Biomechanical Measures to Assess Recovery from Anterior Cruciate Ligament Injury and Reconstructive Surgery

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ABSTRACT

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Anterior cruciate ligament (ACL) injuries are a debilitating injury resulting in abnormal biomechanics. Treatment commonly involves reconstructive surgery, however the tools used to assess the changes in biomechanics due to this procedure may fail to assess movement deficiencies. Therefore, the aim of this thesis was to explore what biomechanical variables are affected by ACL injury and reconstructive surgery and to assess their worth in the monitoring of recovery from ACL injuries and reconstructive surgery.

A systematic review of the changes in lower limb biomechanics that occur due to ACL reconstruction identified 51 articles that presented evidence on balance, joint position sense, gait, pivoting, stair ambulation, and landing tasks. Despite trends in certain variables, such as increased knee flexion excursion, there were inconsistencies between articles in presented changes of gait, pivoting, and landing movements. Tasks that related to the proprioceptive function of the limb exhibited consistent improvements due to surgery. This was the first review to provide a synthesis of the evidence around biomechanical changes due to ACL reconstruction and supported the exploration of variables related to the proprioceptive capacity of the injured limb for the use in assessing function.

Balance data were collected for eight ACL injured participants before and after surgery, and 45 uninjured participants using collection methods that were integrated into clinical practice. The two samples were similar in age, anthropometrics, and sex. Linear measures of the centre of pressure (CoP) provided a measure of balance performance, and complexity at varying timescales calculated using multiscale sample entropy, an approach that had yet to be

explored in ACL injured participants, and complexity index, a summary statistic of the sample entropy at numerous timescales, provided details on the non-linear characteristics of the CoP.

Despite previous evidence linking ACL injuries to a reduction in balance performance, the data did not support the use of linear measures. Linear measures had greater variation in uninjured participants than non-linear measures (e.g. coefficient of variation; CoP path length: 16%; mediolateral CoP complexity index: 10%). No trends, supported by a lack of statistical significance, between the involved and comparison limbs were identified (mean±SD pre-surgery CoP path length; ACL involved: 76±19 cm; ACL uninvolved: 87±27 cm; uninjured controls: 93±28 cm). No significant differences were observed due to surgery (mean±SD post-surgery CoP path length; ACL involved: 79±27 cm).

Complexity of the CoP, in addition to having a reduced variation in uninjured participants, supported that ACL injury was related to a loss of complexity (mean±SD pre-surgery mediolateral complexity index; ACL involved: 4.9±1.3; uninjured controls: 6.0±0.9) and that reconstructive surgery was able to restore this loss (mean±SD ACL involved mediolateral sample entropy at 6.7 Hz; pre-surgery: 0.9±0.3; 19 weeks post-surgery: 1.2±0.2).

The findings provide new evidence to support that ACL injury results in a loss of complexity and that the multiscale sample entropy of the CoP may provide an insight into the changes in lower limb biomechanics that occur due to ACL injury and reconstructive surgery. Comparison of the magnitude of changes in complexity due to ACL reconstructive surgery to uninjured participants, supported that increased complexity may be clinically meaningful. The link between increased complexity and functional outcomes however, is not understood and therefore further research is required to understand this link to establish the usability of complexity as a clinical measure.

Publications

There are no publications or conference abstracts related to this thesis.

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Nomenclature

ACL	Anterior cruciate ligament
AP	Anteroposterior
ApEn	Approximate entropy
CI	Confidence interval
CompInd	Complexity index
CoP	Centre of pressure
CV	Coefficient of variation
DFA	Detrended fluctuation analysis
EMD	Empirical mode decomposition
ICC	Intraclass correlation coefficient
IMF	Intrinsic Mode Function
MAD	Median absolute difference
ML	Mediolateral
MRI	Magnetic resonance imaging
MSE	Multiscale sample entropy
PROM	Patient reported outcome measure
SampEn	Sample entropy
SD	Standard deviation

1. Introduction

1.1 Research Overview

1.1.1 Anterior Cruciate Ligament Injuries

The anterior cruciate ligament (ACL) is one of four major ligaments in the knee joint and has a main role of resisting anterior translation and rotation of the tibia relative to the femur (Arnoczky, 1983; Butler, Noyes, & Grood, 1980). Injury to the ligament is common (Moses, Orchard, & Orchard, 2012) and has a number of debilitating repercussions such as increased risk of degenerative knee cartilage conditions, reduced activity level, and reduced functional capacity (Kessler *et al.*, 2008; Muaidi, Nicholson, Refshauge, Herbert, & Maher, 2007; Papastergiou, Koukoulias, Mikalef, Ziogas, & Voulgaropoulos, 2007). Treatment for such injuries commonly involves reconstructive surgery.

Surgical ACL reconstruction involves the replacement of the damaged ligament by a graft and aims to restore the structural support provided by the intact ligament. Despite the partial success of this surgery in allowing patients to return to previous levels of activity and improved self-reported functional capacity (Webster & Feller, 2018), there still remains a number of long term effects of the injury. Early onset osteoarthritis and increased risk of further injury are both still present in ACL reconstructed populations (Lohmander, Östenberg, Englund, & Roos, 2004; Risberg *et al.*, 2016). These continuing outcomes of ACL injury and treatment are suggested to be related to abnormal biomechanics (Hart *et al.*, 2016), however the assessment of these movement characteristics is often difficult within a clinical setting.

Assessment tools that are able to capture changes in biomechanics and relate these changes to long term outcomes of ACL injury may help inform operative and rehabilitative treatment decisions, ultimately improving prognosis. The National Ligament Registry, an initiative that captures current practice of orthopaedic clinicians working in the United Kingdom, demonstrated that currently used assessment tools within clinical practice focus mainly on patient reported outcome measures (PROMs; The National Ligament Registry, 2019). PROMs form the basis of all clinical assessments regardless of patient characteristics (e.g. activity level). Despite evidence to suggest these questionnaires are valid tools for the assessment of ACL reconstruction outcomes (Salavati, Akhbari, Mohammadi, Mazaheri, & Khorrami, 2011), they may fail to identify some biomechanical deficiencies which would benefit from objective assessment. Where participants aim to return to sport after ACL injury, more dynamic assessments, such as hop tests, are used to gain further insight into limb function, however these may also fail to identify biomechanical deficiencies, and are unsuitable for use in the early stages of treatment. Research into the area of ACL injuries and biomechanical changes is broad (Claes, Neven, Callewaert, Desloovere, & Bellemans, 2011; Hart *et al.*, 2016; Kowalk, Duncan, McCue Iii, & Vaughan, 1997), however often the proposed methodology does not account for the limitations of clinical environments, meaning integration into practice is difficult.

1.1.2 Constraints of Clinically Applicable Findings

The collection of biomechanical markers of recovery from ACL injuries may be useful for clinicians when making treatment and rehabilitation decisions, however for such measures to be widely used the limitations of clinical practice need to be considered. Constraints include required resources and expertise, extrapolation of findings to other patient demographics (e.g. athletic sample and general populace), and the burden placed on the clinician and patient, and therefore the ease of integration. Where new approaches are explored, criterion tools should be used to collect the associated data to ensure scientific rigour is observed. In these cases, the adaptability of the used methodology should be considered so that if useful information is found, cheaper and more accessible methods of collecting the required data can be explored.

1.2 Thesis Aim

The overall aim of this thesis was:

To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

1.3 Research Aims and Thesis Structure

To address the aim of this thesis, four research aims were developed and assessed through three research studies. It was first important to systematically synthesise the current evidence surrounding the changes in biomechanical measures which occur due to ACL reconstruction. This evidence would allow the collection of relevant biomechanical data which could then be assessed for its potential use in the monitoring of ACL injury treatment. No current systematic review of data relating to biomechanical changes due to ACL treatment was available and therefore **Aim I** was developed and will be addressed through a systematic review presented in Chapter 3.

Aim I:

Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery.

The identification of movement tasks and biomechanical variables which appear to be affected by ACL reconstruction informed the development of a data collection protocol which was implemented. This protocol not only took into account the findings relating to **Aim I**, but also the restrictions of clinical practice. Analysis of this data set formed the research studies presented in Chapters 6 and 7.

Where variables are intended to be used for the monitoring of changes in individuals undergoing an intervention, such as ACL reconstruction, it is first important to understand the consistency of these measures (Hopkins, 2000). The consistency of a variable can inform the choice of certain methodologies, and allow comparison of the magnitude of changes due to an intervention against the natural bias within the two measurements. To maximise the applicability of these levels of consistency, the time between observations should be matched to common clinical practice. This led to the development of **Aim II** which will be addressed in Chapter 6.

Aim II:

Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe.

Finally, to establish whether a variable may be suitable for the monitoring of changes due to ACL reconstruction, the effect of surgical intervention needs to be understood. Additionally, the magnitude of the changes should be considered to determine their clinical meaningfulness. This led to **Aims III** and **IV** to be developed, which will be addressed in Chapter 7.

Aim III:

Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons.

Aim IV:

Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.

An overview of the structure of the thesis and the chapters which addressed each research aim is presented in Figure 1.

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

Chapter	Title	Addressed Aims
1	Introduction	
2	Monitoring Functional Recovery from ACL Injuries	
3	Lower Limb Biomechanics Before and After ACL Reconstruction: A Systematic Review	**AIM I**: Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery
4	Assessment of Balance as a Measure of ACL Injury Recovery: A Review of Linear and Non-Linear Approaches	
5	General Methods	
6	Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population	**AIM II**: Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe
7	The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity	**AIM III**: Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons **AIM IV**: Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.
8	Thesis Summary	
9	Conclusion	

Figure 1. Schematic of thesis structure and research aims

2. Monitoring Functional Recovery from Anterior Cruciate Ligament Injuries

2.1 Anterior Cruciate Ligament: Background

2.1.1 Anatomy

Originating from the lateral femoral epicondyle and inserting at the anterior intercondylar area of the tibia, the ACL provides stability to the knee, most notably by resisting tibial anterior draw (Arnoczky, 1983; Butler *et al.*, 1980). The structure of the ligament is controversial, but it is generally accepted to be made up of two major functional bundles. The anteromedial and posterolateral bundles, named for their tibial insertions, have been identified due to their change in tension as the knee moves through its range of motion. This variation in laxity has then been shown to have a direct effect on the contribution of each bundle to resist anterior tibial draw (Amis & Dawkins, 1991) and the tension through each bundle during subluxation (Gabriel, Wong, Woo, Yagi, & Debski, 2004). The ligament also contributes to the neuromuscular system through the presence of mechanoreceptors (Dhillon, Bali, & Prabhakar, 2012) which provide afferent information to the central nervous system (Zimny, Schutte, & Dabezies, 1986).

2.1.2 Epidemiology

ACL injury incidence rates have been reported through registries in Scandinavia and in some cases can be as high as 1-in-500 within certain populations (20-29 year olds; Granan, Forssblad, Lind, & Engebretsen, 2009). Incidence rates are comparable across the world (Gianotti, Marshall, Hume, & Bunt, 2009; Moses *et al.*, 2012) and highlight the prevalence of ACL injuries.

Injury to the ACL has a number of debilitating repercussions including drop in quality of life, loss of earnings, acute discomfort from treatment and increased risk of chronic diseases such as osteoarthritis (Kessler *et al.*, 2008). In addition to the direct effects of injury on the sufferer, the treatment of ACL injuries and secondary disease has a large cost on the health care system which provides treatment.

Gianotti *et al.* (2009) reported that in New Zealand, where the ACL incidence (Moses *et al*., 2012) and economy are comparable to the United Kingdom, patients required an average of 24 treatment visits with a mean cost of NZ$ 11,000 (~GBR£4500).

2.1.3 Injury Mechanism

Injury to the ACL is caused by the strain placed upon the ligament exceeding its mechanical properties, and can be through contact or non-contact mechanisms. The mechanisms of non-contact ACL rupture have been extensively studied (Quatman, Quatman-Yates, & Hewett, 2010; Shimokochi & Shultz, 2008; Shin, Chaudhari, & Andriacchi, 2011). A number of different approaches have been used to describe the injury mechanism, however the inherent limitations with each mean it is difficult to provide a definitive answer. It is generally accepted however, that the mechanism is multi-planar and involves knee movements outside of normal physiological ranges (Hewett, Myer, Ford, Paterno, & Quatman, 2016). The most commonly cited mechanism is a knee valgus collapse, where there is tibial abduction relative to the femur at low knee flexion angles (Quatman *et al.*, 2010).

2.1.4 ACL Deficiency

ACL rupture has a number of acute and long term effects on the function of the involved and uninvolved limbs (Kessler *et al.*, 2008). From an acute perspective further traumatic injuries such as bone bruising and swelling result in short term changes in the function of the joint, however these often subside with rest (Gupte & St Mart, 2013). More concerning are the effects ACL deficiency has on the biomechanics of the knee joint. ACL deficient knees have been shown to have increased laxity (Kittl *et al.*, 2016; Snyder-Mackler, Fitzgerald, Bartolozzi, & Ciccotti, 1997), reduced muscular activation and strength (Kannus, Lanala, & Järvinen, 1987; Limbird, Shiavi, Frazer, & Borra, 1988), and alterations in the performance of tasks such as gait (Knoll, Kocsis, & Kiss, 2004b). The changes in biomechanics of the knee joint have been linked to a number of outcomes from ACL deficiency.

One outcome of ACL deficiency is further musculoskeletal conditions such as cartilage damage. Papastergiou *et al.* (2007) highlighted the effect of ACL deficiency on the risk of meniscal tears. There was a significant increase in meniscus damage when time since injury was longer than three months. ACL deficiency has also been shown to increase the risk of early onset tibiofemoral osteoarthritis (Lohmander *et al.*, 2004), compared to uninjured knees. Other outcomes include reduced quality of life and physical activity levels assessed through PROMs (Filbay, Culvenor, Ackerman, Russell, & Crossley, 2015). These outcomes from ACL deficiency mean that treatment is often advised, and this is most commonly through ACL reconstructive surgery (Grindem, Eitzen, Engebretsen, Snyder-Mackler, & Risberg, 2014).

2.1.5 Reconstructive Surgery

ACL reconstructive surgery involves the replacement of the ruptured ligament with a graft, with the aim of restoring the mechanical stability provided by the intact structure. ACL grafts are commonly autografts (harvested from the affected patient) and are often hamstring (semitendinosus and gracilis) or patellar tendons (The National Ligament Registry, 2019). In addition to graft choice, there are a number of other surgical characteristics which can differ between treatment, including number of bundles and fixation methods. These characteristics are outside the scope of this thesis, however Prentice *et al.* (2018) presented data from national registries and provides a broad overview of current clinical practice.

2.1.6 Rehabilitation

Rehabilitation is generally regarded as a key factor of recovery from ACL reconstruction (Beynnon, Johnson, & Fleming, 2002), however there is no consensus on the optimal protocol (van Grinsven, van Cingel, Holla, & van Loon, 2010). Although there are differences in the method employed, the outcome goals of rehabilitation are consistent. Initial aims are to reduce pain and swelling, and restore full range of motion, and subsequently to restore neuromuscular function and muscular strength (van Grinsven *et al.*, 2010). Despite the importance of rehabilitation, adherence to such protocols is varied. Pizzari, Taylor, McBurney, and Feller (2005) reported the 25-75% percentiles of percentage of prescribed rehabilitation sessions completed, and found adherence rates of 91-100% and 61-87% for scheduled appointments and home exercise, respectively. This range in adherence means the rate of functional recovery may differ between participants undergoing the same treatment. When considering the development of potential measures of recovery from ACL reconstruction, variables should still be able to identify changes in participants with a range of adherence who have undergone surgical intervention.

2.2 Outcomes from ACL Reconstruction

The aim of ACL treatment is to restore structural stability and neuromuscular function of the limb. Evidence supports that current treatment approaches are capable of achieving these aims (Malcom, Daniel, Stone, & Sachs, 1985; Reider *et al.*, 2003), however long term outcomes suggest that function is not restored to pre-injury values. A number of outcomes, such as return to previous activity level, incidence of further injury and degenerative musculoskeletal conditions, and quality of life, have been reported in ACL reconstructed participants (Paterno, Rauh, Schmitt, Ford, & Hewett, 2014; Salmon *et al.*, 2018).

Salmon *et al.* (2018) assessed return to pre-injury activity levels and knee function (using the International Knee Documentation Committee Knee Evaluation questionnaire). At 20 years post-surgery only 31% of people who suffered an ACL rupture as an adolescent and 65% of people who suffered the injury as an adult had similar function compared to the contralateral limb. Additionally, only 80% of all participants returned to their pre-injury level of activity at any time point since surgery, with approximately 18% of participants stating their current knee function was decreasing their activity level. ACL reconstructed limbs have also been shown to have an increased risk of re-injury with Paterno *et al.* (2014) reporting an almost six times increased risk of secondary ACL rupture within two years of return to sport compared to age matched uninjured controls. Meniscal damage is also often accompanied with ACL damage and treatment (Frobell *et al.*, 2015), and for those who suffer meniscal damage long-term osteoarthritis risk has been suggested to be 21-48% (Øiestad, Engebretsen, Storheim, & Risberg, 2009).

The negative outcomes from ACL treatment have been suggested to be as a result of a failure to fully restore lower body and knee biomechanics to normal levels (Grindem, Snyder-Mackler, Moksnes, Engebretsen, & Risberg, 2016). Efforts have been made to reduce a number of outcomes through the use of monitoring tools (Webster & Hewett, 2019), and although these are often used in return to sport there is little implementation in their use to inform treatment decisions before and after ACL reconstructive surgery (Francis, Thomas, & McGregor, 2001; Kapoor, Clement, Kirkley, & Maffulli, 2004). Additionally, the currently available tools may provide limited information on the biomechanics of the lower limbs, and be unsuitable for widespread clinical implementation.

2.3 Assessment Tools for Recovery

2.3.1 Patient Reported Outcomes Measures

One currently used group of assessment tools are PROMs, which are subjective questionnaires covering activity level, knee function, osteoarthritis symptoms, and quality of life. A survey of 1779 clinicians revealed a range of PROMs (Knee Outcome Survey-Activities of Daily Living Scale, Knee Outcome Survey-Sports Activities Scale, Global rating of perceived function, Lysholm Score, International Knee Documentation Committee 2000 Subjective Knee Form, Cincinnati Knee Score, Knee Injury and Osteoarthritis Outcome Score, Tegner Activity Scale, and Marx Activity Rating Scale) were used to assess ACL injury treatment outcomes. PROMs provide an easily implemented method for assessing the current symptoms and impact of the injury, however may not identify biomechanical abnormalities which can still be present up to five years post-surgery (Gokeler *et al.*, 2013). More direct measures of knee biomechanics may therefore provide further information on the recovery from ACL injury.

2.3.2 Measures of Passive Laxity

A key biomechanical characteristic which treatment aims to restore is laxity. Measures of laxity can be either through binary tests such as Lachman and pivot shift tests, or objective assessments using tools such as the KT-2000. Lachman and pivot shift tests involve manual manipulation of the knee joint, and aim to identify whether the graft is providing structural resistance to tibial translation and rotation. Instrumented assessment of laxity through the use of arthrometers provides further information on laxity by assessing anterior tibial translation when force is applied. While these assessments of laxity help to identify whether treatment has resulted in normal levels of laxity, due to their passive nature do not allow the changes in neuromuscular function on joint stability to be assessed, limiting their use in monitoring of changes which occur throughout treatment.

2.3.3 Dynamic Measures of Knee Function

To address the limitations of PROMs and passive assessments of laxity, a number of dynamic assessments have been proposed. The most common of these assessments are variations of hop testing (Gustavsson *et al.*, 2006), where a reduced asymmetry between the injured and uninjured limb is viewed as greater function. Results from these assessments have been shown to be predictors of PROMs of knee function one year after surgery (Logerstedt *et al.*, 2012), however do not provide specific data on how the task was completed and therefore cannot directly assess biomechanical deficiencies which are present (Xergia, Pappas, Zampeli, Georgiou, & Georgoulis, 2013). An additional limitation of hop tests, are the demands placed on the musculoskeletal system make them unsuitable for pre-surgery assessments where joint stability is poor. This means that although these tools may offer insight into asymmetries at return to sport assessments, they have limited use during early stages of treatment. A survey of British based orthopaedic surgeons (n = 192; 60% response rate; Kapoor *et al.*, 2004) evidenced the limited use of functional assessments in informing treatment decisions. Only MRI, arthroscopy and passive range of motion were reported as being used, and in only 7%, 14% and 30% of clinicians, respectively.

2.3.4 Potential of Biomechanical Assessments

The collection of biomechanical data relating to the function of the limb may offer specific objective information which can be used to inform treatment decisions. Biomechanical data on ACL reconstructed participants have been linked to secondary injury (Paterno *et al.*, 2015; Paterno *et al.*, 2010), successful return to sport assessments (Di Stasi, Logerstedt, Gardinier, & Snyder-Mackler, 2013), and osteoarthritis prevalence (van Meer *et al.*, 2015). Collection of biomechanical data often requires resources such as motion capture systems, and large spaces suitable for the completion of tasks such as gait, meaning the application of biomechanical research is limited in general clinical practice. The evidence surrounding the assessment of biomechanics in ACL injured populations suggests it has potential worth in the monitoring of recovery and use in informing treatment decisions, however the exploration of protocols which can be simplified to make them accessible to clinicians is warranted.

3. Lower Limb Biomechanics Before and After Anterior Cruciate Ligament Reconstruction: A Systematic Review

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

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Figure 1. Schematic of thesis structure and research aims

3.1 Preface

Chapter 2 outlined the rationale for exploring the potential use of biomechanical measures in the monitoring of ACL recovery and to inform treatment decisions. The identification of specific movement tasks which are affected by ACL treatment and the currently used analysis methods would allow a data collection protocol to be developed. Therefore this Chapter addressed **Aim I** of this thesis (Figure 1) by systematically synthesising the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery.

3.2 Introduction

The ACL is one of the structures within the knee that provides mechanical resistance to joint laxity and information to the proprioceptive system (Arnoczky, 1983). ACL rupture is a common injury (Moses *et al.*, 2012) and results in knee instability, pain, and early onset of osteoarthritis (Barber, Noyes, Mangine, McCloskey, & Hartman, 1990; von Porat, Roos, & Roos, 2004). ACL deficient knees have been shown to have altered biomechanics, such as reduced strength, increased knee laxity, and alterations in the performance of movement tasks (Georgoulis, Papadonikolakis, Papageorgiou, Mitsou, & Stergiou, 2003; Keays, Bullock-Saxton, Newcombe, & Keays, 2003).

To alleviate these symptoms and return knee biomechanics to normal levels, the damaged ligament is often replaced by a graft during reconstructive surgery. For example, of 143 patients treated as part of the Delaware-Oslo ACL Cohort Study, 70% of patients opted to undergo reconstructive surgery (Grindem *et al.*, 2014). Non-surgical approaches have been shown reduce symptoms of instability, however their long-term effectiveness is not fully understood (Muaidi *et al*., 2007), and surgical intervention remains the most popular treatment choice. Surgical reconstruction aims to improve the stability of an ACL deficient knee by the mechanical role of the original ligament being replaced by the graft. Although reconstruction may also restore the proprioceptive potential of the knee (Dhillon *et al.*, 2012), the loss of the mechanoreceptors in the intact ACL cannot be restored. Proprioceptive potential refers to the capacity of the limb to recover from the loss of the afferent inputs that were provided by the healthy ACL through compensatory mechanisms. The details of these compensatory mechanisms are not fully understood, however as the graft does not provide neurological information they may relate to the restored structural stability facilitating the adaptation of other proprioceptive components. The success of reconstructions measured, as return to previous activity level (Ardern, Webster, Taylor, & Feller, 2011) and avoidance of further musculoskeletal complications (Kessler *et al.*, 2008), although high, is not perfect. An increased risk of reinjury and early onset osteoarthritis compared to uninjured comparison participants have been identified after ACL reconstruction (Paterno, Rauh, Schmitt, Ford, & Hewett, 2012; von Porat *et al.*, 2004). These outcomes may be due to treatment failing to fully restore the biomechanics of lower limb to healthy states, resulting in increased risk of re−injury, or unhealthy joint movement patterns.

Systematic reviews have previously identified altered biomechanics in the ACL deficient and reconstructed knee (Hart *et al.*, 2016; Hart, Ko, Konold, & Pietrosimione, 2010; Petersen, Taheri, Forkel, & Zantop, 2014). These reviews have shown decreases in muscle strength, and altered gait biomechanics, among others, in injured compared with non-injured knees. However, no systematic evaluation of the literature surrounding the changes in biomechanics which occur as a result of reconstructive surgery is currently available. This information may provide further insight into the biomechanical changes that occur following reconstruction to inform the development of pre− and post−operative physical therapy programmes aimed at maximising the effectiveness of treatment, and also into the development of tools aimed at monitoring recovery from such treatments. Therefore this study addressed **Aim I** of this thesis by systematically synthesising the findings of literature which have measured lower limb biomechanics before and after ACL reconstructive surgery in the same participants.

3.3 Methods

This systematic review was designed and presented in accordance with the PRISMA guidelines (Moher *et al.*, 2015).

3.3.1 Search Strategy

Electronic literature searches in CINHAL, MEDLINE, SCOPUS, and SPORTDiscus were performed from inception to 31st December 2018. A search strategy developed using the PICO approach was run in all databases. The PICO strategy involves including terms which identify the population, intervention, comparison, and outcome of interest (O'Connor, Green, & Higgins, 2011). Search terms falling under each heading are combined with an "OR" function, and each search heading combined with an "AND" function. Anterior cruciate ligament (population), reconstruction (intervention), pre- and post-operation (comparison), and biomechanical variables (outcome) formed the four components of the PICO approach. These, and other relating terms, formed the final search strategy (Figure 2) which aimed to maximise the identification of all relevant literature, including non-published articles such as theses and conference abstracts. Truncation allowed the identification of a number of words only using one search input (e.g. biomech* would identify terms such as, biomechanics and biomechanical). Reference lists of accepted articles were manually searched for additional papers that were not included in the list but might meet the inclusion and exclusion criteria.

Population	ACL *or* anterior cruciate ligament

and

Intervention	rupture *or* reconstructi* *or* surg*

and

Comparison (a)	before *or* pre* *or* prior

and

Comparison (b)	after *or* post*

and

Outcome	kinematic* *or* kinetic* *or* biomech* *or* torque *or* angle *or* strength *or* force *or* propriocepti* *or* velocity *or* acceler*

Figure 2. Systematic review search strategy employed using the PICO approach. Truncation was shown as an asterisk.

3.3.2 Study Selection

The titles and abstracts of the identified articles were assessed for inclusion and exclusion criteria by two researchers independently. Inclusion criteria were: 1) human participants with a completely ruptured ACL who underwent reconstructive surgery; 2) data collected within 12 weeks before and 52 weeks after surgery; and 3) biomechanical measures taken. Restrictions on the timing of data collections were included to minimise the influence of longitudinal changes occurring not as a result of the intervention. Exclusion criteria were: 1) participants who had suffered concurrent knee ligament injuries; 2) knee osteotomy; and 3) data on isokinetic torque assessments. Isokinetic strength data were excluded due to the body of evidence showing a clear link between strength deficiencies and ACL reconstruction and subsequent recovery (Ardern & Webster, 2009; Petersen *et al.*, 2014; Xergia, McClelland, Kvist, Vasiliadis, & Georgoulis, 2011). Articles were only excluded if both reviewers assessed that they did not meet the inclusion/exclusion criteria. Where only a single reviewer felt an article should be excluded based on the title and abstract, the article was not excluded. Full texts of all remaining articles were subsequently retrieved and assessed for the same inclusion and exclusion criteria independently by the same two reviewers. No conflicts were identified in the decision to include articles based on the full text.

3.3.3 Article Categorisation

As the biomechanical demands of the knee differ depending on the task which is performed, changes which occur due to ACL reconstruction may vary between movement tasks. Therefore, identified articles were categorised by the movement which was assessed. These movements were stance or balance, joint position sense, gait, pivoting, stair ambulation, and landing.

3.3.4 Methodological Assessment

Methodological quality was assessed using a custom assessment tool to detect risk of bias present in a one group pretest-posttest experimental research (Appendix A). The tool was developed using other available tools such as the Cochrane Collaboration's tool for assessing risk of bias (Higgins *et al.*, 2011), and The Effective Public Practice Health Project: Quality Assessment Tool for Quantitative Studies (Armijo-Olivo, Stiles, Hagen, Biondo, & Cummings, 2012; Thomas, Ciliska, Dobbins, & Micucci, 2004). A grade was given for the methodological strength of how well the participants represented the target population, the number of withdrawals and drop-outs, study design, intervention integrity, and data collection. A grade of strong, moderate, or weak was given to each section. Due to differences in the research question proposed by this review and those in the identified articles, inconsistencies were often present in the intervention or data collections that would not affect the risk of bias related to this review. To account for differences that would not impact the results of this review the effect of differences were also considered in the quality assessment process. No consideration of the research design (i.e. randomised controlled trial) as only pre- to post-surgery values were extracted. An article was then awarded a strong grade (if it had no weak ratings, and there were fewer than four moderate ratings), a moderate grade (if there were more than zero but fewer than two weak, or more than three moderate ratings), or a weak grade (if there were two or more weak ratings).

3.3.5 Data Extraction

Data extraction was completed by one reviewer (JM). Where data were not available, the authors were contacted in attempt to gain this information. Information included details on the study sample and design, intervention details, and data collection methods (Table 1).

Table 1. Data extracted from each article

Category	**Included Information**
Participants	Sample size, and average participant mass and height
Study Design	Time since injury, timing of data collections, and inclusion of other interventions
Surgery Details	Graft type, number of bundles, and any other relevant information
Data Collection Methods	Task analysed, and equipment used
Outcome Variable	Variable of interest, data analysis method, and pre− and post−operative values
Findings	The main finding of the paper, and where applicable the statistical test used to confirm this finding

3.3.6 Data analysis

Cohen's *d* (Equation 1) and 95% confidence intervals (CI; Equation 2) were calculated as (Cohen, 1988; Hedges & Olkin, 1985),

$$d = \frac{\bar{x}_2 - \bar{x}_1}{Pooled\ SD} \tag{1}$$

and

$$95\%\ CI = d \pm \sqrt{\frac{n_1 + n_2}{n_1 \times n_2} + \frac{d^2}{2(n_1 + n_2)}} \times 1.96 \tag{2}$$

where $\bar{x}_i$ and n_i are the mean and sample size, respectively, of pre- (i = 1) and post-surgery (i = 2) data. Negligible (*d*<0.2), small (0.2≤*d*<0.5), medium (0.5≤*d*<0.8), and large (*d*≥0.8) effects were defined using Cohen (1988) guidelines. The effect size was not corrected by Pearson's correlation coefficient as this statistic could not be calculated from the extracted data. Where mean and standard deviations (SD) were not presented for biomechanical variables, values were either provided by the author, or estimated from other measures of central tendency and spread following guidelines by Wan, Wang, Liu, and Tong (2014). If mean and SD were not able to be sourced the variable was excluded from analysis. Where data were presented on two or more groups undergoing reconstructive surgery these were combined to provide an overall mean ($\bar{x}$) and SD (σ) as described by Goon, Gupta, and Dasgupta (1968),

$$\bar{x} = \frac{\sum_i^g n_i \bar{x}_i}{\sum_i^g n_i} \tag{3}$$

and

$$\sigma = \sqrt{\frac{\sum_i^g (n_i - 1) \times {s_i}^2 + \sum_i^g n_i (\bar{x}_i - \bar{x})^2}{(\sum_i^g n_i) - 1}} \tag{4}$$

where $\bar{x}_i$, s_i and n_i are the mean, SD and sample size, respectively, and *g* the number of groups.

Calculated effect sizes were not combined in a meta-analysis. This decision was made due to differences in data collection and analysis methods resulting in heterogeneity between effects. Factors such as the time of extraction of a variable, such as peak knee flexion or average knee flexion, influence what characteristic is being described and therefore combination would not result in a more confident conclusion relating to a specific change in lower limb biomechanics.

Effect size data were presented as *d*±95% CI where a positive effect size was an increase in the variable due to surgery, except measures of balance where an improved balance performance, shown as a reduction in centre of pressure (CoP) length, was presented as a positive effect size. A positive effect size does not always represent a positive outcome from ACL reconstructive surgery, however where a clear link is known between a variable and overall function this is discussed. The research question posed in this review often differed from that in the identified articles, and as a result no information on the statistical significance was available. Therefore, where the 95% CIs of effect size did not include zero, these results were viewed as significant (Hedges & Olkin, 1985), and are identified by a superscript alpha symbol (*d*±95% CI$^{\alpha}$). No information was reported on the statistical approach or outcomes used in the included research.

3.4 Results

3.4.1 Literature Search

After removal of duplicates, the literature search identified 1153 articles. Of these, 51 were found to meet the inclusion criteria and no further articles were identified through manual searches of reference lists (Figure 3). Data on the performance of stance or balance (n = 11), joint position sense (n = 5), gait (n = 31), pivoting (n = 4), stair ambulation (n = 4), and landing (n = 3) were identified. Where data on more than one movement were presented, the article was considered separately for each task.

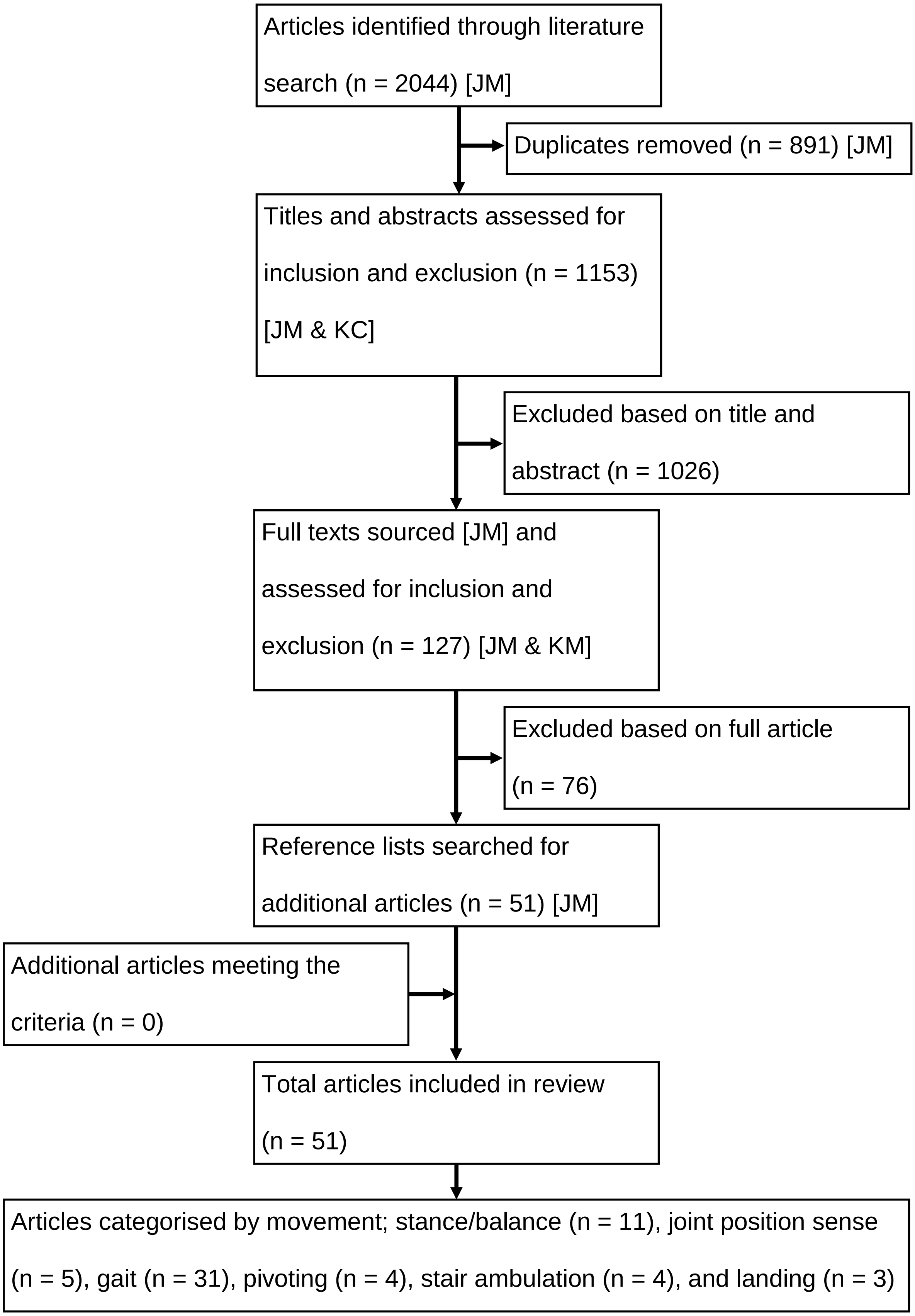

Figure 3. Flow diagram depicting the literature search. Where articles assessed more than one movement task (n = 7) they were included in both categories. Reviewers completing each task are shown in square brackets. There were no conflicts in inclusion and exclusion decisions when reviewing full texts.

3.4.2 Stance or Balance Tasks

3.4.2.1 Identified Articles

Eleven articles analysed the effect of ACL reconstruction on stance or balance tasks (Di Stasi, 2011; Di Stasi, Hartigan, & Snyder-Mackler, 2012; Gokalp *et al.*, 2016; Heijne & Werner, 2007; Kim & Park, 2009; Ma *et al.*, 2014; Ogrodzka-Ciechanowicz, Czechowska, Chwala, Slusarski, & Gadek, 2018; Tagesson & Kvist, 2016; Tagesson, Öberg, & Kvist, 2010; Tagesson, Öberg, Kvist, & Öberg, 2015; Tuğcu *et al.*, 2013), however three articles were not included in the analysis as data were the same as other identified articles (Di Stasi, 2011; Tagesson & Kvist, 2016; Tagesson *et al.*, 2015). Mean and SD were not available in one article (Kim & Park, 2009), resulting in seven articles being analysed (Di Stasi *et al.*, 2012; Gokalp *et al.*, 2016; Heijne & Werner, 2007; Ma *et al.*, 2014; Ogrodzka-Ciechanowicz *et al.*, 2018; Tagesson *et al.*, 2010; Tuğcu *et al.*, 2013).

3.4.2.2 Experimental Procedures

Balance performance was the main outcome for six of the articles, although variations were present in the method of producing this variable. These included movements of the balance board, and different computations using the CoP such as path length. Knee kinematics and muscle activations made up the remaining outcomes. Task constraints also differed between articles, these included unilateral or bilateral stance, eyes opened or closed, and static and dynamic balance. Comprehensive details of the experimental procedure used in articles which assessed balance are presented in Table 2.

Table 2. Details of research assessing changes in balance biomechanics before and after ACL reconstruction

	Sample Size	Height (x̄±SD; m)	Mass (x̄±SD; kg)	Time Since Injury (weeks)	Graft Details	Data Collection Tools	Post-Test Timings (weeks)	Task Analysed	Outcome Measures
Di Stasi *et al.* (2012)	n = 40	NR	NR	11.2±10.2	QB hamstring autograft (n=16) or SB allograft (n=24)	3D motion capture	24	Single leg static balance with eyes open	• Knee flexion angle • Anterior tibia position
Gokalp *et al.* (2016)	n = 30	NR	NR	26.8±18.4	SB BPB autograft	Tetrax Interactive Balance System	4, 8, & 12	Double leg static balance with eyes open and closed, on hard and soft ground	• Stability index combining scores from all conditions
Heijne and Werner (2007)	n = 68	1.74±0.08	73.7±11.1	34 (SD NR)	SB BPB (n=34) or hamstring (n=34) autograft	Kinesthetic Ability Trainer 2000	12 & 20	Single leg static balance with eyes open	• Summation of distance between origin and CoP

Table 2. continued

Ma *et al.* (2014)	n = 67	1.67±0.02	65.1±2.8	18.6±8.3	SB (n=20), SBA (n=21), or DB (n=26) hamstring autograft	Equilibrium Function Meter (G-620)	24	Single leg static balance with eyes closed	• CoP path length
Ogrodzka-Ciechanowicz *et al.* (2018)	n = 31	1.75±0.08	NR	NR	SB hamstring autograft	CQStab2P platform	24	Single leg static balance with eyes open	• CoP path length
Tagesson *et al.* (2010)	n = 19	NR	NR	60 (SD NR)	Quadruple hamstring autograft	Computerised goniometer and EMG	5	Single leg static balance with eyes open	• Maximum anterior tibial translation • Peak EMG activation of the vastus medialis, vastus lateralis, hamstring, gastrocnemius, and soleus
Tuğcu *et al.* (2013)	n = 58	NR	NR	15.8 (median)	BPB autograft	Kinesthetic Ability Trainer 2000	13	Single leg static and dynamic balance with eyes open	• Stability index calculated from fluctuations in balance board

Single bundle (SB), single bundle augmentation (SBA), double bundle (DB), quadruple bundle (QB), bone patella bone (BPB), centre of pressure (CoP), not reported (NR), electromyography (EMG)

3.4.2.3 *Quality Rating*

Table 3 shows the quality rating of all studies including data on stance and balance tasks. All articles had an overall rating of strong or moderate. Di Stasi *et al.* (2012) reported participants underwent surgery using either an allograft or autograft. This discrepancy in the intervention could lead to differences in changes due to surgery, increasing the risk of bias in the results. Other weak ratings occurred due to the participant retention not being reported.

Table 3. Assessment of quality of included studies exploring stance and balance tasks

	Participants	**Withdrawals**	**Study design**	**Intervention integrity**	**Data collection**	**Overall rating**
Di Stasi *et al.* (2012)	1	2	1	3	1	2
Gokalp *et al.* (2016)	1	3	1	1	1	2
Heijne and Werner (2007)	1	1	1	1	1	1
Ma *et al.* (2014)	1	1	1	1	1	1
Ogrodzka-Ciechanowicz *et al.* (2018)	1	1	1	1	1	1
Tagesson *et al.* (2010)	1	3	1	1	1	2
Tuğcu *et al.* (2013)	2	3	1	1	1	2

1 = strong, 2 = moderate, 3 = weak

3.4.2.4 *Main Findings*

Measures of balance performance showed improvements in single leg static balance at 12, 20, 24, and 48 weeks post-surgery with negligible to large effects (Figure 4) (Heijne & Werner, 2007; Ma *et al.*, 2014; Ogrodzka-Ciechanowicz *et al.*, 2018). These improvements appeared to be as a result of both improvements in medio-lateral (ML; 0.22±0.50) and antero-posterior (AP; 0.32±0.50) performance

(Ogrodzka-Ciechanowicz *et al.*, 2018). No comparison at the same time point for eyes open compared against eyes closed was available, however effect size with eyes closed at 24 weeks was larger than eyes open at 20 weeks. Effect sizes could not be calculated for single leg static balance data presented by Tuğcu *et al.* (2013) as no values of variance were presented. However a medium effect size was found for improvements in single leg dynamic balance 12 weeks after reconstructive surgery (Tuğcu *et al.*, 2013) ($0.53 \pm 0.37^{\alpha}$).

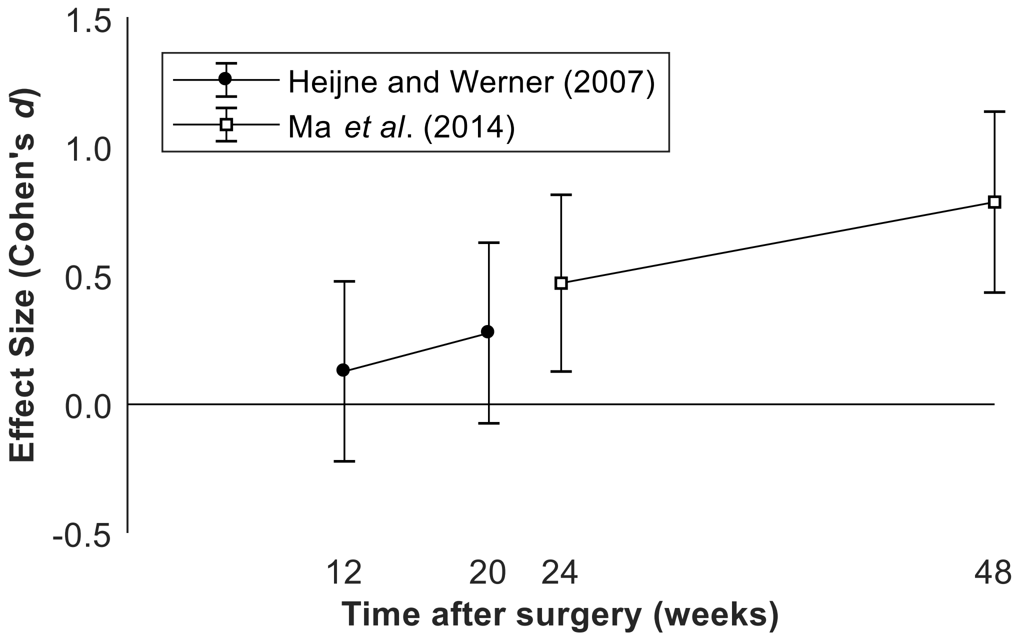

Figure 4. Cohen's d effect sizes and 95% confidence intervals for balance performance comparing pre-surgery to post-surgery data from Heijne and Werner (2007) and Ma *et al.* (2014), where positive effects were improvements.

One study presented data on the performance of bilateral balance under eight different conditions (Gokalp *et al.*, 2016). These included combinations of hard and soft surfaces, eyes open and closed, and varying neck positions. A combined balance score revealed a drop in performance at 4 ($-1.24 \pm 0.55^{\alpha}$) and 8 (-0.12 ± 0.51) weeks post-surgery, before improving to above pre-surgery values ($0.75 \pm 0.52^{\alpha}$) at 12 weeks.

On average, tibial kinematics showed a more anterior position, although effect size was negligible (0.06±0.44), and a small decrease in anterior tibial movement compared to an unloaded position (−0.25±0.61; Di Stasi *et al.*, 2012). Changes in knee flexion were also negligible (0.07±0.44), although participants demonstrated a slightly more flexed knee compared to pre-operation values. Muscle activations were analysed five weeks post-surgery and presented as a percentage of maximum voluntary isometric contraction (Tagesson *et al.*, 2010). Increased activation was found in the vastus medialis (0.42±0.61) and lateralis (0.45±0.61), hamstring (1.04±0.64$^{\alpha}$), gastrocnemius (0.69±0.62$^{\alpha}$), and soleus (0.41±0.61).

3.4.3 Joint Position Sense

3.4.3.1 Identified Articles

Five articles were identified which explored the effect of ACL reconstruction on joint position sense (Jurevičienė *et al.*, 2012; Ma *et al.*, 2014; Ordahan, Küçükşen, Tuncay, Salli, & Uğurlu, 2015; Reider *et al.*, 2003; Shidahara *et al.*, 2011). Two of these articles did not report a measure of variance and were therefore excluded from the analysis (Reider *et al.*, 2003; Shidahara *et al.*, 2011).

3.4.3.2 Experimental Procedures

Outcome variables were threshold for detection of passive movement, and passive and active recall. All data collections were conducted using an isokinetic dynamometer. Differences in movement direction and angular velocity were present between the articles. Full details of the experimental procedure are presented in Table 4.

Table 4. Details of research assessing changes in joint position sense before and after ACL reconstruction

	Sample Size	Height ($\bar{x}$±SD; m)	Mass ($\bar{x}$±SD; kg)	Time Since Injury (weeks)	Graft Details	Post-Test Timings (weeks)	Task Analysed	Outcome Measures
Jurevičienė *et al.* (2012)	n = 15	1.78±0.03	78.9±4.3	NR	SB hamstring autograft	16 & 20	Knee angle recall during passive flexion and extension at 2 and 10 deg·s^{-1}	• Error between target angle and recall value
Ma *et al.* (2014)	n = 67	1.67±0.02	65.1±2.8	18.6±8.3	SB (n=20), SBA (n=21), or DB (n=26) hamstring autograft	24	Knee passively extended or flexed at 0.2 deg·s^{-1} from an angle of 45 deg	• Time from initialisation of movement to time of detection
Ordahan *et al.* (2015)	n = 20	NR	NR	59.6 (SD NR)	Hamstring autograft (number of bundles NR)	24	Knee angle recall during active flexion and extension	• Error between target angle and recall value

Single bundle (SB), single bundle augmentation (SBA), double bundle (DB), not reported (NR)

3.4.3.3 *Quality Rating*

One article received a strong overall rating suggesting a low risk of bias. No data on participant retention resulted in weak participant ratings for the other two articles. Inconsistent data collection timings was the only other risk of bias identified (Table 5).

Table 5. Assessment of quality of included studies exploring joint position sense

	Participants	**Withdrawals**	**Study design**	**Intervention integrity**	**Data collection**	**Overall rating**
Jurevičienė *et al.* (2012)	1	3	3	1	1	3
Ma *et al.* (2014)	1	1	1	1	1	1
Ordahan *et al.* (2015)	1	3	1	1	1	2

1 = strong, 2 = moderate, 3 = weak

3.4.3.4 *Main Findings*

Outcome measures of all identified articles represented proprioceptive function where an increase, and therefore positive effect size, reflected an improvement in function due to surgery. Large effect sizes were found for active and passive joint position sense at 16, 20, and 24 weeks post-surgery compared to pre-surgery values (Jurevičienė *et al.*, 2012; Ordahan *et al.*, 2015; Figure 5). Threshold to detect passive motion also improved 24 weeks post-surgery (Ma *et al.*, 2014). Effect sizes were larger 48 weeks post-surgery (extension: $0.47 \pm 0.34^{\alpha}$; flexion: $1.09 \pm 0.36^{\alpha}$) compared to 24 weeks (extension: 0.33 ± 0.34; flexion: $0.68 \pm 0.35^{\alpha}$).

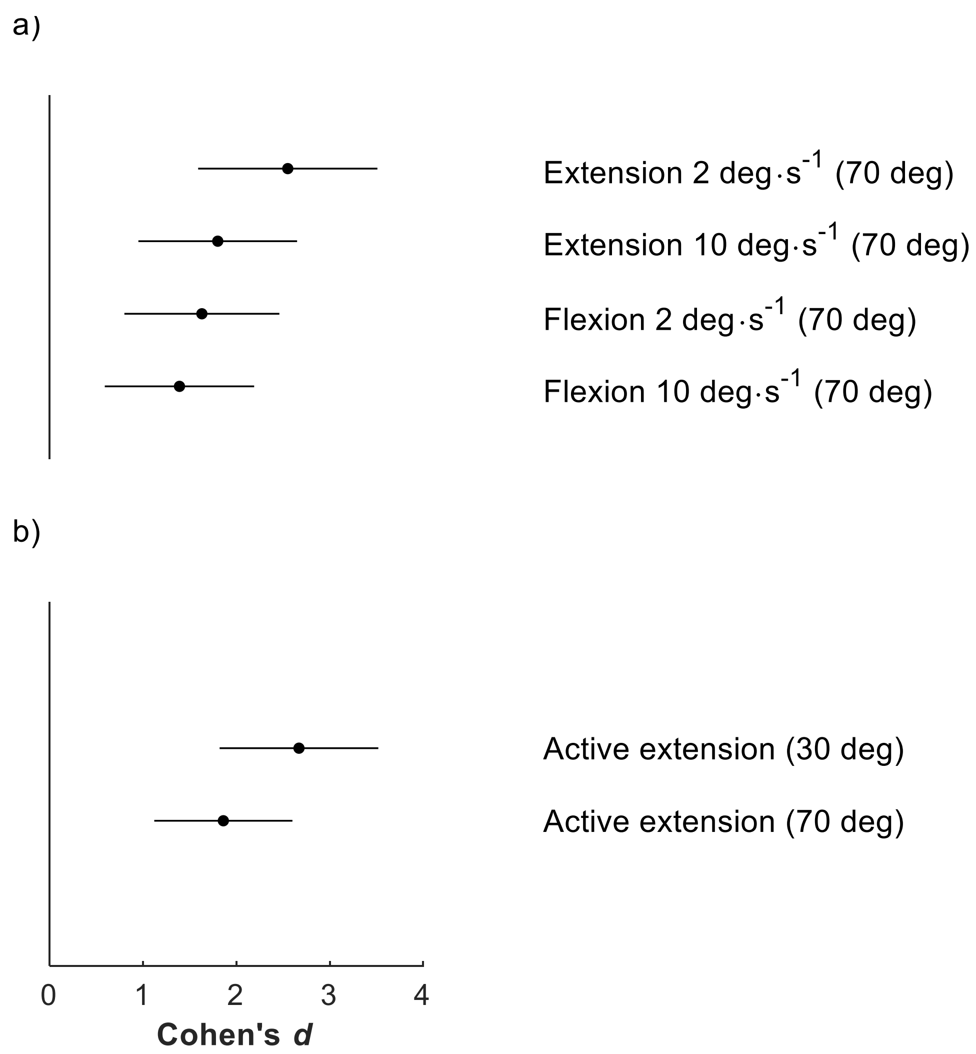

Figure 5. Forest plot of effect sizes and 95% confidence intervals for data on a) passive (Jurevičienė *et al*., 2012) and b) active (Ordahan *et al*., 2015) knee joint position sense at 20 and 24 weeks post−surgery compared to pre−surgery values.

3.4.4 Gait

3.4.4.1 Identified Articles

Thirty-one articles were identified which assessed the effect of ACL reconstruction on gait biomechanics (Asaeda *et al.*, 2017; Azus *et al.*, 2017; Beard *et al.*, 2001; Claes *et al.*, 2011; Devita *et al.*, 1997; DeVita *et al.*, 1996; Di Stasi, Hartigan, & Snyder-Mackler, 2015a; Favre *et al.*, 2006; Ferber, 2001; Ferber, Osternig, Woollacott, Wasielewski, & Lee, 2004; Gardinier, 2013; Hartigan, 2009; Hartigan, Axe, & Snyder-Mackler, 2009; Hartigan, Zeni, Di Stasi, Axe, & Snyder-Mackler, 2012; Knoll, Kiss, & Kocsis, 2004a; Knoll *et al.*, 2004b; Kumar *et al.*, 2018; Laforest, Fuentes, Therrien, & Grimard, 2017; Majewska *et al.*, 2017; Mittlmeier *et al.*, 1999; Moya-Angeler, Vaquero, & Forriol, 2017; Robbins, Clark, & Maly, 2011; Roewer, Di Stasi, & Snyder-Mackler, 2011; Shabani *et al.*, 2015; Tagesson & Kvist, 2016; Tagesson *et al.*, 2010; Tagesson *et al.*, 2015; Teng *et al.*, 2017; Tsivgoulis *et al.*, 2011; Wellsandt *et al.*, 2016; Wellsandt, Zeni, Axe, & Snyder-Mackler, 2017). Eight articles were not included in the analysis as data were either repeated in other identified articles (DeVita *et al.*, 1996; Ferber, 2001; Hartigan, 2009; Knoll *et al.*, 2004a; Tagesson & Kvist, 2016; Tagesson *et al.*, 2015), or were unavailable (Azus *et al.*, 2017; Laforest *et al.*, 2017), resulting in 23 articles which underwent data analysis.

3.4.4.2 Experimental Procedures

Data collection tools included 3D motion capture, 2D videography, accelerometers, gyroscopes, computerised goniometers, force and pressure plates, and electromyography (EMG). Kinematic measures were the most common with 16 articles providing data such as joint excursions and tibial translation. Spectral differential entropy, a method of quantifying movement variability, of pelvis kinematics were presented in one study (Tsivgoulis *et al.*, 2011). Kinetics and muscle activation data were presented in 12 and 1 article(s), respectively. Full details of all articles which analysed changes in gait biomechanics are presented in Table 6.

Table 6. Details of research assessing changes in gait biomechanics before and after anterior cruciate ligament reconstruction

	Sample Size	**Height (x̄±SD; m)**	**Mass (x̄±SD; kg)**	**Time Since injury (weeks)**	**Graft Details**	**Data Collection Tools**	**Post-test timings (weeks)**	**Outcome Measures**
Asaeda *et al.* (2017)	n = 32	1.66±0.09	64.7±11.7	64.4±171.1	SB, SBA or DB hamstring graft	3D motion capture and force plate	48	• Excursion of tibia rotation and knee flexion during stance • Peak internal knee extension and external adduction moment
Beard *et al.* (2001)	n = 11	NR	NR	188.0±120.0	SB hamstring autograft (n=6) and SB BPB autograft (n=5)	3D motion capture and force plate	25	• Patella tendon angle (a measure of tibial translation); ○ during stance ○ at heel strike ○ the average during gait cycle
Claes *et al.* (2011)	n = 16	NR	NR	144.0±92.0	SB (n=8) or DB (n=8) hamstring autograft	3D motion capture	24	• Excursion of tibia rotation during the gait cycle
Devita *et al.* (1997)	n = 9	NR	76.1 (SD NR)	~2	SB BPB autograft	2D video (manually digitised) and force plate	3 & 5	• Average knee and hip angle during stance • Average knee and hip extensor impulse during stance • Negative work at the knee • Positive work at the knee and hip

Table 6. Continued

Di Stasi *et al.* (2015a)	N = 39	NR	NR	11.1±10.1	SB hamstring autograft or SB allograft	3D motion capture and force plate	24	• Average knee and hip angle during stance • Average knee and hip extensor impulse during stance
Favre *et al.* (2006)	N = 2	1.90±0.00	82.0±5.0	30.0±22.0	SB BPB autograft	Two 3D gyroscope units	48	• Knee flexion, rotation, and abduction excursion during one gait cycle
Ferber *et al.* (2004)	N = 10	1.66±0.20	79.1±13.8	273.6±244.8	SB BPB autograft	3D motion capture and force plate	12	• Average knee and hip angle during stance • Knee and hip extensor impulse during stance • Knee and hip work during stance
Gardinier (2013)	N = 13	1.74±0.10	79.0±14.7	8.9±4.4	SB hamstring autograft or SB allograft	3D motion capture and force plate	24	• Estimated peak tibiofemoral contact force during stance • Estimated peak medial compartment contact force during stance
Hartigan *et al.* (2009)	N = 19	NR	NR	11.3±11.3	SB hamstring autograft or SB allograft	3D motion capture and force plate	24	• Knee flexion excursion during mid-stance
Hartigan *et al.* (2012)	N = 38	NR	NR	8.9±8.5	SB hamstring autograft or SB soft tissue allograft	3D motion capture and force plate	24	• Knee flexion moment at peak flexion

Table 6. Continued

Knoll *et al.* (2004b)	N = 25	1.77±0.80	81.4±9.1	81.7 (SD NR)	SB BPB autograft	Ultrasound-based motion tracker system	6, 16,32, & 48	• Peak knee extension and flexion angle
Kumar *et al.* (2018)	N = 37	NR	NR	7.0±3.0	SB hamstring autograft (n=27), and hamstring (n=1), tibialis anterior (n=8) and BPB (n=1) allograft	3D motion capture and force plate	24 & 48	• Knee adduction moment impulse • Peak knee adduction moment and angle
Majewska *et al.* (2017)	N = 40	NR	NR	NR	SB hamstring autograft	3D motion capture	24	• Hip, knee, and ankle excursion in the sagittal plane during a gait cycle
Mittlmeier *et al.* (1999)	N = 10	1.70 (SD NR)	76.2 (SD NR)	NR	SB BPB autograft	Pressure platform	6, 12, & 24	• Total impulse as a percentage of the uninvolved limb • Relative heel loading as a percentage of total impulse
Moya-Angeler *et al.* (2017)	N = 71	NR	85.9±2.1	NR	SB hamstring autograft	Force plate	12, 24, & 48	• Maximum vertical force at heel contact and during single leg stance • Vertical impulse • Maximum anterior and posterior force

Table 6. Continued

Robbins *et al.* (2011)	N = 1	1.58	76.2	16	SB hamstring autograft	3D motion capture and force plate	6, 12, 24, & 36	• Knee flexion, extension, and excursion angle during mid-stance • Peak knee flexion and extension moment during mid-stance • Peak knee adduction moment and impulse
Roewer *et al.* (2011)	N = 26	NR	NR	NR	SB hamstring autograft or SB soft tissue allograft	3D motion capture and force plate	24	• Peak knee flexion angle, and joint excursion during weight acceptance • Internal hip and knee extensor moments at peak knee flexion
Shabani *et al.* (2015)	N = 15	1.72±0.09	70.8±13.7	18.8±17.2	SB BPB autograft	3D motion capture	40	• Average knee angle in the sagittal, axial and frontal planes during the stance and swings phases • Average anteroposterior translation of the tibia during the stance and swing phases
Tagesson *et al.* (2010)	N = 19	NR	NR	60 (SD NR)	Quadruple hamstring autograft	Computerised goniometer and EMG	5	• Maximum anterior tibial translation • Peak EMG activation of the vastus medialis, vastus lateralis, hamstring, gastrocnemius, and soleus during stance

Table 6. Continued

Teng *et al.* (2017)	N = 33	NR	NR	8.1±6.0	SB hamstring autograft (n=23) or SB soft tissue allograft (n=10)	3D motion capture and force plate	24 & 48	• Peak knee flexion angle and moment between first contact to the first knee flexion angle peak • Peak vertical ground reaction force between first contact to the first knee flexion angle peak
Tsivgoulis *et al.* (2011)	N = 20	1.77±0.07	81.5±11.2	≤8	DB hamstring autograft	Waist mounted accelerometer	24 - 36	• Spectral differential entropy (a measure of variability) of pelvis movement in the anteroposterior and mediolateral axes
Wellsandt *et al.* (2016)	N = 22	NR	NR	≤28	QB hamstring autograft or SB soft tissue allograft	3D motion capture, force plate, and EMG	24 & 48	• Peak external knee flexion and adduction moment • Knee adduction impulse during stance • Estimated peak medial compartment contact force during stance
Wellsandt *et al.* (2017)	N = 19	NR	84.8±16.4	14.3±10.3	QB hamstring autograft or SB soft tissue allograft	3D motion capture and force plate	24	• Peak hip extension, and flexion angle and moment during stance • Peak hip adduction angle and moment during the first half of stance • Hip excursion during stance

Single bundle (SB), single bundle augmentation (SBA), double bundle (DB), bone patella bone (BPB), not reported (NR), electromyography (EMG)

3.4.4.3 Quality Rating

Only one of the identified articles received a strong quality rating (Moya-Angeler *et al.*, 2017). Differences in surgical procedure, and no information regarding participant withdrawal levels were the main reasons for weak or moderate ratings (

Table 7). These ratings suggest the risk of bias may be increased and this should be considered when interpreting results.

3.4.4.4 Main Findings

Small to large effect sizes for increases in minimum and maximum knee flexion angles throughout the gait cycle were found at 16, 32, and 48 weeks post operation by Knoll *et al.* (2004b). Negligible, medium, and large increases in peak knee flexion angle were also observed during weight acceptance of stance (24 weeks: 0.15±0.54, 0.66±0.50$^{\alpha}$; 48 weeks: 0.80±0.31$^{\alpha}$) (Roewer *et al.*, 2011; Teng *et al.*, 2017). Average knee angle during stance presented less consistent changes with reduced flexion at 5 (0.34±0.93) and 40 (0.73±0.74) weeks post operation, and increased flexion at 3 (2.47±1.22$^{\alpha}$), 12 (0.63±0.90), and 40 weeks (0.24±0.72) post operation (Devita *et al.*, 1997; Ferber *et al.*, 2004; Shabani *et al.*, 2015). Data on average knee angles during the swing phase were only available in one investigation and showed a small effect of a more flexed position following reconstruction (Shabani *et al.*, 2015). Knee flexion excursion through a full gait cycle was shown to significantly increase at 24 (0.97±0.46$^{\alpha}$) and 48 weeks post operation (3.40±3.06$^{\alpha}$), however both increased and decreased by negligible and small amounts, respectively, when measured during stance (24 weeks: −0.10±0.44, 0.29±0.64; 48 weeks: 0.34±0.49; Asaeda *et al.*, 2017; Di Stasi *et al.*, 2012; Favre *et al.*, 2006; Hartigan *et al.*, 2009; Majewska *et al.*, 2017; Roewer *et al.*, 2011).

Table 7. Assessment of quality of included studies exploring gait

	Participants	**Withdrawals**	**Study design**	**Intervention integrity**	**Data collection**	**Overall rating**
Asaeda *et al.* (2017)	1	3	1	1	1	2
Beard *et al.* (2001)	1	3	1	3	1	3
Claes *et al.* (2011)	1	1	1	3	1	2
Devita *et al.* (1997)	1	3	1	1	1	2
Di Stasi *et al.* (2015a)	1	3	1	3	1	3
Favre *et al.* (2006)	2	3	1	1	1	2
Ferber *et al.* (2004)	1	3	1	1	1	2
Gardinier (2013)	1	2	1	3	1	2
Hartigan *et al.* (2009)	1	3	1	3	1	3
Hartigan *et al.* (2012)	1	3	1	3	1	3
Knoll *et al.* (2004b)	1	3	3	1	1	3
Kumar *et al.* (2018)	1	2	1	3	1	2
Majewska *et al.* (2017)	1	3	1	1	1	2
Mittlmeier *et al.* (1999)	1	3	3	1	1	3
Moya-Angeler *et al.* (2017)	1	1	1	1	1	1
Robbins *et al.* (2011)	3	1	1	1	1	2
Roewer *et al.* (2011)	1	3	3	3	1	3
Shabani *et al.* (2015)	1	3	1	1	1	2
Tagesson *et al.* (2010)	1	3	1	1	1	2
Teng *et al.* (2017)	1	2	1	3	1	2

Tsivgoulis *et al.* (2011)	1	3	3	1	1	3
Wellsandt *et al.* (2016)	1	2	1	3	1	2
Wellsandt *et al.* (2017)	1	1	1	3	1	2

1 = strong, 2 = moderate, 3 = weak

The identified changes in sagittal plane knee kinematics appear to support a general increase in joint range of motion during gait. No comparative evidence is presented in this review meaning interpretation of whether the changes are functionally beneficial is difficult. Increases in joint range of motion however, can be viewed as a positive outcome from ACL reconstructive surgery as these changes suggest participants are not avoiding using the affected limb to aid in the completion of the task. It is also related to one of the outcomes from early stages of rehabilitation of obtaining full passive range of motion in the treated limb.

Surgical intervention resulted in negligible and medium increases in rotation at the knee with equivalent or increased tibial rotation excursion (24 weeks: 0.19±0.69; 48 weeks: 0.00±0.49 & 0.60±2.00; Asaeda *et al.*, 2017; Claes *et al.*, 2011; Favre *et al.*, 2006). This increase appeared to result from a more internally rotated tibia during stance (40 weeks: 0.15±0.72), and a more externally rotated tibia during the swing phase (40 weeks: 0.27±0.72; Shabani *et al.*, 2015). Abduction excursion during gait also increased 48 weeks post-surgery with a medium effect size (0.69±2.00; Favre *et al.*, 2006). During both the swing and stance phases the knee was found to be in a more abducted position at 40 weeks post-surgery (swing: 0.28±0.72; stance: 0.18±0.72; Shabani *et al.*, 2015). Peak knee abduction angle was found to decrease negligible amount at 24 (−0.07±0.46) and 48 (−0.07±0.46) weeks post-surgery (Kumar *et al.*, 2018). No data on tibial rotation or knee abduction were statistically significant. The identified data on knee angles in the frontal and coronal planes should be considered in relation to their potential error. As the magnitude of kinematic data in these planes is small, the errors associated with the calculation of such angles may be greater than the effect of surgery. These potential errors affect the reliability of such variables and although they appear to be able to identify effects of surgery, may be unsuitable for widespread use in monitoring changes due to treatment for ACL injury.

Internal knee extension moment was found to increase as a result of surgical intervention regardless of the time point extracted (Figure 6). In contrast, there was a large reduction in knee extensor impulse at three (−0.87±0.97) and five (−1.39±1.03$^{\alpha}$) weeks post-surgery (Devita *et al.*, 1997), suggesting the contribution of the limb to the gait cycle was acutely reduced by surgery. These effects may only be short term as data at 12 weeks showed a large effect size of an increase in knee extensor impulse (Ferber *et al.*, 2004), supporting the increased use of the injured limb during walking gait. External knee adduction moment has also been explored (Asaeda *et al.*, 2017; Kumar *et al.*, 2018; Wellsandt *et al.*, 2016). A negligible and small increase at 24 weeks (0.11±0.59; 0.37±0.46) were followed by differing results at 48 weeks, with one article showing an increase (0.38±0.46; Kumar *et al.*, 2018) and two showing a decrease (−0.22±0.59; −0.13±0.49; Asaeda *et al.*, 2017; Wellsandt *et al.*, 2016). External knee adduction impulse showed a small and negligible increases at 24 (0.20±0.59; 0.33±0.46) and 48 (0.15±0.59; 0.32±0.46) weeks post-surgery (Kumar *et al.*, 2018; Wellsandt *et al.*, 2016). The size and variation in direction of these effects appear to suggest that they do not relate to any changes in funcitonal outcomes from ACL reconstructive surgery. Negative work at the knee during early stance (0-22% of stance) increased at 3 (0.59±0.94) and 5 (1.72±1.08$^{\alpha}$) weeks post-surgery (Devita *et al.*, 1997). Reductions in positive work were also observed at 3 (2.21±1.17$^{\alpha}$), 5 (2.53±1.24$^{\alpha}$), and 12 (0.56±0.89) weeks post-surgery (Devita *et al.*, 1997; Ferber *et al.*, 2004).

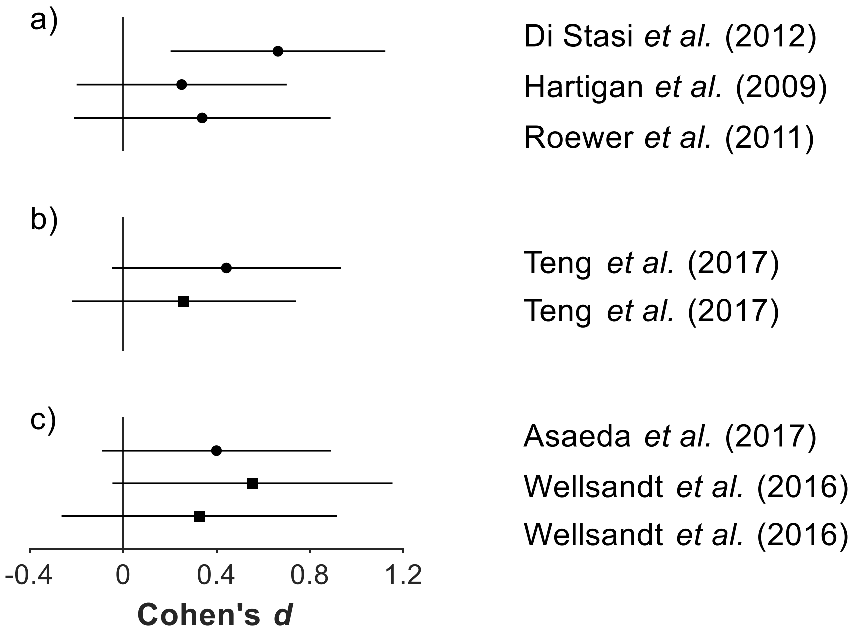

Figure 6. Forest plot of effect sizes for internal knee extension moment during gait a) at peak knee flexion angle during stance, b) maximum during initial stance, and c) maximum during stance at 24 (●) and 48 (■) weeks post anterior cruciate ligament reconstruction.

Average tibial anteroposterior position was found to be more posterior, with a small effect, during stance (0.33±0.37), and swing (0.37±0.37$^{\alpha}$) phases at 40 weeks post-surgery (Shabani *et al.*, 2015). Reduced anterior tibia translation was also identified during stance compared to non-weight bearing values (−0.57±0.33$^{\alpha}$) (Tagesson *et al.*, 2010), supporting the use of reconstructive surgery in restoring the mechanical roles of the healthy ACL. One article found increases in anterior tibial translation at heel-strike (1.07±0.89$^{\alpha}$), during stance (0.61±0.85), and through one gait cycle (0.72±0.86; Beard *et al.*, 2001). However, these values were relative to the uninjured limb and may not reflect changes in the injured limb alone.

Hip excursion angle was shown to increase during gait (24 weeks: 0.49±0.44$^{\alpha}$) (Majewska *et al.*, 2017), and reduce during stance (24 weeks: −0.32±0.64; 48 weeks: −0.02±0.64; Wellsandt *et al.*, 2017) and midstance (24 weeks: −0.72±0.46α; Di Stasi *et al.*, 2015a). This decreased hip range of motion during stance is further evidenced by negligible and small effect sizes for decreases in peak hip flexion (24 weeks: −0.24±0.64; 48 weeks: −0.35±0.64) and extension (24 weeks: −0.05±0.64; 48 weeks: −0.39±0.64) angles (Wellsandt *et al.*, 2017). During stance the hip was in a more flexed position compared to pre-surgery values at 3 (2.77±1.29$^{\alpha}$), 5 (0.95±0.97), and 12 (0.55±0.89) weeks post-surgery. Peak hip adduction angle also increased with a small to medium effect (24 weeks: 0.37±0.64; 48 weeks: 0.56±0.65; Wellsandt *et al.*, 2017). The identified effects ACL reconstruction has on hip biomechanics supports the complex role the surgery has on the entire lower limb and the completion of tasks such as gait.

Further support for the effect ACL reconstruction has on other lower limb joints was identified in hip kinetic data. Surgery resulted in a negligible increase 24 weeks post-surgery (0.06±0.64) in peak internal hip flexion moment during stance, but had a small positive effect 48 weeks post-surgery (0.33±0.64; Wellsandt *et al.*, 2017). In contrast, peak internal hip extensor moment during stance decreased at 24 (−0.35±0.64) and 48 (−0.53±0.65) weeks post-surgery (Wellsandt *et al.*, 2017). When measured at peak flexion, data suggested either negligible negative (−0.02±0.54) or large (1.00±0.47$^{\alpha}$) positive effects at 24 weeks post-surgery (Di Stasi *et al.*, 2015a; Roewer *et al.*, 2011). Peak internal hip abduction also decreased with a small effect (24 weeks: 0.32±0.64; 48 weeks: 0.32±0.64; Wellsandt *et al.*, 2017). No clear outcome was apparent for hip extensor impulse during stance with decreases at 3 (0.64±0.95) and 12 (0.68±0.90) weeks post-surgery, compared with an increase at 5 weeks (0.75±0.96; Devita *et al.*, 1997; Ferber *et al.*, 2004). Similarly, positive work performed at the hip during stance showed decreases at 3 and 12 weeks, and an increase at 5 weeks.

One article presented data on the effect of ACL reconstruction on muscle activation measured using peak EMG (Table 8; Tagesson *et al.*, 2010). The largest change was an increase in peak hamstring and lateral gastrocnemius activation, with negligible effect sizes for muscles of the quadriceps. EMG data were also used to estimate knee contact forces using computer models (Gardinier, 2013; Gardinier, Manal, Buchanan, & Snyder-Mackler, 2012; Manal & Buchanan, 2013; Wellsandt *et al.*, 2016). Negligible effect sizes ($-0.06 \le d \le 0.02$) were identified at 24 weeks post-surgery for peak tibial medial compartment contact forces, which increased at 48 weeks (0.34±0.60). Peak tibiofemoral contact forces were the same pre- and 24 weeks post-surgery (0.00±0.77).

Table 8. Effect sizes of changes in muscle activation as a percentage of maximum isometric voluntary contraction five weeks post anterior cruciate ligament reconstruction from Tagesson *et al.* (2010)

Muscle	Effect Size (Cohen's *d* ± 95%CI)*
Vastus medialis	−0.12 ± 0.64
Vastus lateralis	0.04 ± 0.64
Hamstrings	0.85 ± 0.66$^{\alpha}$
Lateral gastrocnemius	0.46 ± 0.64
Soleus	0.15 ± 0.64

* a negative effect is a reduction in muscle activation

Data from force and pressure platforms were available in three articles (Mittlmeier *et al.*, 1999; Moya-Angeler *et al.*, 2017; Teng *et al.*, 2017). Maximum vertical force was shown to be reduced at heel strike (12 weeks: −1.04±0.35$^{\alpha}$; 24 weeks: −1.65±0.38$^{\alpha}$; 48 weeks: −1.29±0.36$^{\alpha}$) and during stance (12 weeks: −1.45±0.37$^{\alpha}$; 24 weeks: −2.52±0.44$^{\alpha}$; 48 weeks: −1.06±0.35$^{\alpha}$). However, another article found small increases in vertical force when extracted between initial contact and peak knee flexion (24 weeks: 0.20±0.48; 48 weeks: 0.28±0.48). Negligible to small effect sizes were also found for reductions in anterior force during stance (12 weeks: −0.17±0.33; 24 weeks: −0.01±0.33; 48 weeks: −0.42±0.33$^{\alpha}$). Posterior force also showed changes with medium to large effects with a medium increase at 24 weeks (0.75±0.34$^{\alpha}$) and a large decrease 48 weeks (−1.46±0.37$^{\alpha}$) post-surgery. Data on vertical impulse as both a percentage of the uninjured limb and an absolute value were available. Relative impulse appeared to initially decrease with a small effect (6 weeks: −0.16±0.88) before increasing at 12 (0.60±0.90) and 24 (0.65±0.90) weeks post-surgery. In contrast, absolute impulse showed medium to large effects for decreased values at 12 (−0.57±0.34$^{\alpha}$), 24 (−1.82±0.39$^{\alpha}$), and 48 (−1.03±0.35$^{\alpha}$) weeks post-surgery. No clear functional outcomes appeared to be supported through analysis of the force data.

One article investigated the regularity of the ML and AP movement of the pelvis through spectral differential entropy (Tsivgoulis *et al.*, 2011). A lower value represents a more regular signal. In both axes of movement, regularity was increased from pre- to post-surgery (23-36 weeks) with large and medium effect sizes, respectively (ML: 1.07±0.34$^{\alpha}$; AP: 0.71±0.33$^{\alpha}$).

3.4.5 Pivot Tasks

3.4.5.1 Identified Articles

Four articles assessed the changes in lower limb biomechanics during a dynamic cutting task (Claes *et al.*, 2011; Hemmerich, van der Merwe, Batterham, & Vaughan, 2011; Lam *et al.*, 2010, 2011). Data were the same in two of the articles and these were considered together (Lam *et al.*, 2010, 2011), resulting in three data sets being analysed.

3.4.5.2 Experimental Procedures

All articles used motion capture to collect kinematic data, and only one of the articles collected kinetic data through the use of a force plate. A right angled change of direction was the task in all articles, however this was either conducted after a drop or whilst jogging. Rotation of the tibia was the main outcome for all articles. Full details of the experimental procedure are provided in Table 9.

Table 9. Details of research assessing changes in pivot and cutting biomechanics before and after anterior cruciate ligament reconstruction

	Sample Size	**Height (x̄±SD; m)**	**Mass (x̄±SD; kg)**	**Time Since Injury (weeks)**	**Graft Details**	**Data Collection Tools**	**Post-Test Timings (weeks)**	**Task Analysed**	**Outcome Measures**
Claes *et al.* (2011)	n = 16	NR	NR	144.0±92.0	SB (n=8) or DB (n=8) hamstring autograft	3D motion capture	24	Step down and 90° pivot on affected limb	• Rotational excursion of the tibia
Hemmerich *et al.* (2011)	n = 17	1.74±0.08	81.8±13.9	27.6±41.6	SB (n=9) or DB (n=8) hamstring autograft	3D motion capture	18.4±6.4	90° cut whilst jogging	• Max internal and external tibial rotation of the inside and outside limb
Lam *et al.* (2011)	n = 10	1.76±0.10	69.1±9.2	41.2±15.6	DB hamstring autograft	3D motion capture and force plate	41.2±15.6	Two footed drop landing followed by immediate 90° pivot on affected limb	• Rotational excursion of the tibia

Single bundle (SB), single bundle augmentation (SBA), double bundle (DB), bone patella bone (BPB), not reported (NR)

3.4.5.1 Quality Rating

Moderate and strong ratings were assigned to the articles (Table 10). Differences in surgical procedure and timing of post-surgery data collection were the areas which increased the risk of bias.

Table 10. Assessment of quality of included studies exploring pivot tasks

	Participants	**Withdrawals**	**Study design**	**Intervention integrity**	**Data collection**	**Overall rating**
Claes *et al.* (2011)	1	1	1	3	1	2
Hemmerich *et al.* (2011)	1	1	2	3	1	2
Lam *et al.* (2011)	1	1	2	1	1	1

1 = strong, 2 = moderate, 3 = weak

3.4.5.2 Main Findings

During a pivot task, preceded by a step down, rotational excursion of the tibia relative to the femur was found to decrease at 24 and 41 weeks post-surgery with a small (−0.33±0.70; Claes *et al.*, 2011) and large (−0.97±0.93[α]; Lam *et al.*, 2011) effect, respectively. The pivot limb whilst performing a 90° cut, showed a reduced peak internal (−0.37±0.87) and increased peak external (−0.18±0.67) tibial rotation compared to pre-surgery values. Reduced tibial rotation, as shown in the identified articles, supports that ACL reconstruction is able to improve mechanical stability even in high demand tasks such as pivoting.

3.4.6 Stair Ambulation

3.4.6.1 Identified Articles

Four articles were included in the analysis on the effect of ACL reconstruction on stair ambulation biomechanics (Claes *et al.*, 2011; Kowalk *et al.*, 1997; Lepley *et al.*, 2016; Mittlmeier *et al.*, 1999). A further two studies were identified that analysed stair walking biomechanics, however no usable data were able to be accessed (Isaac *et al.*, 2005; McGrath *et al.*, 2017).

3.4.6.2 Experimental procedure

Kinematic and kinetic data on both stair ascent and descent were available. Two articles used a single surgical method, with the other articles using either a combination of graft locations or number of bundles. Full details of the experimental procedures are provided in Table 11.

3.4.6.3 Quality rating

No articles received a strong grade due to no information on participant retention, inconsistent data collection timings, and differing surgical procedures (Table 12).

Table 11. Details of research assessing changes in stair ambulation biomechanics before and after anterior cruciate ligament reconstruction

	Sample Size	Height (x̄±SD; m)	Mass (x̄±SD; kg)	Time Since Injury (weeks)	Graft Details	Data Collection Tools	Post-Test Timings (weeks)	Task Analysed	Outcome Measures
Claes *et al.* (2011)	n = 16	NR	NR	144.0±92.0	SB (n=8) or DB (n=8) hamstring autograft	3D motion capture	24	Stair descent (25 cm rise)	• Rotational excursion of the tibia
Kowalk *et al.* (1997)	n = 7	NR	90.4 (SD NR)	NR	SB BPB autograft	3D motion capture and force plate	24.0 (range: 12.8 – 45.2)	Stair ascent (rise: 23 cm; run 25 cm)	• Sagittal hip, knee, and ankle excursion • Peak internal hip and knee extensor, and ankle plantar flexor moment • Peak hip, knee, and ankle power • Hip, knee, and ankle work
Lepley *et al.* (2016)	n = 20	1.72±0.08	76.2±12.2	5.3±2.2	SB hamstring (n=9) or BPB (n=11) autograft	3D motion capture and force plate	28.3±2.9	Stair ascent and descent (rise: 17 cm; run 25 cm)	• Knee and hip flexion and abduction angle at initial contact, peak during stance, and excursion during one gait cycle • Peak internal knee and hip extension and adduction moment

Table 11. Continued

Mittlmeier *et al.* (1999)	n = 10	1.70 (SD NR)	76.2 (SD NR)	NR	SB BPB autograft	Pressure platform	6, 12, & 24	Stair descent (rise: 17 cm; run 33 cm)	• Total impulse as a percentage of the uninvolved limb

Single bundle (SB), double bundle (DB), bone patella bone (BPB), not reported (NR)

Table 12. Assessment of quality of included studies exploring stair ambulation

	Participants	Withdrawals	Study design	Intervention integrity	Data collection	Overall rating
Claes *et al.* (2011)	1	1	1	3	1	2
Kowalk *et al.* (1997)	1	3	3	1	1	3
Lepley *et al.* (2016)	1	1	2	3	1	2
Mittlmeier *et al.* (1999)	1	3	3	1	1	3

3.4.6.4 Main findings

Sagittal plane knee excursion increased 24 and 28 weeks post-surgery during ascent, and decreased during descent (Table 13), however no differences were significant. Other changes in knee kinematics showed small or negligible effect sizes during both ascent and descent, including increases in knee frontal plane excursion. Sagittal hip excursion showed an increase and decrease at 24 and 28 weeks post-surgery during ascent, and a small decrease during descent. All other hip kinematics showed less than medium effect size changes. Tibial rotation was explored in one article and showed a decrease in excursion during descent 24 weeks post-surgery.

Table 13. Effect sizes of kinematic changes during stair ascent and descent due to anterior cruciate ligament reconstruction

	Ascent	**Descent**
Sagittal hip excursion	0.95±1.11[b]	0.18±0.62[c]
	−0.36±0.62[c]	
Hip extension angle at IC	−0.30±0.62[c]	−0.11±0.62[c]
Peak hip extension angle	0.26±0.62[c]	0.20±0.62[c]
Frontal hip excursion	0.03±0.62[c]	0.21±0.62[c]
Hip abduction angle at IC	−0.24±0.62[c]	0.23±0.62[c]
Peak hip adduction angle	0.27±0.62[c]	−0.36±0.62[c]
Sagittal knee excursion	0.61±1.07[b]	−0.13±0.62[c]
	0.01±0.62[c]	
Knee flexion angle at IC	0.04±0.62[c]	−0.03±0.62[c]
Peak knee flexion angle	−0.31±0.62	−0.13±0.62
Frontal knee excursion	0.31±0.62	0.32±0.62
Knee abduction angle at IC	0.01±0.62	0.29±0.62
Peak knee abduction angle	0.15±0.62	0.06±0.62
Tibial rotation excursion		−0.23±0.70[a]
Sagittal ankle excursion	−0.62±1.07[b]	

[a]Claes; [b]Kowalk; [c]Lepley. Initial contact (IC)

Peak hip and knee extensor moment during stair descent reduced after surgery at 28 weeks (hip: −0.73±0.64[α]; knee: −0.11±0.62; Lepley *et al.*, 2016). Data showed both an increase (24 weeks: 0.48±1.06) and decrease (28 weeks: −0.50±0.63) during ascent in the hip extensor moment, and a large and small decrease in the knee extensor moment (Kowalk *et al.*, 1997; Lepley *et al.*, 2016). Peak internal ankle plantar flexion moment increased with a large effect size 24 weeks post-surgery (Kowalk *et al.*, 1997). Frontal plane kinetics had small or negligible effect sizes for reduced and increased peak knee abduction moment during descent and ascent, respectively. The inconsistency and size of the identified effects in knee kinetics make interpretation difficult, and do not appear to support a link between ACL reconstructive surgery and improved functional performance during stair ambulation.

Peak power and total work completed at the knee reduced post-surgery with large effect sizes (peak power: 2.04±1.29$^{\alpha}$; work: 1.71±1.23$^{\alpha}$). Additionally, peak power at the ankle was found to increase with a medium effect size. Total relative impulse compared to the uninjured limb was found to decrease at 6 weeks post-surgery, before increasing at 12 and 24 weeks (Mittlmeier *et al.*, 1999).

3.4.7 Hop Landing

3.4.7.1 Identified Articles

Three articles were identified that assessed lower limb biomechanics during a hop landing. One article was excluded from analysis as no data were presented (Letchford *et al.*, 2016), meaning two articles were included (Oberländer, Brüggemann, Höher, & Karamanidis, 2014; Oliver, Portabella, & Hernandez, 2018).

3.4.7.2 Experimental Procedure

Oberländer *et al.* (2014) explored landing mechanics of a unilateral hop in 18 participants (height: 1.80±0.08 m; mass: 84.9±12.4 kg) before, and 24 and 48 weeks after ACL reconstruction. All participants received quadrupled hamstring autografts 12-24 weeks after the initial injury. Three dimensional motion capture and a force plate were used during data collection, and peak internal knee extension and abduction, ankle plantar flexion moments, average tibial rotation, and maximum anterior tibial translation were calculated. Oliver *et al.* (2018) investigated the changes in time between initial contact of a hop landing, to peak muscle activation measured using EMG in 23 participants who underwent ACL reconstruction using a bone-patella-bone autograft.

3.4.7.3 Quality Rating

No information on participant retention was provided by Oberländer *et al.* (2014) resulting in a single weak rating, and a moderate overall rating. This suggests there is a small risk of bias in the results. Oliver *et al.* (2018) received all strong ratings, meaning there is a low risk of bias.

3.4.7.4 Main Findings

Internal knee extension moment initially decreased at 24 weeks post-surgery ($-1.76\pm0.77^{\alpha}$), before increasing at 48 weeks ($1.12\pm0.70^{\alpha}$), supporting that initial effects of surgery may reduce the contribution of the injured limb, before improvements above pre-surgery values over longer time periods. Knee abduction moment decreased with a small effect size at 24 (-0.33 ± 0.66) and 48 (-0.38 ± 0.66) weeks post-surgery. No change was seen at 24 weeks for ankle plantar flexion moment, but a medium decrease was observed at 48 weeks. Kinematic changes were reduced tibial rotation (24 weeks: $-1.91\pm0.79^{\alpha}$; 48 weeks: $-1.48\pm0.74^{\alpha}$), and a decrease in anterior tibial translation (24 weeks: $-1.99\pm0.80^{\alpha}$; 48 weeks: $-1.60\pm0.75^{\alpha}$), suggesting decreased joint laxity after ACL reconstruction. Muscle response time was shown to significantly decrease in the quadriceps and hamstring muscles (Figure 7). The magnitude of the effect sizes were larger in the data at 48 weeks compared to 24 weeks.

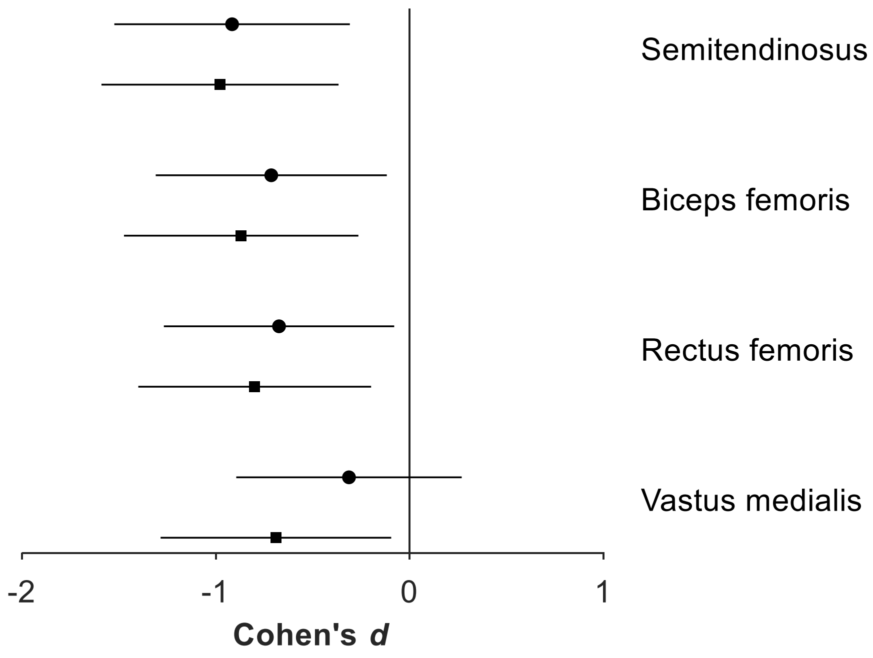

Figure 7. Forest plot of effect sizes for muscle response time during a hop landing at 24 (●) and 48 (■) weeks post anterior cruciate ligament reconstruction (Oliver *et al.*, 2018). A negative effect size represents a reduction in response time.

3.5 Discussion

This review addressed **Aim I** of this thesis, which was to systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery. Data were available on balance, joint position sense, gait, stair ambulation, pivoting, and hop landings. ACL reconstruction was found to result in changes in lower limb biomechanics in all movement tasks. Restoration of the mechanical role of the ACL through reconstruction was evidenced by reductions in tibial translation and rotation in gait and pivotting tasks. Proprioceptive function was also restored with improvements in balance performance, joint position sense, and muscle response time. Findings for other variables such as joint moments, joint angles and muscle activations were inconcsistent. This inconsistency suggests individual responses to surgical intervention exist, and should be considered when making treatment decisions.

Quality ratings identified that a moderate risk of bias was present in most articles. These findings resulted from participant retention, differences in surgical approach, and inconsistent intervention timings. Failure to report information on these factors was the most common reason for weak ratings. Where participant retention is poor or not reported, there is a risk that the presented data is that of only participants who are capable of completing the movement, and therefore a risk of bias towards the study finding greater improvements in biomechanics than would be seen of the whole sample. Differences in surgical intervention were often caused by the research question of the article not matching that of this review, meaning the data processing used in this study introduced this risk of bias. Different surgical interventions have been shown to produce varying findings in biomechanical characteristics in ACL injured participants (Tsai, Wijdicks, Walsh, & LaPrade, 2010), however when considering the potential use of measures in clinical practice variables should be able to identify the effect of treatment regardless of surgery details and future research should provide data to allow the risk of bias to be assessed by the reader.

Balance and joint position sense movements provided the most consistent results, with all articles showing an improvement independent of the task, or performance variable. This improvement appeared to be as a result of changes in the proprioceptive potential of the limb, rather than restored mechanical stability (Di Stasi *et al.*, 2012). Increasing effect size magnitudes with time since surgery (Figure 4) also suggested that the proprioceptive recovery continues up to at least 48 weeks post surgery, providing more evidence of ACL reconstructions enabling the neuromuscular function of the lower limb to recover. Where articles assessed the performance of the balance test, outcome variables were variations of CoP path length. Other assessments of balance performance which have been linked to proprioceptive function such as CoP velocity (Jeka, Kiemel, Creath, Horak, &

Peterka, 2004), and complexity (Busa & van Emmerik, 2016; Gow, Peng, Wayne, & Ahn, 2015) were not conducted and may offer further insight into the effect of ACL reconstruction on balance performance and characteristics.

In gait, stair ambulation, and pivoting tasks, variables included joint kinematics and kinetics, muscle activations, and ground reaction forces. Knee flexion excursion was shown to reduce following reconstruction in most articles identified, except during stair ascent where an increase was shown. There was also evidence of an acute effect of surgery on internal knee extension moment with decreases in data early after surgery (≤5 weeks) compared to later (≥24 weeks). This acute change in knee kinetics was further evidenced by a reduction in positive work done during late stance of gait 3 and 5 weeks post-sugery. An increase and decrease in hamstring and quadriceps activation, respectively, may highlight the mechanism which resulted in the reduced knee extensor moments. Changes in joint kinematics and kinetics were also identified in the hip and ankle joint, highlighting the complexity of the effect ACL reconstruction has on lower limb biomechanics, and this complexity should be considered during rehabilitation. Ground reaction forces showed no clear pattern of change due to ACL reconstruction.

One major aim of reconstructive surgery is to resist tibial translation and rotation relative to the femur, restoring the mechanical role played by the intact ACL. Two articles presented data which showed anterior tibial tranlsation decreased, and one showed an increase. Rotation data also appeared to demonstrate surgical reconstruction is capable of restoring the knee’s natural mechanical stability even when placed under high strain, such as during pivoting movements. Where articles did identify an increase in tibial translation or rotation, these were often derived using the uninjured limb as a comparison, and therefore may include biomechanical changes which occur in the uninjured limb due to ACL injury and treatment (Hart *et al.*, 2010). Other conclusions on how ACL reconstruction alters lower limb biomechanics during high demand movements are difficult to draw due to methodological differences between articles, and contradictory findings. Peak joint angles and moments, and muscle activations were all found to alter, however the magnitude and direction of these changes differed between studies. These differences may be due to treatment variance (Claes *et al.*, 2011; Webster & Feller, 2011), or individual coping strategies. Individual responses to ACL deficiency and reconstruction have been identified within the literature (Alkjær, Simonsen, Jørgensen, & Dyhre-Poulsen, 2003; Alkjær, Simonsen, Peter Magnusson, Aagaard, & Dyhre-Poulsen, 2002; Gardinier, 2013) however, few intra-participant analyses on changes due to ACL reconstruction have been conducted and none were identified in this review.

The data presented in this review provide evidence that biomechanical outcomes during motor tasks such as gait contain individual differences potentially limiting their widespread use as clinical tools. Where a global measure of task performance, such as CoP during balance, was investigated, the data provided more consistent outcomes. The improvements identified in balance and joint position sense tasks suggest that ACL reconstructive surgery is capable of restoring proprioceptive function of the limb, and therefore assessments of this charactersitics may be suitable for exploration as potential assessment tools. Finally, the analysis methods of the identified research focussed almost solely on traditional biomechanical approaches. Variables such as data maxima and minima are considered as linear measures of task performance, and although are informative, have been suggested to provide limited information on how a task is completed (Davids, Glazier, Araújo, & Bartlett, 2003). Non-linear approaches have been theorised to assess the state of the system, and provide information of the internal dynamics related to the demands of the task (van Emmerik, Ducharme, Amado, & Hamill, 2016). Only one identified article explored non-linear outcomes, in the form of variability measured using spectral differential entropy, which was found to differ pre- to post-surgery (Tsivgoulis *et al.*, 2011). Previous research has successfully identified differences in non-linear outcomes in ACL deficient and reconstructed participants (Moraiti, Stergiou, Ristanis, & Georgoulis, 2007; Pollard, Stearns, Hayes, & Heiderscheit, 2015; Skurvydas *et al.*, 2011), however future research should look to explore the potential of these measures in an applied setting, with consideration for implications of their implementation into clinical practice.

3.6 Summary

This systematic review addressed **Aim I** of this thesis; to systematically synthesise current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery. Gait was the most commonly assessed movement, however the findings suggest that although changes in the performance of this task, treatment did not result in clear consistent variations due to surgery. Inconsistent findings were also present in other complex movement tasks such as landing and pivoting. Movements which assessed proprioceptive function provided the most consistent findings, with both joint position sense and balance tasks suggesting ACL reconstructive surgery is capable of restoring the proprioceptive function of the involved limb. Tasks which provide assessments on the proprioceptive function of the limb may therefore be suitable for the monitoring of changes due to ACL reconstructive surgery.

An additional finding of this study was that the analysis methods used within the research exploring biomechanical changes due to ACL reconstructive surgery focus mainly on linear measures of performance. Theoretical frameworks such as dynamical systems theory (Davids *et al.*, 2003) suggest non-linear tools may provide further information into potential changes in the function of the body, and its ability to meet the demands of a task. Due to the lack of current evidence on changes in non-linear biomechanical variables, further exploration into their potential use as monitoring tools is warranted.

4. Assessment of Balance as a Measure of Anterior Cruciate Ligament Injury Recovery: A Review of Linear and Non-Linear Approaches

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

Chapter	Title	Addressed Aims
1	Introduction	
2	Monitoring Functional Recovery from ACL Injuries	
3	Lower Limb Biomechanics Before and After ACL Reconstruction: A Systematic Review	**AIM I**: Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery
4	Assessment of Balance as a Measure of ACL Injury Recovery: A Review of Linear and Non-Linear Approaches	
5	General Methods	
6	Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population	**AIM II**: Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe
7	The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity	**AIM III**: Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons **AIM IV**: Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.
8	Thesis Summary	
9	Conclusion	

Figure 1. Schematic of thesis structure and research aims

4.1 Preface

Chapter 2 highlighted that the currently available assessment tools for monitoring the changes in biomechanics which occur due to ACL rupture and subsequent treatment are sub-optimal, and that these tools have limitations on their ability to monitor the multi-faceted nature of the injury. This highlighted the need to explore what biomechanical changes occur due to treatment, and explore their potential use within the monitoring of treatment success. Chapter 3 addressed **Aim I** of this thesis and identified that tasks which assess the proprioceptive function of the limb may be suitable assessment tools for monitoring ACL injury and recovery.

Joint position sense and threshold to detect passive motion are assessments which aim to directly measure the proprioceptive function of the limb, however often require the use of an isokinetic dynamometer which may limit their potential implementation into clinical practice. Balance tasks also aim to assess proprioceptive function, most commonly by assessments of the CoP (Palmieri, Ingersoll, Stone, & Krause, 2002), however may offer a more easily implemented methodology. Although force and pressure platforms are considered as the criterion measurement tool for collecting CoP data, the collection of such data has been shown to be achievable through cheaper equipment such as a single strain gauge sensor and balance board (Huang, Sue, Abbod, Jiang, & Shieh, 2013). Therefore analysis of balance tasks will be explored in relation to the aim of this thesis, to analyse their potential worth for the monitoring of changes in limb function of ACL injured participants.

Chapter 3 identified that CoP path length improved due to ACL reconstructive surgery, however no other analyses of balance data were presented. Path length is a linear variable of balance, however a number of other analysis methods have been used within balance research and these may offer further insight into the effect of treatment on balance in ACL injured participants, including linear and non-linear approaches. When considering the worth of a variable for the monitoring of recovery it is important to understand the theoretical framework for why injury and treatment would result in changes in the measure. It is also important to explore the consistency of these measures to allow the interpretation of changes due to intervention, and whether they lie outside normal levels of bias. Therefore this chapter will review the current literature around the assessment of balance in ACL injured populations, including the potential worth of linear and non-linear variables, and discuss statistical approaches to assessing levels of bias in relation to interpretation of changes in an ACL injured population undergoing treatment.

4.2 Balance Summary

Balance is achieved through the maintenance of the vertical projection of the centre of mass within the base of support (Hrysomallis, 2007). During stance this is achieved by controlling the movement of the centre of mass and minimising its displacement. This control is achieved through contributions of visual, vestibular, and somatosensory inputs, and the relative contribution of these systems is dependent on the reliability of the information received (Peterka, 2002).The somatosensory system provides information on bodily sensations and includes proprioceptive inputs from mechanoreceptors. Changes to the function of the somatosensory system due to loss of proprioceptive inputs that occur with ACL injury is the theoretical framework behind ACL deficiency resulting in a reduced balance ability (Kapreli & Athanasopoulos, 2006).

Measurements of static balance ability are conducted through assessments of movement of the centre of mass and CoP (Winter, 1995). Assessments of the centre of mass are a philosophically more valid approach due to its relation to the specific demands of balance (Winter, 1995), however the accurate assessment of this is difficult (Lafond, Duarte, & Prince, 2004) and requires equipment that make it unsuitable for clinical use. The CoP is suggested to be related to the centre of mass through the inverted pendulum hypothesis (Winter, 1995). This hypothesis states that changes in the CoP represent a summary measure of the torques which are produced around the centre of mass which aim to stabilise AP and ML movement. The use of inverted pendulums in modelling more dynamic tasks such as gait (Kuo, 2007) may be too simplistic. During static tasks where balance is maintained through moments in the ankle and hip joint however, the inverted pendulum hypothesis appears to provide a suitable paradigm for describing the relationship between the CoP and centre of mass (Gage, Winter, Frank, & Atkin, 2004).

In tasks where the inverted pendulum hypothesis appears to provide a suitably accurate model of balance, analysis of the CoP trace offers insight into the body's ability to control the centre of mass and has been the most common methodology employed in research assessing the effect of ACL injury and balance (Negahban, Mazaheri, Kingma, & van Dieën, 2014). Analyses of the CoP to determine balance ability have traditionally been conducted using linear measures of variance, range, and velocity, where a lower value is considered as a greater ability to control the centre of mass (Palmieri *et al.*, 2002).

4.3 Linear Measures of Balance and ACL Injury

Due to the hypothesised neurophysiological dysfunction that accompanies ACL injury, researchers have looked to explore balance deficits in ACL deficient limbs and the effect reconstruction has on these characteristics. Lehmann, Paschen, and Baumeister (2017) conducted a systematic review on the effects of ACL injury on balance ability, and identified that measures of CoP variance and velocity in the ML and AP axes where higher in ACL injured limbs compared to matched uninjured controls (Cohen's *d*±95% CI; CoP Variance: 0.94±0.62; CoP Velocity: 0.66±0.35). This review did not differentiate between deficient and reconstructed limbs, which may give more insight into the effect of ACL injury and treatment on balance.

Negahban *et al.* (2014) conducted a systematic review of research exploring balance in ACL deficient limbs assessed throughout unilateral balance. The researchers concluded that the evidence supported the hypothesis of reduced balance with ACL deficiency with seven of the ten identified articles reporting an increased postural sway with medium to large effects (Cohen's *d* effect size: 0.56 - 4.32) in the involved limb compared to matched uninjured participants. Two articles reported contradictory evidence with reduced sway in the ACL deficient limb with large effects (Cohen's *d* effect size: −0.72 - −2.92). Outcome measures of balance included variations of sway amplitude and velocity, and although suggested to all represent the ability of participants to control their centre of mass, there were differences in the size of effect between variables when measured in the same sample. Ageberg, Roberts, Holmström, and Fridén (2004) presented data to support a reduction in balance ability with ACL injury, however also identified a greater balance ability in AP velocity of the CoP for ACL deficient limbs, suggesting that comparisons across different variables may not be suitable. A greater balance performance in ACL deficient limbs, assessed through linear measures of the CoP, was also reported in a further study (O'Connell, George, & Stock, 1998). The reason for these contradictory findings is unclear, however as these differences were found between the injured and control limbs, it may be that the injured participants had a higher pre-injury balance ability, meaning the effect of ACL deficiency was not sufficient to see a reduced performance compared to uninjured participants. Despite these limitations, the conclusions of Negahban *et al.* (2014) and further systematic reviews of the evidence (Cooper, Taylor, & Feller, 2005) appear to support that ACL deficiency results in reduced balance performance in the involved limb.

Chapter 3 presented the evidence surrounding changes in balance performance due to ACL reconstructive surgery and found improvements in linear measures of unilateral balance performance. Despite these improvements, ACL reconstructed limbs still appear to have balance deficits compared to ACL intact limbs (Howells, Ardern, & Webster, 2011). As with data on ACL deficient limbs, there were contradictory data identified showing an improved balance in ACL reconstructed participants (Cohen's d effect size; −0.34±0.33), again potentially due to greater baseline performance. One potential approach to increase the effect of ACL injury on measures of balance performance is to maximise the contribution of the somatosensory system to the performance of the task. Performing balance tasks under eyes-closed conditions means that the visual inputs to balance are not present, and the relative contributions of the other systems increase (Peterka, 2002). Howells *et al.* (2011) presented a sub analysis of eyes-closed balance trials and showed that all data suggested a reduced balance ability in ACL reconstructed limbs compared to uninjured participants, suggesting this methodological approach may produce findings that are more consistent.

Linear measures provide insight into the outcome of the task, such as the movement of the centre of mass, by assuming that there is a linear relationship between an input and the output. Measures of balance, such as the spread and velocity of the CoP have been used to establish relationships between ACL injury and balance performance. Despite the clear worth of using such variables in establishing relationships, explorations into the dynamics of how a task is completed have been suggested to offer further insight into the function of a system. One approach to investigating how a task is executed is to use methodologies from dynamical systems theory (Davids *et al.*, 2003; van Emmerik *et al.*, 2016). Within a dynamical systems approach no assumption about the linearity of the system is made, instead variables that are able to capture non-linear characteristics are explored.

No evidence exploring changes in non-linear dynamics of balance due to ACL reconstruction was identified in Chapter 3 however, changes in non-linear balance dynamics have been found due to multiple sclerosis (Busa, Jones, Hamill, & van Emmerik, 2016), Parkinson's disease (Vaillancourt & Newell, 2000), and aging (Manor *et al*., 2010). Manor *et al*. (2010) explored the effect of visual and somatosensory impairments on traditional and dynamical system measures of balance in elderly participants and found that in addition to changes in sway area, the dynamics of the CoP also alluded to changes in feedback loops that contributed to the performance of the task. This finding appears to support that non-linear dynamics may offer a different insight into the performance of a task. Cazzola, Pavei, and Preatoni (2016) assessed race walkers using linear and non-linear analysis methods and found that coordination variability, a measure of the dynamics of a task, was more sensitive at distinguishing skill levels than traditional measures. Non-linear approaches may therefore not only provide insight into the dynamics of a task, but also be more sensitive to distinguishing different populations. Doyle, Newton, & Burnett (2005) provided further support for the application of non-linear approaches in balance analysis. Fractal dimension, a non-linear vairable of the dynamics of the CoP, was shown to have greater relaibility compared to traditional linear measures of balance. Despite the limited evidence on non-linear dynamics of balance in ACL injured populations, the evidence appears to support that the theoretical framework of dynamical systems theory may be a suitable approach to exploring changes in the biomechanics of a balance task due to ACL injury and treatment.

4.4 The Human Body as a Non-Linear Dynamical System

The human physiologic system contains a large number of structural, chemical, and biological components which all contribute to its function. Dynamical systems theory provides a model that suggests these systems and components self-organise to produce outputs which are capable of meeting the demands of varying tasks, and evolve over time (Davids *et al.*, 2003; Kamm, Thelen, & Jensen, 1990; Morrison & Newell, 2015; van Emmerik *et al.*, 2016). Dynamical systems theory challenges the traditional view of homeostasis, where components remain in a steady-state, and instead proposes homeodynamics (Yates, 1994). Homeodynamics refers to processes within a dynamical system where constant changes in individual components interact to meet the requirements of the task. It is theorised that outputs from such dynamical systems, due to the intricacy of the interactions and numbers of degrees of freedom, are complex and non-linear

(Stergiou & Decker, 2011). This has resulted in researchers modelling the human physiology as a non-linear dynamical system, and applying non-linear analysis methods to human biology (DiBerardino, Polk, Rosengren, Spencer-Smith, & Hsiao-Wecksler, 2010; Stergiou & Decker, 2011; Williams *et al.*, 2016).

Traditional biomechanical approaches, have attempted to identify linear relationships within human movement outputs, such as those highlighted in Chapter 3 (Di Stasi, Hartigan, & Snyder-Mackler, 2015b; Tagesson *et al.*, 2015; Wellsandt *et al.*, 2017). These approaches are only capable of identifying growth, decay, or no change in relationships between conditions and outputs. The identification of such relationships has merit, as evidenced by the advancement of knowledge provided by biomechanical research exploring linear relationships, however applying the dynamical systems theory paradigm highlights the limitations of such analyses. Outputs from non-linear systems have characteristics over numerous temporal and spatial scales, and can contain a variety of dynamics such as deterministic chaos, and types of fractal scaling (Goldberger, Peng, & Lipsitz, 2002). As these dynamics are a product of the interaction of numerous complex systems, the ability to quantify and monitor these has been suggested to provide insight into the health or performance of a system (Stergiou & Decker, 2011). As traditional linear approaches are unable to provide information on such characteristics, this has led researchers to apply theoretical concepts from non-linear dynamics to the analysis of human data.

Fractals and chaos, are two key concepts in non-linear dynamical systems, specifically due to their relationship to human physiology. Fractals refer to structures which have a complex geometry, but contain underlying patterns with their irregularity. Structures such as Purkinje fibres, and vascular systems are two examples of fractal structures in the human system. Fractal processes produce structures over differing timescales, and are characterised by long-range correlations within data. Long-range correlations refer to repeating patterns within a signal which occur due to current and past states of the signal influencing future states (Gao *et al.*, 2006). Such processes have been identified in human outputs such as gait parameters (Hausdorff, Peng, Ladin, Wei, & Goldberger, 1995; Hausdorff *et al.*, 1996) and heartbeat interval (Peng, Havlin, Stanley, & Goldberger, 1995). Chaos describes unpredictable behaviours which often occur through the interaction of varying feedback loops (Goldberger, Rigney, & West, 1990). Unlike fractal dynamics, which demonstrate similarities on differing scales, chaotic dynamics do not have a characteristic scale. Chaotic signals often appear "noisy", and have variations which are regularly random and erratic. Chaotic characteristics have been identified within human heartbeat data (Goldberger, 1991). Within biomechanics, researchers have aimed to identify how these signal characteristics affect human movement outputs, specifically changes in the variability and complexity of data (van Emmerik *et al.*, 2016).

4.5 Difference between Variability and Complexity

Within dynamical systems theory two main terms are often used to describe the dynamics of the system: variability and complexity. Each term refers to a different characteristic of the system that may offer insight into its function.

4.5.1 Variability

Statistically, variability refers to the spread of data around an average measure. This perspective models the variability as error, and often data processing methods, such as normalisation, are used to minimise it (Mullineaux, Milner, Davis, & Hamill, 2006). From a human movement perspective, variability can be present in the performance of repeated trials and categorised as either end point variability or coordinative variability (van Emmerik *et al.*, 2016). End point variability refers to the variation in the outcome. Coordinative variability, refers to the variability of how the task is performed. Control theory models both these variability characteristics as resulting from noise within the system, and therefore are both considered undesirable (Bartlett, Wheat, & Robins, 2007). However, from a dynamical systems perspective, variability may not simply be error, yet an important non-linear characteristic of the system (Stergiou, Harbourne, & Cavanaugh, 2006). An example presented by Bernstein (1967) is the accuracy to which a blacksmith can hit a certain point with their hammer (end point variability), and the variability of the path of the hammer to reach that point (coordinate variability). Dynamical systems theory, models lower end point variability as increased task performance, and coordinate variability as a measure of the system's ability to complete the task in a number of different ways.

From a clinical perspective, Stergiou and Decker (2011) presented an argument that there is an optimal level of movement variability where reduced or increased variability relates to a more rigid or noisy system, respectively, and that injury may cause a change in variability. There is some evidence of this alteration in movement variability in ACL reconstructed participants where an increase in coordination variability has been identified in walking (Davis, Williams, Sanford, & Zucker-Levin, 2019) and cutting tasks (Pollard, Stearns, Hayes, & Heiderscheit, 2014). Despite its potential worth in investigating changes in motor function in ACL injured participants, the methods required to provide meaningful data may limit its use within clinical practice.

As movement variability relates to the repeated completion of the same task, a suitable number of trials needs to be collected to gain a true representation of the involved dynamics. One proposed method is to determine the number of trials to establish a stable mean through sequential estimation procedure (Hamill & McNiven, 1990). This method has led to researchers suggesting 10 – 15 trials be used to assess variability in variations of gait (Hamill, van Emmerik, Heiderscheit,

& Li, 1999; Preatoni, Ferrario, Dona, Hamill, & Rodano, 2010). Within an ACL injured population the completion of repeated trials may be unrealistic due to the related effects of the injury, especially during the acute stages of initial injury and recovery. An additional limitation of the use of variability in monitoring changes in function of ACL injured participants within a clinical setting are the required resources. Movement variability is most commonly assessed through analysis of kinematic data collected using motion capture or inertial measurement units (Heiderscheit, 2000). Despite these technologies becoming more readily available, they still contain a number of limitations for their widespread implementation such as cost, and the need for large spaces free from reflections and magnetic metals. The issues related to the collection of suitable data for analysis of movement variability limits its potential use in the monitoring of recovery from ACL injury and reconstruction.

4.5.2 Complexity

Physiological complexity refers to the outputs created by the many interacting systems of human physiology which contain non-random structures which occur over a number of different time-scales (Lipsitz, 2002; Vaillancourt & Newell, 2002; van Emmerik *et al.*, 2016). These structures produce long-range correlations, where similar structures are repeated throughout the signal due to the current state being influenced by past and future states (Gao *et al.*, 2006). These correlations are characterised by a log power spectrum of $1/f^{\alpha}$, where $\alpha=1$ represents the highest level of complexity due to repeating patterns that have a linear relationship between their amplitude and frequency. A log-power spectrum where $\alpha=0$ supports the presence of uncorrelated random white noise, and $\alpha=2$ of Brownian noise characterised by only local similarities (Lipsitz, 2002). Another principle of complexity is the number of variables which are required to predict the signal (Vaillancourt & Newell, 2002). Where a signal is a result of a number of interacting inputs, an increase in the number of these inputs or interactions between them, is theoretically related to an increase in output complexity. As the nature of complexity relies upon the interaction of different systems, quantifying complexity has been suggested to provide information about the current state of a system (Lipsitz & Goldberger, 1992).

It is important to note that although the two concepts of variability and complexity are closely related, and are outcomes of the interacting systems of human physiology, they are not synonyms. Lipsitz (2002) highlighted how a sine wave with a large magnitude is a signal with high variability, but can be described by a simple mathematical function and therefore has low complexity. In contrast, a signal with a low amplitude may contain irregular stochastic noise, therefore having a reduced variability but increased complexity. It is important to ensure researchers clearly define *a priori*; what characteristic they are exploring, and that the correct methodological approach is used (van Emmerik *et al.*, 2016).

Variability and complexity offer insight into the dynamics and health of a system, however complexity may provide a more suitable variable for the use of monitoring recovery from ACL injury in a clinical setting. The assessment of complexity is able to be conducted on a single signal, meaning there is no requirement for repeated trials minimising the burden placed on the patient. Additionally, a commonly assessed signal is that of the CoP during a balance task, an output which has previously been shown to be affected by ACL injury and treatment. Finally, Lipsitz and Goldberger (1992) presented a theoretical framework for the effect pathology may have on complexity, providing potential explanations for any observed changes.

4.6 Loss of Complexity Theory

Lipsitz and Goldberger (1992) proposed that a healthy system produces complex outputs due to the interaction of multiple systems to meet the demands of the task, and that with aging and disease there is a decrease in output complexity. This reduction in complexity was theorised to be due to the loss of certain structures or changes in their interaction. Figure 8 demonstrates how within a four component system, the dynamics can be altered by loss of components and changes in interactions. Within the context of ACL injuries and balance, Figure 8a may represent a healthy limb where the four components are inputs provided by the visual, vestibular, and somatosensory systems. Injury to the ACL and loss of the proprioceptive input provided by the ligament may result in a loss of one of these inputs, as demonstrated in Figure 8b. A reduction in the number of interacting systems, according to the loss of complexity theory, would result in a reduction in the complexity of the output, in this example the CoP.

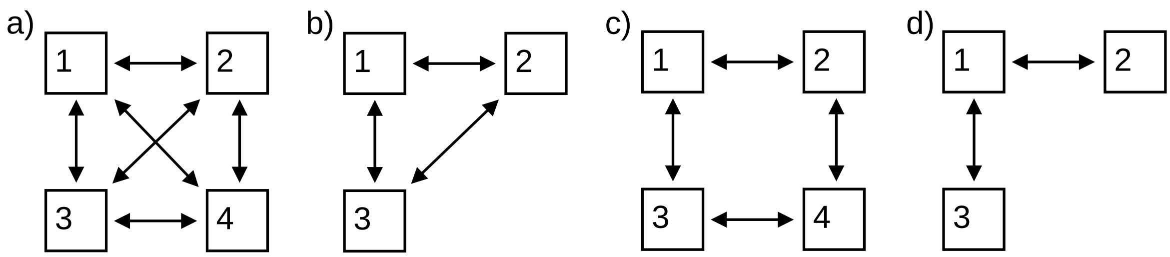

Figure 8. A four component system (a), and theoretical changes in the number of components (b) and interactions (c), and changes in both (d) which may occur due to aging and disease. Adapted from Vaillancourt and Newell (2002).

A reduced complexity in the outcome of a signal has been suggested to be indicative of a less adaptable system, and therefore an undesirable characteristic (Lipsitz, 2002; Lipsitz & Goldberger, 1992; Stergiou & Decker, 2011). Evidence showing pathological and aging participants display a reduced complexity has been used to support this theory (Lake, Richman, Griffin, & Moorman, 2002;

Manor *et al.*, 2010). Busa *et al.* (2016) found women with multiple sclerosis (n=12) had a lower average complexity index (CompInd) in both AP and ML axes compared to healthy women (n=12) during varying balance tasks (mean±SD CompInd; multiple sclerosis: AP =17.43±2.51, ML=16.34±2.38; healthy: AP=18.24±1.69, ML=17.09±1.52). These findings agreed with other investigations into balance complexity in Parkinson's disease (Cattaneo *et al.*, 2016; Vaillancourt & Newell, 2000), idiopathic scoliosis (Gruber *et al.*, 2011), and concussed participants (Purkayastha *et al.*, 2019).

Assessment of static balance tasks appears to identify a loss of complexity with pathology, however Vaillancourt and Newell (2002) proposed that rather than a unidirectional change, ageing and disease can result in a bidirectional change in complexity. Ko and Newell (2016) assessed complexity of the CoP trace in young (19-28 years) and elderly (65-74 years) during two balance tasks with two targets. The targets related to the CoP position and were constant, representing quiet stance, and a sine-wave target. The complexity analysis of the constant target produced results in support of a loss of complexity due to aging, however during the more difficult dynamic target task this relationship was inverted and the elderly participants had a higher complexity. The authors suggested that the difficulty in matching the dynamic target led the elderly participants to increase the degrees of freedom and involved systems in an attempt to meet the demands of the task, and therefore resulted in a more complex signal. The findings of Ko and Newell (2016) support the loss of complexity theory when assessed during static balance, however also highlight the potential role of the participant's ability to utilise the available systems to meet the demands of the task, where a lower complexity may also be indicative of a greater proficiency.

Complexity, as described in section 4.5.2, is a characteristic of a signal which is multifactorial, and difficult to directly measure. One approach which has been used is detrended fluctuation analysis (DFA; Peng *et al.*, 1993). DFA aims to assess fractal dynamics through identifying the presence of short and long-term correlations. The output from DFA is a scaling factor (α) of the log power spectrum of form $1/f^{\alpha}$ as described in section 4.5.2. This approach has been used to assess CoP signals (Wang & Yang, 2012), however Gilfriche, Deschodt-Arsac, Blons, and Arsac (2018) highlighted a potential limitation of this approach. DFA is able to assess the characteristic of complexity at differing temporal scales, however only an overall output is provided meaning it is unclear at what frequencies complexity is present. Frequency-specific fractal analysis may overcome this limitation through the analysis of filtered and simulation data (Gilfriche *et al.*, 2018) however, there is limited evidence to support its use and has not been widely used meaning interpretation with regard to the loss of complexity theory is difficult. Another approach to assessing complexity is through the entropic based measures (van Emmerik *et al.*, 2016). Variants of entropy based measures have been widely implemented to explore complexity of the CoP during balance tasks (Yentes *et al.*, 2013), and formed the methodological approach suggested by Lipsitz and Goldberger (1992) in regard to the proposed loss of complexity with aging and disease.

4.7 Entropy for Measuring Complexity

Entropy based measures stem from information theory and concern the quantification of the regularity and unpredictability of a signal (Costa, Goldberger, & Peng, 2002; Pincus, 1991; Richman & Moorman, 2000; Shannon, 1948). Information theory was proposed by Shannon (1948), and involves quantifying the amount of information in a system. This information is often viewed as uncertainty, which is the foundation for the philosophical link to a measure of complexity, and Shannon quantified this uncertainty as entropy. This entropy differs from the thermodynamics definition, which looks at the level of disorder, and instead quantifies how much information is needed to predict the future state of a system.

Kolmogorov-Sinai complexity (Kolmogorov, 1958; Sinai, 1959) is a variant of Shannon entropy, and is the mean rate of new information relative to the previous states of the system. Algorithms were developed to calculate this entropy (Grassberger & Procaccia, 1983), however these required large noise-free data sets, meaning it was unsuitable for application to physiological systems (Pincus, 1991).

4.7.1 Approximate Entropy

To address the weaknesses related to the calculation of Kolmogorov-Sinai complexity Pincus (1991) developed a family of statistics called approximate entropy (ApEn). This algorithm calculated the logarithmic probability that repeating patterns of a set length remain similar when observed at the next increment, with higher probability producing lower entropy values, and indicating higher signal regularity. The ApEn algorithm was suggested to be able to distinguish between signals with varying complexity characteristics (e.g. chaotic and fractal), in data sets as short as n=100 (Pincus, 1995; Pincus & Huang, 1992). This led to ApEn applications to human signals such as postural control (Deffeyes, Harbourne, Stuberg, & Stergiou, 2011; Rhea *et al.*, 2011), and gait variables (Khandoker, Palaniswami, & Begg, 2008; Tochigi, Segal, Vaseenon, & Brown, 2012). Despite its popularity, the ApEn contains limitations related to the mathematical calculation of the variable: 1) a bias towards regularity due to self−matches; 2) poor relative consistency when the input parameters are changed; and 3) sensitivity to changes in data length. These limitations led to the development of sample entropy (SampEn; Richman & Moorman, 2000).

4.7.2 Sample Entropy

SampEn differs from ApEn in that it does not count self-matches, as it considers the conditional probabilities of template matches across the whole signal rather than on a template-wise approach. A template-wise approach involves calculating the conditional probability that vectors match a single template of length *m* also match for the template of length *m+1*. Comparisons to each new vector in a signal is then completed individually. As the calculation of the conditional probability requires at least one match for both conditions, the ApEn algorithm includes self-matches in the calculation of this probability, resulting in a bias towards regularity. In contrast, SampEn does not calculate the conditional probability until all matches for all templates are counted, excluding self-matches, meaning a reduced bias and the need for only one match across the whole signal to provide a mathematically real result. These differences were intended to reduce the bias related to the calculation of ApEn.

SampEn is defined as the negative natural logarithm for conditional probability that two sequences within a tolerance of *r* for *m* points remain within *r* of each other at the next point (*m*+1), where *m* is a predefined vector length (discussed in section 4.7.2.2), and *r* is a predefined tolerance to determine template matches (discussed in section 4.7.2.3). A worked example of one template comparison is presented in Figure 9. Mathematically, SampEn can be defined as

$$SampEn(m,r) = \lim_{N\to\infty} -\ln[A_{m+1}(r)/B_m(r)] \tag{5}$$

which is predicted by the statistic

$$SampEn(m,r,N) = -\ln[A_{m+1}(r)/B_m(r)] \tag{6}$$

where N is the signal length, and $A_{m+1}(r)$ and $B_m(r)$ are defined as the probability that two sequences will match for *m+1* and *m* points, respectively. $A_{m+1}(r)$ is calculated as

$$A_{m+1}(r) = \frac{\sum_{i=1}^{N-m} A_{m+1}(r)_i}{N-m} \tag{7}$$

where $i = [1, N-m]$, $A_{m+1}(r)_i$ is the number of vectors $x_{m+1}(j)$ which are within a tolerance r of $x_{m+1}(i)$ where $j = [1, N-m]$, and $j \neq i$ to exclude self-matches, divided by the number of comparisons $(N-m-1)$. Similarly $B^m(r)$ is calculated as

$$B_m(r) = \frac{\sum_{i=1}^{N-m} B_m(r)_i}{N-m} \tag{8}$$

with vectors x_m. Richman and Moorman (2000) showed that

$$\frac{A_{m+1}(r)}{B_m(r)} = \frac{A}{B} \tag{9}$$

where B is the total number of template matches of length *m*, and A is the number of matches of lengths *m*+1 across all available templates. Therefore sample entropy can be calculated as

$$SampEn(m, r, N) = -\ln\frac{A}{B} \tag{10}$$

As demonstrated in Figure 9, the value of *A* will always be less than or equal to *B*, meaning SampEn will always be positive, and as with ApEn a larger value is associated with an increased complexity.

SampEn addresses certain biases which were present in the ApEn algorithm (Richman & Moorman, 2000), however it is still affected by data stationarity, input parameter choices, and data length (Gow *et al.*, 2015; Yentes *et al.*, 2013). Researchers have investigated to what extend these factors alter SampEn values on both simulated and real physiological data to provide guidance on what methodology should be selected to provide the most robust and valid measure of complexity (McCamley, Denton, Arnold, Raffalt, & Yentes, 2018; Montesinos, Castaldo, & Pecchia, 2018; Yentes, Denton, McCamley, Raffalt, & Schmid, 2018; Yentes *et al.*, 2013).

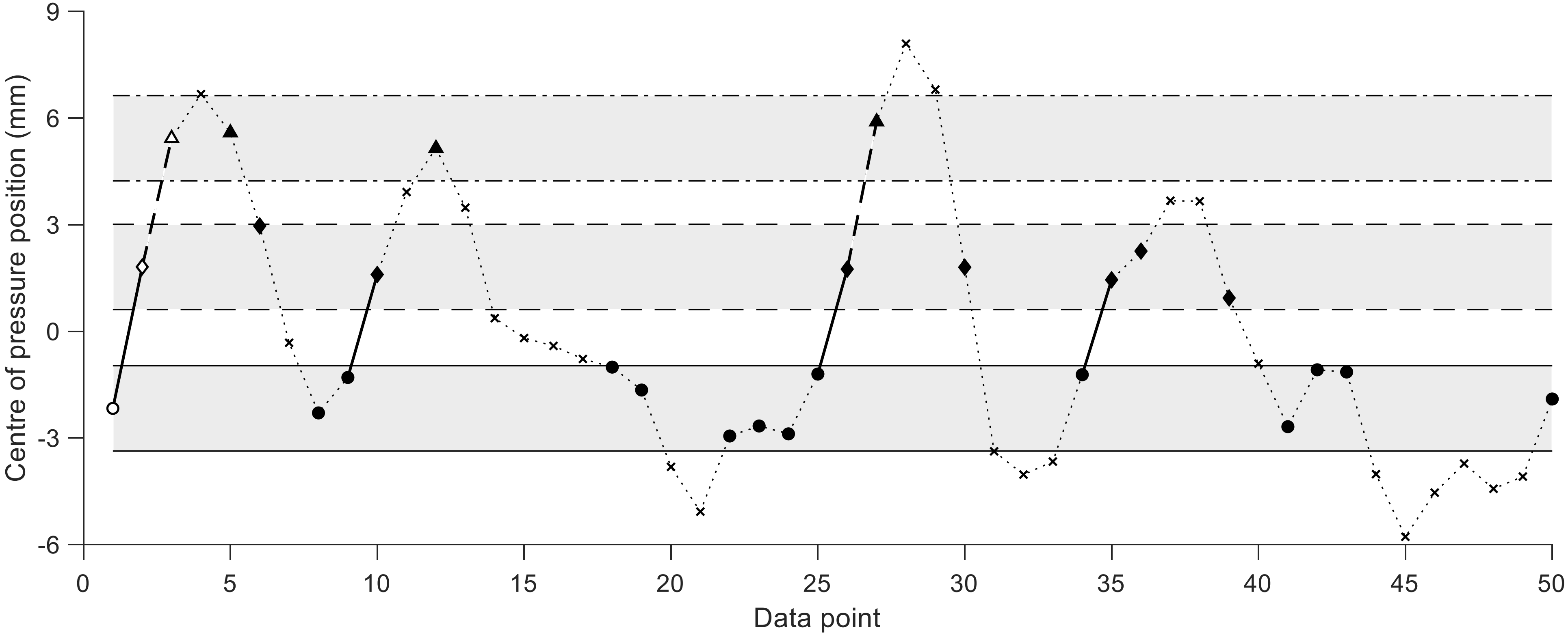

Figure 9. Template matches during a sample entropy calculation on centre of pressure data with a vector length (m) of two. The shaded areas bordered by solid, dashed, and dash-dotted lines represent the tolerance (r) around the first (○), second (◊), and third (Δ) data points, respectively, which form the template vectors m and m+1. Data point matches are shown as filled markers, and none matches as ×. Three observed template matches of length m (solid line), and one of length m+1 (dashed line) are observed. Adapted from Costa, Goldberger, and Peng (2005).

4.7.2.1 Data Length

As SampEn is a probabilistic calculation, confidence in the result will increase with the number of matches identified (Gow *et al.*, 2015). It follows therefore that data length should be maximised to increase the potential for matches. Montesinos *et al.* (2018) provided evidence for this as CoP data of length 35^m produced larger effect sizes between young and elderly participants compared to data 24^m long, *m* is the vector length of the SampEn algorithm. Both the long and short data were taken from the same trial, and the extraction method was not stated. It is therefore possible that the longer data included characteristics related to potential fatigue of the participants. This limitation highlights that data length is also limited by the methodology of the study, particularly the participants. In certain circumstances, such as when the participants are elderly or have pathology, or the task is difficult to complete for long periods of time, the ability to collect a large amount of data is not feasible. Yentes *et al.* (2018) presented evidence for another potential negative to maximising trial length. When comparing complexity of discrete gait variables, poor relative reliability was shown when $N \geq 3000$. The authors did not present an explanation for this outcome, however they did identify that this finding may be related to the methodology employed, and an artefact specific to discrete variables. The data represented 3000 steps leading the authors to theorise this result may have been due to participant fatigue, although this was not measured, and visual inspection of the data did not identify any drift. A study on the effect of input parameters on continuous gait variables calculated SampEn on joint angles on large data sets ($N = 537^m$, 380^m, 268^m, and 190^m; McCamley *et al.*, 2018). The results showed differences in complexity values, which would be expected as data length was changed by down sampling meaning dynamics at different temporal scales were being assessed, however relative consistency was good. This result suggests that sampling frequency must be justified to assess temporal scales specific to the task, but that long data lengths do not reduce the accuracy of SampEn values on continuous data. A systematic review of articles which assessed balance complexity showed CoP data lengths of up to 190^m have been used to distinguish between participants groups during balance tasks. Therefore when collecting continuous data, such as CoP, data length should be as long as possible, taking into account the task demands and participant constraints. To minimise the risk of potential poor relative reliability, data length should be standardised across all comparisons.

The minimum number of data required to produce accurate SampEn values has also been explored. Richman and Moorman (2000) calculated SampEn of independent and identically distributed random variables of lengths N = 100 (10^m), 5000 (~70^m), and 20000 (~141^m), and compared these to theoretically predicted values. The confidence limits of SampEn reduced as N increased, however N = 100 produced values which matched the theoretical values closely. Yentes *et al.* (2013) highlighted that despite the accuracy of the value, the confidence limits were still large, and therefore compared SampEn values of theoretical, and gait data. SampEn was found to be consistent across data lengths of 10^m to 14^m, however the output was more sensitive to changes due to differences in vector length (*m*) and tolerance level (*r*). This led the authors to suggest a minimum data length of 14^m data points, a value that was also presented by Gow *et al.* (2015). These findings demonstrate how the effect data length has on SampEn is still not fully understood, but that continuous data should have a minimum length of 14^m.

4.7.2.2 Vector Length (m)

The vector length input (*m*) of the SampEn algorithm has implications on the number of matches and therefore the confidence of the entropy estimate, and also the timescale which is being assessed (Costa *et al.*, 2002). As the number of comparisons against a template is relative to *m* ($N - m - 1$), a smaller vector length will result in the potential for more matches. The selection of *m* is also limited by the length of the data, where the minimal length has been suggested to be 14^m, meaning a larger vector length will result in a longer required data set. Due to this, and recommendations made by Richman and Moorman (2000), within clinical research *m* of lengths two and three have been used (Clark *et al.*, 2014; Lake *et al.*, 2002; Ramdani, Seigle, Lagarde, Bouchara, & Bernard, 2009).

The choice of vector length, also has implications on the timescale that the SampEn algorithm is assessing. As the SampEn statistic is calculated through the similarities of template vectors, the data which are captured by such vectors relate data of a frequency related to the sampling rate and vector length, referred to as the timescale. Busa and van Emmerik (2016) suggested that the timescale which is being assessed should be reported by using the following equation

$$Timescale = \frac{Sample\ frequency}{(m+1)\times\tau} \tag{11}$$

where τ is a timescale factor which for SampEn is set to one. It is important that the timescale being analysed is able to assess the complexity of dynamics which are related to the performance of the movement, as doing so will result in biologically relevant assessments. For example the data related to somatosensory feedback during balance tasks mostly has a frequency between 2 and 20 Hz (Dietz, Mauritz, & Dichgans, 1980; Golomer, Dupui, & Bessou, 1994). Equation 11 shows how the sampling frequency and *m* determine this timescale. It shows that both *m* and the sampling frequency should be considered together to assess the most valuable timescale, however this consideration is overcome when using a variant of SampEn, multiscale sample entropy (MSE), which is described in Section 4.7.3.

4.7.2.3 Tolerance (r)

During template vector comparison, a match is defined by the data points of the vector being within a pre-set tolerance level (*r*). As demonstrated in Figure 9, the magnitude of *r* affects the number of matches of both length *m* and *m+1*, and therefore should be carefully selected. A larger tolerance would result in an increase in matches, something that theoretically would increase the confidence of the statistic, however it would also result in Equation 9 tending towards one. Within the literature, *r* is often selected in relation to the variance of the signal, and either kept constant between trials, or calculated as a percentage of a variance statistic such as SD (Gow *et al.*, 2015; Pincus, 1991; Yentes *et al.*, 2018; Yentes *et al.*, 2013). A fixed tolerance level has been shown to have potential benefits for providing results with good relative reliability (Yentes *et al.*, 2018). However, when *r* is fixed, no adjustment for the magnitude of the signal is taken, meaning the complexity algorithm may be being affected by the variability of the signal. As discussed in section 4.5, the dynamics of variability and complexity are different and should therefore not be considered together, meaning a fixed tolerance level is potentially limited by its interaction with variability. No exploration of the effect of signal range and constant tolerance levels has been conducted, however by calculating *r* as a percentage of the variance this potential limitation may be avoided.

In the original ApEn algorithm Pincus (1991) suggested using an *r* value which was 10-20% of the signal SD. Duarte and Sternad (2008) explored the effect of tolerance levels of 10%, 15%, 25%, and 30% of the SD on balance complexity of young and elderly participants using the SampEn algorithm. No specific data on the comparisons were presented, however relative reliability was reported as good for all comparisons despite changes in the levels of complexity. The optimal level of tolerance is still not fully understood, however the presented evidence suggests that tolerance level should be set as a percentage between 10-30% of the SD of the signal, and should remain constant for all comparisons.

One limitation of using the SD to inform the tolerance level is that *r* has the same limitations as the SD statistic, specifically the effect of outliers and non-stationarities (Hampel, 1971; Mullineaux & Irwin, 2017). Outliers refer to anomalies that exceed the general variance of a distribution and are often viewed as error. Stationarity is a characteristic of a signal where the mean and variance are consistent across the data, and non-stationarities are data which cause a violation of this characteristic. Stationarity can be violated through the presence of drift or outliers. When one or more outliers are present within a data set, the SD provides a non-robust measure of the spread, meaning the statistic is susceptible to large changes in the presence of spikes such as that in Figure 10. The magnitude of this effect is increased as the proportion of outliers to the data size increases. This increased SD would then have a direct effect on the tolerance level of the SampEn, which has already been discussed to alter the output.

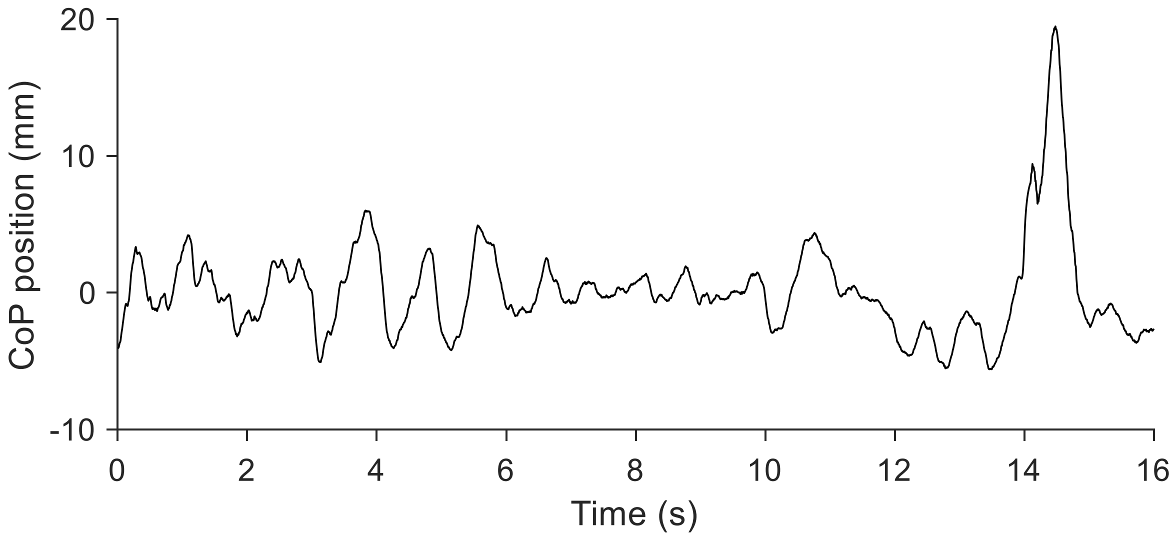

Figure 10. Example centre of pressure (CoP) position (100 Hz) during unilateral balance with an outlier between 14 – 15 s, which may be caused by the participant shifting their foot. Adapted from Gow et al. (2015). Standard deviation for all the data (0-16 s) = 3.5 mm and before the outlier (0-14 s) = 2.3 mm.

The removal of outliers would remove the effect they have on the tolerance input to SampEn, however the removal of such data may remove dynamics of the movement which are inherent to the completion of the movement (Gow *et al.*, 2015). Therefore, a more attractive proposition is to use a more robust method of assessing the variance, and therefore less susceptible to changes due to outliers. One example is the use of the median absolute deviation (MAD; Govindan, Wilson, Eswaran, Lowery, & Preißl, 2007). This statistic is calculated as the median of the residuals between each value and the median of the data. For a data set x $(x_1, x_2, \dots, x_n)$ MAD can be calculated as

$$MAD = median(|x - \tilde{x}|) \tag{12}$$

where $\tilde{x}$ is the median of x. This measure of variability is more robust, meaning it is less susceptible to change due to outliers, and therefore may provide a suitable statistic to allow the SampEn algorithm to take into account the variability of the signal without being affected by non-stationarities. While the MAD may offer a robust measure of the variance of a signal (Rousseeuw & Croux, 1993), and therefore may be a suitable approach for the calculation of tolerance in the SampEn algorithm, it does not resolve the issues related to drift and there is no research into how different percentages of the statistic will affect the measured complexity value. MAD may offer a useful approach, however further explorations into its use with biomechanical data such as CoP, and its effectiveness at distinguishing between populations is needed.

Gow *et al.* (2015) proposed an alternate method to calculate the variability as the median of the SDs from a moving window of length n that is shifted one data point forward until the $N-n^{th}$ data point, where N is the length of the data. To ensure an acceptable level of accuracy of the window SD in comparison to the whole data set, a minimum of n=240 points is suggested to be used. Gow *et al.* (2015) demonstrated on example data, how the windowed SD method produced similar values when no outliers were present, but was less susceptible to increases when the outliers were included. SD increased by 48% when the outlier was included compared to excluded in the data presented in Figure 10. In comparison, using the windowed SD method, the difference was reduced to 6%. No comprehensive evaluation of this method has been conducted, however the data presented by Gow *et al.* (2015) suggests the windowed SD method is a suitable approach for determining the tolerance level of the SampEn algorithm in data which are prone to outliers and non-stationarities such as CoP during balance.

4.7.2.4 Filtering

One final consideration that should be taken into account when conducting SampEn analysis is the filtering process. Data collection tools often introduce noise into a signal. This noise does not provide information into the dynamics of the system, and is therefore undesirable (Derrick & Robertson, 2018). Filtering tools aim to primarily remove noise whilst retaining the desired signal, however this is often difficult. As a result, there exists a trade-off between the rigours of filtering processes to maximise the removal of noise without altering the true signal. This is an issue which is present in most biomechanical data, and that can lead to errors for common analysis tools. SampEn poses a further requirement on the data processing, by the effect non-stationarities and drift have on the output. Drift and non-stationarities, not only have an effect on the tolerance level, but also reduce the number of matches and therefore the confidence in the statistic. Data processing methods should therefore aim to maintain the characteristics of the signal whilst removing both high frequency data introduced due to data collection tools and therefore not relevant to biological processes, and lower frequency data related to drift. Two approaches have been used within the research, band-pass filtering, and empirical mode decomposition (EMD; Huang *et al.*, 1998).

Band-pass filters pass data that lie within a predefined frequency band, and attenuates data outside of this band. By selecting suitable limits for the frequency band, data can be processed to remove both low frequency data which may have an effect on the confidence of the SampEn statistic, and high frequency data which may influence the complexity of the signal due to noise. Although band-pass filters are computationally able to remove undesirable characteristics of a signal related to the calculation of SampEn, they may be unsuitable for the processing of non-linear signals where non-stationarities are present. The most commonly applied filtering approach for assessments of complexity of balance has been EMD a tool specifically developed to process non-linear and non-stationary time series data (Gow *et al.,* 2015).

EMD involves decomposing a signal into a number of intrinsic mode functions (IMFs) and a residual through an iterative sifting process. These IMFs contain the intrinsic characteristics of the signal, with each function having a predominant frequency of $sf/2^{i+1}$, where sf is the sampling frequency, and i the IMF number. The resulting IMFs and residual can then be summed to recreate the signal. Through the exclusion of certain IMFs at unwanted frequencies, such as those not relating to biological processes, the EMD algorithm can be used to create a signal which only contains characteristics which occur at frequencies of interest.

The EMD algorithm is an iterative process where the same data processing is conducted until the output meets the criteria of an IMF. These criteria are: that the number of local extrema and zero crossings are equal or differ by no more than one; and that the mean of the lower and upper envelopes, defined as the cubic splines fitted to local minima and maxima, respectively, is equal to zero. Once an IMF meets the criteria, the algorithm is repeated with a new signal created by subtracting the IMF from the signal. The algorithm for the identification of one IMF is demonstrated in Figure 11 and contains the following steps:

1. Locate the local minima and maxima of the signal [$X_i(t)$], where i is the iteration number
2. Interpolate the located extrema data points with a cubic spline, of the same length (t) as the signal, to obtain the upper [$U_i(t)$] and lower [$L_i(t)$] envelopes
3. Find the mean of the upper and lower envelopes

$$M_i(t) = \frac{U_i(t) + L_i(t)}{2}$$

4. Subtract the mean from the original signal to calculate a new signal [$H_{i,s}(t)$] where s is the sift number

$$H_{i,s}(t) = X_i(t) - M_i(t)$$

5. Check whether the new signal [$H_{i,s}(t)$] meets the criteria for an IMF:
    a. If the criteria are met, $H_{i,s}(t)$ is saved as IMF_i, and a new signal [$X_{i+1}(t)$] is created by subtracting IMF_i from $X_i(t)$ and the next iteration is conducted
    b. If the criteria are not met, another sift is completed by repeating steps 1-5 with $H_{i,s}(t)$ substituted for $X_i(t)$

The purpose of the sifting process (step 5) is to ensure the IMF contains the best representation of the characteristics of the signal on a distinct timescale (Huang *et al.*, 1998). However, over sifting can result in distinctions of the data being removed. Therefore a stopping criterion is also employed. Huang *et al.* (1998) presented a method whereby a consistency threshold is set, and the sifting process stops when the two subsequent iterations are similar. Similarity is determined by comparing a difference statistic ($Error_{IMF}$; Equation 13) using a threshold, set between 0.2-0.3 to align with similar process using Fourier analysis (Huang *et al.*, 1998; Wang, Chen, Qiao, Wu, & Huang, 2010).

$$Error_{IMF} = \frac{[H_{i,s-1}(t) - H_{i,s}(t)]^2}{H_{i,s-1}^2(t)} \qquad (13)$$

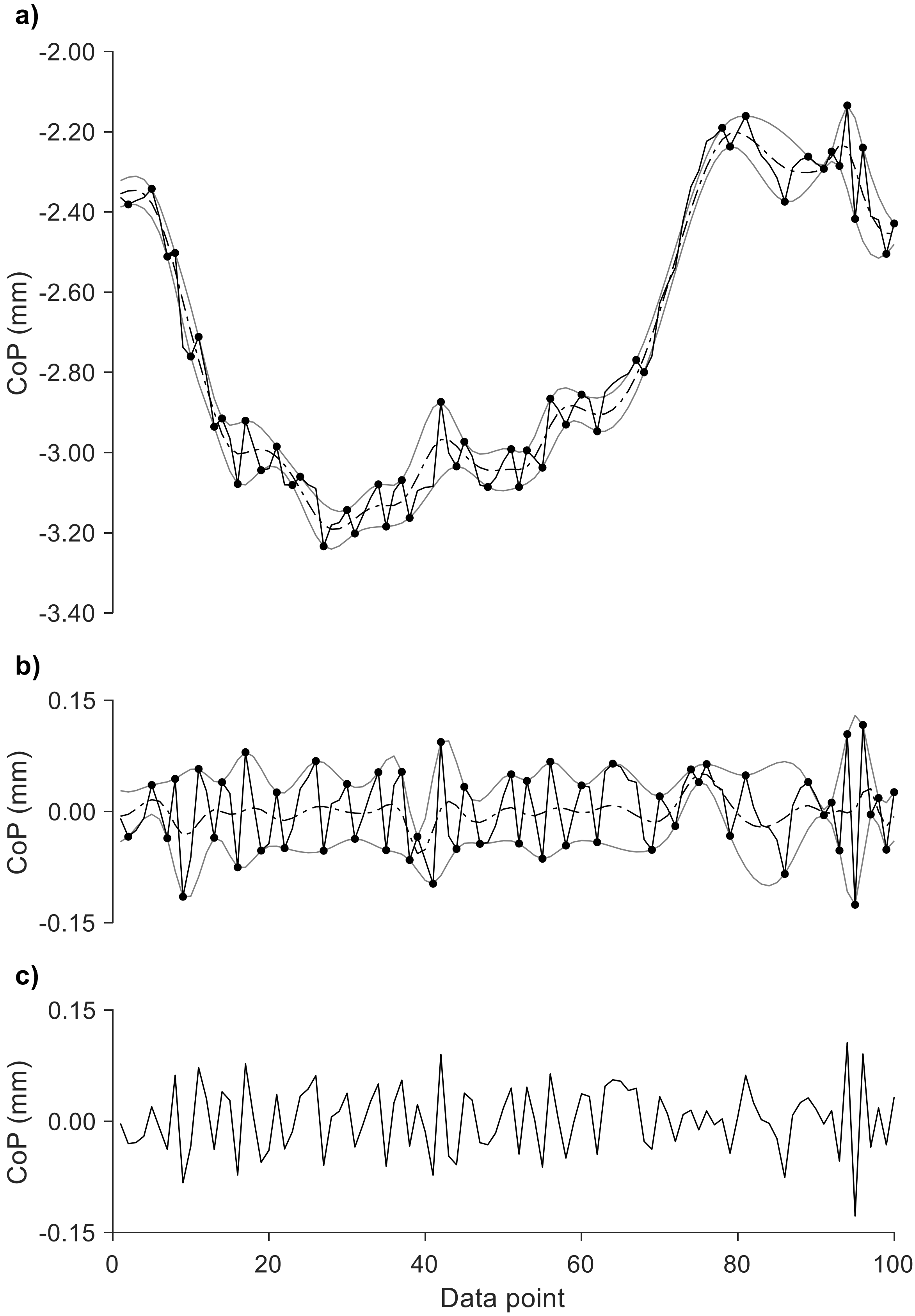

Figure 11. Stages of empirical mode decomposition, showing a) the original signal, b) the first sift, and c) the first intrinsic mode function (Huang *et al.*, 1998).

The number of factors affecting the output from the SampEn limits the ability to compare results across different methodologies. It is therefore important that authors provide a detailed methodology and justification for the selection of data processing methods, and input parameters when using SampEn to assess the complexity of a system.

4.7.3 Multiscale Sample Entropy

The aim of SampEn is to assess the complexity of a system, however as described in section 4.5.2 the inherent properties of a complex signal are spread over different temporal scales. As SampEn is only capable of assessing one timescale, as shown by Equation 11, this limits its ability to truly evaluate the complexity of a system. To address this Costa *et al.* (2002) developed the MSE algorithm.

The algorithm uses the same method as SampEn to calculate complexity, however it does this on coarse-grained data sets (Figure 12) to provide an output at increasingly longer timescales. The coarse-graining procedure calculates the mean of consecutive non-overlapping windows. The size of this window is the timescale factor (τ), which is related to the timescale the SampEn algorithm will calculate complexity for (Equation 11). Complexity is then calculated over a series of signals of length N/τ.

The output from the MSE algorithm is termed the complexity-timescale curve, where each value provides a measure of complexity of the characteristics of the signal at certain frequencies. A CompInd can also be calculated as the area under the curve (Busa & van Emmerik, 2016). The ability of the MSE algorithm to provide a value of entropy at a number of timescales provides a more comprehensive exploration of the complexity of a signal. Additionally, it offers the ability to link differences in entropy to specific frequencies that can in turn be linked to specific biological process that occur at certain timescales (Gow *et al.*, 2015). The interpretation of the complexity-timescale curve is limited to comparisons at each timescale. This is due to differences in entropy that would be present due to the number of comparisons and effects of using a constant tolerance input despite changes in the variance of the coarse-grained signal. The shape of the complexity-timescale curve does not therefore provide further information beyond providing insight into higher and lower frequency biological process.

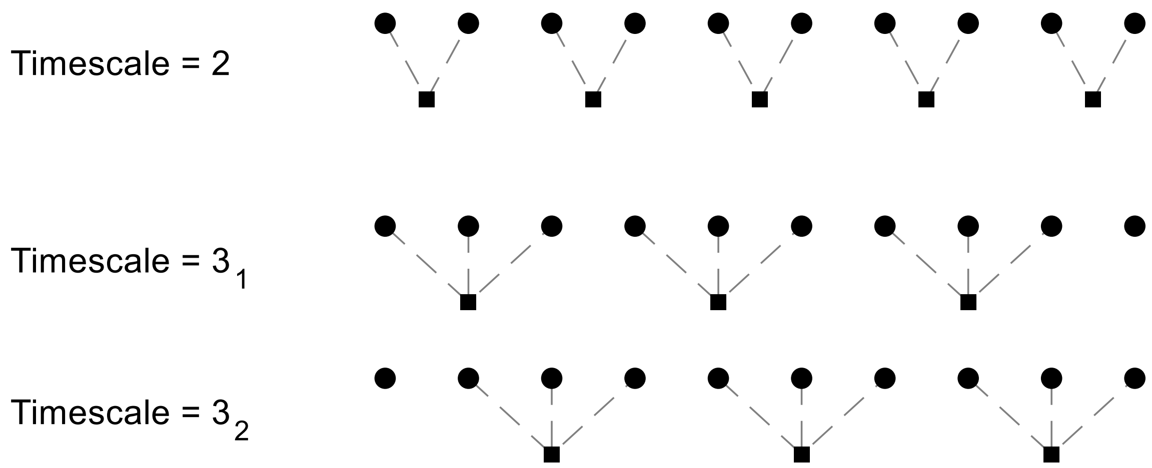

Figure 12. Coarse graining procedure of a signal (n=10; ●) at timescale factors 2 and 3 (■), including demonstration of output signals when the signal length divided by the timescale factor is not an integer.

4.7.3.1 Composite Multiscale Sample Entropy

As N/τ does not always result in an integer, the coarse-graining process can produce data lengths which are of length $(N-(\tau-1))/\tau$, and have up to τ variations. Figure 12 demonstrates how a signal of length N=10 can result in two different coarse-grained signals when τ=3. Wu, Wu, Lin, Wang, and Lee (2013) presented a method to address this weakness by calculating the SampEn of all possible coarse-grained signals at a certain timescale factor, and using the mean entropy value. When both MSE and composite MSE were calculated for a series of simulated and experimental data with theoretically constant complexity levels, the SD of the entropy values were smaller for the composite MSE compared to the MSE algorithm (τ=9; white noise: MSE = 0.07, Composite MSE = 0.05; $1/f$ noise: MSE = 0.16, Composite MSE = 0.11).

4.7.3.2 Multiscale Sample Entropy Limitations

As the MSE method uses the SampEn algorithm, the same limitations which are discussed in section 4.7.2 are present. Specifically, due to the coarse graining procedure, the minimum data length now needs to be considered in relation to the largest timescale factor. As at the largest timescale factor the data length should be at least 14^m to provide an accurate measure of complexity (Yentes *et al.*, 2013), the timescale which can be analysed is limited by the length and sampling frequency of the original signal. This limitation has implications on the MSE algorithm to provide complexity at meaningful timescales, and where trial length is limited by the difficulty of the task, or participant pathology, may be unable to analyse complexity at low frequencies.

4.7.3.3 MSE and Balance Tasks

MSE analysis provides the ability to assess complexity at varying timescales, where the timescale should be selected to identify complexity at meaningful frequencies. This causes a specific challenge for studies into balance complexity. The frequency characteristics of balance have been explored (Bizid *et al.*, 2009; Nagy *et al.*, 2004; Soames & Atha, 1982), and have produced differing conclusions. Commonly, power spectral analyses identify that low frequencies (≤3 Hz) form the majority of the data (Baratto, Morasso, Re, & Spada, 2002; Fitzpatrick, Gorman, Burke, & Gandevia, 1992). Proprioceptive control which forms part of the somatosensory contributions to balance has been suggested to be present in the high frequencies (2-20 Hz) of the signal (Dietz *et al.*, 1980; Golomer, Crémieux, Dupui, Isableu, & Ohlmann, 1999; Nagy *et al.*, 2004). As discussed in section 4.2 rupture to the ACL results in a loss of the proprioceptive input provided by the intact ligament, meaning if a loss of complexity is present due to ACL injury it would be present at timescales between 2 and 20 Hz.

Despite the evidence suggesting low frequencies are predominant in CoP data, explorations into balance complexity suggest characteristics at higher frequencies may still provide information into the health of the system. Costa *et al.* (2007) identified a significantly decreased CompInd of balance in elderly participants with timescales ranging between 60.0 and 7.5 Hz. Similarly, Wayne *et al.* (2014) identified changes in balance complexity due to Tai Chi participation, using frequencies below 20.0 Hz. Differences in complexity identified at frequencies which may not relate to biological processes suggest the MSE algorithm, when conducted at short timescales, is affected by low frequency characteristics of the data. This potential crosstalk between MSE timescales, although not a limitation of the algorithm to assess complexity, which by its definition contains information at varying timescales, may limit the ability to attribute changes in complexity to specific biological process.

Evidence of differences in complexity at frequencies considered to not be related to biological processes, demonstrates that it is unclear which frequencies to analyse when exploring the complexity of CoP during balance. Although spectral analyses have identified that data are predominantly of low frequency (<3 Hz), this does not provide evidence on whether the higher frequencies still contain information relevant to the dynamics of the signal. The articles which explored differences in CompInd may also be misleading, as this variable takes into account the SampEn at each timescale, and therefore does not provide evidence to support the analyses of specific timescales, rather a range. Due to the proprioceptive role of the ACL, when exploring complexity of CoP during balance trials in ACL injured participants frequencies up to 20 Hz may provide meaningful information into the potential loss of complexity. Additionally, the longest timescales should include the lowest frequency which can be reliably assessed with consideration for the limitations of trial length and minimum data length as discussed in section 4.7.3.2.

4.8 ACL Injuries and Balance Complexity

ACL injury has been shown to alter the neurological function of the limb (Pap, Machner, Nebelung, & Awiszus, 1999), and reconstructive surgery is suggested to restore the proprioceptive potential (Dhillon *et al.*, 2012). Within the context of the loss of complexity theory, these changes may result in changes in the number of components, or interaction between components. This may then theoretically alter the complexity of an output where such components are required to meet the demands of the task, such as balance. However the body of evidence surrounding ACL injury and balance complexity is limited.

Balance deficits appear to be greatest in the ACL deficient knee, with reconstruction showing improvements, as identified in Chapter 3. Only one article has previously explored the effect of ACL deficiency on the complexity of balance (Negahban *et al.*, 2010). ACL deficient participants (n=27) completed unilateral and bilateral balance tasks at 1.80±2.23 (mean±SD) years after initial injury. ML and AP CoP data were analysed using a recurrence quantification analysis, a method of quantifying the repetitions of a dynamical system within its phase space (Riley, Balasubramaniam, & Turvey, 1999). Shannon Entropy is an output from this analysis and represents the complexity of the deterministic characteristics of the dynamical system. Shannon Entropy was found to be higher in the ACL deficient participants for all unilateral balance, compared to a matched uninjured comparison group (ML: $F = 9.55$, $p \leq 0.01$; AP: $F = 6.55$, $p = 0.02$). This increased complexity appears to be in disagreement to the loss of complexity theory, however as Shannon Entropy provides a conceptually different outcome to other entropic methods, the relationship between pathology and complexity may be different. Seigle, Ramdani, and Bernard (2009) reinforce this hypothesis by discussing that as Shannon Entropy gives the complexity of the deterministic characteristics, it does not provide a value of whole system complexity on which Goldberger *et al.* (2002) based their theoretical framework. Therefore no articles have currently assessed ACL deficiency, balance, and the loss of complexity theory.

Despite improvements in balance performance, proprioceptive function has still been shown to be reduced in ACL reconstructed participants. Clark *et al.* (2014) presented traditional measures of balance performance relating to amplitude, velocity, and variance of the CoP in ACL reconstructed participants (n = 45). Additionally, SampEn was completed on the incremental CoP trace. Balance deficits were identified for all measurements in the ACL reconstructed group, compared to uninjured comparisons. Complexity, assessed using SampEn, was not found to differ between groups (mean±SD; ACL reconstructed: 1.70±0.03; Uninjured: 1.70±0.05). There appeared to be no loss of complexity in the ACL reconstructed group, however a number of limitations place doubt on this conclusion. ACL reconstruction is said to restore the proprioceptive potential of the limb, therefore at varying points along the treatment timeline, balance performance will change. Clark *et al.* (2014) used participants who had undergone reconstructive surgery between 22.6 to 81.6 weeks prior to testing. The deficits identified using traditional methods suggest that a proprioceptive deficit was still present in all participants, however the relationship between ACL reconstruction and complexity is currently unknown and this variance in timing may have affected the findings. A second limitation relates to the application of the SampEn algorithm. Data were sampled at 100 Hz and vector length was set at m = 3. As per Equation 11, this resulted in a complexity value which was assessed at a timescale of 25 Hz. This value itself may be higher than the frequency of meaningful biological characteristics, however data were also run through a low-pass filter with a cut-off of 6.75 Hz. Therefore data of a frequency which were assessed using the SampEn algorithm were removed through the filtering process. Finally, as only one timescale were used, as described in section 4.7.3, the true complexity of the signal may not be assessed. No assessment of balance complexity in ACL deficient or reconstructed participants has been conducted using the MSE algorithm.

The current evidence surrounding ACL injury and complexity is limited and contains methodological weaknesses which mean the relationship of the injury to the loss of complexity theory is still unknown, and therefore warrants investigation into its potential use as a monitoring tool for recovery from treatment of ACL injuries. In addition to exploring whether changes occur due to treatment, for measures of balance to provide clinically relevant information it is important to understand the magnitude of changes in the measures in participants not undergoing treatment over the same time period as the pathological patients, this is termed the consistency of the measure. By understand the consistency of a measure in an unaffected population, the magnitude of changes identified in a pathological population due to treatment can be interpreted. A number of statistical tools are able to evaluate consistency, most commonly by assessing the presence of bias between two measures (Atkinson & Nevill, 1998; Hopkins, 2000).

4.9 Methods for Quantifying Consistency

Two approaches to exploring the potential of a variable to monitor the changes in an individual due to treatment are: 1) to compare a single measurement to a comparison group, and 2) to compare the change in the measurement to a comparison group. The first approach involves the use inferential statistics to determine whether the distributions of the target group, and comparison group are different. The second approach requires the quantification of the changes which occur in a healthy comparison population, most commonly completed through the use of reliability statistics. Hopkins (2000) highlighted how this approach allows a practitioner to determine whether a meaningful change has occurred due to treatment, by comparing the change in a variable to the consistency without intervention. It was also highlighted that this consistency should be assessed over the same time period the target population is assessed over. This is to ensure that error due to the measurement is assessed as well as changes which occur in addition to any changes due to the intervention (Hopkins, 2000).

Quantifying the difference between two measurements can be completed by using a number of statistical approaches. There is currently no consensus as to which approach is optimal (Atkinson & Nevill, 1998; Hopkins, 2000; Ludbrook, 2010a), as each offer different benefits and limitations. A visual inspection of a scatter plot of the data initially provides information that the relationship is linear, and therefore linear statistical assessment is suitable. The second step is to test the data for normality and scedasticity, where these are assumptions of the test. Testing for normality is a common test performed on data within sports medicine, completed for example through qualitative inspection of the distribution curve, and formal assessment using a Kolmogorov–Smirnov test. Scedasticity is a more rarely discussed assumption and one which is of particular importance in consistency assessments. It may often be necessary to perform a logarithmic transformation on the data to satisfy the assumptions of normality and homoscedasticity (Hopkins, 2000).

Scedasticity refers to whether the distribution of the data around the regression line is additive (homoscedastic), or multiplicative (heteroscedastic). Additive error is where points are evenly distributed around the regression line throughout the entire range of the data. Atkinson and Nevill (1998) argued that error is rarely additive within sports medicine, and is more likely to be multiplicative.

Multiplicative error occurs when the spread is not constant, observed as an increasing or decreasing spread as the measured value increases.

Confirmation of multiplicative error can be completed either through qualitative assessment of a scatter plot of the two measurements (Mullineaux et al., 1999), or formal assessment by performing a correlation on the absolute difference against the average score (Neville & Atkinson, 1997). If heteroscedasticity is determined then data should be explored and transformation maybe warranted. Neville and Atkinson (1997) employed a formal approach to identifying heteroscedasticity and found even small amounts of multiplicative error could be reduced using a logarithmic transformation on the data. They therefore advised that even if the correlation between absolute difference in the measures and the mean was non-significant but positive, a transformation should be completed. Despite logarithmic transformations reducing the risk of violating the assumptions of the chosen statistical test, they do result in the findings of those tests referring to the transformed data. This has implications on the simplicity of the results, and their ease of understanding. Therefore despite potential benefits of reducing multiplicative error, unnecessary processing of the data should be discouraged. Due to the limitations discussed, when transformations are ran, the justification for this decision should be documented. As qualitative assessment is based on subjective opinion, different researchers may come to different conclusions on the appropriate course of action. Therefore, a justified set of criteria for formal assessment of heteroscedasticity may offer the most rigorous methodology.

Regardless of the processes applied to the data the aims of assessment remain the same. This is to quantify the difference between the two measurements, which can be split into the presence of bias, and the level of random error. Both these factors contribute to the total error and must be taken into account. A number of articles have addressed the issue of the suitability of certain tests when comparing two measurements (Atkinson & Nevill, 1998; Hopkins, 2000; Mullineaux, Barnes, & Batterham, 1999). Although each author provides an argument for certain tests, all acknowledge that no method is perfect. Therefore it is essential to fully understand the limitations associated with each test and how each handles certain characteristics such as forms of bias, levels of error, and the range of the data.

4.9.1 Systematic and Proportional Bias

Two forms of bias can be present when comparing paired data sets; systematic and proportional. Systematic or fixed bias refers to consistent differences between each pair of data points regardless of the magnitude of the original measurement (Ludbrook, 2010; Atkinson and Neville, 1989). When graphically represented, the gradient of the regression line between the two data points would be near one, but would be shifted away from the line of identity (Figure 13a). In contrast, proportional bias is characterised by a difference which is relative to the magnitude of the measurement. As shown in Figure 13b, a regression analysis ran on data with this form of bias will produce a line with a gradient which differs notably from one. Greater bias will be shown by an increasing difference between the gradient of the line of identify and regression. Data will rarely contain only one form of bias, and the detection of both provides a specific challenge for statistical assessment.

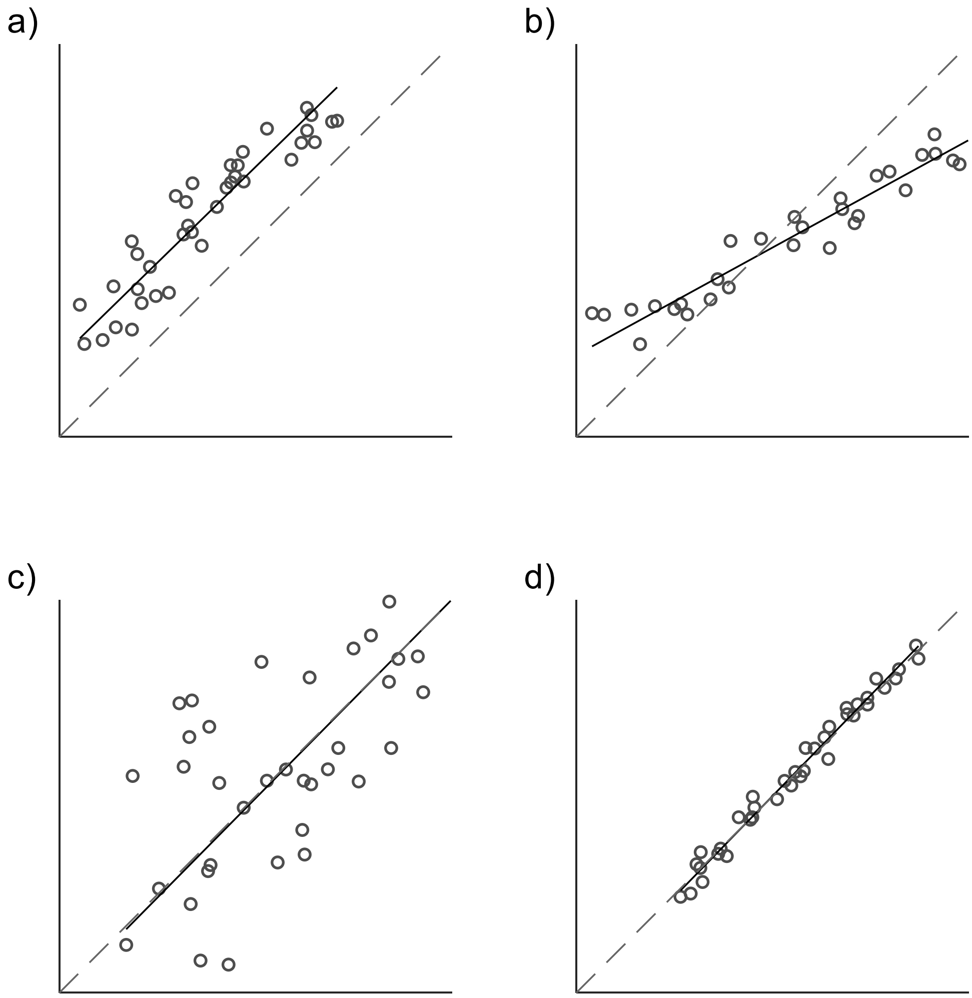

Figure 13. Plots showing line of identity (dashed line), example data, and regression line with; a) systematic and b) proportional bias, and c) low and d) high random error.

4.9.2 Methods for Assessing Levels of Bias

A number of methods are available to provide a measure of the systematic and proportional bias. These include; correlations, regression, and absolute reliability. The strengths and weaknesses of each approach are discussed in turn. Other methods that have been used in the literature (Atkinson & Nevill, 1998), include traditional hypothesis testing using tests such as *t*-tests. Such methods are not discussed as they do not quantify the difference between two measures, rather define whether the difference between two distributions is due to chance to an accepted level of probability.

4.9.2.1 Correlations

The two most commonly seen methods of correlations used in agreements are Pearson's correlations and intra-class correlations (ICCs). Despite its widespread use, Atkinson and Nevill (1998), describe how Pearson's *r* is unsuitable for assessment of agreement. Pearson's correlation does not provide information on agreement, rather how well the data points fit along a straight line. This means the gradient of the line, such as that which would be caused by the presence of proportional bias would not alter the correlation coefficient.

The ICC provides a value of the relationship between the overall variance of the sample and the average difference between the two measurements. There are six variations of ICC, and the output varies between different methods (Müller & Büttner, 1994). An ICC of one is viewed as perfect reliability, however in certain instance the value can be higher than this due to its calculation. These limitations of the ICC mean that even when the specific method is reported, their use is associated with potential error and spurious results.

4.9.2.2 Regressions

Unlike correlations, specific types of regression analysis provide measures of proportional and systematic bias, as well as an estimate of random error. This is done by examining the equation of the regression line and the R value. As regression provides a measure of all these factors it has been said this is the only philosophically correct measure of agreement (Mullineaux *et al.*, 1999). Ludbrook (2010a) provides a comprehensive explanation of the correct method of regression when looking at agreement between two measures. Ordinary least squares regression, which fits a line by minimising error in one axis, has often been used. This method uses an incorrect assumption that error is only present in one measurement, meaning both the estimates of bias and error would be incorrect. Instead, least products regression fits a line by minimising the total error contributed by both measurements.

Despite being considered a true measure of agreement, regression does also contain limitations. Similarly to correlations, regressions analysis is sensitive to the range of the data, where a smaller range will often result in a poorer outcome. A second limitation is the relationship between proportional and systematic bias. Quantification of these types of bias are provided as the equation of the calculated line. The gradient of the line provides a good measure of the proportional bias, however the intercept only provides a good value of the systematic bias when little or no proportional bias is present. This is due to the effect the gradient has on the line. This limitation is specifically prominent when the value of the measures differs greatly from zero, increasing the effect the gradient will have on the intersect. This means that other tests may need to be adopted to establish the level of systematic bias within the system.

4.9.2.3 Measures of Absolute Consistency

A final group of methods which can be used to assess the level of agreement is measures of absolute consistency. These measures, rather than looking at the agreement between two measures look to quantify the amount of difference, to provide a useable measure of how much the two measures differ. These tests are of particular use when looking to monitor changes over a period of time or provide information on the amount of error which can occur. Examples of these measures are standard error of measurement, limits of agreement (Altman & Bland, 1983), and coefficient of variation (CV).

The standard error of the measurement provides a value of the variance between the measures and is therefore quantifies the random error. The statistic is in the same scale as the original value meaning it is suitable in the monitoring of changes in a certain population. The statistic can be calculated using the value of the ICC, mean square error term of a repeated measures ANOVA, or the SD of the errors (Hopkins, 2000). Atkinson and Nevill (1998) highlight that these three methods can produce different results, and that each is related to the limitations associated with the statistical test involved. It should also be noted that when applying this statistic for the purpose of determining whether changes occur which are greater than the measured error, the statistic only spans approximately 68% of the true variance between two measures (Atkinson & Nevill, 1998). Traditional approaches to determining differences have employed 95% confidence limits, meaning this statistic may underestimate the difference between two samples.

CV provides a relative measure of consistency by dividing the SD between two measures by the mean. CV is often presented as a percentage meaning it is not in the same scale as the original measure. CV has limited use when looking to quantify the consistency between two measures with the aim of comparing the magnitude of the difference, to changes due to an intervention. However CV is suitable for other analytical goals such as comparing consistency between variables with different measurement scales (Hopkins, 2000). One limitation of the use of CV as a relative measure of bias is the predisposition to tend towards larger values as the mean of the measure decreases, meaning the value of CV should be interpreted with consideration of the magnitude of the original value.

The quantification of random error is one aspect of quantifying the difference between measures however, as discussed in section 4.9.1, values of proportional and systematic bias are also needed. Regression analysis between two measures provides information on the presence of proportional bias, however it has limitations in the measurement of systematic bias and does not provide a measure of random error on the same scale as the data. One method that can provide both a measure of systematic bias and random error is limits of agreement (Altman &

Bland, 1983; Bland & Altman, 1986). This method involves calculating the systematic bias as the mean of the differences, and random error as the SD multiplied by 1.96. This method provides a measure of two types of error on the same scale as the original data meaning it is suitable for the application of monitoring changes due to interventions. As the limits of agreement approach uses the mean and SD of the difference as estimates of systematic and random bias, the normality and homoscedasticity of the differences are assumed. Violation of these assumptions means the identified limits may not truly represent the bias within the data. Another factor which may alter the confidence in the calculated limits is the presence of proportional bias. For example, if two measures have the presence of proportional bias, shown by a regression line gradient not equal to one, but has a high R^2 value it would suggest the measure has low random bias. However limits of agreement would over estimate this random bias due to the range of the errors resulting from the presence of proportional bias. This limitation highlights the need to conduct a number of statistical tests to fully explore the presence of different types of bias with consideration for the violation of certain statistical assumptions.

All of the presented methods of assessing consistency contain certain advantages and disadvantages, and these should be considered when choosing the correct methodological approach. Despite this, there are certain guidelines that should be followed. Firstly, as assessing levels of consistency is not related to statistical significance, and therefore the use of hypothesis testing is unsuitable. The chosen methods should provide measures systematic, proportional, and random bias. Where measures of consistency are intended to be used to inform the interpretation of future data, the measures of absolute and random bias should be in the same measurement scale as the analysed variable. The limits of agreement method would therefore provide a suitable approach to assessing the consistency of these two types of bias. As discussed the limits of agreement approach does not allow the assessment of proportional bias, and therefore it is suggested that least products regression is conducted and the gradient of the regression line used to explore the presence of proportional bias.

4.10 Summary

This Chapter reviewed the current literature around the use of linear and non-linear measures of balance in relation to the monitoring of ACL injuries and recovery. Injury to the ACL results in the loss of proprioceptive feedback and therefore may alter the somatosensory inputs during balance. Linear measures have identified that ACL deficient limbs have poorer balance performance, but that reconstruction is able to improve the proprioceptive potential limb. Linear measures therefore have worth in monitoring changes due to ACL injury and treatment, however may be limited in their ability to assess changes in the non-linear dynamics of the system. The loss of complexity theory hypothesises that with ACL injury the complexity of the CoP will reduce due to changes in the systems contributing to balance. There are currently no assessments of the loss of complexity due to ACL injury which are without limitations, and may provide useful information into the potential of treatment to restore normal dynamics. MSE offers the most suitable method for assessments of complexity during balance due to its ability to assess entropy at different timescales which may be linked to biological processes.

The aim of this thesis is to explore the potential worth of biomechanical measures in the monitoring of ACL injuries and recovery. One aspect of this aim is to establish the consistency of these measures to aid in the interpretation of data in a pathological population. A number of statistical methods are available for the assessment of consistency between two measures, however estimates of the systematic, proportional and random bias should be calculated, and the usability of the output statistic should be considered.

5. General Methods

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

Chapter	Title	Addressed Aims
1	Introduction	
2	Monitoring Functional Recovery from ACL Injuries	
3	Lower Limb Biomechanics Before and After ACL Reconstruction: A Systematic Review	**AIM I**: Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery
4	Assessment of Balance as a Measure of ACL Injury Recovery: A Review of Linear and Non-Linear Approaches	
5	General Methods	
6	Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population	**AIM II**: Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe
7	The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity	**AIM III**: Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons **AIM IV**: Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.
8	Thesis Summary	
9	Conclusion	

Figure 1. Schematic of thesis structure and research aims

5.1 Preface

Chapter 2 highlighted the limitations with current tools used to monitor recovery from ACL reconstruction, and how biomechanical assessments of movement tasks may provide information into the function of the injured limb. Due to the restraints of clinical practice, certain biomechanical assessments are not viable due to required resources and expertise. Considering the limitations of current assessment tools, the possible worth of biomechanical measures, and constraints of clinical practice, data were collected on a number of movement tasks which may assess the functional state of an ACL injured participant and that would be suitable for simplification and implementation into health care systems. This Chapter describes the methodology used to collect the data, which are used in Chapters 6 and 7 to address **Aims II**, **III**, and **IV** of this thesis (Figure 1).

Chapter 3 identified that analysis of balance trials before and after ACL reconstructive surgery have consistently shown treatment was successful in improving balance ability. Chapter 4 reviewed the current evidence surrounding the assessment of balance tasks as a mode for assessing the function of the limb and how ACL injury and treatment may affect this. Linear and non-linear variables of the CoP during balance tasks formed the focus of the subsequent chapters of this thesis. The data analysis methods which are universal to future chapters are described here.

5.2 Ethical Approval

Ethical approval for this research was granted by National Research Ethics Service Committee East Midlands (Derby; 14/EM/1130), and by the Health Research Authority. This approval allowed the implementation of the research protocol into any NHS trust, where the local research and design departments confirmed their willingness to participate. United Lincolnshire Hospitals NHS Trust and Portsmouth Hospitals NHS Trust both confirmed their willingness to participate. The University of Lincoln and University of Portsmouth were included as data collection sites as part of the protocol, and the approvals met the requirements of each local ethics committee, therefore no further ethical approvals were required.

5.3 Recruitment

ACL-deficient participants were identified and recruited through one orthopaedic surgeon's caseloads. During weekly orthopaedic clinic hours patients who had suspected ACL rupture were provided with participant information by a principal investigator. Patients subsequently underwent magnetic resonance imaging (MRI) to further diagnose the injury and a decision on course of treatment was made by the clinician. Once a decision to treat with surgical intervention was made, the researcher contacted the patient to discuss their willingness to participate in the research. Uninjured participants were recruited from the local population of the research site through recruitment media and word of mouth. Inclusion and exclusion criteria were the same for injured and uninjured participants, except for ACL rupture requirement (Table 14). ACL deficiency was diagnosed by an orthopaedic surgeon using the Lachman and pivot shift tests, and MRI. MRI is considered the gold standard non-invasive diagnostic tool for ACL rupture (Leblanc *et al.*, 2015). Lachman and pivot shift tests have been shown to have a sensitivity of 96% (95CI: 0.90-1.00) and 86% (95CI: 0.68-0.99) compared to MRI

(Leblanc *et al.*, 2015). Confirmation of ACL rupture was then completed during arthroscopic surgery. No participants were incorrectly diagnosed. Limb dominance was defined as the limb the participants would feel most comfortable kicking a ball with prior to injury.

Table 14. Inclusion and exclusion criteria for participants

Inclusion Criteria	**Exclusion Criteria**
18 – 45 years old	Combined posterior and anterior cruciate ligament rupture
Unilateral anterior cruciate ligament rupture*	Multi-ligament instability (including medial or lateral collateral ligament injury)
	Other lower limb surgery in the past 3 months
	Current significant acute injury affecting other lower-extremity joints
	Neurological or musculo-skeletal pathology effecting lower limb biomechanics
	Previous anterior cruciate ligament injury

* Only applicable for anterior cruciate ligament deficient participants and diagnosed by an orthopaedic surgeon

5.4 Participants

ACL deficient (n=10) and uninjured participants (n=45) were recruited for this research**.** Two ACL deficient participants were unable to complete the full data collection protocol due to acute pain experienced during unilateral weight bearing movements and were excluded from analysis resulting in eight ACL injured participants being included in this research. All ACL injured participants were recruited through the Lincoln research site. Uninjured participants were recruited through Lincoln (n=32) and Portsmouth (n=13) research sites. Participant information for all included participants is presented in Table 15.

Table 15. Participant information. Data presented as mean ± SD

	ACL Deficient	Uninjured
N	8 (Male: 4; Female: 4)	45 (Male: 24; Female: 21)
Age (years)	25 ± 10	27 ± 5
Height (m)	1.74 ± 0.10	1.75 ± 0.09
Mass (kg)	79 ± 17	75 ± 14
Time since injury (weeks)	34 ± 29	Not applicable
Limb Dominance	Right: 8; Left: 0	Right: 38, Left: 7
Injured Limb	Right: 4; Left: 4	Not applicable
% of injured dominant limb	50%	Not applicable

5.5 Timeline

Data collection timings were intended to be within four weeks prior to surgery, and 18 and 32 weeks after surgery for ACL deficient participants. Uninjured participant data collections were a baseline visit, and a second at approximately 18 weeks to match the ACL participants. Based on facility and participant availability, data collections were completed one week prior to surgery (mean ± SD; 1.0 ± 0.6 weeks), and at 19 (19.4 ± 2.7) and 33 (32.8 ± 2.9) weeks post-surgery for ACL deficient participants. Uninjured participants completed a baseline testing session, and 27 completed a second testing session at 18 (17.7 ± 0.9) weeks.

5.6 Surgical Intervention and Physiotherapy

Arthroscopic ACL reconstructions were conducted by the same consultant orthopaedic surgeon. Tibial and femoral tunnels were drilled in the footprint of the ruptured ligament. Where meniscal and/or cartilage damage was present, this was repaired. A four-strand hamstring autograft was prepared and tensioned. Graft fixation was completed with the use of an Endobutton and RCI screw (Smith & Nephew, UK). All participants were provided with a standardised ACL rehabilitation program, and received four to six supervised sessions with a physiotherapist (Appendix B).

5.7 Data Collection

The data collection protocol was developed with consideration for a number of research questions based across the multiple sites involved in this research project. The full data collection protocol is presented here, and all participants completed every section. Due to the findings of Chapter 3 the research questions addressed in the following chapters of this thesis relate to the balance trials only, and therefore only the data analysis methods of these trials are presented. The multi-component nature of the data collection protocol led to methodological decisions to be made. One such decision was that participants completed all data collection tasks whilst wearing shorts and trainers as movements such as the isometric strength assessments (section 5.7.4.1) required footwear to be worn.

Data collections were conducted at Pilgrim Hospital, the University of Lincoln, and the University of Portsmouth. At all research locations, no specialised biomechanics equipment was installed, and all equipment used during collections were portable. The data collection procedures were developed with consideration for the constraints of working within a clinical environment. Specifically being suitable to be completed in limited space, for example the Clinical Research Facility at Pilgrim Hospital had floor dimensions of 2.5 × 4.5 m. All data collections followed the same protocol and consisted of movement analysis and self-reported questionnaires (see section 5.7.4.4).

5.7.1 Custom Seating Rig

A custom built seating rig (Figure 14a) was used for all movement analysis during data collection. Each data collection site had one rig of the same specifications. The rig consisted of an aluminium frame, and a seat on a hydraulic jack to allow for adjustments in height. A force plate (Kistler, Switzerland; 9281CA) was fixed to the aluminium frame to allow collection of kinetic data. A removable foot restraint was attached to the force plate to resist foot movement during isometric tasks (Figure 14b). The foot restraint consisted of two sections that could be adjusted to fit different shoe sizes.

a) b)

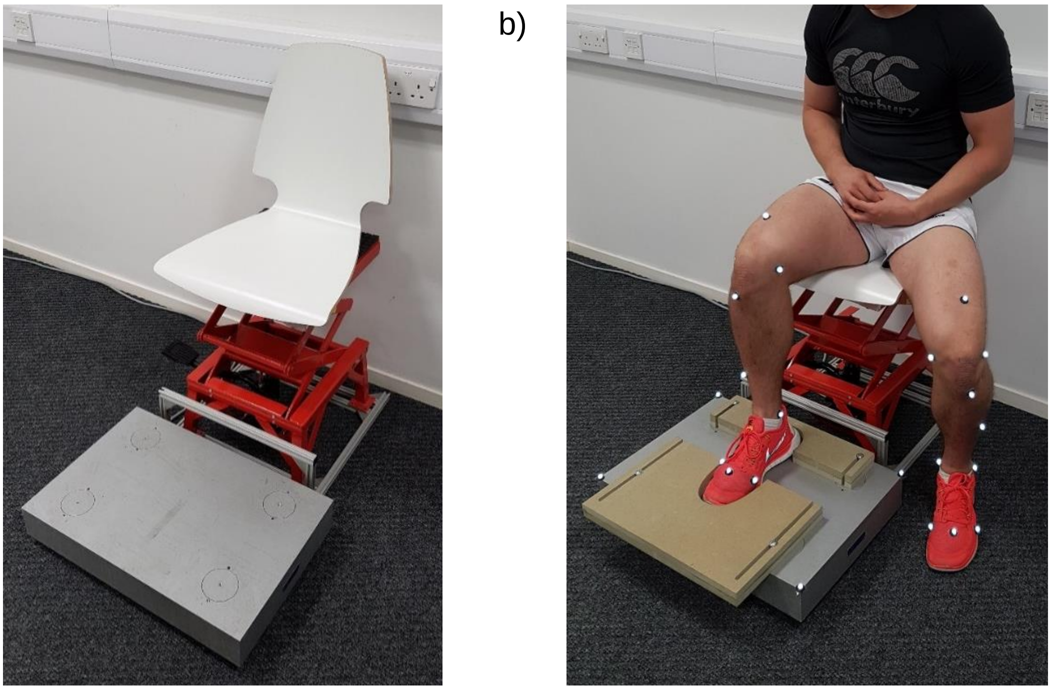

Figure 14. A custom built testing rig (a) with adjustable seat, force plate, and detachable foot restraint (b)

5.7.2 Data Capture

Kinematic and kinetic data were collected using a three-dimensional motion capture system and force plate (section 5.7.1; 3000 Hz). Motion capture setup varied between sites (Table 16). Each system was calibrated using an L-frame placed on the force plate, and maximum marker residual error was set at 0.5 mm. If residuals were seen to be above this level, recalibration was completed.

Table 16. Motion capture system setup details for each data collection site.

Site	**Motion Capture System**	**Number of Cameras**	**Sampling Frequency (Hz)**
University of Lincoln	Motion Analysis Corporation	Six	150
Pilgrim Hospital	Motion Analysis Corporation	Four	150
University of Portsmouth	Qualisys	Eight	150

5.7.3 Marker Locations

Twenty 9 mm diameter reflective markers were placed on to the skin and shoes, superficial to specific anatomical landmarks, to track the movements of the lower limb (Figure 15). The landmarks on each leg were: the heads of the first and fifth metatarsal, third metatarsophalangeal joint, medial and lateral calcaneus, shank, most anterior point of the tibial tuberosity, medial and lateral epicondyle of the femur, and anterior thigh. An additional four markers were placed on the corners of the force plate. The chosen marker set was dictated by the limited field of view that could be captured whilst collecting data at Pilgrim Hospital. Marker data were only used to define the foot segment in subsequent analyses however, data were also able to define the shank segment and orientation of the thigh segment.

Figure 15. Reflective marker placements

5.7.4 Protocol

Movement analysis was split into three sections: isometric strength assessments, movement and balance tasks, and a force matching task. The order of these sections remained constant, however the trial order within each was randomised using a random number generator.

5.7.4.1 Isometric Strength Assessments

The testing rig was adjusted so that when the participant was in a seated position their knee was in 90±3° of flexion, confirmed as the angle in the sagittal plane between the 2D vectors created by the virtual ankle and knee joint centres and thigh marker, where the angle during upright stance was offset to represent 0° of flexion. The participant’s foot was then placed within the foot restraint attached to the force plate (Figure 14b). Participants were instructed to push their foot against the wooden jig as hard as possible for 10 s, starting on a verbal signal that was given 1 s into the recording of the trial. Hip adduction, and knee internal rotation, extension and flexion trials were completed twice for each leg in a randomised order. Extension and flexion trials were completed to gain a measure of quadriceps and hamstring strength, respectively. Hip adduction and knee internal rotation were included to evaluate the participant’s ability to produce and withstand a knee valgus torque.

5.7.4.2 Movement and Balance Tasks

Sit-to-stands, unilateral and bilateral squats, and unilateral and bilateral balance tasks were performed in a randomised order. To allow sufficient rest (≥10 s) and to allow the force plate to be reset participants were asked to step off the force plate between each trial. Squat and sit-to-stand trials consisted of three repetitions during a single trial. During sit-to-stand trials participants were instructed to rise from the chair and return to a seated position in a controlled manner, and to remain seated for 1 s before beginning the next repetition. Squats were performed to a self-selected depth, and balance, defined as not needing to use the non-weight bearing limb to stabilise, had to be maintained throughout the repetition to be valid.

Balance tasks were completed with eyes closed and unilateral on both limbs, and bilateral balance conditions were completed twice. During unilateral balance participants were instructed to align their weight baring limb with the edge of the force plate, to approximately match the force plate axis with their ML and AP axis, within the boundaries of the force sensors. Participants were instructed to establish balance on one or two legs, for unilateral and bilateral balance respectively, with their eyes open. On a cue they were asked to close their eyes and the trial was begun 2 s after this. This was to ensure the dynamics related to the change in task demands were not included in the trial. During balance conditions, trial length was set to 20 s, and a minimum of 10 s without falling and no foot movement was required for a trial to be deemed successful.

5.7.4.3 Force matching task

Previous deficiencies in force matching ability has been identified in ACL reconstructed knees (Perraton *et al.*, 2017), however this has been evaluated using single joint tasks using an isokinetic dynamometer. To assess whether these deficiencies are present in a task involving inputs from multiple joints, a novel force matching task was developed. Whilst seated, the participant was required to produce a downward vertical force of 50 N using a single limb over a 40 s time period. Feedback was provided using the BioFeedTrak function in the Cortex software (Motion Analysis Corporation) or live force reading using Qualysis Track Manager at Lincoln and Portsmouth research sites, respectively. A custom written Visual Basic script resulted in 20 s of feedback on vertical force, provided as an integer in numerical form, and a graph ranging from 45 – 55 N (Figure 16). After this initial 20 s, feedback was stopped and the participant was required to maintain the same downward force for a further 20 s.

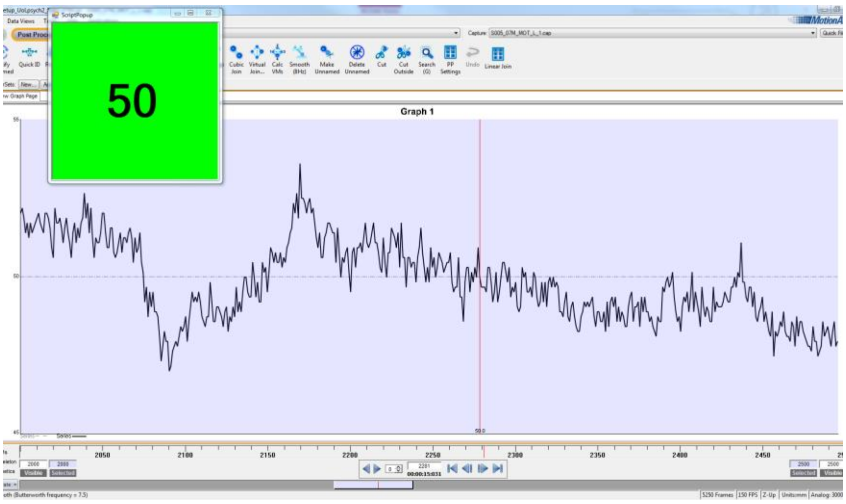

Figure 16. A screenshot of visual feedback provided during a force matching task.

5.7.4.4 Questionnaires

All participants completed Tegner Activity Level Scale, International Knee Documentation Committee subjective form, and Lysholm Knee Score questionnaires which are valid and reliable assessments of patient reported outcomes from arthroscopic knee surgery (Briggs *et al.*, 2009; Irrgang *et al.*, 2001). The Tegner Activity Level Scale (Tegner & Lysholm, 1985) is a questionnaire which asks patients to recall their activity level at prior to, and during different stages of their treatment. The Lysholm Knee Score (Lysholm & Gillquist,

1982) and International Knee Documentation Committee subjective form (Irrgang *et al.*, 2001), contain questions on severity of symptoms.

5.8 Data Analysis

Kinematic and kinetic data from the balance trials (section 5.7.4.2) were analysed using custom written MATLAB codes. The methods used to calculate linear and non-linear measures of the CoP are described here.

5.8.1 Extracting Anteroposterior and Mediolateral Data

During the data collection, although instruction on foot placement was provided the repeated trials may have resulted in differences between trials and participants, therefore the coordinate system of the force plate was unsuitable to determine ML and AP axes. To overcome this, foot kinematics were used to establish the sagittal plane (Figure 17), and subsequently used to calculate ML and AP CoP data relevant to foot placement. During unilateral balance, the vector from the mean of the 1st and 5th metatarsal head markers to the mean of the medial and lateral ankle markers defined the sagittal plane, and during bilateral balance, the mean of the left and right 5th metatarsal head and lateral ankle markers were used.

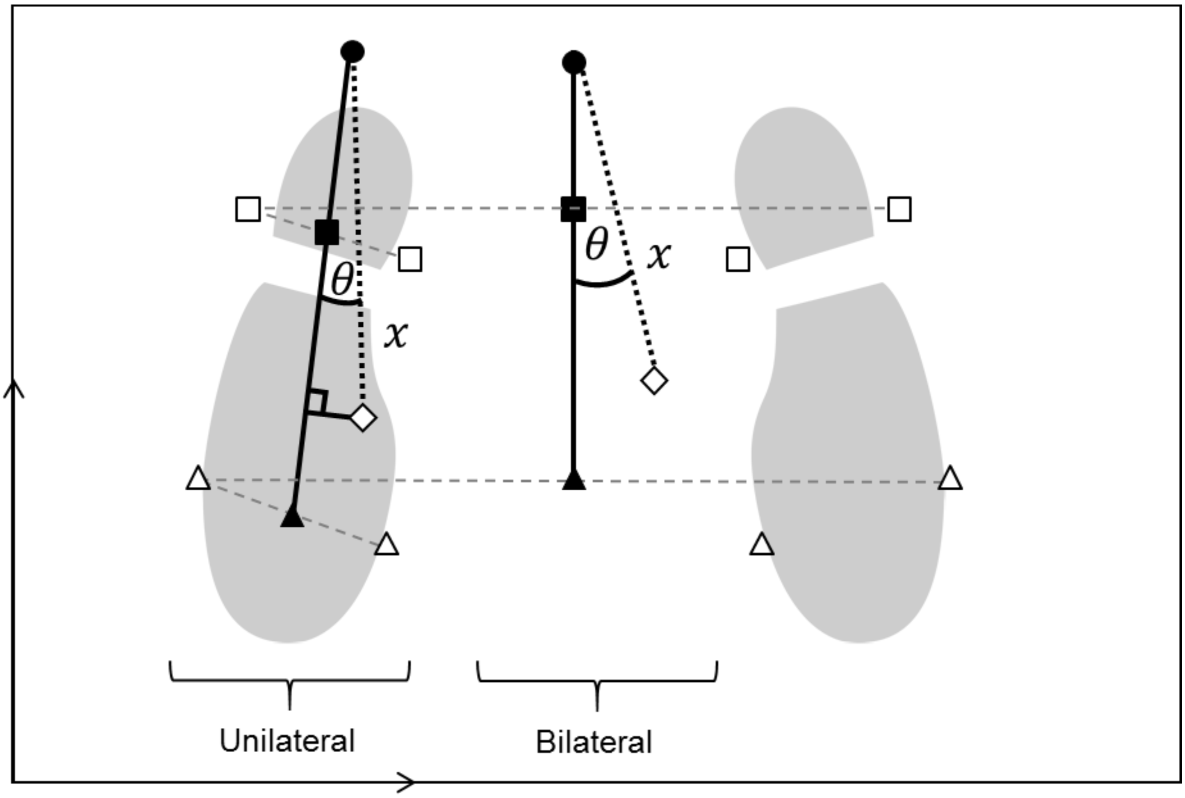

Figure 17. Method of calculating medio-lateral (*ML=xsinθ*) and antero-posterior (*AP=xcosθ*) centre of pressure data based on medial and lateral toe (triangle) and ankle (square) markers, and centre of pressure (diamond) data. ● is a coordinate 50% of the foot length from the mid-ankle coordinate on the sagittal plane. Open and closed shapes represent raw and calculated data points, respectively.

Trigonometry was used to calculate ML and AP data in relation to the sagittal axis (Figure 17). Changes in the sign of inputs to trigonometric calculations may result in incorrect outputs, therefore a reference coordinate was defined at a point along the sagittal axis which was a distance of 50% the length of the foot from the mean of the ankle markers. This reference coordinate was therefore outside the base of support, and would ensure vectors remained positive. As kinematic data includes error related to motion capture equipment, its inclusion in the calculation of CoP data would result in additional noise included in the ML and AP signals. To remove this, the sagittal axis and reference coordinate were calculated from the first frame, and were assumed to remain constant throughout the trial. Another vector, referred to as the CoP vector, was from the CoP to the reference coordinate. ML and AP data were then calculated as the length of the CoP vector multiplied by the sine or cosine of the angle between the CoP vector and sagittal plane (Figure 17).

5.8.2 Measures of Balance Performance

To provide a measure of balance performance, linear measures of variance, range, and velocity of CoP data were calculated. To provide measures of the complexity of the data, MSE analyses were completed. Different data processing approaches were used for each analysis and are described separately. CoP data were down sampled to 200 Hz based on the requirements of the chosen analysis, including assessing complexity at biologically relevant timescales (section 4.7.3.3) and the effect oversampling can have on linear measures of balance (Ruhe, Fejer, & Walker, 2010).

Due to the effect of non-stationarities on linear and non-linear measures of balance (see section 4.7.2.4), an additional data extraction step to locate the data with lowest variance over the two trials for each balance condition was conducted. As a result data representing the best balance performance, defined as the lowest CoP sway, for each condition was used for analysis. The measure of sway variance was the area of the 95% CI ellipse fitted to the ML and AP data using the principal component analysis method as described by Duarte and Zatsiorsky (2002); Table 17.

Due to difficulties performing unilateral balance and a technical artefact resulting in a loss of frames (≤50 frames) at the end bilateral trials, extracted trial length (t_{ell}) was set at 10.0 s and 19.5 s for unilateral and bilateral balance, respectively. To identify the data representing the best balance, the area of 95% CI ellipses were calculated for a moving window of length t_{ell}, resulting in $N - (t_{ell} \times 200)$ ellipses for each trial, where N is the trial length. The data resulting in the smallest ellipse area over the two trials was used for analysis.

5.8.2.1 Linear Measures of Balance Performance

Table 17. Equations used to calculate linear measure of balance.

Variable	Equation
CoP SD (mm)	Mediolateral $SD_{ML} = \sqrt{\frac{\sum_{i=1}^{N} \lvert ML_i - \overline{ML} \rvert^2}{N-1}}$ Anteroposterior $SD_{AP} = \sqrt{\frac{\sum_{i=1}^{N} \lvert AP_i - \overline{AP} \rvert^2}{N-1}}$
CoP Mean Velocity (mm/s)	Mediolateral $Vel_{ML} = \frac{\sum_{i=1}^{N-1} \lvert ML_{i+1} - ML_i \rvert}{t}$ Anteroposterior $Vel_{AP} = \frac{\sum_{i=1}^{N-1} \lvert AP_{i+1} - AP_i \rvert}{t}$ Resultant $Vel_{Res} = \frac{\sum_{i=1}^{N-1} \sqrt{(ML_{i+1} - ML_i)^2 + (AP_{i+1} - AP_i)^2}}{t}$
CoP Path Length (cm)	$Dist = \sum_{i=1}^{N-1} \sqrt{(ML_{i+1} - ML_i)^2 + (AP_{i+1} - AP_i)^2}$
95% CI Ellipse Area (cm^2)	*Covariance matrix* $\begin{bmatrix} A & C \\ B & D \end{bmatrix} = \begin{bmatrix} 1/(n-1)\sum_{i=1}^{n}(ML_i - \overline{ML})^2 & 1/(n-1)\sum_{i=1}^{n}(ML_i - \overline{ML})(AP_i - \overline{AP}) \\ 1/(n-1)\sum_{i=1}^{n}(ML_i - \overline{ML})(AP_i - \overline{AP}) & 1/(n-1)\sum_{i=1}^{n}(AP_i - AP)^2 \end{bmatrix}$ *Eigenvalues where $b = A + D$ and $d = AD - BC$* $\lambda_1 = (b - \sqrt{b^2 - 4d})/2 \quad \& \quad \lambda_2 = (b + \sqrt{b^2 - 4d})/2$ *Scaled ellipse axes* $[x_{ell}, y_{ell}] = 1.96 \times \sqrt{svd[\lambda_1, \lambda_2]}$ *Ellipse area* $Ell_{area} = \pi \times x_{ell} \times y_{ell}$

ML and AP are mediolateral and anteroposterior CoP data, N the number of data points, and i the current data point number

Extracted CoP data were further down sampled to 100 Hz and filtered using a low pass 2nd order zero-lag Butterworth filter with a cut off of 10 Hz, in line with a systematic review on CoP data processing methods which resulted in the most reliable measures of balance (Ruhe *et al.*, 2010). SD, mean velocity, path length and 95% confidence ellipse area were calculated as described in Table 17.

5.8.2.2 MSE

To provide complexity measures at meaningful frequencies and minimise the risk of aliasing, kinetic data were down sampled to 200 Hz (Gow *et al.*, 2015). In line with previous research and the limitations of the MSE analysis on short data sets, entropy was calculated at frequencies between 22.2 Hz, and 6.7 Hz for unilateral and 3.3 Hz for bilateral balance. Entropy at lower frequencies were unable to be analysed due to a required minimum of 200 data points for use in the SampEn algorithm. As the equation used to determine the frequency being assessed includes the sampling frequency, down sampling the data did not limit the frequency that could be analysed.

To exclude data of a frequency that would not be included in the MSE analysis, EMD (Huang *et al.*, 1998) was used. A detailed description of the EMD process is provided in detail in section 4.7.2.4. Briefly, EMD results in a number of IMFs which contain characteristics and have a predominant frequency of $sf/2^{n+1}$, where sf is the sampling frequency (200 Hz), and n is the IMF number (Table 18). EMD was completed on AP and ML data, and IMFs 2-4 and 2-5 were summed for unilateral and bilateral balance, respectively. This resulted in signals which only contained data of a frequency that could be assessed using the MSE algorithm (Table 18).

Table 18. Predominant frequency of intrinsic mode functions created from a signal sampled at 200 Hz.

Intrinsic Mode Function	Predominant Frequency (Hz)
1	50.0
2	25.0
3	12.5
4	6.3
5	3.1
6	1.6

MSE analysis (Costa *et al.*, 2002) was then ran on the data to obtain a measure of complexity. A detailed description of the MSE algorithm is provided in section 4.7. Vector length (m) was set as 2, and tolerance level as 0.2×SD using the windowed-MSE method (Gow *et al.*, 2015), as described in section 4.7.2.3. Timescales are limited by the number of data points, with a minimum of 200 required at the largest timescale to ensure complexity values are reliable (Yentes *et al.*, 2013). Timescale factors 1 and 2 representing complexity at 66.7 and 33.3 Hz, respectively (Equation 11), were excluded from all balance conditions as they assessed timescales which were unlikely to be related to the dynamics of balance (see section 4.7.3.3). Unilateral balance trials were 2000 data points meaning the maximum timescale factor was 10. This resulted in complexity values for 22.2, 16.7, 13.3, 11.1, 9.5, 8.3, 7.4, and 6.7 Hz. Bilateral balance trials were 4000 data points meaning the maximum timescale factor was 20. This resulted in complexity values at further timescales of 6.1, 5.6, 5.1, 4.8, 4.4, 4.2, 3.9, 3.7, 3.5, and 3.3 Hz. In addition to complexity values at each timescale, a CompInd was calculated as the area under the complexity-timescale curve using the trapezoidal method (Busa & van Emmerik, 2016).

5.9 Summary

This chapter described the methods for the collection of biomechanical data on a number of movement tasks which may be affected by ACL injury and subsequent treatment. Balance tasks were chosen for further analysis due to the effect surgery has on linear variables of the CoP (Chapter 3), and the potential of non-linear measures which have yet to be fully explored within the context of ACL injury and treatment (Chapter 4). Variables describing unilateral and bilateral balance were calculated for ACL injured participants before and after (approximately 19 and 33 weeks) surgery, and uninjured participants (0 and approximately 18 weeks). Calculated variables were:

Linear Measures

- ML and AP CoP SD
- ML, AP, and resultant CoP mean velocity
- Resultant CoP path length
- Resultant CoP 95% CI ellipse area

Non-Linear Measures

- ML and AP CoP MSE at timescales
    - unilateral; 22.2, 16.7, 13.3, 11.1, 9.5, 8.3, 7.4 and 6.7 Hz, and
    - bilateral; 22.2, 16.7, 13.3, 11.1, 9.5, 8.3, 7.4, 6.7, 6.1, 5.6, 5.1, 4.8, 4.4, 4.2, 3.9, 3.7, 3.5 and 3.3 Hz
- CompInd

6. Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

Chapter	**Title**	**Addressed Aims**
1	Introduction	
2	Monitoring Functional Recovery from ACL Injuries	
3	Lower Limb Biomechanics Before and After ACL Reconstruction: A Systematic Review	**AIM I**: Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery
4	Assessment of Balance as a Measure of ACL Injury Recovery: A Review of Linear and Non-Linear Approaches	
5	General Methods	
6	Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population	**AIM II**: Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe
7	The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity	**AIM III**: Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons **AIM IV**: Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.
8	Thesis Summary	
9	Conclusion	

Figure 1. Schematic of thesis structure and research aims

6.1 Preface

Chapter 3 addressed **Aim I** of this thesis, and identified that ACL reconstructive surgery resulted in improvements in balance ability assessed through analyses of the CoP during unilateral and bilateral stance. The findings advocated the exploration of balance assessments in the monitoring of recovery from ACL injury and reconstructive surgery. Chapter 4 provided an overview of the worth and limitations of traditional linear measures of the CoP, and presented the loss of complexity theory (Lipsitz & Goldberger, 1992) as a theoretical framework for assessing non-linear measures of balance in an ACL injured population.

Where the purpose of a measure is to monitor the changes which occur due to treatment, it is important to understand the consistency of this measure without intervention. The availability of usable magnitudes of consistency allow the interpretation of the size of changes which occur in a pathological population, such as ACL deficient participants, due to treatment. This Chapter addressed **Aim II** of this thesis by quantifying and comparing the consistency of measures of balance performance in an uninjured population over a common clinical observational timeframe relating to ACL injuries.

6.2 Introduction

During quiet standing, balance is maintained through the use of visual, somatosensory, and vestibular inputs (Shumway-Cook & Woollacott, 2007). Successful balance is considered as the absence of falling (Winter, 1995), however analyses of the characteristics of how this is achieved can offer insight into the function of the involved systems (Duarte & Zatsiorsky, 2002; Paillard & Noé, 2015). As certain pathologies, such as ACL injuries, can have effects on the systems involved in maintaining balance, one application of the analysis of stance is to establish whether treatments are able to restore the function to these systems (Lehmann *et al.*, 2017; Paterno *et al.*, 2010). It is important however, to understand the consistency, or magnitude of differences between two measurements in an untreated or unaffected population, to establish whether observed changes due to medical interventions are greater in size. The intended use of levels of difference, or bias, between two measures influences the methodological approach required (Atkinson & Nevill, 1998; Hopkins, 2000). These include the time period over which the two measures are taken and the choice of statistical tests used to quantify the differences.

Hopkins (2000) discussed that the time between trials can have a substantial effect on the magnitude of bias. The magnitude of the bias will be equal to the sum of the error within the measurement system plus changes in the performance of the task. The error within the measurement system may be unaffected by the time between trials, however the performance of the task may change. When using measures of difference to determine whether intervention results in changes in balance performance, both measurement error and natural changes in balance performance without intervention need to be considered. Therefore the time between trials should be matched to the time between clinical assessments in general practice. In the context of ACL injuries, regular monitoring is often not achievable due to limitations within clinical support. More commonly measurements are taken 12-24 weeks apart, as demonstrated by the timings in Tables (list SysRev tables) in Chapter 3. By matching the time between measurements to common clinical practice, estimates of the bias might provide practically usable comparative data to changes that occur in the observed patients.

When assessing the differences between two measurements, it is important to obtain measures of systematic, proportional and random bias (Altman & Bland, 1983; Atkinson & Nevill, 1998; Hopkins, 2000; Ludbrook, 2010b; Mullineaux *et al.*, 1999). A detailed description of each type of bias is provided in Section 4.6. Systematic bias refers to the difference between two measures having a general trend in a particular direction, proportional bias identifies whether there is a relationship between the magnitude of the baseline measure and the difference between the measures, and random bias is the spread of the differences between measures (Hopkins, 2000). Measures of systematic bias and random error can therefore be used to help assess whether changes in pathological populations are greater than estimated bias limits of a healthy population, and the presence of proportional bias highlights the need to consider the size of the baseline measure in addition to the difference. A number of statistical approaches are available to estimate bias, as described in Section 4.6.

6.2.1 Linear Measures of Balance and ACL Injury

Chapter 3 identified that ACL reconstructive surgery resulted in improvements in balance performance. Ogrodzka-Ciechanowicz *et al.* (2018) analysed a 30 s single leg stance task with eyes open before and 24 weeks after ACL reconstruction. Total (mean±SD; Pre- vs. Post-surgery: 1187±323 vs. 1024±319 mm), AP (805±313 vs. 731±351 mm), and ML (792±267 vs. 709±2589 mm) CoP path length decreased post-operatively compared to pre-operative values in the injured limb.

The findings were in agreement with data presented by Heijne and Werner (2007), and Ma *et al.* (2014) who also identified improvements in CoP path length 12, 20, and 24 weeks after reconstructive surgery. CoP path length is an example of a linear measure of balance performance which may offer insight into function after ACL reconstructive surgery. No other measures of balance performance were identified in Chapter 3, however a systematic review and meta-analysis by Lehmann *et al.* (2017) synthesised evidence of balance performance in ACL injured knees. Deficits in the linear measures of CoP variance and velocity in resultant, AP, and ML axes were identified in ACL injured knees, which may therefore be suitable linear variables to assess changes in balance due to ACL injury treatment.

Investigations into the changes in linear measures of balance performance in uninjured populations are available, however these relate to the test-retest reliability over short timeframes (0-1 week), meaning their relation to assessing the meaningfulness of changes due to intervention over longer time periods is limited (Ruhe *et al.*, 2010). Additionally, the statistical approaches used to assess the reliability have been varied, and often do not provide a useable measure of systematic or random bias. Ruhe *et al.* (2010) conducted a systematic review on the reliability of measures of bipedal stance and showed that excellent intra-class correlations (>0.75) were identified for path length, variance, and mean velocity of the CoP. The high ICCs suggest the measurement error related to linear measures of balance may be low. However, ICCs are less clinically useable as the magnitude of these changes are dimensionless, and not in the same unit of measurement that a practitioner can easily interpret and use.

6.2.2 Non-Linear Measures of Balance and ACL Injury

Linear measures of CoP have been widely used to assess balance ability (Duarte & Freitas, 2010; Lehmann *et al.*, 2017; Ruhe *et al.*, 2010), however as discussed in Chapter 4 non-linear measures may offer further insight into the function of the involved systems. These analyses are based on dynamical systems theory which models the human body as a number of interacting systems that can produce both linear and non-linear outputs (Section 4.4). One non-linear output is complexity which refers to the amount of information present in a signal and is often measured using variants of approximate and sample entropy (Busa & van Emmerik, 2016; Pincus, 1995; Richman & Moorman, 2000). In relation to pathology Lipsitz and Goldberger (1992) proposed the loss of complexity theory which postulates that aging and disease result in changes in the interaction and function of the systems involved in human control, causing a reduction in the complexity of movement outputs. There is limited research into the loss of complexity theory and balance in ACL injured populations, with no assessment using MSE, a method which provides a measure of complexity over different timescales (Costa *et al.*, 2002). Changes in CoP complexity have been identified in other pathological populations such as multiple sclerosis (Busa *et al.*, 2016), concussion (Purkayastha *et al.*, 2019), and idiopathic scoliosis (Gruber *et al.*, 2011) suggesting that balance complexity may be a useful tool in assessing balance function in ACL injured participants.

No data are available on the magnitude of the changes which occur in CoP entropy over any time period, however two articles have presented the reliability of fractal dimension, another non-linear measure of balance (Doyle *et al*., 2005; Santos, Delisle, Lariviere, Plamondon, & Imbeau, 2008). Fractal dimension is a measure of the self-similarity of a signal at different scales, with a higher dimension being suggested to be a more complex signal. Doyle *et al.* (2005) showed fractal dimension showed higher ICCs (0.62 - 0.90) compared to linear measures of balance (0.05 - 0.71) during a 10 s trial. Santos *et al.* (2008) reported comparable reliability between fractal dimension and linear measures of balance performance, however variables were calculated for a 60 s trial. These results show that bias between measures due to error of non-linear measures may be comparable or smaller compared to traditional linear measures.

6.2.3 Consideration of Limb Dominance

Where balance is completed on a single limb the performance may be affected by whether the limb is the participant's preferred or dominant side. Alonso, Brech, Bourquin, and Greve (2011) explored inter-limb differences in balance performance and found no significant differences between the dominant and non-dominant limbs. Despite no difference in balance performance, no exploration of the consistency of balance over clinically relevant timeframes have been conducted, and therefore the effect of limb dominance on consistency is unknown. Understanding whether the consistency of balance measures is affected by limb dominance would inform the use of limb specific or general guidelines for the interpretation of changes due to intervention.

6.2.4 Study Aim

This study addressed **Aim II** of this thesis, specifically to quantify and compare the consistency of linear and non-linear measures of balance in an uninjured population over a common clinical observational timeframe. To address this aim, three research questions, and where applicable hypotheses, were developed:

RQ$_{2.1}$: What is the level of systematic, proportional, and random bias in linear and non-linear measures of balance between baseline and 19 weeks measures?

RQ$_{2.2}$: Do linear and non-linear measures of balance performance have different consistency over 19 weeks?

RQ$_{2.3}$: Is the consistency of balance variables different for unilateral balance performed on the dominant compared to non-dominant limbs?

***H*$_{2.1}$: There will be no significant difference between changes in ML CoP CompInd in the dominant limb compared to the non-dominant limb

***H*$_{2.2}$: There will be no significant difference between changes in AP CoP CompInd in the dominant limb compared to the non-dominant limb

***H*$_{2.3}$: There will be no significant difference between changes in ML CoP SD in the dominant limb compared to the non-dominant limb

***H*$_{2.4}$: There will be no significant difference between changes in AP CoP SD in the dominant limb compared to the non-dominant limb

***H*$_{2.5}$: There will be no significant difference between changes in ML CoP velocity in the dominant limb compared to the non-dominant limb

***H*$_{2.6}$: There will be no significant difference between changes in AP CoP velocity in the dominant limb compared to the non-dominant limb

***H*$_{2.7}$: There will be no significant difference between changes in resultant CoP velocity in the dominant limb compared to the non-dominant limb

***H*$_{2.8}$: There will be no significant difference between changes in CoP path length in the dominant limb compared to the non-dominant limb

***H*$_{2.9}$: There will be no significant difference between changes in CoP 95% confidence ellipse area in the dominant limb compared to the non-dominant limb

6.3 Methods

6.3.1 Data Analysis

Balance data from uninjured participants (n=33), as described in Chapter 5, were analysed for this study. Levels of bias between baseline and approximately 19 weeks (mean±SD: 18.8±2.6 weeks) trials were quantified for linear and non-linear measures of balance performance. Linear measures were SD and mean velocity of ML and AP CoP data, and path length and 95% CI ellipse area (Duarte & Zatsiorsky, 2002) of resultant CoP. Non-linear measures were complexity at timescales between 22.2 Hz and 6.7 Hz for unilateral balance and 22.2 Hz and 3.5 Hz for bilateral balance, and CompInd from MSE analysis (Costa *et al.*, 2002). Analyses were completed using a custom written MATLAB (R2018a; MathWorks, Natick, MA) script, and SPSS (v.25; IBM, Armonk, NY).

6.3.2 Statistical Analysis

Statistical assumption of normality was confirmed prior to statistical analysis using a Shapiro-Wilk test with an alpha level of 0.05. The presence of homoscedasticity was explored through visual inspection of the relationship between absolute differences and mean score (Mullineaux *et al.*, 1999). No transformations were completed where heteroscedasticity was present due to the implications related to the usability of the statistic, and instead the findings were considered in relation to the violation of the assumption.

To address **RQ$_{2.1}$** systematic, random, and proportional bias between trials were assessed for linear and non-linear measures of balance performance. Systematic bias was calculated as the mean of the differences ($\bar{X}$),

$$\bar{X} = \frac{\sum_{i=1}^{n}(y_i - x_i)}{n} \tag{14}$$

and random bias as the 95% confidence intervals of the differences ($95\%CI_{diff}$),

$$95\%CI_{diff} = 1.96 \times \sqrt{\frac{\sum_{i=1}^{n}((y_i - x_i) - \bar{X})^2}{n-1}} \tag{15}$$

where x and y were baseline and 19 week measures, and n was sample size (Altman & Bland, 1983). Proportional bias was assessed as the slope and 95% CIs of the least products regression line (Ludbrook, 2010b). Least products regression was completed using SPSS as described by Mullineaux *et al.* (1999).

Confidence intervals were calculated from standard error estimated using a bootstrapping technique.

To provide a comparable measure of bias across variables of different scales (Atkinson & Nevill, 1998; Hopkins, 2000), and address **RQ2.2**, CV was calculated as ($\%CV$),

$$\%CV = \frac{\sum_{i=1}^{n} s_i \div \bar{m}_i}{n} \times 100 \tag{16}$$

where $\%CV$ is the CV as a percentage, and s_i and $\bar{m}_i$ are the SD and mean of the baseline and 19 week data for each participant.

To address **RQ2.3** paired samples *t*-tests between changes in measures of unilateral balance on the dominant compared to the non-dominant limb were conducted to test the hypotheses ***H*2.1-9**.

6.4 Results

Systematic, random, and proportional bias of linear and non-linear measures of unilateral balance on the dominant limb are presented in Table 19 and Table 20, respectively. Systematic bias data suggested linear measures of balance tended towards a smaller value at 19 weeks compared to baseline measures in both dominant (Table 19) and non-dominant unilateral balance (Appendix C). No pattern was present in linear measures of bilateral balance (Appendix D), however the magnitude of the systematic bias was lower in all variables compared to unilateral data except ML SD for dominant unilateral balance (mean difference; bilateral: 0.42 mm; dominant unilateral: −0.19 mm). Random bias, measured as the 95% CI of the difference, were greater than systematic bias in all variables and conditions. Random bias was higher in the ML compared to the AP axis for standard deviation (difference: 1.49 mm) and mean velocity (difference: 2.10 mm/s;) for unilateral balance on the dominant limb. Proportional bias ranged from

0.73 to 1.56, however 95% confidence limits included a gradient of 1.00 for all variables and conditions.

Table 19. Mean ± 95% confidence interval (CI) of the difference (systematic and random bias), least products regression slope ± 95% CI (proportional bias), and coefficient of variation (%CV) between linear measures of unilateral balance on the dominant limb at baseline and 19 weeks

	Mean ± 95% CI Difference	**Regression Slope ± 95% CI**	**%CV**
ML SD (mm)	-0.19 ± 6.59	1.08 ± 0.43	18.39
AP SD (mm)	-0.47 ± 5.10	0.89 ± 0.37	15.32
ML Velocity (mm/s)	-5.96 ± 34.23	1.06 ± 0.38	17.08
AP Velocity (mm/s)	-2.41 ± 32.13	1.08 ± 0.35	17.40
Resultant Velocity (mm/s)	-6.78 ± 47.88	1.08 ± 0.31	15.98
Path Length (cm)	-6.85 ± 48.26	1.08 ± 0.31	16.00
95% CI Ellipse Area (cm^2)	-0.75 ± 11.13	1.01 ± 0.32	29.24

Heteroscedasticity was present in 95% CI ellipse area for bilateral and non-dominant unilateral balance (Figure 18) and appeared to be as a result of a number of data points which had a greater level of bias. CompInd of bilateral balance also appeared to be heteroscedastic (Figure 19a and Figure 20a), however unilateral balance was homoscedastic in both the dominant (Figure 19c and Figure 20c) and non-dominant limb (Figure 19e and Figure 20e). Heteroscedasticity was not visually present in any other variable.

Table 20. Mean ± 95% confidence interval (CI) of the difference (systematic and random bias), least products regression slope ± 95% CI (proportional bias), and coefficient of variation (%CV) between non-linear measures of unilateral balance on the dominant limb at baseline and 19 weeks

MSE Output	Mean ± 95% CI Difference	Regression Slope ± 95% CI	%CV
Medio-lateral			
CompInd	-0.23 ± 2.10	0.81 ± 0.55	9.95
22.2 Hz	0.00 ± 0.21	1.53 ± 0.99	8.60
16.7 Hz	0.00 ± 0.20	1.13 ± 0.89	8.22
13.3 Hz	-0.01 ± 0.22	0.76 ± 0.38	8.44
11.1 Hz	-0.03 ± 0.28	0.73 ± 0.39	9.40
9.5 Hz	-0.04 ± 0.34	0.81 ± 0.36	10.57
8.3 Hz	-0.05 ± 0.42	0.90 ± 0.37	11.84
7.4 Hz	-0.08 ± 0.47	0.97 ± 0.38	13.37
6.7 Hz	-0.06 ± 0.55	1.09 ± 0.37	14.42
Antero-Posterior			
CompInd	0.01 ± 2.48	1.10 ± 0.40	10.88
22.2 Hz	0.01 ± 0.18	0.99 ± 0.46	9.19
16.7 Hz	0.00 ± 0.23	0.96 ± 0.57	9.31
13.3 Hz	0.00 ± 0.29	1.02 ± 0.30	10.49
11.1 Hz	0.00 ± 0.37	1.06 ± 0.40	11.67
9.5 Hz	0.01 ± 0.40	1.07 ± 0.40	11.59
8.3 Hz	0.00 ± 0.44	1.18 ± 0.41	11.68
7.4 Hz	0.02 ± 0.51	1.17 ± 0.43	11.87
6.7 Hz	0.02 ± 0.49	1.24 ± 0.38	11.00

Complexity index (CompInd)

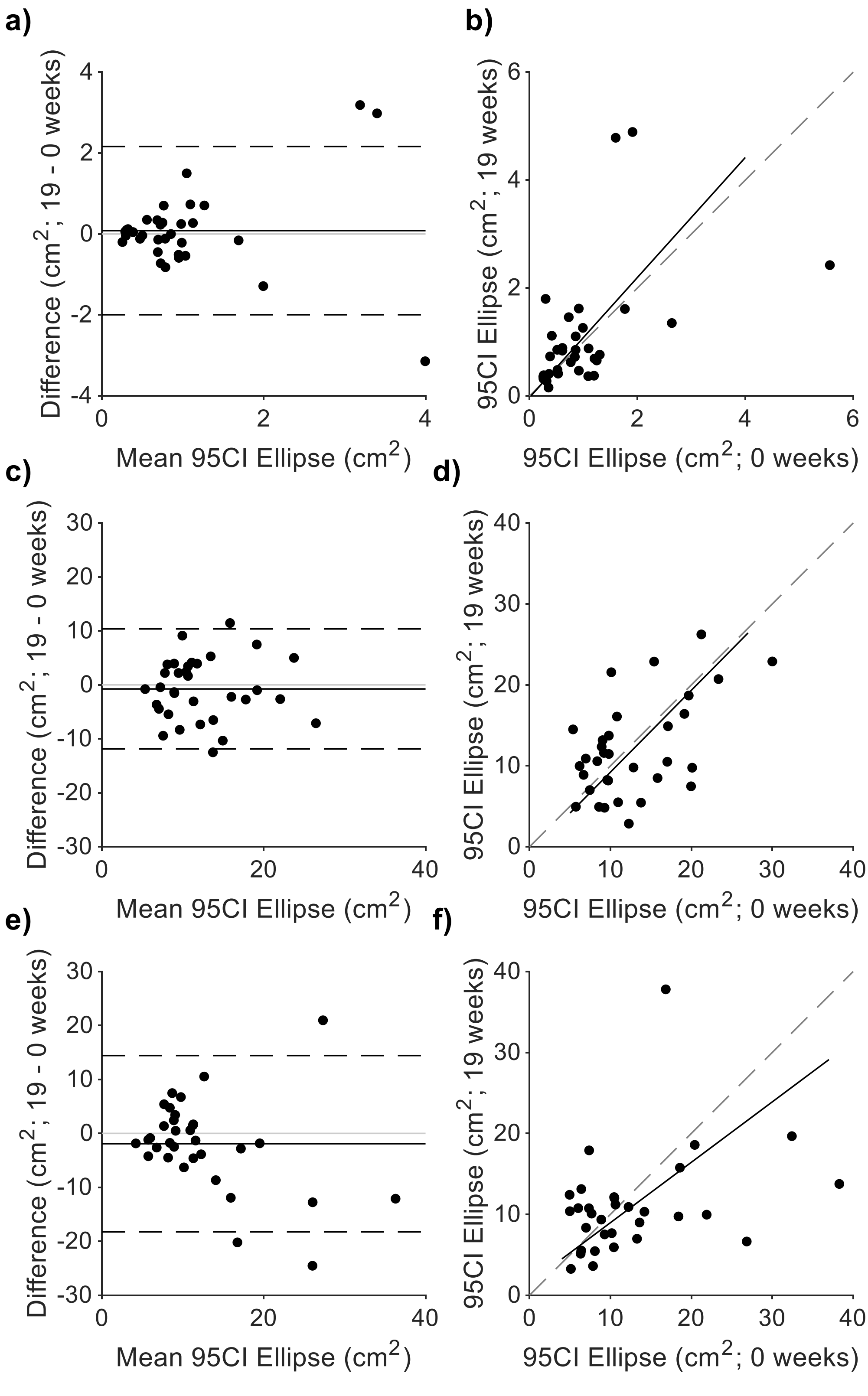

Figure 18. Bland-Altman (a, c, e; systematic and random bias) and least products regression (b, d, f; proportional bias) plots of 95% CI ellipse area (95CI Ellipse) during bilateral balance (a, b), and unilateral balance on the dominant (c, d) and non-dominant limb (e, f) between 0 and 19 weeks

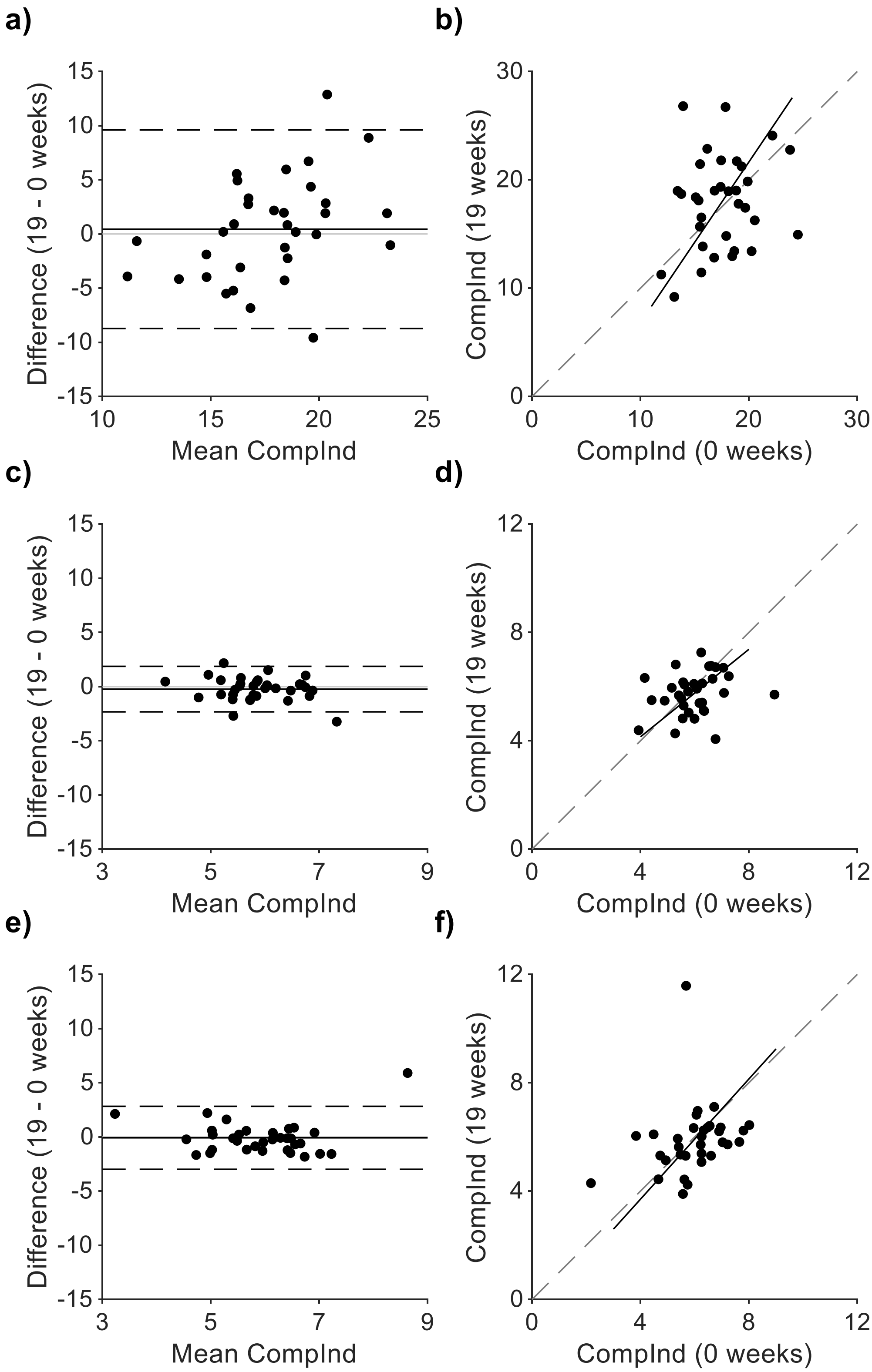

Figure 19. Bland-Altman (a, c, e; systematic and random bias) and least products regression (b, d, f; proportional bias) plots of medio-lateral complexity index (CompInd) during bilateral balance (a, b), and unilateral balance on the dominant (c, d) and non-dominant limb (e, f) between 0 and 19 weeks

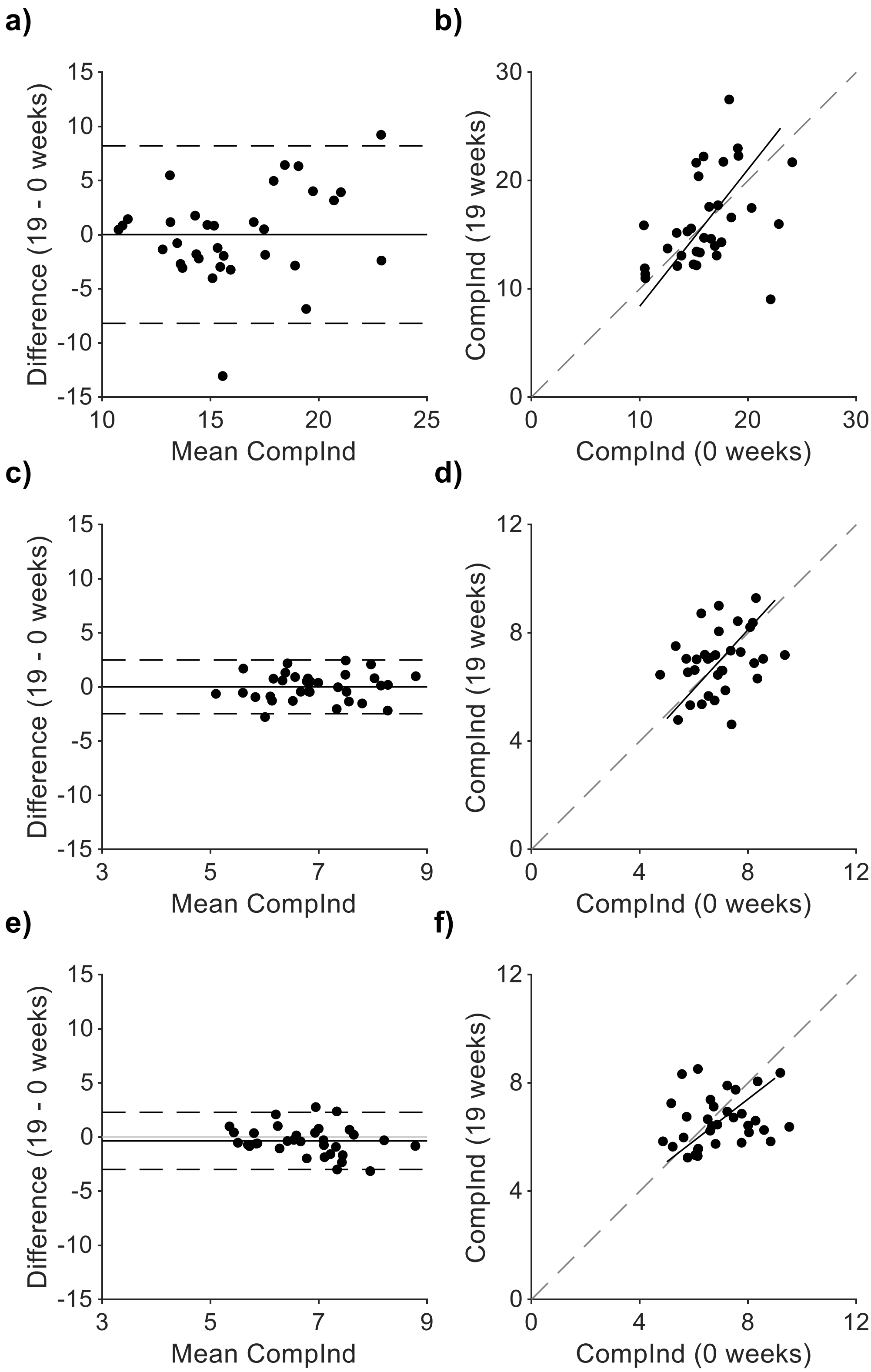

Figure 20. Bland-Altman (a, c, e; systematic and random bias) and least products regression (b, d, f; proportional bias) plots of antero-posterior complexity index (CompInd) during bilateral balance (a, b), and unilateral balance on the dominant (c, d) and non-dominant limb (e, f) between 0 and 19 weeks

CV was lower in all non-linear measures of unilateral balance compared to linear measures (Table 19 & Table 20). AP SD and resultant velocity provided the smallest CV of linear measures of balance. ML CompInd had a smaller CV (9.95%) compared to AP CompInd (10.88%), however showed a greater range of relative bias in complexity at the timescales analysed (min – max CV; ML: 8.22% – 14.42%; AP: 9.19% – 11.87%). CompInd for bilateral balance were higher than unilateral balance in the ML (14.86%) and AP (13.47%) direction regardless of tested limb dominance. There were no significant differences between changes in balance measures in dominant and non-dominant unilateral balance from baseline to 19 weeks (Table 21).

Table 21. Mean ± SD differences between baseline and 19 week measures of unilateral balance in the dominant and non-dominant limb

	Dominant	**Non-Dominant**
ML SD (mm)	-0.19 ± 3.41	-0.46 ± 4.24
AP SD (mm)	-0.47 ± 2.64	-0.80 ± 2.70
ML Velocity (mm/s)	-5.96 ± 17.74	-3.40 ± 18.81
AP Velocity (mm/s)	-2.41 ± 16.65	-2.66 ± 21.39
Resultant Velocity (mm/s)	-6.78 ± 24.81	-4.91 ± 29.79
Path Length (cm)	-6.85 ± 25.00	-4.94 ± 30.03
95% Confidence Ellipse Area (cm^2)	-0.75 ± 5.76	-1.91 ± 8.47
CompInd ML	-0.23 ± 1.09	-0.08 ± 1.51
CompInd AP	0.01 ± 1.28	-0.36 ± 1.37

No statistical differences were observed between limbs

6.5 Discussion

The results of this study provide information on the use of linear and non-linear measures of balance in the monitoring of changes which may occur due to pathology and treatment. Specifically, providing a measure of systematic and random bias in the same measurement scale as the variable, allowing results of future tests to be directly compared to determine whether changes are greater than that observed in an uninjured population. The results also suggest complexity of CoP calculated using MSE analysis may provide a more consistent measure than traditional linear measures of balance, however as no data on a pathological population are presented it is unclear whether changes in complexity in a pathological population would also be smaller than in linear measures. Finally there appears to be no difference between changes that occur in the dominant limb and those in the non-dominant limb, suggesting accounting of limb dominance is not required when assessing balance.

6.5.1 Systematic, Random, and Proportional Bias

Within a clinical setting, it is often the aim to both determine whether intervention results in change in a measured variable, and the magnitude of that change (Gardner & Altman, 1986). To aid in determining whether this change is clinically significant, the consistency of the measure in a population who has not undergone intervention can be used. Ma *et al.* (2014) assessed changes in resultant CoP path length during unilateral balance with eyes closed prior to and 24 weeks after ACL reconstructive surgery. The difference between the mean path length pre- and post-surgery was −34 cm (mean±SD; pre-surgery: 158±63 cm; post-surgery 124±39 cm), and was found to be statistically significant. The results of the current study suggest that to be 95% confident that a difference does not lie within the changes seen in an untreated population it should be greater in magnitude than 48 cm (Table 19). This suggests that the results presented by Ma *et al.* (2014), although statistically significant, may not represent a clinically significant change in balance performance.

Interpretation of the systematic and random bias in relation to previously published data, such as that of Ma *et al.* (2014) should be done with care. Firstly, although the mean difference can be calculated from data included as part of a manuscript, individual differences are required to calculate the variance of those changes (random bias). As a result, where a mean difference is smaller than the levels of consistency presented in this chapter it may lead to a conclusion that the change was smaller than the natural variation in balance performance. However, there may be certain individuals within the sample who did result in a change greater than the variation meaning that conclusion is not fully correct. Secondly, it has previously been shown that methodological choices such as trial length, sampling time, and filtering parameters can affect balance variables (Ruhe *et al.*, 2010), meaning comparisons between different methodologies may not be suitable. Lastly, although 95% is often viewed as a suitable CI, Hopkins (2000) suggested this may be too rigorous, and smaller intervals such as 68% may provide a more suitable cut off for assessing whether observed change is clinically significant. In addition to the size of the CI used, the presence of heteroscedasticity and proportional bias may also result in unsuitable limits of bias.

Heteroscedasticity is where an increase in the value of a variable coincides with an increase in the magnitude of the error, and has said to be present within most biological systems (Atkinson & Nevill, 1998). The presence of heteroscedasticity not only violates statistical assumptions, but also means the random bias measure may under and over estimate at the end ranges of the data. Some authors have advocated performing a natural log transformation of the data (Altman & Bland, 1983; Atkinson & Nevill, 1998), however this has a number of negative effects on its usability. Specifically any calculated measures of bias will now refer to the transformed data, limiting its use. Heteroscedasticity was present in 95% CI ellipse area as shown in Figure 18, suggesting the presented random bias may be too large. Figure 19 and Figure 20 show the CompInd of the same trials, and highlight that the heteroscedasticity has been reduced in certain outputs. Most notably this is in the non-dominant unilateral balance trials, where the data appear homoscedastic and have a smaller number of visual outliers. Homoscedasticity was present in all other variables, however the presented random bias of the 95% CI ellipse area and CompInd of bilateral balance should be used with care due to the presence of heteroscedasticity.

The data presented in this study suggested that small levels of proportional bias were present in most variables, as demonstrated by slopes of the least products regression line varying from one. However, the 95% CI of these data do not provide evidence to confirm the presence of proportional bias as all included the possibility of the slope being equal to one. No previous research has presented on the proportional bias between assessments of balance tasks (Ruhe *et al.*, 2010) so comparisons cannot be made. The conclusion of no proportional bias being present suggests that the change in balance measures is not affected by a participant’s baseline balance ability. For the purposes of applying levels of bias to determine clinically significant differences, the lack of proportional bias presents as a strength for using balance as a method of monitoring function.

When applying the results from this study to other data there is a number of steps that would increase the confidence of the interpretations. Firstly the variance of the changes of the intervention group should be considered either through a measure of random bias, or on an individual participant basis. Secondly, methodology should be matched to minimise differences due to timing of data collections and data analysis methods. Finally, the presence of heteroscedasticity highlights that certain measures of bilateral balance should be used with care due to errors between the estimates of bias and the true difference between participant results.

6.5.2 Comparisons between Linear and Non-Linear Variables

Measures of bias in the same measurement scale as the assessed variable provide results which can be compared and interpreted in relation to future measurements, however they do not allow comparisons between variables. Measures of relative bias such as CV provide a value of the bias in relation to the magnitude of the variable, meaning comparisons between variables can be made (Hopkins, 2000). The calculation of the CV allowed the **RQ$_{2.2}$** to be addressed; *do linear and non-linear measures of balance performance have different consistency over 19 weeks?* Complexity measures (Table 20) had lower coefficients of variation compared to linear measures of balance performance (Table 19), and therefore had greater consistency. This finding is in agreement with previous research that identified non-linear measures of balance may have reduced bias between measures taken within one week of each other (Doyle *et al.*, 2005). The data presented is the first to quantify the bias over a timeframe often used in clinical practice. The data suggests that complexity may offer a more consistent measure of balance performance, however as no data on a pathological population is presented here it is unclear how non-linear measures will change due to disease and treatment.

One possible explanation for complexity presenting a greater consistency relates to the characteristic the variable is suggested to represent. Complexity is a measure of the amount of information within a signal (van Emmerik *et al.*, 2016). From a balance perspective the complexity of the CoP has been suggested to be related to the function of the systems contributing to balance and how these systems interact to produce an output (Busa & van Emmerik, 2016). Linear measures such as the 95% CI ellipse area, which is a measure of the variance of the CoP, provide a measure of the control of the CoP movement (Duarte & Zatsiorsky, 2002). It is theoretically possible for outputs which differ in certain characteristics such as variance to be produced by the same number of interacting systems (van Emmerik *et al.*, 2016), meaning changes in linear measures of balance do not necessarily result in changes in non-linear measures such as complexity. The discrepancy between the relative biases therefore may be resulting from poorer consistency in the participants ability to control their CoP, compared to the number and interaction of the systems contributing to that task. Complexity measures may therefore offer a more consistent measure of the function of the systems contributing to balance, and how pathology and treatment may influence these.

A second possible explanation for the reduced relative bias in the complexity variables refers to the methods used to calculate the value. One limitation of the SampEn and MSE algorithms is the number of data points required for acceptable levels of relative reliability (Yentes *et al.*, 2013). As the MSE procedure uses a method of down sampling to explore complexity at lower frequencies, the timescale that can be analysed is limited by trial length (Gow *et al.*, 2015). Due to this limitation unilateral balance data of a low frequency (≤3.1 Hz) were excluded through EMD as the complexity could not be assessed at frequencies below 6.7 Hz. The exclusion of this data may have removed characteristics of the data which resulted in increased bias between visits in some participants, which were included in the analysis for linear measures. CompInd of the bilateral trials (Figure 19a & Figure 20a) provide evidence for differences in relative bias being related to the exclusion of lower frequency data. Due to a longer bilateral trial (19.5 s), lower frequency data (3.1 Hz) could be included in the analysis, and CV was higher than that of unilateral trials. Longer trial lengths would minimise the effect of this limitation of entropy calculations, however it is often not possible to collect long trials due to fatigue or difficulty of the task.

Conclusions as to the cause of the differences in relative bias are difficult to draw due to no data on pathological participants where a change in the interaction and function of the systems contributing to balance are presented. It should also be noted that, despite being advocated as a measure of bias across different measurement scales, CV does contain limitations. To provide a relative measure of bias, the statistic divides the bias by the mean of the two measures. Coefficient of variation therefore tends to provide a larger measure of relative bias for measures with a lower mean value. The data does not support this limitation being a factor within the findings of this study as the measures of complexity had lower average values and coefficients of variation.

6.5.3 Difference between the Dominant and Non-Dominant Limb

To answer $\mathbf{RQ_{2.3}}$ of this study; is the consistency of balance variables different for unilateral balance performed on the dominant compared to non-dominant limbs, the hypotheses $\mathbf{H_{2.1\text{-}9}}$ were tested and no significant differences were identified between changes in the dominant compared to non-dominant limbs in any variables. Previous data has identified that there was no difference between dominant and non-dominant balance measures at one time point (Alonso *et al.*, 2011), however it was unknown whether there would be differences in consistency over a longer time period. The results of the study suggest that limb dominance does not need to be taken into account when using balance to assess changes due to pathology or treatment.

6.6 Summary

This study addressed **Aim II** of this thesis; to quantify and compare the consistency of linear and non-linear measures of balance in an uninjured population over a common clinical observational timeframe. This was addressed by answering three research questions.

$RQ_{2.1}$: What is the level of systematic, proportional, and random bias in linear and non-linear measures of balance between baseline and 19 weeks?

Systematic and random bias of linear and non-linear measures of balance are presented in the same measurement scale as the assessed variable and can be used to inform conclusions on whether observed changes in other populations are clinically relevant. The data did not support the consideration of proportional bias in the application of these data.

$RQ_{2.2}$: Do linear and non-linear measures of balance performance have different consistency over 19 weeks?

Non-linear measures had greater consistency compared to linear measures of balance. Non-linear variables may therefore provide a more sensitive approach to monitoring change in pathological populations where a loss of complexity is theorised to occur.

$RQ_{2.3}$: Is the consistency of balance variables different for unilateral balance performed on the dominant compared to non-dominant limbs?

Consistency was not significantly different between balance variables completed on the dominant compared to non-dominant limb. This finding suggests limb dominance does not need to be taken into account when assessing changes in balance.

In summary, both linear and non-linear measures may offer useful tools to monitor changes in neuromuscular function due to pathology and treatment, however the observed changes should be interpreted alongside the identified systematic and random bias of uninjured participants. Non-linear measures of balance may provide a more useful tool due to greater relative consistency over a common observation timeline. However there are currently limited data on changes in balance complexity that occur due to pathology meaning it is difficult to identify the reason for the greater consistency. Additionally, there is only limited data on changes in balance complexity that occur due to ACL reconstruction therefore the magnitude of the systematic and random bias cannot be interpreted. To further explore the worth of linear and non-linear measures of balance as monitoring tools, the changes in a pathological population should be assessed to determine whether the loss of complexity theorised to occur due to disease or injury, such as ACL tears, can be restored through treatment.

7. The Effect of Anterior Cruciate Ligament Injury and Reconstruction on Balance Performance and Complexity

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

Chapter	Title	Addressed Aims
1	Introduction	
2	Monitoring Functional Recovery from ACL Injuries	
3	Lower Limb Biomechanics Before and After ACL Reconstruction: A Systematic Review	**AIM I**: Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery
4	Assessment of Balance as a Measure of ACL Injury Recovery: A Review of Linear and Non-Linear Approaches	
5	General Methods	
6	Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population	**AIM II**: Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe
7	The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity	**AIM III**: Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons **AIM IV**: Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.
8	Thesis Summary	
9	Conclusion	

Figure 1. Schematic of thesis structure and research aims

7.1 Preface

Chapter 6 addressed **Aim II** of this thesis and provided data on the consistency of measures of balance performance which were previously identified as potential tools to help assess the treatment and recovery from ACL injury. Complexity of the CoP signal appeared to offer a more consistent measure of balance than traditional linear variables, however levels of bias have limited use without consideration of the magnitude of changes which occur due to ACL deficiency and reconstructive surgery as it is unclear what an acceptable level of bias is. This chapter addresses **Aims III** and **IV** of this thesis by assessing balance in ACL injured participants before and after reconstructive surgery. Linear and non-linear balance measures were compared to uninjured control participants to establish whether ACL injury does result in balance deficits and a loss of complexity. Changes in measures were compared to the findings of Chapter 6 to establish their potential use in the monitoring of recovery from ACL injury and reconstruction.

7.2 Introduction

7.2.1 The Effects of Anterior Cruciate Ligament Injury and Reconstruction

The ACL contributes to the structural support of the knee and to the neurological function through its contribution to proprioception (Arnoczky, 1983; Butler *et al.*, 1980; Zimny *et al.*, 1986). Rupture of this ligament has been shown to result in reduced proprioceptive function (Pap *et al.*, 1999; Relph, Herrington, & Tyson, 2014), increased laxity (Snyder-Mackler *et al.*, 1997), and altered muscle activation patterns (Limbird *et al.*, 1988). These effects have all been suggested to cause a number of outcomes of ACL injuries such as reduced activity levels (Muaidi *et al.*, 2007), increased risk of future knee trauma (Papastergiou *et al.*, 2007), and early onset osteoarthritis (Kessler *et al.*, 2008). To attempt to restore the function of the affected limb, and reduce the impact of the negative outcomes of ACL deficiency, surgical reconstruction of the ligament is often undertaken (Jameson *et al.*, 2012).

Surgical reconstruction of the ACL has been suggested to restore the mechanical stability and proprioceptive potential of the limb (Dhillon *et al.*, 2012; Ruiz, Kelly, & Nutton, 2002). Biomechanical assessments have supported the benefits of reconstructive surgery, showing improved joint position sense and threshold to detect passive motion (Ma *et al.*, 2014; Ordahan *et al.*, 2015), and reduced kinematic excursions during movement tasks (Shabani *et al.*, 2015; Tagesson *et al.*, 2010). Collection of these types of biomechanical variables requires the use of specialist equipment such as isokinetic dynamometers or motion capture systems. The financial cost and required resources of such methodological approaches mean these are unsuitable for widespread clinical application. One task which may offer a suitable approach to assessing the effectiveness of clinical intervention is the assessment of balance tasks. Analysis of balance tasks is commonly completed through calculation of characteristics of the CoP trace, a signal which is able to be measured through simple relatively low cost technology (Huang *et al.*, 2013), and is not related to large space requirements, meaning it may be more suitable for widespread integration into clinical practice.

7.2.2 Anterior Cruciate Ligament Injuries and Balance

A number of studies have explored whether ACL deficiency leads to a reduced balance ability, most commonly through the analysis of characteristics of the CoP (Negahban *et al.*, 2014). Negahban *et al.* (2009) identified that during unilateral balance ACL deficient limbs (n=27) had significantly greater mean velocity (mean±SD; ACL deficient: 1.50±0.23 cm/s; uninjured: 1.37±0.11 cm/s) of the CoP, which was associated with poorer balance, compared to matched uninjured controls (n=27). A systematic review of balance performance in ACL deficient limbs provided further evidence for a reduced ability to control the CoP (Negahban *et al.*, 2014). No meta-analyses of the findings were conducted, however medium to large effect sizes (Cohen's d = 0.56–4.32) for poorer balance in ACL deficient limbs was found in over 76% of articles identified when compared to matched uninjured controls. Poorer balance ability of the ACL deficient limb was also identified when compared to the uninjured limb, however this was only present in eyes closed conditions, with no significant differences reported for eyes open conditions (Negahban *et al.*, 2014).

Comparisons between the involved limb of ACL injured participants, and the uninvolved limb and healthy uninjured controls both should be interpreted with considerations of the limitations. Firstly it has previously been shown that the uninvolved limb also has a reduced balance ability when compared to uninjured participants (Negahban *et al.*, 2014), meaning the uninvolved limb cannot be considered as an estimate of the participant's uninjured balance ability. Secondly, although uninjured matched controls may have similar demographics, the balance ability of the control group and the injured participants prior to injury may not have been the same, and a number of other factors can affect balance ability such as previous sporting experience (Matsuda, Demura, & Uchiyama, 2008; Winter, 1995). One methodological approach which may overcome these limitations is to explore the effects of clinical intervention, such as ACL reconstruction, on measures of balance ability which would allow a within limb comparison.

Section 3.3.2 presented a systematic review of changes in balance performance in ACL injured participants due to reconstructive surgery. The results of all identified studies suggested that reconstructive surgery resulted in improvements in measure of balance performance (e.g. Heijne & Werner, 2007; Ma *et al.*, 2014; Ogrodzka-Ciechanowicz *et al.*, 2018). This finding suggests that ACL deficiency does cause deficits in balance performance, and that clinical intervention is able to mitigate these outcomes. Despite these apparent improvements in balance, research has identified that there still appear to be balance deficits in ACL reconstructed knees compared to uninjured comparisons (Howells *et al.*, 2011). A systematic review of studies assessing postural control following ACL reconstruction found medium to large effect sizes for an improved stability in the uninjured control group during eyes open (Cohen's d; 0.32-1.40) and eyes closed (Cohen's d; 0.41-0.94) balance tasks in the majority of the identified articles (Howells *et al.*, 2011). Only one article found ACL reconstructed limbs had greater balance with a medium effect size (Cohen's d; -0.37), and all other articles had negligible effect sizes (Cohen's d; $-0.2 \leq d \leq 0.2$). These effect sizes support the conclusion that there is a trend towards poorer balance in ACL reconstructed participants compared to matched healthy controls in both eyes open and closed conditions (Howells *et al.*, 2011). No comparisons to the uninvolved limb were presented, however Mohammadi *et al.* (2012) compared balance measures in an

ACL reconstructed athletic population and identified that the involved limb had significantly poorer balance compared to both match uninjured controls and the uninvolved limb (mean± SD ML mean velocity [cm/s]; ACL involved: 1.7±0.1; ACL uninvolved: 1.6±0.1; Uninjured control: 1.6±0.1).

The evidence suggests that ACL injury results in balance deficits, and that treatment is able to partially restore this ability. The methodological approaches to establish this link have focussed on traditional linear measures of the CoP, such as variance and magnitudes of velocity. Applying a dynamical systems approach to these findings suggests that although having worth, the analysis approaches may fail to fully explore the non-linear dynamics of the balance task which offer more insight into the function of the involved systems (van Emmerik *et al.*, 2016). One potential theoretical framework which may relate to ACL injury and treatment is the loss of complexity theory (Lipsitz & Goldberger, 1992).

7.2.3 Loss of Complexity and Anterior Cruciate Ligament Injuries

The loss of complexity theory postulates that with aging and disease the outputs of human movement, such as the CoP during balance, have a reduced complexity (Lipsitz & Goldberger, 1992). Complexity is a term which is difficult to define, however it relates to the amount of meaningful information present within a signal, and is often linked to the number of inputs which are contributing to an output. Within the context of ACL injuries the loss of structural support and proprioceptive input from the mechanoreceptors in a healthy ACL may lead to a reduced complexity of the CoP during balance tasks.

Only two articles have explored CoP complexity in ACL injured populations (Clark *et al.*, 2014; Negahban *et al.*, 2010), however both contain limitations in relation to the loss of complexity theory. Negahban *et al.* (2010) assessed balance complexity in ACL deficient limbs in comparison to uninjured match controls using

Shannon entropy (Shannon, 1948). Shannon entropy rather than assessing the complexity of the whole signal, explores the complexity of deterministic structure. Although the complexity of the deterministic structure is not related to the loss of complexity theory, ACL deficient limbs were found to have significantly different Shannon entropy to healthy matched controls evidencing the potential link between ACL injury and non-linear dynamics (Negahban *et al.*, 2010). Clark *et al.* (2014) assessed the complexity of the CoP during balance in participants with ACL reconstructed knees through SampEn analysis, an entropic based method of estimating the complexity at certain timescale (Busa & van Emmerik, 2016; Richman & Moorman, 2000). SampEn data suggested there were no differences between the reconstructed and matched uninjured limbs, however analysis methods may have masked any potential differences. Specifically data were low-pass filtered with a cut-off frequency lower than the timescale which was being assessed through the SampEn analysis (cut-off: 6.75 Hz; SampEn timescale: 25 Hz [see Equation 11]). These limitations suggest that there is currently no adequate assessment of the loss of complexity theory in relation to ACL injuries, and its potential use as a method of monitoring recovery from treatment.

A further limitation of the evidence surrounding ACL injuries and the loss of complexity is the lack of data exploring the effect of ACL reconstructive surgery on the non-linear dynamics of balance. As described in Chapter 2, reconstructive surgery is the most popular treatment pathway for ACL injury, and monitoring tools using biomechanical measures may offer insight into this treatment. Negahban *et al.* (2010) and Clark *et al.* (2014) have only provided data on deficient and reconstructed knees, respectively. Explorations into changes due to surgery would provide further insight into treatment and the loss of complexity theory, and the potential use of balance trials to inform treatment of ACL ruptures.

7.2.4 Clinically Meaningful Differences

When assessing the use of measures to detect changes due to intervention, the presence of statistical significance alone is not sufficient justification for their use. Significance testing does not provide information on the magnitude of the effect, rather whether differences are not due to chance. It is possible to use statistics such as the *t* statistic to inform on the magnitude of the difference, however as these are not in the same measurement scale as the analysed variable their use in assessing clinical meaningfulness is limited. It is therefore important to understand whether the magnitude of the change is clinically meaningful. One approach to interpret observed changes is to compare their magnitude to observed changes without intervention. As previously discussed, the uninvolved limb of ACL injured participants may not provide a suitable comparison due to the effect injury and treatment has on the limb's ability to balance, and therefore changes in an uninjured population over a similar timeframe may offer the most suitable comparison to aid with determining the meaningfulness of identified differences.

7.2.5 Study Aims

This study addresses **Aims III** and **IV** of this thesis. Firstly **Aim III** is to identify whether measures of unilateral balance differ between limbs with ACL deficient and reconstructed knees compared to limbs with ACL intact knees. Secondly **Aim IV** is to identify whether ACL reconstruction results in changes in measures of unilateral balance of the involved limb, and to explore the magnitude of these changes in relation to changes in an uninjured control population over a similar timeframe. To address these aims four research questions and related hypotheses were developed. Where hypotheses only differed by the dependent variable a template hypothesis was provided and "*balance variables"* used to represent the variables: ML CoP SD, AP CoP SD, ML CoP mean velocity, AP CoP mean velocity, resultant CoP mean velocity, CoP path length, CoP 95% CI ellipse area, ML CoP CompInd, AP CoP CompInd, and ML and AP CoP entropy at 22.2, 16.7, 13.3, 11.1, 9.5, 8.3, 7.4 and 6.7 Hz, which are described in section 7.3.1.

$RQ_{3.1}$: Do measures of unilateral balance differ between the involved and uninvolved limb of ACL injured participants before and after ACL reconstructive surgery?

> **$H_{3.1}$:** There will be no significant difference between *balance variables* of the involved and uninvolved limb before ACL reconstructive surgery
>
> **$H_{3.2}$:** There will be no significant difference between *balance variables* of the involved and uninvolved limb 19 weeks after ACL reconstructive surgery
>
> **$H_{3.3}$:** There will be no significant difference between *balance variable* of the involved and uninvolved limb 32 weeks after ACL reconstructive surgery

$RQ_{3.2}$: Do measures of unilateral balance differ between the involved limb of ACL injured participants and the dominant limb of uninjured control participants before and after ACL reconstructive surgery?

> **$H_{3.4}$:** There will be no significant difference between *balance variables* of limbs with ACL deficient knees and limbs of uninjured control participants
>
> **$H_{3.5}$:** There will be no significant difference between *balance variables* of limbs with ACL reconstructed knees 19 weeks after surgery and limbs of uninjured participants
>
> **$H_{3.6}$:** There will be no significant difference between *balance variables* of limbs with ACL reconstructed knees 32 weeks after surgery and limbs of uninjured participants

$RQ_{4.1}$: Does ACL reconstructive surgery and treatment result in changes in measures of unilateral balance in the involved limb of ACL injured participants?

$H_{4.1}$: There will be no significant differences in *balance variables* of limbs with ACL injured knees 1 week before, and 19 and 32 weeks after ACL reconstructive surgery

$RQ_{4.2}$: Are changes in measures of unilateral balance in the involved limb of ACL injured participants due to ACL reconstructive surgery greater in magnitude than changes in uninjured control participants over a similar time frame?

7.3 Methods

7.3.1 Data Analysis

Unilateral balance data from 45 uninjured control participants (male: n=24; female: n=21; mean±SD; age: 27±5 years; height: 1.75±0.09 m; mass: 75.1±14.2 kg) at baseline, and from eight ACL injured participants (Table 22) approximately 1 (mean±SD; 0.9±0.6 weeks) week before, and 19 (19.4±3.1 weeks) and 32 (32.4±3.0 weeks) weeks after ACL reconstructive surgery as described in Chapter 5 were used. Balance measures were SD, mean velocity and complexity measures from MSE analysis (Costa *et al.*, 2002) of ML and AP data, and path length, mean velocity, and 95% CI ellipse area (Duarte & Zatsiorsky, 2002) of resultant CoP data (see section 5.8.2). SD, mean velocity, path length, and ellipse area are examples of linear measures of balance, and provide information on the body's ability to control the movement of the centre of mass (Winter, 1995). Lower values of these variables have therefore been suggested to represent better and more stable balance (Lehmann *et al.*, 2017). Entropy, calculated through MSE analysis, is a non-linear measure of the complexity of the signal, where a lower value represents a less complex signal (Costa *et al.*, 2002; Richman & Moorman, 2000). Values of systematic and random bias of these variables between measures 19 (18.8±2.6) weeks apart in uninjured participants (n=33) calculated as the limits of agreement (Bland & Altman, 1986) as described in Chapter 6 (Table 19 & 20) were also used.

Table 22. Details of ACL injured participants

Code	**Age (years)**	**Sex**	**Height (m)**	**Mass (kg)**	**Time Since Injury (weeks)**	**Injured Limb**
A	19	M	1.80	107	52	Left
B	18	F	1.65	76	30	Right
C	42	F	1.61	64	20	Right
D	19	M	1.83	68	34	Right
E	41	F	1.68	67	11	Right
F	20	F	1.68	83	98	Left
G	23	M	1.90	101	14	Left
H	18	M	1.73	66	18	Left
Mean±SD	25±10	-	1.74±0.10	79±17	34±29	-

7.3.2 Statistical Analysis

All statistical tests were performed in MATLAB using the Statistics and Machine Learning Toolbox (R2018a; MathWorks, Natick, MA). Acceptable type I error rate was set to 5% and therefore an alpha level of 0.05 was considered statistically significant for all tests. Due to the limited sample size, no correction for multiple tests was implemented due to their effects on statistical power (Nakagawa, 2004). To address **RQ$_{3.1}$** paired samples *t*-tests and Wilcoxon signed-rank tests were used to test **H$_{3.1\text{-}3}$** where the assumption of normality was confirmed or violated, respectively. The distributions of the between limb differences of the ACL injured participants were assessed for the assumption of normality using a Shapiro-Wilk assessment. To address **RQ$_{3.2}$** independent samples *t*-tests and Mann-Whitney U tests were used to test **H$_{3.4\text{-}6}$** where the assumption of normality was confirmed or violated, respectively. The distributions of the uninjured participants and involved limb of the ACL injured participants were assessed for the assumption of normality using a Shapiro-Wilk assessment.

To address **RQ$_{4.1}$** one-way repeated measures analysis of variance (ANOVA) tests were used to test **H$_{4.1}$**. The violation of the assumption of sphericity was identified as a significant Mauchly's test of sphericity, and where present the degrees of freedom were adjusted through a Greenhouse-Geisser correction. Where a significant difference was identified this was further explored *post hoc* using Fisher's least significant difference method for multiple comparisons. To address **RQ$_{4.2}$** the magnitude of differences observed due to treatment were compared to the limits of agreement of changes in an uninjured population calculated in Chapter 6.

7.4 Results

Linear measures of balance in the involved limb compared to the uninvolved limb at the pre-surgery measure were not significantly different (Table 23), except ML SD (mean difference: −2.7 mm; $p < 0.05$) leading to the rejection of the null hypothesis **H$_{3.1}$** for ML SD, and acceptance for all other linear variables. No other significant differences between the involved and uninvolved limb were present meaning null hypotheses **H$_{3.2}$** and **H$_{3.3}$** were accepted for linear variables. **H$_{3.1}$**, **H$_{3.2}$**, and **H$_{3.3}$** were all accepted as no significant between limb differences in measures of complexity in the ACL injured participants were identified.

Table 23. Linear and non-linear measures (Mean±SD) of unilateral balance of the dominant limb of uninjured participants, and the involved and uninvolved limb of ACL injured participants before, and 19 and 32 weeks after reconstructive surgery

	Uninjured Controls	**ACL Injured**					
		Pre-Surgery		19 weeks Post-Surgery		32 weeks Post-Surgery	
		Involved	*Uninvolved*	*Involved*	*Uninvolved*	*Involved*	*Uninvolved*
ML SD (mm)	10.0±2.9	**9.7±2.7***	**12.4±3.0***	10.2±4.0	9.6±3.5	9.5±2.7	8.7±2.1
AP SD (mm)	9.8±2.5	9.2±1.1	10.6±3.0	8.7±2.7	9.0±2.6	9.4±1.5	8.8±1.1
ML Velocity (mm/s)	62.9±18.5	49.6±9.7	53.4±13.3	50.8±14.2	54.7±15.2	53.4±14.9	48.9±6.8
AP Velocity (mm/s)	**54.7±19.7**$^{\theta(np)}$	46.2±15.7	56.0±21.0	49.4±22.4	51.0±20.5	**42.5±13.8**$^{\theta(np)}$	43.2±10.2
Resultant Velocity (mm/s)	92.3±28.1	76.0±18.5	87.0±27.2	79.3±27.2	83.2±24.6	75.8±21.1	72.1±9.1
Path Length (cm)	92.90±28.33	76.39±18.60	87.43±27.27	79.85±27.54	83.69±24.90	76.18±21.34	72.46±9.23
95%CI Ellipse Area (cm^2)	11.86±5.45	10.92±4.23	16.01±7.65	11.39±6.07	10.96±6.37	10.37±2.42	8.56±2.98
ML CompInd	**5.98±0.93**$^{\theta}$	**4.90±1.29**$^{\theta}$	5.00±0.77	5.88±1.01	5.41±1.11	5.50±0.89	5.31±1.28
AP CompInd	7.03±1.10	6.31±0.84	6.06±1.27	7.26±1.02	6.75±1.15	7.04±1.01	6.45±0.94

*****significant difference between involved and uninvolved limbs; $^{\theta}$significant difference between uninjured and ACL involved limbs; $^{(np)}$non-parametric test

Mean linear measures of balance in the involved limb of the ACL injured participants were not significantly different compared to the uninjured participants, except AP mean velocity, which was significantly less at 32 weeks leading to $\mathbf{H_{3.5}}$ being rejected for this variable (mean difference: −12.2 mm/s; $p < 0.05$). Null hypotheses $\mathbf{H_{3.4}}$ and $\mathbf{H_{3.5}}$ were accepted for all linear variables and $\mathbf{H_{3.6}}$ for all linear variables except AP mean velocity were accepted.

All complexity variables were lower in the involved limb of the ACL injured participants when compared to uninjured participants (Table 23 & Figure 21). ML CompInd was significantly lower in the involved limb of the ACL injured participants compared to uninjured controls (mean difference: −1.08; $p < 0.05$) before surgery, meaning $\mathbf{H_{3.4}}$ was rejected for this variable. $\mathbf{H_{3.5}}$ and $\mathbf{H_{3.6}}$ were accepted for ML CompInd as this difference was not present after surgery (mean difference: −0.10 [19 weeks]; −0.48 [32 weeks]; $p > 0.05$). AP CompInd was not significantly different resulting in $\mathbf{H_{3.4}}$, $\mathbf{H_{3.4}}$, and $\mathbf{H_{3.5}}$ being accepted, however showed a similar pattern as ML CompInd with a lower complexity before surgery and a reduced mean difference at measures post-surgery (Table 23). Figure 21 presents a comparison of the ML (a) and AP (b) entropy at different timescales of the involved limb of the ACL injured participants before surgery and uninjured participants. The involved limb had significantly lower ML entropy at all timescales and AP entropy at 6.7 and 8.3 Hz ($p < 0.05$; rejected $\mathbf{H_{3.4}}$). Mean difference between participants was higher at lower compared to higher timescales in both the ML (22.2 Hz: 0.06; 6.7 Hz: 0.30) and AP (22.2 Hz: 0.03; 6.7 Hz: 0.16) directions (Figure 21).

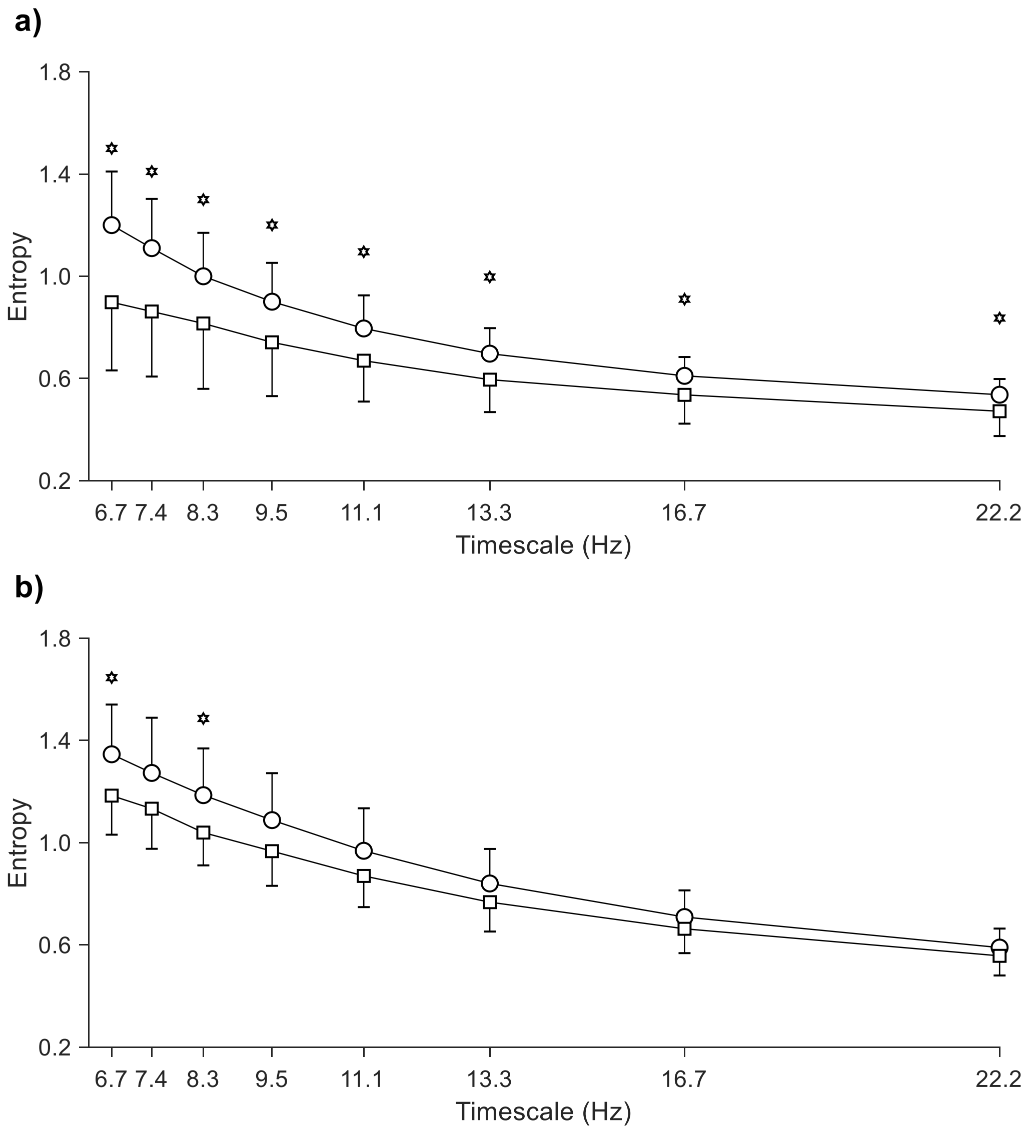

Figure 21. Mean±SD multiscale entropy of a) ML and b) AP CoP data during unilateral balance for ACL deficient limbs (□), and uninjured participants (○). ✡ shows statistically significant difference between limbs.

$H_{4.1}$ was accepted for linear measures of balance as reconstructive surgery did not result in any significant changes in linear variables of the involved limb (Table 23). No individual changes in linear measures from before to 19 weeks after ACL reconstruction were greater than the natural variation, shown by the 95% confidence limits, of a healthy population (Figure 22a-g; **$RQ_{4.2}$**).

Mean post-surgery complexity measures were all greater than pre-surgery at both time points (Table 23 & Figure 23), however only **$H_{4.1}$** for MSE of the ML CoP at

6.7 Hz was rejected due to a significant increase from pre-surgery to 19 weeks post-surgery (mean difference: 0.29). There was also a significant decrease in MSE of the ML CoP at 6.7 Hz from 19 to 32 weeks post-surgery (mean difference: −0.09). Participants G and H, and D and F had changes in CompInd of ML and AP CoP data, respectively, from pre-surgery to 19 weeks post-surgery that were greater in magnitude than the variation of a healthy control population (Figure 22h-i; **RQ$_{4.2}$**).

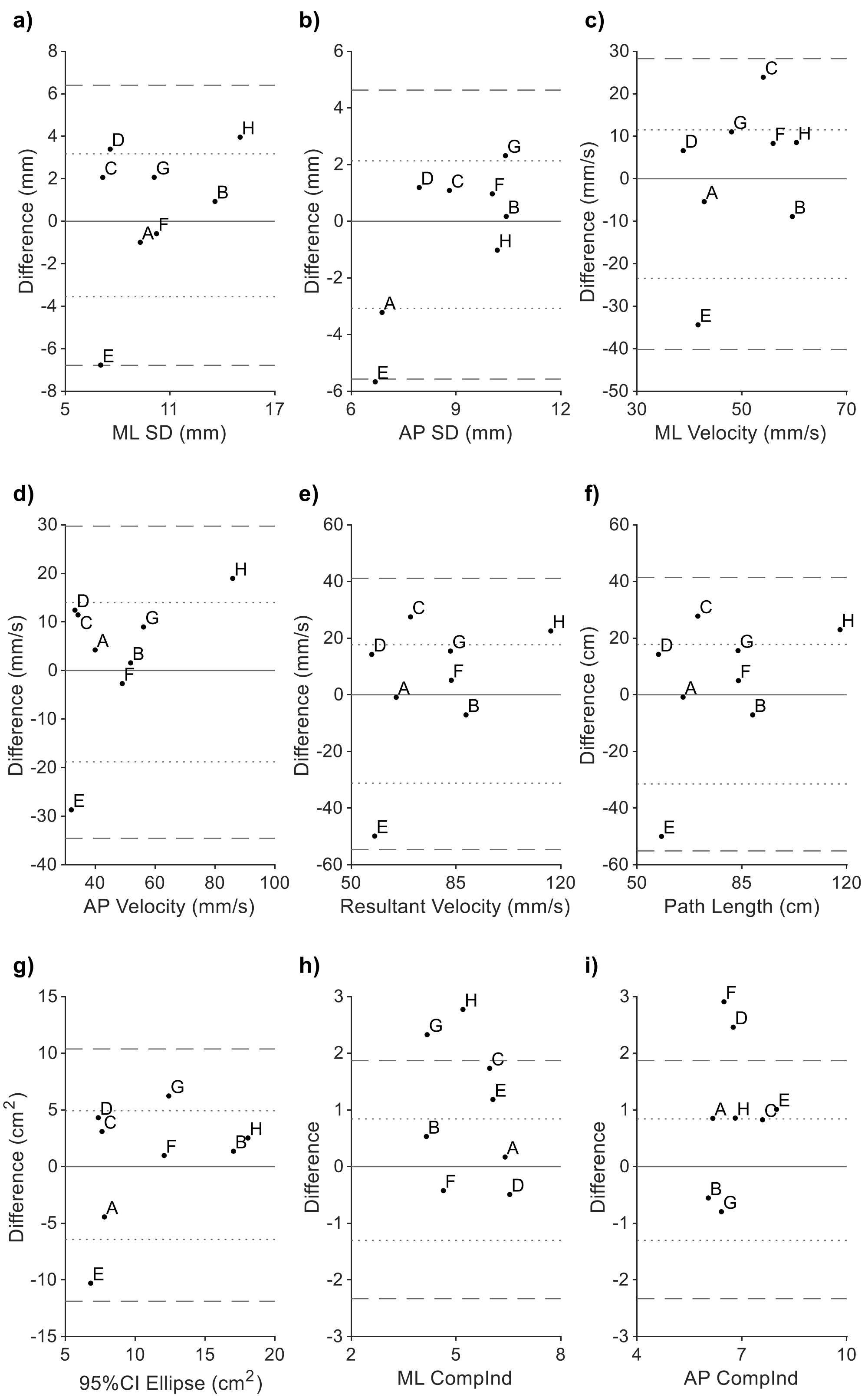

Figure 22. Individual differences in balance variable in the involved limb of ACL injured participants between pre-surgery and 19 weeks post-surgery, where a positive value is an increase due to surgery. Dotted and dashed lines represent 68% and 95% limits of agreement of changes in an uninjured control population, respectively (Chapter 6).

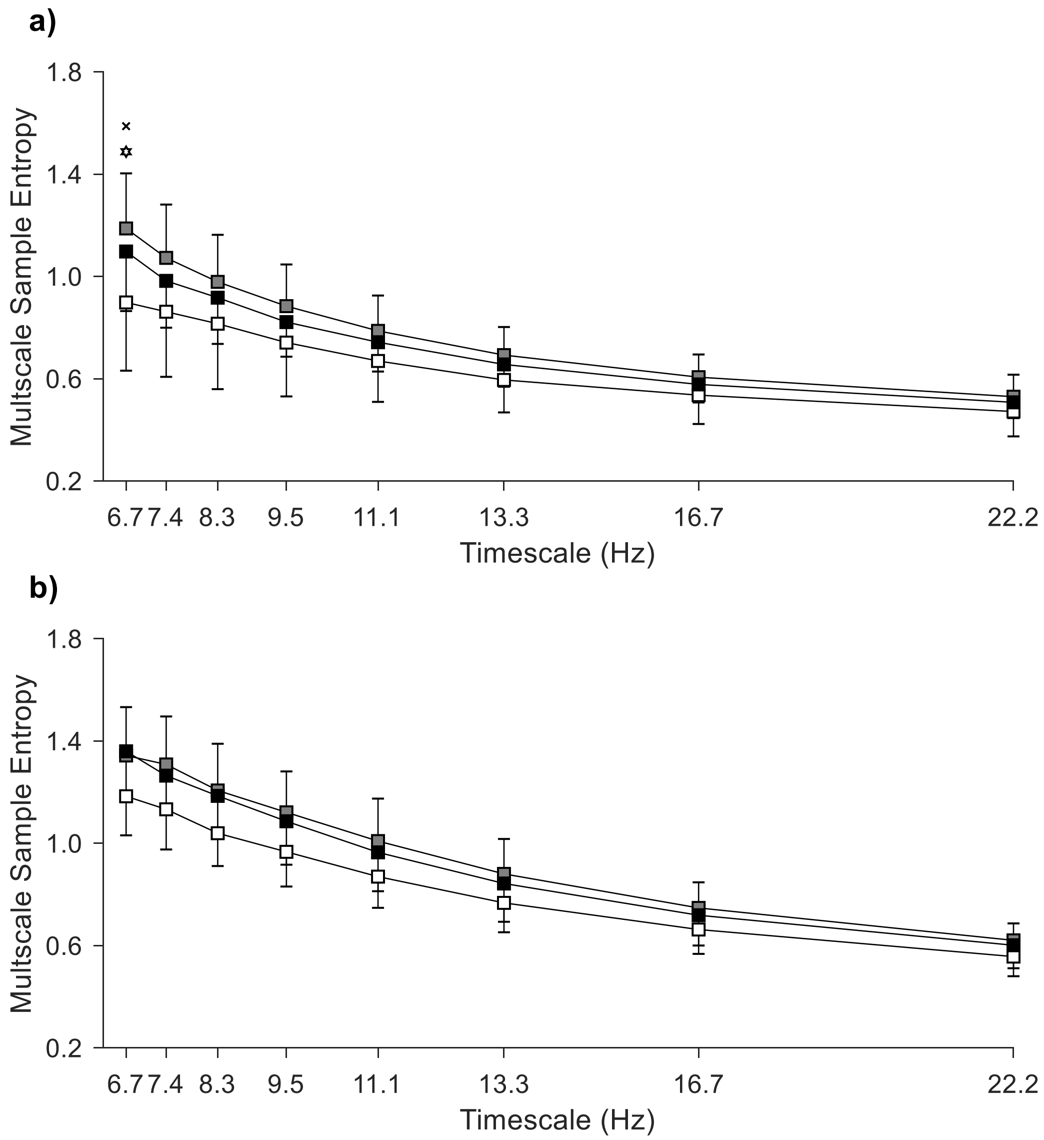

Figure 23. Mean±SD a) ML and b) AP CoP multiscale sample entropy of the involved limb in ACL injured participants before (white), and 19 (grey) and 32 (black) weeks after surgery. ✡ significant difference between pre- and 19 weeks post-surgery; × significant difference between 19 and 32 weeks post-surgery

Individual changes in MSE at 6.7 Hz in the ML direction in the involved limb in the ACL injured participants from pre-surgery to post-surgery are presented in Figure 24. MSE increased in all ACL injured participants at 19 weeks post-surgery, however only three of eight were greater than the 95% confidence limits of changes in an uninjured population over the same time (Chapter 6). All but one participant had a reduction in MSE from 19 to 32 weeks post-surgery, however the magnitude of these changes were smaller in magnitude than the uninjured confidence limits.

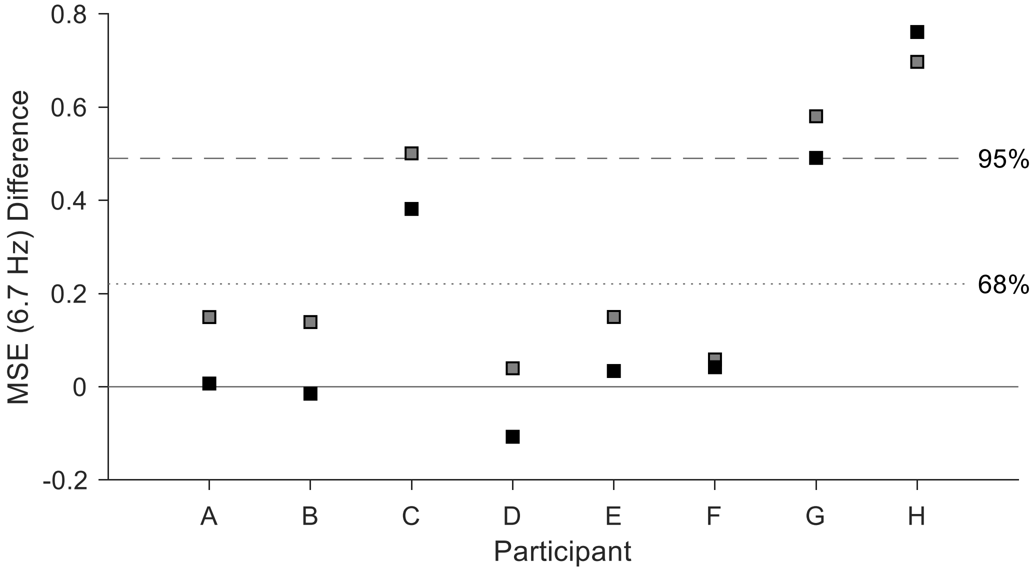

Figure 24. Change in multiscale entropy (MSE) at 6.7 Hz timescale in the involved limb of ACL injured participants from pre-surgery to 19 (grey) and 32 (black) weeks post-surgery. The 95% (dashed) and 68% (dotted) confidence limits of changes over 19 weeks in an uninjured control population are indicated.

7.5 Discussion

The results of this study suggest that the involved limb of ACL injured participants did not differ in balance ability. Only **H$_{3.1}$** for ML SD and **H$_{3.6}$** for AP mean velocity were rejected and all other null hypotheses related to **RQ$_{3.1}$** and **RQ$_{3.2}$** were accepted. The significantly lower SD and mean velocity may suggest that ACL injured participants were able to control their centre of mass through less extreme mechanisms, however the number of other non-significant findings in variables cast doubt on this conclusion and suggest no true differences were present. The presented data does not therefore support that ACL injury results in a reduced balance ability that has been shown in previous research (Howells *et al.*, 2011; Negahban *et al.*, 2014). There were no differences in balance performance between the involved and uninvolved limb after ACL reconstructive surgery, however changes in the uninvolved limb indicative of improved balance performance were present, however these differences were not statistically assessed so conclusions are difficult to draw. Despite changes in the uninvolved limb not being analysed, previous research has identified improvements in functional tests of the uninvolved limb and discussed the implications on symmetry indexes (Rohman, Steubs, & Tompkins, 2015). Future research may therefore look to explore changes in in the balance ability of the uninvolved limb of ACL injured participants undergoing reconstructive surgery. There were no significant changes in balance performance in the ACL injured limb due to ACL reconstructive surgery, contradicting the evidence reviewed in Chapter 3 and suggesting that linear measures of balance may not be suitable variables for the monitoring of balance function during treatment for ACL injuries.

Non-linear assessments of balance suggested that ACL limbs had significantly lower output complexity compared to uninjured comparisons, supporting the loss of complexity theory (Lipsitz & Goldberger, 1992). There were no significant differences in complexity measures between the involved and uninvolved limb supporting the effect that ACL injury has on both limbs (Reider *et al.*, 2003). ACL injury treatment appeared to restore the loss of complexity, specifically in measures of ML complexity at lower timescales. These increases in complexity may suggest that ACL reconstruction is able to partially restore the contributions of the healthy ligament to the performance of balance tasks, and that complexity may provide further information into the changes of the proprioceptive system due to ACL injury and treatment.

7.5.1 Changes in Linear Measures of Balance

Research has previously suggested that ACL deficient and reconstructed limbs have poorer balance performance assessed through linear measures of the CoP compared to ACL intact limbs (Howells *et al.*, 2011; Lehmann *et al.*, 2017; Negahban *et al.*, 2014), however the current results do not support this conclusion. Data showed that the ACL injured limb either did not differ or had significantly better balance compared to comparison knees. These conclusions are in agreement with Ageberg, Zätterström, Moritz, and Fridén (2001) and O'Connell *et al.* (1998) who present evidence to support no difference or greater balance performance in ACL injured limbs. The loss of the proprioceptive input from the ligament has been shown to result in decreased proprioception in tasks which isolate the knee joint such as joint position sense and threshold to detect passive motion (Relph *et al.*, 2014). This apparent reduction in proprioception paired with an increased balance ability identified in the presented data suggest that linear measures of unilateral balance are not sensitive to allow the assessment of the specific effects of ACL injury due to other factors affecting measures of balance.

One possible factor for an improved balance in the ACL deficient limbs may be improvements between injury and testing. Time between injury and data collection was on average 34 weeks and it is possible that during this time the effects of the injury on balance were mitigated. Lee, Lee, Ahn, and Park (2015) presented data to suggest that time since injury did not solely result in improvements in proprioception of the involved limb, however it is unclear whether participants in their study undertook any rehabilitation during this time, which has been shown to improve balance performance in ACL deficient limbs (Zätterström, Friden, Lindstrand, & Moritz, 1994). Participants within this research did not receive any pre-operative physiotherapy or guidance on exercise, however pre-operative activity was not recorded as part of the participant screening and therefore may have occurred.

Differences in the chosen methodology may have also contributed to differing results to other research. Participants completed unilateral balance whilst their eyes were closed, and due to difficulties completing this task for extended periods of time, only ten seconds of data were used for analysis. Although this trial length is sufficient to produce reliable results for the non-linear analyses used, assessments on acceptable reliability of linear measures of balance have suggested trial lengths in excess of 15 s are required (Riemann, Piersol, & Davies, 2017). This limitation does suggest that the employed methods may not be capable of identifying the balance deficits which may be caused by ACL injury and provides evidence against the use of unilateral balance with obscured vision as a method for assessing differences in balance performance in ACL injured populations.

7.5.2 Changes in Complexity

7.5.2.1 ACL Injury and Loss of Complexity

The loss of complexity theory states that the diminished function of systems, which occurs due to aging and disease, leads to a reduction in the complexity of biological outputs (Goldberger *et al.*, 2002; Lipsitz & Goldberger, 1992). The data presented are the first to assess this theory in relation to balance and ACL injury using MSE, a method which measures complexity in different timescales (Costa *et al.*, 2002). ACL deficient limbs had a significantly lower CoP complexity during unilateral balance when compared to uninjured limbs. A reduced complexity suggests that the effects of ACL injury do result in a change in the function of and interaction between the systems contributing to balance performance. Although this is the first assessment of complexity in ACL deficient limbs, evidence for a loss of complexity during balance tasks has also been identified due to Parkinson's disease (Cattaneo *et al.*, 2016), idiopathic scoliosis (Gruber *et al.*, 2011), and concussion (Purkayastha *et al.*, 2019), further supporting the relationship between disease or injury and a loss of complexity.

One characteristic of complexity is that the signal contains structures and information at a number of different timescales (Vaillancourt & Newell, 2002). The MSE analysis used in this study allows the assessment of this characteristic, and the data presented appears to show that differences in complexity due to ACL injury occur in lower timescales. Specifically, the mean difference in entropy between the involved limb of ACL injured participants and dominant limbs of uninjured control participants increased as the timescale decreased. This can be explained by the relation of the assessed timescale to physiological meaningful frequencies (Busa & van Emmerik, 2016). Previous research and data in the ML axis of this study show that there is still an identifiable loss of complexity at timescales which have previously been assumed to not relate to physiological mechanisms (Busa & van Emmerik, 2016), however frequency analysis has previously identified that the majority of a CoP signal during balance consists of lower frequency data (≤ 3Hz; Bizid *et al.*, 2009; Golomer *et al.*, 1994; Soames & Atha, 1982). Limitations of the MSE algorithm relating to the minimum number of data points required, and the trial length analysed in this research mean that the lowest timescale analysed was 6.7 Hz. A significant loss of complexity compared to uninjured comparisons was identified in both the ML and AP in timescales 6.7 and 8.3 Hz, suggesting these are suitable frequencies for assessing complexity in ACL deficient limbs, however it may be that lower timescales provide greater differences due to their suggested relevance to physiological processes.

7.5.2.2 ACL Treatment and Complexity

The aim of ACL surgical treatment is to improve the function of the knee by providing structural support and restoring the proprioceptive potential of the limb. The identified increase in complexity at 19 weeks post-surgery does not provide information on the ability of the limb to complete a balance task, however it suggests that treatment was capable of increasing the number of biological inputs and interactions between the systems which are contributing to the CoP. This increase in complexity may therefore be viewed as a measure of improved function (Lipsitz & Goldberger, 1992; Vaillancourt & Newell, 2002), suggesting that treatment was successful. However, the results also show a significant decrease in complexity from 19 to 32 weeks post-surgery, providing evidence against an increase in complexity being related to improved function. There have been no other assessments of the effects of surgical intervention on balance complexity meaning there is little evidence to support theoretical explanations for these changes, however the identified changes in complexity may be explained by motor learning principles.

Mitra, Amazeen, and Turvey (1998) hypothesised that motor learning results in a decrease in the active degrees of freedom resulting in more deterministic dynamics. Newell and Vaillancourt (2001) expanded on this hypothesis by suggesting that unlike the loss of complexity theory, which models a more deterministic output as an undesirable change, the reduction in degrees of freedom, and therefore reduction in complexity, postulated by Mitra *et al.* (1998) would be indicative of an increase in the ability to complete a task. In relation to the presented results, the initial significant increase in complexity may be due to a desirable increase in the number of interacting inputs responsible for the completion of the task and therefore function of the limb. However, the higher complexity may also be as a result of a poorer ability to utilise the additional inputs to meet the demands of the task. The significant decrease between 19 and 32 weeks post-surgery may therefore relate to a reduction in active degrees of freedom which have been hypothesised to occur with learning (Newell & Vaillancourt, 2001). Future explorations into the effect of surgical treatment should further explore the acute and chronic effects clinical intervention have on measures of complexity to further understand the relationship between complexity and biological function.

7.5.3 Use of Balance Variables for Monitoring Recovery from ACL Injury

Despite previous evidence to suggest that ACL injury results in poorer linear measures of balance performance, the results from this study, and those of Ageberg *et al.* (2001) and O'Connell *et al.* (1998) show that this relationship is not universal in all investigations. Additionally, despite previous evidence to show ACL reconstructive surgery was capable of improving balance performance (Chapter 3), the presented data did not support this. These findings provide evidence against the use of linear measures of balance for the monitoring of limb function due to ACL injury and treatment. Additional evidence for this conclusion is provided in the individual analysis of the magnitude of changes due to surgery, where no observed change was greater in magnitude than the observed change in uninjured participants.

Evidence on the potential use of measures of balance complexity for the monitoring of ACL injury and recovery is limited, however the findings of this study suggest these may be more sensitive to changes due to injury and reconstruction. Changes in complexity measures were the only calculated variables that had individual magnitudes greater than that observed in uninjured participants. Specifically ML MSE at 6.7 Hz timescale, which may provide the most biologically relevant information of the assessed non-linear variables, identified three of eight participants as having changes greater than the 95% confidence limits of uninjured participants. Measures of complexity at lower timescales, not assessed in this research, may also identify larger differences due to ACL injury and have potentially greater worth for the monitoring of changes in ACL injured populations. It is currently unclear whether the identified changes in complexity are related to improved functional outcomes from ACL treatment or how they may change over longer periods of time (>32 weeks), however they may offer a unique insight into the dynamics and the function of the system which is not able to be assessed using traditional linear approaches.

A final consideration should also be taken into account when assessing the magnitude of the individual changes in the data presented in this research. As discussed in section 6.5.1 the use of 95% confidence limits has previously been considered as conservative when assessing whether differences lie outside the normal variation of the variable (Hopkins, 2000). By assessing changes against such conservative boundaries, it is possible that meaningful differences were disregarded. This limitation may be particularly relevant to the study design employed in this research, as although assessing the natural variation over the same time frame as the observation period around clinical treatment is the correct approach, the time may have introduced large amounts of error. The 68% confidence limits of changes in an uninjured population are also presented in Figures 22 and 24, and using these boundaries does identify more participants as having undergone meaningful changes. Future research should look to explore the relationship between the use of different boundary limits in predicting whether changes lay outside natural variation and their relation to improved functional outcomes.

7.6 Summary

This study addressed **Aims III** and **IV** of this thesis:

III. to identify whether measures of unilateral balance differ between limbs with ACL deficient and reconstructed knees compared to limbs with ACL intact knees; and

IV. to Identify whether ACL reconstruction results in changes in measures of unilateral balance of the involved limb, and explore the magnitude of these changes in relation to changes in an uninjured population.

These aims were addressed by answering four research questions.

$RQ_{3.1}$: Are measures of unilateral balance different in the involved limb compared to uninvolved limb of ACL injured participants before and after ACL reconstructive surgery?

Linear measures of unilateral balance suggested the involved limb of ACL injured participants had the same balance ability compared to the uninvolved limb before surgical reconstruction. There were no differences between limb differences in the ACL injured participants after surgery. Measures of complexity did not differ between the involved and uninvolved limb at any time point.

$RQ_{3.2}$: Are measures of unilateral balance different in limbs with ACL injured knees before and after ACL reconstructive surgery compared to limbs of uninjured participants?

The involved limb of ACL injured participants and uninjured comparisons did not differ in balance performance assessed through linear measures, except AP velocity at 32 weeks. The involved limb had significantly lower complexity before surgery compared to uninjured participants suggesting ACL deficiency results in a loss of complexity.

RQ$_{4.1}$: Does ACL reconstructive surgery and treatment result in changes in measures of unilateral balance?

There was no significant effect of treatment on linear measures of balance in the involved limb of ACL injured participants. ML complexity assessed at a timescale of 6.7 Hz significantly increased from pre-surgery to 19 weeks post-surgery, and then significantly decreased from 19 to 32 weeks post-surgery.

RQ$_{4.2}$: Are changes in measures of unilateral balance due to ACL reconstructive surgery greater in magnitude than changes in uninjured participants over a similar time frame?

No individual changes in linear measures of balance performance were greater than the observed 95% confidence limits of uninjured participants identified in Chapter 6. Measures of complexity did have changes greater in magnitude than observed confidence limits for some individuals. Three of eight ACL injured participants had changes in ML complexity at 6.7 Hz greater than uninjured participants.

In summary the presented results suggest that ACL injured limbs have similar balance ability compared to the uninvolved limb of the same participants and the dominant limb of uninjured participants. This finding is in contrast to the general trend of the research although it is supported by some published articles, and highlights the limitations with the use of linear measures of balance in the monitoring of ACL injuries. The results provide further evidence against the use of linear measures of balance as treatment did not result in any significant changes, and the magnitude of individual changes did not appear to be clinically meaningful. Complexity assessed using MSE may be more sensitive than linear approaches in assessing changes in limb function due to ACL injury and treatment. ACL deficient limbs had significantly lower complexity, and treatment resulted in significant changes where the magnitude of some individuals were greater than observed variations in uninjured participants over a similar time period. To assess the worth of measures of complexity and ACL injury studies with larger sample sizes should be conducted and the relationship between functional outcomes and complexity should be explored.

8. Thesis Summary

Thesis aim: To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

Chapter	Title	Addressed Aims
1	Introduction	
2	Monitoring Functional Recovery from ACL Injuries	
3	Lower Limb Biomechanics Before and After ACL Reconstruction: A Systematic Review	**AIM I**: Systematically synthesise the current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery
4	Assessment of Balance as a Measure of ACL Injury Recovery: A Review of Linear and Non-Linear Approaches	
5	General Methods	
6	Consistency of Linear and Non-Linear Measures of Balance in an Uninjured Population	**AIM II**: Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe
7	The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity	**AIM III**: Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons **AIM IV**: Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population.
8	Thesis Summary	
9	Conclusion	

Figure 1. Schematic of thesis structure and research aims

8.1 Addressing the Thesis and Study Aims

The aim of this thesis was:

To explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery.

As presented in Chapter 1 and Figure 1, three studies (Chapters 3, 6, & 7) which addressed four study aims were presented in this thesis. The main findings relating to these aims are presented here, and discussed in relation to the overall thesis aim.

8.1.1 Aim I

Systematically synthesise current evidence surrounding changes in biomechanical variables which occur due to ACL reconstructive surgery.

Chapter 3 presented a systematic review of the research that has assessed lower limb biomechanics before and after ACL reconstructive surgery. Previous systematic reviews have identified changes in biomechanics in ACL deficient and reconstructed participants, however this review was the first to synthesise the evidence on changes in lower limb biomechanics due to ACL reconstruction. Data were available on balance, joint position sense, gait, stair ambulation, pivoting, and hopping tasks. Analyses of linear kinematic and kinetic variables were the most common methodological approaches. Inconsistent surgical characteristics and uncertainty on participant retention resulted in moderate risk of bias for most articles. There was a common finding of an effect of ACL reconstruction on lower limb biomechanics, including changes in structural support and neuromuscular function in all tasks, however the direction and magnitude of these changes often differed between studies. Assessments of proprioception appeared to provide the most consistent findings with improvements in balance tasks and joint position sense being found.

In relation to the overall thesis aim, the findings suggest that biomechanical measures do change due to surgery. Despite being the most commonly assessed movement task, variables related to the performance of gait did not provide clear conclusions as to the effect of ACL reconstruction. The inconsistent conclusions drawn from assessments of gait may suggest that participants demonstrate individual coping strategies when undertaking dynamic tasks. The presented variables of gait are therefore unsuitable approaches to monitor changes in lower limb function due to ACL injury and reconstruction. Variables that related to the proprioceptive function of the limb supported the hypothesis that ACL reconstruction is capable of restoring the proprioceptive potential of the limb. Assessments of tasks whose performance is predominately reliant on the proprioceptive system may provide a more specific assessment of one of the effects of ACL injury, and therefore may be less susceptible to individual coping strategies that appeared to be present in tasks such as gait. Analysis of the proprioceptive function of the limb through analysis of tasks such as balance and joint position sense may therefore offer insight into the effects of ACL reconstruction and be suitable for the assessment of lower limb function. As the collection of balance data is able to be completed with minimal resources, variables related to the performance of balance may offer the most clinically suitable approach to assessing the function of the involved limb of ACL injured participants.

8.1.2 Collection of Biomechanical Data

To address **Aims II**, **III** and **IV** an innovative and novel data collection protocol was developed and implemented to gather biomechanical data on ACL injured (Figure 25) and uninjured matched control participants (Chapter 5). Recruitment and collection of data for ACL injured participants took place within Pilgrim Hospital. The constraints related to conducting research within a National Health Service hospital resulted in weekly attendance at orthopaedic clinics to maximise participant recruitment from a limited pool (see section 8.2.2), and the creation of custom equipment for data collection (see section 8.2.1).

Recruitment

- Recruited through attending weekly orthopaedic clinics
- From approximately eight ACL reconstructions per year
- Broad inclusion criteria

Data Collection

- Generic clinical space
- Space restrictions
- Custom data collection equipment and protocol

Figure 25. Characteristics of the recruitment and data collection for ACL injured participants

Due to the findings of Chapter 3, analyses of balance trials were conducted for their potential worth in assessing recovery from ACL injuries and reconstructive surgery. Traditional linear analyses were conducted to provide evidence on the suitability of the developed protocol in identifying the previously identified link between ACL injuries and balance performance. Additionally, MSE was performed to estimate the complexity of the signal, an approach which had not previously been applied to assessing ACL injuries, or monitoring changes due to surgical intervention.

8.1.3 Aim II

Quantify and compare the consistency of identified biomechanical variables in an uninjured population over a common clinical observational timeframe.

One desirable characteristic of a measure for monitoring changes due to an intervention is its consistency over a period of time that does not include an intervention. A greater consistency and therefore smaller natural variance in a measure reduces the required size of an observed change to be interpreted as clinically meaningful (Figure 26). Consistency over short time periods (<1 week) has been explored, however for the purpose of assessing clinical meaningfulness, the levels of consistency should be assessed over a commonly used observation timeframe. Chapter 6 presented the first study to explore the consistency of linear and non-linear measures of balance performance over a relevant timeframe to ACL injuries (mean±SD; 18.8±2.6 weeks) in an uninjured sample (n = 33). No balance measure contained proportional bias demonstrated through the 95% CI of the gradient of the least products regression always including one (e.g. gradient±95% CI; CoP Path Length: 1.08±0.32; ML CoP CompInd: 0.81±0.55). Using the limits of agreement method, systematic bias was smaller than random bias in all assessed variables (e.g. Mean±95% CI of differences; Unilateral CoP Path Length: −7±48 cm; Unilateral ML CoP CompInd: −0.23±2.10). Relative consistency was assessed through CV and showed that non-linear measures were more consistent (e.g. unilateral balance ranging from 8.2-14.4%) compared to linear measures (e.g. unilateral balance ranging from 15.3-29.2%). This was the first study to suggest that CoP complexity is a more consistent measure of balance than traditional linear measures, and support its use in monitoring changes due to an intervention. There were no significant differences (*p*>0.05) in the observed changes between the dominant and non-dominant limbs for all variables suggesting limb dominance does not alter the natural variation in a measure over 19 weeks.

Non-linear measures of balance provide tools that are more consistent and are less susceptible to variation over a 19 week period. Magnitudes of systematic and random bias presented in Chapter 6 provide useable criteria for determining whether observed changes due to intervention lay outside natural variation of the variable and are therefore clinically meaningful (Figure 26), and will therefore allow more informed interpretation of future research into balance.

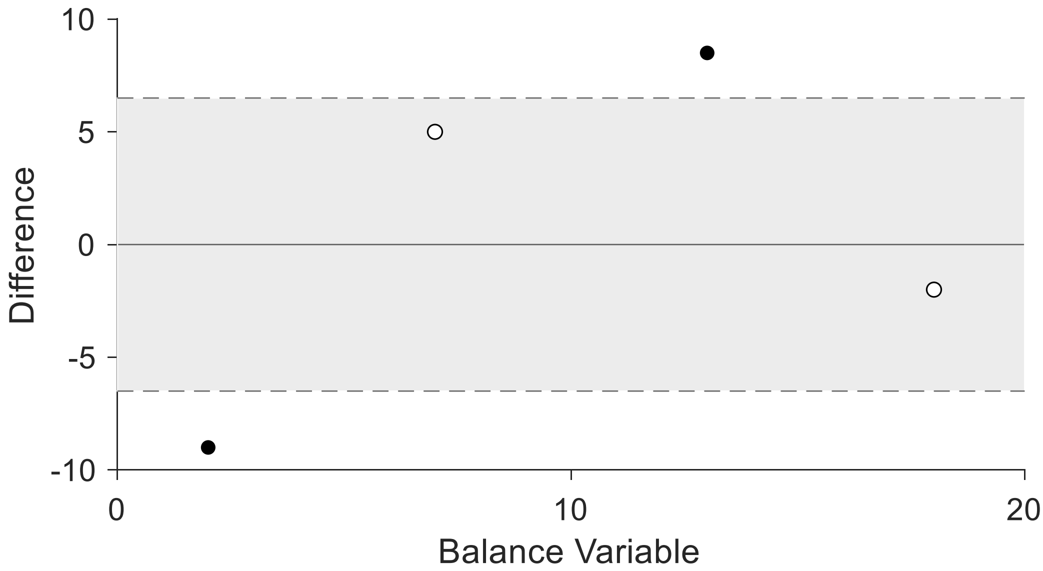

Figure 26. A Bland-Altman plot demonstrating the use of levels of consistency (dashed lines) to determine the clinical meaningfulness of future observed changes (meaningful - ●; not meaningful - ○)

8.1.4 Aim III

Identify whether ACL deficient and reconstructed knees differ in the identified biomechanical variables compared to ACL intact comparisons

Due the presence of mechanoreceptors within the intact ACL, injury to the ligament appears to result in a reduction in the proprioceptive function of the limb (Dhillon *et al.*, 2012). The findings of Chapter 7 do not support this proposed reduced proprioceptive function in the involved limb. Greater or the same balance ability was found in the involved limb of ACL injured participants before and after surgery compared to the uninvolved limb (e.g. pre-surgery mean±SD ML CoP SD; involved: 9.7±2.7 mm & uninvolved: 12.4±3.0 mm; $p<0.05$) and uninjured matched controls (e.g. 32 weeks post-surgery AP CoP mean velocity; involved: 42.5±13.8 mm/s & uninjured control: 54.7±19.7 mm/s; $p<0.05$). The finding of improved balance ability in ACL injured participants, assessed through linear measures of the CoP, is inconsistent with previous research that has identified that ACL deficient and reconstructed limbs have larger linear measures of balance performance (Howells *et al.*, 2011; Negahban *et al.*, 2014), and therefore poorer balance ability. There are several factors causing this contradiction such as differences in pre-injury balance ability between groups may have masked any effect ACL rupture had on balance, and that the selected task was unable to fully assess the proprioceptive function of the limb. These factors may limit the potential use of linear measures of balance to assess limb function in ACL injured participants in a clinical setting.

Non-linear characteristics were measured using MSE to estimate CoP complexity, an approach which has not previously been applied to ACL injured participants. Complexity of balance was used to provide new knowledge on the loss of complexity theory (Lipsitz & Goldberger, 1992) and musculoskeletal injuries, specifically ACL ruptures. The involved limb of the ACL injured participants had significantly lower complexity before surgery compared to uninjured control participants (e.g. mean±SD ML CoP CompInd; involved 4.90±1.29 & uninjured control: 5.98±0.93; $p<0.05$) supporting the theory that pathology is associated with a loss of complexity (Lipsitz & Goldberger, 1992). There were no significant differences ($p>0.05$) after surgery or between the limbs of ACL injured participants. Previous research into complexity and ACL injury has not identified differences between the involved limb and intact comparison limbs (Clark *et al.*, 2014; Negahban *et al.*, 2010), however the methodology used is associated with limitations (see section 4.8) which are addressed in this research. <u>These are the first data to support that ACL deficiency results in a loss of complexity, and therefore may offer a suitable variable to assess changes in function due to treatment.</u>

Linear measures of balance did not identify a negative outcome of ACL injury and therefore may be less suitable for use in the monitoring of function after ACL injury. Specifically, the data suggest that other factors not related to ACL injury, such as pre-injury proprioceptive function, have too greater effect on the measured variables to allow the changes due to injury to be detected. Complexity data suggests that non-linear variables may provide a more sensitive approach to assessing changes in the proprioceptive function of the involved limb. The loss of complexity was only significant pre-operatively suggesting ACL reconstruction may lead to changes in complexity and proprioceptive function.

8.1.5 Aim IV

Identify whether ACL reconstruction results in changes in the identified biomechanical variables, and explore the magnitude of these changes in relation to changes in an uninjured population

Previous research has reported that ACL reconstruction results in improvements in linear measure of unilateral balance in the involved limb, as described in Chapter 3. The measures of balance that have previously been used to establish the effect of ACL reconstructive surgery are limited to CoP path length. <u>Other linear measures of balance had yet to be used in assessing changes due to reconstructive surgery, but were assessed in Chapter 7</u>. There were <u>no significant changes in any linear measures of balance from pre-surgery to post-surgery</u>

measures (e.g. involved limb mean±SD 95%CI ellipse area; pre-surgery: 10.9±4.2 cm^2; 19 weeks post-surgery: 11.4±6.1 cm^2; 32 weeks post-surgery: 10.4±2.4 cm^2). This finding did not support the use of linear measures of balance to monitor the changes in limb function due to ACL injury and reconstructive surgery contradicting the evidence presented in Chapter 3. It is unclear why the presented data did not agree with other published research, however may be related to the limitations associated with the clinical nature of the recruitment and data collection which are described in sections 8.2.1 and 8.2.2, respectively.

<u>This thesis was the first to explore changes in CoP complexity due to any surgical intervention, including ACL reconstructive surgery</u>. There was a general trend in all measures of complexity for an increase at 19 weeks post-surgery compared to pre-surgery values with most (7 out of 8) participants then showing a decrease from 19 to 32 weeks post-surgery. Only <u>ML CoP MSE at 6.7 Hz showed statistically significant changes due to surgery</u> (involved limb mean±SD ML CoP MSE at 6.7 Hz; pre-surgery 0.90±0.27; 19 weeks post-surgery: 1.19±0.22; 32 weeks post-surgery: 1.10±0.23), suggesting that <u>ML complexity at lower frequencies may offer insight into the changes in limb function due to ACL reconstruction</u> and be suitable for the monitoring of changes due to treatment in ACL injured participants. <u>These findings provide new knowledge about the effects of ACL reconstructive surgery on the interacting systems contributing to the performance of a balance task, and lay the foundation for further investigations into the worth of non-linear measures in the assessment of changes due to clinical intervention.</u>

Previous research into changes in balance complexity have focussed solely on inference based statistics to establish whether a difference between groups is present, however to interpret the clinical meaningfulness of these changes their magnitude relative to natural variation should be considered. This thesis presented the only data on the natural variation, in the form of systematic, proportional, and random bias, of complexity measures without intervention over a clinically relevant timeframe (Chapter 6) and therefore could explore the potential clinical meaningfulness of complexity measures. The magnitude of changes in complexity compared to the variance of measures in an uninjured population supports the potential use of non-linear measures. Changes in MSE at 6.7 Hz for three of eight individuals were greater in magnitude than the random bias of uninjured participants. This suggests that these changes may be clinically meaningful, however no data are presented on long term outcomes meaning it is unclear whether these differences are favourable or what caused between participant differences. Future research into the link between changes in complexity due to treatment and long term outcomes is required to further explore the worth of such measures to inform clinical practice (see section 8.2.3).

Chapter 3

- Evidence supports improved proprioceptive function after ACL reconstructive surgery
- Currently employed analysis methods are limited

The synthesised evidence on changes in balance performance showed analysis of this task may provide a suitable approach to monitoring changes in ACL injured participants, and that there had been no investigation into non-linear approaches.

Chapter 6

- Complexity offers a more consistent measure than linear variables of balance over 19 weeks
- Provided useable measures of bias over a timeframe relevant to ACL injuries and treatment

Consistency data supported the use of complexity measures for monitoring changes over long time periods (19 weeks) and provided data to allow the interpretation of changes in a pathological population

Chapter 7

- ACL deficiency results in a loss of complexity
- ACL reconstructive surgery significantly increases CoP complexity

ACL injuries do result in changes in CoP complexity, however future research should aim to determine the link between these changes and outcomes from injury and treatment

Figure 27. Key new findings from this thesis, and how they informed each subsequent study

8.1.6 Summary

The findings of this thesis provide new evidence for the potential use of CoP complexity during balance tasks to assess changes in limb function which occur due to ACL injury and reconstructive surgery. This evidence was collected through progressive studies, which provided information that informed the approach of subsequent studies (

Figure **27**). Previous research had identified a loss of complexity in various pathological states, however the evidence presented in this thesis is the first to support the loss of complexity in relation to ACL injuries. No previous investigations into the effect of surgery have been conducted, however the findings of this thesis suggest that ACL reconstruction increases the complexity of the CoP. Increased CoP complexity suggests that surgery either increases the number of systems contributing to balance, or changes in the interaction between the already present systems. The mechanism for increased complexity is not fully understood, however the loss of complexity theory models this as a positive functional change related to the adaptability of the system (Lipsitz & Goldberger, 1992).

Additionally, the magnitudes of these changes were larger for certain ACL injured participants than the natural variation in uninjured participants meaning that these may be clinically relevant. The findings of this thesis should also be considered in relation to the clinical applicability of the methodology, showing that the employed methodologies are capable of identifying changes in ACL injured participants recruited from the general population with no specific sporting experience and using data collection approaches which are suitable for simplification.

8.2 Research Approach

Throughout this thesis a number of research approaches were considered and explored, and are related to a number of characteristics, limitations, and future directions. Three key approaches central to this thesis are discussed sequentially: collection of data suitable for clinical implementation, the applicability of results to the general population, and ACL injuries and a loss of complexity.

8.2.1 Collection of Data Suitable for Clinical Implementation

The aim of this thesis incorporated the need for the findings to be applicable to the current clinical practice for the treatment of ACL injuries, and to be suitable for simplification to allow their widespread implementation with minimal financial cost and required resources. The implementation of evidence based findings into clinical practice is associated with a number of constraints such as limited space and resources, which make traditional biomechanical methodologies difficult. This meant that innovative approaches were required to ensure the research met the applied nature of the thesis aim.

Biomechanical assessments often take place in dedicated laboratories with the use of in-built specialised equipment such as motion capture systems and force plates. The required resources for such facilities mean that they are unobtainable within most clinical environments. These restrictions led to the development of an innovative data collection protocol presented in Chapter 5 with consideration for the constraints of clinical practice. Specifically the method was suitable for use within a small clinic sized room (2.5 × 4.5 m) by using a custom rig for the housing of a force plate (Figure 28), and assessing movements which are able to be completed in a restricted area. Specialised equipment was still used to ensure the collection of high quality data, meaning the motion capture system was transported between data collection sites within each research site. Despite the use of motion capture equipment and piezoelectric force plates, this thesis was further delimited by analysing the CoP during balance tasks, data which are able to be collected through simpler and cheaper equipment (Huang *et al.*, 2013). Finally, although the data analysis process including a number of calculations, these were all conducted using a custom written MATLAB code meaning the methods can be used on any future CoP with minimal expertise using the created code.

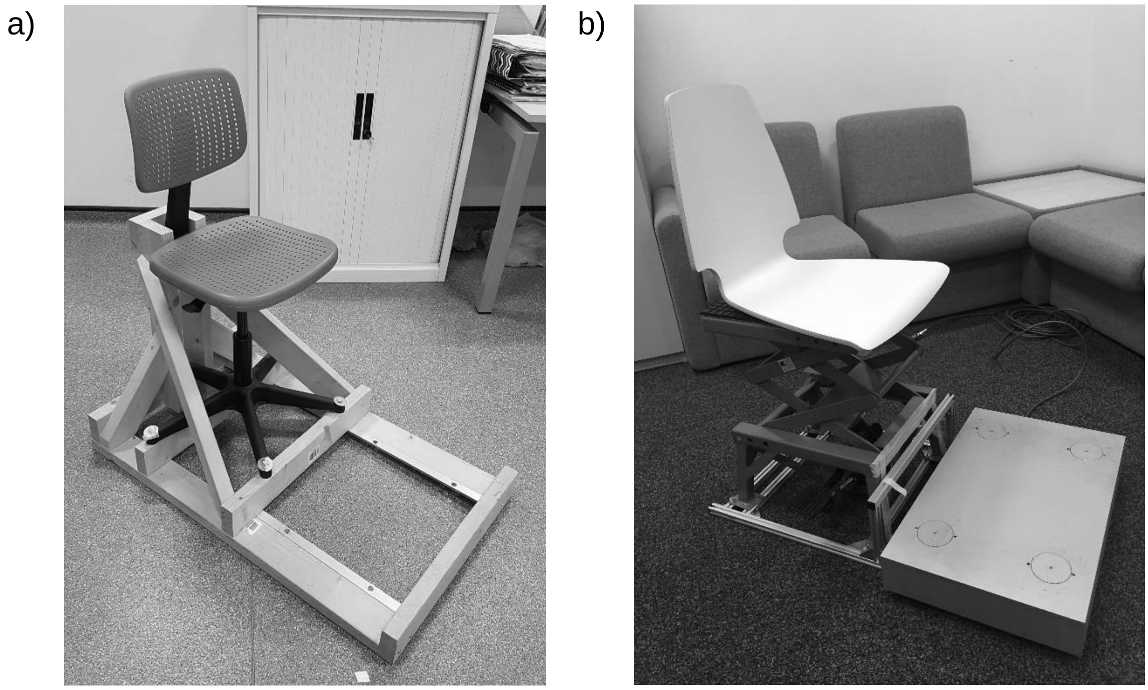

Figure 28. Development of a custom built seating rig to house a force plate from a) early to b) final design

The use of methodologies which are suitable for simplification and the evidence to support the collection of meaningful data within a clinical setting are a strength of this thesis. By collecting the data within the processes of general clinical practice the results provide data collection and analysis processes which are applicable to a wide range of health care settings, and are able to function within the National Health Service. The analysis of balance tasks is just one analysis approach to the collected data set, and different analyses may provide further support for the collection of biomechanical data using the presented methods.

One limitation which emerged through the research approach of clinically applicable data was the unavailability of clinic spaces outside of normal working hours (9:00 – 17:00) resulting in a number of potential participants being unable to participate. Data collections took place in the most convenient location for the recruited participants, however due to the rural nature of the County of Lincolnshire, ACL injured participants were often unable and unwilling to travel between the location of the Hospital and the University of Lincoln (approximate travel time of 1 hour). Data collections at Pilgrim Hospital took place in the Clinical Research Facility which although providing clinically applicable results, resulted in a reduced sample size and therefore limited the power of the statistical approaches used, and limited the potential research questions which could be addressed.

The collection of accurate and meaningful biomechanical data within a clinical setting would allow the further exploration of findings such as those presented in this thesis for the use within clinical practice. Specifically the development of cheaper and more accessible technologies that are able to measure the kinematics and kinetics of human movement is of worth. Technologies such as inertial measurement units (Lebel, Boissy, Hamel, & Duval, 2013) and mobile phone based accelerometers (Nishiguchi *et al.*, 2012) may allow the collection of complex data within pre-existing clinical spaces, and future research should investigate the suitability and worth of such approaches within clinical settings.

8.2.2 Participants

As outlined in the The National Ligament Registry (2019) although sporting activities are the most common cause of ACL injuries, median pre-injury Tegner activity score was approximately 3, representing non-pivoting recreation sports like swimming (Tegner & Lysholm, 1985), for the 9794 patients registered evidencing that the population suffering ACL injuries are often non-athletic. As the aim of this thesis concerned the exploration of variables to aid in the monitoring of such injuries, the findings needed to be relevant to both athletic and non-athletic populations. For findings to be applicable to a wide range of participant demographics it was assumed that changes in biomechanics due to ACL injury and reconstructive surgery would be consistent across different populations and that the selected recruitment procedures would allow a suitably broad sample.

To ensure a wide range of ACL patient demographics were included in this research, recruitment of ACL injured participants was through an orthopaedic surgeon's caseload within the National Health Service, as described in section 5.3. No inclusion or exclusion criteria related to activity or sporting level were imposed.

By assessing the biomechanics of participants not from a specific population, the potential impact of the findings of this thesis is wider due to their relation to the general population who suffer ACL injuries. If constraints had been placed on the tested sample, such as activity level, the findings may not have represented the changes which occur in other populations, limiting their worth.

Despite the advantage of wider applicability, the use of the general population resulted in a number of limitations in this thesis. During balance tasks participants were required to perform unilateral balance with their eyes closed for 20 s or as long as possible. A number of ACL injured, and uninjured participants were unable to complete this task for the full allotted time and therefore only 10 s of data were used. As described in section 4.7.3 the timescale which can be assessed in the MSE analysis is limited by the trial length, and the shortened trial led to frequencies that may provide further information into the performance of a balance task not being analysed, potentially limiting the findings. The inability to complete certain tasks highlights that the biomechanical proficiency of the recruited participants varied, and the proposed tasks may not be suitable for all ACL injured patients.

A further limitation related to the recruitment process, was differences in the timing of the intervention. As the research was delimited to recruit participants through the National Health Service, the timing of the intervention was based upon the schedule of the hospital, and this resulted in a wide range in the time since injury for participants (mean±SD: 34±29 weeks). It has previously been shown that lower limb biomechanics continue to change without surgical intervention for ACL injury

(Button, van Deursen, & Price, 2005). The variations in time between injury and the first data collection may have influenced the before surgery data and also the response to surgical intervention, resulting in inconsistent effects of treatment across the group.

A final limitation of the recruitment approach related to the barriers faced whilst trying to recruit ACL injured participants. During initial stages of this research recruitment of ACL injured participants was completed through an information sheet provided at initial consultation by the orthopaedic surgeon, and contact with the researcher was only initiated once the patient had been scheduled for ACL reconstructive surgery. It became apparent this approach was not successful in recruiting participants due to patients not returning calls, or not being interested in volunteering. To overcome this limitation changes were made to the recruitment process (Figure 29).

Original recruitment pathway	*Information sheet given to patient by surgeon and confirmed consent for researcher to contact*	*Patient contact number provided to researcher to query patient interest*	*Schedule data collection*
ACL patient pathway	Attend orthopaedic clinic	Scheduled for ACL reconstruction through booking service	Receive operation date and attend pre-assessment
Adapted recruitment pathway	*Researcher attended clinic and provided information sheet and discussed research with patient*	*Researcher contact patient to confirm willingness to participate once treatment decision confirmed*	*Schedule data collection*

Figure 29. Treatment and recruitment pathway for ACL injured participants

To increase the effectiveness of the recruitment pathway rather than initial contact with the researcher being once a treatment decision had been made and the patients were placed on the waiting list for surgery, the researcher attended fortnightly orthopaedic clinics at Pilgrim Hospital. Approximately eight ACL injured participants per year were eligible for recruitment meaning during most clinic visits no participants were recruited, however by ensuring that the research and the associated benefits were described in full by the researcher, recruitment was more successful lessening the impact of the limitations associated with the recruitment delimitations.

The results of this study suggested that a loss of complexity was present in ACL injured participants when completing a balance task with eyes closed, and that this was most prominent in timescales that may be more relevant to biological processes of balance (Chapter 7). The limitation of difficulties completing balance tasks for longer than 10 s led to complexity at lower frequencies not being analysed. Future research should therefore look to explore whether a loss of complexity can be observed in tasks which are easier to perform, such as balance with eyes open, to allow the assessment of complexity at further timescales. Additionally, the same research protocol should look to be implemented in additional hospitals with other orthopaedic surgeons to determine whether the identified findings are also observed with different practitioners.

8.2.3 ACL Injuries and a Loss of Complexity

One theoretical framework that was used to support the chosen analysis was the loss of complexity theory (Lipsitz & Goldberger, 1992). According to this theory the loss of the proprioceptive inputs which are provided by an intact ACL would result in a reduced output complexity. The results supported this hypothesis, however certain assumptions and limitations should be considered in relation to this finding. The loss of complexity theory assumes that a reduction in the inputs that contribute to the completion of a balance task result in a reduction in the complexity of the output (CoP) from that task. This assumption is based on the theory that more inputs and interactions between systems are directly related to the complexity of the signal, or the amount of biologically relevant information present within a signal.

The presented research was delimited in relation to the loss of complexity theory in the data collection methods and analysis. The CoP is suggested to relate to the mechanisms used to stabilise the participant's centre of mass. These mechanisms are created through inputs from the visual, vestibular, and somatosensory systems. During data collections, balance was completed with the participant's eyes closed to increase the relative contribution of the somatosensory system (Peterka, 2002), which is theorised to be affected by ACL injury (Dhillon *et al.*, 2012). Complexity of the CoP was therefore chosen to establish whether the changes in the somatosensory system caused by ACL rupture would lead to a loss of complexity in this task output.

The use of balance tests to assess whether ACL injury results in a loss of complexity has advantages in relation to the required resources required to collect this data in a clinical setting as described in section 8.2.1. Other advantages relate to the validation of such approaches to identify a loss of complexity which occur with pathology (Gow *et al.*, 2015). One limitation of balance tasks is their relevance to day to day activities. As described in section 4.2 the aim of balance is to minimise movement of the centre of mass, and within this thesis this was conducted during a static task with no external perturbations. Despite this approach being suitable for determining whether there has been a loss of complexity due to ACL injury, it may have limited relevance to more dynamic tasks which are completed during physical activity that may involve different mechanisms for controlling the centre of mass. Future research should therefore explore whether there are changes in the CoP during other more dynamic balance tasks such as unilateral squats or dual-task balance trials.

Delimitations related to the analysis tools to assess the loss of complexity due to ACL injury are also related to certain limitations. As described in section 4.5.2, complexity is a characteristic which is difficult to define, and measure. MSE analysis was used within this research to provide a statistical value of the regularity of a signal, where a lack of regularity was assumed to be related to an increased complexity. MSE allows this process to be completed over a number of timescales to gain a more thorough estimate of the overall complexity of a signal. MSE has similar advantages to the use of balance tasks in that it has previously been shown to be able to identify differences between pathological and healthy participants. A further advantage of MSE is by calculating the CompInd a single value that represents the complexity of the system is provided, which may provide clinicians with an easy to understand outcome measure for ACL injured participants.

The MSE algorithm, despite its use in identifying differences due to pathology, is related to certain limitations. Complexity does not only refer to the irregularity of the signal, but the amount of biologically relevant information. For example, a completely random signal would have high MSE due to its irregularity, however it would have low biological complexity (Rhea *et al.*, 2011). Therefore where a change in MSE is observed, it is not certain that this is due to a loss of complexity and may be resulting from other mechanisms which are currently not understood. The final limitation is that although complexity has been linked to disease and injury, as demonstrated in Chapter 7 other factors such as task proficiency may also alter complexity (Newell & Vaillancourt, 2001). Therefore, interpreting the causes of changes in complexity is difficult, and cannot be solely attributed to changes due to disease.

The differences in MSE of ACL injured participants in comparison to uninjured healthy controls and effect of surgery (Figure 30) suggest that the loss of complexity theory may be a suitable framework to explore the worth of such measures in the monitoring of ACL injuries. However, to address the limitations related to this approach the development of further analysis approaches which are able to explore the biological relevance of the information within the signal in addition to the regularity would enable more worthwhile conclusions to be drawn. Additionally, the exploration of summary statistics which take into account a number of analytical approaches may allow researchers to gain a more thorough understanding of complexity whilst keeping the outcome measure simple to facilitate implementation into clinical practice (see section 8.2.1).

To further explore the worth of the loss of complexity theory in the monitoring of ACL injuries future research should look to establish a link between observed changes in complexity and long term functional outcomes. For example when making return-to-sport decisions a neuromuscular integration of the inputs from the graft are suggested to be related to more favourable outcomes (Herbst *et al.*, 2015; Paterno *et al.*, 2010) and complexity may provide insight into the dynamics of the limb’s proprioceptive systems. Other outcomes could include quality of life, osteoarthritis prevalence, and re-injury risk.

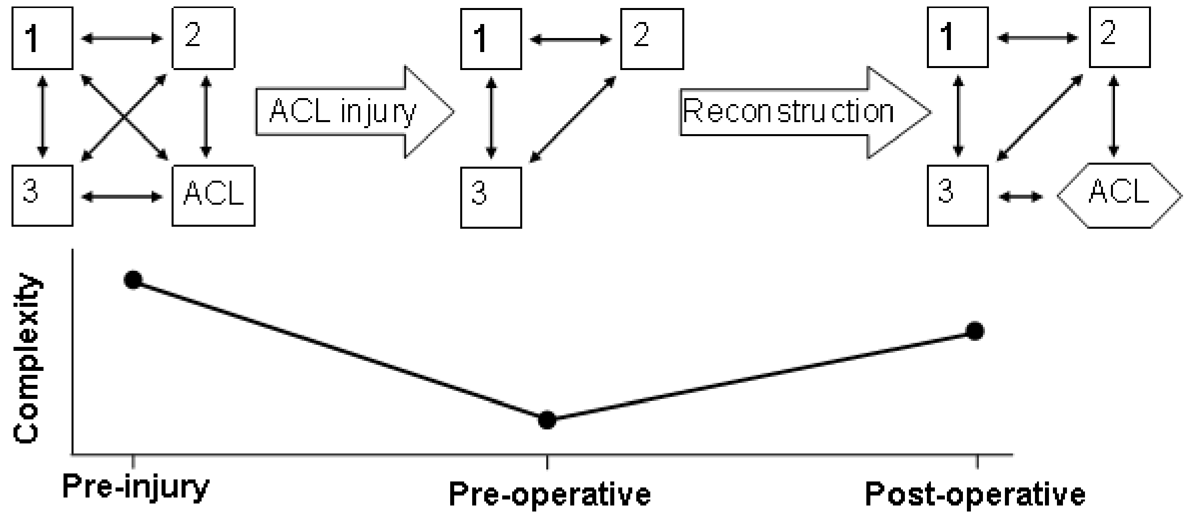

Figure 30. Diagram representing the findings of this thesis on complexity of balance outputs. The systems that contribute to the performance of a balance task, including the ACL, are modelled as boxes with arrows showing their interactions. The systems after ACL rupture and reconstruction are shown to represent the theoretical changes that occur due to injury and treatment. The theoretical changes in complexity, which are supported by the findings of this thesis, are presented below to show a loss with injury and an increase due to surgery.

9. Conclusion

9.1 Thesis Overview

The aim of this thesis was to explore what biomechanical variables are affected by ACL injury and reconstructive surgery and assess their potential worth in the monitoring of recovery from ACL injury and reconstructive surgery. To achieve this aim four study aims were developed and were addressed in the three studies presented in Chapters 3, 6, and 7.

9.1.1 Lower Limb Biomechanics Before and After Anterior Cruciate Ligament Reconstruction: A Systematic Review

- A synthesis of the evidence supported that ACL reconstructive surgery results in changes in balance, joint position sense, gait, stair ambulation, pivoting, and hopping tasks.
- Inconsistent changes were identified due to ACL reconstruction for gait, stair ambulation, pivoting, and hopping tasks.
- Movements assessing proprioceptive function (balance and joint position sense) appear to show consistent improvements due to ACL reconstruction.

9.1.2 Consistency of Linear and Non Linear Measures of Balance in an Uninjured Population

- Changes in linear and non-linear measures in an uninjured sample over 19 weeks did not present with proportional bias.
- Random bias of measures of balance between visits was greater in magnitude than systematic bias.
- Complexity variables had greater relative consistency than linear measures of balance.

- There were no differences in consistency between the dominant and non-dominant limb.

9.1.3 The Effect of ACL Injury and Reconstruction on Balance Performance and Complexity

- The involved limb of ACL injured participants before and after reconstructive surgery appeared to have the same, or greater balance ability compared to the uninvolved limb and uninjured control participants.
- ACL reconstruction did not result in any significant changes in linear measures of balance in the involved limb of ACL injured participants.
- The involved limb of the ACL injured participants had significantly lower complexity compared to uninjured control participants.
- ACL reconstruction resulted in a significant increase in ML complexity in the involved limb of ACL injured participants.

9.2 Thesis Findings

A number of main conclusions can be drawn regarding the use of biomechanical measures for the monitoring of recovery from ACL injuries through reconstructive surgery. The main conclusions are presented, in addition to the main limitations and future directions.

9.2.1 Main Findings

- ACL reconstruction results in changes in biomechanics of the lower limbs during a number of movement tasks
- Non-linear variables (e.g. complexity) of balance performance appear to provide more consistent measures in uninjured participants suggesting these may offer suitable approaches to monitor changes in injured participants

- Despite current evidence (e.g. Howells *et al.*, 2011), linear measures of balance do not appear to be affected by ACL injury or reconstructive surgery and therefore are unsuitable for monitoring changes in ACL injured participants
- CoP complexity during balance, measured using the MSE algorithm, is affected by ACL injury and reconstruction, and changes may be clinically meaningful and offer insight into the function of the involved limb
- Complexity at lower frequencies (e.g. 6.7 Hz) which may relate to biological processed appeared to be more sensitive at identifying differences between uninjured and injured participants.

9.2.2 Main Limitations

- This study was conducted with consideration of the constraints of clinical practice, and only considered approaches which would be suitable for simplification to allow implementation into practice. This approach may have excluded a number of worthwhile measures which would provide further information about the function of the ACL injured limb.
- ACL injured participants were recruited from the general population and therefore had varying levels of sporting activity. This broad range of participant demographics resulted in difficulties completing certain tasks within the data collection protocol, resulting in limitations of the analysis. Additionally the range of task proficiency may have resulted in less consistent changes in biomechanical measures due to ACL injury and reconstruction.
- The data supported the loss of complexity with ACL injury, however these outcomes were not able to be linked to long term function outcomes so it is currently unclear whether changes in complexity are related to desirable treatment outcomes.
- The data presented in this thesis were from a limited number of ACL injured participants resulting in limited confidence on the generalisability of the

findings. Increasing the sample size, and the surgical procedure utilised would build the confidence in the conclusions and support its generalisability to other clinical settings.

9.2.3 Main Future Directions

- Exploration of the use of developing technologies to allow the collection of biomechanical variables by people with little expertise and access to minimal resources
- Explore whether the loss of complexity identified in this research is present in less demanding balance tasks which allow lower frequency complexity to assessed.
- Establish the link between complexity of balance and functional outcomes from ACL reconstructive surgery to explore their potential use in improving injury prognosis.

9.3 Thesis Conclusion

The main findings of this thesis suggest that non-linear biomechanical measures of balance tasks may have worth in the monitoring of changes which occur due to ACL injury and reconstruction. The collection of such data in a clinical setting also provides evidence to suggest that the implementation of biomechanical approaches to other clinical settings is viable. The variation in task proficiency of ACL patients within the National Health Service provides a barrier to the widespread implementation of these findings and exploration of more easily performed tasks is warranted. The presented data although supporting the worth of complexity measures, do not provide information on whether differences in the magnitude of changes due to treatment are related to more favourable outcomes such as reinjury risk and osteoarthritis prevalence, and this should therefore be explored in future studies.

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11. Appendices

11.1 Appendix A

QUALITY ASSESSMENT TOOL FOR ONE GROUP PRETEST-POSTTEST EXPERIMENTAL RESEARCH: QUALITY ASSESSMENT FORM

UNIVERSITY OF LINCOLN
LINCOLN INSTITUTE FOR HEALTH

ARTICLE CODE: ________________ YEAR: ________ 1st AUTHOR: ______________________________

REVIEWER (initials):____ DATE: _____ / _____ / _____

COMPONENT RATINGS

A) PARTICIPANTS

Q1. Are the individuals selected to participate in the study likely to be representative of the target population?

1 Very likely
2 Somewhat likely
3 Not likely
4 Can't tell

Section	STRONG	MODERATE	WEAK
A) Participants			

Strong = answer 1; Moderate = answer 2; Weak = answers 3 & 4

B) WITHDRAWALS AND DROP-OUTS

Q1. Indicate the percentage of participants completing the study.

1 80 -100%
2 60 - 79%
3 less than 60%
4 Can't tell

Section	STRONG	MODERATE	WEAK
B) Withdrawals and Drop-outs			

Q1: Strong = answer 1; Moderate = answer 2; Weak = answers 3 & 4

C) STUDY DESIGN

Q1. Were the timings of the data collections and interventions consistent for all participants?

1 Yes
2 No
3 Can't tell

Q2. Is it likely that any differences in timings influenced the results?

1 Yes
2 No

Section	STRONG	MODERATE	WEAK
C) Study Design			

If Q1 is yes (1) then the score is strong. If Q1 is no (2) then the score is moderate (Q2 = no) or weak (Q2 = yes) depending on Q2. If Q1 is can't tell (3) then the score is weak.

D) <u>INTERVENTION INTEGRITY</u>

Q1. Was the intervention consistent across all participants?

1 Yes
2 No
3 Can't tell

Q2. Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?

1 Yes
2 No
3 Can't tell

Section	STRONG	MODERATE	WEAK
D) Intervention Integrity			

Strong = Q1 answer 1 (yes) & Q2 answer 2 (no). Moderate = Q1 answer 1 (yes) & Q2 answer 3 (can't tell) OR Q1 answer 3 (can't tell) & Q2 answer 2 (no). Weak = either Q1 answer 2 (no) OR Q2 answer 1 (yes).

E) <u>DATA COLLECTION</u>

Q1. Were pre- and post-tests identical?

1 Yes
2 No

Q2. Were differences like to alter the results?

1 Yes
2 No

Section	STRONG	MODERATE	WEAK
E) Data Collection			

If Q1 is yes (1) then score is strong. If Q1 is no (2) then score is either moderate (Q2 = no) or weak (Q2 = yes) depending on Q2.

SUMMARY

Section	STRONG	MODERATE	WEAK
A) Participants			
B) Withdrawals and Drop-outs			
C) Study Design			
D) Intervention Integrity			
E) Data Collection			

GLOBAL RATING

Using the summary above please provide a global rating for the assessed research.

<u>Guidance</u>

STRONG – no weak ratings and less than four moderate ratings
MODERATE – less than two weak ratings
WEAK – two or more weak ratings

	STRONG	MODERATE	WEAK
OVERALL			

11.2 Appendix B

ACL Rehabilitation Programme

You should have a physiotherapy appointment at the time of discharge from the hospital. If you do not have an appointment within a week of discharge, please contact my secretary. You may be given a brace to use from 1 to 4 weeks post-operatively

WEEK ONE
In the first few days after surgery your knee will be swollen and you can expect some pain. For comfort and to speed up the removal of swelling follow the RICE programme.
REST as much as possible
ICE the knee at regular intervals for the first 48 hours
COMPRESSION – leave the knee bandaged for at least 48 hours or until swelling subsides
ELEVATION of your leg is recommended when sitting

EXERCISES
You are encouraged to develop a range of motion from full extension (0^o) to 90^o flexion. The exercises described below will help improve the condition of the muscle about the knee joint and enhance your stability.

Knee Stretch
Sit on a flat surface (floor, bed or lounge chair) with you leg straight our in front of you. Place a pillow or cushion under your heel. Relax the muscles in your leg and let gravity straighten the knee fully. Hold this position for as long as possible. You should spend 20 minutes twice per day in this position.

Knee Flexion
Sit on a table or high chair with the knee bent comfortably. Cross your operated leg over the top of your good leg at the ankle. Use your good leg to extend to 45^o (half way to full extension) and then back to 90^o. In a controlled manner do three sets of repetitions with one minute rests between each set. You should try two or three sessions each day aiming to get the knee bending easily to 90^o.

Static Quadriceps
Sit or lie with the operated leg straight our in front of you – tighten thigh muscle and hold for 5 seconds. Repeat three sets of ten and perform ten times each day.

WALKING
If you have a splint or brace use it when walking. You do not need to wear your splint when sitting or sleeping. Crutches improve balance during walking. Use your crutches outside, particularly on uneven ground or when moving amongst people. At home you do not need to use your crutches. Practice walking without crutches in an uncluttered room, aiming for a heel toe walking pattern.

STANDING
- holding on to a table or other support, practice taking weight on the operated leg. For 30 seconds, hold a position with the knee as straight as possible with all your weight on the leg. Do this five times, having a rest of one minute between each set.
- to progress this exercise, maintain the one-legged stance and push up at the ankle to stand on your toes. Hold this position for 10 seconds.
- further progression of this exercise – start with a one-leg stance and the knee extended. Flex the knee about 30^o, then extend. Do three sets of 10 repetitions.
- sideways step – holding on to a table or wall bar, feet apart approximately 45cm, step sideways slowly, two steps left then two steps right. Repeat these steps 20 times.

WEEK TWO TO FOUR

WALKING
Spend more time walking without crutches. Increase your walking outside up to 15-20 minutes per day. Take your crutches if necessary for longer walks on uneven terrain and amongst crowds. Practice walking sideways and backwards. Dispense with your splint once you are confident walking without crutches.

EXCERCISES
Continue your previous exercises from week one and progress.

Knee Stretch
You should now be able to stretch the knee fully straight without difficulty. If your knee is still tight you should spend more time on stretching to make sure the knee straightens fully.

Knee Flexion
Once you can flex the knee easily to 90^{0} with support from your good leg, continue this exercise with your operated leg without support.

Hamstring
Lying on your stomach with your knee extended, cross your operated leg over your good leg at the ankle. Now flex and use the good leg to assist the motion. Do three sets and rest for one minute between sets.

STANDING
Progress your standing exercise by not holding a support. Increase the time you spend standing on one leg, flexing and extending 30^{0}. As you are able, do this with your eyes closed.

EXERCLYCLE
Once you can flex your knee easily to 90^{0} you can begin exercycling. Put the seat up higher if necessary. Make it easy so you do not have to push hard on the pedals. Build up to at least 20 minutes a day.

POOL
If you have access to a pool this can be helpful for early rehabilitation. In the pool progress your walking exercises in chest deep water. Start kicking but do not kick hard.

DO NOT use breaststroke (frog) kick as this involves abnormal knee movement.

GYMNASIUM
If you have access to a gymnasium you can use the following equipment:
- stepping machine
- leg press – quadriceps (closed chain)
- leg curl – hamstrings
- rower

Make these exercises easy at first with little or no resistance and slow speed.

DRIVING

Once you are confident walking without crutches and without your splint you can start driving. You *must* have full control of your leg to be safe driving.

PHYSIOTHERAPY
At this stage you may need treatment to help regain full range of movement and strength. Arrange this through you Physiotherapist.

WEEK FOUR TO TEN

EXERCYCLE
You should be able to manage up to 30 minutes in one session. Add in some resistance for short periods to work your muscles harder.

WALKING
Walk up to 30 to 40 minutes each day. Increase your stride length and speed as you get more confident. Start figure eight walking with large 20 to 30 metre length figure eights. Do ten in each direction. As you get more confident, decrease the side of the figure eight to five to ten metres and increase your walking speed.

Square Walking: walk 20 paces then turn left, another 20 paces then turn left, another 20 paces then turn left and return to the start point. Do ten in each direction.

Walking Swerves: position ten objects (real or imaginary) at ten feet intervals directly in front of you. Weave between the objects. Progress this exercise by increasing the speed of walking.

JOGGING
Some people *may* be ready to start light jogging at six weeks following surgery. If you are quite comfortable cycling for up to 30 minutes you can start light jogging in a straight line on even ground. Ensure you do not limp by keeping stride short and slow.

EXERCISES
Your Physiotherapist will work through the following exercises with you:
▪ strengthening of lower abdominals and gluteals – to promote strength around the pelvis and so gain stability.
▪ walking with correct alignment and co-contraction (using gluteals, hamstrings and quadriceps) – may develop new pains if poor alignment, limping, or not tightening muscles correctly.
▪ gymnasium for closed kinetic chain exercise – leg press, squats, calf raises, phantom chair, step-up's and step-down's, lunges, hopping, skipping.
▪ balance on balance board, rebounder, exa -slide, swiss ball – poor balance could contribute to the risk of re-injury. You may need to be reviewed by a Sports Physician at this stage to ensure adequate progress is being made.

WEEK TEN TO SIXTEEN

EXERCYCLE / BICYCLE
Continue cycling to the limit of your tolerance.

JOGGING
You can increase your jogging as you gain confidence. Progress by incorporating sideways and backwards jogging. Progress by introducing figure eight and square jogging.

EXERCISES
Your Physiotherapist will work through the following exercises with you:
- gymnasium for open kinetic chain exercises – leg curl, hip extension, hip abduction.

All gym exercises need to be progressed through various types of strengthening eg. concentric, eccentric, catch-exercises as well as varying speeds and directions of movement. A generalised gym programme for upper limb and trunk can be formalised with your trainer.

SPORTS SPECIFIC REHABILITATION
It is necessary to co-ordinate the strengthening and balance work so that specific drills can be practiced and perfected before a return to your particulate sport. These will include jumping and landing, hopping, carioca running and pylometrics.
The addition of ball skills and grids will precede a return to training sessions – initially training will be un-opposed and then against opposition as capable.
A fitness test including co-ordination, resisted movement, speed and balance will precede a return to sport.
NB: at *no* stage should exercises cause an increase in pain or swelling – if this happens discuss with your Physiotherapist who will normally suggest a return to the previous level of activity which was asymptomatic.

COMPETITIVE SPORT TRAINING
You can start training for competitive sport after six to twelve months from surgery, once you are confident in jogging and passed a fitness test.

COMPETITIVE CONTACT SPORT
You may be ready for competitive contact sport by nine to twelve months following surgery.

11.3 Appendix C

Mean ± 95% confidence interval (CI) of the difference (systematic and random bias), least products regression slope ± 95% CI (proportional bias), and coefficient of variation (%CV) between linear measures of unilateral balance on the non-dominant limb at baseline and 19 weeks

	Mean Difference	**Random Bias (95% CI)**	**Regression Slope**	**CV (%)**
ML SD (mm)	-0.46	8.19	0.75	21.08
AP SD (mm)	-0.80	5.21	0.94	15.88
ML Velocity (mm/s)	-3.40	36.30	1.01	19.93
AP Velocity (mm/s)	-2.66	41.29	0.97	20.96
Resultant Velocity (mm/s)	-4.90	57.50	0.98	19.54
Path Length (cm)	-4.94	57.96	0.98	19.58
95% CI Ellipse (cm^2)	-1.91	16.34	0.75	31.40

11.4 Appendix D

Mean ± 95% confidence interval (CI) of the difference (systematic and random bias), least products regression slope ± 95% CI (proportional bias), and coefficient of variation (%CV) between linear measures of bilateral balance at baseline and 19 weeks

	Mean Difference	**Random Bias (95% CI)**	**Regression Slope**	**CV (%)**
ML SD (mm)	0.42	4.05	1.51	18.67
AP SD (mm)	-0.06	1.92	1.00	28.12
ML Velocity (mm/s)	-0.41	3.84	1.05	17.75
AP Velocity (mm/s)	0.11	6.89	1.05	19.43
Resultant Velocity (mm/s)	-0.20	7.77	1.06	17.09
Path Length (cm)	-0.38	15.17	1.06	16.96
95% CI Ellipse (cm^2)	0.08	2.08	1.11	35.41

11.5 Appendix E

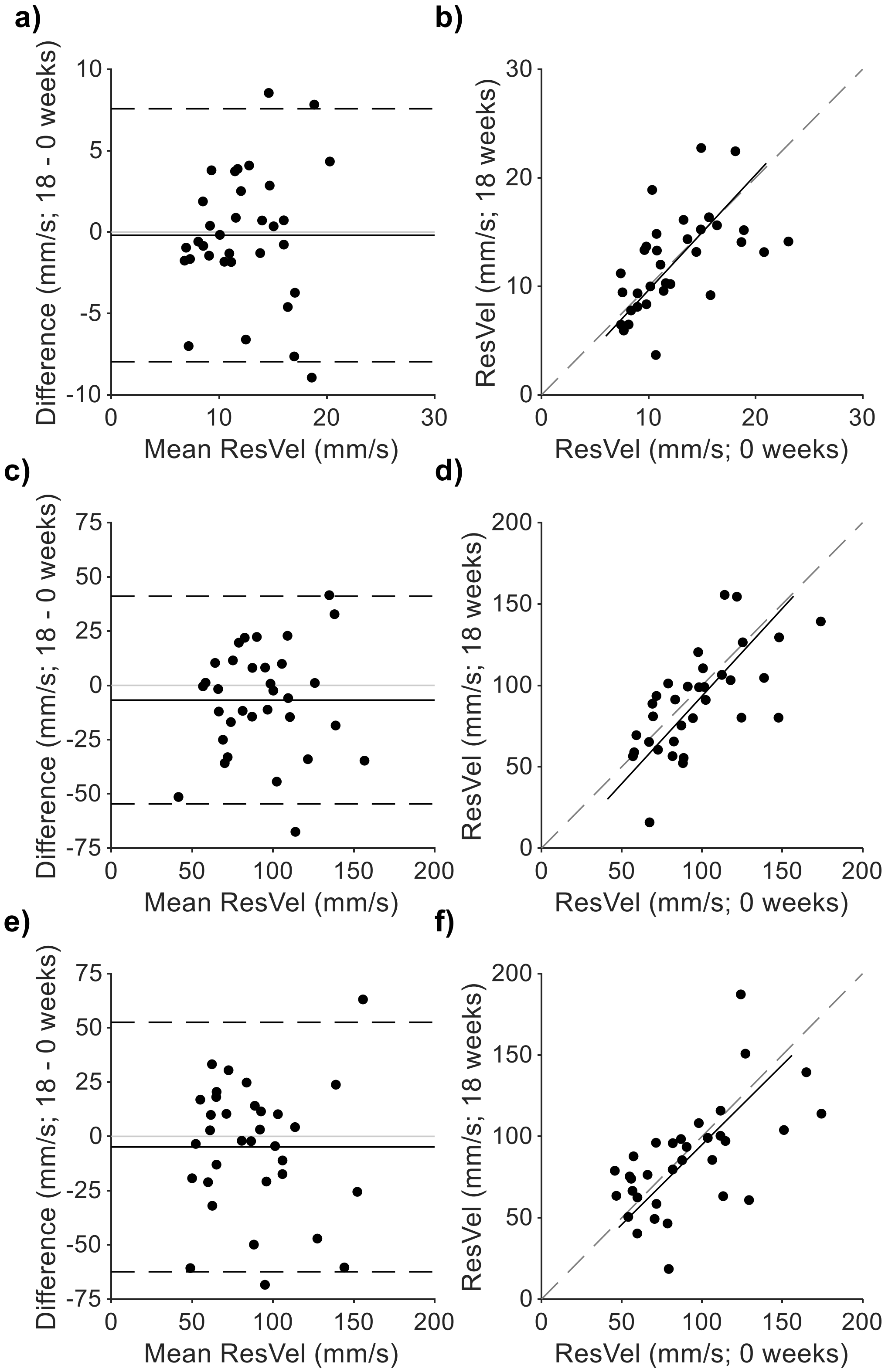

Figure E. Bland-Altman (a, c, e; systematic and random bias) and least products regression (b, d, f; proportional bias) plots of mean resultant velocity (ResVel) during bilateral balance (a, b), and unilateral balance on the dominant (c, d) and non-dominant limb (e, f) between 0 and 19 weeks