant relationship may be explained by the exclusion of individuals with symptoms of instability such as clicking or catching during functional tasks. These patients were excluded to ensure that all participants could safely complete the functional tests; however, the exclusion of these participants should be considered when interpreting this finding (Tengrootenhuysen *et al.*, 2010).

The lack of association between meniscal surgery at the time of ACLR and knee joint function in this study could be related to ongoing improvements in surgical techniques. As the menisci are important secondary stabilizers of the tibiofemoral joint (Shoemaker & Markolf, 1986), the preservation and stabilization of meniscal tissue is important for the structural stability of the knee joint (Georgoulis *et al.*, 2003). Current surgical practices which prioritize repair and preservation of meniscal tissue may therefore contribute to greater structural stability of the knee joint (Sofu *et al.*, 2014). Improved structural knee stability, combined with the average time since surgery of 18 months, may mean that patients with symptomatic or unstable meniscal pathology at the time of ACLR are able to function at a similar level to those without meniscal injuries (Keays *et al.*, 2010; Takeda *et al.*, 2011).

An important finding of this study was that anterior knee laxity was significantly associated with knee joint function in both bivariate multivariate analyses. This finding is contrary to a several previous investigations that have reported no significant relationship between anterior knee laxity and self-reported knee function (Eastlack, 1999; Kocher *et al.*, 2004; Snyder Mackler *et al.*, 1997). Of the three variables included in the logistic regression model, knee laxity was the strongest predictor of knee joint function (IQR OR 5.5). To the author's knowledge, this is the first study to report a significant and large association between anterior knee joint laxity and knee function after ACLR. The average knee laxity values of the ACLR group (2.3 mm, SD = 2.4 mm) were similar to those of previous ACLR studies that have included patients with



greater than 3 mm side-to-side difference (Kocher *et al.*, 2004; Lentz *et al.*, 2009; Lorbach *et al.*, 2011; Risberg *et al.*, 1999c).

The significant association between knee function and knee laxity may be attributed to the use of a battery of tests to assess knee joint function, rather than a single test. Moreover, the use of multiple measures of knee function may have been more sensitive in identifying individuals who demonstrate functional limitations following ACLR that were related to knee joint laxity (Gustavsson *et al.*, 2006; Thomeé *et al.*, 2012). The significant association could also be explained by the recruitment of individuals who had meniscal surgery and/or chondral injuries at the time of ACLR. These individuals are often excluded from studies that use functional performance tests to evaluate knee function (see Section 2.2.3). A combination of greater anterior knee joint laxity and meniscal and/or chondral pathology may compromise the structural integrity of the knee joint and be associated with both neuromuscular adaptations and knee functional limitations (Boeth *et al.*, 2013). This hypothesis will be tested in the proceeding chapters.

## **3.8 Summary**

### **3.8.1 Overview and clinical implications**

Although numerous studies have investigated factors that relate to or predict knee function, many have limited their assessment of knee function to one or two knee functional measures. Knee function is a broad construct that encompasses a range of activities; therefore the use of multiple functional measures to determine knee function has been recommended (Fitzgerald *et al.*, 2001; Reiman & Manske, 2011). To the author's knowledge, this is the first study to investigate the associations between sports participation, participant characteristics and a range of knee functional assessments following ACLR. The findings of this study will inform future research aimed at identifying predictors of poor knee function following ACLR and help clinicians to identify sub-groups of individuals who may benefit from more specific or individualised rehabilitation following ACLR.

In this study, ACLR participants demonstrated limitations in all aspects of their self-reported and physical knee function. The greatest knee function limitations were related to sports activities. Although the average LSIs of ACLR participants were above or near the minimum acceptable level for return to sport (Thomee et al. 2012), the distance and number of hops performed by ACLR participants was significantly lower than the healthy control participants for two of the three hop tests. Furthermore, half of the ACLR participants scored less than 85% on at least one of the functional measures and only 41 ACLR participants (62%) achieved a LSI of 85% or more on the side hop test. These findings demonstrate that many individuals continue to experience ongoing knee functional limitations well after the conclusion of rehabilitation following ACLR. These limitations may have implications for the quality of movement observed during functional tasks and the structural integrity of the knee joint (Ingersoll *et al.*, 2008).

Greater anterior knee joint laxity, older age and higher BMI were significant predictors of failing the functional test battery. Patients with greater anterior knee joint laxity, higher BMI and neuromuscular impairments following ACLR may place greater demands on passive joint restraints and knee joint cartilage (Boeth *et al.*, 2013; Ingersoll *et al.*, 2008). Therefore, patients with greater anterior knee joint laxity, or patients who are older and have a higher BMI, may require additional or specialised rehabilitation in order to optimise knee function and joint health after ACLR. As BMI is modifiable, clinicians could potentially improve knee functional outcomes following ACLR by guiding patients, with various interventions, to achieve a healthy BMI. In addition to identifying sub-groups of individuals who may be at risk of poor knee functional outcomes, clinicians could use the findings of this study to identify patients who may benefit from additional neuromuscular re-training following ACLR. The relationship between knee function and neuromuscular control is the focus of the final chapter of this thesis.

Level of sports participation, having returned to the pre-injury level of sports participation at the time of testing and the psychological response to returning to sport were not associated with knee function in this study. The clinical implication of this finding is that returning to sport, or participating at a higher level of sport, does not necessarily mean that an individual has acceptable knee joint function. Participating in

high-level sport with poor knee joint function may predispose some individuals following ACLR to develop knee osteoarthritis, particularly when combined with chondral or meniscal injuries (Keays *et al.*, 2010). Grade III or IV chondral injuries and meniscal surgery at the time of ACLR were not significantly associated with knee joint function in this study. However, given the long-term implications of concomitant chondral and meniscal injuries, these variables should be accounted for in future research. The prevalence of grade III or IV chondral injuries in this study (11%) is comparable to the prevalence reported in a large multicentre study (Borchers *et al.*, 2011). Therefore, although chondral and meniscal injury was not associated with knee function in this study, the inclusion of these individuals may have increased the external generalizability of these findings.

### **3.8.2 Limitations**

There are several limitations to this study:

1. Due to the cross-sectional design it is not possible to infer causation from the associations that were found.
2. The participants were limited to patients with ACLR and healthy control participants who volunteered for the study, hence the participants were not a truly random sample of the population and care should be taken when generalizing the findings of this study to the wider ACLR population. Furthermore, individuals with ACLR who were aged less than 18 years at the time of testing were excluded from the study. The exclusion of adolescents could have introduced sampling bias and the findings of this study may not be generalisable these individuals.
3. Although all participants were encouraged to follow a similar post-operative protocol, including early weight-bearing and quadriceps activation and range of motion exercises, the rehabilitation program was not standardised. Therefore, variability in the quality, volume and structure of rehabilitation may have contributed to some of the unaccounted variance in functional scores.
4. Only participants with hamstring grafts who were at least 12 months and no more than 24 months post-surgery and aged between 18 and 50 years were eligible for the study, therefore the relevance of the results to individuals with different types of

grafts, at different time-points post ACLR, adolescents or individuals who are over 50 years old is unknown.

5. Despite efforts to match the ACLR and control groups for demographic variables, the ACLR group were an average of 2.6 years older and had a BMI that was 1.3 kg/m<sup>2</sup> higher than control participants. This is important because age and BMI were significant predictors of knee function; hence, the slightly older age and greater BMI of the ACLR group may have influenced the size of the ACLR and control group differences. However, considering the IQR of age (8.2 years) and BMI (3.7), the size of these differences may not be clinically important.
6. Significantly more control participants were tested on their dominant limb; defined as the preferred leg for kicking a ball (Brown *et al.*, 2009). Healthy control populations have previously been found to hop further on their dominant compared to non-dominant limb (van der Harst *et al.*, 2007). Although, limb dominance was not significantly associated with knee function in the ACLR group, it is possible that the greater proportion of individuals tested on their dominant limb in the control group contributed to the size of the differences found between the ACLR and control group.
7. Although relatively broad eligibility were used, the exclusion of individuals with grade three collateral ligament injuries at the time of ACLR and revision ACLR means that the results of this study cannot be generalized to these individuals.
8. Although there were no significant differences in the proportion of women using or not using the MOCP at the time of testing between the ACLR and control groups, this variable only provides an approximation of estrogen levels. It is not known whether variability in estrogen levels within the ACLR group were associated with knee function.
9. The recruitment of participants from two surgeons was necessary to recruit the required number of participants within the restricted time-frame of the study. Although both surgeons use very similar surgical techniques and there were no differences between surgeons in knee function scores, the recruitment of participants from different surgeons may have introduced variability that was not accounted for in the regression analyses. Furthermore, it was not possible to randomly sample the required number of subjects within the timeframe of the study; hence, the study population may not have been a true representation of the wider ACLR population.

10. The psychological response to returning to sport, as assessed with the ACL-RSI scale, is only one of a number of psychological variables that may be associated with knee functional outcomes. Fear of movement or injury during functional tasks may also influence knee function, particularly around the time of return to sport (Chiemlewski *et al.*, 2008). Although fear of re-injury was a component of the ACL-RSI; fear of movement was not assessed in this study.
11. The binary categorisation of chondral injuries and meniscal surgery and the creation of a dichotomous variable from the self-reported and functional performance test scores (overall knee function) may have resulted in less precise estimates of these variables (Altman & Royston, 2006). However, these classifications are commonly used in clinical practice (Hartigan *et al.*, 2010; Røtterud *et al.*, 2013); hence, these methods can be argued to have clinical utility.

### **3.9 Conclusions and recommendations**

ACLR participants demonstrated limitations in a range of self-reported and performance measures of knee function. Greater anterior knee joint laxity, older age, and higher BMI were significantly associated with greater odds of failing a battery of knee function tests. Level I or II sports participation, having returned to the pre-injury level of sports participation, the psychological response to returning to sport, sex, grade III or IV chondral injury and meniscal surgery at the time of ACLR were not associated with knee function; however, future research is warranted to confirm these findings given their potential relevance to rehabilitation following ACLR.

The variables included in this study only accounted a third of the variance in knee joint function. Greater variance in knee joint function may be explained by exploring the relationship between knee function and neuromuscular control. Therefore, the aims of the following three chapters are to assess the neuromuscular control of individuals following ACLR in the open (Study 2) and closed kinetic chain (Study 3), and determine the strength of the associations between neuromuscular variables and knee function (Study 4).

# Chapter 4

## Study 2

### **Quadriceps force control and thigh muscle activation strategies after anterior cruciate ligament reconstruction**

#### **4.1 Chapter Overview**

The study reported in this chapter investigated the neuromuscular control of ACLR and healthy control participants during open kinetic chain testing. The quadriceps force control and thigh muscle activation strategies of ACLR and control participants were assessed using a novel force-matching task. The associations between quadriceps force control and thigh muscle activation strategies were then investigated.

#### **4.2 Introduction**

Rupture of the ACL is associated with a range of neuromuscular, biomechanical and clinical impairments such as anterior tibial translation and internal tibial rotation (DeFrate *et al.*, 2006), quadriceps weakness (Eitzen *et al.*, 2009), quadriceps atrophy (Williams *et al.*, 2005a) and altered patterns of muscle activation (Chmielewski *et al.*, 2005; Lustosa *et al.*). In an attempt to address these impairments and improve knee function, ACL reconstruction (ACLR) is commonly performed (Ingersoll *et al.*, 2008). Following ACLR, and despite the restoration of knee joint stability, many individuals continue to demonstrate impairments in quadriceps strength (Eitzen *et al.*, 2009; Thomeé *et al.*, 2011) in combination with altered quadriceps and hamstrings activation strategies (Bryant *et al.*, 2009b; Madhavan & Shields, 2011; Williams *et al.*, 2005b).

Quadriceps impairments are particularly problematic given the role of the quadriceps in attenuating ground reaction forces (Lewek *et al.*, 2002; McLean & Samorezov, 2009)

and providing dynamic knee stability during functional tasks (Lustosa *et al.*, 2011; Palmieri-Smith *et al.*, 2009). Impairments in the strength, activation and control of the quadriceps after ACLR may be associated with increased knee joint loading, which may accelerate the onset or progression of knee OA (Palmieri Smith, 2009). Quadriceps strength deficits are also associated with knee functional limitations (Eitzen *et al.*, 2009; Logerstedt *et al.*, 2012c; Schmitt *et al.*, 2012). Therefore, knowledge of the factors that relate to or predict quadriceps impairments after ACLR may inform the development of more effective rehabilitation strategies.

Quadriceps weakness identified with open kinetic chain assessments may be associated with reduced quality of functional movements. For example, individuals following ACLR with quadriceps weakness use smaller knee flexion angles in walking than individuals with strong quadriceps (Lewek *et al.*, 2002). In stair climbing and single leg landing tasks, lower quadriceps strength has previously been associated with greater peak trunk flexion and lower peak knee flexion moments (Hall *et al.*, 2012; Oberländer *et al.*, 2012a). These findings indicate that some individuals following ACLR compensate for quadriceps strength deficits by incorporating kinematic, kinetic or neuromuscular adaptations within the kinetic chain. Hence, open kinetic chain testing of quadriceps strength may be beneficial to isolate and assess quadriceps strength deficits following ACLR (Augustsson & Thomeé, 2000).

Quadriceps strength is important for optimal knee function after ACLR (Eitzen *et al.*, 2009); however, the ability to produce force accurately with the quadriceps may also be functionally relevant. The majority of activities of daily living, and many sporting activities, require only sub-maximal intensities of muscle contraction (Pandy & Andriacchi, 2010). For example, during moderate speed walking (~1.49 m/s), quadriceps forces have been estimated to range from ≈10-30% of their predicted maximal isometric forces (Besier *et al.*, 2009). Therefore, in addition to the assessment of quadriceps strength following ACLR, it may be relevant to assess quadriceps control at sub-maximal intensities.

The previous investigations that have assessed open kinetic chain quadriceps force control after ACLR have required participants to reproduce a static target force at a percentage of their maximal voluntary isometric contraction (MVIC; (Baumeister *et al.*,

2011; Williams *et al.*, 2005b). However, static quadriceps contractions are used infrequently in sports and everyday tasks (Madhavan & Shields, 2011); hence, a sub-maximal force matching task that varies in intensity may better represent functional activities. As a foundation to this study, a more demanding, isometric quadriceps force matching protocol was developed, where the target force fluctuated between 5 to 30% of MVIC. This pilot study involved a group of ACLR (n = 28) and control (n = 29) participants, and in this study the quadriceps force matching test was able to discriminate large deficits in quadriceps force control (i.e. 23%) in the ACLR group (Telianidis *et al.*, 2014).

In the Telianidis *et al.* (2014) study, impaired quadriceps force control (i.e., less-accurate quadriceps force production) was found to be associated with reduced magnitude of hamstrings muscle activation. This finding may be clinically relevant, as a higher magnitude of quadriceps activation and hamstrings coactivation during low-intensity functional movements is associated with less effective responses to external perturbations (Lustosa *et al.*, 2011; Madhavan & Shields, 2011). Hence, generalized muscle coactivation and less-accurate quadriceps force production may affect the quality of functional movements. Altered muscle activation may also contribute to higher knee joint forces and long-term structural changes (Tsai *et al.*, 2012).

The previous investigations that have evaluated quadriceps force control after ACLR are limited by their use of small, homogenous samples (Baumeister *et al.*, 2011; Bryant *et al.*, 2009a; Telianidis *et al.*, 2014; Williams *et al.*, 2005b). Consequently, the findings of these investigations are difficult to generalize to the wider ACLR population, and their relevance to specific sub-groups of individuals following ACLR is also unknown. For example, a lower level of sports participation has previously been associated with greater quadriceps activation during a single leg landing task (Nyland *et al.*, 2013) and participant characteristics such as age and sex may confound the relationship between quadriceps force control and muscle activation (see Section 2.3.3). Hence, it is important to assess quadriceps force control impairments and thigh muscle activation strategies within a larger group of individuals following ACLR and determine the cross-sectional associations between quadriceps force control, muscle activation strategies, sports participation and participant characteristics.



### 4.3 Aims

Based on this rationale and the overall aims of the research in this thesis, the aims of the study reported in this chapter were to:

1. Compare the quadriceps force control of ACLR and healthy control participants using a novel, sub-maximal, quadriceps force-matching task
2. Compare the quadriceps and hamstring muscle activation strategies of ACLR and healthy control participants during the quadriceps force-matching task
3. In the ACLR group, determine the cross-sectional associations between quadriceps force control and:
  - a) Vastus medialis, vastus lateralis and rectus femoris muscle activation during the task
  - b) Medial and lateral hamstrings muscle activation during the task
  - c) Sports participation and participant characteristics (see Section 3.5.5)

### 4.4 Hypotheses

Based on the current literature the following hypotheses were proposed:

1. ACLR participants would demonstrate less-accurate quadriceps force production (Telianidis *et al.*, 2014)
2. ACLR participants would demonstrate significantly higher levels of quadriceps activation and hamstrings coactivation compared to control participants (Árnason *et al.*, 2014; Bryant *et al.*, 2010; Madhavan & Shields, 2011)
3. In the ACLR group, less-accurate quadriceps force production would be significantly associated with:
  - a) Higher vastus medialis (Telianidis *et al.*, 2014), vastus lateralis and rectus femoris muscle activation (Kouzaki *et al.*, 2004; Lustosa *et al.*, 2011)
  - b) Lower medial and lateral hamstrings coactivation (Telianidis *et al.*, 2014)
  - c) Older age at the time of testing, female sex, lack of current participation in level I or II sport, limb dominance, concomitant meniscal surgery, grade III or IV chondral injury at the time of ACLR and greater anterior knee joint laxity (see Section 2.3.3)

## **4.5 Methods**

### **4.5.1 Participants**

The participants in this study were the same as those described in Study 1 (66 individuals with ACLR and 41 uninjured individuals; see Section 3.6). Eligibility criteria and participant characteristics are reported in Tables 3.1 and 3.2 respectively.

### **4.5.2 Overview of experimental protocol**

All data were collected by the PhD candidate during the testing session described in Study 1 (see Section 3.5) at the CHESM movement laboratory at the University of Melbourne. The testing protocol and data analysis procedures were developed by the PhD candidate with the assistance of supervisors. The testing protocol was refined using rationale from the literature and pilot testing with 15 healthy volunteers (see Appendix 2). Pilot testing volunteers met the eligibility criteria for the study (see Section 3.5.1) but were not included in the control group.

The inter-session reliability of quadriceps force control, muscle activation strategies and isometric quadriceps and hamstrings strength was assessed with a group of control participants ( $n = 26$ ) who were willing and able to repeat the testing session within 5-7 days of the first assessment (see Appendix 8). It was not possible to assess the inter-session reliability within the ACLR group due to their concurrent involvement in another, unrelated PhD study (see Appendix 1).

### **4.5.3 Self-reported measures**

#### *Sports participation and participant characteristics*

The assessment of sports participation and participant characteristics, including demographic variables, concomitant chondral and meniscal injuries and anterior knee joint laxity was described in Chapter 3 (see Section 3.6.1).

### *Limb dominance and involved limb*

The method of assessing limb dominance was outlined in Study 1 (see Section 3.5.6). The involved limb of the ACLR group was compared to the right limb of the control group. The right limb of control participants was assessed, rather than the dominant limb, to improve the efficiency of data collection procedures. Consequently, and as expected, when the data were analysed it was found that more control participants were tested on their dominant limb than on their non-dominant limb (see Section 3.6.1). To account for the possible influence of limb dominance on between-group (Aims 1 and 2) measures, additional statistical analyses were performed. These procedures are described below in Section 4.5.7.

The contralateral limb of ACLR participants was not compared to the involved limb because subject preparation, experimental setup, familiarisation trials and equipment calibration took approximately 45 minutes for a single limb. Furthermore, the main aim of the study was to investigate the associations between muscle activation strategies and quadriceps force control within the ACLR limb. Assessing the contralateral side, in addition to the testing for Studies 1 and 3, may have increased the risk of participant fatigue as the testing session as performed in this study took approximately 3 hours.

### *Pain during testing protocol*

Pain during or after hopping, or activities of daily living, was an exclusion criterion for the study; therefore, it was anticipated that participants would not report pain during the quadriceps force control test, given the sub-maximal intensity of the task. However, pain may influence the measurement of strength and muscle activation during maximal voluntary contractions (Eccleston & Crombez, 1999); hence, the severity and intensity of any pain that occurred during testing was recorded. After the performance of the task, participants were asked whether they experienced any pain (yes or no). If a participant answered yes, they were asked to record the pain intensity on a 100 millimetre visual analogue scale from 0 (no pain) to 100 (extreme pain).

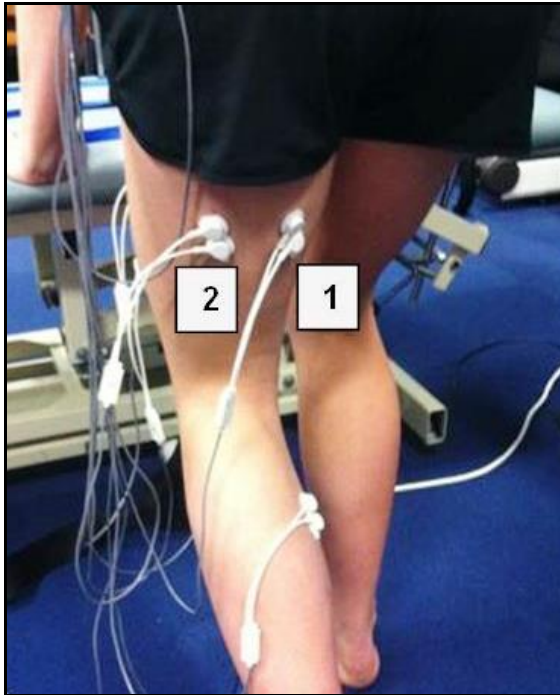
#### 4.5.4 Subject preparation

##### *Muscle activation strategies*

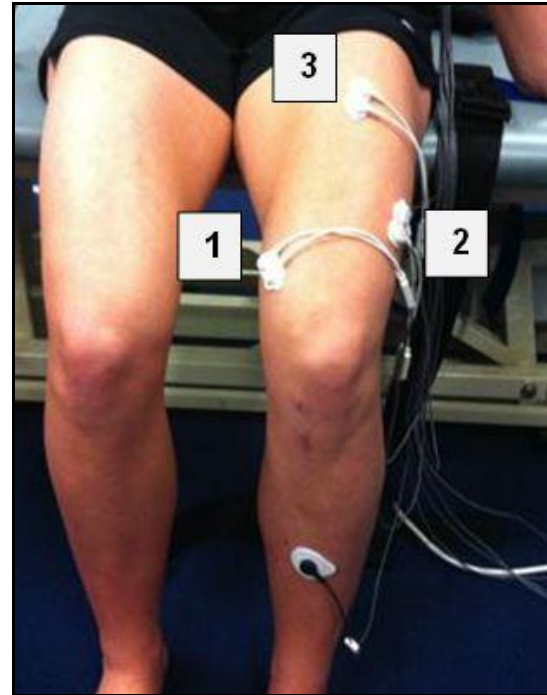
An eight channel electromyographic (EMG) system (Noraxon Inc., Scottsdale, AZ) was used to measure the level of activation of three quadriceps muscles (vastus medialis, vastus lateralis and rectus femoris), the lateral hamstring (biceps femoris) and the medial hamstring (semitendinosus and semimembranosus) muscles of the involved limb during the force matching task. The terms medial and lateral hamstrings was used because the semitendinosus and semimembranosus muscles have a close anatomical relationship in the thigh and it is difficult to accurately measure the muscle activation of these muscles separately using surface EMG (Koh & Grabiner, 1992).

To identify the site of electrode attachments for the hamstrings, participants were asked to stand on their uninvolved limb, put their hands on a bench and flex their involved knee to  $60^\circ$  against manual resistance (see Figure 4.1a). The medial hamstring electrode was positioned at the mid-point of a line connecting the ischial tuberosity and the medial femoral epicondyle (Ristanis *et al.*, 2011). The lateral hamstring electrode was placed at the mid-point of a line connecting the ischial tuberosity and the lateral femoral epicondyle (Patras *et al.*, 2009).

The site of electrode attachment for the quadriceps was determined with the participant seated on the edge of a bench (see Figure 4.1b). Participants were asked to flex their hip and knee to  $60^\circ$  and extend their knee against manual resistance while electrode placement sites were palpated and marked with a non-permanent marker (Daanen *et al.*, 1990). The vastus medialis electrode was located on the area of greatest muscle bulk on a line connecting the medial femoral epicondyle and the anterior superior iliac spine (ASIS) and orientated  $60^\circ$  to the longitudinal axis of the thigh (Cowan *et al.*, 2009). The vastus lateralis electrode was positioned at the junction of the distal and middle third of the thigh on a line connecting the lateral femoral epicondyle and the ASIS (Patras *et al.*, 2009). The rectus femoris electrode was placed at the mid-point of a line connecting the anterior inferior iliac spine and the superior pole of the patella (Cowling *et al.*, 2003).



**Figure 4.1a.** Example of the electrode placement of the medial (1) and lateral (2) hamstrings



**Figure 4.1b.** Example of the electrode placement of the vastus medialis (1), vastus lateralis (2) and rectus femoris (3) muscles

Prior to electrode placement the site of electrode attachment was shaved, abraded with fine sandpaper and cleaned with alcohol to reduce impedance (Clancy *et al.*, 2002). Silver-silver chloride non-amplified surface electrodes (Duotrode, Myotronics) were placed on the prepared site with an inter-electrode distance of 20 millimetres (Daanen *et al.*, 1990). Care was taken to position each electrode parallel with the underlying muscle fibres, as oblique electrode placement can cause attenuation of EMG signals (Clancy *et al.*, 2002). The reference electrode was located over the anteromedial surface of the tibia (Shultz *et al.*, 2009). Electrodes were stabilised using tape to minimise motion artefact and the quality of EMG signals was inspected during walking and isolated muscles contractions (Cowling *et al.*, 2003). When artefact or crosstalk were detected, the electrode was removed and the process was repeated until an acceptable signal quality was achieved.

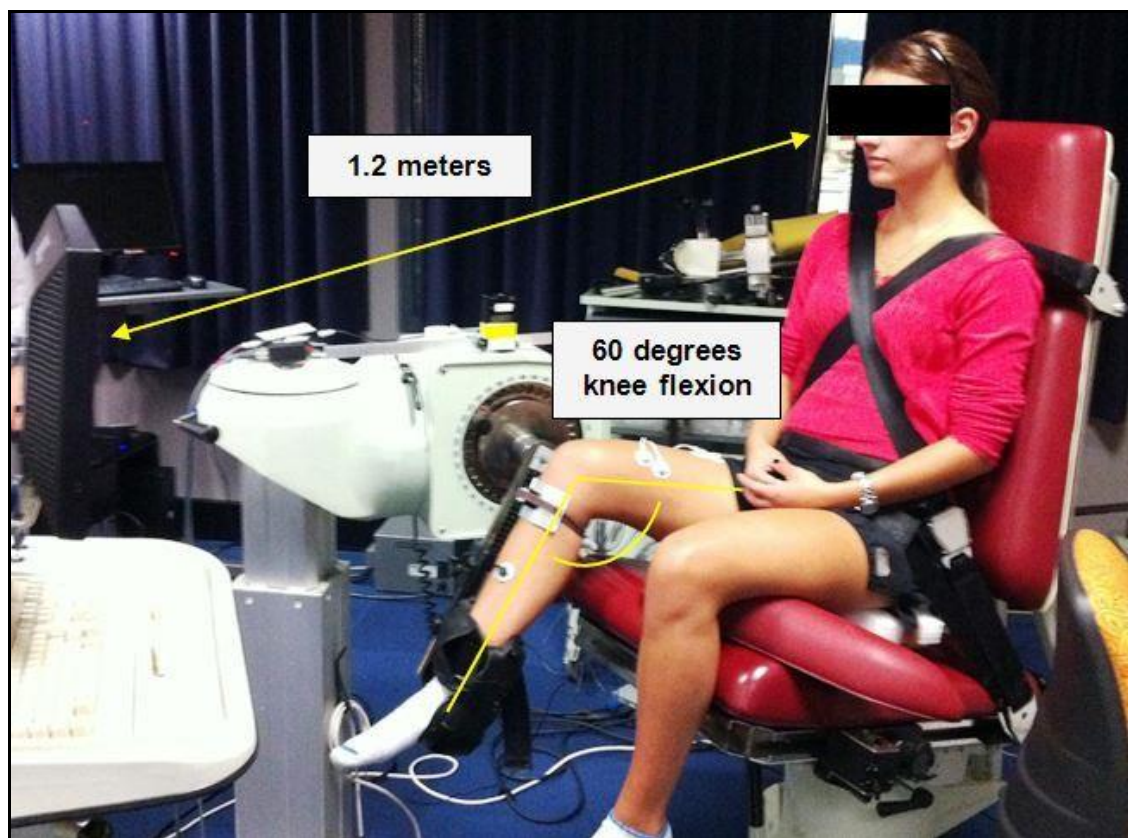
### *Isometric test set-up*

Participants were seated on a small foam platform on the seat of a KinCom isokinetic dynamometer (KinCom, U.S.A.) with their upper body stabilised by waist and chest straps. The thigh was elevated so that the only points of contact of the thighs were the ischial tuberosities (see Figure 4.2). The purpose of the foam platform was to transfer weight through the ischial tuberosity rather than through the thigh, thereby creating a less stable base of support and facilitating greater recruitment of trunk and gluteal muscles to maintain stability (Telianidis *et al.*, 2014; Williams *et al.*, 2004; Williams *et al.*, 2005b). These methods may make the task more generalisable to functional movements, since trunk and gluteal muscles assist with stability during locomotion (Anders *et al.*, 2007).



**Figure 4.2.** Isometric testing position with participants seated on a foam platform on the seat of a KinCom isokinetic dynamometer with the thigh elevated.

After stabilising the ankle to the lever arm of the dynamometer with Velcro straps, the dynamometer head was elevated until the participant's hip was flexed to 90° and the knee was then flexed to 60° by adjusting the lever arm. Both angles were confirmed with a manual goniometer. Sixty degrees of knee flexion was chosen because this angle has been shown to produce the least strain on the ACL (Beynon *et al.*, 1995) and the length-tension relationship of the quadriceps is optimal for force production (Krishnan *et al.*, 2011). The ankle strap was attached two centimetres proximal to the lateral malleolus. The lateral epicondyle of the femur was used to approximate the flexion-extension axis of the knee and this axis was aligned with the axis of the dynamometer lever arm. A computer screen was positioned at a standardised distance (1.2 metres) in front of the participant and was used to provide visual feedback during testing (see Figure 4.3).



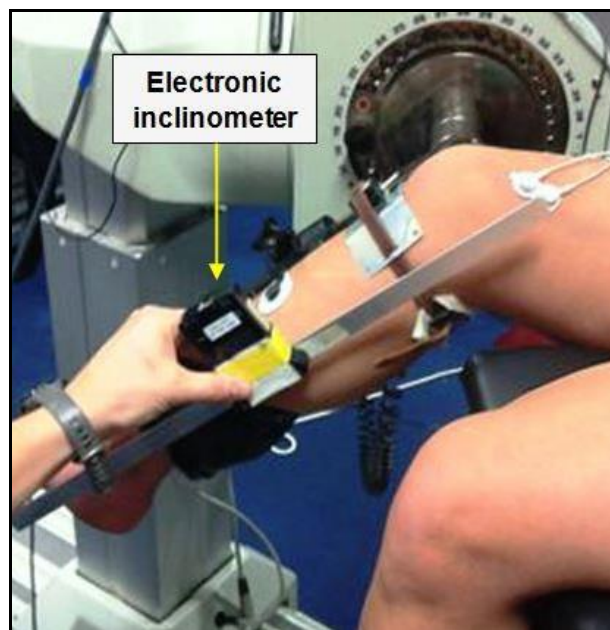
**Figure 4.3.** The testing position for quadriceps and hamstrings isometric strength testing and the quadriceps force matching test.



An electronic goniometer was attached to the lateral aspect of the thigh and leg, spanning the knee joint (see Figure 4.4a). The goniometer output was used to monitor and record any changes to the knee joint angle during testing. An electronic inclinometer (The Dualer, U.S.A.) was used to more precisely position the involved limb in 60° knee flexion (see Figure 4.4b). Prior to testing, calibrations were performed to account for the weight of the test limb and the effect of gravity. With the participant's leg completely relaxed, data from the electronic goniometer and torque data from the KinCom were collected using custom LabVIEW software (National Instruments, Texas, U.S.A.) and a cosine-based calibration factor was used to account for differences in the weight of participant's limbs. The raw data from the electronic goniometer was calibrated and used to monitor the angle of knee flexion during testing.



**Figure 4.4a.** The electronic goniometer that was used to monitor knee flexion angle during testing



**Figure 4.4b.** The electronic inclinometer (The Dualer, U.S.A.) that was used to position the involved limb in 60° knee flexion

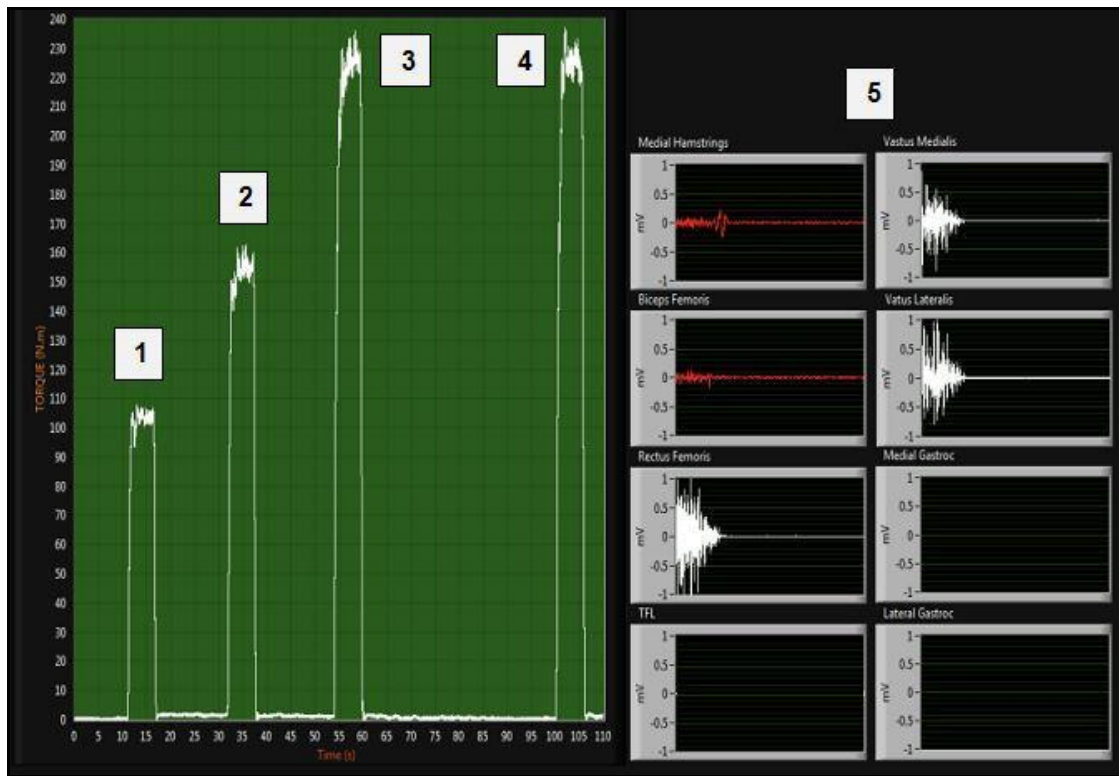


#### **4.5.5 Experimental protocol**

##### *Isometric strength testing*

In the position described above, subjects completed two five-second MVICs with their quadriceps and hamstrings muscles with 40 seconds rest between each trial. To assess quadriceps strength, participants were instructed to kick forward with their leg as hard as possible. For hamstring strength testing, participants were instructed to pull back as hard as possible. Two sub-maximal practice trials were performed for each muscle group; one at approximately 50% and one at approximately 75% of perceived MVIC.

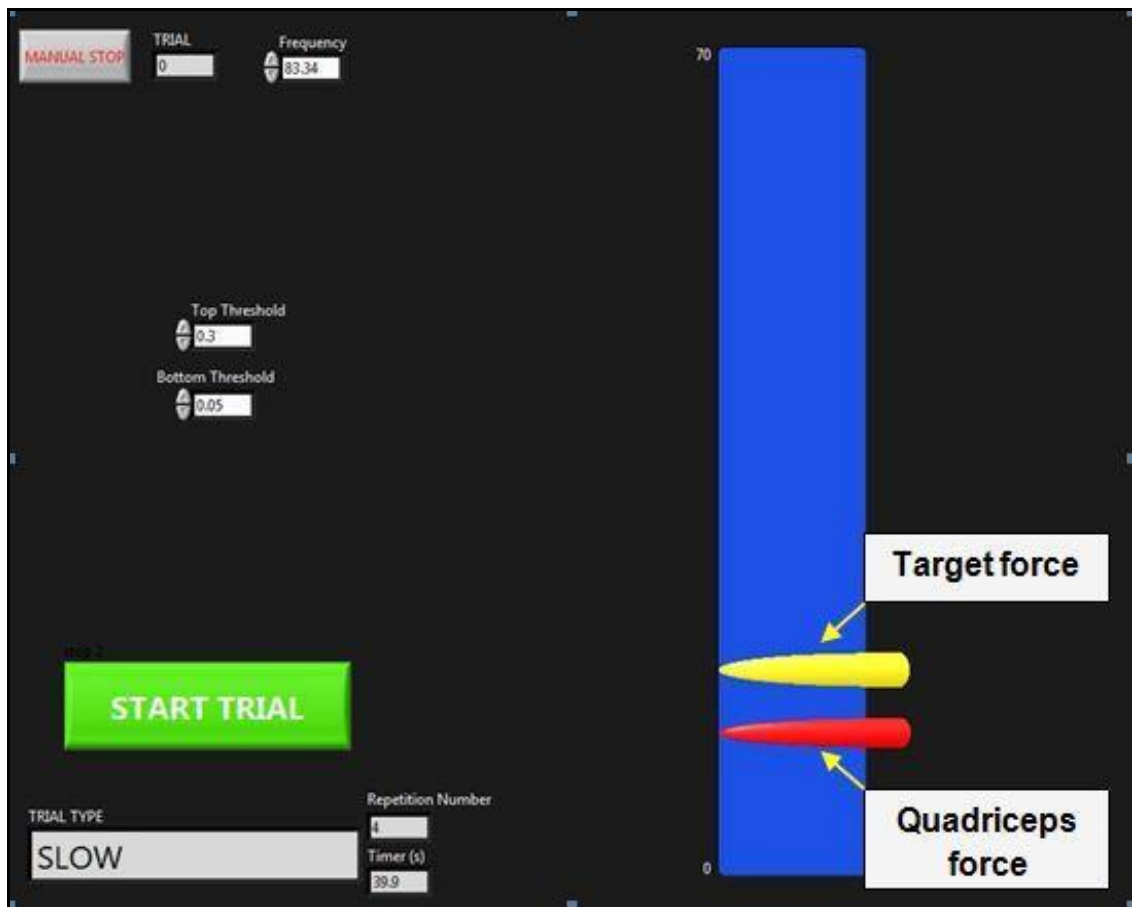
Isometric strength testing was necessary to determine the limits for the force matching test and to obtain maximal muscle activation levels for which to normalise the EMG measured during the test (Williams *et al.*, 2005b). Isokinetic strength testing was not conducted because of the risk of inducing fatigue, which may confound the measurement of quadriceps force control and muscle activation (Johnston *et al.*, 1998; Singh *et al.*, 2010). However, a recent study found moderate to strong correlations between measures of isometric and isokinetic quadriceps strength after ACLR (Knezevic *et al.*, 2014). For both MVIC trials, a standardised script of strong verbal encouragement was provided and the force output was displayed in real time on the computer monitor to encourage maximum effort (Krishnan & Williams, 2011). The EMG output was monitored in real time using the same custom LabVIEW software. An example of this visual feedback is provided in Figure 4.5.



**Figure 4.5.** The visual feedback provided to participants on the computer screen: (1) 50% and (2) 75% of perceived MVIC. (3) and (4) are MVIC trials. Scale is torque (Newton metres). Raw hamstrings and quadriceps EMG activity can be seen on the right of screen (5)

### *Force matching test*

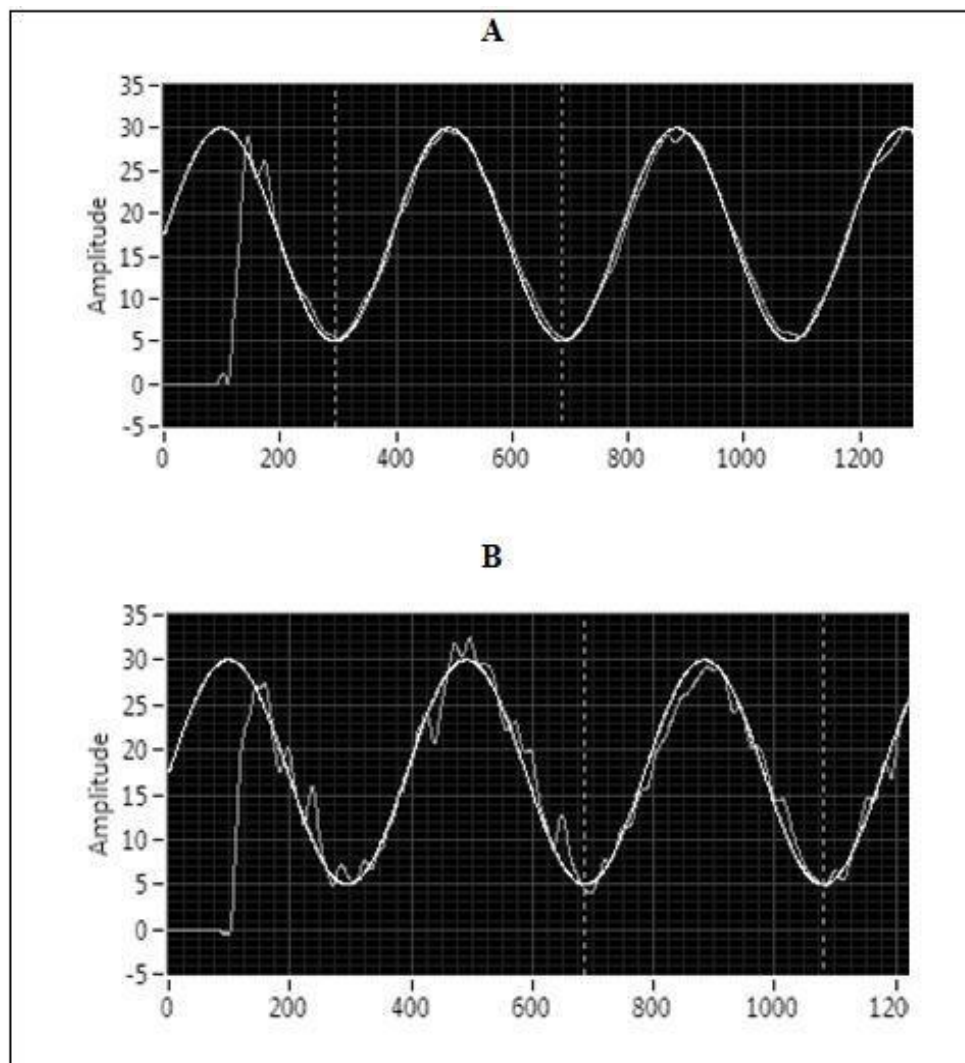
In the same position that was used for the isometric strength testing, participants completed a force-matching task using their quadriceps to match a target force displayed on the computer screen. The target force was represented by a yellow arrow that moved up and down the screen at a pre-set frequency. The participant's quadriceps force was represented by a red arrow that moved up the screen with increasing quadriceps force and down the screen with decreasing quadriceps force (Figure 4.6). Participants were asked to focus on the computer screen and not to talk during the trial. This was repeated continuously for one minute and was preceded by three practice trials with 30 seconds rest between each trial. No feedback was provided during testing and the laboratory environment was kept free of noise and visual distractions.



**Figure 4.6.** Quadriceps force matching test. The target arrow oscillated slowly up and down on the screen and the participant attempted to match this target force using quadriceps force.

The intensity of the force matching test was normalised by calculating the most consistent two seconds of the participant's quadriceps MVIC. The target torque oscillated between 5 and 30% of this value in a sinusoidal pattern. Normalisation of the intensity of the task to the steadiest part of the MVIC allowed for comparison between individuals with different levels of quadriceps strength and accounted for any spikes in torque during MVIC testing. The frequency of the oscillations was 0.128 Hertz (Hz), equivalent to eight cycles per minute, or four seconds of increasing force then four seconds of decreasing force. To familiarise participants with the task but minimise the effect of learning, the first practice trial was performed at a different frequency; slow (0.094 Hz, six cycles per trial). The second practice trial was performed at the same

frequency as the task (0.128 Hz) and the third practice trial was performed at a non-sinusoidal frequency (0.133 Hz for the increasing force and 0.111 Hz for the decreasing force). Visual feedback of performance was provided after each practice trial using a graph which displayed the participants force throughout the trial, superimposed over the target force (see Figure 4.7).



**Figure 4.7.** An example of the visual feedback provided to participants after each trial of the quadriceps force matching test, including an example of good (A) and poor (B) performance. The Y axis is torque (Newton metres standardised to MVIC) and the X axis is time. The thicker line was the target torque which alternated between 5 and 30% MVIC. The thinner line was the torque produced by the participant using quadriceps torque.

The intensity, frequency, duration and number of practice trials of the force matching test were selected based on inspection of pilot data, interviewing participants during pilot testing and rationale from the literature (see Section 2.4.2). Muscle fatigue is associated with reductions in movement accuracy and changes in muscle activation (Missenard *et al.*, 2008). Feedback from pilot participants confirmed that testing intensities greater than 30% MVIC, test durations greater than one minute, greater numbers of practice trials and higher frequencies of force oscillation were associated with greater self-reported fatigue and worse task performance. Hence, the duration, intensity, frequency and number of practice trials were chosen based on the most challenging test that pilot participants could complete without reporting excessive fatigue or errors related to concentration.

The intensity of the force-matching task was chosen to reflect the intensity of muscle contractions involved in everyday tasks like walking. Quadriceps force in moderate speed walking (1.49 metres/second) has been shown to range from 10-30% of its predicted maximum isometric force (Besier *et al.*, 2009). A dynamic, rather than a static target force was chosen to reflect the dynamic forces that occur during locomotion and other functional tasks. Although the task involved isometric muscle contraction, the changing target torque resulted in small increases and decreases in muscle and tendon length that may be more representative of functional movement (Manini, 2005).

A sinusoidal pattern was chosen instead of a randomly changing or non-sinusoidal pattern so that changes in the direction of the target force would be less abrupt and easier to follow. A randomly fluctuating force or a non-sinusoidal pattern may have resulted in some individuals not being able to complete the task, therefore introducing floor effects. The presence of floor and ceiling effects was assessed by inspecting the range of scores during pilot tests and interviewing participants about the subjective difficulty of performing the task (Barber-Westin *et al.*, 1999).

## 4.5.6 Data processing and analysis

### *Instrumentation*

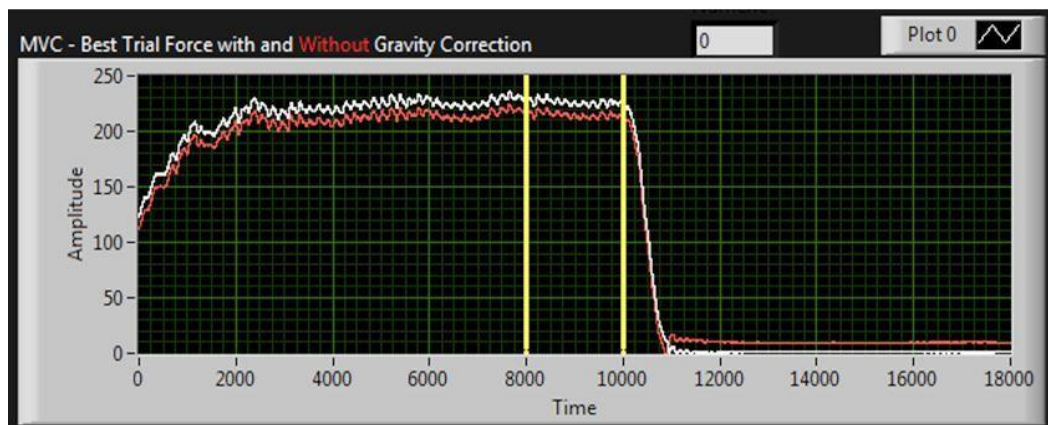
Raw force and EMG data were collected with a CompactDAQ with BNC 9125 modules (National Instruments, U.S.A.) and sampled at 2000 Hz using a desktop computer and customised LabVIEW software.

### *Quadriceps and hamstrings strength*

Raw force data in Newtons (N) from both the quadriceps and hamstrings MVIC trials and the quadriceps force matching task were filtered with a 62.5 Hz low-pass Symlet-8 undecimated wavelet filter. The filtered raw force data was converted to torque by multiplying by the lever arm length in metres (Nm). Quadriceps and hamstrings torque (Nm) relative to body mass (Nm/kg) were reported (Shultz *et al.*, 2009).

### *Quadriceps force control*

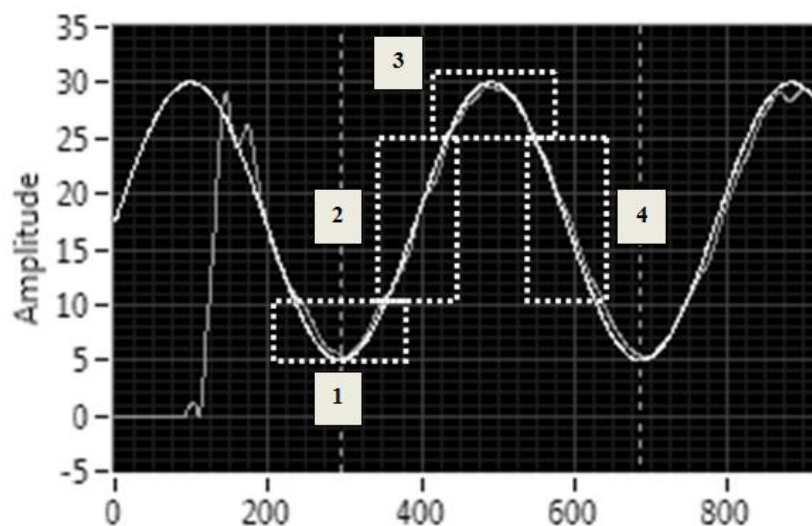
Raw force data (in Newtons) collected during the force matching task was filtered and converted to torque as per the quadriceps and hamstrings strength tests. The steadiest two seconds of the isometric torque value obtained during MVIC testing was automatically identified using a minimal coefficient of variation algorithm. The average torque value in this epoch, and not the body-weight normalised torque value, was used to define the intensity (5-30%) of the force matching test (see Figure 4.8).



**Figure 4.8** The steadiest two second segment of an MVIC trial, represented by the section between the two yellow cursors; white = raw torque, red = torque after gravity calibration. The average gravity-calibrated torque within the steadiest two second segment was used to define the intensity (5-30%) of the force matching test

Quadriceps force control was determined by calculating the root mean square error (RMSE) of the quadriceps torque data relative to the target force over the one minute trial. Quadriceps torque error can be positive or negative (i.e., too much or too little force). Calculating the root mean square provided positive numbers, with higher numbers indicating greater target matching error. The first and last repetitions of the sine wave were removed to account for any variability related to the beginning or end of the trial. The RMSE for the remaining cycles was averaged to produce a final measure of quadriceps force control for the one minute trial.

The force matching test involved periods of increasing and decreasing force, and periods where the force changed between increasing and decreasing force. To determine whether these periods of different force intensity were associated with differences in quadriceps force control, the average RMSE during four periods was calculated; 1) low intensity (5-10% MVIC), 2) increasing intensity (10-25% MVIC), 3) highest intensity (25-30%) and 4) decreasing intensity (25-10% MVIC). These periods are highlighted in Figure 4.9.



**Figure 4.9.** The four periods of quadriceps force intensity that were analysed; 1) low intensity (5-10% MVIC), 2) increasing intensity (10-25% MVIC), 3) highest intensity (25-30%) and 4) decreasing intensity (25-10% MVIC).

### *Muscle activation during the force matching task*

A fourth-order Butterworth filter with a band-pass of 10-500 Hz was applied to the raw EMG data. For the MVIC trial, the average root mean square (RMS) EMG value was calculated during the steadiest two-second segment extracted (see Section 4.5.6) and a linear envelope was created by applying a 10 Hz low-pass filter. The linear envelope EMG was normalised to the EMG recorded during this two-second segment. Quadriceps activation and hamstrings coactivation were analysed separately (Shultz *et al.*, 2009), rather than calculate an index of coactivation (Rudolph *et al.* 2001), as it was hypothesised that both quadriceps activation and hamstrings coactivation would be higher in the ACLR group (hypothesis 2). Therefore, a ratio of quadriceps and hamstrings activation may not accurately reflect the hypothesised differences in quadriceps activation and hamstrings coactivation between the groups.

#### **4.5.7 Statistical analyses**

##### *Reliability*

The inter-session reliability of measures was assessed using a sub-group of control participants ( $n = 26$ ). All control participants were invited to attend a second assessment 5-7 days following their initial assessment until the required sample size was obtained. A detailed summary of the methods (including sample size calculation) and findings of this reliability study is provided in Appendix 8, and the findings are referred to in this chapter. Ideally, reliability should be established within the clinical population of interest, i.e. within the ACLR group, to optimise the generalizability of the findings (Milner *et al.*, 2011). However, due to the involvement of the ACLR participants in another, unrelated PhD study, this was not possible (see Appendix 1).

In summary, intraclass correlation coefficients ( $ICC_{3,k}$ ) with 95% confidence intervals (CIs) were used to determine the inter-session reliability of quadriceps force control (RMSE) and quadriceps and hamstrings MVIC. The ICC defines the ability of a variable to discriminate between individuals (Stratford & Goldsmith, 1997). ICC values range from 0 (no reliability) to 1 (perfect reliability), with values less than 0.4 rated as poor, 0.4 to 0.59 rated as fair, 0.6 to 0.74 rated as good, and values greater than or equal to 0.75 rated as excellent (Bruton *et al.*, 2000).



The ICC is a dimensionless value; hence, the standard error of measurement (SEM) was calculated for each variable by calculating the square root of the mean square residual from analysis of variance derived from the ICC calculation (Stratford & Goldsmith, 1997). In this case, the SEM was an estimate of an individual control subject's measurement error, expressed in the same units as the variable (Meldrum *et al.*, 2014). 95% CIs of the SEM were calculated by dividing the sum of squares error from the analysis of variance derived from the ICC calculation by the upper and lower critical values of the  $\chi^2$  distribution (Stratford & Goldsmith, 1997). The SEM and 95% CI were used to determine the repeatability of the testing protocol, and whether significant differences found between the ACLR and control groups were larger or smaller than the measurement error for each variable (Singh *et al.*, 2010).

#### *ACLR and control group comparisons*

The statistical methods used to compare the participant characteristics of the ACLR and control group were reported in Study 1 (see Section 3.5.8). In summary, descriptive statistics were calculated for age at the time of testing and anterior knee joint laxity and frequencies with percentages were used to describe sex, limb dominance, level of sports participation, meniscal surgery at the time of ACLR and grade III or IV chondral injuries at the time of ACLR.

Normality and equality of variance of RMSE, quadriceps and hamstrings strength and EMG variables were confirmed with Shapiro-Wilk and Levene Median tests respectively. Means and standard deviations were then calculated for each variable and independent t-tests were used to compare the groups statistically. Between-group differences as absolute measures and 95% CIs of these differences were calculated to determine the precision of each estimate. Box plots were created to present RMSE and muscle activation to identify any outlying scores. Percentage differences were calculated for between group differences. To provide an interpretation of the size and clinical utility of the findings, the group differences in RMSE, quadriceps and hamstring strength and muscle activation were interpreted with respect to the standard error of measurement, as determined from reliability testing (see Appendix 8).

Redundancy analyses were performed within the ACLR group to determine whether the average RMSE values calculated in the four periods of the sine wave (lowest intensity, increasing intensity, highest intensity and decreasing intensity) were related to the average RMSE for the whole curve. After confirming the linearity of relationships with scattergraphs, the strength of relationships was determined using Pearson product moment correlation coefficients (Mason & Perreault Jr, 1991; Osborne & Waters, 2002). The strength of relationships were categorised as very strong when  $r > 0.75$ , strong when  $r = 0.75$  to  $0.51$ , moderate when  $r = 0.50$  to  $0.25$  and weak/no relationship when  $r < 0.25$  (Portney & Watkins, 2008).

As described in Study 1, the ACLR group were an average of 2.6 years older ( $p = 0.03$ ) and had an average BMI that was  $1.3 \text{ kg/m}^2$  higher than control participants ( $p = 0.03$ ). Furthermore, significantly more control participants were tested on their dominant leg ( $p = 0.02$ ). The bivariate relationships between age at the time of testing and neuromuscular variables within the ACLR group were assessed as a part of aim 2 (see Section 4.6.3). To determine whether differences could have influenced the results of ACLR and control group comparisons, logistic or linear regression was used to assess the univariate relationship between these variables and quadriceps strength, hamstrings strength and EMG variables within the ACLR group.

#### *Candidate predictors of quadriceps force control*

Multivariate linear regression was used to determine predictors of quadriceps force control in the ACLR group. The following variables, determined based on the literature review reported in Chapter 2 (see Section 2.4), were candidate predictors of quadriceps force control:

- a) EMG variables: Average EMG RMS values for the vastus medialis, vastus lateralis, rectus femoris, medial hamstring and lateral hamstring during the force-matching test, as a percentage of muscle activation during MVIC
- b) Age at the time of testing, sex, current participation in level I or II sport, limb dominance, concomitant meniscal surgery or grade III or IV chondral injury at the time of ACLR and anterior knee joint laxity

Quadriceps strength was not hypothesised to be associated with quadriceps force control, because quadriceps force control was assessed at a standardised intensity (5-30% of quadriceps MVIC); hence, RMSE was experimentally controlled for quadriceps strength. To confirm this assumption, quadriceps strength relative to body mass was included as a candidate predictor variable. Due to the significant relationship found between level I or II sports participation and having returned to the pre-injury level of sport (see Section 3.6.5), only level I or II sports participation was included in the analysis. Due to the low intensity and open kinetic chain nature of the task ACL-RSI score was also excluded from the analysis, since the ACL-RSI relates to the performance of high-intensity sporting tasks which are associated with a risk of ACL injury (see Section 3.5.5).

#### *Bivariate relationships between candidate predictor variables*

The statistical methods used to assess the linearity and strength of the bivariate relationships between predictor variables were the same as those described in Study 1 (see Section 3.5.8). Due to the known variability in EMG measurements between testing sessions (Rainoldi *et al.*, 2001), it was anticipated that the ICCs for EMG variables would, at best, be fair to good (Mathur *et al.*, 2005). Therefore, only EMG variables with an ICC < 0.40 (i.e. poor) were excluded from the regression analysis.

#### *Bivariate relationships between candidate predictors and quadriceps force control*

The selection of predictor variables for the linear regression model was determined by a combination of the strength of relationships between each variable and quadriceps force control as well as subject matter expertise, previous literature and the clinimetric properties of variables (Harrell, 2001). The linearity and strength of the correlations between continuous predictor variables and RMSE were assessed with scattergraphs and Pearson product moment correlation coefficients (Mason & Perreault Jr, 1991; Osborne & Waters, 2002). Odds ratios were used to assess the strength of the relationships between RMSE and binary candidate predictor variables (i.e., sex, level I or II sports participation, limb dominance, grade III or IV chondral injury and meniscal surgery at the time of ACLR).

To determine the maximum number of predictor variables in the model, a power calculation was performed. Based on the acquired sample of 66 ACLR participants, a maximum of six predictor variables would provide over 95% power, with an alpha level of 0.05 to detect an adjusted R square ( $R^2$ ) of 0.4 (Faul, 2009). Hence, the model was powered to include a maximum of six predictor variables.

### *Missing data*

Due to failure and subsequent repair of a component inside the EMG transmitter during some of the testing period, EMG data were missing for six (9%) of the ACLR participants. As discussed in Study 1, data that are missing completely at random do not introduce bias to estimates, but reduce statistical power and the precision of estimates (Rubin, 1976; Sterne *et al.*, 2009). Therefore, rather than exclude the six participants with missing EMG data from the analysis, multiple imputation was used to impute the missing values. The assumption that the missing data were missing completely at random was tested using Little's  $\chi^2$  statistic (Little, 1988).

Five imputations of the dataset were performed with 100 iterations (Allison, 2000; Schafer, 1999). RMSE was included in the imputation model, as standard errors and regression coefficients can be biased by the omission of outcome variables from multiple imputation models (Moons *et al.*, 2006). A sensitivity analysis (see Appendix 6) was then performed to determine the effect of the data imputation on between-groups differences, regression coefficients and standard errors (Sterne *et al.*, 2009).

### *Linear regression analysis*

A maximum of six predictor variables identified from the bivariate analyses were entered into a multivariate linear regression model. Adjusted  $R^2$  values were used to determine the amount of variation in RMSE that was explained by the predictor variables, adjusted by the number of variables in the analysis (Heijne *et al.*, 2009). As the analysis was performed on five imputations of the dataset, the average of the adjusted  $R^2$  values were reported (Schafer, 1999).

Regression coefficients for continuous variables were scaled by their respective interquartile range (IQR) by multiplying each coefficient and confidence interval by its

IQR (Harrell, 2001). Hence the interpretation of the regression coefficient was the average difference in target matching error for a participant at the 75<sup>th</sup> compared to the 25<sup>th</sup> percentile of the predictor variable. The dataset included the imputed EMG data; hence, regression coefficients were pooled from the five imputations of the dataset (Schafer, 1999).

#### *Evaluation of the linear regression model*

As described in Study 1, tolerance and variance inflation factors were used to assess the overall model for collinearity (O'Brien, 2007). Standardised residuals were assessed using histograms, scattergraphs and normal probability plots for normality, linearity and homoscedasticity (Osborne & Waters, 2002). An *a priori* alpha level of 0.05 was used to determine statistical significance. All analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 21.0 (Armonk, NY: IBM Corp).

## **4.6 Results**

### **4.6.1 Reliability and repeatability of measures**

The inter-session reliability of RMSE, quadriceps strength and hamstrings strength was excellent, with ICCs ranging from 0.90 to 0.93. EMG variables demonstrated good reliability (ICC > 0.6). ICCs and SEM for each variable with 95% CIs are summarised in Appendix 8.

### **4.6.2 ACLR and control group comparisons**

#### *Participant characteristics*

A complete summary of the participant characteristics of the ACLR and control groups was reported in Chapter 3 (see Section 3.6.1). In summary, there were no significant differences between the ACLR and control groups in the proportion of men and women, physical activity levels (Tegner score), level of sports participation, or the proportion of women who were taking the monophasic oral contraceptive pill (e.g. Organon, Femodene) or within days 1-14 of their menstrual cycle at the time of testing. In the ACLR group, twenty one participants (32%) had meniscal surgery (partial

menisectomies or meniscal repairs to either meniscus) and seven participants (11%) had grade III or IV chondral injuries at the time of ACLR. The mean (SD) KT-1000 side-to-side difference was 2.3 (2.4) mm. No significant univariate relationships were observed between neuromuscular variables and either limb dominance or BMI. The *p* values from these relationships are provided in Table 4.1.

**Table 4.1.** Significance of the relationships between neuromuscular variables and 1) limb dominance and 2) body mass index - derived from univariate regression

Neuromuscular variables	Tested on dominant limb (binary variable)	Body mass index (kg/m <sup>2</sup> )
Quadriceps strength relative to body mass	0.59	0.99
Hamstrings strength relative to body mass	0.88	0.32
Quadriceps force control	0.25	0.50
Vastus medialis activation	0.21	0.64
Vastus lateralis activation	0.22	0.76
Rectus femoris activation	0.63	0.20
Medial hamstring activation	0.90	0.42
Lateral hamstring activation	0.37	0.63

*P* values were derived from univariate regression. Logistic regression was used to assess the significance of the relationships between limb dominance and neuromuscular variables

#### *Quadriceps and hamstrings strength*

No participant reported pain or any other symptom during the strength testing; therefore, VAS data were not recorded. There was no difference in quadriceps strength between the ACLR and control groups; either as an absolute measurement (*p* = 0.81) or relative to body mass (*p* = 0.28). The ACLR group had 11% lower absolute hamstrings strength (*p* = 0.10) and 17% lower hamstrings strength relative to body mass (*p* = 0.008). Quadriceps and hamstrings strength values are presented in Table 4.2.

**Table 4.2** Quadriceps and hamstrings isometric strength values derived from maximal voluntary isometric strength testing. Values are means and standard deviations with between-groups differences (95% confidence intervals) and statistical comparisons

Variable	ACLR (66)		Control (41)		Difference (95% CI)	p value*
	Mean	SD	Mean	SD		
Quadriceps strength (Nm)	144.4	57.9	147.4	65.8	3.0 (-20.8 to 26.8)	0.81
Quadriceps strength relative to body mass (Nm/kg) <sup>†</sup>	1.85	0.66	1.99	0.69	0.14 (-0.12 to 0.41)	0.28
Hamstrings strength (Nm)	71.3	23.1	79.2	26.3	7.9 (-1.6 to 17.4)	0.10
Hamstrings strength relative to body mass (Nm/kg) <sup>†</sup>	0.93	0.31	1.09	0.30	0.16 (0.04 to 0.28)	0.008*

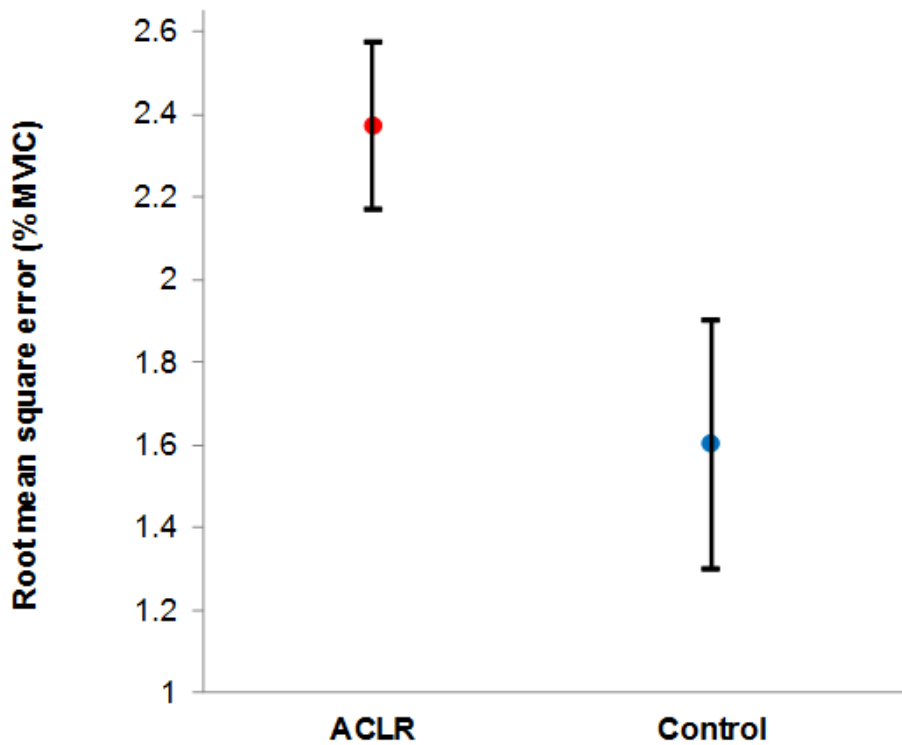
Strength values represent the steadiest two seconds of torque in Newton metres (Nm) during a maximum voluntary isometric contraction (MVIC); SD = standard deviation

<sup>†</sup> Strength values (Nm) normalised to the participant's body weight in kilograms (Nm/kg)

\*  $p < 0.01$  (independent groups t-test)

### *Quadriceps force control*

The redundancy analyses revealed strong relationships ( $r > 0.75$ ) between average RMSE and all four periods of the curve (lowest intensity, increasing intensity, highest intensity and decreasing intensity). Hence, no further analyses were performed with these variables. The ACLR group demonstrated significantly higher average RMSE values than the control group (48% difference,  $p < 0.001$ ), indicative of less-accurate quadriceps force production. The average difference in RMSE between the ACLR and control group (0.77% MVIC) was larger than the SEM (0.30% MVIC; see Appendix 8). The average RMSE of the ACLR and control groups during the force matching test, with 95% confidence intervals are presented in Figure 4.10.

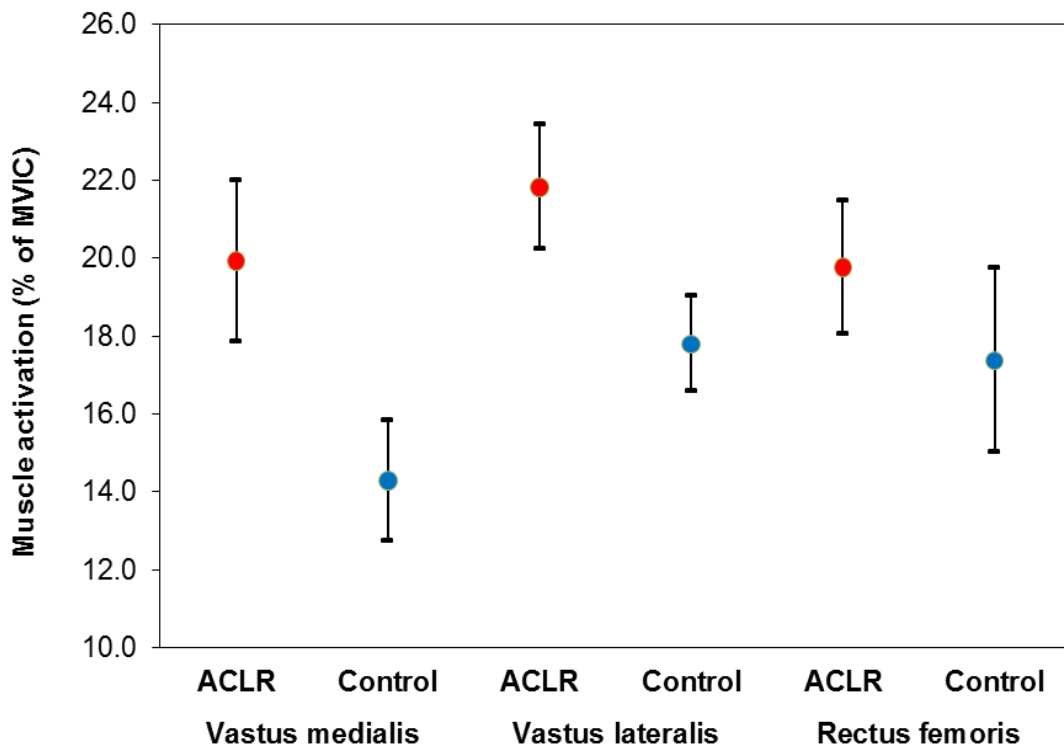


**Figure 4.10** Average root mean square error (RMSE) of the ACLR and control groups during the force matching test with 95% confidence intervals. Greater RMSE values represent greater quadriceps force variability.

*Quadriceps activation*

The ACLR group demonstrated significantly higher activation of the vastus medialis (39% difference,  $p < 0.001$ ) and vastus lateralis muscles (23% difference,  $p < 0.001$ ) than control participants and both differences were larger than the SEM (see Appendix 8). There was a trend for higher rectus femoris activation in the ACLR group (14% difference), but this difference was not statistically significant ( $p = 0.19$ ) and the difference (2.4%) was smaller than the SEM (6.5%, 95% CI 4.7 to 8.4). The mean quadriceps muscle activation levels during the force matching task of the ACLR and control groups are presented in Figure 4.11.

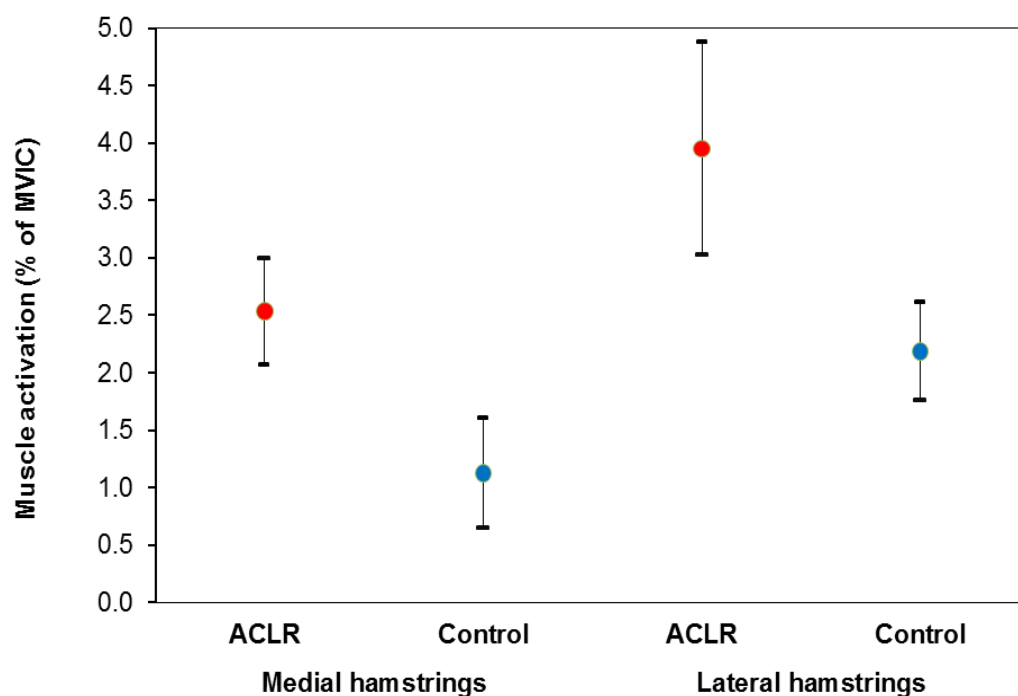




**Figure 4.11** Average vastus medialis, vastus lateralis and rectus femoris activation for the ACLR and control groups during the force matching task with 95% confidence intervals. EMG was normalised to the muscle activation recorded during maximum voluntary isometric contraction (MVIC).

#### *Hamstrings coactivation*

The ACLR group demonstrated significantly higher coactivation of both the medial and lateral hamstrings during the force matching test compared to the control group. Medial hamstrings coactivation was 25% ( $p < 0.001$ ) greater than the control group and lateral hamstrings activation was almost double that of the control group (81% difference,  $p < 0.001$ ). The lateral hamstring had higher average levels of activation for both groups. Despite the size of these relative differences, the absolute levels of hamstrings coactivation were low in both groups (range 1.1% to 4.0% of MVIC). The mean hamstrings muscle activation levels during the force matching task of the ACLR and control groups are presented in Figure 4.12.



**Figure 4.12** Average medial and lateral hamstring activation for the ACLR and control groups during the force matching task with 95% confidence intervals. EMG was normalised to the muscle activation recorded during maximum voluntary isometric contraction (MVIC).

### 4.6.3 Predictors of quadriceps force control following ACLR

#### *Bivariate relationships between candidate predictor variables*

As reported in Study 1 (see Section 3.6.5), significant positive relationships were found between age at the time of testing and grade III or IV chondral injury ( $p = 0.01$ ). Significant relationships were also observed between medial and lateral hamstring coactivation ( $r = 0.56$ ,  $p < 0.01$ ) and between vastus medialis and vastus lateralis activation ( $r = 0.68$ ,  $p < 0.01$ ). However, all four variables were retained as candidate predictor variables because the size of the relationships was below the level set *a priori* for removal of correlated variables ( $r = 0.75$ ) and primarily because of the potential importance of altered medial and lateral thigh muscle activation strategies on knee joint function (Nyland et al. 2013) and knee joint loading (Palmieri Smith et al. 2009). Weak to moderate relationships, or no relationships were observed between other candidate predictor variables.

*Bivariate relationships between candidate predictors and quadriceps force control.*

Significant bivariate relationships were found between RMSE and age at time of testing ( $p = 0.02$ ), sex ( $p = 0.01$ ), anterior knee joint laxity ( $p < 0.01$ ) and meniscal surgery the time of ACLR ( $p = 0.03$ ). Considering that each of these variables were independently related to RMSE and could potentially influence the association between RMSE and the magnitude of thigh muscle activation, these variables were included in the linear regression model. No significant relationships were found between RMSE and level I or II sports participation ( $p = 0.76$ ), limb dominance ( $p = 0.91$ ) and grade III or IV chondral injury ( $p = 0.72$ ).

Significant correlations were observed between RMSE and medial ( $r = -0.31$ ,  $p < 0.05$ ) and lateral ( $r = -0.33$ ,  $p < 0.05$ ) hamstring coactivation (i.e., greater hamstring coactivation was related to less-accurate quadriceps force production). Significant correlations were also observed between RMSE and vastus medialis activation ( $r = 0.38$ ,  $p < 0.01$ ), vastus lateralis activation ( $r = 0.40$ ,  $p < 0.01$ ). No significant correlations were observed between RMSE and quadriceps strength or rectus femoris activation. As the linear regression model was only powered to include six predictor variables, and moderate correlations were observed between vastus medialis and lateralis and between the medial and lateral hamstring muscles, the quadriceps and hamstring muscles with the strongest correlation to RMSE were included in the model (vastus lateralis and lateral hamstrings). The bivariate correlations between continuous predictor variables and RMSE are presented in Table 4.3.

**Table 4.3** Relationships between candidate predictor variables (continuous data) for the regression analysis for quadriceps force control in the ACLR group. Values are Pearson product moment correlation coefficients

Variables	Quadriceps force control	Quadriceps strength	Medial hamstring coactivation	Lateral hamstring coactivation	Rectus femoris activation	Vastus medialis activation	Vastus lateralis activation	Age at time of testing
Quadriceps strength	-0.20	-	-	-	-	-	-	-
Medial hamstring coactivation	-0.31*	0.11	-	-	-	-	-	-
Lateral hamstring coactivation	-0.33*	0.16	0.56**	-	-	-	-	-
Rectus femoris activation	0.08	-0.21	0.29	0.19	-	-	-	-
Vastus medialis activation	0.38**	0.01	0.05	0.21*	0.06	-	-	-
Vastus lateralis activation	0.40**	-0.05	0.07	0.35**	0.19	0.68**	-	-
Age at time of testing	0.29**	0.20	0.26*	0.10	0.19	0.06	0.06	-
Anterior knee laxity	0.42**	-0.03	0.27*	0.32*	0.10	0.24	0.30*	-0.01

Quadriceps force control: Root mean square error (RMSE; % MVIC) assessed between 5-30% MVIC

Quadriceps strength was normalised to body mass –Newton metres per kilogram of body weight (Nm/kg)

Muscle activation values are the average linear envelope EMG during the force matching test.

Age at time of testing is in years; anterior knee laxity = KT-1000 side-to-side difference in millimetres \*  $p < 0.05$ ; \*\*  $p < 0.01$

### *Predictors of quadriceps force control (RMSE)*

Age at the time of testing, female sex, anterior knee joint laxity, meniscal surgery at the time of ACLR, vastus lateralis activation and lateral hamstring coactivation explained 42% of the variance in quadriceps force control (average adjusted  $R^2 = 0.42$ ). Vastus lateralis activation was directly associated with quadriceps force control (IQR coefficient 0.57); while lateral hamstring coactivation was inversely associated with quadriceps force control (IQR coefficient -0.22). These coefficients should be interpreted within the context of the range (0.63 to 6.86) and interquartile range (1.24) of RMSE.

Female sex was associated with worse quadriceps force control; women were predicted to have a RMSE that was 0.56 units higher than men. Likewise, older age at the time of testing (IQR coefficient 0.49) and greater anterior knee laxity (IQR coefficient 0.71) were significantly associated with worse quadriceps force control. However, meniscal surgery at the time of ACLR was significantly associated with *better* quadriceps force control; individuals who had partial meniscectomy or meniscal repair at the time of ACLR were estimated to have a RMSE that was 0.64 units lower than individuals without significant meniscal injury (95% CI -0.12 to -1.16). The regression coefficients and *p* values for age at the time of testing, female sex, anterior knee joint laxity, meniscal surgery at the time of ACLR, vastus lateralis activation and lateral hamstring coactivation as predictors of RMSE are summarised in Table 4.4.

**Table 4.4** Predictors of quadriceps force root mean square error (RMSE) in the ACLR group with interquartile range regression coefficients and *p* values. Greater RMSE values indicate less-accurate quadriceps force production. The model was powered to include a maximum of six predictor variables.

Predictor variables	Median of variable (25 <sup>th</sup> and 75 <sup>th</sup> percentiles)	Regression coefficient (95% CI)	<i>p</i> value
Age at time of testing (years)	27.1 (23.8, 32.0)	0.49 (0.16, 0.78)	0.002**
Female sex †	-	0.56 (0.24, 1.05)	0.03*
Anterior knee joint laxity (KT-1000 difference in mm)	2.6 (0.7, 4.0)	0.71 (0.34, 1.07)	0.0001**
Meniscal surgery at the time of ACLR †	-	-0.64 (-0.12, -1.16)	0.02*
Vastus lateralis activation §	20.7 (17.9, 27.1)	0.57 (0.18, 0.96)	0.004**
Lateral hamstring coactivation §	2.6 (1.8, 4.6)	-0.22 (-0.05, -0.42)	0.04*

For continuous variables, regression coefficients represent the difference in quadriceps force control, or RMSE (root mean square error) between individuals at the 75<sup>th</sup> to the 25<sup>th</sup> percentile of each predictor variable. For example, participants at the 75<sup>th</sup> percentile of age (32.0 years) are predicted to have a RMSE that was 0.46 units higher than participants at the 25<sup>th</sup> percentile of age (23.8 years)

† For binary categorical variables, the adjusted difference represents *yes* versus *no*

§ Represents average root mean square EMG values during the force matching test relative to the value obtained during maximum voluntary isometric contraction

\* *p* < 0.05; \*\* *p* < 0.01

#### 4.6.4 Evaluation of the regression model

##### *Assumptions of linear regression and sensitivity analysis*

Tolerances (range 0.76 to 0.99) and variance inflation factors (range 1.01 to 1.32) were within acceptable limits (Mason & Perreault Jr, 1991; O'Brien, 2007). The standardised residuals of the regression coefficients demonstrated normality, linearity and homoscedasticity (Osborne & Waters, 2002). Imputed EMG data were included in the final model; hence a sensitivity analysis was performed (see Appendix 6). Little's  $\chi^2$  test confirmed that missing EMG data were missing completely at random (*p* = 0.1).

## **4.7 Discussion**

### **4.7.1 Overview of findings**

The main finding of this study was that at an average of 18 months following ACLR, participants demonstrated significantly greater quadriceps target matching error, indicative of less-accurate quadriceps force production. Furthermore, ACLR participants demonstrated significantly higher levels of thigh muscle activation during a dynamic quadriceps force matching task. Greater magnitude of vastus medialis and vastus lateralis activation was associated with less-accurate quadriceps force production and greater hamstrings coactivation was associated with more-accurate quadriceps force production. In a multivariate model, greater vastus lateralis activation, lower lateral hamstring coactivation, older age, female sex and anterior knee joint laxity were associated with worse quadriceps force control; whereas, meniscal surgery at the time of ACLR was associated with more-accurate quadriceps force production.

This study has added new knowledge to the existing body of literature by quantifying the associations between quadriceps force control, sports participation and participant characteristics following ACLR – including chondral and meniscal injuries and anterior knee joint laxity. The findings of this study inform the development of the final two studies in this thesis, which explore movement adaptations and the relationship between neuromuscular control and knee function following ACLR. A detailed discussion of the findings of the study follows.

### **4.7.2 Quadriceps force control**

Supporting hypothesis 1, the ACLR group demonstrated significantly greater RMSE during the force matching task than the control group. Although the methods used in this study are novel and cannot be directly compared to those of previous research, the finding that quadriceps force production is less-accurate, after ACLR is consistent with previous investigations that have used static open kinetic chain target matching protocols (Williams *et al.*, 2005b), dynamic closed kinetic chain force matching protocols (Kiefer *et al.*, 2013; Madhavan & Shields, 2011; Yosmaoglu *et al.*, 2011) and maximal isokinetic testing protocols (Bryant *et al.*, 2009a).

Less-accurate quadriceps force production following ACLR may have important clinical implications. Greater quadriceps and hamstrings activation during closed kinetic chain tasks, such as walking and squatting, is associated with less-effective responses to external perturbations (Lustosa *et al.*, 2011; Madhavan & Shields, 2011). Given the relationships that were found between muscle activation and quadriceps force control in this study, it is possible that less-accurate quadriceps force output could be associated with mal-adaptive neuromuscular responses during functional activities. During demanding activities, less-accurate quadriceps force production could impair task performance, or increase the risk of ACL graft rupture (Bryant *et al.*, 2009a).

This study and the previous investigation by Telianidis *et al.* (2014) are the first to assess quadriceps force control after ACLR using an open kinetic chain task with a fluctuating target torque. The strength of this approach is that, unlike the findings of Kiefer *et al.* (2013), Madhavan *et al.* (2011) and Yosmaoglu *et al.* (2011) who assessed lower limb force control using closed kinetic chain tests, the less-accurate force output observed in this study can be attributed more directly to the quadriceps. Importantly, unlike previous investigations, this study assessed the reliability and SEM of variables. The main outcome variable, RMSE, demonstrated excellent reliability, and the average difference in RMSE between the ACLR and control group was larger than the SEM derived from reliability testing (see Appendix 8).

The findings of this study are contrary to those of Baumeister *et al.* (2011) who found no difference in quadriceps target matching error between a group of patients with ACLR and a group of matched control participants. The findings of Baumeister *et al.* (2011) could also be attributed to the relatively small sample size ( $n = 9$ ), or to the use of a static target force, which may have been less-demanding. Although the target matching task used in this study involved isometric quadriceps contraction at a relatively low intensity, the target force constantly varied; thereby creating a quasi-static isometric contraction. This constantly varying target force may therefore have been more challenging for some participants. The elevated position of the thigh that was used in this study may also have made it more difficult to produce accurate force with the quadriceps. Collectively, these factors may have increased the sensitivity of the test



when compared to the protocol used in the Baumeister *et al.* (2011) study, and help account for the difference in findings between the studies.

The relatively large sample used in this study and the inclusion of individuals of both genders, with meniscal and chondral injuries, higher anterior knee joint laxity measurements and lower levels of sports participation, may make the findings of this study more generalisable than some previous investigations. However, before these results can be generalized to the wider ACLR population, it is necessary to understand the muscle activation strategies observed during quadriceps force control testing, to identify possible mechanisms of quadriceps force control impairments.

### **4.7.3 Quadriceps and hamstrings muscle activation**

Neurophysiological impairments, such as changes in cortical activity (Baumeister *et al.*, 2008) and altered muscle reflexes (Madhavan & Shields, 2011) are thought to be a part of the aetiology of neuromuscular impairments after ACLR (Ingersoll *et al.*, 2008). It was not possible to assess central nervous system adaptations in this study; however, in an attempt to understand some of the neuromuscular mechanisms of quadriceps force control impairments, muscle activation strategies were assessed.

Supporting hypothesis 2, higher levels of vastus medialis and vastus lateralis activation were observed for the ACLR group. This finding is similar to Telianidis *et al.* (2014) who also found greater vastus medialis activation in a similar group of ACLR individuals. Comparison of these findings to those of previous investigations is difficult because of the novel methodology used in this study; for example, the elevated and non-supported thigh position and constantly varying target force. However, previous studies that have assessed quadriceps muscle activation strategies after ACLR in walking (Lustosa *et al.*, 2011) and single leg squatting (Madhavan & Shields, 2011) have also found greater levels of quadriceps activation in ACLR compared to control participants. Greater levels of quadriceps muscle activation after ACLR during sub-maximal tasks may also be related to ongoing quadriceps atrophy (Williams *et al.*, 2005a) or changes in the contractile properties of the quadriceps (Krishnan & Williams, 2011) which necessitate greater muscle activation to produce force (Palmieri Smith *et al.*, 2008).

Contrary to hypothesis 2, no significant differences in rectus femoris activation were observed between the ACLR and control groups. Greater rectus femoris activation has previously been observed during open kinetic chain tasks following ACLR; for example, in kicking a soccer ball (Cordeiro *et al.*, 2014). The finding that the magnitude of rectus femoris activation in the ACLR group was not significantly different from the control group may be related, in part, to variability in rectus femoris EMG measurement. For example, changes in the magnitude of muscle activation may result from cross-talk from the adjacent vasti muscles, or individual variability in muscle fibre orientation, given its pennate fibre alignment of rectus femoris (Rainoldi *et al.*, 2001).

Supporting hypothesis 2, higher coactivation of the medial and lateral hamstrings was observed for the ACLR group. Although the ACLR group co-activated their medial and lateral hamstrings at approximately twice the intensity of the control group, the absolute levels of hamstrings coactivation were relatively low in both groups, ranging from 1.1 to 4% of MVIC. Relatively low intensity hamstrings coactivation was expected during the task because it was performed at 5-30% of quadriceps MVIC; however, it is not known whether such low intensities of muscle activation are clinically important. Furthermore, when interpreting the possible effect of greater hamstrings muscle coactivation on movement patterns and knee joint loading, it is important to consider that the relationship between EMG and muscle force may not be linear (Woods & Bigland-Ritchie, 1983); hence, greater muscle activation in the ACLR group may not be directly associated with muscle or joint loading.

The greater levels of hamstrings muscle activation observed in the ACLR group should also be interpreted with respect to the lower levels of hamstrings strength relative to body mass observed for the ACLR group. Hamstrings strength deficits were not unexpected; a reduction in hamstrings strength has been observed up to two years following ACLR with a hamstring tendon graft (Aune *et al.*, 2001). Muscle activation during the force matching task was normalised to the EMG values that were obtained during MVIC testing; hence, if ACLR participants were not able to produce a true MVIC, then the hamstrings coactivation observed during the sub-maximal task may have been artificially inflated.

A reduced capacity to generate torque with the hamstrings may be associated with ongoing morphological changes in the semitendinosus muscle and tendon which are related to the graft harvest at the time of ACLR. An investigation by (Nomura *et al.*, 2014), involving 24 male and female patients with ACLR who had returned to sport, found that hamstrings strength deficits were correlated with the amount of shortening, atrophy and healing of the semitendinosus muscle, as confirmed by MRI. Therefore, although hamstring muscle morphology was not assessed in this study, it is possible that the reduced hamstrings strength and greater hamstrings coactivation observed in the ACLR group was related to the harvesting of the hamstring graft (Árnason *et al.*, 2014).

#### **4.7.4 Predictors of quadriceps force control following ACLR**

##### *Overall model findings*

When age, sex and concurrent meniscal surgery were included in the model, the activation levels of the lateral thigh muscles (lateral hamstring and vastus lateralis) explained 42% of the variance in quadriceps force control. It is possible that specific sub-groups of individuals following ACLR, i.e. older individuals and those with higher levels of anterior knee joint laxity and a history of meniscal injuries, may have inherent differences in their neuromuscular control that may influence the association between quadriceps force control and muscle activation. The relationships between the candidate predictor variables and quadriceps force control are potentially complex and may have important clinical implications. Therefore, a discussion of these associations is presented below:

##### *Muscle activation strategies*

In support of hypothesis 3a, greater vastus lateralis activation during the force matching task was associated with less-accurate quadriceps force production. Vastus lateralis activation was subsequently included in the multivariate linear regression model, and was found to be a significant predictor of quadriceps force control; in that, greater vastus lateralis activation was associated with higher RMSE. It is difficult to compare these findings to those of previous studies due to the novel methodology used in this study. However, the finding that greater vastus lateralis activation is associated with poor quality of movement during a sub-maximal intensity task is consistent with

previous ACLR investigations. For example, unexpected perturbations applied during walking (Lustosa *et al.*, 2011) and single leg squatting (Madhavan & Shields, 2011) are associated with greater vastus lateralis activation after ACLR.

Greater vastus lateralis activation may be a response to ongoing atrophy or weakness in this muscle; that is, changes to the local force-generating capacity of the muscle may necessitate greater muscle activation to generate the same amount of force (Stockmar *et al.*, 2006; Williams *et al.*, 2005a). Alternatively, greater vastus lateralis activation may share a common aetiology with quadriceps force control impairments; that is, the disruption of normal supraspinal neuronal pathways from ligament afferents (Sjölander *et al.*, 2002) and altered cortical activation (Baumeister *et al.*, 2008; Kapreli *et al.*, 2009).

In support of hypothesis 3a, greater vastus medialis activation during the force matching task was associated with less-accurate quadriceps force production in bivariate analysis. However, due to the multivariate model being limited to six predictor variables and the prior inclusion of four non-neuromuscular variables, vastus medialis activation was not included in the multivariate model. Although the correlation between vastus medialis and lateralis activation ( $r = 0.68$ ) was below the level that was set *a priori* for removal of correlated variables ( $r = 0.75$ ), only two EMG variables could be included in the model after the inclusion of age, sex, anterior knee joint laxity and meniscal surgery, because the model was only powered to include 6 variables. Therefore, it was deemed appropriate to include one quadriceps and one hamstring muscle in the model.

The magnitude of vastus medialis activation may be more important in closed, rather than open kinetic chain activities, particularly more demanding activities which involve landing and changing direction (Barendrecht *et al.*, 2011; Bencke & Zebis, 2011; Besier *et al.*, 2003). The obliquity of the fibre orientation of vastus medialis and its proximal attachment to the linea aspera of the femur may enhance its capacity to stabilise the knee joint in preparation for the large knee abduction moments that occur at ground contact during single leg landing (Nyland *et al.*, 2013; Palmieri-Smith *et al.*, 2009). Hence, it is possible that the relatively small correlation observed between vastus medialis activation and quadriceps force control in this study was related to the open kinetic chain task, relatively low task intensity and the linear nature of the task.

It was hypothesised that greater rectus femoris activation in the ACLR group would be associated with worse quadriceps force control, as rectus femoris is a two-joint muscle which does not attach directly to the femur, and may be less-capable of producing force accurately at low intensities (Cordeiro *et al.*, 2014). Furthermore, greater rectus femoris activation has previously been associated with greater force variability during low-intensity quadriceps contractions in a group of healthy control subjects (Kouzaki *et al.*, 2004).

However, contrary to hypothesis 3a, rectus femoris activation was not associated with quadriceps force control. The lack of association between these variables in the current study may be related to the low intensity of the task. High-intensity open kinetic chain tasks such as kicking and sprinting, are known to involve significant levels of rectus femoris activation (Mero *et al.*, 1992). A recent investigation of soccer players with ACLR performing a kicking task found that greater rectus femoris activation was associated with greater kinematic variability during kicking (Cordeiro *et al.*, 2014). Hence, rectus femoris activation may also be related to the quality of movement observed in other functional tasks; for example, locomotion or landing tasks. Although rectus femoris activation was not associated with quadriceps force control in this study, the assessment of rectus femoris activation strategies may be important to include in future investigations using similar protocols.

In support of hypothesis 3b, lower medial and lateral hamstring coactivation was associated with less-accurate quadriceps force production. As hypothesised, this was the opposite direction of association than what was found for vastus lateralis activation and RMSE, but the same direction of association found by (Telianidis *et al.*, 2014). Hamstring coactivation during maximal isokinetic contractions may be an adaptation that serves to reduce anterior tibial translation (Bryant *et al.*, 2009a). In contrast, the sub-maximal intensity task that was used to assess quadriceps force control in this study may not have generated sufficient shear force and anterior tibial translation to necessitate hamstring coactivation. Instead, the greater hamstring coactivation observed in this study may have been related to the visual feedback provided on the screen (Schiffman *et al.*, 2002); specifically, greater hamstrings coactivation may have been an

adaptation used by ACLR participations to improve the accuracy of their quadriceps force output.

Hamstrings coactivation during functional, closed kinetic chain tasks may serve a different purpose to the coactivation observed in open kinetic chain tasks. The level of muscle coactivation during functional tasks may be associated with age and learning (Chapman *et al.*, 2008), sex (Myer *et al.*, 2005b), level of expertise (Sigward & Powers, 2006) and the specific demands of tasks (McNitt-Gray, 1993). In more demanding functional tasks, earlier timing of preparatory hamstring activation is associated with better knee function (Bryant *et al.*, 2009b). However, generalized hamstring coactivation may also be considered mal-adaptive, in that it may protect the knee from episodes of instability, at the expense of normal knee function (Lustosa *et al.*, 2011; Rudolph *et al.*, 1998). This hypothesis will be explored in the following two chapters of this thesis.

### *Quadriceps strength*

Quadriceps force control was obtained at a fixed percentage (5-30%) of each participant's MVIC. Hence, quadriceps strength relative to body mass was not hypothesised to be associated with quadriceps force control, as quadriceps force control was experimentally adjusted for quadriceps strength. As expected, isometric quadriceps strength was not associated with quadriceps force control. However, it is unclear whether the lack of association was biologically based, because the measurement of quadriceps force control was specific to each participant's previously determined MVIC.

In a prospective investigation, Yosmaoglu and colleagues (2011) reported that the force matching ability of 20 individuals following ACLR performing a closed kinetic chain task did not improve despite improvements in quadriceps strength and horizontal hop distance. The findings of this study, and those of the current study, support the contention that impairments in quadriceps force control may persist after ACLR despite the restoration of quadriceps strength. Therefore, specific neuromuscular training may be required to improve quadriceps control deficits after ACLR, in addition to the training required to normalise strength, power and endurance.

### *Sports participation and participant characteristics*

Contrary to hypothesis 3c, quadriceps force control was not associated with current participation in level I or II sport. Level I or II sports participation was included in the analysis because level of sports participation has previously been associated with the magnitude of quadriceps muscle activation observed during single leg landing tasks (Nyland *et al.*, 2013). The low intensity and open kinetic chain nature of the task used in this study may have contributed to the lack of association. Importantly, participation in Level I or II sport only provides a gross indication of current sports participation, and does not account for the type of sport or the training performed by individuals.

Supporting hypothesis 3c, and consistent with previous investigations involving non-ACLR populations (Christou *et al.*, 2003; Manini, 2005; Tracy & Enoka, 2002), older age at the time of testing was associated with reduced quadriceps force control. Given that the IQR of age at the time of testing in the ACLR group was 8.2 years (see Section 3.6.1), these findings indicate that relatively small differences in age (i.e., less than a decade) may be important when assessing neuromuscular control, particularly quadriceps force control after ACLR. Age-related changes in muscle fiber number and size have been found to affect quadriceps strength following ACLR (Richardson *et al.*, 2006). It is possible that similar neuromuscular changes contribute to the impairments in muscle force control and the significant association between age and quadriceps force control that was observed in this study

Supporting hypothesis 3c, female sex was also significantly associated with worse quadriceps force control. This finding is consistent with previous investigations that have found gender-related differences in neuromuscular control during functional tasks after ACLR (Miranda *et al.*, 2013; Webster *et al.*, 2011). Musculotendinous stiffness is lower in women than in men performing the same functional tasks (Cammarata & Dhaher, 2008) and musculotendinous stiffness may influence kinematics, kinetics and muscle activation in functional tasks (Blackburn *et al.*, 2013; Bryant *et al.*, 2010; Eiling *et al.*, 2007). It is possible that differences in musculotendinous stiffness between men and women contributed to the relationship that was observed between quadriceps force control and female sex. This is an area for future research.

### *Clinical impairments and surgical findings*

An important finding of this study was that anterior knee joint laxity and meniscal surgery at the time of ACLR were associated with quadriceps force control, in both bivariate and multivariate analyses. Anterior knee laxity has previously been found to correlate weakly with measures of neuromuscular control (Gokeler *et al.*, 2003; Lentz *et al.*, 2009). However, in this study greater anterior knee joint laxity was associated with less-accurate quadriceps force production. The significant association found between anterior knee laxity and quadriceps force control could be attributed to the recruitment of individuals with knee laxity measurements greater than the conventional research selection criteria of 3 mm side-to-side difference (see Section 2.3.4).

Meniscal surgery at the time of ACLR was associated with better, not worse, quadriceps force control. The menisci provide an important secondary and stabilizing role to the knee, in both the sagittal and transverse planes (Shoemaker & Markolf, 1986). Unstable meniscal tears can lead to greater passive knee instability (Andriacchi & Dyrby, 2005; Melton *et al.*, 2011). Participants with unstable meniscal injuries may have demonstrated different neuromuscular adaptations throughout the course of their rehabilitation to compensate for knee instability associated with the injury. However, the precise mechanisms of the association between meniscal surgery at the time of ACLR and quadriceps force control are unclear, as it was anticipated that there would either be no relationship, or an inverse relationship, between these variables.

The presence of grade III or IV chondral injury at the time of ACLR was not associated with reduced quadriceps force control. It is possible that grade III or IV chondral injuries are more strongly associated with neuromuscular control in more demanding tasks that result in greater shear and compressive forces in the knee, such as single leg landing (Haughom *et al.*, 2012). This hypothesis will be tested in the following chapter, which examines neuromuscular responses during a single leg landing task.

Grade III and IV chondral injuries are associated with a greater risk of knee OA and reduced knee function (Potter *et al.*, 2011); hence, a combination of chondral injury and impaired neuromuscular control may increase that risk (Keays *et al.*, 2010). Osteoarthritic changes have been found in ACLR knees as early as one year following



surgery (Frobell *et al.*, 2009), and individuals with mild to moderate knee OA have been shown to have reduced accuracy of quadriceps contractions during a static force matching task (Hortobágyi *et al.*, 2004). Therefore, although Grade III or IV chondral injuries at the time of ACLR were not associated with quadriceps force control in this study, they may be predictive of worse quadriceps force control in the longer term. This is an area for future research.

## **4.8 Summary**

### **4.8.1 Overview and clinical implications**

To the author's knowledge, this study and the foundational study by Telianidis *et al.* (2014) are the first to assess the accuracy of quadriceps force output after ACLR using a dynamic force matching task. Furthermore, this is the first known study to investigate the multivariate associations between quadriceps force control, participant characteristics and muscle activation after ACLR. The main findings of this study were that significant differences in quadriceps force control were observed between the ACLR and control groups, and that ACLR participants performed the force matching task with greater activation of both their quadriceps and hamstrings muscles. Furthermore, older age at the time of testing, female sex, greater anterior knee joint laxity, concomitant meniscal surgery, higher vastus lateralis activation and lower lateral hamstring coactivation explained 42% of the variance in quadriceps force control.

The clinical implication of these findings is that older patients with ACLR, particularly women and those with greater anterior knee joint laxity, are sub-groups for whom quadriceps force control impairments may be more relevant. Impairments in the accuracy of quadriceps force production may be related to factors other than local muscle activation; such as altered cortical activation (Baumeister *et al.*, 2008) or altered reflex profiles (Madhavan *et al.* 2011). Likewise, the greater thigh muscle activation observed in this study may be associated with changes in local muscle conductivity, muscle atrophy, or arthrogenic muscle inhibition (Ingersoll *et al.*, 2008). Further research is required to determine the mechanisms of quadriceps force control

impairments and greater thigh muscle activation after ACLR and whether they may be modifiable through rehabilitation.

Despite the relatively low intensity of the task used in this study, ACLR participants demonstrated a global increase in thigh muscle activation. This finding has implications for future research into the mechanisms of OA after ACLR (Tourville *et al.*, 2014). Greater thigh muscle activation has been speculated to increase compressive forces within the tibiofemoral joint (Palmieri Smith, 2009; Tsai *et al.*, 2012), which may hasten the onset or progression of OA (Ingersoll *et al.*, 2008). This study demonstrated that neuromuscular impairments following ACLR can be observed at relatively low levels of intensity; intensities that are comparable to those required for many functional activities such as walking and running (Besier *et al.*, 2009). Clinicians assessing locomotion in individuals following ACLR should therefore consider the potential impact of altered muscle activation strategies on the quality of functional movement following ACLR.

#### **4.8.2 Limitations**

There are a number of limitations to this study:

1. The participants were recruited using convenience sampling and this approach may have introduced selection bias. In particular, the study design excluded adolescents and people aged over 50 years. As a result, the study participants may not have been a truly random sample of the population and the results of the study may not be generalizable to all ACLR individuals.
2. Although the eligibility criteria for the study were relatively broad, the results may not be generalizable to the wider ACLR population, such as older adults, adolescents, children or elite athletes.
3. Although a control group was used to establish the size and statistical significance of neuromuscular impairments, the cross-sectional study design prevented the establishment of cause and effect. There is a need for prospective research to determine the causes of quadriceps force control impairments and altered muscle activation strategies. Furthermore, test-retest reliability was not established within

the ACLR group and estimates of error may differ between the ACLR and control groups.

4. It is unclear whether the neuromuscular adaptations demonstrated on the involved limb of the ACLR group were present in the contralateral limb. However, if a significant inter-limb difference had been observed it would still be unclear whether the injury and/or subsequent surgery caused the asymmetry or whether the asymmetry was present prior to injury. Additionally, previous studies have reported bilateral quadriceps activation deficits following unilateral ACL injury and ACLR; hence the contralateral limb may not be a stable denominator (Konishi *et al.*, 2003; Urbach *et al.*, 1999; Urbach & Awiszus, 2002). Nonetheless, given the significant differences in RMSE and muscle activation found between the ACLR and control groups in this study, future research is warranted to determine whether inter-limb differences are present in these variables following ACLR.
5. The assessment of quadriceps force control without visual feedback may have provided additional information about the possible mechanisms of quadriceps force control deficits; however, no such data were obtained. Pilot testing revealed that participants were not able to adequately perform the test without visual feedback due to the constantly varying target torque. Assessment of quadriceps force control without visual feedback may be more feasible with a constant force protocol (Baumeister *et al.*, 2011).
6. More control participants were tested on their dominant limb. Although limb dominance was not associated with quadriceps force control ( $p = 0.91$ ), differences in EMG variables have previously been observed between the dominant and non-dominant limbs of uninjured individuals (Gokeler *et al.*, 2010). Hence, differences in limb dominance may have affected muscle activation.
7. Considering that age at the time of testing was a significant predictor of RMSE, the significant difference in age between the ACLR and control groups could be argued to have influenced the size of the differences in RMSE that was observed between the groups. However, the difference in age between the groups (2.6 years) was relatively small compared to the IQR of age in the ACLR group (8.2 years), which were used to scale both estimates.
8. Although a constantly varying isometric target force was used, the isometric nature of the task and the task of matching muscle and target forces with visual feedback

means that the findings may not be generalizable to normal functional movements that occur during daily living and sports. It is not known from this study whether fatigue, a factor in many functional tasks, can affect dynamic quadriceps force control (Singh *et al.*, 2010).

9. Only isometric quadriceps and hamstrings strength were assessed in this study; hence, it is not known whether quadriceps force control is associated with deficits in isokinetic or eccentric quadriceps or hamstrings strength.
10. The use of surface EMG introduces the possibility of movement of electrodes and cross-talk between electrodes (Merletti & Lo Conte, 1997) that may not have occurred with the use of fine wire EMG (Cowan *et al.*, 2009). However, surface EMG has the advantage of being painless and non-invasive.
11. Quadriceps force control may be associated with other neuromuscular factors that were not accounted for in this study, such as spinal reflexes (Madhavan *et al.* 2011), central processing (Baumeister *et al.*, 2011) or the presence of muscular fatigue (Missenard *et al.*, 2008; Singh *et al.*, 2010). Different neuromuscular adaptations may have been revealed by conducting the test under fatigued conditions. This is an area for future research.

## **4.9 Conclusions and recommendations**

The ability to produce quadriceps force accurately is impaired and thigh muscle activation is greater after ACLR. When age, sex, anterior knee joint laxity and concomitant chondral and meniscal injuries are accounted for, less-accurate quadriceps force production is associated with a higher magnitude of quadriceps activation and a lower magnitude of hamstring coactivation. Future research is needed to determine the relationship of these impairments to knee joint function, knee loading and osteoarthritis.

This study assessed neuromuscular control following ACLR in the open kinetic chain; however, most functional activities are performed in the closed kinetic chain. Therefore, the next chapter in this thesis (Study 3) assessed the neuromuscular control of ACLR and control participants during a dynamic closed kinetic chain task.

## *Chapter 5*

### **Study 3**

#### **Neuromuscular adaptations in single leg landing after anterior cruciate ligament reconstruction**

##### **5.1 Chapter Overview**

The research reported in this chapter investigated the neuromuscular control of ACLR and healthy control participants in the closed kinetic chain, using a novel hopping task - developed specifically for the study. The task involved involving a walking approach and dynamic take-off. Hop distance and take-off velocity were standardised to minimise variability in task performance between individuals. The trunk, hip, knee and ankle kinematics and kinetics of ACLR and control participants were compared in the landing phase of the task. To explore potential mechanisms of biomechanical adaptations, the associations between knee flexion excursion and muscle activation strategies were explored within the ACLR group.

##### **5.2 Introduction**

Biomechanical and neuromuscular adaptations such as smaller knee flexion angles and greater preparatory muscle activation can persist following ACLR, despite the restoration of mechanical knee stability (Delahunt *et al.*, 2012a; Oberländer *et al.*, 2012a; Scanlan *et al.*, 2010; Tashman *et al.*, 2004). These adaptations are believed to be related to neuroplastic changes in the higher motor centres (Kapreli *et al.*, 2009; Madhavan & Shields, 2011) and the need to minimise strain to the ACL graft in the acute perioperative period (Laughlin *et al.*, 2011). However, in the long term, particularly following return to sport, biomechanical adaptations such as reduced knee flexion excursion could be considered maladaptive, given the potential impact on

sporting performance (Xergia & Pappas, 2013) and knee joint loading (Chaudhari *et al.*, 2008).

Biomechanical analysis of more demanding activities after ACLR, such as single leg hopping tasks, may identify kinematic or kinetic adaptations that are less apparent during low-intensity activities such as walking (Oberländer *et al.*, 2012a; Orishimo *et al.*, 2010; Xergia & Pappas, 2013). Assessing the quality of movement during single leg landing tasks is particularly important for individuals who have returned to unrestricted sporting activity as they are demanding and simulate some of the requirements of sport (Reid *et al.*, 2007). Numerous previous investigations have used single leg hopping and landing tasks to evaluate neuromuscular control after ACLR (see Chapter 2, Section 2.5). However, most of these investigations have not standardized the hop distance or the velocity of the participant's centre of mass prior to ground contact, or accounted for these variables in statistical analyses (Myer *et al.*, 2012; Roos *et al.*, 2013).

Standardizing, or accounting for these variables is potentially important because increasing horizontal hop distances are associated with smaller peak knee flexion angles and increasing trunk and hip flexion angles in healthy individuals (Ali *et al.*, 2012). Increasing hip and trunk flexion angles are associated with altered activation of the quadriceps and hamstrings after ACLR (Nyland *et al.*, 2010). In straight-line hopping tasks, individuals are capable of reducing the velocity of their centre of mass prior to landing by modifying their take-off (Phillips & van Deursen, 2008), and in doing so they may reduce GRF following landing (Ali *et al.*, 2012). Therefore, variability in hopping performance should be accounted for when investigating the mechanistic associations between kinematic, kinetic and neuromuscular adaptations after ACLR (McNitt-Gray, 1993; Phillips & van Deursen, 2008; Shimokochi *et al.*, 2013).

Another limitation of previous investigations is the use of small and homogenous samples of relatively high functioning participants (see Chapter 2 Section 2.5). These small samples sizes, often less than 20 subjects, have necessitated the exclusion of individuals with greater anterior knee joint laxity (Gokeler *et al.*, 2010; Ortiz *et al.*, 2011) and significant chondral and meniscal injuries (Deneweth *et al.*, 2010; Gokeler *et al.*, 2010; Oberländer *et al.*, 2012a) and those participating in lower levels of sport (Bryant *et al.*, 2009b; Gokeler *et al.*, 2010; Oberländer *et al.*, 2012a). Consequently,

although these studies provide valuable knowledge of the biomechanical adaptations that are present following ACLR, it is difficult to generalize their findings to the wider ACLR population.

Numerous biomechanical adaptations have been observed after ACLR (see Sections 2.4 and 2.5). From a clinical perspective, it is important to identify impairments that are modifiable and are related to improved quality of movement within the kinetic chain, so that these impairments can be focus of rehabilitation. Knee flexion kinematics in single leg landing tasks have been found to be modifiable through verbal instruction (Laughlin *et al.*, 2011; Tsai & Powers, 2013) and neuromuscular training (Hartigan *et al.*, 2009; Myer *et al.*, 2005b) and are related to postural control and the biomechanics of other joints within the kinetic chain (Oberländer *et al.*, 2012a).

However, it is unclear from the literature whether knee flexion excursion deficits after ACLR are related to muscle activation strategies, quadriceps strength or quadriceps control (see Section 2.4.3). It is also unclear whether the smaller knee flexion excursion observed following ACLR is associated with current level of sports participation, the psychological response to returning to sport or other participant characteristics such as sex or BMI (Miranda *et al.*, 2013). Knowledge of these associations will help clinicians to identify sub-groups of patients for whom biomechanical impairments may be most relevant following ACLR.

### **5.3 Aims**

Based on this rationale and the overall aims of the study, the specific aims of the research reported in this chapter were to:

1. Compare the knee, hip, ankle and trunk kinematics and the hip, knee and ankle kinetics of ACLR and healthy control individuals during the landing phase of a standardized hopping task
2. In the ACLR group, determine the cross-sectional associations between knee flexion excursion in landing (see Section 2.4.3) and:

- a) Quadriceps strength relative to body mass (see Section 4.5.5)
- b) Quadriceps force control (see Section 4.5.5)
- c) Preparatory vastus medialis, vastus lateralis, rectus femoris, medial gastrocnemius, medial and lateral hamstring activation in the 100 milliseconds prior to initial ground contact
- d) Sports participation and participant characteristics (see Section 3.5.5)

## 5.4 Hypotheses

Based on the specific demands of the task used in the study, the current literature (cited below and summarised in Chapter 2, Section 2.2.3) and the findings of Study 2, the following hypotheses were proposed:

1. Compared to healthy control participants, ACLR participants would demonstrate the following kinematic and kinetic adaptations during the landing phase of a standardized hopping task:

*Knee kinematic variables:*

- a) Significantly smaller peak knee flexion angles (Xergia & Pappas, 2013)
- b) Significantly smaller knee flexion excursion (Miranda *et al.*, 2013)
- c) Significantly smaller peak knee abduction angles (Tashman *et al.*, 2007)
- d) Significantly smaller peak knee internal rotation angles (Scanlan *et al.*, 2010)

*Trunk, hip and ankle kinematic variables:*

- e) Significantly larger peak trunk flexion angles (Oberländer *et al.*, 2012a)
- f) Significantly larger peak hip flexion angles (Vairo *et al.*, 2008)
- g) Significantly smaller peak ankle dorsiflexion angles (Xergia & Pappas, 2013)

*Kinetic variables:*

- h) Significantly larger peak hip extensor moments (Orishimo *et al.*, 2010)
- i) Significantly smaller peak knee extensor moments (Ortiz *et al.*, 2007)
- j) Significantly larger peak ankle plantarflexor moments (Laughlin *et al.*, 2011; Oberländer *et al.*, 2012a)



2. In the ACLR group, smaller knee flexion excursion in the landing phase of the standardised hopping task would be significantly associated with:
  - a) Lower levels of quadriceps strength relative to body mass (Morrissey *et al.*, 2004)
  - b) Less-accurate quadriceps force production
  - c) Lower levels of preparatory vastus medialis (Vairo *et al.*, 2008), vastus lateralis (Gokeler *et al.*, 2010) and rectus femoris (Ortiz *et al.*, 2008) activation in the 100 milliseconds prior to initial ground contact
  - d) Greater preparatory medial and lateral hamstring and medial gastrocnemius activation in the 100 milliseconds prior to initial ground contact (Gokeler *et al.*, 2010; Ortiz *et al.*, 2008; Vairo *et al.*, 2008)
  - e) Female sex (Miranda *et al.*, 2013), lack of participation in level I or II sports, a more negative psychological response to returning to sport (lower ACL-RSI scores), concomitant chondral and meniscal injuries and greater anterior knee joint laxity

## **5.5 Methods**

### **5.5.1 Participants**

The participants in this study were the same participants tested in Studies 1 and 2 (n = 66, see Section 3.6). Eligibility criteria and participant characteristics are reported in Tables 3.1 and 3.2 respectively.

### **5.5.2 Overview of experimental protocol**

All data were collected during the same testing session described in Study 1 (Chapter 3) at the CHESM movement laboratory at the University of Melbourne. The testing protocol described in this chapter was developed by the PhD candidate and were refined based on the findings of pilot testing involving 15 healthy volunteers (see Appendix 2). The inter-session reliability of the kinematic and kinetic variables reported in this chapter were assessed with the same group of control participants (n = 26) described in Chapter 2 (see Section 4.5.2) and Appendix 8.

### **5.5.3 Self-reported measures**

#### *Sports participation and participant characteristics*

The assessment of sports participation and participant characteristics, including demographic variables, concomitant chondral and meniscal injuries and anterior knee joint laxity was described in Chapter 3, Section 3.6.1.

#### *Limb dominance and involved limb*

The method used to assess limb dominance was described in Study 1 (Chapter 3, Section 3.5.5). The reconstructed limb of ACLR participants was compared to the right limb of control participants. As described in Study 2, the right limb of control participants was assessed, rather than the dominant limb, to improve the efficiency of data collection procedures. The involved and uninvolved limbs of ACLR participants were not compared because subject preparation, experimental setup, familiarisation trials and equipment calibration for the task took considerable time. Hence, assessing the contralateral side, in addition to completing the testing for Studies 1 and 3 may have increased the risk of participant fatigue. Furthermore, the aim of the study was to assess the mechanisms of neuromuscular adaptations within the closed kinetic chain, i.e. within the involved limb. This approach allowed a more comprehensive analysis of biomechanical and neuromuscular variables within the involved limb of ACLR participants to be performed.

#### *Pain during testing protocol*

As described in Studies 1 and 2, the presence of pain was assessed subjectively after the completion of the task. Participants were asked whether they experienced any knee pain (yes or no). If a participant answered yes, they were asked to record the intensity of the pain on a 100 millimetre visual analogue scale from 0 (no pain) to 100 (extreme pain).

#### **5.5.4 Experimental protocol**

##### *Instrumentation*

Kinematic data were acquired using a 12 camera (MX F20 CMOS) Vicon motion analysis system (Oxford Metrics, Oxford, U.K.) at a sampling frequency of 120 Hertz (Hz). Kinetic data were acquired using an Advanced Mechanical Technology, Inc (AMTI Watertown, MA, U.S.A.) force plate embedded in the laboratory floor (AMTI model BP600900-6-2000) and time-synchronised with the motion analysis data. Analogue signals from the force plate were recorded using a 16-bit analogue to digital converter at a sampling frequency of 2400 Hz. Electromyographic (EMG) data were collected simultaneously for ACLR participants with an eight channel electromyographic (EMG) system at a sampling frequency of 2400 Hz (Noraxon Inc., Scottsdale, AZ). Kinematic, kinetic and EMG data were processed using Vicon Nexus software (version 1.5.2) and custom LabVIEW software (National Instruments, Texas, U.S.A).

##### *System calibration*

The motion capture area was assessed for any reflective material that may cause light artefact, and reflective materials (e.g. metal objects) were covered or removed. The three-dimensional (3D) position of each camera was calibrated immediately prior to each testing session. A T shaped calibration wand (MX calibration wand) with five reflective markers attached to it was moved in a figure of eight pattern through the motion capture area.

The Vicon Nexus calibration software performed simultaneous recording of two-dimensional (2D) positions of each marker and calculated the physical 3D position of each camera in the room using at least 1000 valid frames. The mean calibration residuals were inspected to determine the likely error of marker measurement in millimetres from each camera. Mean calibration residuals greater than 1 were deemed unacceptable and the calibration was performed again (Meldrum *et al.*, 2014). The three planes of reference (analogous to the sagittal, coronal and transverse planes) known as the XYZ global co-ordinate system were then calibrated. An L shaped frame with three

reflective markers attached was placed on the corner of the force plate and the position of each camera was orientated into this reference plane.

### *Subject preparation*

Participants were barefoot, dressed in non-reflective shorts and a t-shirt that was modified to allow markers to be placed on the manubrium, T2, T10 and S2 spinous processes. Non-reflective tape was used to secure loose clothing so it did not obscure reflective markers and all jewellery was removed. A total of 40 retro-reflective markers (13 millimetre diameter) were attached to the trunk, pelvis and lower limbs of participants. The markers were attached to standardised anatomical landmarks using double sided tape. The precise locations of reflective markers are listed in Appendix 9 and can be observed in Figure 5.1.



**Figure 5.1** Locations of the 40 retro-reflective markers on the trunk, pelvis, thighs, legs and feet of a participant. The exact anatomical locations and orientations of each marker are provided in Appendix 9.

A single researcher (the PhD candidate) was responsible for identifying the anatomical landmarks and attaching reflective markers, as changes in the placement of markers can affect the reliability of 3D motion analysis (Della Croce *et al.*, 2005). The position of each marker was determined by careful visual inspection and palpation of the anatomical landmark. The accuracy of marker placement was evaluated by observing the participant performing functional movements.

#### *Static and dynamic calibration of kinematic model*

Static and dynamic calibration trials were used to determine anatomical and technical frames of the foot, leg, thigh, pelvis and trunk and the knee joint flexion extension axis. Additional reflective markers were placed on the medial epicondyle of the femur, the medial malleolus of the ankle, the proximal calcaneus and the nail of the big toe for the static trial (Schache *et al.*, 2006). With the participant standing quietly with their arms folded, three seconds of kinematic data were collected. The additional static markers were removed and a dynamic calibration trial was performed. The participant stood on their uninvolved leg, used a cane held in the contralateral hand for balance and slowly flexed their involved knee to a horizontal position and back to a vertical position three times.

#### *Muscle activation strategies*

An eight channel non-preamplified electromyographic (EMG) system (Noraxon Inc., Scottsdale, AZ) was used to measure the level of preparatory activation of the quadriceps (vastus medialis, vastus lateralis and rectus femoris), lateral hamstring (biceps femoris), medial hamstrings (semitendinosus and semimembranosus) and medial gastrocnemius of the involved limb of ACLR participants. Silver-silver chloride non-amplified surface electrodes (Duotrode, Myotronics) were placed on the prepared site with an inter-electrode distance of 20 millimetres (Daanen *et al.*, 1990). The site and method of electrode attachments for the quadriceps and hamstrings was described in Chapter 4 (see Section 4.5.4). The medial gastrocnemius electrode location was determined with the participant standing. The electrode was placed over the area of greatest muscle bulk at the junction of the upper and middle third of the medial leg, at a 10° angle parallel to the muscle fibres (Klyne *et al.*, 2012).

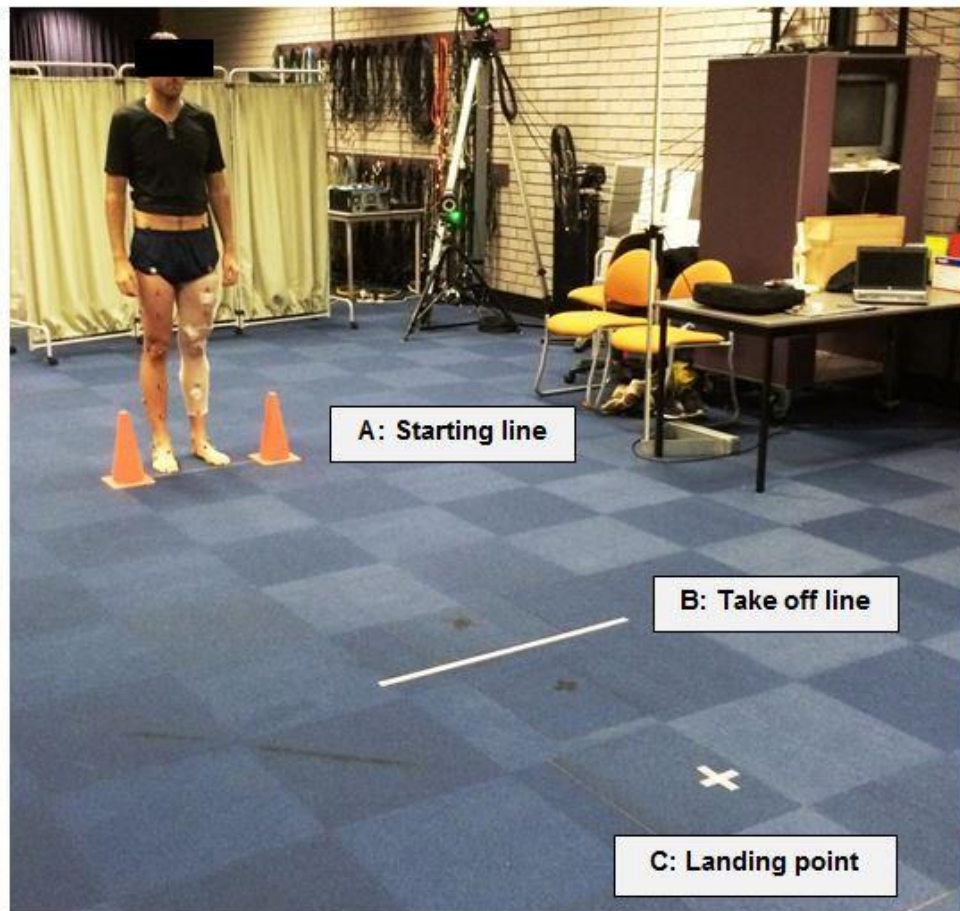
### **5.5.5 Testing protocol**

#### *Overview of hopping task*

A novel testing protocol was developed to assess kinematic, kinetic and neuromuscular adaptations within the closed kinetic chain during the landing phase of a hopping task. The protocol utilised a dynamic rather than a stationary take-off to standardise the velocity of the participant's centre of mass prior to landing (Phillips & van Deursen, 2008). Participants were instructed to walk forwards at a standardised cadence, hop with their involved limb and land on a force plate without losing balance.

#### *Set-up of hopping task*

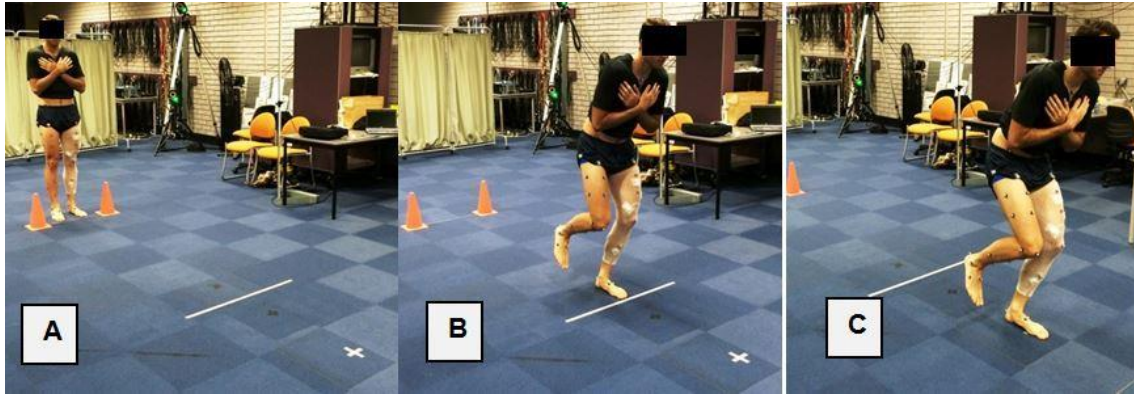
The distance of the hop was normalised to the participant's leg length. Leg length was determined by measuring from the lateral aspect of the greater trochanter to the floor with a tape measure (Gribble *et al.*, 2012). The take-off line was marked with white tape on the floor and a cross was marked in the centre of a force plate at a distance from the take-off line equal to the participant's leg length. Participants were asked to take three steps backwards and another white line was marked on the floor with tape to indicate the starting line. The start line, take-off line and landing point are indicated in Figure 5.2.



**Figure 5.2** The set up for the standardised hopping task indicating the starting line (A), the take-off line (B) and the landing point (C). The distance of the hop (B to C) was normalised to the participant's leg length (lateral aspect of the greater trochanter to the floor in centimetres).

### *Procedure*

Participants were instructed to stand with both toes behind the starting line and fold their arms across their chest. Throughout the test, participants were instructed to keep their arms folded to standardise the contribution of the upper body during the task (Gokeler *et al.*, 2010). The task involved taking three steps forward, taking off with the involved limb from behind the line and landing on the target with the take-off foot. The cadence of the walking approach was standardised to 100 beats per minute (bpm), by asking participants to walk, take off and land in time with a digital metronome that made an audible beeping sound. A demonstration of the test is provided in Figure 5.3.



**Figure 5.3** A participant performing the landing task. A: Standing behind the starting line, B: The participant has taken three steps forward in time with the metronome (100bpm) and is about to hop from the take-off line. C: The participant has hopped from the take-off line to the landing point and will attempt to regain balance without using their arms or uninjured leg.

The purpose of the walking approach was to standardise the velocity of the participant's approach and thereby standardise the velocity of their body prior to landing. These methods were designed to be clinically feasible and allow more accurate comparisons of kinematics, kinetics and muscle activation to be made between individuals (Roos *et al.*, 2013). The cadence of 100 bpm for the approach was selected based on pilot testing; in summary, 100 bpm was challenging for all participants, but all participants were able to complete the task. The number of missed trials was recorded for both groups as a measure of the relative difficulty of the task.

The hopping task was performed barefoot because differences in the mass and design of shoes have been shown to influence landing kinetics (Steele & Milburn, 1988) and the sub-maximal hop distance was not expected to cause foot discomfort during landing. Shoe surface friction has also been shown to influence lower limb kinematics during side-stepping tasks (Dowling *et al.*, 2010). Furthermore, three degrees greater knee flexion excursion and significantly reduced rates of loading of vertical GRF have been observed for ACLR and uninjured individuals in shod versus barefoot conditions (Lafortune *et al.*, 1996; Webster *et al.*, 2004b). Therefore, the task was completed barefoot to remove this potential source of variability.



A standardised, scripted explanation and demonstration was provided. The trial was deemed valid if balance was maintained for at least two seconds after landing (Reid *et al.*, 2007). If participants shuffled or took additional steps or hops after landing, or moved their trunk or contralateral limb greater than 45 degrees from the vertical plane the trial was discarded from the analysis. A maximum of five practice trials were completed with verbal feedback to ensure participants were completing the task in the same manner (Delahunt *et al.*, 2012b). No further practice trials were permitted so as to standardise the effect of learning, which may influence performance of the task (Milner *et al.*, 2012). The participants were given no specific instructions on how to land, as verbal instructions such as ‘land softly’ have been shown to increase hip and knee flexion angles and decrease ACL loads during single leg landing tasks (Laughlin *et al.*, 2011; Tsai & Powers, 2013).

The task was repeated until five successful trials were recorded. Five trials were performed rather than the commonly used approach of performing three trials (Blackburn & Padua, 2008; Orishimo *et al.*, 2010; Vairo *et al.*, 2008; Xergia & Pappas, 2013) to increase the accuracy of estimates. In previous research, a minimum of five trials were needed to obtain acceptable reliability for peak knee flexion angle during a single leg landing task (Ortiz *et al.*, 2007). A greater number of trials were not used to avoid participant fatigue, which has been associated with reduced knee flexion excursion on both the ipsilateral (Cortes *et al.*, 2013; Lucci *et al.*, 2011; Webster *et al.*, 2012b) and contralateral (McLean & Samorezov, 2009) limbs during functional tasks.

The demands of the hopping task were carefully considered. A countermovement or side stepping task was not used because both groups included individuals from lower levels of sport (see Section 3.6.1) and these individuals may have less experience in performing these tasks. Importantly, the knee valgus angles and knee abduction moments associated with these tasks may have placed some participants at risk of ACL graft injury (Hewett *et al.*, 2005; Paterno *et al.*, 2010). Notwithstanding this limitation, the task was anticipated to be demanding enough to challenge participants without exposing participants to an unnecessary risk of injury. Due to the linear nature of the task, the aims and hypotheses of the study were predominately based around sagittal plane biomechanics and muscle activation strategies.

## 5.5.6 Data processing and analysis

### *Data cleaning and filtering*

Successful trials were individually reconstructed using the Nexus reconstruct pipeline. Each marker was manually labelled using the marker names listed in Appendix 9 and any gaps in marker trajectories were filled by selecting a nearby marker with a similar trajectory and using the Nexus copy pattern algorithm. Trials were trimmed from heel contact of the last step of the walking approach to the point where the participant appeared to have returned to quiet standing. The static calibration trial was inspected for any body movement that may affect the calibration and was trimmed if necessary. The labelled marker trajectories, force plate data and raw EMG data were inspected for artefact and trials containing missing or unusable data were excluded from the analysis.

Kinematic and GRF data were filtered using a fourth order zero-lag Butterworth filter at a frequency of 20 Hz (Bisseling & Hof, 2006). Low-pass filtering of kinematic and kinetic data is needed to remove random noise (Kristianslund *et al.*, 2012). Random noise in kinematic data can originate from subtle movement of cameras or skin motion artefact (Benoit *et al.*, 2006; Reinschmidt *et al.*, 1997). Reflective markers mounted on the leg have been found to vibrate at a frequency of 23-51 Hz during functional activities (Karlsson & Tranberg, 1999) and filtering frequencies above 20 Hz result in kinematic data that are too noisy (Kristianslund *et al.*, 2012). The noise is amplified when position data are differentiated to calculate segment inertia during inverse dynamic calculations. This can result in inaccurate estimates of joint moments from unfiltered kinematic data (Kristianslund *et al.*, 2012). The accuracy of joint moments can be further affected by filtering kinematic and kinetic data at different cut-off frequencies (Bisseling & Hof, 2006); hence, the GRF data and kinematic data were filtered at the same frequency.

The filtering frequency of 20 Hz is comparable to previous studies that have reported joint moments during high-frequency movements such as jumping (Miranda *et al.*, 2013), hopping (Gokeler *et al.*, 2010) and cutting (Dempsey *et al.*, 2009) tasks. The impact phase of a hop produces a large high frequency acceleration of body segments and a spike in vertical GRF between 0 and 30 milliseconds after landing (Camenga *et al.*, 2013; Miranda *et al.*, 2013). The high frequency acceleration and spike in GRF are

removed or attenuated by low-pass filtering (Kristianslund *et al.*, 2012). Hence, it is difficult to accurately measure the magnitude of joint moments using marker-based motion analysis systems if the moments occur close to (i.e., within 20 milliseconds) the time of ground contact.

Based on previous studies using similar hopping tasks it was anticipated that peak sagittal plane moments would occur later in the landing phase and not at the point of impact (Oberländer *et al.*, 2012a; Orishimo *et al.*, 2010) and would therefore not be affected by filtering of the impact spike in GRF. In contrast, the peak frontal and transverse plane (internal abduction and external rotation) moments were anticipated to occur around the point of peak GRF, and therefore be influenced by the impact of landing (Bisseling & Hof, 2006).

To determine whether this was the case, graphs of the peak internal hip and knee extensor and ankle plantar flexor moments were produced for the first 10 ACLR and control participants using filtered and unfiltered data. The time between the peak vertical GRF and peak joint moments and the magnitude of peak moments were visually inspected. Based on this preliminary work, the magnitude of frontal and transverse plane knee moments were deemed to be negatively affected by filtering and were not included in the analysis. However, peak hip extensor, knee extensor and ankle plantar flexor moments occurred after the impact spike in the GRF data and did not appear to be affected by filtering. Hence, these variables were included for further analysis.

#### *Kinematic data*

The calibration of the kinematic model and the calculation of joint angles and moments were performed using Vicon Nexus software and custom Vicon BodyBuilder code (Oxford Metrics, Oxford, U.K.) written by the developer of the kinematic model (Dr. Anthony Schache, Department of Mechanical Engineering, The University of Melbourne). The static calibration trial was used to reconstruct a technical frame for each body segment (trunk, pelvis, thigh, leg and foot). The static calibration markers were used to reconstruct the anatomical frame of each segment to improve the accuracy of the estimate of the anatomical position of the underlying bones (Schache *et al.*, 2007).

The dynamic calibration trial was used to determine the knee flexion extension axis (Schache *et al.*, 2006). An optimisation procedure was performed that rotated the estimated knee flexion extension axis around the longitudinal axis of the femur until the variance in the knee valgus and varus profile was minimised (Schache *et al.*, 2006). This procedure has been found to result in more repeatable hip and knee kinematics than traditional methods of estimating the knee flexion extension axis (Schache *et al.*, 2006). The hip joint centre was defined relative to the pelvic anatomical frame using the inter ASIS distance based on the methods of (Davis *et al.*, 1991).

Knee and ankle joint segments were calculated using BodyBuilder code based on the static marker locations. The calibrated kinematic model consisted of eight rigid body segments; the trunk, pelvis, two thigh segments, two leg segments and two foot segments. The co-ordinates of markers throughout each dynamic trial were used to determine the immediate orientation of each segment. Joint angles were calculated using a joint co-ordinate system approach which determined the orientation of each segment with respect to the XYZ global co-ordinate system of the laboratory (Grood *et al.*, 1984). Calculations were performed using the BodyBuilder code within the Nexus program.

#### *Kinetic data*

Internal sagittal plane joint moments were calculated for the hip, knee and ankle joints using force plate data, kinematic data from the pelvic and six lower limb segments and the BodyBuilder code described in Section 5.5.7. Joint moments represent an estimate of the rotational torque within the joint and can be considered a product of the magnitude of the ground reaction force vector and the distance from this vector to the estimated joint centre (Oberländer *et al.*, 2012a). The vertical ground reaction force originates from the centre of pressure under the foot and is a summation of medial, anterior-posterior and vertical ground reaction forces (Phillips & van Deursen, 2008).

Joint moments were calculated using Newton-Euler inverse dynamics, which incorporates the joint centre, the magnitude and direction of the ground reaction force (GRF) vector, the mass of limb segments and the estimated inertial force of each limb segment produced by acceleration of that segment (Winter, 2009). The kinematic model

estimated the mass and centre of mass of each segment based on a proportion of the participant's total body mass. The model then differentiated the kinematic data to calculate accelerations of each segment. Joint moments were expressed in the proximal tibial anatomical frame in units of Newton metres (Nm) (Schache *et al.*, 2007). The filtered kinematic and kinetic data for each trial, the unfiltered EMG data and the joint angles and moments derived from the model were saved together in a C3D (Co-ordinate 3D) file. A second copy of the C3D file was made with unfiltered GRF data to calculate peak vertical GRF and time to stabilise vertical GRF.

#### *Data extraction and analysis*

The kinematic, kinetic and EMG variables were extracted using a custom LabVIEW analysis program. The program used the C3D file containing the raw unfiltered GRF data to calculate peak vertical GRF and time to stabilise vertical GRF. Unfiltered data was used to calculate these variables because filtering was observed to reduce the magnitude of peak GRF and time to stabilise GRF. The C3D file containing the filtered and modelled data was used to calculate the joint angles, moments and EMG data. The median, rather than the mean value, of the five successful trials was used for statistical analysis because the mean may be skewed by outlying scores (Petrie, 2006).

##### *1. Variables related to the standardisation of the hopping task*

The landing phase of the hopping task was defined as the time-point where the peak unfiltered vertical GRF first exceeded 10 Newtons (N), until the participant returned to quiet standing (Decker, 2003; Ford *et al.*, 2007). The entire stabilisation period was included in the analysis rather than using a standardised event (e.g. peak knee flexion) to define the landing phase, to allow the time taken to stabilise vertical GRF to be measured (Webster & Gribble, 2010). The number of missed trials were summed for each participant and averaged for the group (Phillips & van Deursen, 2008).

The velocity prior to landing in metres per second (m/sec) was determined by calculating the average velocity of the sacral marker from the heel contact of the last step of the walking approach to the point of initial ground contact (Phillips & van Deursen, 2008). This variable was used to compare the average velocity prior to landing to determine the effectiveness of the methods used to standardise performance of the

task. Peak vertical ground reaction force (N), normalised to body weight in kilograms (N/kg) and the time taken to stabilise peak vertical GRF to within  $\pm 5\%$  of body weight for more than one second were assessed to provide additional measures of task performance (Gribble *et al.*, 2012; Miranda *et al.*, 2013). The magnitude of peak vertical GRF and the time to stabilise vertical GRF were calculated using unfiltered force plate data because low-pass filtering was found to reduce the magnitude of peak vertical GRF (see Section 5.5.7).

## 2. Kinematic and kinetic variables

Peak trunk, hip and knee flexion, ankle dorsiflexion, knee abduction and knee internal rotation angles relative to adjacent segments were calculated in degrees. Knee flexion excursion was calculated by subtracting the knee flexion angle at initial ground contact from the peak knee flexion angle (Gokeler *et al.*, 2010; Miranda *et al.*, 2013; Rudolph *et al.*, 1998). Knee flexion excursion was the primary focus of the study, rather than peak knee flexion angle, so that the knee flexion angle at initial ground contact could be accounted for (Miranda *et al.*, 2013). To interpret the hypothesised differences in knee flexion excursion between the ACLR and control groups, the knee flexion angle at initial contact and the peak knee flexion angle were also reported.

Peak internal hip and knee extensor moments and ankle plantar flexor moments during landing were normalised to each participant's height and weight using the formula  $\text{Nm}/(\text{height} \times \text{weight})$  (Andriacchi & Dyrby, 2005). The normalisation to height and weight allowed for comparison to previous studies (see Section 2.2.3) and helped account for differences in weight and height between the ACLR and control groups (see Section 5.5.8). Normalising joint moments by height and weight has been found to be a more effective method of accounting for gender-related differences in weight and height than normalising moments by weight alone (Moisio *et al.*, 2003).

## 3. EMG variables

Raw EMG data were filtered with a fourth-order Butterworth filter with a band-pass of 10-500 Hz. These data were then converted into positive values using a root mean square technique, and a linear envelope was created by applying a 10 Hz low-pass filter. The mean linear envelope value between initial ground contact and 100 milliseconds

prior to ground contact was extracted for each trial to determine preparatory muscle activity (Vairo *et al.* 2008). The values for each muscle were normalised to the peak linear envelope EMG value recorded during the two quadriceps and hamstring MVICs (see Chapter 4, Section 4.5.6). Gastrocnemius MVIC was not assessed in Study 2; therefore, all medial gastrocnemius EMG was normalised to the peak linear envelope value measured after ground contact. Preliminary inspection of the data revealed that peak linear envelope values were higher during the landing phase (i.e. after initial ground contact) than during the MVIC trials for some trials. Therefore, the peak linear envelope value prior to initial contact was normalised to the larger of either the peak value recorded during the MVIC or the peak linear envelope value during the landing task (Palmieri Smith *et al.* 2009).

To determine an appropriate epoch in which to assess peak muscle activation after landing, the timing of peak sagittal plane joint angles and time to stabilise vertical GRF to within 5% of body weight was determined. Previous research has established a relationship between larger preparatory muscle activity and smaller vertical ground reaction forces (McNair & Marshall, 1994). The time to stabilise vertical GRF ranged from 250 milliseconds to 1 second; therefore, the peak linear envelope value in the 1 second period after ground contact was used to assess peak muscle activation after landing. Previous studies have used a 250 ms epoch after initial ground contact to assess reactive muscle activity after landing (McNair & Marshall, 1994; Swanik *et al.*, 2004). In the current study, a larger epoch was used so the maximum muscle activation during the task could be determined, rather than only assessing the reactive muscle activity near the point of ground contact.

Normalised values of muscle activation for each muscle group were reported instead of coactivation indices (Shultz *et al.*, 2009) so that the associations between individual muscle activation and knee flexion excursion could be evaluated. The use of a coactivation index (e.g. vastus lateralis and lateral hamstring coactivation) is difficult to interpret because the denominator is not constant. For example, a higher coactivation index could be a result of 1) greater hamstring activation or 2) lower quadriceps activation (Houck, 2005). Hence, normalised linear envelope EMG values were reported for individual muscles.

### 5.5.7 Statistical analyses

#### *Reliability*

Previous studies have reported moderate to excellent reliability for the kinematic and kinetic variables reported in this study during drop jumps (Ford *et al.*, 2007; Ortiz *et al.*, 2007; Whatman *et al.*, 2012), box jumping (Ortiz *et al.*, 2007) and stop-jumps (Milner *et al.*, 2011). However, to the author's knowledge, no previous study has evaluated the reliability of kinematic and kinetic variables derived from single leg landings.

The movement of reflective markers and overlying skin has been shown to cause errors in the estimate of joint angles and moments in functional movements (Benoit *et al.*, 2006). Although knee flexion measurements are less affected by skin and marker movement than frontal and transverse plane movement (Reinschmidt *et al.*, 1997), absolute errors in peak knee flexion measurements have been found to range from 2.2° in walking (Houck & Yack, 2003) to 5.5° in running (Reinschmidt *et al.*, 1997). Therefore, previous authors have recommended reporting the SEM, in addition to the reliability (ICC) of kinematic and kinetic variables (Benoit *et al.*, 2006).

To determine the inter-session reliability and the SEM of variables, a reliability study was conducted involving the same control participants (n = 26) described in Study 2 (see Section 4.5.7 and Appendix 8). In summary, all control participants were invited to attend a second assessment 5-7 days following their initial assessment until the required sample size was obtained. The rationale for using control participants, rather than ACLR participants to establish the reliability of variables is described in Study 2 (see Section 4.5.7) and Appendices 1 and 8.

Intraclass correlation coefficients (ICC<sub>3,k</sub>) with 95% confidence intervals (CIs) were used to determine the inter-session reliability of kinematic and kinetic variables. EMG variables were not assessed in the control group and were therefore not able to be included in reliability analyses; however, (Goodwin *et al.*, 1999) established the reliability of surface EMG in measuring the magnitude of muscle activation in the vastus medialis and rectus femoris during jumping and landing.



ICC values less than 0.4 were rated as poor, 0.4 to 0.59 were rated as fair, 0.6 to 0.74 were rated as good, and values greater than or equal to 0.75 were rated as excellent (Bruton *et al.*, 2000). The standard error of measurement (SEM) and 95% CIs were calculated for each variable using the methods described in Study 2 (see Appendix 8). The SEM and 95% CI were used to determine the repeatability of the testing protocol, and whether significant differences found between the ACLR and control groups were larger or smaller than the measurement error estimated for an individual (Singh *et al.*, 2010).

#### *ACLR and control group comparisons*

The descriptive statistics and between-group statistical analyses for participant characteristics were provided in Study 1 (see Section 3.6.1). Normality and equality of variance of kinematic and kinetic variables and the number of missed trials were assessed with Shapiro-Wilk and Levene Median tests respectively. Histograms were inspected for normality and skewness. Absolute and percentage differences between the ACLR and control groups were calculated for each variable with 95% confidence intervals. After confirming normality, independent t-tests were used to compare the groups statistically and *a priori* alpha level of 0.05 was used to determine statistical significance.

Whilst all ten variables were carefully chosen, it is recognised that larger numbers of variables increase the risk of Type 1 error (Petrie *et al.* 2006). However, the cost of incurring a Type 1 error was deemed appropriate given the exploratory nature of the study. Furthermore, rather than rely on *p* values alone, the group differences in variables were interpreted with respect to the standard error of measurement (SEM), as determined from reliability testing (see Appendix 8).

As described in Studies 1 and 2, the ACLR group were an average of 2.6 years older ( $p = 0.03$ ), had an average BMI that was 1.3 kg/m<sup>2</sup> higher than control participants ( $p = 0.03$ ) and significantly more control participants were tested on their dominant leg ( $p = 0.02$ ). To determine whether these differences could have influenced the results of ACLR and control group comparisons, logistic or linear regression was used to assess the univariate relationship between these variables and biomechanical variables.

### *Candidate predictors of knee flexion excursion*

Multivariate linear regression was used to determine predictors of knee flexion excursion in the ACLR group. The following variables, determined based on the literature review reported in Chapter 2 (see Section 2.5), were candidate predictors of knee flexion excursion:

- a) Isometric quadriceps strength relative to body mass (Nm/kg; see Section 4.5.5)
- b) Quadriceps force control (RMSE; see Section 4.5.5)
- c) Mean linear envelope EMG values in the 100 milliseconds prior to ground contact for the vastus medialis, vastus lateralis, rectus femoris, medial and lateral hamstrings and medial gastrocnemius muscles (% of maximum activation)
- d) Sex, current participation in level I or II sport, the psychological response to returning to sport (ACL-RSI), greater BMI, concomitant chondral and meniscal injuries and greater anterior knee joint laxity.

Due to the significant relationship found between level I or II sports participation and having returned to the pre-injury level of sport (see Section 3.6.5), only level I or II sports participation was included in the analysis.

### *Bivariate relationships between candidate predictor variables*

The statistical methods used to assess the linearity and strength of the bivariate relationships between predictor variables were the same as those described in Studies 1 and 2 (see Section 3.5.8).

### *Bivariate relationships between candidate predictors and knee flexion excursion*

The selection of predictor variables for the linear regression model was determined by considering the strength of relationships between each variable and quadriceps force control, subject matter expertise, previous literature, the clinimetric properties of variables (Harrell, 2001). The linearity and strength of the correlations between pairs of continuous predictor variables were assessed with scattergraphs and Pearson product moment correlation coefficients (Osborne & Waters, 2002). Odds ratios were used to quantify relationships between knee flexion excursion and binary candidate predictor variables (i.e., sex, level I or II sports participation, limb dominance, Grade III or IV

chondral injury and meniscal surgery at the time of ACLR). A maximum of six predictor variables were included in the regression model, according to the power calculation performed in Study 2 (see Section 4.5.7).

#### *Missing data*

As described in Study 2, EMG data were missing for six ACLR participants (see Section 4.5.7). Hence, rather than incur a loss of statistical power and loss of precision of estimates, multiple imputation was used to impute the missing EMG values, (Sterne *et al.*, 2009). Firstly, Little's  $\chi^2$  statistic was used to determine whether the EMG data were missing completely at random (Little, 1988). Secondly, five imputations of the dataset were performed with 100 iterations (Allison, 2000; Schafer, 1999). Finally, a sensitivity analysis was performed to determine the effect of the data imputation on regression coefficients and standard errors (Sterne *et al.*, 2009). The methods and findings of this analysis are reported in Appendix 6.

#### *Linear regression analysis*

A maximum of six predictor variables identified from the bivariate analyses were entered into a multivariate linear regression model with the dependent variable being knee flexion excursion (degrees). Adjusted  $R^2$  values were used to determine the amount of variance in knee flexion excursion that was explained by the predictor variables, adjusted by the number of variables in the analysis (Heijne *et al.*, 2009). As the analysis was performed on five imputations of the dataset, the average of the adjusted  $R^2$  values were reported (Schafer, 1999).

Regression coefficients were pooled from the five imputations of the dataset (Schafer, 1999). As described in Studies 1 and 2, regression coefficients for continuous variables were scaled by their interquartile ranges by multiplying the coefficient by the interquartile range of the predictor variable (Harrell, 2001). Hence, the interpretation was the average difference in knee flexion excursion for a participant at the 75<sup>th</sup> compared to the 25<sup>th</sup> percentile of the predictor variable.

#### *Evaluation of the linear regression model*

As described in Appendix 6, the model was assessed for collinearity using tolerance and variance inflation factors (Mason & Perreault Jr, 1991; O'Brien, 2007). The assumptions of linear regression (normality, linearity and homoscedasticity) were assessed using histograms, scattergraphs and normal probability plots of standardised residuals (Osborne & Waters, 2002). An *a priori* alpha level of 0.05 was used to determine statistical significance. All analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 21.0 (Armonk, NY: IBM Corp).

## **5.6 Results**

### **5.6.1 Reliability and repeatability of measures**

The inter-session reliability of the kinematic and kinetic variables was excellent, with ICCs ranging from 0.76 to 0.96 (see Appendix 8).

### **5.6.2 ACLR and control group comparisons**

#### *Participant characteristics*

A complete analysis of participant characteristics was reported in Study 1 (see Section 3.6.1). In summary, there were no significant differences between the ACLR and control groups for physical activity level (Tegner score), level of sports participation, the proportion of men and women or the proportion of women who were taking the monophasic oral contraceptive pill (e.g. Organon, Femodene; see Section 3.6.1). Twenty one participants (32%) had meniscal injuries and six participants (9%) had full-thickness chondral injuries at the time of ACLR. The mean KT-1000 side-to-side difference was 2.3 mm. (SD 2.4 mm.).

No significant relationships were observed between biomechanical variables and limb dominance or age at the time of testing. Significant correlations were observed between BMI and peak hip extensor moment ( $r = -0.44$ ), peak knee extensor moment ( $r = -0.66$ ) and peak ankle plantarflexor moment ( $r = -0.58$ ). The *p* values from these relationships are provided in Table 5.1.

**Table 5.1.** Significance of the relationships between biomechanical variables and 1) limb dominance, 2) body mass index and 3) age at the time of testing - derived from univariate regression

Biomechanical variables	Tested on dominant limb	Body mass index	Age at testing
Peak knee flexion angle	0.99	0.41	0.52
Knee flexion excursion	0.63	0.90	0.68
Peak knee abduction angle	0.55	0.21	0.43
Peak knee internal rotation angle	0.84	0.93	0.61
Peak trunk flexion angle	0.12	0.49	0.36
Peak hip flexion angle	0.94	0.87	0.70
Peak ankle dorsiflexion angle	0.18	0.35	0.96
Peak hip extensor moment	0.78	< 0.01	0.27
Peak knee extensor moment	0.91	< 0.01	0.38
Peak ankle plantarflexor moment	0.14	< 0.01	0.25

*P* values were derived from univariate regression. Logistic regression was used to assess the significance of the relationships between limb dominance and neuromuscular variables

#### *Performance of the hopping task*

There were no significant differences in velocity prior to landing (mean difference 0.02 seconds,  $p = 0.44$ ), peak vertical ground reaction force (1.4 N,  $p = 0.31$ ) or time to stabilise vertical ground reaction force (0.01 seconds,  $p = 0.81$ ) between the ACLR and control groups. The average number of missed trials in the ACLR group (mean = 3.9, SD = 1.7) was higher than that of the control group (mean = 3.5, SD = 1.8); however, this difference was not statistically significant ( $p = 0.22$ ). No participant reported pain during the hopping task; therefore a rating of pain during the test was not required. No discomfort related to barefoot landings was reported during testing.

#### *Kinematic and kinetic adaptations*

The ACLR group demonstrated  $4.4^\circ$  less knee flexion excursion than the healthy control group (% difference = 11,  $p < 0.001$ ) and the average peak knee flexion angle in the ACLR group ( $61.0^\circ$ ), was  $7.2^\circ$  less than that of the control group ( $68.2^\circ$ ;  $p < 0.001$ ). The

group differences in knee flexion excursion and peak knee flexion angle were larger than the individual SEM determined during reliability testing (see Appendix 8). Although the ACLR group landed with smaller peak knee flexion angle, they also landed with smaller knee flexion angles at initial ground contact ( $21.3^{\circ}$ ) compared to the control group ( $24.1^{\circ}$ ;  $p = 0.01$ ).

The ACLR group demonstrated  $1.3^{\circ}$  less peak knee abduction angle than the control group; although this difference was not statistically significant ( $p = 0.18$ ) and was smaller than the SEM ( $1.6^{\circ}$ ; 95% CI 1.1 to 2.0). The ACLR group also landed with  $2.2^{\circ}$  greater peak knee internal rotation angle ( $p = 0.02$ ); however this difference was also smaller than the SEM ( $2.7^{\circ}$ ; 95% CI 1.9 to 3.6). The average peak trunk flexion angle in the ACLR group ( $10.7^{\circ}$ ) was almost double that of the control group ( $5.6^{\circ}$ ;  $p = 0.004$ ); however, there was no significant difference in peak hip flexion angle between the groups. The ACLR group demonstrated significantly less peak ankle dorsiflexion angle (8% difference,  $p = 0.01$ ).

There was no significant difference in peak hip extensor moment between the groups. However, the average peak knee extensor moment of the ACLR group (27.3 Nm/kg) was 19% smaller than the control group (33.7 Nm/kg;  $p < 0.001$ ) and the average peak ankle plantarflexor moment was 13% smaller than the control group ( $p = 0.004$ ). These differences were greater than the SEM (see Appendix 8). The kinematic and kinetic variables for the ACLR and control groups are summarized in Table 5.2.

**Table 5.2** Kinematic and kinetic variables during the landing phase of the hopping task. Peak joint angles and peak internal joint moments (Nm) are reported for the involved limb of ACLR and control group. Values are means (standard deviations) with between-groups differences with 95% confidence intervals

Variables	ACLR (66)		Control (41)		Difference (95% CI)	p value
	Mean	SD	Mean	SD		
<i>Knee kinematic variables</i>						
Peak knee flexion angle (°)	61.0	7.6	68.2	5.4	7.2 (4.6 to 9.6)	< 0.001**
Knee flexion excursion (°)	39.7	5.5	44.1	4.5	4.4 (2.3 to 6.4)	< 0.001**
Peak knee abduction angle (°)	1.7	4.8	3.0	4.8	1.3 (-0.6 to 3.2)	0.18
Peak knee internal rotation angle (°)	10.8	4.5	13.0	5.0	2.2 (0.4 to 4.1)	0.02*
<i>Trunk, hip and ankle kinematic variables</i>						
Peak trunk flexion angle (°)	10.7	9.3	5.6	7.7	5.1 (1.6 to 8.5)	0.004**
Peak hip flexion angle (°)	51.3	9.0	51.7	8.5	-0.4 (-3.1 to 3.9)	0.83
Peak ankle dorsiflexion angle (°)	21.6	4.0	23.5	3.8	-1.9 (-3.5 to -0.4)	0.01*
<i>Kinetic variables</i>						
Peak hip extensor moment (Nm/kg)	12.6	3.4	13.3	4.0	-0.7 (-2.1 to 0.8)	0.36
Peak knee extensor moment (Nm/kg)	27.3	6.6	33.7	6.3	-6.4 (-9.0 to -3.9)	< 0.001**
Peak ankle plantarflexor moment (Nm/kg)	10.9	2.8	12.6	3.2	-1.7 (-2.9 to -0.6)	0.004**

Joint angles (°) = degrees; joint moments = Newton Metres (Nm) normalised to weight\*height (Nm/weight\*height); SD = standard deviation; \*  $p < 0.05$ , \*\*  $p < 0.01$  (independent groups  $t$ -test)

### 5.6.3 Predictors of knee flexion excursion following ACLR

#### *Bivariate relationships between candidate predictor variables*

As reported in Study 1 (see Section 3.6.5), significant relationships were found between age at the time of testing and grade III or IV chondral injury ( $p = 0.01$ ), between sex and BMI ( $p = 0.03$ ) and between quadriceps force control and knee joint laxity ( $p < 0.01$ ). Moderate relationships were observed between vastus medialis and vastus lateralis

activation ( $r = 0.54$ ,  $p < 0.01$ ), between medial and lateral hamstring activation ( $r = 0.39$ ,  $p < 0.05$ ) and between rectus femoris and vastus medialis ( $r = 0.36$ ,  $p < 0.05$ ) and vastus lateralis activation ( $r = 0.44$ ,  $p < 0.01$ ). However, all variables were retained as candidate predictors of knee flexion excursion because the size of the relationships was below the level set *a priori* for removal of correlated variables ( $r = 0.75$ ). No significant relationships were observed between the other candidate predictor variables.

#### *Bivariate relationships between candidate predictors and knee flexion excursion*

Significant relationships were found between knee flexion excursion and quadriceps strength relative to body mass ( $r = 0.26$ ,  $p < 0.05$ ), vastus medialis activation ( $r = -0.55$ ,  $p < 0.01$ ), vastus lateralis activation ( $r = -0.40$ ,  $p < 0.01$ ) and medial hamstring activation in the 100ms prior to ground contact ( $r = 0.49$ ,  $p < 0.01$ ). A significant relationship was also found between knee flexion excursion and anterior knee joint laxity ( $r = -0.32$ ,  $p < 0.01$ ). Considering that these variables were independently related to knee flexion excursion and were physiologically meaningful when modelled together, they were included in the linear regression model.

No significant relationships were observed between knee flexion excursion and quadriceps force control ( $p = 0.12$ ), rectus femoris activation ( $p = 0.09$ ), lateral hamstring activation ( $p = 0.82$ ), medial gastrocnemius activation ( $p = 0.48$ ), age at the time of testing ( $p = 0.68$ ), BMI ( $p = 0.90$ ), sex ( $p = 0.79$ ), level I or II sports participation ( $p = 0.32$ ), limb dominance ( $p = 0.63$ ), grade III or IV chondral injury ( $p = 0.57$ ) or meniscal surgery at the time of ACLR ( $p = 0.85$ ). The bivariate relationships between knee flexion excursion and continuous predictor variables are presented in Table 5.3.



**Table 5.3** Bivariate relationships between candidate predictor variables (continuous data) for the regression analysis for knee flexion excursion in the ACLR group. Values are Pearson product moment correlation coefficients

Variables	Knee flexion excursion	Quadriceps strength	Vastus medialis activation	Vastus lateralis activation	Rectus femoris activation	Medial hamstrings activation	Lateral hamstrings activation	Medial gastrocnemius activation	Age at time of testing	Body mass index
Quadriceps strength	0.26*	-	-	-	-	-	-	-	-	-
Vastus medialis activation	-0.55**	-0.07	-	-	-	-	-	-	-	-
Vastus lateralis activation	-0.40**	-0.03	0.54**	-	-	-	-	-	-	-
Rectus femoris activation	-0.21	-0.12	0.36*	0.44**	-	-	-	-	-	-
Medial hamstrings activation	0.49**	0.03	-0.26*	-0.20	-0.12	-	-	-	-	-
Lateral hamstrings activation	-0.03	-0.20	0.05	0.01	-0.01	0.39*	-	-	-	-
Medial gastrocnemius activation	-0.09	0.00	-0.07	-0.03	-0.11	-0.11	0.17	-	-	-
Age at time of testing	-0.05	-0.20	0.01	0.12	0.10	-0.16	0.05	-0.19	-	-
Body mass index	0.02	-0.10	-0.02	0.24	0.02	0.10	-0.15	-0.08	0.01	-
Anterior knee joint laxity	-0.32**	-0.03	0.05	-0.03	0.07	-0.24	0.05	0.03	0.00	-0.26

Knee flexion excursion = the difference in degrees between the peak knee flexion angle and knee flexion angle at initial ground contact (Miranda *et al.*, 2013); Quadriceps strength was normalised to body mass (Nm/kg); muscle activation variables are mean linear envelope EMG in the 100 millisecond window prior to initial ground contact (see Study 2, Chapter 4); body mass index = kg/m<sup>2</sup>; anterior knee laxity = KT-1000 side-to-side difference in millimetres

\*  $p < 0.05$ ; \*\*  $p < 0.01$

### *Predictors of knee flexion excursion*

Quadriceps strength relative to body mass, anterior knee joint laxity, preparatory vastus medialis and vastus lateralis activation and preparatory medial hamstring activation explained 54% of the variance in knee flexion excursion during the landing phase of the hopping task (average adjusted  $R^2 = 0.54$ ). Although vastus lateralis activation was significantly associated with knee flexion excursion in the bivariate analysis, within the multivariate model it was not a significant predictor of knee flexion excursion ( $p = 0.28$ ). Furthermore, the omission of vastus lateralis activation from the model did no change the  $R^2$  value of the model (average adjusted  $R^2 = 0.54$ ). Hence, vastus lateralis activation was omitted from the model.

An interquartile increase in quadriceps strength relative to body mass was associated with an average  $2^\circ$  increase in knee flexion excursion ( $p = 0.02$ ); however, an interquartile (19%) increase in vastus medialis activation prior to landing was associated with an average  $3.4^\circ$  decrease in knee flexion excursion. The opposite direction of association was observed for medial hamstring activation; that is, participants who activated their medial hamstrings at 81% (the 75% percentile) of their maximum activation prior to landing were predicted to use  $2.1^\circ$  more knee flexion excursion than participants who activated their hamstrings at 42% (the 25<sup>th</sup> percentile).

The only non-neuromuscular variable that was significantly associated with knee flexion excursion was anterior knee joint laxity. ACLR participants at the 75<sup>th</sup> percentile of anterior knee laxity were predicted to use  $1.7^\circ$  less knee flexion excursion during the landing phase of the hopping task than individuals at the 25<sup>th</sup> percentile (95% confidence interval 0.2 to 3.1,  $p < 0.02$ ). The regression coefficients and  $p$  values for quadriceps strength relative to body mass, vastus medialis activation, medial hamstring activation and anterior knee joint laxity as predictors of knee flexion excursion are summarised in Table 5.4.

**Table 5.4** Predictors of the knee flexion excursion in the ACLR group with interquartile range regression coefficients and p values. The model was powered to include a maximum of six predictor variables.

Predictor variables	Median of variable (25 <sup>th</sup> and 75 <sup>th</sup> percentiles)	Regression coefficient (95% CI)	p value
Quadriceps strength relative to body mass (Nm/kg)	1.8 (1.3, 2.4)	2.0 (0.3, 3.6)	0.02*
Vastus medialis activation §	28.5 (19.1, 38.0)	-3.4 (-4.9, -2.0)	0.004**
Medial hamstring activation §	61.5 (42.2, 81.6)	2.1 (0.7, 3.5)	0.001**
Anterior knee joint laxity (KT-1000 difference in mm)	2.6 (0.7, 4.0)	-1.7 (-3.1, -0.2)	0.02*

The dependent variable knee flexion excursion (degrees) = the difference between peak knee flexion angle and the knee flexion angle at initial ground contact. Quadriceps strength was determined during maximum voluntary isometric contraction (see Chapter 4, Section 4.5.6) and normalised to body weight in kilograms (Nm/kg)

§ Muscle activation values (% of MVIC) represent the mean linear envelope in the 100 millisecond window prior to initial ground contact, normalised to the larger of either the mean linear envelope EMG value recorded during the MVIC (Study 2, Chapter 4), or the mean linear envelope value recorded after ground contact (Palmieri-Smith *et al.*, 2009).

Regression coefficients represent the difference in knee flexion excursion of individuals at the 75<sup>th</sup> to the 25<sup>th</sup> percentile of each predictor variable. For example, participants at the 75<sup>th</sup> percentile of quadriceps strength (2.42 Nm/kg) would have an average of 2° more knee flexion excursion than participants at the 25<sup>th</sup> percentile of quadriceps strength (1.35 Nm/kg).

\*  $p < 0.05$ ; \*\*  $p < 0.01$

### *Evaluation of regression model*

*Assumptions of linear regression:* Tolerance (range 0.86 to 0.99) and variance inflation factor (range 1.00 to 1.14) were within acceptable limits, indicating that the findings of the model were not affected by collinearity or model under-fitting (O'Brien, 2007). Standardised residuals demonstrated normality, linearity and homoscedasticity and the model was deemed to be valid in terms of these assumptions.

*Sensitivity analysis:* Imputed EMG data were included in the final model; hence a sensitivity analysis was performed. Little's  $\chi^2$  test confirmed that missing EMG data were missing completely at random ( $p = 0.08$ ). The average adjusted  $R^2$  value derived from the imputed dataset ( $R^2 = 0.54$ ), was similar to that of the  $R^2$  value derived from the original dataset ( $R^2 = 0.53$ ). The unstandardized regression coefficients and standard errors derived from the imputed data set were smaller than those derived from the original data (see Appendix 6). The estimate for quadriceps strength from the imputed

dataset was considerably *smaller* than from the original data (percentage difference 21.5%), indicating that the regression coefficient for quadriceps strength may have been more conservative than anticipated. However, more conservative estimates were deemed to be preferable to inflated estimates; hence, the imputed dataset and results were retained (Harrell, 2001).

## **5.7 Discussion**

### **5.7.1 Overview**

To the author's knowledge, this is the first study to use a single leg landing task with a standardised approach velocity to investigate kinematic, kinetic and neuromuscular adaptations following ACLR. Furthermore, this is the first study to investigate the multivariate associations between both neuromuscular and non-neuromuscular variables and knee flexion excursion in single leg landing after ACLR.

The main findings of the study were that 1) ACLR participants demonstrated smaller knee flexion excursion, smaller knee extension moments and greater peak trunk flexion angles during landing, and 2) smaller knee flexion excursion was associated with lower levels of quadriceps strength relative to body mass, greater anterior knee joint laxity, lower levels of preparatory vastus medialis activation and greater preparatory medial hamstring activation. This study has added new knowledge to the existing body of ACLR literature by neuromuscular variables and participant characteristics that are associated with smaller knee flexion excursion, which is a common observation following ACLR (see Section 2.4.3). A detailed discussion of the findings of the study follows.

### **5.7.2 Knee kinematics**

Supporting hypotheses 1a and 1b, the ACLR group demonstrated significantly smaller peak knee flexion angles and knee flexion excursion compared to the control group. The ACLR group not only demonstrated smaller peak knee flexion angles but also smaller knee flexion angle at initial ground contact. The smaller knee flexion excursion therefore represented a shift towards more extended knee angles throughout the entire landing phase.

Previous research in ACLR (Miranda *et al.*, 2013) and control populations (Podraza & White, 2010) has found that reduced knee flexion excursion is associated with reduced knee flexion angles at knee at the point of peak vertical GRF (Miranda *et al.*, 2013; Podraza & White, 2010). Reduced knee flexion angle at peak vertical GRF is associated with a greater risk of ACL graft re-injury (Paterno *et al.*, 2010) and over time, this adaptation may also affect the structural integrity of knee joint cartilage by contributing to higher joint contact pressures (Chaudhari *et al.*, 2008; Scanlan *et al.*, 2013). Hence, the knee flexion kinematics observed in the ACLR group may have important implications for patients following ACLR who return to activities that involve single leg landings.

Smaller peak knee flexion compared to uninjured subjects, or compared to the contralateral side, has previously been reported in groups of patients with ACLR during the stance phase of walking (Hart *et al.*, 2010; Lewek *et al.*, 2002) and single leg landing tasks (Deneweth *et al.*, 2010; Gokeler *et al.*, 2010; Orishimo *et al.*, 2010; Xergia & Pappas, 2013). Interestingly, a smaller peak knee flexion angles during walking are observed for individuals with knee OA (McCarthy *et al.*, 2013). It is unknown whether the reduction in knee flexion movement was a response, or part of the aetiology of knee OA (McCarthy *et al.*, 2013).

Likewise, in this study, it is unclear whether ACLR is causative of reduced knee flexion movement or a trait of the ACLR group. In a recent prospective investigation, (Goerger *et al.*, 2014) assessed the lower limb biomechanics of individuals before ACL injury and after ACLR. In this study, ACLR participants demonstrated smaller hip and knee flexion angles during a jump landing task than they did prior to ACL injury. These findings provide some evidence that ACL injury and ACLR may be causative of the reduced knee flexion angles that were observed in the current study.

Understanding the associations between muscle activation and knee kinematics may inform the development of improved rehabilitation strategies after ACLR. However, the muscle activation strategies of the thigh and leg may be affected by the kinematic and kinetic variability in the trunk, hip or ankle (Nyland *et al.*, 2010). Therefore, the following section discusses the comparisons of the trunk, hip, knee and ankle biomechanics of the ACLR and control groups.

### 5.7.3 Kinematic and kinetic deficits within the closed kinetic chain

Supporting hypothesis 1e, significantly greater peak trunk flexion angle was observed in the ACLR group. This finding is consistent with previous investigations that have assessed trunk kinematics during single leg landing tasks after ACLR (Ernst *et al.*, 2000; Oberländer *et al.*, 2012a). Greater peak trunk flexion in landing has previously been associated with smaller peak GRF and smaller knee flexion angles in healthy individuals (Shimokochi *et al.*, 2013) and with smaller knee extensor moments in individuals following ACLR (Oberländer *et al.*, 2012a).

Trunk flexion after ground contact may be a mechanism by which individuals reduce GRF and transfer loads away from the knee joint following ACLR (Oberländer *et al.*, 2012a). Based on previous investigations, the reduced knee flexion excursion observed in the ACLR group would be expected to be associated with greater GRF and ACL forces (Kulas *et al.*, 2011; Shimokochi *et al.*, 2013). In this study, no significant differences in peak GRF were observed between the ACLR and control groups, despite the ACLR group demonstrating significantly less knee flexion excursion. The greater trunk flexion demonstrated by ACLR participants may have been a compensatory mechanism to reduce the GRF and ACL forces that would normally increase as knee flexion excursion decreases (Kulas *et al.*, 2011; Laughlin *et al.*, 2011; Oberländer *et al.*, 2012a).

Contrary to hypothesis 1f, the ACLR group did not demonstrate significantly greater peak hip flexion angles than the control group. Greater peak hip flexion angles have previously been observed for individuals following ACLR compared to uninjured individuals during vertical drop landings (Vairo *et al.*, 2008). However, previous studies have found no difference between ACLR and control groups in peak hip flexion angles during the landing phase of single leg hopping tasks (Gokeler *et al.*, 2010; Xergia & Pappas, 2013). It is possible that due to the forward momentum of their centre of gravity, individuals following ACLR are unable to compensate for deficits in knee flexion excursion by increasing their peak hip flexion angle, and may instead compensate by increasing their peak trunk flexion (Oberländer *et al.*, 2012a).

Supporting hypotheses 1g, ACLR participants demonstrated significantly smaller peak ankle dorsiflexion angles than control participants. However, contrary to hypothesis 1j, ACLR participants demonstrated significantly smaller peak ankle plantarflexor moments. In athletic populations, smaller peak ankle dorsiflexion angles and smaller peak ankle plantarflexor moments have been associated with reduced knee flexion angles (Norcross *et al.*, 2010). In this study, smaller knee flexion excursion may have necessitated a reduction in peak ankle dorsiflexion angle and a concomitant decrease in peak ankle plantarflexor moment, as knee flexion and ankle dorsiflexion movement in landing tasks are closely related (DeVita & Skelly, 1992; Gokeler *et al.*, 2010).

Another possible explanation for the differences in peak ankle dorsiflexion angle and plantarflexor moment observed between the ACLR and control groups is related to differences in muscle activation and musculotendinous stiffness prior to, or during landing. Individuals following ACLR have been shown to have higher levels of lower limb musculotendinous stiffness in their involved limb compared to recreationally active control subjects during single leg hopping (Bryant *et al.*, 2008b). The ankle plantarflexors have been shown to provide the largest contribution to the regulation of musculotendinous stiffness in the lower limb during hopping (Farley & Morgenroth, 1999). Greater musculotendinous stiffness of the plantarflexors, combined with greater trunk flexion, may have allowed ACLR participants to reduce their knee flexion and ankle dorsiflexion angles without increasing GRFs (DeVita & Skelly, 1992). Smaller peak ankle dorsiflexion angles and peak ankle plantarflexor moments may therefore be a part of an overall pattern of mal-adaptive compensatory movement and altered joint loading that persists after ACLR (Ernst *et al.*, 2000).

Contrary to hypothesis 1h, no significant difference in peak hip extensor moment was observed between the groups. During the landing phase of the hop for distance test, greater hip extensor moments may allow individuals following ACLR to compensate for reduced knee extensor moments and knee flexion excursion by transferring forces proximally (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010). However, the combination of a dynamic take-off and sub-maximal hop distance used in this study meant that participants landed with forward momentum from the walking approach which had to be attenuated upon landing. The forward momentum of the body and reduced knee

flexion excursion may have reduced the capacity of the hip joint to contribute to the landing, instead facilitating greater compensatory trunk flexion (Oberländer *et al.*, 2012a; Phillips & van Deursen, 2008).

Supporting hypothesis 1i, significantly smaller knee extensor moments were observed in the ACLR group. Smaller peak knee extensor moments in landing have previously been associated with greater peak trunk flexion angles (Oberländer *et al.*, 2012a) and a more anterior position of the contralateral limb (Gokeler *et al.*, 2010). Greater trunk and contralateral lower limb flexion result in a more anterior GRF vector with respect to the ipsilateral knee joint axis, resulting in a reduced knee extensor moment (Gokeler *et al.*, 2010; Oberländer *et al.*, 2012a). In contrast, the more upright posture demonstrated by control participants may explain the significantly larger knee extensor moments observed in this group (Shimokochi *et al.*, 2013).

#### **5.7.4 Predictors of knee flexion excursion following ACLR**

##### *Overall model findings*

Considering that only four candidate predictor variables were included in the multivariate model, the model explained a relatively large amount of the variance ( $R^2 = 0.54$ ) in knee flexion excursion, when compared to the model reported in Study 2, which explained only 42% of the variance in quadriceps force control. The relationships that were identified between the predictor variables and knee flexion excursion are potentially complex and have important clinical implications. Therefore, a discussion of these associations is presented below.

##### *Quadriceps strength relative to body mass*

In support of hypothesis 2a, a lower level of quadriceps strength relative to body mass was significantly associated with smaller knee flexion excursion in both the bivariate and multivariate analyses. This finding is consistent with previous studies; for example, quadriceps strength deficits after ACLR are associated with smaller peak knee flexion angles in both walking and jogging (Morrissey *et al.*, 2004). At the group level, individuals following ACLR with quadriceps strength deficits have been found to use smaller peak knee flexion angles in walking compared to those with greater quadriceps strength (Lewek *et al.*, 2002). Due to the cross-sectional nature of this study, it is



unclear whether individuals with impairments in quadriceps strength had adapted to these impairments by reducing their knee flexion excursion, or whether reduced knee flexion excursion, over time, contributes to quadriceps weakness. Nonetheless, these findings provide further evidence of the association between quadriceps strength deficits and quality of movement after ACLR.

Most previous studies that have investigated the relationship between quadriceps strength and lower limb kinematics after ACLR have chosen to assess isokinetic, rather than isometric quadriceps strength. Furthermore, most studies have presented quadriceps strength as a ratio of the unaffected side (Bryant *et al.*, 2008b; Eitzen *et al.*, 2009; Logerstedt *et al.*, 2012c; Schmitt *et al.*, 2012). In this study, body weight normalised isometric quadriceps strength was used instead of isokinetic strength as a ratio of the uninvolved side, because 1) it was not possible to assess both isometric and isokinetic quadriceps strength in Study 2 (see Section 4.5.5) and 2) the aim of the study was to determine the neuromuscular mechanisms of knee flexion kinematics within the involved limb (Shultz *et al.*, 2009).

The findings of this study indicate that individual differences in body weight normalised quadriceps strength are associated with knee flexion excursion in landing after ACLR. These findings suggest that consideration should therefore be given to both the symmetry and absolute level of quadriceps strength relative to body mass when assessing the implications of quadriceps strength on knee biomechanics after ACLR.

#### *Quadriceps force control*

Contrary to hypothesis 2b quadriceps force control was not significantly associated with knee flexion excursion. It is possible that differences in the intensity of the task used to assess quadriceps force control in Study 2 (see Section 4.5.5) and the landing task used in this study contributed to the lack of association between the variables. The lack of association could also be attributed to the assessment of quadriceps force control with an open kinetic chain task, which isolated force production to the quadriceps muscle. Closed kinetic chain landing tasks involve most, if not all, muscle groups within the trunk and lower limb; hence, the accuracy of force output during a more functional,

closed kinetic chain force matching task may be significantly related to knee flexion excursion (Madhavan & Shields, 2011).

### *Muscle activation strategies*

In support of hypothesis 2c, greater preparatory vastus medialis and vastus lateralis activation were associated with smaller knee flexion excursion. However, contrary to hypothesis 2c, greater rectus femoris activation was not significantly associated with knee flexion excursion. Due to the finding that the addition of vastus lateralis activation to the multivariate model did not increase the  $R^2$  value and was not a significant predictor of knee flexion excursion within the model, only vastus medialis activation was included in the model. However, both variables demonstrated moderate bivariate correlations with knee flexion excursion. These findings are consistent with those of previous ACLR studies using comparable populations (Bryant *et al.*, 2009b; Gokeler *et al.*, 2010; Vairo *et al.*, 2008). Greater preparatory vastus medialis and vastus lateralis activation may represent a neuromuscular feed-forward response whereby the knee joint is stiffened prior to landing, in anticipation of the considerable knee extensor moments that occur in landing (Bryant *et al.*, 2009b; Gokeler *et al.*, 2010).

Atrophy of the quadriceps occurs rapidly after ACL rupture (Williams *et al.*, 2005a). Although it was not assessed in this study, greater activation of the vastus medialis and vastus lateralis muscles may have been adaptation which allowed some ACLR participants to generate sufficient knee extensor muscle force in light of ongoing quadriceps atrophy (Williams *et al.*, 2005a). Greater preparatory vastus medialis and vastus lateralis activation may also have increased the musculotendinous stiffness of the quadriceps prior to landing, allowing some ACLR participants to perform the task successfully, albeit with reduced knee flexion excursion (Swanik *et al.*, 1999). Quadriceps activation prior to landing may also result in a more extended knee during the flight phase of the hop, which could help to explain the more extended knee angles that were observed at initial contact in the ACLR group.

Vastus medialis is also an important medial stabiliser of the patellofemoral and tibiofemoral joints, and is particularly affected by the quadriceps atrophy that is associated with ACL injury and ACLR (Stockmar *et al.*, 2006). Recreational athletes participating in lower levels of sport have been found to use greater activation of vastus

medialis during forward hopping compared to higher level athletes (Nyland *et al.*, 2013). This observation is believed to be an adaptation that protects the knee from potential episodes of instability by increasing tibiofemoral compressive forces; however, it may also result in greater knee joint compressive forces (Nyland *et al.*, 2013).

It was anticipated that greater hamstring coactivation would be associated with smaller knee flexion excursion. However, contrary to hypothesis 2d, higher levels of medial hamstring activation were associated with larger, rather than smaller knee flexion excursion, and contrary to hypothesis 2d, lateral hamstring activation was not associated with knee flexion excursion. Interestingly, it was the medial thigh muscle (vastus medialis and the medial hamstrings) that were significantly associated with reduced knee flexion excursion in the multivariate model. Although it was not assessed in this study, it is possible that greater preparatory medial thigh muscle activation in landing following ACLR is an adaptation that prepares the knee joint for the considerable knee abduction moments that occur following ground contact (Besier *et al.*, 2003; Hewett *et al.*, 2005; Nyland *et al.*, 2013). Such changes in muscle activation may help to explain the three-dimensional reduction in knee movement observed in the ACLR group (Scanlan *et al.*, 2010; Tashman *et al.*, 2007).

Altered medial hamstring activation may be an ongoing mal-adaptive response to the procurement of the ACL graft from the semitendinosus and gracilis tendons (Ingersoll *et al.*, 2008). Previous studies have demonstrated that the semitendinosus and gracilis tendons may take 1-3 years to regenerate after ACLR and that graft procurement may alter the moment arm of the semitendinosus muscle (Carofino & Fulkerson, 2005). Such a change in muscle morphology may mean that greater motor unit activation would be required to generate equivalent amounts of muscle force (Árnason *et al.*, 2014). This notion is consistent with the significantly lower levels of hamstring strength relative to body mass observed in the ACLR group in Study 2 (see Section 4.6.2).

Contrary to hypothesis 2d, preparatory medial gastrocnemius activation was not associated with knee flexion excursion. The hopping task used in this study was novel in that it required participants to arrest the momentum that was generated by the walking approach. Hence, it was anticipated that individuals who demonstrated mal-

adaptive landing strategies, such as smaller knee flexion excursion and greater peak trunk flexion angle, would require greater medial gastrocnemius activation in order to control this momentum and stabilise their centre of mass (Oberländer *et al.*, 2012a). Conversely, lower levels of medial gastrocnemius activation prior to and during landing may be a positive adaptation that serves to reduce pathological medial knee joint loads; that is, arthrogenic muscle inhibition (Nyland *et al.*, 2010).

The lack of association found in this study between gastrocnemius activation and knee flexion excursion may be related to the timing of its measurement (i.e. prior to ground contact) and the fact that gastrocnemius EMG was normalised to the peak activation during the task rather than MVIC (see Section 5.5.7). Furthermore, given the anterior knee laxity observed within the ACLR group, the magnitude of medial gastrocnemius activation around the time of peak ground reaction force may have been more strongly associated with knee biomechanics, given the greater need for muscular stabilisation of the knee joint at this time-point for individuals with greater knee joint laxity (Klyne *et al.*, 2012).

#### *Sports participation and participant characteristics*

Women have been found to perform single leg landing tasks with smaller knee flexion excursion than men (Miranda *et al.*, 2013). However, contrary to hypothesis 2e, sex was not significantly associated with knee flexion excursion in this study. The lack of association between sex and knee flexion excursion could be explained by the finding that no significant relationship was observed between sex and quadriceps strength relative to body mass. Women, on average, have lower levels of body weight normalised strength because they possess a lower proportion of lean body mass than men for the same body weight (Shultz *et al.*, 2009). Because of this relative disadvantage, it was anticipated that women would be required to activate their quadriceps at higher levels than men during landing. Given the hypothesised association between quadriceps activation, quadriceps strength and knee flexion excursion, it was expected that female sex would also be associated with reduced knee flexion excursion (Miranda *et al.*, 2013).

The lack of significant association between sex and knee flexion excursion could also be related to variability in the level of sports participation within the group. Although

level of sports participation was not independently associated with knee flexion excursion, participants of either gender who regularly participate in sports which involve single leg landings, such as basketball, or who have greater experience in performing hopping tasks, may have learned to increase their knee flexion excursion in order to improve landing performance.

An important finding from this study was that greater anterior knee joint laxity was associated with smaller knee flexion excursion. Previous studies have found that greater anterior knee laxity is not correlated with knee flexion excursion during the stance phase of walking (Eastlack, 1999; Gokeler *et al.*, 2003). The conflicting findings of this study and previous studies may be related to the greater demands placed on the neuromuscular system and knee joint during single leg landing tasks compared to walking (Kiapour *et al.*, 2014). Specifically, single leg landing tasks involve an abrupt impact and deceleration which may place greater demands on joint structures and the ACL graft (Bryant *et al.*, 2009b; Laughlin *et al.*, 2011).

In this study, ACLR participants landed with their knee in a more extended position at initial ground contact. More extended knee positions in single leg landings are associated with greater anterior tibial translation in uninjured subjects (Podraza & White, 2010). Moreover, after ACLR, more extended knee angles at initial ground contact, combined with greater levels of anterior knee joint laxity, may increase the need for mal-adaptive thigh muscle activation and compressive forces to maintain dynamic joint stability (Boeth *et al.*, 2013; Kiapour *et al.*, 2014). These adaptations may have implications for knee joint function and the risk of future knee OA.

The menisci are important secondary stabilizers of the knee joint (Thorlund *et al.*, 2014); hence, it was anticipated that a history of meniscal instability may influence the associations between other predictor variables and knee flexion excursion. However, contrary to hypothesis 2e, meniscal surgery at the time of ACLR was not associated with reduced knee flexion excursion. It is possible that the method of assessing meniscal injuries (those who did or did not require meniscal surgery at the time of ACLR) was not sensitive enough to allow this association to be found. Likewise, the small number of participants with grade III or IV chondral injuries (n = 7, 11%) may have contributed to the non-significant relationship between this variable and knee

flexion excursion (Harrell, 2001). On the other hand, chondral injuries are associated with a reduction in the tolerance of knee joint cartilage to higher compressive forces and it is possible that a history of chondral and/or meniscal injury is associated with knee kinematics during tasks that involve greater shear or impact forces (Dye, 1998).

The sub-maximal intensity of the landing task may also have contributed to the lack of association between ACL-RSI score and knee flexion excursion. To the author's knowledge, this is the first study to investigate the relationship between the psychological response to returning to sport and a specific biomechanical variable. It is possible that some ACLR demonstrated smaller knee flexion excursion despite having high ACL-RSI scores because of other factors such as quadriceps strength deficits, knee joint laxity or altered muscle activation strategies.

## **5.8 Summary**

### **5.8.1 Overview and clinical implications**

To the author's knowledge, this is the first study to investigate the multivariate associations between knee kinematics, neuromuscular variables and participant characteristics after ACLR. The findings of this study have contributed to a greater understanding of the mechanisms of kinematic adaptations after ACLR. The use of a novel, standardised hopping task allowed comparisons of kinematics, kinetics and muscle activation to be made between individuals with different physical characteristics and levels of sports participation, by reducing variability in the performance of the task (Swearingen *et al.*). The recruitment of a larger sample of ACLR participants allowed a number of important variables to be included in the analysis that would not have otherwise been accounted for; such as anterior knee joint laxity.

The association that was found between knee joint laxity and knee flexion excursion is consistent with the findings of Study 2, where anterior knee laxity was negatively associated with quadriceps force control. Individuals with side-to-side differences in anterior knee laxity greater than 3 mm are often excluded from biomechanical investigations (see Section 2.3.4). The exclusion of these individuals has contributed to a lack of understanding of the associations between knee laxity, muscle activation and

movement patterns. Although further research is required to establish the prospective associations between knee laxity and knee flexion excursion, the findings of this study suggest that individuals with ACLR with greater ACL graft laxity may require more specialised rehabilitation to normalise knee joint kinematics compared to individuals who do not have increased laxity. Clinicians prescribing interventions such as landing re-training to improve knee joint kinematics for patients following ACLR should consider the potential impact of increased anterior knee joint laxity on movement strategies and muscle activation patterns. Landing re-training may be most effective when combined with interventions such as perturbation training, which is known to improve mal-adaptive muscle activation patterns following ACLR (Hartigan *et al.*, 2009). Further prospective research is required to confirm these hypotheses.

The multivariate associations observed between quadriceps strength relative to body mass, anterior knee laxity, thigh muscle activation strategies and knee flexion excursion indicate that greater anterior knee joint laxity may be associated with quality of movement in more demanding tasks. Knee flexion excursion deficits after ACLR have previously been found to be modifiable through neuromuscular training (Hartigan *et al.*, 2009; Myer *et al.*, 2008) and verbal instruction (Tsai & Powers, 2013). Therefore, the findings of this study have implications for the design of prospective research; for example, the effectiveness of neuromuscular training programs to improve knee kinematics after ACLR.

### **5.8.2 Limitations**

In addition to the limitations discussed in Studies 1 and 2, there are several limitations to this study:

1. Individuals with ACLR who were aged less than 18 years or greater than 50 years at the time of testing were excluded from the study. Hence, these participants may not have been a truly random sample of the ACLR population and care should be taken when generalizing the findings to all patients following ACLR.
2. The analysis was limited mainly to peak sagittal plane joint moments and joint angles. Knee adduction and internal rotation moments may have important implications for knee joint loading and post-traumatic osteoarthritis (Palmieri Smith,

2009). Frontal and transverse plane knee joint moments derived from jumping and countermovement tasks are commonly analysed in biomechanical research (Breen *et al.*, 2014; Delahunt *et al.*, 2012c; Paterno *et al.*, 2010). However, the impact phase of the hopping task precluded the use of these variables in this study. Despite this limitation, sagittal plane joint moments may still have important functional implications after ACLR; for example, smaller knee extensor moments in drop vertical jump tasks are associated with a greater risk of ACL graft rupture (Paterno *et al.*, 2010).

3. The analysis was limited to the landing phase of the hopping task. Neuromuscular adaptations may also be present in the propulsion phase (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010; Xergia & Pappas, 2013) and stabilisation phase of landing tasks (Oberländer *et al.*, 2012a). The multivariate analysis was limited to one dependent variable and to the ACLR group; hence, it is unknown whether muscle activation is related to other biomechanical adaptations and whether the results are also generalisable to the control group.
4. It is possible that the significantly greater BMI of the ACLR group contributed to the smaller peak knee extensor and peak ankle plantarflexor moments that were observed in the ACLR group, considering that greater BMI was related to smaller peak knee extensor and peak ankle plantarflexor moments (see Section 5.6.2).
5. Previous investigations evaluating muscle activation strategies after ACL injury and ACLR have expressed muscle coactivation as an index, whereas in this study, muscle activation was reported for each muscle group for the ACLR limb only. Using this approach, the relative activation of muscle groups as a proportion of the contralateral side or as an index of their antagonist is unclear. However, the use of a coactivation index is also problematic, as it is unclear whether higher values are a result of higher activation of the agonist or lower values of the antagonist (e.g. the quadriceps and hamstrings). Furthermore, the medial and lateral thigh muscle groups may have different levels of activation during single leg landing tasks (Nyland *et al.*, 2014). A flexor/extensor coactivation index would require either calculating an average measure of quadriceps and hamstring activation, or the reporting of separate indexes between individual muscle groups (e.g. vastus lateralis and medial gastrocnemius, medial hamstring and vastus medialis). For the purposes of this study, it was decided that the absolute level of muscle activation would



provide a more understandable and informative interpretation of muscle activation (Shultz *et al.*, 2009).

6. Gastrocnemius MVIC was not assessed; hence, gastrocnemius EMG was normalised to the highest value obtained during the landing task, rather than MVIC. The difference in normalisation for gastrocnemius may have contributed to the lack of significant association with knee flexion excursion.
7. The period of the landing from initial contact to peak knee flexion involved an abrupt deceleration of the tibia, necessitating a powerful eccentric contraction of the quadriceps, soleus and gluteus maximus muscles (Bryant *et al.*, 2009b; Gokeler *et al.*, 2010). Hence, measures of quadriceps power, rather than isometric strength, may have been more closely associated with knee flexion excursion. Furthermore, assessing the activation of the soleus and gluteus maximus muscles may have provided greater insight into the muscle activation strategies associated with knee kinematics. The rapid acceleration of the tibia could be measured using accelerometry, which could measure the high-frequency acceleration of the tibia directly. This method would avoid the problem of low-pass filtering and high frequency GRF data discussed earlier and may be associated with altered muscle activation prior to ground contact (Bryant *et al.*, 2009b). This is an area for future research.
8. The use of vertical GRF provided a starting point for assessing whether the standardised hop task resulted in similar performance of the task between groups and individuals. However, posterior GRF (i.e., anterior shear force) may be more strongly associated with knee kinetics in hopping tasks (Ali *et al.*, 2012). The posterior ground reaction force has previously been used to estimate shear forces between the femur and tibia that may have helped to predict knee flexion excursion in this population (Sell *et al.*, 2007). It is unknown whether the methods used to standardise the hop task resulted in similar posterior GRF between groups and individuals.
9. Barefoot landings may be less generalizable to sports for which footwear is mandatory and provide differing kinematics/kinetics to landings performed in shoes.
10. EMG variables were not assessed in the control group; hence the reliability of EMG variables was not able to be determined. Furthermore, because no group differences

in EMG variables were possible, it is not known whether quadriceps or hamstring activation was higher in the ACLR group.

11. The relationship between EMG and muscle force is known to be highly non-linear (Alkner *et al.*, 2000; Kouzaki *et al.*, 2004; Woods & Bigland-Ritchie, 1983). Furthermore, the magnitude of muscle activation determined by EMG varies with electrode position, skin impedance and individual task performance (Goodwin *et al.*, 1999). In addition, the force required to generate movement at the knee joint varies with joint position, as the moment arm of the quadriceps and hamstring muscles changes (Bryant *et al.*, 2008a). Future research using musculoskeletal modelling may reveal whether altered kinematics and kinetics after ACLR are associated with changes in estimates of muscle forces (Laughlin *et al.*, 2011).
12. Quadriceps strength was assessed using a maximum voluntary contraction and a burst superimposition technique was not used to determine true maximum muscle activation (Lewek *et al.*, 2004; Snyder Mackler, 1994). It is possible that some participants with ongoing quadriceps muscle inhibition may have appeared to possess larger muscle activation deficits due to a failure to produce their true maximal quadriceps activation during voluntary testing (Shultz *et al.*, 2009).
13. Fatigue of the lower limb muscles has been associated with smaller knee flexion angles and larger hip and knee flexion angles at initial contact during landing tasks (Lucci *et al.*, 2011; Ortiz *et al.*, 2010; Webster *et al.*, 2012b). To account for this potential source of variability the number of trials was limited to five with a maximum of five practice trials. However, different neuromuscular adaptations may have been revealed by conducting the test under fatigued conditions (Webster *et al.*, 2014b).
14. No contralateral leg comparison was included in the study. Due to the cross-sectional study design, it is unclear whether impairments existed before, and were causative of, ACL injury, or whether they are adaptations to ACLR. However, impairments on the contralateral side have been found for quadriceps strength (Hiemstra *et al.*, 2007) and postural control (Howells *et al.*, 2013) at similar time points after ACLR. Therefore if a significant inter-limb difference had been observed it would still be unclear whether the injury and/or subsequent surgery caused the asymmetry or whether the asymmetry was present prior to injury.

15. Anticipated tasks may not accurately reflect the demands of sport and everyday functional activities (Borotikar *et al.*, 2008). Furthermore, the use of a standardised landing task with the arms folded may not reflect functional movement. The use of an unplanned landing task which allows free movement of the upper limbs may reveal associations between EMG and knee kinematics that are not observed during planned tasks (Besier *et al.*, 2001). This is an area for future research.

## **5.9 Conclusions and recommendations**

At an average of 18 months following surgery, individuals following ACLR continue to demonstrate kinematic and kinetic adaptations during single leg landings. These adaptations include smaller knee flexion excursion, greater peak trunk flexion angles and smaller peak knee extensor and ankle plantarflexor moments. Smaller knee flexion excursion after ACLR is associated with lower levels of quadriceps strength relative to body mass, greater anterior knee joint laxity, greater preparatory vastus medialis activation and lower levels of preparatory medial hamstring activation. Age, sex, BMI, level of sports participation, meniscal surgery and grade III or IV chondral injuries at the time of ACLR were not significantly associated with knee flexion excursion in this study; however, these variables are worthy of investigation in future studies, particularly those involving higher-intensity tasks.

The findings of this study have implications for both future research and current clinical practice. Individuals with a combination of greater ACL graft laxity and poor neuromuscular control may require more specialised rehabilitation prior to return to sport. Specifically, interventions such as neuromuscular and landing technique training may improve knee flexion excursion deficits by normalising preparatory thigh muscle activation strategies. Individuals with ACLR who demonstrate knee flexion excursion deficits may benefit from combining these interventions with quadriceps strengthening and sports-specific training. However, prospective research is needed to determine whether improving neuromuscular control following ACLR leads to improved knee function and a reduced risk of knee osteoarthritis.

Collectively, the findings of this study, and those of Study 2 of this thesis, demonstrate that at an average of 18 months following surgery, individuals with ACLR continue to demonstrate significant neuromuscular impairments during both open and closed kinetic chain tasks. The results of the current study have provided insight into variables that predict knee flexion excursion following ACLR. However, it is unclear whether these impairments are associated with knee joint function. Therefore, the final study included in this thesis will examine the relationship between knee joint function and the biomechanical and neuromuscular variables reported in Studies 2 and 3.

## *Chapter 6*

### **Study 4**

#### **The relationship between neuromuscular control and knee function after anterior cruciate ligament reconstruction**

### **6.1 Chapter Overview**

This chapter addresses the primary aim of the thesis; that is, the relationship between neuromuscular control and knee function after ACLR. To address this aim, the multivariate associations between knee joint function and the neuromuscular and biomechanical variables reported in Studies 2 and 3 of this thesis were assessed. Hence, this chapter consists of two parts:

- **Part 1:** The associations between knee joint function and neuromuscular variables derived from open kinetic chain testing (Study 2)
- **Part 2:** The associations between knee joint function and biomechanical/neuromuscular measures derived from closed kinetic chain testing (Study 3)

### **6.2 Introduction**

Functional outcomes after ACLR are variable - particularly amongst recreational athletes (Eitzen *et al.*, 2009; Kostogiannis *et al.*, 2007). Following ACLR, some recreational athletes achieve a level of knee joint function that is acceptable for pivoting and/or landing sports (Feller & Webster, 2013; Thomeé *et al.*, 2012; Zaffagnini *et al.*, 2014). Other athletes fail to return to their previous level of sport (Arderm *et al.*, 2011b), or return to sport with sub-optimal knee joint function (de Jong *et al.*, 2007; Myer *et al.*, 2012). The factors that may predict poor knee function following ACLR are numerous, and include participant characteristics, impairments and biomechanical/neuromuscular variables (Ross *et al.*, 2002). However, few studies have directly investigated the multivariate associations between these variables and knee joint function after ACLR.

The bivariate relationships between neuromuscular control and knee joint function have been investigated in previous studies (Bryant *et al.*, 2008b; Bryant *et al.*, 2009b; Wilk, 1994; Zouita Ben Moussa *et al.*, 2009). These studies provide an important foundation for assessing the convergent validity of neuromuscular and biomechanical variables following ACLR. However, a number of non-modifiable factors, such as age, sex, BMI, level of sports participation, chondral injuries and knee joint laxity, may influence these relationships (see Section 2.3).

Previous investigations of the relationship between knee function and neuromuscular control following ACLR are limited by their small sample sizes and exclusion of important sub-groups of individuals. The exclusion of these sub-groups may make these data less generalizable to the wider ACLR population. For example, some previous studies have excluded women, individuals with lower levels of knee function and individuals with greater anterior knee joint laxity or chondral injuries (see Chapter 2, Section 2.6). The lack of knowledge of the relationship between knee joint function and neuromuscular control following ACLR represents a significant gap in the literature. Better understanding of this relationship will help to explain the variability in knee function that is observed following ACLR and inform the development of more effective interventions to improve knee joint function.

### **6.3 Aims**

Based on this rationale and the overall aims of the study, the aim of this study was to explore the multivariate associations between knee joint function (pass vs fail) following ACLR and the biomechanical/neuromuscular variables reported in Studies 2 and 3.

### **6.4 Hypotheses**

#### **Part 1: Variables derived from open kinetic chain testing (Study 2)**

Based on the current literature and the findings of Studies 1 and 2, the following variables would be significantly associated with worse knee joint function (i.e., greater

odds of failing the battery of functional tests by scoring less than 85% on any one of three hop tests or the CKRS):

- a) Less-accurate quadriceps force production (Lustosa *et al.*, 2011; Williams *et al.*, 2005b)
- b) Greater vastus medialis, vastus lateralis and rectus femoris activation during quadriceps force control testing (Lustosa *et al.*, 2011)
- c) Greater medial (Madhavan & Shields, 2011) and lateral (Lustosa *et al.*, 2011) hamstring activation during quadriceps force control testing
- d) Lower quadriceps strength relative to body mass (Schmitt *et al.*, 2012)
- e) Lower hamstring strength relative to body mass (Hamilton *et al.*, 2008)

### **Part 2: Variables derived from closed kinetic chain testing (Study 3)**

Based on the current literature and the findings of Study 3, the following variables would be significantly associated with worse knee joint function (i.e., greater odds of scoring less than 85% on any one of three hop tests or the CKRS):

- a) Smaller knee flexion excursion (Miranda *et al.*, 2013)
- b) Greater peak trunk flexion angle (Oberländer *et al.*, 2012a)
- c) Greater peak ankle dorsiflexion angle (Gokeler *et al.*, 2010; Orishimo *et al.*, 2010)
- d) Smaller peak knee extensor moment (Xergia *et al.*, 2014)
- e) Smaller peak ankle plantarflexor moment (Orishimo *et al.*, 2010)
- f) Greater preparatory vastus medialis, rectus femoris, vastus lateralis and medial gastrocnemius activation in the 100 milliseconds prior to ground contact (Bryant *et al.*, 2009b; Cordeiro *et al.*, 2014)
- g) Lower levels of preparatory medial and lateral hamstring activation in the 100 milliseconds prior to ground contact (Bryant *et al.*, 2009b; Gokeler *et al.*, 2010)

## **6.5 Methods**

### **6.5.1 Participants**

The participants in this study (n = 66) were described in Studies 1-3 (see Section 3.6). Eligibility criteria and participant characteristics are reported in Tables 3.1 and 3.2 respectively. The inter-session reliability and standard error of measurement of the variables described within this study are reported in Appendix 8.

### **6.5.2 Experimental protocol and data analysis**

Detailed descriptions of the methods used to assess knee function are described in Study 1 (see Sections 3.5.6 and 3.5.7). The methods and data analysis procedures used to assess neuromuscular control in the open and closed kinetic chain are provided in Studies 2 and 3 (see Sections 4.5.4 and 5.4.4).

### **6.5.3 Statistical analyses**

#### *Predictors of knee joint function in the ACLR group*

The statistical methods used to determine variables that were predictive of knee joint function (pass vs fail) were identical to those described in detail in Study 1 (see Sections 3.5.8). The selection of predictor variables for the regression model was determined by assessing the bivariate relationships between knee joint function and candidate predictor variables, as well as subject matter expertise and the findings of Studies 1 - 3 (Harrell, 2001). As described in Study 1, the dependent variable (knee joint function) was a dichotomous (pass vs fail) variable (see section 3.5.7).

Multivariate binary logistic regression analyses were used to quantify the associations between knee function and the neuromuscular and biomechanical variables reported in Studies 2 and 3. As described in Study 1 (see Section 3.5.2) a maximum of three predictor variables were included in the multivariate models. Based on the literature review reported in Chapter 2 (see Section 2.3), the findings of Studies 2 and 3 and the aims of the study, the following neuromuscular variables were candidate predictors of knee joint function (pass vs fail):



### *Part 1*

- a) Quadriceps force control: Average RMSE during the quadriceps force-matching test (see Section 4.5.6)
- b) EMG variables: Average linear envelope EMG values during the quadriceps force-matching test for the vastus medialis, vastus lateralis, rectus femoris, medial hamstrings and lateral hamstrings, normalised to MVIC (see Section 4.5.6)
- c) Quadriceps and hamstring strength relative to body mass (see Section 4.5.6)

### *Part 2*

- a) Kinematic variables: Knee flexion excursion, peak trunk flexion angle, peak ankle dorsiflexion angle (see Section 5.5.7)
- b) Kinetic variables: Peak knee extensor moment and peak ankle plantarflexor moment (see Section 5.5.7)
- c) EMG variables: Preparatory vastus medialis, rectus femoris, vastus lateralis, medial gastrocnemius, medial hamstring and lateral hamstring activation (see Section 5.5.7)

For Part 2, peak hip flexion angle, peak knee internal rotation angle, peak knee abduction angle and peak hip extensor moment were not included in the analysis because these variables were either not significantly different from the control group or the average differences between the ACLR and control groups were smaller than the SEM (see Appendix 8).

Anterior knee joint laxity, age at the time of testing and BMI were significant predictors of knee joint function in Study 1 (see Section 3.6.5) and were therefore included as candidate predictors of knee function in this study. Female sex was not significantly associated with knee function in Study 1 ( $p = 0.18$ ); however, 1) women, on average, have lower levels of quadriceps and hamstrings strength relative to body mass than men (Shultz *et al.*, 2009), and 2) women have been found to use less knee flexion excursion than men during single leg landing tasks (Miranda *et al.*, 2013). Hence, gender may influence the association between knee flexion excursion and knee joint function and was included as a candidate predictor of knee function in this study.

### *Missing data*

As described in Studies 2 and 3, EMG data were missing for six participants. Rather than incur a loss of statistical power and precision, multiple imputation was used to impute the missing values (see Sections 4.5.7 and 5.5.8). Sensitivity analyses were then performed (see Appendix 6) to determine the effect of the data imputation on between-groups differences, regression coefficients and standard errors (Sterne *et al.*, 2009).

### *Logistic regression analyses*

A maximum of three predictor variables identified from bivariate analyses were entered into each logistic regression model and the Nagelkerke  $R^2$  value and the area under the receiver operator curve (AUC) were calculated. If models contained EMG variables (i.e., imputed data), the average adjusted Nagelkerke  $R^2$  value was reported (Heijne *et al.*, 2009; Schafer, 1999).

Interquartile range odds ratios (ORs) with 95% confidence intervals were calculated for the three predictor variables to determine the odds of failing the battery of functional tests (i.e., scoring < 85% on one or more functional measures; see Section 3.5.8). If ORs were < 1, the inverse of the OR was calculated to allow more direct comparison of ORs between predictor variables; in this case, the OR represented the odds of passing the battery of functional tests (Harrell, 2001).

### *Evaluation of regression models*

Tolerance and variance inflation factors were calculated to assess the model for collinearity (Mason & Perreault Jr, 1991; O'Brien, 2007). The linearity, homoscedasticity and normality of the standardised residuals of regression models were assessed using scattergraphs, normal probability plots and histograms (Osborne & Waters, 2002). An *a priori* alpha level of 0.05 was used to determine statistical significance. The Statistical Package for the Social Sciences (SPSS) version 21.0 (Armonk, NY: IBM Corp) was used for all analyses.

## 6.6 Results

### 6.6.1 Part 1: Open kinetic chain predictors of knee joint function (pass vs fail)

#### *Bivariate relationships between candidate predictor variables*

In Study 2, moderate to strong correlations were observed between medial hamstring and lateral hamstring activation ( $r = 0.56$ ,  $p < 0.01$ ) and vastus medialis and vastus lateralis activation ( $r = 0.68$ ,  $p < 0.01$ ) during the force-matching task. Furthermore, moderate correlations were observed between quadriceps force control and all EMG variables, apart from rectus femoris activation (see Section 4.6.3, Table 2.3). As reported in Study 1, a significant bivariate relationship was found between sex and BMI ( $p = 0.03$ ); however, no other significant relationships were observed between the other non-neuromuscular variables (see Section 3.6.5). Despite the presence of statistically significant relationships between some candidate predictor variables, all variables were retained in the analysis because the size of the relationships was below the level set *a priori* for removal of correlated variables ( $r = 0.75$ ).

#### *Bivariate relationships between candidate predictors and knee joint function*

Significant relationships were found between knee function and quadriceps force control ( $p = 0.002$ ) and lateral hamstring coactivation ( $p = 0.02$ ). Considering the potential importance of these variables to the quality of functional movement and knee joint loading (see Sections 4.7.2 and 4.7.3); both variables were included in the logistic regression model. No significant relationships were observed between knee function and vastus medialis activation ( $p = 0.15$ ), vastus lateralis activation ( $p = 0.11$ ), rectus femoris activation ( $p = 0.09$ ) or quadriceps strength relative to body mass ( $p = 0.58$ ). Hamstring strength relative to body mass ( $p = 0.07$ ) and medial hamstring coactivation ( $p = 0.05$ ) trended towards a significant relationship with knee function; however, as these relationships were not statistically significant neither variable was included in the model.

In Study 1, female sex was not associated with knee function ( $p = 0.18$ ). However, differences in hamstring and quadriceps EMG have been observed between men and women during functional tasks (Bencke & Zebis, 2011; Myer *et al.*, 2005a; Zeller *et al.*,

2003). Hence, it is possible that sex could confound the relationship between knee function and hamstring coactivation. Although anterior knee joint laxity was significantly associated with knee function in Study 1 (see Section 3.6.5); sex was included in the multivariate model in place of anterior knee joint laxity because the testing position for the force-matching task was designed to minimize shear forces and strain on the ACL graft (see Section 4.5.4). It was therefore considered more important to account for sex within the model.

#### *Open kinetic chain predictors of knee joint function*

Quadriceps force control, lateral hamstring activation during the quadriceps force matching task and female sex explained 47% of the variance in knee function (average Nagelkerke  $R^2 = 0.47$ ;  $p < 0.001$ , AUC = 0.88;  $p < 0.0001$ ). An interquartile increase in RMSE (i.e., less accurate quadriceps force production) was associated with 4.4 times the odds of scoring less than 85% on at least one functional test and therefore failing the test battery (95% CI 1.7 to 11.4). An interquartile increase in lateral hamstring coactivation was associated with 3.8 times the odds of failing the test battery (95% CI 1.1 to 14.2). Female sex was the strongest predictor of knee function within the multivariate model (IQR OR 5.1, 95% CI 1.0 to 25.7). The interquartile-scaled odds ratios and  $p$  values for quadriceps force control, lateral hamstring activation and sex are summarised in Table 6.1.

**Table 6.1** Open kinetic chain predictors of knee joint function (pass vs fail) in the ACLR group, with interquartile range odds ratios and *p* values (logistic regression model). The model was powered to include a maximum of three predictor variables.

Predictor variables	Median of variable (25 <sup>th</sup> and 75 <sup>th</sup> percentiles)	Odds ratio (95% CI)	<i>p</i> value
Quadriceps force control (RMSE)	2.0 (1.4, 2.7)	4.4 (1.7, 11.4)	0.002**
Average lateral hamstring activation §	2.6 (1.8, 4.6)	3.8 (1.1, 14.2)	0.047*
Female sex †	-	5.1 (1.0, 25.7)	0.044*

Interquartile-scaled ORs represent the odds of failing the battery of functional tests (i.e., scoring < 85% on the CKRS or scoring <85% limb symmetry index on any one of the hop tests).

For continuous variables, ORs represent the difference in odds of failing the battery of knee functional tests for individuals at the 75<sup>th</sup> and the 25<sup>th</sup> percentile of the predictor variable. For example, participants at the 75<sup>th</sup> percentile of RMSE (2.7% MVIC) would have 4.4 times greater odds of failing than participants at the 25<sup>th</sup> percentile (1.4% MVIC; 95% CI 1.06 to 5.46)

† For sex, ORs represent the difference in log odds of failing the battery of functional tests for *women* versus *men*

RMSE = Root mean square error, greater values are indicative of reduced quadriceps force control

§ Represents the average linear envelope EMG value during the quadriceps force matching test relative to the value obtained during maximum voluntary isometric contraction; \* *p* < 0.05; \*\* *p* < 0.01

## 6.6.2 Evaluation of logistic regression model

*Assumptions of logistic regression:* Despite the significant associations found between quadriceps force control and both lateral hamstring activation and sex in Study 2 (see Section 4.6.3), the inclusion of these variables in the regression model did not result in unacceptable collinearity between variables. Tolerance and variance inflation factors were within acceptable limits (Mason & Perreault Jr, 1991; Osborne & Waters, 2002). The standardised residuals demonstrated normality, linearity and homoscedasticity.

*Sensitivity analysis:* As expected, changes to *p* values were small, and smaller standard errors were noted when using the imputed dataset. Moreover, the imputed dataset yielded more conservative estimates than the original data; therefore, these differences were deemed to be acceptable (see Appendix 6). Histograms of the residuals from the analysis using imputed data were normally distributed and demonstrated linearity and homoscedasticity.

### 6.6.3 Part 2: Closed kinetic chain predictors of knee joint function (pass vs fail)

#### *Bivariate relationships between candidate predictor variables*

In Study 3, significant relationships were found between knee flexion excursion and 1) anterior knee joint laxity, 2) preparatory vastus medialis activation and 3) preparatory vastus lateralis activation (see Section 4.6.3). In the current study, significant relationships were found between BMI and peak knee extensor moment ( $r = -0.66$ ) and peak ankle plantar flexor moment ( $r = -0.58$ ). Significant relationships were also observed between knee flexion excursion and peak ankle dorsiflexion angle ( $r = 0.48$ ) and between peak knee extensor moment and peak ankle plantarflexor moment ( $r = 0.56$ ). However, the size of these correlations were below the level set *a priori* for removal of correlated variables ( $r = 0.75$ ).

#### *Bivariate relationships between candidate predictor variables and knee joint function*

Significant relationships were observed between knee joint function and knee flexion excursion ( $p = 0.001$ ) and peak knee extensor moment ( $p = 0.004$ ). Considering the relevance of these variables to the risk of ACL injury and knee joint loading (see Section 2.5.3), both variables were included in the multivariate model. Anterior knee joint laxity was included as the third predictor variable because of its association with knee joint function in Study 1 and because of the potential for anterior knee joint laxity to influence the relationship between knee kinematics/kinetics and knee joint function in functional tasks known to load the ACL (Boeth *et al.*, 2013).

No significant relationships were observed between knee joint function and peak trunk flexion angle ( $p = 0.09$ ) or peak ankle dorsiflexion angle ( $p = 0.45$ ). Likewise, knee function was not significantly related to preparatory rectus femoris ( $p = 0.94$ ), lateral hamstring ( $p = 0.82$ ) or medial gastrocnemius activation ( $p = 0.61$ ). Significant relationships were observed between knee function and peak ankle plantarflexor moment (IQR OR = 2.1,  $p = 0.04$ ) and medial hamstring activation (IQR OR = 2.7,  $p = 0.02$ ). Significant relationships were also observed between knee function and vastus lateralis (IQR OR = 2.0,  $p = 0.04$ ) and vastus medialis activation (IQR OR = 2.3,  $p = 0.04$ ).

### *Closed kinetic chain predictors of knee joint function*

Knee flexion excursion, peak knee extensor moment and anterior knee joint laxity explained 51% of the variance in knee joint function (Nagelkerke  $R^2 = 0.51$ ;  $p < 0.001$ ,  $AUC = 0.86$   $p < 0.0001$ ). Odds ratios for knee flexion excursion and peak knee extensor moment were less than one; therefore, they were expressed as the odds of passing the battery of functional tests. An interquartile increase in knee flexion excursion ( $7.2^\circ$ ) was associated with 2.9 times greater odds of passing (95% CI 1.1 to 7.8). An interquartile increase in knee extensor moment was associated with 4.9 times greater odds of passing the functional test battery. As found in Study 1 (see Section 3.6.5), greater anterior knee joint laxity was significantly associated with greater odds of failing the battery of tests (IQR OR 4.7). The interquartile range ORs and  $p$  values for knee flexion excursion, peak knee extensor moment and anterior knee joint laxity are summarised in Table 6.2.

**Table 6.2** Closed kinetic chain predictors of knee joint function (pass vs fail) in the ACLR group, with interquartile range odds ratios and  $p$  values (logistic regression model). The model was powered to include a maximum of three predictor variables.

Predictor variables	Median of variable (25 <sup>th</sup> and 75 <sup>th</sup> percentiles)	Odds ratio (95% CI)	$p$ value
Knee flexion excursion ( $^\circ$ )	39.8 (36.3, 43.5)	2.9 (1.1, 7.8)	0.03*
Peak knee extensor moment (Nm/kg)	27.8 (22.5, 31.7)	4.9 (1.6, 14.3)	0.004**
Anterior knee joint laxity (mm)	2.6 (0.7, 4.0)	4.7 (1.5, 14.9)	0.009*

Interquartile-scaled ORs represent the odds of failing the battery of functional tests (i.e., scoring  $< 85\%$  on the CKRS or scoring  $< 85\%$  limb symmetry index on any one of the hop tests).

For knee flexion excursion and peak knee extensor moment, ORs represent the odds of *passing* the battery of functional tests.

ORs represent the difference in odds of passing or failing the test battery for individuals at the 75<sup>th</sup> and the 25<sup>th</sup> percentile of the predictor variable. For example, a participant at the 75<sup>th</sup> percentile of knee flexion excursion ( $43.5^\circ$ ); \*  $p < 0.05$ ; \*\*  $p < 0.01$

#### **6.6.4 Evaluation of logistic regression model**

*Assumptions of linear regression:* Tolerance and variance inflation factors were within acceptable limits for all imputations of the dataset, indicating that collinearity between variables was acceptable (Mason & Perreault Jr, 1991; O'Brien, 2007). Standardised residuals demonstrated normality, linearity and homoscedasticity (Osborne & Waters, 2002).

## **6.7 Discussion**

### **6.7.1 Overview**

This study addressed the primary aim of the thesis; that is, to explore the relationship between knee joint function (pass vs fail) and neuromuscular control following ACLR. To achieve this aim, two multivariate regression models were developed, one including open kinetic chain variables and the other including closed kinetic chain variables. The discriminative ability and overall strength of both models was good, indicating that the variables assessed in studies 2 and 3 were useful in explaining the variability observed in knee joint function scores in Study 1.

The main findings of this study were that worse knee joint function (greater odds of failing a battery of knee functional assessments) was associated with; 1) less-accurate quadriceps force production, 2) greater lateral hamstring coactivation during a voluntary quadriceps force matching task, 3) female sex, 4) smaller knee flexion excursion in a hop landing, 5) smaller peak knee extensor moment in hop landing and 6) greater anterior knee joint laxity.

This study has added new knowledge to the existing ACLR literature by quantifying the multivariate associations between knee function and a range of biomechanical and neuromuscular variables derived from open and closed kinetic chain tasks, whilst also accounting for participant characteristics. The relatively large sample size and the use of multivariate regression analyses may make the findings of this study more generalisable to the wider ACLR population than some previous studies (see Section 2.5.3). A detailed discussion of the findings of this study follows:

### **6.7.2 Part 1: Open kinetic chain predictors of knee joint function (pass vs fail)**

#### *Quadriceps force control*

In support of hypothesis 1a, quadriceps force control was significantly associated with knee joint function (i.e. greater odds of scoring less than 85% on one or more of the four knee functional assessments). This finding builds on the findings of (Telianidis *et al.*, 2014), who also found that individuals with ACLR demonstrate less-accurate



quadriceps force production; however, Telianidis *et al.*, (2014) did not explore the relationship between quadriceps force control and knee joint function. In Study 2, large deficits in quadriceps force control were identified in the ACLR group (48% difference; see Section 4.6.2). It was hypothesised that less-accurate quadriceps force production would be associated with worse knee joint function; given that lower levels of knee function following ACLR are associated with greater thigh muscle activation in walking (Lustosa *et al.*, 2011) and thigh muscle activation was a significant predictor of quadriceps force control in Study 1 (see Section 4.6.3).

In Study 2, quadriceps force control was assessed using a challenging open kinetic chain protocol, which involved following a constantly moving target torque. The thigh was also elevated, arguably making it more difficult to produce force accurately (Williams *et al.* 2005). Indeed, participants reported greater difficulty in performing the force matching task with their thigh elevated, compared to having their thigh supported during pilot testing (see Appendix 2). Although closed kinetic chain force matching tasks may more closely resemble functional movements (Kiefer *et al.*, 2013; Madhavan & Shields, 2011; Yosmaoglu *et al.*, 2011), these tasks employ multiple joints and muscles, and the specific contributions of individual muscles are less clear.

An advantage of assessing quadriceps force control in the open kinetic chain is that the variability in force output can be more directly attributed to the quadriceps muscle group. The protocol that was used in this study involved a fluctuating target force which required participants to accurately increase and decrease force, similar to the demands of many functional activities (Madhavan & Shields, 2011). Hence, this task was quite different to constant force matching protocols (Baumeister *et al.*, 2011; Williams *et al.*, 2005b), where the participant may adopt a strategy of augmented coactivation in order to produce a steady force.

Importantly, female sex was a predictor of worse quadriceps force control in Study 2, and was significantly associated with worse knee function in this study. The association between sex and neuromuscular control after ACLR has been investigated extensively in the literature. In general, women demonstrate lower levels of musculotendinous stiffness than men (Cammarata & Dhaher, 2008) and use different muscle activation strategies than men during the same functional tasks (Beaulieu & McLean, 2012).

Therefore, the clinical relevance of the association found between knee function and quadriceps force control is strengthened by the inclusion of gender in the multivariate model. Future research should determine whether less-accurate quadriceps force production is associated with an increased risk of ACL or ACL graft injury in female athletes.

Future prospective research should determine whether impairments in quadriceps force control are a cause or an effect of ACLR injury and reconstruction, and whether a prospective association exists between quadriceps force control and knee joint function. Such research would inform the development of specific rehabilitation techniques to address quadriceps force control impairments, such as neuromuscular and perturbation training (Hartigan *et al.*, 2009; Myer *et al.*, 2005b; Risberg *et al.*, 2007).

#### *Quadriceps activation during quadriceps force control testing*

Contrary to hypothesis 1b, greater levels of vastus lateralis, vastus medialis and rectus femoris activation during the quadriceps force matching test were not associated with knee joint function (pass vs fail). The significantly higher quadriceps activation that was observed in the ACLR group in Study 2 (see Section 4.6.2), and the considerable functional limitations observed in the ACLR group lead to the hypothesis that greater quadriceps activation would be associated with worse knee function. This hypothesis is supported by the literature; for example, greater vastus lateralis activation has previously been associated with reduced quality of movement in walking (Lustosa *et al.*, 2011) and single leg squatting (Madhavan & Shields, 2011).

The lack of association found in this study between quadriceps activation and knee function may be related to the relatively low-intensity (5-30% MVIC) of the quadriceps force matching task. This intensity was specifically chosen to replicate the demands of low-intensity functional tasks such as walking (Besier *et al.*, 2003). During activities that require greater intensities of muscular contraction, such as running and isokinetic strength testing, individuals following ACLR have been found to have *lower* levels of vastus lateralis activation compared to uninjured individuals (Patras *et al.*, 2009). Hence, maximum hopping tasks and the higher-intensity tasks described in the CKRS, may be more strongly associated with muscle activation during similar, high-intensity

tasks (Bryant *et al.*, 2009b). Although quadriceps activation was not related to knee joint function in this study, further research is needed to determine whether greater quadriceps activation at sub-maximal intensities is related to other aspects of knee function, such as walking or activities of daily living.

#### *Hamstring coactivation during quadriceps force control testing*

In support of hypothesis 1c, greater lateral hamstring coactivation during the quadriceps force control task was associated with worse knee joint function (pass vs fail). However, in Study 2, greater lateral hamstring coactivation was associated with better quadriceps force control. Although the neurophysiological mechanisms of these associations are still unclear, it is possible that less-accurate quadriceps force production and greater hamstring coactivation share a common aetiology; that is, they may both be related to neurophysiological changes such as altered cortical activation and altered mechanoreceptor feedback (Baumeister *et al.*, 2008; Kapreli *et al.*, 2009).

Hamstring coactivation during a sub-maximal open kinetic chain task with visual feedback may serve a different purpose than the hamstring coactivation observed during functional tasks. The level of hamstring coactivation during functional tasks is known to be associated with age and learning (Chapman *et al.*, 2008), sex (Myer *et al.*, 2005a) level of expertise (Sigward & Powers, 2006) and the specific demands of tasks (McNitt-Gray *et al.*, 2001). In more demanding functional tasks, particularly for individuals with ACLR who experience subtle knee instability, greater hamstring coactivation may be mal-adaptive, in that it stabilises the knee at the expense of normal knee function (Lustosa *et al.*, 2011). Hence, the relatively high levels of anterior knee laxity within the group (mean 2.3 mm, SD 2.4mm) may have contributed to the association between greater lateral hamstring coactivation and worse knee function.

Contrary to hypothesis 1c, greater medial hamstring coactivation was not associated with worse knee joint function. As discussed in Study 2, the higher levels of medial hamstring coactivation observed in the ACLR group may have been a neuromuscular response to the procurement of the ACL graft from the semitendinosus and gracilis tendons (Árnason *et al.*, 2014; Ristanis *et al.*, 2011). In the current study, it was hypothesized that greater medial hamstring coactivation would impair the performance

of high-intensity tasks, particularly those involving countermovement, and would therefore be associated with worse hopping performance (Vairo *et al.*, 2008). For example, hamstring muscle coactivation during the take-off phase may reduce the force generating capacity of the quadriceps, resulting in impairments in hop distance on the involved limb (Gokeler *et al.*, 2010).

In ACL deficient individuals, an inverse association has been reported between hamstring activation and hamstring stiffness; a measure of the passive resistance of muscle to elongation (McNair & Marshall, 1994). Following ACLR, greater lower limb stiffness in hopping is associated with better knee function (Bryant *et al.*, 2008b). In more demanding functional tasks, such as single leg landings, greater hamstring stiffness and hamstring coactivation may introduce rigidity to the lower limb that helps to stabilise the knee joint and improves functional performance (Arampatzis *et al.*, 2001; Bryant *et al.*, 2009b). Greater hamstring stiffness and coactivation may also improve performance of some open kinetic chain tasks, such as kicking a soccer ball (Cordeiro *et al.*, 2014), or the force matching task used in Study 2 of this thesis.

#### *Quadriceps and hamstring strength*

Contrary to hypothesis 1d, quadriceps strength relative to body mass was not associated with knee function. Previous investigations have found that quadriceps weakness relative to the uninvolved side is related to worse knee function after ACLR (Eitzen *et al.*, 2009; Logerstedt *et al.*, 2012c). Given the significant functional limitations observed in the ACLR group (see Study 1, Section 3.6.2), it was anticipated that quadriceps strength deficits would also be related to worse knee function in this study. The novel elevated testing position, isometric testing protocol and use of body weight normalized strength values, rather than an index of the contralateral side, may have contributed to the lack of association. It is difficult to compare these findings to those of previous ACLR studies because most studies have reported side-to-side differences in isokinetic quadriceps strength (Schmitt *et al.*, 2012; Wilk, 1994; Xergia *et al.*, 2014).

In Study 3, the inclusion of body weight normalized quadriceps strength rather than a LSI in the regression analysis was advantageous, because the analysis performed in this study focused on variables within the involved limb (Shultz *et al.*, 2009). The ACL

group included men and women, and women typically have lower levels quadriceps strength relative to body mass (Shultz *et al.*, 2009) and use less knee flexion excursion in landing tasks (Miranda *et al.*, 2013). Therefore, it was important to account for differences in body weight normalized quadriceps strength when investigating predictors of knee flexion excursion in this study. It is accepted that inter-limb differences in isokinetic quadriceps strength may have been more strongly associated with knee function than strength relative to body mass, because the functional performance measures used to assess knee function were ratios of the unaffected side.

Contrary to hypothesis 1e, hamstring strength relative to body mass was not associated with knee function. In Study 2, significantly lower levels of hamstring strength were observed in the ACLR group (see Study 1, Section 4.5.3). The hamstrings play an important role in stabilizing the knee joint and providing propulsion during hopping tasks (Bryant *et al.*, 2010). Hence, it was anticipated that individuals with hamstring strength deficits would demonstrate impaired functional performance (Hamilton *et al.*, 2008) and limitations in ADLs and sporting tasks. As previously discussed, hamstring strength relative to the contralateral side, or isokinetic hamstring strength measures, may have been more strongly associated with knee function.

### **6.7.3 Part 2: Closed kinetic chain predictors of knee joint function (pass vs fail)**

#### *Kinematic variables*

Supporting hypothesis 2a, reduced knee flexion excursion was associated with greater odds of failing the battery of functional tests. This finding is important because smaller knee flexion excursion in single leg landing tasks is associated with greater vertical GRF (Shimokochi *et al.*, 2013) and greater ACL forces (Laughlin *et al.*, 2011). These adaptations may affect the structural integrity of knee joint cartilage (Chaudhari *et al.*, 2008; Scanlan *et al.*, 2013) and increase the risk of ACL graft rupture (Hewett *et al.*, 2005; Paterno *et al.*, 2010; Paterno *et al.*, 2014).

Decreased knee flexion excursion after ACLR is modifiable through verbal instruction (Tsai & Powers, 2013) and neuromuscular training (Hartigan *et al.*, 2009). Hence, interventions that increase knee flexion excursion during landing tasks could reduce detrimental joint and ACL forces (Tsai & Powers, 2013) and improve knee joint

function after ACLR. However, due to the cross-sectional design of this study it is not possible to determine whether knee flexion excursion is causative of functional limitations, or vice versa. Nonetheless, these findings provide a foundation for further research in this area.

Smaller knee flexion excursion in single leg landings may also be associated with altered frontal or transverse plane kinematics (Pollard *et al.*, 2010). Peak knee abduction and tibial internal rotation angles were not candidate predictors of knee function in this study due to their large SEM and lower reliability (see Chapter 5, Section 5.6.2). However, smaller peak knee abduction and decreased peak tibial internal rotation angles were observed within the ACLR group in Study 3. Smaller knee abduction and tibial internal rotation may also be harmful when combined with smaller knee flexion excursion, in that they may increase tibiofemoral joint compressive forces (Takeda *et al.*, 2011). Altered knee joint loading, or changes to the areas of loading of knee joint cartilage, may contribute to the higher rates of knee OA observed after ACLR (Scanlan *et al.*, 2013).

Despite screening participants for knee instability during functional activities, 11 participants reported activity limitations due to partial giving way of their knee and five participants reported activity limitations due to full giving way of their knee on the CKRS (see Appendix 7). Individuals following ACLR who experience episodes of minor knee instability, or lack confidence in more demanding functional tasks, may have learned to avoid positions of potential knee instability (i.e., knee abduction, internal rotation and anterior tibial translation) by altering their landing strategies (Hewett *et al.*, 2013).

This hypothesis is supported by the finding that greater anterior knee joint laxity was associated with greater odds of failing the battery of functional tests. Interventions such as perturbation training and neuromuscular training, are effective in reducing episodes of knee instability and improving knee joint function (Fitzgerald *et al.*, 2000; Risberg *et al.*, 2007) and improving knee kinematics (Hartigan *et al.*, 2009) after ACL injury. Based on the findings of the research presented in this thesis, individuals who experience greater graft laxity following ACLR could be offered perturbation and neuromuscular training in an attempt to optimise their neuromuscular control and knee

function. However, further research is required to determine whether these interventions are safe and effective in improving kinematics and neuromuscular responses during more demanding tasks, and for all patient sub-groups following ACLR.

Another potentially modifiable kinematic adaptation that was observed in the ACLR group was greater peak trunk flexion during the landing phase of the hopping task. However, contrary to hypothesis 2b, greater peak trunk flexion angle was not associated with greater odds of failing the knee functional tests. It was hypothesised that greater peak trunk flexion angle would be associated with worse functional performance because greater trunk flexion angles have previously been associated with reduced postural stability after landing from a hop (Oberländer *et al.*, 2012a). Greater peak trunk flexion angles may be a compensatory adaptation that normalizes GRF and ACL forces, that would normally be increased when landing with the knee in a more extended position or reducing knee flexion excursion (Kulas *et al.*, 2011; Laughlin *et al.*, 2011; Oberländer *et al.*, 2012a).

Contrary to hypothesis 2c, greater peak ankle dorsiflexion angle was not associated with greater odds of failing the functional test battery. Although the ACLR group demonstrated less peak ankle dorsiflexion angle than the control group (see Chapter 5, Section 5.6.2), it was hypothesised that ACLR participants with poor knee function would increase their peak ankle dorsiflexion angle as a compensation for impairments in dynamic postural control and smaller knee flexion excursion (Gokeler *et al.*, 2010; Oberländer *et al.*, 2012a; Orishimo *et al.*, 2010). Greater peak ankle dorsiflexion angle, combined with greater peak trunk flexion angle, may help to reduce the GRF and ACL forces that are associated with smaller knee flexion angles (Kulas *et al.*, 2011; Laughlin *et al.*, 2011). Greater peak trunk flexion and ankle dorsiflexion angles in landing may allow individuals following ACLR with poor balance to lower their centre of gravity and stabilise their centre of mass more effectively, without increasing their knee flexion excursion (Oberländer *et al.*, 2012a; Phillips & van Deursen, 2008).

#### *Kinetic variables*

In support of hypothesis 2d, reduced peak knee extensor moment in landing was a significant predictor of failing the battery of knee functional assessments. A number of

previous studies have found smaller knee extensor moments in the involved limb of ACLR participants in hopping and landing tasks (Ernst *et al.*, 2000; Gokeler *et al.*, 2010; Orishimo *et al.*, 2010; Xergia & Pappas, 2013). However, few studies have investigated the association between these impairments and knee joint function (see Section 2.6). The findings of this study add to those of Hartigan *et al.* (2012), who found that smaller knee extensor moment in walking predicted whether individuals with ACLR passed or failed a battery of knee functional assessments, aimed at assessing readiness to return to sport.

A recent prospective study demonstrated that ACLR is not only associated with, but may be causative of reduced knee extensor moments in landing (Goerger *et al.*, 2014). A group of individuals who had undergone baseline biomechanical testing, and subsequently ruptured their ACL, were reassessed following ACLR. Compared to their pre-injury assessment, the group demonstrated smaller knee extensor moments as well as high-risk knee kinematics; that is, increased hip abduction and knee valgus movement. Based on the findings of this study and the study by Goerger *et al.*, (2014), rehabilitation programs should place greater emphasis on interventions which may improve knee kinematics and kinetics, such as neuromuscular training and technique modification (Fitzgerald *et al.*, 2000; Hartigan *et al.*, 2010; Tsai & Powers, 2013).

In drop landing tasks and in the landing phase of the hop for distance test, some individuals following ACLR compensate for reduced knee extensor moments by increasing hip extensor and ankle plantarflexor moments, thereby transferring forces from the knee to the hip and ankle joints (Ernst *et al.*, 2000; Gokeler *et al.*, 2010; Orishimo *et al.*, 2010). In Study 3, no difference was found in the peak hip extensor moments of ACLR and control participants, and the ACLR group demonstrated significantly smaller peak ankle plantarflexor moments (see Chapter 5, Section 5.6.2). This was despite there being no significant difference between the ACLR and control groups in peak vertical ground reaction force. It was speculated that ACLR participants landed with greater peak trunk flexion as an adaptation for their smaller knee extensor moments, a finding also reported by Oberlander *et al.*, (2012). It was therefore hypothesised that smaller peak ankle plantarflexor moments would be associated with *worse* knee function.



Supporting hypothesis 2e, smaller ankle plantarflexor moment was associated with greater odds of failing the battery of functional tests. This hypothesis may seem counterintuitive, because it was also hypothesised that greater ankle dorsiflexion angles would be associated with worse knee function and greater ankle dorsiflexion angles could increase the ankle moment arm, thus increasing the peak ankle joint moment (Oberländer *et al.*, 2012a). However, unlike a drop landing or vertical jump, in which individuals with ACLR may increase ankle plantarflexor moments and reduce knee extensor moments (Vairo *et al.*, 2008), the hopping task used in this study involved a dynamic approach, followed by an abrupt landing. The landing and stabilisation period were challenging for many ACLR participants.

It is possible that ACLR participants with poor knee function responded to this challenge by landing with smaller knee extensor and ankle plantarflexor moments, and greater peak trunk flexion angles (Oberländer *et al.*, 2012a). This adaptation may have allowed these participants to perform the landing task despite compromised quality of movement (Hewett *et al.*, 2013). However, poor quality of movement may come at a cost; namely, a greater risk of ACL graft re-injury (Laughlin *et al.*, 2011; Paterno *et al.*, 2010) and structural changes within knee joint cartilage (Scanlan *et al.*, 2013).

#### *Neuromuscular variables*

Supporting hypotheses 2f and 2g, significant associations were observed between knee function and preparatory vastus medialis, hamstring and gastrocnemius activation, although these variables were not included in the regression model. This finding is consistent with (Bryant *et al.*, 2009b), who reported that individuals following ACLR with better knee function activated their quadriceps earlier prior to ground contact in a hopping task. In that study, peak quadriceps activation occurred less than 60 milliseconds following initial ground contact, which may be too fast to be a result of reflexive muscle activity (Beard *et al.*, 1994; Swanik *et al.*, 2004). Instead, it was hypothesised that ACLR participants with better knee function pre-activated their quadriceps prior to landing in order to synchronize peak quadriceps activity with peak ground reaction forces.

The relationship that was observed between greater muscle activation and worse knee function found in this study may also be related to the need of some ACLR participants to use greater muscle activation to cope with subtle knee joint instability (Boeth *et al.*, 2013). The ability to pre-activate the hamstrings and synchronize peak hamstring activity closer to peak ground reaction force or peak joint loads may allow more functional patients to perform functional tasks with greater dynamic knee stability (Bryant *et al.*, 2009b). However, although it was not assessed in Study 3, higher levels of reflexive hamstring coactivation may affect the ability to execute a powerful countermovement hop on the involved limb, as is required for the crossover and side hop tests (Ortiz *et al.*, 2011). This is an area for future research.

## **6.8 Summary**

### **6.8.1 Overview and clinical implications**

To the author's knowledge, this is the first study to assess the multivariate associations between knee joint function and neuromuscular control after ACLR using both open and closed kinetic chain tasks. By identifying neuromuscular adaptations that are associated with knee function, the findings of this study help to explain the variability that is observed in knee function following ACLR. Future prospective research should determine whether similar associations exist between neuromuscular control and long-term knee function and whether knee functional outcomes can be improved by targeting specific neuromuscular impairments following ACLR.

This study also highlights the importance of considering the wider ACLR population in the design and interpretation of laboratory-based investigations. Although recreational athletes are often included in biomechanical studies, individuals who participate in lower levels of sports are often excluded (see Chapter 2, Section 2.6). Furthermore, although concomitant chondral and meniscal injuries are prevalent, individuals following ACLR with these injuries and/or higher knee laxity measurements are commonly excluded from biomechanical studies (see Chapter 2, Section 2.3.4). A strong association was found between greater anterior knee joint laxity and worse knee

joint function (i.e. greater odds of failing the battery of functional tests) in this study. Hence, patients who present with a combination of greater anterior knee joint laxity and neuromuscular impairment could be identified and targeted by clinicians as candidates for additional or specialized rehabilitation (see Section 5.8.1) to optimize neuromuscular strategies and knee joint function after ACLR.

### **6.8.2 Limitations**

In addition to the limitations discussed in Studies 1-3 (Chapters 3-5), there were a number of other limitations to this study:

1. The study participants were volunteers and therefore not a truly random sample of the ACLR population. Specifically, the exclusion of adolescents could have introduced sampling bias which should be considered when generalizing the findings of this study to the wider ACLR population.
2. The study only involved individuals with hamstring grafts who were 12-24 months post-surgery and aged between 18 and 50 years. Hence, the study findings may not be generalisable to patients with other types of ACL grafts (e.g. allografts, patella tendon or synthetic grafts), younger or older patients, or patients at earlier or later time-points post ACLR.
3. Due to the cross-sectional study design, it is not known whether the neuromuscular adaptations identified in Studies 2 and 3 are causative of poor knee function, or vice versa. It is also unknown whether these neuromuscular adaptations were a result of ACLR, or were traits that existed prior to ACL injury.
4. The associations that were found between knee function and neuromuscular control are limited to those tests used in Studies 1-3; hence, it is not possible to generalize these findings to other aspects of neuromuscular control; for example, postural control or rate of force development (Angelozzi, 2012; Trulsson *et al.*, 2010).
5. The levels of hamstring activation observed in Study 2 were relatively small; hence, although a significant association was identified between lateral hamstring activation and knee function, it is not known whether such small levels of muscle activation are clinically relevant.
6. Interpretation of muscle activation prior to initial ground contact is limited by the non-linear relationship between muscle activation and muscle force (Kouzaki *et al.*,

2004). Future studies using musculoskeletal modelling to estimate muscle forces may reveal whether individuals with poor knee function also demonstrate altered muscle forces after ACLR, and if so, whether these changes are related to better, or worse, knee joint function.

7. Peak trunk and hip flexion angles were not associated with knee function; however, it is possible that trunk or hip flexion excursion may be more closely associated with knee function.
8. The relationships between neuromuscular control and knee function reported in this study were limited to the involved (ipsilateral) limb. It is unclear whether the neuromuscular adaptations demonstrated on the involved limb of the ACLR group were present in the contralateral limb, and if so, whether this limb asymmetry is related to knee function.

## **6.9 Conclusions and recommendations**

Knee functional limitations following ACLR are associated with less-accurate quadriceps force production, greater hamstring coactivation during a voluntary quadriceps force matching task, female sex, smaller knee flexion excursion and peak knee extensor moment in a hop landing and anterior knee joint laxity. Importantly, the associations identified in this study between knee joint function, participant characteristics and neuromuscular control were derived from multivariate analyses conducted with a relatively large and representative sample of patients with ACLR. Hence, the findings of this study may be more generalisable to the wider ACLR population than some previous studies. Prospective investigations are now needed to determine whether the biomechanical and neuromuscular variables identified by this research are predictive of knee function and knee osteoarthritis in the immediate and longer term.

## *Chapter 7*

### **Summary of findings and clinical implications**

#### **7.1 Summary of findings**

This thesis investigated the multivariate associations between knee joint function, sports participation, participant characteristics and neuromuscular control following ACLR. An important part of this thesis was that individuals from lower levels of sport and were not excluded from the studies. Furthermore, patients with full-thickness chondral injuries and greater anterior knee joint laxity were also included. This approach was taken to address an important gap in the literature; namely, a lack of knowledge of the relationship between knee function, sports participation, participant characteristics (including surgical findings) and neuromuscular control. The inclusion of a more diverse ACLR population may have made the results of the studies more generalisable to the wider ACLR population. By determining predictors of knee joint function; this thesis has contributed to a better understanding of the variability in knee functional outcomes that are observed following ACLR, particularly amongst recreational athletes. A summary of the findings of the four studies included in this thesis follows.

##### **7.1.1 Study 1: Knee function following ACLR**

The first study in this thesis (Study 1, Chapter 3) assessed the self-reported knee function and functional performance of ACLR and uninjured control participants. Compared to control participants, ACLR participants demonstrated significant limitations in both self-reported knee function and functional performance. Specifically, the median Cincinnati Knee Rating Scale (CKRS) score for the ACLR group (88.6%) was significantly lower than that of the control group (100%). The greatest self-reported functional limitations in the ACLR group were related to sport; the sports sub-scale of the CKRS was 22% lower than that of the control group.

Although the median LSIs for the hop for distance (96%), crossover hop (97%) and side hop test (89%) were significantly lower for the ACLR than the control group; they were within the lower limit of the range that is considered normal in the literature (85%; see

Section 2.2.3). However, a significant proportion of the ACLR group scored < 85% for the hop for distance (38%), the crossover hop (20%) and the side hop test (38%) compared to the control group. Likewise, 30% of the ACLR group scored less than 85% on the CKRS. Overall, 50% of ACLR participants scored less than 85% on one or more of these functional tests.

These findings confirm that knee functional outcomes are variable following ACLR, particularly amongst recreational athletes. For example, the CKRS scores of the ACLR group ranged from 43 to 100% and the LSI for the crossover hop test ranged from 68 to 113%, an average of 18 months post-surgery. To help explain this variability it was necessary to explore the relationships between knee function, sports participation and participant characteristics. The review of the literature (Chapter 2) identified that concomitant chondral or meniscal injuries, knee impairments and participant characteristics such as age, sex and BMI may be associated with knee joint function, or confound the relationship between knee function and neuromuscular control. Hence, the relationships between these variables and knee joint function were assessed.

In a multivariate logistic regression model, greater anterior knee joint laxity, older age at the time of testing and greater BMI were associated with worse knee joint function. Collectively, these variables explained 33% of the variance in knee function. Although anterior knee joint laxity was not hypothesized to be a predictor of overall knee joint function, an interquartile increase in anterior knee joint laxity (3.3 mm) was associated with 5.5 times greater odds of failing the battery of knee functional tests. Factors related to sports participation (level of sports participation, having returned to the pre-injury level of sport and the psychological response to returning to sport were not significantly associated with knee joint function.

Despite the finding that anterior knee joint laxity, age at the time of testing and BMI were significant predictors of knee joint function, these variables only accounted for a third of the variability in knee function that was observed within the ACLR group. To explain more of this variability, the neuromuscular control of ACLR and control participants was assessed in the open and closed kinetic chain.

### **7.1.2 Study 2: Open kinetic chain neuromuscular control**

The second study in this thesis (Study 2, Chapter 4) assessed neuromuscular control in the open kinetic chain with the same group of ACLR and control participants reported in Study 1. Specifically, the quadriceps force control and thigh muscle activation strategies of ACLR and control participants were assessed using a novel, sub-maximal target matching task that was developed specifically for the study.

The quadriceps force matching task involved reproducing a target torque which varied between 5 to 30% of the participant's previously-determined maximum voluntary isometric contraction (MVIC). Quadriceps force control was quantified by calculating the root mean square error (RMSE) of the quadriceps force output (i.e., the average difference between the target torque and quadriceps force expressed as a percentage of MVIC) during the trial. Thigh muscle activation strategies were assessed with surface electromyography (EMG). The inter-session reliability of RMSE, quadriceps strength and hamstring strength was excellent, with ICCs ranging from 0.90 to 0.93. The EMG variables demonstrated fair to good reliability ( $ICC > 0.6$ ).

The ACLR group demonstrated significantly greater RMSE than the control group, indicative of less-accurate quadriceps force production. Furthermore, ACLR participants demonstrated significantly higher levels of activation of the vastus medialis, vastus lateralis, medial hamstrings and lateral hamstrings during the trial. These differences were larger than their respective SEMs derived from reliability testing (see Appendix 8). Due to the novelty of the task and the limited literature relating to quadriceps force control following ACLR, the mechanisms of the quadriceps force control deficits observed in the ACLR group were unclear. Hence, multivariate linear regression analysis was performed to determine the multivariate associations between thigh muscle activation strategies, sports participation, participant characteristics and quadriceps force control.

In a multivariate linear regression model, older age at the time of testing, female sex, greater vastus lateralis activation, lower lateral hamstring coactivation and greater anterior knee joint laxity were associated with worse quadriceps force control. Meniscal surgery at the time of ACLR was associated with more-accurate quadriceps force

production. Together, these variables explained 42% of the variance in quadriceps force control. Greater vastus lateralis activation was associated with less-accurate quadriceps force production (IQR coefficient 0.57); whereas, greater lateral hamstring coactivation was associated with more-accurate quadriceps force production (IQR coefficient -0.22).

The impairments in quadriceps force control and altered thigh muscle activation strategies that were observed in this study were assessed during an isolated, open kinetic chain movement. However, most functional movements occur in the closed kinetic chain. Therefore, in Study 3, the neuromuscular control of ACLR and control participants was assessed using a sub-maximal closed kinetic chain task.

### **7.1.3 Study 3: Closed kinetic chain neuromuscular control**

The third study in this thesis (Study 3, Chapter 5) assessed neuromuscular control in the closed kinetic chain with the same group of ACLR and control participants reported in Studies 1 and 2. The biomechanics of ACLR and control participants were assessed during the landing phase of a standardised hopping task. The task involved a walking approach, which was standardised by asking participants to walk in time with a metronome. Hop distance was normalised to the participant's leg length. Analysis of ground reaction forces and velocity prior to landing revealed time to stabilise. The purpose of standardising the approach velocity and hop distance was to reduce variability in the performance of the task between individuals. It was therefore concluded that the task had been performed in a similar way between the ACLR and control groups.

Despite the performance of the hopping task being similar between the groups, the ACLR group demonstrated significantly smaller knee flexion excursion, smaller knee extensor moment and greater peak trunk flexion angle during landing than control participants. In a multivariate linear regression model, lower levels of quadriceps strength relative to body mass, greater anterior knee joint laxity, greater preparatory vastus medialis activation and lower preparatory medial hamstring activation were associated with smaller knee flexion excursion. Together, these variables explained 54% of the variance in knee flexion excursion.



The findings of Studies 2 and 3 provided insight into some of the possible mechanisms of poor neuromuscular control following ACLR. However, it was unclear whether the biomechanical and neuromuscular adaptations revealed in Studies 2 and 3 were associated with knee joint function. Therefore, the final study included in this thesis explored the relationship between knee joint function and the biomechanical and neuromuscular variables reported in Studies 2 and 3.

#### **7.1.4 Study 4: Association between neuromuscular control and knee function**

The final study in this thesis (Study 4, Chapter 6) addressed the main aim of the thesis; that is, the relationship between neuromuscular control and knee function after ACLR. Two separate logistic regression models were developed to determine whether variables derived from open and closed kinetic chain assessments were predictive of knee joint function. Multivariate models were developed based on the findings of Studies 1 – 3, review of the literature and the bivariate relationships between candidate predictor variables and knee joint function.

Less-accurate quadriceps force production, greater lateral hamstring coactivation and female sex were associated with greater odds of failing the battery of knee functional tests. Collectively, these variables explained 47% of the variance in knee function. Greater knee flexion excursion and greater peak knee extensor moment were associated with greater odds of passing the functional test battery. When anterior knee joint laxity was included in the model, these variables explained 51% of the variance in knee joint function. Significant relationships were observed between knee function and peak ankle plantarflexor moment and preparatory medial hamstring, vastus lateralis and vastus medialis activation; however, these variables were not included in the multivariate model.

### 7.1.5 Summary of model findings: Studies 1 and 4

The candidate predictors of knee joint function and the predictors of overall knee function identified through multivariate logistic regression analyses in Studies 1 and 4 are summarised in Table 7.1.

**Table 7.1** Summary of candidate predictor variables and significant predictors of failing the battery of knee function tests in Studies 1 and 4 of this thesis. All models were powered to contain a maximum of three predictor variables.

Study 1	Study 4	
	Part 1	Part 2
<b>Candidate predictors</b>		
<ul style="list-style-type: none"> <li>• Age, sex, BMI</li> <li>• Tested on dominant limb</li> <li>• Returned to the pre-injury level of sport</li> <li>• Psychological response to return to sport (ACL-RSI)</li> <li>• Anterior knee joint laxity</li> <li>• Meniscal surgery at the time of ACLR</li> <li>• Grade III or IV chondral injury</li> </ul>	<ul style="list-style-type: none"> <li>• Age, sex, BMI</li> <li>• Anterior knee joint laxity</li> <li>• Quadriceps force control</li> <li>• Quadriceps and hamstring strength relative to body mass</li> <li>• Quadriceps and hamstring muscle activation strategies</li> </ul>	<ul style="list-style-type: none"> <li>• Age, sex, BMI</li> <li>• Anterior knee joint laxity</li> <li>• Kinematic, kinetic and EMG variables derived from standardised landing task</li> </ul>
<b>Predictors of failing the battery of functional tests</b>		
<ul style="list-style-type: none"> <li>• Older age at the time of testing</li> <li>• Greater body mass index</li> <li>• Greater anterior knee joint laxity</li> </ul>	<ul style="list-style-type: none"> <li>• Less-accurate quadriceps force production (greater RMSE)</li> <li>• Greater lateral hamstring coactivation</li> <li>• Female sex</li> </ul>	<ul style="list-style-type: none"> <li>• Smaller knee flexion excursion</li> <li>• Smaller peak knee extensor moment</li> <li>• Greater anterior knee joint laxity</li> </ul>
<b>Variables significantly associated with knee joint function – not included in models</b>		
		<ul style="list-style-type: none"> <li>• Smaller peak ankle plantarflexor moment</li> <li>• Greater preparatory vastus medialis, vastus lateralis and medial hamstring activation</li> </ul>
<b>Evaluation of model</b>		
<ul style="list-style-type: none"> <li>• Nagelkerke <math>r^2 = 0.33</math> (<math>p &lt; 0.05</math>)</li> <li>• AUC = 0.78 (<math>p &lt; 0.0001</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Average Nagelkerke <math>r^2 = 0.47</math> (<math>p &lt; 0.001</math>)</li> <li>• AUC = 0.88 (<math>p &lt; 0.0001</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Nagelkerke <math>r^2 = 0.51</math> (<math>p &lt; 0.001</math>)</li> <li>• AUC = 0.86 (<math>p &lt; 0.0001</math>)</li> </ul>

RMSE = Root mean square error, EMG = electromyography, BMI = body mass index; AUC = area under the curve

## 7.2 Clinical implications

There are a number of important clinical implications of the findings of the studies that were reported in this thesis. The first aim of the research, addressed in Study 1, was to explore the relationship between knee joint function and sports participation after ACLR. Level of sports participation, having returned to the pre-injury level of sports participation at the time of testing and the psychological response to returning to sport were not associated with knee function in this study. The clinical implication of this finding is that having returned to sport following ACLR does not necessarily mean that an individual has developed an acceptable level of knee joint function.

Participating in high-level sport with poor knee joint function may predispose individuals with ACLR to the development of knee osteoarthritis, particularly when combined with chondral or meniscal injuries (Keays *et al.*, 2010). Clinicians should therefore continue to emphasise functional outcomes with patients and use functional criteria to inform rehabilitation decisions, regardless of whether or not patients have returned to sport following ACLR. For example, individuals who have returned to sport but score less than 85% on self-reported or objective functional tests, should be offered additional neuromuscular and strength training with the aim of restoring knee joint function.

The second aim of the research reported in this thesis, addressed in Study 1, was to explore the associations between knee joint function and participant characteristics, including surgical findings and anterior knee joint laxity. In Study 1, greater anterior knee joint laxity, older age at the time of testing and higher BMI were significant predictors of failing a battery of knee functional tests. Given the cross-sectional study design it is unknown whether these variables are predictive of long-term knee joint function. Notwithstanding this limitation, anterior knee joint laxity, BMI and age at the time of testing are important factors for clinicians to consider when assessing knee joint function following ACLR. BMI in particular, is modifiable and is related to the presence of chondral and meniscal injuries (Bowers *et al.*, 2005) and the development of knee osteoarthritis (Øiestad *et al.*, 2011).

The final aim of the research reported in this thesis, addressed in Study 4, was to explore the relationships between knee joint function (assessed in Study 1) and neuromuscular control (assessed in Studies 2 and 3). The finding that quadriceps force control was associated with knee joint function is important, because many functional activities involve only sub-maximal intensities of muscle activation (Besier *et al.*, 2009). Although quadriceps strength deficits are commonly assessed following ACLR, the findings of Studies 2 and 4 of this thesis indicate that the accuracy of quadriceps force production is impaired following ACLR, and that less-accurate quadriceps force production is related to worse knee function.

Less-accurate quadriceps force production during low-intensity functional tasks such as walking may contribute to altered knee joint loading, especially if it is combined with altered muscle activation strategies (Chaudhari *et al.*, 2008). Hence, in the long-term, impairments in quadriceps force control and greater thigh muscle activation may contribute to the development or progression of knee OA. Although the methods used in this study to assess quadriceps force control and thigh muscle activation following ACLR are not yet clinically feasible, clinicians should consider the potential impact of altered quadriceps force control and increased muscle activation on the quality of functional movements, such as walking and sports-performance.

To the author's knowledge, this is the first study to investigate the relationship between knee joint function (i.e., self-reported knee function and functional performance) and kinetics and kinematics during a single leg landing task. The finding that smaller knee flexion excursion and smaller knee extensor moment were associated with worse knee function is clinically important, because these variables are potentially modifiable through verbal instruction and training (Gokeler *et al.*, 2014a) and neuromuscular training (Myer *et al.*, 2008). Smaller knee flexion excursion is associated with greater ACL forces in uninjured individuals (Laughlin *et al.*, 2011) and greater knee contact pressures following ACLR (Tsai & Powers, 2013) and may therefore increase the risk of post-operative knee OA. Smaller knee flexion excursion and knee extensor moments, combined with greater knee valgus angles and forces may increase the risk of second ACL injury following return to sport (Paterno *et al.*, 2010). The findings of this study indicate that smaller knee flexion excursion and smaller knee extensor moment are also

associated with worse knee joint function. Clinicians should therefore be aware of the valid, reliable and clinically-feasible screening assessments that can be used to identify deficits in lower limb kinematics, including reduced knee flexion excursion, following ACLR (Myer *et al.*, 2010; Padua *et al.*, 2009). The routine assessment of knee flexion and lower limb kinematics in clinical settings could help identify individuals who are at risk of poor knee functional outcomes or further injury following ACLR.

### **7.3 Strengths of the study**

The strengths of the studies included in this thesis have been discussed at length within their respective chapters; hence, only an overview of the major strengths of each study is provided in this section. The main strength of the research reported in this thesis is the relatively broad inclusion criteria and large sample size compared to many previous investigations. The broad inclusion criteria resulted in the recruitment of individuals at all levels of sport and those with concomitant chondral or meniscal injuries and greater levels of anterior knee joint laxity. The larger sample size allowed for detailed statistical analyses of the relationships between these variables and knee joint function. Hence, to the author's knowledge, this is the first study to use multivariate analyses to investigate the mechanisms of quadriceps force control deficits and reduced knee flexion excursion and the relationship between these variables and knee joint function.

Besides the issue of external generalizability, a major strength of this research was the design and piloting of novel tests of neuromuscular control which addressed important limitations in previous research. The reliability and standard error of measurement of the variables derived from these tests were also assessed. This allowed the size of the differences between the ACLR and control groups to be interpreted within the context of an estimate of measurement error. This approach ensured that the most reliable and important variables were selected for regression analyses. Furthermore, rather than simply reporting differences in neuromuscular control between the ACLR and control groups, the mechanisms of neuromuscular adaptations were explored using linear regression analyses.

A major strength of this research was the effort that was put into developing a battery of knee functional assessments that was appropriate to the function and participation level of the study participants. Batteries of knee function tests have greater sensitivity in detecting knee functional limitations than single functional measures (Logerstedt *et al.*, 2012a). Hence, the use of a battery of knee functional assessments in this study may have helped to identify predictors of knee joint function that would not have been identified if only a single measure of knee function or an average functional score was used.

Finally, the major strength of this research was the use of multivariate regression analyses to determine predictors of knee joint function, and consideration of a range of variables that could impact on knee function, including participation, participant characteristics and neuromuscular control. The consideration of these variables is important when considering sub-groups of ACLR participants to which this research can be generalized.

#### **7.4 Limitations of the study**

The limitations of each study have been discussed in detail within their respective chapters; hence, the following section provides an overview of the main limitations of the research. An important limitation is the cross-sectional nature of the studies, which precludes any claim of causation from the associations that were found. A prospective study design was not feasible given time-constraints; however, knowledge of the prospective associations between knee function, sports participation, participant characteristics and neuromuscular control are needed before the findings of this research can be translated to clinical practice.

Another important limitation was the use of convenience sampling. Although considerable effort was put into recruiting individuals who were representative of the wider ACLR population, the study was limited to participants who volunteered. Hence, the study participants may not have been a truly random sample of the ACLR population. Importantly, the study design excluded adolescent individuals, an important

sub-group of patients following ACLR. Therefore, care should be taken when generalizing the findings of these studies to the wider ACLR population.

Another limitation of this research is that only patients with hamstring autografts harvested from the ipsilateral limb and adults aged 18-50 years were included. Furthermore, the studies only included individuals who were between 12 and 24 months following ACLR. As a result, the findings of this study may not be generalisable to individuals with different graft types and patients at different post-operative time-points. The lack of standardised rehabilitation is also a limitation of the research. Although all participants were encouraged to follow a similar post-operative protocol, including early weight-bearing and quadriceps activation and range of motion exercises, the rehabilitation program was not standardised. Therefore, variability in the quality, volume and structure of rehabilitation may have contributed to some of the unaccounted variance in functional scores.

## **7.5 Recommendations for further research**

Several recommendations for future research were identified within the chapters that comprise this thesis. Importantly, future research is needed to allow the findings of this study to be generalized to other sub-groups of individuals following ACLR; for example, adolescents, patients at different post-operative time-points or patients with different types of grafts (e.g. allografts or patella tendon grafts). Further research is needed to determine the cross-sectional associations between neuromuscular control and knee joint function within these populations, as a foundation for prospective cohort and experimental studies.

Asymmetry in movement patterns and neuromuscular control may have important functional implications after ACLR. Future investigations should determine whether side-to-side asymmetry in quadriceps force control, knee flexion excursion and knee extensor moments are associated with worse knee function after ACLR. The tasks used to assess neuromuscular control were linear in nature (i.e., performed in the sagittal plane) and did not involve any unexpected components. Further research is needed to

assess the relationship between neuromuscular variables derived from multidirectional and unexpected landing tasks and knee joint function after ACLR.

Although effort was made to recruit a larger number of participants for this research and include variables related to impairment, function and participation, other variables which may affect knee function were not included in the analysis. These variables include impairments such as knee range of motion, radiographic findings and other psychological variables such as fear of movement. Due to the inherent variability of many of the variables that were included in the analysis, the confidence intervals for many of the odds ratios were wide. Hence, future research involving larger sample sizes may be required to further quantify the strength of these associations.

Knowledge of the relationship between neuromuscular control and knee joint function derived from this study will also inform the development of future experimental and observational research. For example, prospective observational studies are now needed to determine whether impairments in quadriceps force control and biomechanical landing strategies are predictive of long-term knee function (i.e., greater than two years). Future research is required to determine whether neuromuscular training and related interventions are able to change knee functional outcomes, and whether improving knee function and neuromuscular control following ACLR leads to improvements in knee joint loading and knee osteoarthritis.

In conclusion, this thesis has produced new and clinically-relevant information about the mechanisms of neuromuscular impairments and the predictors of knee joint function after ACLR. It is anticipated that this research will inform the development of prospective research to refine and improve rehabilitation protocols following ACLR.



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## Appendices

1. Human Ethics Approval
2. Pilot testing
3. Menstrual cycle and monophasic oral contraceptive pill use
4. The Anterior Cruciate Ligament Return to Sport after Injury (ACL-RSI) Scale
5. The Cincinnati Knee Rating Scale
6. Sensitivity analyses for logistic and linear regression models
7. Cincinnati Knee Rating Scale sub-scale scores
8. Reliability of open and closed kinetic chain neuromuscular variables
9. Reflective marker locations and orientations

# Appendix 1

## Human Ethics Approval

A copy of correspondence from the University of Melbourne's Human Research Ethics Committee confirming approval to conduct the research described within this thesis (ethics ID 1136167). Note that this study was conducted concurrently with another PhD study titled Patellofemoral Joint Changes 12 months after anterior cruciate ligament reconstruction

15 August 2011

Dr K.M. Crossley  
Physiotherapy  
The University of Melbourne

Dear Dr Crossley

I am pleased to advise that the Behavioural and Social Sciences Human Ethics Sub-Committee approved the following Project:

Project title: **Patellofemoral joint changes 12 months after anterior cruciate ligament reconstruction**  
Researchers: **Dr A L Bryant, Mr T Wrigley, Dr K M Crossley, Mr T Whitehead, Mr H Morris, Dr N Collins, A/Prof J L Cook, A Culvenor, L Perraton**  
Ethics ID: **1136167**

The Project has been approved for the period: **15-Aug-2011 to 31-Dec-2011.**

It is your responsibility to ensure that all people associated with the Project are made aware of what has actually been approved.

Research projects are normally approved to 31 December of the year of approval. Projects may be renewed yearly for up to a total of five years upon receipt of a satisfactory annual report. If a project is to continue beyond five years a new application will normally need to be submitted.

Please note that the following conditions apply to your approval. Failure to abide by these conditions may result in suspension or discontinuation of approval and/or disciplinary action.

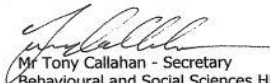
- (a) **Limit of Approval:** Approval is limited strictly to the research as submitted in your Project application.
- (b) **Variation to Project:** Any subsequent variations or modifications you might wish to make to the Project must be notified formally to the Human Ethics Sub-Committee for further consideration and approval. If the Sub-Committee considers that the proposed changes are significant, you may be required to submit a new application for approval of the revised Project.
- (c) **Incidents or adverse effects:** Researchers must report immediately to the Sub-Committee anything which might affect the ethical acceptance of the protocol including adverse effects on participants or unforeseen events that might affect continued ethical acceptability of the Project. Failure to do so may result in suspension or cancellation of approval.
- (d) **Monitoring:** All projects are subject to monitoring at any time by the Human Research Ethics Committee.
- (e) **Annual Report:** Please be aware that the Human Research Ethics Committee requires that researchers submit an annual report on each of their projects at the end of the year, or at the conclusion of a project if it continues for less than this time. Failure to submit an annual report will mean that ethics approval will lapse.
- (f) **Auditing:** All projects may be subject to audit by members of the Sub-Committee.

If you have any queries on these matters, or require additional information, please contact me using the details below.

Please quote the ethics ID number and the title of the Project in any future correspondence.

On behalf of the Sub-Committee I wish you well in your research.

Yours sincerely

  
Mr Tony Callahan - Secretary  
Behavioural and Social Sciences HESC  
Phone: 8344 2067, Email: t.callahan@unimelb.edu.au

## **Appendix 2**

### **Pilot testing**

Following ethical approval for the project and prior to data collection, pilot testing of the quadriceps force matching task and standardised hop landing task described in Studies 2 and 3 was conducted. The pilot testing involved 15 healthy colleagues and fellow students at the Melbourne University who fulfilled the eligibility criteria for the control group study (see Chapter 3, Section 3.5.1).

The purpose of pilot testing was to rehearse data collection procedures, refine the parameters of the tests, check the quality of the data and seek subjective feedback from participants on important aspects of the testing that may have confounded the results of the study. These aspects included confidence in performing the tasks, the relative difficulty of the tasks and any discomfort experienced during the tasks –including muscular fatigue or pain.

To objectify this process, participants were asked to indicate on a visual analogue scale their confidence in performing the tasks, the relative difficulty of the tasks and any discomfort experienced during the tasks. This information was used to refine the parameters of the testing. For example, to select the approach cadence of 100 beats per minute (bpm) for the hopping task in Study 3, cadences of 90, 100, 110 and 120 bpm were trialled with all 15 participants. Discussions with participants, inspection of VAS data and inspection of the number of successful and unsuccessful trials revealed that an approach cadence of 100 bpm was challenging, but able to be completed by all participants. A copy of these visual analogue scales is provided below.

Visual analogue scales used during pilot testing to assess confidence, difficulty in performing the task and discomfort during the task

1. How **confident** did you feel with that task?

\_\_\_\_\_

No confidence Full confidence

2. How **difficult** was that task?

\_\_\_\_\_

No difficulty Extreme difficulty

3. How much **discomfort**, if any, did you have with that task?

\_\_\_\_\_

No discomfort Extreme discomfort

### Appendix 3

#### Menstrual cycle and monophasic oral contraceptive pill use

The questionnaire that was used to assess menstrual cycle status and monophasic oral contraceptive pill use at the time of testing is included below:

<b>Participant ID:</b> _____		
<b>Date</b> _____		
<b>Oral contraceptive pill and menstrual cycle questionnaire</b>		
<b>Oral contraceptive pill (OCP) use</b>		
	Are you currently using the oral contraceptive pill?	Yes <input type="checkbox"/> No <input type="checkbox"/>
<b>If yes</b>	Which brand?	
	How long have you used the OCP? (years)	
<b>If no</b>	Have you previously used the OCP?	
	When did you stop using the OCP? (years)	
	Which brand?	
<b>Your menstrual cycle</b>		
	Is your menstrual cycle currently irregular (less than 8 cycles in a year or more than 35 days between cycles)	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
	What was the date of the start of your last menstrual period?	N/A <input type="checkbox"/>
	What is the average length of your menstrual period?	N/A <input type="checkbox"/>

## Appendix 4

### The Anterior Cruciate Ligament Return to Sport after Injury Scale

The 12-item Anterior Cruciate Ligament Return to Sport after Injury Scale (ACL-RSI; Webster et al. 2008) is included below:

ACL – Return to Sport after Injury Scale	
Participant Code: _____	Date: _____
1. Are you confident that you can perform at your previous level of sport participation?	
Not at all _____	Extremely
2. Do you think you are likely to re-injure your knee by participating in your sport?	
Not at all _____	Extremely
3. Are you nervous about playing your sport?	
Not at all _____	Extremely
4. Are you confident that your knee will not give way by playing your sport?	
Not at all _____	Extremely
5. Are you confident that you could play your sport without concern for your knee?	
Not at all _____	Extremely
6. Do you find it frustrating to have to consider your knee with respect to your sport?	
Not at all _____	Extremely



7. Are you fearful of re-injuring your knee by playing your sport?

Not at all \_\_\_\_\_ Extremely

8. Are you confident about your knee holding up under pressure?

Not at all \_\_\_\_\_ Extremely

9. Are you afraid of accidentally injuring your knee by playing your sport?

Not at all \_\_\_\_\_ Extremely

10. Do thoughts of having to go through surgery and rehabilitation again prevent you from playing your sport?

Not at all \_\_\_\_\_ Extremely

11. Are you confident about your ability to perform well at your sport?

Not at all \_\_\_\_\_ Extremely

12. Do you feel relaxed about playing your sport?

Not at all \_\_\_\_\_ Extremely

## Appendix 5

### The Cincinnati Knee Rating Scale

The Cincinnati Knee Rating Scale (CKRS) was used to evaluate self-reported knee function (Noyes 1984). The modified CKRS, used commonly in ACLR research (see Section 2.2.3.1), evaluates activity limitations related to symptoms, activities of daily living (ADLs) and sport using three separate ordinal sub-scales. The symptoms sub-scale evaluates activity limitations related to pain, swelling, partial giving way and full giving way (20 points), the ADL sub-scale evaluates walking and stair climbing (6 points), and the sports activities sub-scale evaluates running, jumping and hard twisting/cutting/pivoting (9 points). The scores of the three sub-scales are summed and converted to a percentage. The symptoms, ADLs and sports sub-scales of the CKRS used in this thesis are included below:

**Symptom Rating Scales, Patient Perception Scale**

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**DIRECTIONS:** Using the key below, circle the appropriate boxes on the four scales below which indicate the highest level you can reach **WITHOUT** having symptoms.

Scale	Description
10	Normal knee, able to do strenuous work/sports with jumping, hard pivoting
8	Able to do moderate work/sports with running, turning and twisting; symptoms with strenuous work/sports
6	Able to do light work/sports with no running, twisting or jumping; symptoms with moderate work/sports
4	Able to do activities of daily living alone; symptoms with light work/sports
2	Moderate symptoms (frequent, limiting) with activities of daily living
0	Severe symptoms (constant, not relieved) with activities of daily living

**1. PAIN**

10 — 8 — 6 — 4 — 2 — 0

---

**2. SWELLING** (actual fluid in the knee; obvious puffiness)

10 — 8 — 6 — 4 — 2 — 0

---

**3. PARTIAL GIVING-WAY** (partial knee collapse, no fall to the ground)

10 — 8 — 6 — 4 — 2 — 0

---

**4. FULL GIVING-WAY** (knee collapse occurs with actual falling to the ground)

10 — 8 — 6 — 4 — 2 — 0

---

**Activities of Daily Living Function Scales**

<p><b>1. Walking</b> check one box: 40 <input type="checkbox"/> normal, unlimited 30 <input type="checkbox"/> some limitations 20 <input type="checkbox"/> only 3-4 blocks possible 0 <input type="checkbox"/> less than 1 block; cane, crutch</p>	<p><b>2. Stairs</b> check one box: 40 <input type="checkbox"/> normal, unlimited 30 <input type="checkbox"/> some limitations 20 <input type="checkbox"/> only 11-30 steps possible 0 <input type="checkbox"/> only 1-10 steps possible</p>	<p><b>3. Squatting / kneeling</b> check one box: 40 <input type="checkbox"/> normal, unlimited 30 <input type="checkbox"/> some limitations 20 <input type="checkbox"/> only 6-10 possible 0 <input type="checkbox"/> only 0-5 possible</p>
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**Sports Function Scales**

<p><b>1. Straight running</b> check one box: 100 <input type="checkbox"/> fully competitive 80 <input type="checkbox"/> some limitations, guarding 60 <input type="checkbox"/> definite limitations, half speed 40 <input type="checkbox"/> not able to do</p>	<p><b>2. Jumping / landing on affected leg</b> check one box: 100 <input type="checkbox"/> fully competitive 80 <input type="checkbox"/> some limitations, guarding 60 <input type="checkbox"/> definite limitations, half speed 40 <input type="checkbox"/> not able to do</p>	<p><b>3. Hard twists / cuts / pivots</b> check one box: 100 <input type="checkbox"/> fully competitive 80 <input type="checkbox"/> some limitations, guarding 60 <input type="checkbox"/> definite limitations, half speed 40 <input type="checkbox"/> not able to do</p>
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The original CKRS combines the three sub-scales that were used in this thesis, with categorical data derived from functional performance tests, clinical impairments (range of movement and anterior knee joint laxity) and radiographic findings (Barber-Westin *et al.*, 1999). In this thesis, these impairments were assessed separately, and the associations between impairments and knee function were determined.

**Cincinnati Knee Rating System: Overall Rating Scheme**

		Excellent		Good		Fair		Poor		
		Level	Pts.	Level	Pts.	Level	Pts.	Level	Pts.	
<b>Subjective: 20 points</b>		10 = Normal knee, able to do strenuous work/sports with jumping, hard pivoting 8 = Able to do moderate work/sports with running, twisting, turning, symptoms with strenuous work/sports 6 = Able to do light work/sports with no running, twisting, turning, symptoms with moderate work/sports 4 = Able to do activities of daily living alone, symptoms with light work/sports 2 = Moderate symptoms (frequent, limiting) with ADL 0 = Severe symptoms (constant, not relieved) with ADL <small>*highest level possible with no or rare symptoms</small>		10	8	6	4	2	0	
<b>Activity Level: 15 points</b>		Pts 3 Normal, unlimited Pts 2 Some limitations Pts 1 Only 3-4 blocks possible Pts 0 Less than 1 block, cane Only 1-10 steps possible Only 0-5 possible Not able to do Definite limitations, 1/2 speed Definite limitations, 1/2 speed Not able to do		10	8	6	4	2	0	
<b>Examination: 25 points</b>		NL Effusion Lack of Flexion Lack of Extension Tibiofemoral Crepitus Patellofemoral Crepitus		Pts 5 5 5 5 5	MILD ≤25 cc 6-15° 4-5°	MOD 26-60 cc 16-30° 6-10° Mod* Mod*	SEV >60 cc >30° >10° Sev* Sev*	Pts 4 4 4 4 4	Pts 0 0 0 0 0	
<b>Instability: 20 points</b>		Anterior (KT-1000) Pivot Shift		Pts 10 negative 10	Pts 4 slip	Pts 6 mm definite 4	Pts 4 4 4 4	Pts 0 0 0 0		
<b>Radiographs: 10 points</b>		Medial Tibiofemoral Lateral Tibiofemoral Patellofemoral		4 pts NL NL NL	3 pts Mild Mod Mod	2 pts Mod Mod Mod	0 pt Sev Sev Sev	Pts 0 0 0 0	Convert sum x-ray pts: 12 x-ray pts = 10 final pts	5-0 x-ray pts = 0 final pts
<b>Function Testing: 10 points</b>		One-Legged Hop, 1 hop for distance One-Legged Hop, 3 hops for distance One-Legged Hop, timed hop over 6 meters One-Legged Hop, cross-over for distance		% limb symmetry % limb symmetry % limb symmetry % limb symmetry	average % limb symmetry	Sum points:	Pts 7 7 7 7	Pts 0 0 0 0	Symmetry Pts. 100-85 10	Symmetry Pts. 84-75 7 74-65 4 <65 0
<b>Final Rating Acute Injury Studies: Category</b>		Excellent: all in "excellent" (may have one in "good"); Good: all in "excellent" and "good" Fair: any one in "fair"; Poor: any one in "poor"		Final Rating Chronic Injury Studies: Point Sum						

## Appendix 6

### Sensitivity analyses for logistic and linear regression models

In studies 1-3 of this thesis, multiple imputation was used to impute missing ACL-RSI questionnaire scores and EMG data prior to regression analyses. Multiple imputation is a form of regression analysis that uses all available data to predict missing values, based on multiple iterations of the dataset (Schafer, 1999). This appendix outlines the methods and results of these analyses.

In each of the multiple imputation processes, five imputations of the dataset were performed with 100 iterations (Allison, 2000; Schafer, 1999). The logistic and linear regression analyses described in Studies 1-4 were performed on the imputed data sets ( $n = 66$ ); thus, if ACL-RSI questionnaire scores or EMG data were included in the final model, the regression coefficients and odds ratios (ORs) derived from the model were pooled from the five imputations of the data set.

The average and range of adjusted R square ( $R^2$ ) values were reported and sensitivity analyses were performed to compare the model output using original and imputed data (Sterne *et al.*, 2009). The  $p$  values and standard errors of regression coefficients and ORs were compared. Percentage differences were calculated for coefficients or ORs and their respective standard errors. The normality, linearity and homoscedasticity of the standardised residuals of regression coefficients and ORs from imputed and original data sets were also compared. If ACL-RSI questionnaire scores and EMG data were not included in the final model, this process was redundant and was not undertaken. A summary of the sensitivity analyses included in this thesis follows:

#### Study 2: Multivariate linear regression model

Imputed EMG data were included in the final model; hence a sensitivity analysis was performed. The  $R^2$  value derived from the original dataset ( $n= 60$ ) was 0.43 and the average adjusted  $R^2$  value reported in the thesis was 0.42. The unstandardized regression coefficients derived from the imputed data were smaller than those derived from the original data (average percentage difference -1.6%, range -4.8 to 8.2%).

Therefore the imputed data yielded slightly more conservative estimates. As expected, the standard errors derived from the imputed data were smaller than those derived from the original dataset (average percentage difference -5.6%, range -9.8 to -2.6%; see Table 1).

### **Study 3: Multivariate linear regression model**

In Study 3, imputed EMG data were included in the final model; hence a sensitivity analysis was performed. The average adjusted  $R^2$  value reported in the thesis that was derived from the imputed dataset ( $R^2 = 0.54$ ), was similar to that of the  $R^2$  value derived from the original dataset ( $R^2 = 0.53$ ). The unstandardized regression coefficients derived from the imputed data set ( $n = 66$ ) were smaller than those derived from the original data ( $n = 60$ ). The estimate for quadriceps strength was considerably smaller for the imputed dataset (percentage difference 21.5%), indicating that the estimate for quadriceps strength reported in Study 3 may have been more conservative than anticipated. As expected, the standard errors derived from the imputed data were smaller than those derived from the original dataset (average percentage difference = -6.0%, range 0 to -13.7%; see Table 2).

### **Study 4: Multivariate logistic regression models**

Two logistic regression models were included in Study 4. The analysis reported in Part 1 (open kinetic chain variables) contained imputed EMG data. Therefore a sensitivity analysis was performed. The Nagelkerke  $R^2$  value derived from the original dataset (0.52) was larger than the average Nagelkerke  $R^2$  value derived from the imputed dataset (0.47). Smaller ORs were observed for the imputed dataset (average percentage difference -9.8%). Histograms of the residuals from the analysis using imputed data were normally distributed and demonstrated linearity and homoscedasticity. As expected, standard errors were also observed (average percentage difference -12.3%, see Table 3).

**Table 1.** Comparison of regression coefficients, standard errors and p values derived from original (n = 60) and imputed datasets for the linear regression analysis reported in Study 2 of this thesis (see Chapter 4, Section 4.5.4).

Variable	Unstandardized coefficient			Standard error			p value	
	Original	Imputed	% diff	Original	Imputed	% diff	Original	Imputed
Vastus lateralis activation (%)	0.063	0.062	-1.6	0.022	0.021	-4.5	0.005	0.004
Lateral hamstring activation (%)	-0.080	-0.077	-3.8	0.039	0.038	-2.6	0.04	0.04
Female sex †	0.514	0.556	8.2	0.268	0.251	-6.3	0.03	0.03
Age at time of testing (years)	0.063	0.060	-4.8	0.021	0.019	-9.5	0.004	0.002
Anterior knee joint laxity (mm)	0.220	0.214	-2.7	0.060	0.056	-6.7	0.001	0.0001
Meniscal surgery at time of ACLR †	-0.672	-0.637	-5.2	0.276	0.265	-4.0	0.02	0.02

† Binary variable; mm = millimetres; % diff = percentage difference

**Table 2.** Comparison of regression coefficients, standard errors and p values derived from original (n = 60) and imputed (n = 66) datasets for the linear regression analysis reported in Study 3 of this thesis (see Chapter 5, Section 5.6.3).

Variable	Unstandardized coefficient			Standard error			p value	
	Original	Imputed	% diff	Original	Imputed	% diff	Original	Imputed
Quadriceps strength (Nm/kg)	2.279	1.788	-21.5	0.879	0.759	-13.7	0.012	0.019
Vastus medialis activation (%)	-0.196	-0.180	-8.2	0.041	0.038	-7.3	0.001	0.001
Medial hamstring activation (%)	0.054	0.054	0	0.018	0.018	0	0.004	0.004
Anterior knee joint laxity (mm)	-0.531	-0.508	-4.3	0.228	0.221	-3.1	0.024	0.022

† Binary variable; mm = millimetres; % diff = percentage difference

**Table 3.** Comparison of odds ratios, standard errors and p values derived from original (n = 60) and imputed (n = 66) datasets for the logistic regression analysis reported in Study 4, Part 1 of this thesis (see Chapter 6, Section 6.6.1).

Variable	Odds ratio			Standard error			p value	
	Original	Imputed	% diff	Original	Imputed	% diff	Original	Imputed
Quadriceps force control (RMSE)	3.867	3.326	-14.0	0.441	0.385	-12.7	0.002	0.002
Lateral hamstring activation (%)	1.858	1.634	-12.1	0.275	0.242	-12	0.024	0.047
Female sex †	5.236	5.057	-3.4	0.946	0.830	-12.6	0.023	0.044

† Binary variable; mm = millimetres; % diff = percentage difference

## Appendix 7

### Cincinnati Knee Rating Scale sub-scale scores

Appendix 7 summarises the individual sub-scale items of the Cincinnati Knee Rating Scale, reported in Chapter 3, Section 3.6.2 of this thesis. 47% of the ACLR group reported having knee pain with strenuous work or sports (see Table 1).

**Table 1.** The proportion of ACLR participants (n = 66) reporting activity limitations related to pain, swelling, partial giving way and full giving way.

Symptoms sub-scale of the Cincinnati Knee Rating Scale	Pain	Swelling	Partial giving way	Full giving way
Normal knee	33 (50%)	46 (70%)	52 (79%)	61 (92%)
Symptoms with strenuous work/sports	31 (47%)	17 (26%)	11 (16%)	5 (8%)
Symptoms with moderate work/sports	2 (3%)	3 (4%)	3 (5%)	0
Symptoms with light work/sports	0	0	0	0
Moderate symptoms (frequent limiting) with ADL	0	0	0	0
Severe symptoms (constant not relieving) with ADL	0	0	0	0

Of the four activities within the activities of daily living (ADL) sub-scale of the CKRS, stair negotiation was the most limited; 50% of ACLR participants reported some limitations, or guarding with these activities (see Table 2). The greatest limitations identified by the sports sub-scale were hard twists, cuts and pivots. 65% of the ACLR group reported some limitations, or guarding with these activities.



**Table 2.** The proportion of ACLR participants (n = 66) reporting activity limitations in activities of daily living and sport.

Activity limitation	Activities of daily living sub-scale			Sports sub-scale		
	Walking	Stairs	Squatting/ kneeling	Straight running	Jumping/ landing	Hard twists/ cuts/pivots
Normal/fully competitive	66 (100%)	32 (49%)	35 (53%)	44 (66%)	26 (39%)	16 (24%)
Some limitations or guarding	0	33 (50%)	30 (45%)	20 (30%)	36 (55%)	43 (65%)
Definite limitations	0	1 (1%)	1 (1%)	2 (3%)	4 (6%)	5 (8%)
Not able to do	0	0	0	0	0	2 (3%)

The average scores for each item of the CKRS are presented in Table 3. ACLR participants had significantly greater functional limitations than control participants for all questions except for full giving way ( $p = 0.07$ ) and walking ( $p = 1.00$ ). No participant in either group reported pain, instability, apprehension or any other symptoms during the testing session. The average score for hard twisting/cutting/pivoting was 30% lower than that of controls, indicating that ACLR participants reported significant functional limitations with this activity.

**Table 3.** The mean, standard deviation, difference and p value for scores for individuals items of the Cincinnati Knee Rating Scale for the ACLR (n = 66) and control (n = 41) groups.

Activity limitation	ACLR	Control	Percentage difference	p value
<b>Symptoms sub-scale</b>				
Pain	3.94 (1.12)	5.00 (0.00)	-21%	< 0.001*
Swelling	4.30 (1.14)	5.00 (0.00)	-14%	< 0.001*
Partial giving way	4.50 (1.13)	5.00 (0.00)	-10%	0.002*
Full giving way	4.85 (0.53)	5.00 (0.00)	-3%	0.07
<b>Activities of daily living sub-scale</b>				
Walking	3.00 (0.00)	3.00 (0.00)	0%	1.00
Stairs	2.47 (0.53)	3.00 (0.00)	-18%	< 0.001*
Squatting/kneeling	2.52 (0.53)	3.00 (0.00)	-16%	< 0.001*
<b>Sports sub-scale</b>				
Straight running	2.64 (0.54)	3.00 (0.00)	-12%	< 0.001*
Jumping/landing	2.33 (0.59)	3.00 (0.00)	-22%	< 0.001*
Hard twists/cuts/pivots	2.11 (0.66)	3.00 (0.00)	-30%	< 0.001*

## Appendix 8

### Reliability of open and closed kinetic chain neuromuscular variables

#### Methods

##### Participants

This study involved a sub-group ( $n = 26$ ) of the healthy control participants described in Studies 1-3, who were available and willing to repeat the testing session within 5-7 days of the first assessment. Eligibility criteria are reported in Chapter 3, Section 3.5.1. In summary, participants were aged between 18 and 50 years, were recreationally active, i.e., regularly participating in sport at least 50 hours a year and currently involved in recreational or competitive sport (Hefti *et al.*, 1993) and had not history of injury or any other condition affecting their physical function.

##### Procedures

All control participants were invited to attend the second testing session until the required sample size was obtained. Ideally, reliability should be established within the clinical population of interest, i.e., within the ACLR group, to optimise the generalizability of the findings (Milner *et al.*, 2011). However, due to the involvement of the ACLR participants in another, unrelated PhD study, this was not possible.

To determine the minimum number of participants for the study, an *a priori* power analysis were performed according to the methods of (Donner & Eliasziw, 1987). An intraclass correlation coefficient (ICC) of  $\geq 0.75$  was set a priori as the optimal target level of reliability (Bruton *et al.*, 2000). A sample size of 20 participants were needed to provide 80% power at the 5% level of significance to test a null hypothesis between variables using intraclass correlation coefficients (ICCs) derived from a one-way analysis of variance model (Donner & Eliasziw, 1987). To account for potential loss of data, 30 participants were recruited. This more conservative sample size was also chosen in light of the limitation of having to establish the reliability of variables within the control group, rather than the ACLR group.

The assessment of demographic variables and physical characteristics, including physical activity level, level of sports participation, limb dominance and body mass index were described in Chapter 3. The right limb of control participants was assessed, rather than the dominant limb, to improve the efficiency of data collection procedures. Convenience sampling was used to recruit participants for this study; hence, the demographic variables and knee functional data of the study sample ( $n = 26$ ) were compared to the control group ( $n = 41$ ) from which they were sampled, to determine whether any differences existed between the groups. In addition to the biomechanical and neuromuscular variables, the Cincinnati Knee Rating Scale (see Appendix 5) was repeated to confirm that participants were not experiencing knee functional limitations.

### **Data and statistical analysis**

The data analysis procedures were identical to the procedures outlined in Study 2 (see Chapter 4, Section 4.4.6) and Study 3 (see Chapter 5, Section 5.5.7). After testing for normality with Shapiro-Wilk tests and equality of variance with Levene Median tests, the demographic and knee functional data of the control ( $n = 41$ ) and reliability sample ( $n = 26$ ) were compared using either independent t tests or independent samples Mann-Whitney U tests (Portney & Watkins, 2008). Differences in means and standard deviations (SD), or medians and interquartile ranges (IQRs), with 95% confidence intervals (CIs) were reported as appropriate.

To determine the reliability of variables, intraclass correlation coefficients; two way mixed, average measures (ICC 3, k), with 95% confidence intervals (CIs) were used. Average measures ICCs were used because all variables were derived from multiple trials, and the final values were measures of central tendency (i.e mean or median; ref). The magnitude of the ICC defines the ability of a variable to discriminate between individuals; therefore, the interpretation of the ICC throughout this thesis is the ability to discriminate between healthy individuals on repeated days of testing (Stratford & Goldsmith, 1997). ICC values range from 0 (no reliability) to 1 (perfect reliability), with values less than 0.4 rated as poor, 0.4 to 0.59 rated as fair, 0.6 to 0.74 rated as good, and values greater than or equal to 0.75 rated as excellent (Bruton *et al.*, 2000).

To determine the repeatability and measurement error of biomechanical and neuromuscular variables, the standard error of measurement (SEM) was calculated. The

SEM was derived by calculating the square root of the mean square residual from the analysis of variance output, which is derived during the ICC calculation (Stratford & Goldsmith, 1997). In this case, the SEM was an estimate of an individual control subject's measurement error, expressed in the same units as the variable (Meldrum *et al.*, 2014). After confirming normality and equality of variance with Shapiro-Wilk and Levene Median tests respectively, paired t tests were used to determine whether participants demonstrated significantly different performance of the tasks between testing occasions (Mathur *et al.*, 2005).

The minimum detectable change (MDC) and minimum clinically important difference were not calculated in this study because the convergent validity of neuromuscular and biomechanical variables was not established until Study 4 of this thesis. Hence, it was deemed that the difference in means between testing sessions, reliability and SEM were sufficient for describing the measurement properties of variables (Hinman *et al.*, 2013).

Ninety-five percent confidence intervals (CI) of both the ICC and the SEM were calculated for each variable. For the SEM, 95% CIs were calculated manually by dividing the sum of squares error from the analysis of variance derived from the ICC calculation by the upper and lower critical values of the chi-square distribution (Stratford & Goldsmith, 1997). The SEM and 95% CI were used to determine the repeatability of the testing protocol, and whether significant differences found between the ACLR and control groups were larger or smaller than the measurement error for each variable (Singh *et al.*, 2010).

## **Results and discussion**

### **Demographic variables**

The time between testing sessions was 7 days for all participants. Cincinnati Knee Rating Scale scores were 100% for both sessions. No significant differences in demographic variables or knee function scores were observed between the reliability study participants and the control group from which the participants for this study were recruited (see Table 1). Therefore, the results of this study may be easier to generalize to the control participants described in Studies 2 and 3.

**Table 1** Demographic variables and knee function of reliability study participants (n = 26) and control group from which participants were recruited (n = 41).

<b>Continuous variables</b>	<b>Sample (n = 26)</b>		<b>Control (n =41)</b>		<b>Difference (95% CI)</b>	<b>p value</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>		
<i>Demographic variables</i>						
Age at testing (years)	24.7	4.8	25.8	5.3	1.1 (-3.7 to 1.4)	0.37
Height (metres)	1.75	0.07	1.74	0.08	0.01 (-0.02 to 0.05)	0.56
Weight (kilograms)	71.9	11.6	72.5	11.1	0.6 (-4.4 to 6.6)	0.61
BMI (kg/m <sup>2</sup> )	23.7	2.6	24.0	2.6	0.3 (-1.4 to 1.2)	0.98
Tegner Activity Scale (/10)	6.3	2.2	6.0	2.0	0.3 (-0.5 to 1.6)	0.46
Hop for distance (cm/height)	81.4	13.9	78.4	14.9	3.0 (-3.3 to 9.7)	0.27
Crossover hop (cm/height)	239.8	54.9	227.1	56.5	12.7 (-11.7 to 24.6)	0.25
Side hop (number)	37.7	14.8	35.0	14.5	2.7 (-4.4 to 10.3)	0.43
<i>Knee function</i>						
Cincinnati Knee Rating Scale (%)	100.0	0.0	100.0	0.0	N/A	N/A
Hop for distance LSI (%)	100.8	5.8	100.0	6.6	0.8 (-3.5 to 2.1)	0.61
Crossover hop LSI (%)	97.8	9.1	100.5	9.7	2.7 (-4.8 to 1.4)	0.28
Side hop LSI (%)	100.0	25.9	104.2	21.9	4.2 (-9.1 to 5.8)	0.63
<b>Categorical (binary data)</b>						
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>		
Female sex	8	31	16	39	8% (-6% to 14%)	0.21
MOCP or day 1-14 of menstrual cycle	6	75	11	69	6% (-22% to 26%)	0.43
Tested on dominant limb	19	73	30	73	0% (-12% to 13%)	0.64
Level I or II sports at time of testing	18	69	28	68	1% (-15% to 17%)	0.94

Difference in means with standard deviation (SD) for continuous data, difference in proportions for categorical data, CI = 95% confidence interval;

Hop test LSIs were compared with independent samples Mann-Whitney U tests

Chi square tests were used to compare categorical variables

MOCP = monophasic oral contraceptive pill; BMI = body mass index, n = number of participants; SD = standard deviation; LSI = limb symmetry index

\*  $p < 0.05$

## Variables derived from open kinetic chain testing

Reliability analyses of the variables derived from open kinetic chain testing revealed excellent reliability for quadriceps force control and quadriceps and hamstring MVIC. EMG variables demonstrated good reliability (ICC > 0.6). Vastus medialis activation was significantly higher in the second testing session ( $p = 0.02$ ); however, the SEM (3.2%) was smaller than the difference between the ACLR and control group (5.8%; see Study 2). The other open kinetic chain variables demonstrated no significant differences between sessions. However, a 23% improvement in quadriceps force control was noted between sessions. The reliability, group differences and SEM of the variables derived from Study 2 are provided in Table 2.

**Table 2.** The mean (standard deviation), reliability (intraclass correlation coefficients; ICCs) and standard error of measurement (SEM) with 95% confidence intervals (CIs) for variables derived from open kinetic chain testing in Study 2.

Variable	Session 1	Session 2	ICC (95% CI)	SEM (95% CI)
	Mean (SD)	Mean (SD)		
Quadriceps force control (RMSE)	1.62 (0.7)	1.30 (0.6)	0.91 (0.22, 0.99)	0.30 (0.22, 0.39)
Quadriceps MVIC relative to body mass (Nm/kg)	2.0 (0.7)	2.1 (0.7)	0.93 (0.75, 0.98)	0.11 (0.07, 0.16)
Hamstring MVIC relative to body mass (Nm/kg)	1.1 (0.3)	1.2 (0.3)	0.88 (0.62, 0.96)	0.13 (0.09, 0.18)
Vastus medialis activation (%)	13.9 (3.2)	15.7 (4.6) *	0.61 (-0.06, 0.80)	3.2 (2.3, 4.1)
Vastus lateralis activation (%)	18.4 (2.3)	18.7 (3.9)	0.65 (0.22, 0.85)	2.6 (1.9, 3.3)
Rectus femoris activation (%)	18.2 (8.3)	20.9 (8.9)	0.60 (0.10, 0.83)	6.5 (4.7, 8.4)
Medial hamstrings activation (%)	1.1 (0.5)	1.3 (0.7)	0.62 (0.14, 0.83)	0.9 (0.7, 1.2)
Lateral hamstrings activation (%)	2.3 (1.0)	2.9 (1.5)	0.65 (0.22, 0.85)	0.4 (0.3, 0.6)

ICC = Intraclass correlation coefficient (average measures; 3, k); SEM = Standard error of measurement (in original units); RMSE = root mean square error; MVIC = maximum voluntary isometric contraction in Newton metres, normalised to body weight in kilograms (NM/kg); SD = standard deviation;

\* significantly different from session 1;  $p < 0.05$

## Variables derived from closed kinetic chain testing

Reliability analyses for closed kinetic chain variables revealed good to excellent reliability. There were no significant differences between the sessions for most variables; however, peak knee abduction angle was significantly larger in the second testing session ( $p = 0.003$ ). Peak knee abduction angle was reliable (ICC 0.91, 95% CI 0.80 to 0.96); however, the SEM (1.6°; 95% CI 1.1 to 2.0) was larger than the differences found between the ACLR and control groups (1.3°; 95% CI -0.6 to 3.2). The reliability, group differences and SEM of kinematic and kinetic variables are provided in Table 3.

**Table 3.** The mean (standard deviation), reliability (intraclass correlation coefficients; ICCs) and standard error of measurement (SEM) with 95% confidence intervals (CIs) for variables derived from closed kinetic chain testing in Study 3.

Variable	Session 1	Session 2	ICC (95% CI)	SEM (95% CI)
	Mean (SD)	Mean (SD)		
Approach velocity (m/sec)	1.57 (0.10)	1.59 (0.09)	0.88 (0.72, 0.94)	0.05 (0.03, 0.06)
Time to stabilise GRF (sec)	0.62 (1.7)	0.59 (1.7)	0.86 (0.69, 0.94)	0.08 (0.06, 0.11)
Peak vertical GRF (N/kg)	37.0 (7.2)	36.5 (7.4)	0.94 (0.87, 0.93)	2.5 (1.7, 3.2)
<i>Kinematic variables</i>				
Peak knee flexion angle (°)	68.1 (5.9)	67.4 (6.0)	0.95 (0.88, 0.98)	1.8 (1.3, 2.5)
Knee flexion excursion (°)	44.3 (5.6)	44.6 (4.1)	0.85 (0.67, 0.93)	2.2 (1.5, 2.9)
Peak knee abduction angle (°)	2.5 (3.8)	3.9 (3.8) *	0.91 (0.80, 0.96)	1.6 (1.1, 2.0)
Peak knee internal rotation angle (°)	12.5 (4.7)	13.3 (4.1)	0.76 (0.46, 0.89)	2.7 (1.9, 3.6)
Peak trunk flexion angle (°)	4.2 (7.0)	3.8 (7.1)	0.92 (0.83, 0.97)	2.7 (1.9, 3.5)
Peak hip flexion angle (°)	50.5 (9.5)	51.6 (8.2)	0.92 (0.83, 0.97)	3.3 (2.3, 4.3)
Peak ankle dorsiflexion angle (°)	23.3 (3.8)	22.8 (3.9)	0.91 (0.83, 0.97)	1.5 (0.9, 2.0)
<i>Joint moments</i>				
Peak hip extensor moment (Nm/kg)	13.1 (3.9)	13.4 (3.2)	0.88 (0.74, 0.95)	1.6 (1.1, 2.1)
Peak knee extensor moment (Nm/kg)	35.8 (5.6)	34.9 (5.2)	0.96 (0.91, 0.98)	1.5 (1.0, 2.0)
Peak ankle plantarflexor moment (Nm/kg)	13.7 (3.0)	12.9 (2.7)	0.93 (0.84, 0.97)	1.0 (0.7, 1.4)

ICC = Intraclass correlation coefficient (average measures; 3, k); SEM = Standard error of measurement (in original units); Time to stabilise vertical ground reaction force (GRF) to +/- 5% of body weight; sec = seconds; N = Newtons; kg = kilograms; m/sec = metres per second; § Muscle activation values (% of MVIC) represent the mean linear envelope in the 100 millisecond window prior to initial ground contact \* significantly different from session 1;  $p < 0.05$ , \*\*  $p < 0.05$

## *Appendix 9*

### **Reflective marker locations and orientations**

Marker (13mm)	Description
<b>Trunk/upper limb</b>	
Man	Jugular notch
T2	2 <sup>nd</sup> thoracic vertebrae
T10	10 <sup>th</sup> thoracic vertebrae
<b>Pelvis</b>	
LASIS/RASIS	Anterior superior iliac spines
SACR	Midpoint of posterior superior iliac spines
<b>Thigh</b>	
LTHAP/RTHAP	Proximal anterior thigh
LTHAD/RTHAD	Distal anterior thigh
LTHLP/RTHLP	Proximal lateral thigh
LTHLD/RTHLD	Distal lateral thigh
LLEPI/RLEPI	Lateral epicondyle of knee
LMEPI/RMEPI*	Medial epicondyle of knee *
RPAT/LPAT	Patella
<b>Tibia</b>	
LTIAP/RTIAP	Proximal anterior tibia (1/3 from lateral epicondyle to lateral malleolus)
LTIAD/LTIAD	Distal anterior tibia (2/3 from lateral epicondyle to lateral malleolus)
LTILAT/RTILAT	Lateral tibia (1/2 from lateral epicondyle to lateral malleolus)
LLMAL/RLMAL	Lateral malleolus
LMMAL/RMMAL*	Medial malleolus *
<b>Foot</b>	
LHEEL/RHEEL	Distal calcaneus
LHEEL2/RHEEL2*	Proximal calcaneus *
LMFS/RMFS	Mid-foot superior
LMFL/RMFL	Mid-foot lateral
LTOE/RTOE	Nail of 1 <sup>st</sup> toe *
* = static calibration only	





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