Neuromuscular markers of non-contact anterior cruciate ligament injury during dynamic tasks

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Abstract

This thesis explores the added value of neuromuscular markers of non-contact ACL injury risk. First, a systematic review was conducted to establish the existing evidence from the literature. The outcome of this review served to select candidate neuromuscular observations to be included in a large-scale prospective study. The two main risk factors that were found to be supported with some evidence were the (i) hamstrings to quadriceps ratio (HQR) and (ii) a unique neuromuscular activation pattern during side cutting. These parameters were included in a prospective cohort study to establish injury risk factors. After two years of data collection we still had not seen any non-contact ACL injuries in our study sample. As a fall back plan, the collected database was explored in search of evidence that can help support previous findings. First, we showed that quadriceps strength meaningfully affects HQRs (as quadriceps gets stronger, HQR value gets lower), introducing bias when profiling individuals for injury risk. We demonstrated how through an allometric approach this bias can be removed for future investigation into HQR as a risk factor for injury. Second, we evaluated whether HQR explains neuromuscular activations of the knee musculature during the execution a dynamic task. We found that variations between individuals in muscle (co-)activations were not explained by differences in muscle strength or HQR. Overall, through this work we have obtained a clear overview on the limited evidence on neuromuscular risk factors of non-contact ACL injury, provided in-depth insights into HQR as a measure of muscular capacity, and demonstrated how one should be

careful in linking observations of muscular capacity with observations of muscular activation and vice versa.

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Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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List of Abbreviations, Acronyms and Symbols

β	beta coefficient
x^2	chi-square
ACL	anterior cruciate ligament
ACL-D	ACL deficient
ACL-R	ACL reconstruction
ATSF	anterior tibial shear force
BF	biceps femoris
CI	confidence interval
DHQR	dynamic/functional hamstrings to quadriceps ratio
EMG	electromyography
Hcon	hamstrings concentric
Hecc	hamstrings eccentric
HQR	hamstrings to quadriceps ratio
Qcon	quadriceps concentric
SDHQR	Scaled dynamic hamstrings to quadriceps ratio
SHQR	scaled hamstrings to quadriceps ratio
ST	semitendinosus
VL	vastus lateralis
VM	vastus medialis

Chapter 1 General Introduction

The knee joint is one of the largest joints in the human anatomy and one of the most important stabilizers during dynamic weight-bearing activities. There is a major demand on this joint on a daily basis covering movements such as walking, running, and jumping. A severe impairment on this joint may significantly impair an individual’s quality of life in hindering functional efficiency to perform day-to-day activities. In a sporting environment, the importance to safeguard this joint from being injured is arguably even more crucial, with a particularly prominent need for an intact Anterior Cruciate Ligament (ACL). The ACL connects the lateral femoral condyle (thigh bone) to the medial tibial plateau (shin bone). The main functions of the ACL is to prevent excessive anterior translation of the tibia relative to the femur (keeping the shin bone from moving too far forward), prevent excessive internal rotation of the tibia (inward rotation of the shin bone), and prevent knee hyperextension. The ACL also helps protect the knee from excessive valgus forces (bending the knee sideways toward the body). By preventing these motions, the ACL provides stability to the knee joint and allows for very dynamic motions. When the ACL is stretched or torn, the knee can become very unstable and will oftentimes "give way". Although surgical repair after ACL rupture is a common treatment, the ligament’s functionality will often not be the same as prior to injury and an athlete who suffers an ACL injury is often unable to perform similarly during dynamic activities as before the injury (Kvist et al. 2005), possibly added with long term health consequences such as post traumatic knee osteoarthritis (Simon et al. 2015).

Due to its crucial role the ACL is the most commonly injured knee ligament during sports participation (Kiapour and Murray 2014, Kapoor et al. 2004). In most cases, ACL injury derives from a non-contact situation with nearly three quarters of ACL injuries being non-contact injuries (Boden et al. 2000, McNair et al. 1990). In the United States, an estimated 250,000 ACL injuries occur each year, many in young, active individuals with injury rates as high as 2.8 and 3.2 injuries per 10,000 hours of exposure in women's collegiate basketball and soccer, respectively (Smith et al. 2012a, Griffin et al. 2006). In the United Kingdom alone, the National Ligament Registry of 2017 recorded 9,378 cases of individuals who acquired an ACL injury between December 2012 and January 2016, amounting to approximately 3,000 annual cases, where 85% of the individuals who suffered an ACL injury engaged in sport activities (Gabr et al. 2017). Within the sport setting, when comparing elite and amateur levels of competition, the rate of injury is considerably higher in professional or elite levels (ranging from 0.15% to 3.67%) than amateur levels (ranging from 0.03% and 1.62%) (Moses et al. 2012). Females more often acquire an ACL injury compared to their male counterparts within the same sport setting and level of competition (Walden et al. 2011, Prodromos et al. 2007). The high ACL injury incidence and prevalence remains to be a major concern, justifying a need for continued research efforts towards a greater understanding of injury risk factors. Such understanding is important to support the development of injury prevention programs.

Research efforts towards preventing ACL injury have seen a major growth throughout the past decades. A particular emphasis has been on studies trying to identify risk factors associated with non-contact ACL injury. There is, however, general consensus that certain risk factors are still not fully understood, particularly concerning some of the risk factors which are considered to be modifiable (Volpi et al. 2016, Wojtys 2015, Sandra J. Shultz et al. 2015, Shultz 2008). The exploration of these risk factors is not an easy task, as in many cases this requires costly large-scale prospective cohort studies. Only through such prospective cohort studies one can ensure that markers of non-contact ACL injuries become fully understood and that preventative programs are supported with strong evidence. The importance of acquiring strong research evidence has been highlighted in the ACL injury prevention model (Donnelly et al. 2012), an adaptation from the Translating Research Into Injury Prevention Practice (TRIPP) model (Finch 2006) and the preceding 4-step injury prevention model (van Mechelen et al. 1992).

One particular category of modifiable non-contact ACL injury risk factors is that of the so-called neuromuscular risk factors. Neuromuscular risk factors encompass often intertwined facets of the neural and muscular systems, and previous research has focused mainly on knee musculature. The knee musculature consists mainly of the knee flexors (hamstrings) and extensors (quadriceps). Neuromuscular capacity of these muscles can be defined as the ability of the muscles to generate sufficient contractile force at the right time during dynamic tasks, often assessed through measures of strength and/or co-activation. In other words, neuromuscular capacity associated with non-contact ACL injury includes the study of (i) weakness and imbalance of hamstring and quadriceps muscle strength and (ii) imbalance of hamstring and quadriceps co-contractions or co-activations during dynamic tasks. Unfortunately, the evidence underpinning the extent to which deficits in muscle strength or aberrant muscle co-activations, or a combination of the two, lead to an increased risk of an ACL injury is still largely unknown.

In summary, there is a need for high quality research to better understand neuromuscular risk factors of non-contact ACL injury in dynamic sporting activities. Obtaining a better understanding of neuromuscular capacity as a risk factor for ACL injury requires prospective cohort studies that can reveal a causal relationship between deviating neuromuscular observations and consequent injury. Ultimately, this will enable a more robust development of screening tools to identify those who are more susceptible of sustaining non-contact ACL injury in dynamic sporting activities and provide evidence in support of the continued development of injury prevention programs.

Chapter 2 Literature Review

2.1 Introduction

This chapter aims to review the research evidence relating to neuromuscular risk factors of a non-contact ACL injury. The review will cover (i) the epidemiology of non-contact ACL injuries, (ii) framework for injury prevention research, (iii) mechanisms of ACL injury in a dynamic setting, (iv) existing beliefs concerning muscular capacity and neuromuscular (co-)activations as risk factor for non-contact ACL injury and (v) importance of prospective evidence in the neuromuscular literature associated with non-contact ACL injury. This review will specifically cover those aspects within a dynamic sport setting and only focus on non-contact ACL injury. At the end of the literature review, the aim and objectives of the thesis will be described.

2.2 Epidemiology of non-contact ACL injuries

2.2.1 Anatomy of the ACL: Why is it prone to injury?

The knee joint encapsulates the thighbone (femur), shinbone (tibia), fibula and kneecap (patella) in a complex articulation. Surrounding the knee are ligaments and tendons to aid in the function of the knee. The ligaments hold the knee bones together as passive constraints, providing stability to the knee while tendons connect the knee bones to the leg muscles that also provide stability but primarily move the knee joint. Ligaments are tough yet elastic fibrous tissues. On the medial and lateral side of the knee are the medial collateral ligament (MCL) and lateral collateral ligament (LCL). The MCL and LCL prevent the knee from moving too far in a side-to side direction, i.e. adduction or abduction. Inside the knee joint, two other important ligaments stretch between the femur and the tibia, the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL). These ligaments cross each other (hence the name cruciate) and primarily control the front-to-back movement of the knee joint, with the ACL preventing anterior tibial translation and PCL preventing posterior tibial translation. Some further detail on the function of the ACL was already provided in Chapter 1.

Participation in sports activities requires rapid and fast-paced movements whether it be leaping, running or side-cutting; these movements can lead to high intersegmental forces (typically referred to as joint reaction forces) and consequently high stresses on the various ligaments. Considering that the knee extensors play a primary role in generating these movements, particularly the ACL is often exposed to stress from the high anterior tibial shear forces these extensors create (Beynnon and Fleming 1998, DeMorat et al. 2004, Hashemi et al. 2011, Sell et al. 2007, Yu and Garrett 2007). Add to that the notion that a non-sagittal component to the movement can add further loading of the ACL (Markolf et al. 1995), that a lack of anticipation also increases the loading to the knee in general (Almonroeder et al. 2015), and that repetitive knee loading can lead to detrimental fatigue of the ligament tissues (Wojtys et al. 2016). This makes that the ACL is a vulnerable ligament in sports involving rapid manoeuvres.

2.2.2 ACL injury incidence and its societal impact

Reviews of national registries indicate ACL injury incidences of 34 per 100,000 people in Norway, 38 per 100,000 people in Denmark, 32 per 100,000 people in Sweden, 32 per 100,000 people in Germany and 37 per 100,000 people in New Zealand (Neeraj 2018). These incidences are a great concern for health care (Gabr et al. 2017, Smith et al. 2012a, Griffin et al. 2006), and show an incrementally increased probability of getting injured due to participation in sports (Sayampanathan et al. 2017), playing at an elite level (Moses et al. 2012) and being female (Walden et al. 2011, Prodromos et al. 2007), respectively. These high incidences cause a considerable socio-economic burden, particularly with reconstructive surgery often needed after ACL injury. For example, in the US alone, over 100,000 surgeries are done each year. Besides the orthopedic challenges associated with these surgeries, these also require extensive post-operative rehabilitation typically of 6-12 months in duration (Csintalan et al. 2008). As such, the treatment and rehabilitation of ACL injuries has been associated with an estimated total annual cost of $3 billion for the US. Also, beyond the rehabilitation processes there is a considerable post traumatic concern, with the majority of the ACL injured population having residual muscle imbalances, muscle weakness, and altered lower extremity mechanics at the time of return-to-play, often persisting for up to two years following ACL reconstruction (Nagelli and Hewett 2017). In the worst case, and this is the case for up to 29% of all ACL reconstruction patients, they will suffer a secondary tear (Queen 2017). Finally, there are also possible long term concerns, with those who suffered an ACL injury being more susceptible to develop knee osteoarthritis (Hill et al. 2005), affecting 59% up to 70% of the injured population (American Academy of Orthopaedic Surgeons 2007).

2.3 Framework for injury prevention research

Considering the burden of ACL injuries on our society, a systematic approach in the prevention of this injury is important. Almost three decades ago an injury prevention framework was proposed (van Mechelen et al. 1992). Several recent adaptations have been introduced in the literature (Van Tiggelen et al. 2008, Finch 2006). With regards to ACL injury, a specific framework for ACL prevention incorporates recent evidence surrounding the non-contact ACL injury literature as shown in Figure 2.1 (Donnelly et al. 2012).

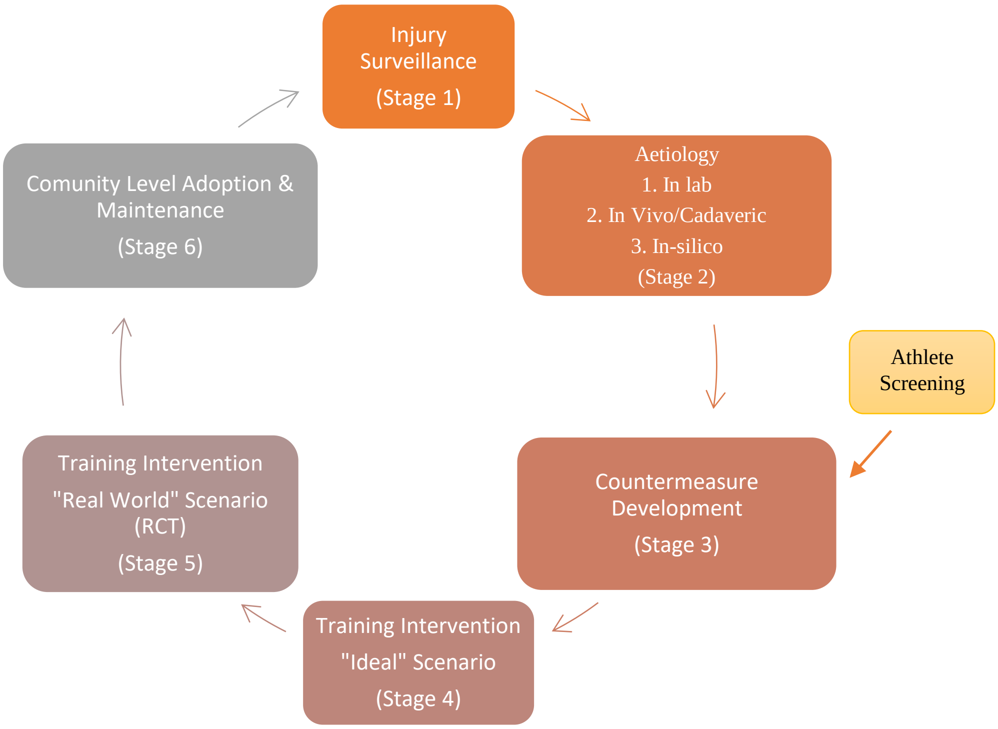

Figure 2.1 Non-contact ACL injury prevention framework (Donnelly et al. 2012)

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Adopted from the TRIPP framework (Finch 2006), the Donnelly framework is specific to risk factors associated with non-contact ACL injuries to support the design of ACL injury prevention training protocols. The first four steps of this framework are similar with the TRIPP framework. Step 1 consists of injury surveillance of non-contact ACL injury, for example through retrospective surveys and video analyses, primarily to observe the prevalence of non-contact ACL injuries. This step helps observe the significance of non-contact ACL injuries. Step 2 is to establish the aetiology and mechanisms of non-contact ACL injury through in vitro, in vivo and in silico studies. This step helps in understanding risk of injury, as well as understanding what loading patterns and possibly joint kinematics may put an individual at increased risk of an injurious event. An establishment of injury risk could only be done through prospective work as it allows to capture potential markers associated with the subsequent occurrence of a non-contact ACL injury. Step 3 involves the identification of possible options to avoid non-contact ACL injury and develop corresponding preventive interventions. This step mainly aims at selecting the most appropriate modifiable markers related to non-contact ACL injury, followed by developing interventions and observing the progression of selected markers throughout these interventions. Step 4 consists of subjecting the preventive measures to evaluation under "ideal conditions", typically laboratory based or controlled clinical or field settings in which researchers deliver the intervention to coaches and athletes who have been convinced and helped to participate through incentives and reminders. Step 5 focuses at testing the efficacy of step four in a “real world” setting. This is then followed by the last step, dealing with the challenges associated to implementing the “real world” training interventions within community-level training environments. Ultimately, step 5 aims at measuring the efficacy of the intervention while step 6 evaluates the efficiency of using the recommended intervention in the “real world”. This thesis aimed at identifying neuromuscular risk factors associated with non-contact ACL injury through prospective work in order to provide strong evidence that will aid in further exploration and understanding of the relationship. Therefore, it fits in stage 2 of the ACL injury prevention framework.

2.4 Mechanism of non-contact ACL injury in a dynamic setting

As mentioned in the non-contact ACL injury prevention framework, it is necessary to understand the mechanisms behind a non-contact ACL injurious event in order to identify risk factors associated to the occurrence of such an event. Non-contact ACL injury usually occurs in a dynamic movement, especially during jump-landing tasks, changing of direction, or any combination of acceleration-deceleration tasks. During these tasks, various external forces acting on the body may lead to accumulated stress on the ACL ligament. An inability of the ACL to withstand these stresses, or an inability of the individual to avoiding excessive external forces in the first place, may result in a tear or in the worst case, rupture. The most common mechanism of non-contact ACL injury has been well described in a systematic review, summarizing the outcomes from various in vivo (studies using living organisms), in vitro (studies using isolated tissue, organ or cell in an artificial environment), and in silico (computer simulation studies) research studies (Shimokochi and Shultz 2008). Generally, retrospective studies assessing the non-contact ACL injury mechanism found that the knee typically moves in multiple planes of motion prior to the time of an injury. This is for example a combination of valgus motion with either internal or external rotation, typically while the knee was near full extension or even hyperextended (Yu and Garrett 2007). Further in vivo and in vitro examination was made to observe ACL injury mechanisms based on ACL loading patterns due to loads applied to bones and/or muscles that make up the knee joint. In terms of knee muscle force, the ACL is loaded when an anterior directed force is applied to the tibia. This force is known as the anterior tibial shear force (ATSF) and the ACL serves as the primary restraint to ATSF. This force disrupts the ACL by pushing the tibia anteriorly in relation to the femur. An excessive amount of ATSF could solely tear the ACL ligament. Whilst external forces acting on the body could cause ATSF, also the force generated by the quadriceps muscle to extend the knee can pull the tibia forwards based on the large moment arm at which the patellar tendon acts on the tibia, particularly when the knee is in an extended position (Sakane et al. 1999, Woo et al. 1998). Considering most movement in an individual’s daily life involves running and jumping, high ATSF can be expected in those activities (Sell et al. 2014, Brown et al. 2014, Levine et al. 2013, Shimokochi and Meyer 2011, Bennett et al. 2008, Cowling and Steele 2001). Whilst quadriceps contractions near full knee extension can theoretically increase ATSF and may be harmful to the ACL, hamstrings muscle contraction is assumed to produce posterior tibial shear forces (PTSF) thereby countering the ATSF (Baratta et al. 1988, Solomonow et al. 1987). The effectiveness of hamstring contractions to prevent ATSF increases as knee flexion angle increases (Markolf et al. 2004, Fleming et al. 2003, Li et al. 1999, Durselen et al. 1995, Markolf et al. 1990, Draganich and Vahey 1990, Renstrom et al. 1986). So, it is clear that hamstring co-activation at times of high quadriceps activation is needed to prevent excessive ATSF, but near full knee extension the ACL is at greater vulnerability for strain and tension as the co-contraction of hamstrings is then not very effective due to a reduced moment arm.

Besides the evidence of high ATSF, frequently observed movements that have been reported during non-contact ACL injuries include valgus-varus (frontal) and knee internal-external rotation (transverse) motions (Cochrane et al. 2007, Fauno and Wulff Jakobsen 2006, Olsen et al. 2004, Boden et al. 2000, Ferretti et al. 1992). These non-sagittal movements have been identified as a potential mechanism of ACL injury (Shimokochi and Shultz 2008, Yu and Garrett 2007). In fact, one of the most cited prospective cohort studies showed that individuals who would eventually get injured demonstrated increased abduction loads and increased knee valgus motion compared to healthy controls (Hewett et al. 2005). However this particular study has had its share of controversies, first of all considering the small sample size of injured individuals (n=9), and second considering that numerous studies have found that knee valgus loading solely is unlikely to be the main ACL loading mechanism (Fleming et al. 2001, Markolf et al. 1995, Berns et al. 1992).

Overall, the literature describing non-contact ACL injury mechanisms seems to suggest that this type of injury occurs due to a combination of excessive forces in all three planes during highly dynamic movements. If individuals have the ability to withstand these multi-planar forces, or to avoid these forces from occurring in the first place, then that may well help prevent the injury. Improving an individual's neuromuscular capacity to generate adequate movement patterns may well be the solution.

2.5 Prospective evidence on neuromuscular risk factors

As mentioned in the injury prevention framework, neuromuscular risk factors can only be identified in a prospective manner, considering the impact that an injury is expected to have on both neuromuscular capacity and neuromuscular co-activations. These prospective studies provide stronger evidence on injury risk than, for example, retrospective studies in which already injured individuals are compared to healthy controls, and they form the foundation for other studies or associating other observations with the known risk factors. Based on an initial exploration of the literature, only very few studies were found that report on the prospective identification of neuromuscular risk factors. Yet there is a vast body of research addressing neuromuscular facets of non-contact ACL injury, whether that be trying to better understand the risk of injury (Boden et al. 2010, Pfeifer et al. 2018, Shima et al. 2017) or developing prevention strategies (Gokeler et al. 2018, Grindstaff et al. 2006, Taylor et al. 2015). Altogether, in recent years there appears to be a trend of progression away from gathering prospective evidence and more appealing towards engaging in retrospective and associative studies.

2.6 Muscular capacity and neuromuscular (co-)activation: risk factors of non-contact ACL injury?

Work focusing in particular on the main knee musculature (quadriceps and hamstrings) has seen considerable and growing interest over the recent years. Weaknesses and/or imbalance in the quadriceps and hamstrings activations have been associated with smaller knee flexion angles during dynamic manoeuvres (Walsh et al. 2012, Podraza and White 2010). Often, deficits in neuromuscular activation have been linked to an imbalance of the knee musculature strength. For example, the hamstring-to-quadriceps ratio (HQR) has been prospectively demonstrated as a risk factor for non-contact ACL injury in female athletes (Söderman et al. 2001). It has also been proposed that female athletes take a longer time to generate maximum hamstring torque (Huston and Wojtys 1996), suggesting the link with neuromuscular co-activation deficits. However, a recent paper suggested that weak HQR alone is not a significant predictor of increased ATSF in a jump landing task (Bennett et al. 2008). Contractile forces resulting from maximal strength testing may not represent forces produced during an actual landing, as it is unlikely that landing requires maximal effort. Therefore, the question whether deficits in muscular capacity (i.e. low HQR) and neuromuscular (co-)activations are linked to explain increased injury risk remains unanswered and requires further exploration.

The non-sagittal aspects of injury mechanisms, where the knee is pushed into a valgus state and usually also knee external rotation, has also been associated with neuromuscular factors. Namely, a low medial-to-lateral quadriceps and hamstrings co-activation during dynamic landing tasks has been suggested to result in knee valgus and knee external rotation. The medial muscles of the lower limb tend to have a varus moment arm and assist the tibial internal rotators, and the lateral muscles have a valgus moment arm and assist tibial external rotators (Palmieri-Smith et al. 2009). Therefore, the need to balance medial and lateral quadriceps and hamstrings activations may help resist the abduction (valgus) and knee external rotation loads about the knee and may help diminish the risk of ACL injury (Besier et al. 2003). Particularly when changes of direction are executed during running, the medial and lateral hamstrings contribute differently to knee stability; semitendinosus and semimembranosus (medial hamstring) are responsible for internal rotation and varus stress about the knee, and bicep femoris (lateral hamstring) for external and valgus rotation (Opar 2013). Additionally, a prospective study observing pre-activations of a side-cutting manoeuvre showed that female athletes with reduced pre-activity of the semitendinosus (medial hamstring muscles) and increased pre-activity of the vastus lateralis (lateral quadriceps muscles) during side-cutting were at increased risk of future non-contact ACL rupture (Zebis et al. 2009). The lower activation of the hamstring muscles, especially low neuromuscular activity of the semitendinosus, may insufficiently compress the medial knee joint compartment, thereby increasing the risk of dynamic knee joint valgus and knee external rotation.

To summarize, both in terms of muscular capacity and neuromuscular (co-)activations of the primary knee musculature, there have been ample suggestions that an imbalance would lead to increased risk of non-contact ACL injury. However, many studies have alluded to a direct connection between both types of observation, but for as far as we are aware no clear evidence exists yet that this connection in fact exists. Despite this gap in the literature, we have seen more and more emerging studies that are using the HQR as proven indicator of non-contact ACL injury risk (Ahmad et al. 2006, Bowerman et al. 2006, Holcomb et al. 2007, Bee-Oh et al. 2009, Grygorowicz et al. 2010, Hosokawa et al. 2011, Grygorowicz et al. 2017a), or that associate observations of neuromuscular (co-)activation with non-contact ACL injury risk (Malinzak et al. 2001, Besier et al. 2003, Ford et al. 2003, McLean et al. 2004, Palmieri-Smith et al. 2009, Zebis et al. 2009, Bencke and Zebis 2011, Opar 2013). We believe this to be a dangerous trend, and that more research is needed to generate a more solid evidence base for this kind of work.

2.7 Conclusion

The need to prevent non-contact ACL injury incidence rate is a growing concern and many efforts have been undertaken to investigate neuromuscular risk factors associated to non-contact ACL injury. However, the evidence available in the neuromuscular literature seems to still be unclear. The need to explore and evaluate neuromuscular injury risk factors is essential to understand why non-contact ACL injury within a dynamic setting happens, and to ultimately develop prevention programs.

2.8 Aim and Objectives

2.8.1 Aim

The overall aim of this research was to gain a better understanding of neuromuscular risk factors of a non-contact ACL injury during dynamic sporting tasks.

2.8.2 Objectives

i. To systematically review the existing evidence on neuromuscular risk factors of non-contact ACL injury in team sports participation, and to critically evaluate whether current research trends are supported by adequate evidence (Chapter 3).

ii. To conduct a prospective study to identify neuromuscular risk factors of non-contact ACL injury in team sports participation (Chapter 4).

iii. To critically evaluate HQR as indicator of imbalance in muscular strength and as potential risk factor of non-contact ACL injury in team sports participation (Chapter 5).

iv. To observe if neuromuscular (co-)activation patterns are associated with muscular strength imbalance.

Chapter 3 Systematic Review

3.1 Abstract

The aim of this systematic review was (i) to identify neuromuscular markers that have been predictive of a primary non-contact ACL injury, (ii) to assess whether proposed risk factors have been supported or refuted in the literature from cohort and case-control studies, and (iii) to reflect on the body of research that aims at developing field based tools to assess risk through an association with these risk factors. Electronic searches were undertaken, of PubMed, SCOPUS, Web of Science, CINAHL and SPORTDiscus examining neuromuscular risk factors associated with ACL injury published between January 1990 and July 2015. The evidence supporting neuromuscular risk factors of ACL injury is limited where only four prospective cohort studies were found. Three of which looked into muscular strength imbalance and 1 looked into neuromuscular activation patterns but none of the studies found strong evidence on how these neuromuscular capacity deficits are a risk factor for a primary non-contact ACL injury. A number of factors associated to neuromuscular capacity have been suggested to be related to non-contact ACL injury risk but the level of evidence supporting these risk factors remains often elusive, leaving researchers and practitioners uncertain when developing evidence-based injury prevention programs.

3.2 Introduction

In an effort to investigate what is known of the neuromuscular markers associated with ACL injury, the study will systematically review the literature by category as follows; level 1 – prospective studies, level 2 – case-control studies and level 3 – associative studies. The specifics of these studies were further explained in Table 3.1. Generally, prospective cohort studies provide the strongest evidence to support the development of intervention and prevention programs, as outlined in the Translating Research into Injury Prevention Framework, (Finch 2006) where the success of the programs are based on modifying known risks associated with incurring the injury. The high costs associated with running prospective cohort studies tends to limit the amount of direct evidence on risk, particularly when experimental observations are time consuming or only possible in a lab environment, such as is often the case in the investigation of neuromuscular factors.

Table 3.1 Classification of studies for risk factor studies

Classification	Description
Prospective Cohort Studies	Study designs in which neuromuscular characteristics of one or more samples (called cohorts) are assessed and the occurrences of a non-contact ACL injury is followed prospectively to determine which initial participants' characteristics (risk factors) are associated with increases risk of incurring an ACL injury.
Case Control Studies	Study designs that compared people who have suffered a non-contact ACL injury (cases) with people from the same source population but without significant knee injury (healthy controls), to examine changes in neuromuscular characteristics after injury. Whilst these changes may reflect person-specific differences prior to injury, they also reflect post-injury adaptations due to prolonged deficiency (ACL-D) or reconstruction (ACL-R).
Associative Studies	Study designs that used previously suggested risk factors in their work to establish associations with (a combination of) other characteristics of that population sample, typically to detect surrogate observations that are easier/ cheaper when screening for non-contact ACL injury risk on a large scale or in the field.

To date, a number of risk factors associated with neuromuscular capacity, which includes muscular strength imbalance and neuromuscular control, have been suggested to be related to non-contact ACL injury risk. The level of evidence supporting the suggested neuromuscular risk factors remains to our knowledge often elusive, leaving researchers and practitioners uncertain when developing evidence-based injury prevention programs. Therefore the aim of this systematic review of the literature was (i) to identify those neuromuscular markers that have been predictive of a primary non-contact ACL injury, (ii) to assess whether the identified risk factors have seen supportive evidence from cohort and case-control studies, and (iii) to reflect on the body of research that aims at developing field based tools to assess risk through an association with these risk factors.

3.3 Method

The Cochrane Handbook (Higgins and Green 2009) and the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) (Liberati et al.) guidelines were used in conducting this systematic review.

3.3.1 Electronic Literature search

The literature selection process consisted of exploring electronic databases from PubMed, Scopus, Web of Science, CINAHL and SPORTDiscus between January 1990 and July 2015. The search terms were constructed and tested prior to the initial search so that the key terms cover as much as possible the existing literature of neuromuscular risk factors for non-contact ACL injury. In addition, a hand search was done on the reference lists of included articles. The search terms were divided into four groups. Between groups, the search terms were connected with AND, and within groups the search terms were connected with OR. Depending on the search database, the appropriate search term notation technique was applied. The result of this search strategy is described in Table 3.2.

Table 3.2 Search Strategy

Step	Strategy	PubMed	Scopus	Web of Science	CINAHL	SPORTDiscus
#1	Search "ACL injur*" OR "anterior cruciate ligament injur*"	9,626	4,159	22,358	4,632	2,022
#2	Search neuromuscular OR musc* OR timing OR activation OR isokinetic dynam* OR EMG OR electromyography	1,406,853	167,905	17,061,970	145,331	112,873
#3	Search #1 AND #2	1,809	383	9,703	1,165	733
#4	Search jump* OR land* OR run* OR sprint* OR side* OR cut* OR crossover OR hop* OR one-leg* OR one leg* OR single-leg OR single leg OR isokinetic OR isometric OR isotonic OR flexion OR extension OR contraction*	1,336,769	78,845	6,538,119	171,728	223,533
#5	Search #3 AND #4	1,171	130	2,658	695	463
#6	Search risk OR prevent* OR predict* OR screening OR associat* OR sensitivity OR specificity OR reproducibility OR reliability OR validity	8,354,639	11,308,360	23,799,549	1,322,386	354,238
#7	Search #5 AND #6	696	99	712	409	344

3.3.2 Literature Selection

From the titles and abstracts (first stage), two authors (R.S. and M.R.) independently selected the result of the searches to avoid risk of bias in identifying potentially relevant papers for full review. If there were any disagreements between the two reviewers, consensus was sought through discussion between them. If no consensus was reached, a moderator (J.V.) was consulted to reach a final consensus. Selection based on full text assessment (second stage) was done by two other reviewers (R.R. and J.V.) and if there were any disagreements between the two reviewers, consensus was sought through discussion between them. If no consensus was reached, a moderator (M.R.) was consulted to reach a final consensus. For these titles, categorization as well as inclusion and exclusion criteria were implemented in a study classification system using EndNote® (version X7.0.1, Thomson Reuters) to select the relevant titles. Inclusion criteria across studies were as follows: (i) studies that measure neuromuscular variables (e.g.: isokinetic dynamometry, isometric strength, electromyography or EMG); and (ii) studies measuring other variables (e.g.: biomechanical or physiological variables) but still containing neuromuscular assessments. Classification of included studies is described in Table 3.1. Exclusion criteria were (i) studies without abstracts; (ii) invited reviews or systematic reviews; (iii) studies that focused on the effect and impact of treatment/training; (iv) studies that only looked into orthopaedic and rehabilitative aspects of ACL reconstruction; (v) in-vitro studies; (vi) studies on non-team sports (such as golf, walking, etc); (vii) technical studies and (viii) studies that were not in English.

3.3.3 Data Extraction

The first author (R.R.) extracted data from each included article based on their respective study designs. For prospective cohort studies, data supporting the strength of the prospective evidence (e.g.; number of participants, monitoring/follow-up period and injury rate) and the neuromuscular variables measured were extracted. For retrospective and case-control studies the assessed task, neuromuscular variable measured, and findings were extracted. For associative studies, data that were extracted provided an insight to enable reflection on the amount of ongoing research that takes prospectively identified ACL injury risk factors as a foundation for their experimental research paradigm(s).

3.3.4 Methodological Quality Assessment

The first author (R.R.) assessed the methodological quality of the studies based on the Risk of Bias Tool by the Cochrane Bias Methods Group (Group) for prospective cohort, case-control studies, evaluating criteria associated to e.g. cohort selection, exposure assessment, case-control matching, etc. (See full list at bottom of table 3.3). For each item, one point could be scored and the total score of the methodological quality ranged between 0 – 7 (prospective cohort) and 0 – 6 (case-control studies). If an item was not present, not reported or insufficient information was given, 0 points were scored. Some items were not applicable, depending on the study design of the included studies, and then these items were excluded from calculation of the quality scores.

Table 3.3 Methodological quality of studies

	Study	Quality Score	A	B	C	D	E	F	G	H	I
Prospective Cohort	(Myer et al. 2009)	6/7	Y	Y	Y	N/A	N/A	N	Y	Y	Y
	(Söderman *et al.,* 2001)	6/7	Y	Y	Y	N/A	N/A	Y	N	Y	Y
	(Uhorchak *et al.,* 2003)	7/7	Y	Y	Y	N/A	N/A	Y	Y	Y	Y
	(Zebis *et al.,* 2009)	4/7	Y	NR	Y	N/A	N/A	Y	N	N	Y
Case-control Studies	(Hsiao et al. 2014)	3/6	N/A	N	Y	Y	N	Y	N	N/A	N/A
	(Konishi *et al.,* 2011)	2/6	N/A	N	N	Y	N	Y	N	N/A	N/A
	(Swanik *et al.,* 2004)	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	(Tsepis *et al.*,2004)	4/6	N/A	Y	N	Y	Y	Y	N	N/A	N/A
	(Urbach *et al.*,2001)	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	(Holsgaard-Larsen *et al.*,2013)	3/6	N/A	Y	N	Y	N	Y	N	N/A	N/A
	(Xergia *et al.*,2013)	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	(Drechsler *et al.*,2006)	2/6	N/A	N	N	Y	N	Y	N	N/A	N/A
	(Aalbersberg *et al.*,2009)	3/6	N/A	Y	Y	N	N	Y	N	N/A	N/A
	(DeMont *et al.*,1999)	3/6	N/A	Y	N	Y	N	Y	N	N/A	N/A
	(Steele *et al.*,1999)	3/6	N/A	Y	N	N	Y	Y	N	N/A	N/A
	(Swanik *et al.*,1999)	3/6	N/A	Y	Y	Y	N	N	N	N/A	N/A
	(Ortiz *et al.*,2008)	2/6	N/A	N	N	N	Y	Y	N	N/A	N/A
	(Ortiz *et al.*,2011)	2/6	N/A	N	N	N	Y	Y	N	N/A	N/A

NA not applicable, N no or insufficient information, NR not reported, Y yes

a Was selection of the prospective cohorts drawn from the same population

b Can we be confident in the assessment of activity exposure in participants

c Can we be confident that any injury was not present at start of the study (prospective) or had suffered from ACL injury and controls had not (case-control)

d Were the cases (those who acquired ACL injury) appropriately selected

e Were the controls appropriately selected

f Did the study match injured and uninjured participants (prospective) or cases and controls (case-control) for all variables that are associated with the potential risk factor or did the statistical analysis adjust for these prognostic variables

g Was the nature/cause of the ACL injury well defined

h Can we be confident in the assessment of the ACL injury

i Was the follow up of cohorts adequate

3.4 Results

3.4.1 Search Findings

Table 3.1 shows the overall process and outcome of keyword searches. The initial search retrieved a total number of 2,260 studies: PubMed (696), Scopus (99), Web of Science (712), CINAHL (409) and SPORTDiscus (344) (see Figure 3.1). Removing duplicates between database searches resulted in a total of 2,204 titles. From the title and abstract assessment (1st stage), 269 studies were retrieved and eligible for full text assessment. From full text review (2nd stage), a further 221 papers were excluded retaining 4 prospective studies, 14 case-control studies and 30 associative studies. The mean methodological quality score for prospective studies was 5.75 (range 4 to 7) and for case-control studies was 3.21 (range 2 to 5).

3.4.2 Prospective Studies

Of the 4 prospective studies observing the neuromuscular markers of ACL injury, 3 evaluated muscular capacity (comprising of isokinetic knee strength and HQR) as risk factor of non-contact ACL injury (Myer et al. 2009, Söderman et al. 2001, Uhorchak et al. 2003), and 1 study evaluated muscular activation patterns (Zebis et al. 2009) (see Table 4).

3.4.2.1 Muscular Capacity

Myer (Myer et al. 2009) found that females who went on to suffer an ACL injury had decreased hamstring strength whereas matched female healthy controls who did not suffer from ACL injury had decreased quadriceps strength, in both cases compared to male controls. Söderman (Söderman et al. 2001) found that an imbalance of the hamstrings to quadriceps ratio (HQR) between legs in female athletes was predictive of players who suffered an ACL injury, with a lower HQR on the side that would become

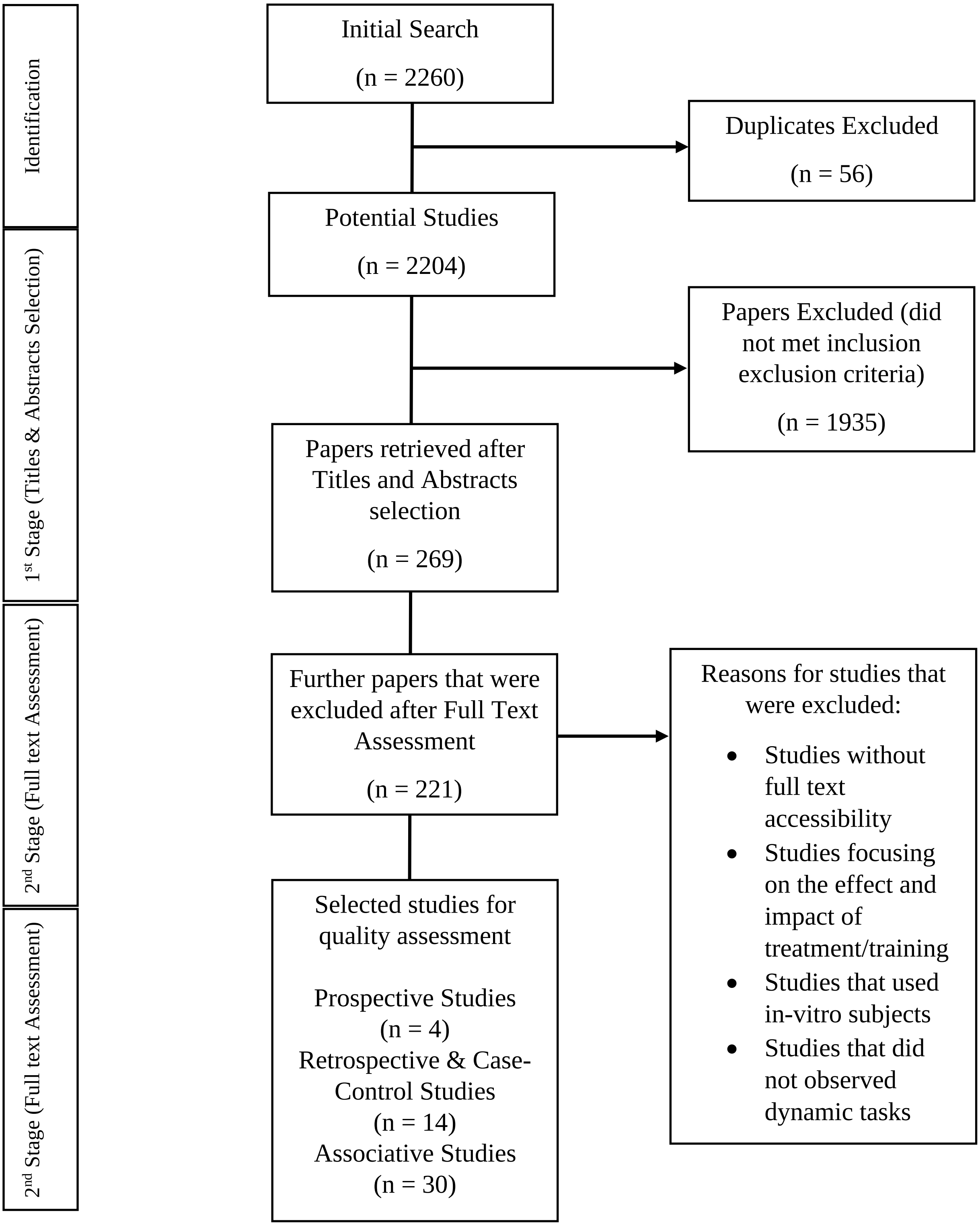


Figure 3.1 Flow diagram of the overall selection and exclusion process

injured. On the contrary, Uhorchak (Uhorchak et al. 2003) did not find differences in HQRs for males and females who go on to suffer ACL injury.

3.4.2.2 Muscular Activation Pattern

Zebis (2009) focused on muscle co-activation patterns during side cutting in elite female athletes and found that reduced pre-activity of the semitendinosus (ST) combined with increased pre-activity of the vastus lateralis (VL) indicates an increased risk of future non-contact ACL injury.

3.4.3 Case-Control studies.

Fourteen studies were included in the review to assess the consistency of findings of the identified neuromuscular risk factors associated with non-contact ACL injury from the prospective studies (see Table 3.5). In this section, studies were further separated based on whether the study observed differences between participants with ACL deficiency (ACL-D) and healthy controls, or differences between ACL reconstructed participants (ACL-R) and healthy controls.

3.4.3.1 Muscular Capacity

Five case-control studies analyzed deficits in muscular capacity in ACL-D subjects compared to healthy controls (Hsiao et al. 2014, Konishi et al. 2011, Swanik et al. 2004, Tsepis et al. 2004, Urbach et al. 2001). ACL-D subjects showed a deficit of the peak quadriceps torque in both isometric testing in males (Urbach et al. 2001) and isokinetic testing (Konishi et al. 2011, Tsepis et al. 2004) in males and females. Another study found quadriceps and hamstring deficits for isometric and isokinetic tests in male and females (Hsiao et al. 2014). In contrast, one study found greater isokinetic hamstring strength in ACL-D females (Swanik et al. 2004). Finally, one study found no difference in quadriceps strength between ACL-D and healthy controls.

Five case-control studies looked into the muscular capacity deficits of ACL-R compared to healthy controls (Hsiao et al. 2014, Urbach et al. 2001, Holsgaard-Larsen et al. 2013, Xergia et al. 2013, Drechsler et al. 2006). Two studies demonstrated weaknesses in quadriceps strength that were still present at both 1 and 3 months after injury in males and females during isometric and isokinetic contraction (Hsiao et al. 2014, Drechsler et al. 2006). Another study also found a decrement of isokinetic strength in the quadriceps in males (Xergia et al. 2013). One study that found a deficit in peak quadriceps torque in isometric contraction in males after ACL-R went on to observe that this deficit had disappeared two years after reconstruction (Urbach et al. 2001). Another study also found a reduced function of the operated leg, 2 years post ACL-reconstruction, for hamstring isometric contraction where asymmetry in hamstring strength was greater after ACL-R (Holsgaard-Larsen et al. 2013).

3.4.3.2 Muscular Activation Patterns

Five case-control studies examined deficits in muscular activation pattern between ACL-D and healthy controls (Swanik et al. 2004, Aalbersberg et al. 2009, DeMont et al. 1999, Steele and Brown 1999, Swanik et al. 1999). One study found that the hamstrings were activated more in ACL-D subjects and this increased activation was more apparent in extended than in flexed knee angles (Aalbersberg et al. 2009). Another study focusing on a deceleration task found delayed biceps femoris (BF) and semimembranosus (SM) activation (Steele and Brown 1999). Further studies observed muscle activations in ACL-D females (Swanik et al. 2004, DeMont et al. 1999, Swanik et al. 1999). Muscle pre-activity strategies appeared to be different depending on the task being done with vastus lateralis (VL) activation being higher during hopping and vastus medialis obliquus (VMO) activation being lower during downhill walking (DeMont et al. 1999). Reactive muscle activity (after ground contact) during running was seen to be greater when observing peak activity in the BF and vastus medialis

(VM), but smaller when observing overall EMG activity (Swanik et al. 1999). During landing, the ACL-D group demonstrated significantly less overall activity in the vastus lateralis (VL) (Swanik et al. 1999). A final study found that ACL-D females had significantly increased preparatory muscle activity in the BF before landing, but no differences in reactive muscle activity during landing or reflex latency after joint perturbations were observed (Swanik et al. 2004).

Two case-control studies described differences in muscular activation patterns between ACL-R and healthy controls (Ortiz et al. 2008, Ortiz et al. 2011). One study demonstrated co-contraction ratios between normalised hamstring and quadriceps activations that were significantly closer to 1 in the ACL-R group during drop jumps, and greater gluteus maximus (Gmax) and rectus femoris (RF) activations (Ortiz et al. 2008). Another study from the same research group showed that neuromuscular recruitment strategies during two side hopping tasks in ACL-R females did not differ from healthy controls (Ortiz et al. 2011).

3.4.4 Associative studies

Thirty associative studies were retained (see Table 3.6). Out of these studies, 11 studies investigated associations with muscular capacity as a risk factor. Five of the studies assessed isokinetic and isometric peak torques where four of the studies observed deficits in quadriceps and hamstring strength (Hiemstra et al. 2007, Mattacola et al. 2002, Roberts et al. 2007, Zebis et al. 2011b) and 1 study focused on increments of isokinetic strength from an intervention to prevent ACL injury (Wilkerson et al. 2004). The other 6 studies assessed HQRs in a variety of ways (Ahmad et al. 2006, Bee-Oh et al. 2009, Bowerman et al. 2006, Grygorowicz et al. 2010, Holcomb et al. 2007, Hosokawa et al. 2011).

Twenty studies investigated associations between muscular activation patterns risk of ACL injury. Five of the 20 studies looked into an intervention to improve on quadriceps and hamstring activation or co-activation (Begalle et al. 2012, Elias et al. 2015, Nagano et al. 2011, R. Shultz et al. 2015, Wilderman et al. 2009), 3 studies focused on pre-activation of the lower limbs in different tasks (Bencke and Zebis 2011, Hannah et al. 2015, McLean et al. 2010), 1 study investigated detraining effects on lower extremity EMG (Dai et al. 2012), 1 study assessed lower extremity neuromechanics relative to leg dominance during an unanticipated sidestep cutting task, with differing states of fatigue and training (Greska 2012), 5 studies investigated the differences in muscle synergy strategy between gender (Hughes and Daily 2015, Kipp et al. 2014, Landry et al. 2009, Lategan 2012, Liebensteiner et al. 2012, Palmieri-Smith et al. 2009), 2 studies observed the relationship between muscle co-contraction and knee flexion angle (Podraza and White 2010, Walsh et al. 2012), 1 study identified the phases of sidestep cutting that may place athletes at a greater risk for ACL injuries (Xie et al. 2013), and 1 study investigated the effect of muscle fatigue on neuromuscular strategy during a functional side cutting movement (Zebis et al. 2011b).

Table 3.4 Study characteristics and outcomes (Prospective Studies)

Author	Subjects Characteristics	Monitoring/Follow up period	Neuromuscular Measurement	Injury Rate (%)	Objective	Results/Findings
(Myer et al. 2009)	Females = 1692 19 Postpubertal and 3 pubertal (only on injured subjects) High school and collegiate soccer and basketball players	5 years	Isokinetic Knee Strength	22 non-contact ACL injuries (1.3%)	To determine the association of quadriceps and hamstrings strength to anterior cruciate ligament (ACL) injury risk in female athletes.	Female ACL subjects had decreased hamstrings strength compared to MC (15%; 95% CI, 1 to 27%; P = 0.04). FC were not different from MC in hamstrings strength. Conversely, Female ACL subjects did not differ compared to the MC in quadriceps strength, and the FC demonstrated decreased quadriceps strength relative to MC (10%; 95% CI, 3 to 18%; P = 0.01).
(Söderman et al. 2001)	Female = 221 146 (75 dropouts) 20.6 ± 4.7 years Soccer players from 13 teams of 2nd and 3rd Swedish division	6 months (1 out-door season)	Isokinetic Knee Strength	5 ACL injuries- did not mentioned contact or non-contact (2.3%)	To study possible risk factors for leg injuries in female soccer players.	Multivariate logistic regression showed hyperextension of the knee joint, a low postural sway, reduced HQR during concentric action, and a higher exposure to soccer to significantly increase the risk of traumatic leg injury. All five players who suffered an anterior cruciate ligament injury during the study period had a lower hamstring to quadriceps ratio during concentric action on the injured side than on their non-injured side. Three of them had a HQR lower than 50%, and the other two had a HQR of 52% and 53% on the injured side.
(Uhorchak et al. 2003)	1198 Male = 1021 Female = 177 18.4 years (ranged from 17 to 23) Military cadets playing in competitive club and varsity sports	4 years	Isokinetic Knee Strength	24 non-contact ACL injuries (16 Males with 1.56% and 8 Females, with 4.52%)	To prospectively evaluate risk factors for noncontact anterior cruciate ligament injuries in a large population of young athletic people.	Men - Knee extensor and flexor strength ratios, including the eccentric hamstring muscles to concentric quadriceps muscles and end-range of motion ratios (P = 0.353 to 0.961) were not significantly different between the groups. Women - The strength ratios evaluating relationships between the quadriceps and hamstring muscle groups as well as strength in the end-range of motion (P = 0.424 to 0.700) were not significantly different between groups.
(Zebis et al. 2009)	Female = 55 24 ± 5 years Elite female handball and soccer athletes	2 years (2 subsequent season)	Muscle Activation (vastus lateralis & medialis, rectus femoris, semitendinosus and bicep femoris) during side cutting.	5 non-contact ACL injuries- did not mentioned contact or non-contact (9.0%)	To identify risk factors that have high clinical relevance in the prevention of ACL rupture.	In the present study, currently non-injured female athletes with reduced EMG pre-activity of the ST and increased EMG pre-activity of the VL during side cutting were at increased risk of future noncontact ACL rupture. The study's data indicate that a high-risk zone can be used to identify non-injured players at high risk of future ACL rupture. Consequently, individual preventive efforts can be introduced in time. However, large prospective studies are needed to confirm this finding before definitive clinical recommendations can be made.

Table 3.5 Study characteristics and outcomes (Retrospective and Case-Control Studies)

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Hsiao et al. 2014)	12 ACL-D to ACL-R subjects (9 Males & 3 Females) 25.7 ± 9.3 years Non-active participants except for 3 subjects 15 Healthy Controls (11 Males & 4 Females) 23.0 ± 3.3 years Did not report control subjects sports participation	KIN-COM Isokinetic Dynamometer	Isometric knee strength - a series of contractions over a knee range between 10 and 90 of flexion, at 20° decrement (10°, 30°, 50°, 70°, and 90° of knee flexion) in random order. After a practice trial, 3 attempts of 5-second MVCs from quadriceps and hamstrings were allowed in each joint position with a 15-second rest in between and the highest force of contraction among 3 attempts was measured. Isokinetic knee strength - a series of contractions of the quadriceps and hamstrings over a knee joint range between 10 and 90° of flexion, in the form of 3 reciprocal concentric-concentric cycles with a 15-second rest in between. Contractions were performed in a random order at angular velocities of 50, 100, 150, 200, and 250°.s^{-1}. In each case, the highest force of contraction among 3 attempts was measured.	***Before Reconstruction*** Both quadriceps and hamstrings of the uninjured knees showed similar isometric performance to the control subjects; there was no significant difference between the uninjured and control groups at all testing knee angles in isometric MVCs. Compared with the uninjured knees, the injured knees showed significant weakness in both quadriceps and hamstrings ($p < 0.05$) across the whole range of knee angles tested. Before the reconstruction, there was no significant difference in the isokinetic force production in uninjured knees when comparing with the control group in all testing velocities for both quadriceps and hamstrings. The isokinetic MVCs from both quadriceps and hamstrings of the injured knees before reconstruction showed significant weakness at all movement velocities ($p < 0.05$) ***After Reconstruction*** There was no significant difference among the isometric MVCs produced by the uninjured knees preoperatively, 3 and 6 months after the ACL reconstruction, for both quadriceps and hamstrings. The isokinetic performance of the quadriceps and hamstrings also showed no significant change throughout the follow-up period at all testing movement velocities. Compared with the preoperative stage, isometric MVCs of the quadriceps at the 3-month follow-up was significantly weaker especially at positions that were more flexed ($p < 0.005$ at 90 and 70° of knee flexion). Unlike the quadriceps, there were no significant changes in isometric hamstrings MVCs of the injured knee at the 3 or 6-month follow-up. Quadriceps showed a more profound weakness during isokinetic contractions at the 3-month follow-up, with a diminished pattern of force: velocity relationship. There was a slight return of force and pattern of force production at 6-month follow-up when compared with that in the preoperative stage. Hamstrings showed slight though non-significant improvement in the isokinetic force production continuing through- out the 6-month follow-up period

Table 3.5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Konishi et al. 2011)	22 ACLD (11 Males & 11 Women) 24.7 ± 5.3 years 10 competitive, 10 recreational and 2 occasional sports participation) 22 Healthy Controls (13 Males & 9 Women) 24.3 ± 5.7 years Various levels of sports activity were reported	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength - All subjects performed maximum concentric knee extensions ranging from 90-degree knee flexion to full extension. Isokinetic knee extension torque at preset angle velocities of 60 and 180°/s and were performed 5 times by each subject for each velocity. Patients with ACL injury were measured starting from the uninjured side and then continued on the injured side. Each trial was separated by a rest period of 2 min.	The mean torque values for knee extension of the injured and uninjured sides analyzed using a paired t-test indicated that mean torque values of the injured side at both 60 and 180°/s were significantly lower than those of the uninjured side ($p < 0.01$ at 60°/s, $p <0.01$ at 180°/s). Peak torque for the groups at 60°/s and 180°/s were, injured side (134 ± 45, 97 ± 33), uninjured side (171 ± 46, 113 ± 28) and Control group (182 ± 46, 125 ± 42) respectively.
(Swanik et al. 2004)	12 ACLD 25.2 ± 7.3 years 17 Healthy Controls 22.7 ± 4.0 years Tegner activity score with an average of 5.4 All Females	Surface EMG (Noraxon) were placed on the VM, VL, Medial Hamstrings & Lateral Hamstrings. Biodex 2 Isokinetic Dynamometer	Muscular activation - The subject stood on a 20-cm step, balanced momentarily on the test limb, and hopped to a target (x) placed 30 cm horizontally. The subject did 2 practice attempts followed by 3 test trials and the ensemble peak was used for amplitude normalization. EMG preparatory muscle activity was represented by a 150-ms period before landing and reactive muscle activity was described by a 250-ms period after ground contact. Isokinetic knee strength - a standardized knee position was assumed, and testing was done at speeds of 60°/second with torque values automatically adjusted for gravity. Warm-up procedures consisted of two submaximal (50% and 75%), and one maximal repetition followed by data collection during five reciprocal maximum repetitions.	Females with anterior cruciate ligament deficiencies had significantly increased preparatory muscle activity in the lateral hamstring before landing, but no differences in reactive muscle activity during landing or reflex latency after joint perturbation. Female ACLD also had greater peak torque and torque development for knee flexion.
(Tsepis et al. 2004)	32 ACLD (3 groups of knee function High, Intermediate and Low) 27.7 ± 7.3 years 12 Healthy Control 22.1 ± 2.9 Amateur soccer players All Males	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength - A warm up on the dynamometer consisted of five repetitions of incremental intensity from 50% to 100% of each subject's estimated maximal effort. After one minute of complete rest, 5 maximal repetitions of concentric extensions and flexions were performed at 60°/s. The testing order of the knees was randomized.	The average peak torque (APT) of the quadriceps of the injured knee was significantly lower than the APT of the intact knee in all-experimental groups (lowest $F= 6.8$; $P<0.001$). Regarding the hamstrings, the APT in the injured knee was significantly lower than the APT of the intact knee in the low knee function (L3) group only ($F= 11.08$, $P<0.001$).

Table 3.5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Urbach et al. 2001)	12 ACL-D to ACL-R subjects 26.9 years (ranged from 14.9 to 43.5) 12 Healthy Controls 26.4 years (ranged from 15.3 to 42.3) Tegner activity score with an average of 7.9 only on injured subjects were reported All Males	Purpose-built Chair (Urbach et al., 2001)	Isometric knee strength - Patients were seated in an upright position on a purpose-built chair. For electrical stimulation of the muscle aluminium-plate electrodes were strapped to the quadriceps and a constant current was applied (Dantec Counterpoint K II, Skovlunde, Denmark). The subjects were instructed to extend their knee fully for 5 seconds to determine the force at maximum voluntary contraction (MVC) measured as extension torque and for maximal potentiation of the twitch response. Immediately after twitch potentiation, the subjects performed isometric contractions with 90%, 75%, 50% and 100% of their MVC force by matching the visualized torque level on the monitor with the desired torque. When the torque was stable three single stimuli were applied to the muscle.	Before operation we found a deficit of voluntary activation of the quadriceps on both the injured (mean ± SEM 74.9 ± 3.5%) and the uninjured side (74.6 ± 3.0%) in comparison with the control group (91 ± 0.9%). Two years after reconstruction of the ACL the voluntary activation of the quadriceps improved significantly on both sides but remained less than that of the controls.
(Holsgaard-Larsen et al. 2013)	23 ACL-R 27.2 ± 7.5 years 25 Healthy Controls 27.2 ± 5.4 years MET score with an average of 36 All Males	Stabilized Dynamometry (Jensen et al., 2011)	Isometric knee strength & HQR - For each muscle group, 3 trials of approximately 4-s duration were performed and the trial with highest isometric strength (joint moment) was selected for further analysis. All contractions were performed in the sitting position with 90° of knee flexion. Pauses between successive contractions were 20–30 s. To stabilize the body, subjects were secured with a waist strap positioned across the proximal part of the thigh and participants were allowed to hold on to the construction for further support.	Maximal hamstring voluntary contraction was reduced by 0.22 Nm kg^{-1} in the operated versus non-operated limb in patients, resulting in a greater (p b 0.001) asymmetry in ACL-patients (77.4%) than controls (101.3%). In contrast, no limb-to-limb asymmetry was detected for maximal quadriceps strength. An 11.1% reduction in H/Q-ratio was observed in the ACL-patients on the operated side while no difference (0.5%) between legs was observed in controls, leading to greater ($p < 0.001$) asymmetry in ACL-patients (85.7% vs. 103.4%).
(Xergia et al. 2013)	22 ACL-R 28.8 ± 11.2 years 22 Healthy Controls 24.8 ± 9.1 years Tegner activity score with an average of 6.5 All Males	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength - The range of motion was set from 90° of flexion to full extension (0°) and was performed at 120°/s, 180°/s, and 300°/s. All tests were first performed on the intact lower extremity, followed by the involved lower extremity. For the control group, the dominant lower extremity was tested first. The test consists of 5 repetitions with a 1-minute rest period in between.	Compared to the control group, the ACLR group had greater isokinetic knee extension torque deficits at all speeds (P<0.001) When averaged across speeds, the ACLR group had a lower Limb Symmetry Index (LSI) compared to the control group (76.9% versus 98.2%).

Table 3.5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Drechsler et al. 2006)	31 ACLR (25 Males & 6 Females) 30.0 ± 8.0 years 20 Inactive Healthy Controls - RC (10 Males & 10 Females) 24.0 ± 4.0 years 5 Active Healthy Controls - SC (2 Males & 3 Females) 28.0 ± 3.0 High performance sporting activities	Purpose Built Chair (refer to Drechsler et al., 2006) Surface EMG were placed on the RF. Digitizer DS7 current stimulator	Isometric knee strength and muscular activation - Subjects performed 3 or more MVCs (5-s duration) of quadriceps femoris, with a 2 min rest period between each MVC.The first 2 MVCs acted as trial attempts and were undertaken without stimulation. On the third occasion, the stimulator delivered 1 Hz stimuli for 5-s to the relaxed muscle.If the subject was unable to activate fully (i.e. the twitch augmented the MVC by more than 5%), MVC testing with twitch superimposition was repeated up to two additional times.	There were no significant differences in mean isometric MVC of the quadriceps femoris of uninjured limbs of the ACLR group, one month after surgery and of the RC and SC groups. In contrast the mean isometric MVC of quadriceps of the injured limbs of the ACLR group was significantly less (P = 0.0001) than that of the uninjured limb at both 1 and 3 months after surgery despite increases of I/U% from 1 to 3 months of 23 ± 3% and 16 ± 4% for male and female subjects, respectively.
(Aalbersberg et al. 2009)	11 ACL-D (4 Males & 7 Females) 35.0 years (ranged from 20.0 to 46.0) 15 Healthy Controls (10 Males & 5 Females) 23.0 years (ranged from 18.0 to 51.0) Did not report subjects sport participation	Custom-build seat (Aalbersberg et al., 2009) Kistler Force Plate Surface EMG were placed on the VM, RF, VL, SM, ST, BF & MG muscles.	Muscular activation - Subjects performed 3 maximum voluntary isometric contractions (MVIC) for both the quadriceps and the hamstrings at 90° of knee flexion in 3 positions (knee behind, over and in front of the ankle). Another series of 3 MVIC was performed for the GM muscle at 90° of ankle flexion.	No significance in muscle activation variables nor the moments between ACL-deficient and control subjects during knee behind the ankle position In postures with the knee in front of the ankle, ACL-deficient subjects showed, averaged over three force levels and three knee angles, a median activation level of 6.6% MVC (range 3.2–12.3) hamstrings activation, against 4.2% (range 1.8–17.4) in control subjects.In postures with the knee over the ankle hamstrings activation were 9.1% MVC (range 2.0–29.0) for ACL-deficient and 4.0% MVC (range 2.2–35.7) for control subjects. The differences between ACL-deficient and control subjects (2.4% MVC for postures with the knee in front of the ankle and 5.1% MVC for postures with the knee over the ankle) were significant.

Table 3.5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(DeMont et al. 1999)	6 ACL-D 12 ACL-R 6 Healthy Controls 29.4 ± 10.4 years (all subjects) Tegner activity score with an average of 6.8 ± 1.5 (All Females)	Integrated EMG on the VMO, VL, MH, LH, MG and LG.	Muscular activation- Subjects performed 4 dynamic activities for IEMG assessment of downhill walking at 0.92 m/s, running at 2.08 m/s, 10 step hopping task and jump-landing task from a 20.3 cm step.	Side-side differences. Landing – ACLD shows side-to-side differences between the LG (involved 36.4% ±19.7% and uninvolved 60.1% ±23.6%, $P < 0.05$).], Running – ACLD shows side differences in the VMO (involved 11.4% ±3.8%, uninvolved 7.2% ±3.1%, $P < 0.05$) and VL (involved 13.3% ±2.7%, uninvolved 8.9% ±1.9%, $P < 0.05$) and Downhill Walking – ACL shows side differences between the VMO (involved 9.2% ±4.2%, uninvolved 19.5% ±7.3%, $P < 0.05$). Mean amplitude of IEMG. Running – ACLD differences between the VMO (involved 78.2% ±23.2%, uninvolved 45.8% ±18.9%, $P < 0.05$), Downhill Walking – ACLD shows differences between the LG (involved 79.7% ±30.3% and uninvolved 122.3% ±34.9%, $P < 0.05$) and Hopping – ACLR shows a side-to-side differences on the LG Landing – ACLD shows differences between the LG (involved 74.7% ±40.0% and uninvolved 52.8% ±14.3%, $P < 0.05$). ANOVA revealed group differences on the involved VL during hop and the VMO when walking downhill. ACLD had significantly higher IEMG area than controls in VL (ACLD 12.9% ±5.8% and Controls 7.1% ±3.9%, $P < 0.05$) but lower in VMO (ACLD 9.2% ±4.2% and Controls 15.7% ±3.6%, $P < 0.05$). The side-to-side differences of the ACLD and ACLR groups, as well as the group differences between ACL-D and control, suggest that different muscle activation strategies are used by females when performing different dynamic activities. Therefore, muscle unit differentiation may be the cause of our results. These changes appear to be reversed through surgery or the associated postoperative rehabilitation.
(Steele and Brown 1999)	11 ACL-D (8 Males & 3 Females) 31.6 ± 7.6 years 11 Healthy Controls (8 Males & 3 Females) 30.4 ± 8.3 years Did not report subjects sport participation	Surface EMG (Noraxon) were placed on the VM, RF, VL, SM, BF & MG muscles.	Muscular activation - Subjects performed 5 trials of a dynamic and abrupt deceleration task in which they accelerated forward for three steps to receive a chest level pass, landed on the test limb in single-limb stance, and stabilized their position without raising the landing foot.	Peak BF & SM activity displayed by the control subjects' involved limbs occurred earlier than that for their non-involved limbs while the ACLD subjects displayed the reverse trend.

Table 3.5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Swanik et al. 1999)	6 ACL-D 12 ACL-R 6 Healthy Controls 29.4 ± 10.4 years (all subjects) Tegner activity score with an average of 6.8 ± 1.5 (All Females)	Intergrated EMG (Noraxon) were placed on the VM, VL, Medial Hamstrings & Lateral Hamstrings.	Muscular activation- Subjects performed 4 dynamic activities for IEMG assessment of downhill walking at 0.92 m/s, running at 2.08 m/s, 10 step hopping task and jump-landing task from a 20.3 cm step.	During running, the ACLD group demonstrated significantly greater area and peak IEMG activity in the MH in comparison with the ACLR group (30.3 ± 5.7, P<0.05, CI =19.1 to 41.5 and 365.4 ± 123.3, P<0.05, CI =123.7 to 607.1 respectively) and greater peak activity in the LH when compared with the control group (379.5 ± 105.5, P<0.05, CI =172.7 to 586.3). The ACLD group also demonstrated greater peak activity in the VM (428.2 ± 110.2, P<0.05, CI =212.2 to 644.2) and less area of IEMG activity in the LH than the control group (30.1 ± 6.9, P<0.05, CI =16.57 to 43.6) during running. During landing, the ACLD group demonstrated significantly less area of IEMG activity in the VL when compared with the control group (109.7 ± 50.3, P<0.05, CI =11.1 to 208.3)
(Ortiz et al. 2008)	13 ACL-R 25.4 ± 3.1 years 15 Healthy Controls 24.6 ± 2.6 years Recreational fitness activities (All Females)	Surface EMG were placed on GMax, RF, LH and MH (Cram et al., 1998).	Muscular activation - 5 trials of a 40-cm single-legged drop jump and a 20-cm up down hop task. These tasks were randomly ordered. Each participant was allowed to rest as much as she wanted to prevent fatigue. No participant was allowed to rest less than 1 minute between trials.	Multivariate analysis for EMG variables showed statistically significant differences between groups ($F_{4,23}$ = 6.47, P = .001; ES = 0.53, β = 0.97) during drop jumps. Follow-up analyses of variance on each EMG variable showed significantly greater co-contraction ratios ($F_{1,26}$ = 8.83, P = .006; ES = 0.25, β = 0.82), greater gluteus maximus full-wave rectified normalized EMG (F1,26 = 10.64, P = .003; ES = 0.29, β = 0.88), and greater rectus femoris full-wave rectified normalized EMG (F1,26 = 14.73, P = .001; ES = 0.36, β = 0.96) in the group with ACL reconstruction .
(Ortiz et al. 2011)	14 ACL-R 25.4 ± 3.1 years 15 Healthy Controls 24.6 ± 2.6 years Recreational fitness activities (All Females)	Surface EMG were placed on GMax, RF, LH and MH (Cram et al., 1998).	Muscular activation - The participant stood on the force plate of her preference and started jumping single-legged from one force plate to another for 10 consecutive times across the marked lines. One jump was defined as jumping away and back to the same force plate. A side-hopping manoeuvre was defined as the direction of movement to the opposite side of the weight-bearing leg whereas a crossover hop was defined as the direction of movement toward the same side of the weight-bearing leg	In neither group did group × manoeuvre interaction ($F_{4,22}$ = 1.05; P = 0.402; effect size: 0.16; power: 0.28), group main effect ($F_{4,22}$ = 2.05; P = 0.12; effect size: 0.27; power: 0.52), or manoeuvre main effect ($F_{4,22}$ = 2.20; P = 0.10; effect size: 0.29; power: 0.55) in the gluteus, rectus femoris, and hamstrings muscles or the co-contraction ratios reach statistical significance. Electromyographic data revealed no statistically significantly differences between the groups.

VL vastus lateralis ***VM*** vastus medialis ***VMO*** vastus medialis obliquus ***RF*** rectus femoris ***LH*** lateral hamstring ***MH*** medial hamstring ***BF*** biceps femoris ***ST*** semitendinosus ***LG*** lateral gastrocnemius ***MG*** medial gastrocnemius ***Gmax*** gluteus maximus ***ACLD*** anterior cruciate ligament deficiency ***ACLR*** anterior cruciate ligament reconstructed ***MVC*** maximum voluntary contraction***MVIC*** maximum voluntary isometric contraction ***RC*** inactive controls ***SC*** active controls ***H/Q*** hamstring/quadriceps ***EMG*** electromyography***IEMG*** integrated electromyography

Table 3.6 Associative studies

Neuromuscular Risk Factor	Papers	Variables Observed
Muscular Capacity	(Hiemstra et al. 2007, Mattacola et al. 2002, Roberts et al. 2007, Wilkerson et al. 2004, Zebis et al. 2011b)	Isokinetic and isometric peak torques
	(Ahmad et al. 2006, Bee-Oh et al. 2009, Bowerman et al. 2006, Grygorowicz et al. 2010, Holcomb et al. 2007, Hosokawa et al. 2011).	HQR
Muscular Activation	(Begalle et al. 2012, Elias et al. 2015, Nagano et al. 2011, R. Shultz et al. 2015, Wilderman et al. 2009)	Intervention to improve on quadriceps and hamstring activation or co-activation
	(Bencke and Zebis 2011, Hannah et al. 2015, McLean et al. 2010)	Pre-activation of the lower limbs in different tasks
	(Dai et al. 2012)	Detraining effects on lower extremity EMG
	(Greska 2012)	Lower extremity neuromechanics relative to leg dominance during an unanticipated sidestep cutting task, with differing states of fatigue and training
	(Hughes and Daily 2015, Kipp et al. 2014, Landry et al. 2009, Lategan 2012, Liebensteiner et al. 2012, Palmieri-Smith et al. 2009)	Differences in muscle synergy strategy between gender
	(Podraza and White 2010, Walsh et al. 2012)	Relationship between muscle co-contraction and knee flexion angle
	(Xie et al. 2013)	Phases of sidestep cutting that may place athletes at a greater risk for ACL injuries
	(Zebis et al. 2011b).	Muscle fatigue on neuromuscular strategy during a functional side cutting movement

3.5 Discussion

3.5.1 Prospective evidence

The evidence supporting risk factors of ACL injury associated with muscular capacity or muscular activation patterns is limited. This systematic review found only four prospective studies of which three studies looked into muscular capacity (Myer et al. 2009, Söderman et al. 2001, Uhorchak et al. 2003) and only one study into muscular activation patterns (Zebis et al. 2009). From the studied cohorts, there were only a small number of individuals who incurred an injury with injury rates ranging from 1.3% to 9.0%. Although the incidence rate of ACL injury is high as highlighted in Chapter 1 and 2, the observation of prevalence in ACL injuries at a specific time has not necessarily been highlighted. From the numerous prospective studies that are available, it seems to demonstrate that the prevalence rate of acquiring ACL injuries during prospective monitoring periods are relatively low (Zebis et al. 2009, Söderman et al. 2001). Therefore, to compensate studies have incorporated substantially large cohorts to increase ACL injuries observation (Uhorchak et al. 2003, Krosshaug et al. 2016).

In prospective risk factor studies, the power of the study is determined by (i) the association strength of the risk factor and injury risk (the stronger the association, the fewer cases are needed), (ii) the rate of injury (the more frequent the injury, the fewer cases are needed), and (iii) the chosen significance level (Bahr and Holme 2003). With low rates of injury, suggestions for future work have been that risk of ACL injury would need to be studied in substantially larger cohorts than typically done but the cost associated to that is simply too high. The relatively higher incidence of injury in females has led to most cohort studies only involving females (Myer et al. 2009, Söderman et al. 2001, Zebis et al. 2009). Considering the knowledge that injury mechanisms in females are different than in males and other risk factors such as laxity and hormonal factors may also differ between males and females (Smith, et al., 2012) , this makes translating the risk factors to male populations highly ambiguous. Differences between injured and non-injured individuals were small, providing relatively low sensitivity and specificity of the measure to predict injury (Myer et al. 2009, Söderman et al. 2001, Uhorchak et al. 2003, Zebis et al. 2009). The value of the risk factors for targeted screening with a focus on differentiating interventions based on risk is therefore limited.

Particularly, a good research practice would require proposed risk factors to be confirmed in an independent study with an independent cohort, yet no risk factors have been independently confirmed to date. Altogether, whilst one may advise future research to involve greater cohorts, for example through multi-centre studies, such efforts should probably focus on multi-factorial risk. Particularly concerning neuromuscular factors, the link between muscular activation patterns and muscles' capacity to generate torque is often referred to when interpreting findings of one or the other (Myer et al. 2009, Söderman et al. 2001, Uhorchak et al. 2003, Zebis et al. 2009), but whether this link holds true in the context of ACL injury risk remains unknown. Also, muscular capacity as well as muscular activation patterns at the knee are related to capacity and activation patterns at the ankle and probably at hip and abdominal musculature (Zazulak et al. 2005, Zeller et al. 2003, Shultz et al. 2012).

No papers on this topic fit our exclusion criteria, but the focus on knee musculature based on the premise that this is the closest evidence to predicting ACL injury may well not hold true. Another approach may still be suggested based on a recent systematic literature review on the effectiveness of prevention programmes (Grimm et al. 2015). This review revealed that the prevention of ACL injury has until now mostly been ineffective, yet the prevention of knee injuries in general has seen more success. Considering some suggestions that non-contact lower limb injuries can have similar causality, a potentially viable approach to making prospective studies more cost-effective may be to explore risk factors of any knee injury rather than only ACL injury.

3.5.2 Post-injury case-control evidence

Whilst one may focus on the fact that sample characteristics of the various studies were diffuse, the overarching message concerning post-injury supportive evidence to risk factors is that the effect of injury is greater than any remaining person-specific effects of risk prior to the injury. Clear and often long-term reductions in muscular capacity were found for quadriceps muscles in ACL-D (Hsiao et al. 2014, Konishi et al. 2011, Tsepis et al. 2004, Urbach et al. 2001) and ACL-R (Hsiao et al. 2014, Xergia et al. 2013, Drechsler et al. 2006) patients compared to healthy controls suggesting substantial consequences of post-injury inactivity, detrimental effects of kinesiofobia (Drechsler et al. 2006), autograft repair (Hiemstra et al. 2004), and potentially lack of rehabilitation compliance.

These considerable changes in muscular capacity and likely alterations in muscular activation patterns altogether suggest that risk of re-injury is based on very different factors than risk of primary injury. Rather than hamstring weakness combined with high quadriceps strength (low HQRs), re-injury risk may need to be explored through the consequences of quadriceps weakness and/or lack of quadriceps activation in the injured leg, particularly in the context of compensation mechanisms in the contralateral leg where re-injury is most prevalent (Wright et al. 2011). Hamstring weakness was in most post-injury case-control studies not an indication of risk, with hamstring strength being the same between injured and non-injured limb, and between injured and healthy controls (Swanik et al. 2004, Tsepis et al. 2004, Xergia et al. 2013, Drechsler et al. 2006). This may reflect the effectiveness of many ACL rehabilitation protocols that focus on strengthening the hamstrings as an ACL protective measure. The evidence on hamstring weakness as a risk factor for primary ACL injury remains poor, and is confounded by many other factors, including the fact that hamstring inadequacy may well be joint-angle and joint-angular velocity specific, or as mentioned above, that muscular capacity may well be dissociated from risk inducing activation patterns.

In muscular activation pattern assessment, only two case-control studies (Swanik et al. 2004, Swanik et al. 1999) found reduced activation of the semitendinosus combined with increased activation of the vastus lateralis during dynamic tasks as was found through prospective work (Zebis et al. 2009). These observations again suggest discrepancies between risk factors of a primary injury versus re-injury. Changes observed in muscular activation patterns post ACL injury likely also result from adaptations associated with protective behavior when performing selected tasks and/or as a result of rehabilitation focus.

3.5.3 Reflection on associative studies

The last decade has seen a substantial increase in studies that aim at translating evidence on risk into field-based screening tools through associating observations that are easy to assess in a clinical or field context with previously identified risk factors. For muscular capacity, 11 studies have looked into its association with sustaining a non-contact ACL injury (Hiemstra et al. 2007, Mattacola et al. 2002, Roberts et al. 2007, Wilkerson et al. 2004, Zebis et al. 2011b, Ahmad et al. 2006, Bee-Oh et al. 2009, Bowerman et al. 2006, Grygorowicz et al. 2010, Holcomb et al. 2007, Hosokawa et al. 2011). These studies have associated muscular capacity with risks of acquiring ACL injury, validating ACL screening tools to be used in intervention programs to prevent ACL injury.

Considering that the 3 prospective studies (Myer et al. 2009, Söderman et al. 2001, Uhorchak et al. 2003) did not find strong evidence of how muscular capacity deficits are a potential risk factor for non-contact ACL injury, the actual predictive value of screening tools with a moderately strong association to the actual risk factor is potentially very weak. The same case applies to screening for muscular activation deficits. There were 20 studies in the last few years that addressed an association with motion pattern deficits, seeking opportunities to observe risk from motion analysis (Zebis et al. 2011b, Begalle et al. 2012, Bencke and Zebis 2011, Dai et al. 2012, Elias et al. 2015, Greska 2012, Hannah et al. 2015, Hughes and Daily 2015, Kipp et al. 2014, Landry et al. 2009, Lategan 2012, Liebensteiner et al. 2012, McLean et al. 2010, Nagano et al. 2011, Palmieri-Smith et al. 2009, Podraza and White 2010, R. Shultz et al. 2015, Walsh et al. 2012, Wilderman et al. 2009, Xie et al. 2013).

Whilst there is value in understanding how motion patterns relate to the underlying activation of muscles, it is important to keep in mind that the proposed risk due to imbalance in activation between medial hamstring and lateral quadriceps muscles was based on a limited sample (5 injuries), one particular task (side cut), and a very small window of pre-activity observation (10 ms before touchdown) (Zebis et al. 2009), and that this has until now not been confirmed independently. With none of the associative studies strictly adhering to these criteria when measuring muscle activation patterns, any subsequent suggestions made around risk of ACL injury through a screening tool that is based on associations with the suggested muscle activation deficit should be interpreted with great care.

3.6 Limitations

This review was bound by the chosen search terms and may still not have captured all studies identifying neuromuscular risk factors associated with non-contact ACL injury. We undertook careful hand-searching to detect masquerading articles (articles that were not properly indexed) in an attempt to ensure that all relevant studies were included. Also, the neuromuscular risk factors observed in this systematic review were solely based on attributes of muscular capacity and muscular activation patterns, whereas the term ‘neuromuscular’ has in the past been used to cover a broader grouping of observations, for example including kinematic (motion) and kinetic (force) observations. Our review was based on published and accessible work only (articles that may have been relevant but were not available for access were excluded from the study), whereas we are aware of more recent unpublished prospective work. To our knowledge, none of that unpublished work seems to direct towards any convincing evidence for neuromuscular risk factors of primary ACL injury.

The sample demographics in the prospective studies varied across studies with respect to age, sex, playing level and type of sport, therefore different risk factors may apply to different subject characteristics as been observed in the ACL prognostic literature.

3.7 Conclusion

To date, (i) the neuromuscular markers that have been predictive of a primary non-contact ACL injury from prospective evidence are weak, (ii) post-injury case-control studies cannot be used as support for pre-injury risk and (iii) despite a substantial body of research that has studied various neuromuscular risk factors for ACL injury, current evidence is contradictory and ongoing efforts are limited largely to case-control and associative investigations. This means that the evidence-base for the development of field-based and/or large-scale screening, as well as the development of prevention programmes, is currently weak. With high costs involved in prospective cohort studies, a change in approach to create stronger evidence may well be necessary.

Chapter 4 Prospective Study Outcome

4.1 Abstract

The aim of this study was to prospectively investigate the identified neuromuscular markers that have been predictive of a primary non-contact ACL injury which are (i) muscular strength imbalance and (ii) neuromuscular (co-)activations. Over the course of two consecutive academic years, 103 recreational athletes participated in our study. These were 55 male recreational athletes (age: 21.3 ± 3.4 years, stature: 175.6 ± 8.1 cm, mass: 75 ± 11.7 kg) and 49 female recreational athletes (age: 22.3 ± 3.8 years, stature: 164.1 ± 7.8 cm, mass: 64.3 ± 10.4 kg). Activity levels (sporting exposure) and history of injuries were taken before the start of testing and were subsequent to testing registered and monitored weekly through a monitoring app for the next nine months. During testing, subjects performed a muscular strength test with an isokinetic dynamometer for concentric and eccentric knee flexions and extensions at speeds of 60°/s and 120°/s. They also performed 5 trials of 4 dynamic movement tasks; bilateral drop vertical jump, single-legged drop vertical jump, single-legged hop for distance and an anticipated side-cutting manoeuvre, during which kinematics and kinetics was measured as well as muscle activations of prime knee movers. Over the period of 9 months, the study achieved a compliance rate of 51%, however, to our surprise no non-contact ACL injuries were recorded. Injuries that were acquired consisted of muscle soreness, ankle sprain and strain, and quadriceps and hamstring injuries. Based on the lack of ACL injuries in the cohort, it was decided to not continue recruiting for a third academic year but to move towards the next two objectives of this work (Chapters 5 and 6). In the proceeding chapter, procedures for running the prospective study are reported, as well as an overview of participant compliance.

4.2 Introduction

Few prospective studies have assessed the risk factors associated with non-contact ACL injury during dynamic tasks. The prospective studies that were addressed in Chapter 1 had important limitations, such as (i) being based on a small sample of injured individuals, (ii) a restricted set of subject cohorts (not multisport), (iii) non-standardized assessment methods (different measuring tools and protocols) and (iv) predominantly focusing on female athletes. There is a definite need for more and better prospective evidence on neuromuscular risk factors.

Muscular strength imbalance has been identified in prospective studies as an indicator of being at risk of ACL injury. Assessment of peak torque of the quadriceps and hamstrings and deriving a HQR is one of the most commonly reported measures of muscular strength imbalance. Although it has been contested, a minimum threshold of 0.6 has been reported for a HQR based on concentric hamstring and quadriceps peak strengths (Coombs and Garbutt 2002, Grygorowicz et al. 2017a, Heiser et al. 1984), where values lower than 0.6 may indicate increased injury risk. However, prospective evidence has been contradictory (see chapter 3). Considering that actions of agonists and antagonists do not happen simultaneously during movement, a more functional HQR based on hamstring eccentric and quadriceps concentric strength has been proposed to be more representative of muscular capacity (Coombs and Garbutt 2002). Vice versa, considering that injuries usually occur during landing, observing quadriceps eccentric strength as well could be beneficial to aid further understanding of the knee musculature during this specific phase. However, we did not include this assessment in our prospective work as there was no literature on supporting quadriceps eccentric strength as injury risk of primary non-contact ACL injury through the observations made in the systematic review (Chapter 3). Future research investigating the role of muscular strength imbalance and its relationship with non-contact ACL injury should consider including quadriceps eccentric assessments to observe its association with non-contact ACL injury through prospective work.

Studies have also assessed neuromuscular function using muscular activation patterns through EMG. However, to date, only one study has done this prospectively (Zebis et al. 2009), and the rather detailed deficit in pre-activation prior to the contact phase of a side stepping manoeuvre, as observed in a very small sample (5 injured athletes), was never confirmed. Further prospective observations are needed to confirm whether this particular risk factor can be confirmed, or else if more comprehensive analyses could reveal neuromuscular co-activation differences between those who go on to get injured and those who do not.

Altogether, there is currently only weak and inconclusive evidence on muscular strength imbalance and neuromuscular co-activations as risk factors of non-contact ACL injury. This study set out to prospectively assess whether based on these factors it is indeed possible to predict non-contact ACL injury.

4.3 Method

4.3.1 Recruitment

The aim of the study was to recruit as many participants as possible (male and female) between the age of 19 – 35 years of age. Participants should at least engage not less than 2 hours (≥ 2 hours) per week to be eligible for recruitment and no recent (< 12 month) major injury is present in order to be recruited. All participants were involved in dynamic team-based sports such as football, rugby, field hockey, basketball, volleyball and lacrosse.

The prospective cohort study was known as the Liverpool Knee Injury Study (LKIS). Prior to testing, participants were given an injury history questionnaire (Appendix A), readiness to exercise questionnaire (Appendix B), informed consent form (Appendix C) and sporting exposure questionnaire (Appendix D). Participants then performed a 10-minute warm up that included light jogging and dynamic stretching. Afterwards, the participants underwent a series of anthropometric, isokinetic and dynamic movement assessments. Written consent was obtained from all participants and the study was performed in accordance with the university ethics committee guidelines (14/SPS/032).

4.3.2 Anthropometry Measurements

Anthropometry measurement included measurements of mass, height, and leg length as the distance between greater trochanter to lateral malleolus (to determine the target distance for single leg hop for distance).

4.3.3 Sporting Exposure and Injury History Questionnaire

A participant’s activeness in a typical week was determined with a sporting exposure questionnaire (Appendix D). History of injuries was also taken (Appendix A).

4.3.4 Assessment of muscular strength through isokinetic dynamometry

Maximal isokinetic torques were measured on an isokinetic dynamometer (Biodex System 3, Shirley, NY). Participants were seated with the trunk reclined at 15° from the vertical plane. Stabilization straps to the trunk, thigh, and tibia were attached to prevent any extraneous joint movement. The axis of rotation of the dynamometer lever arm was visually aligned with the lateral femoral condyle, and the lower leg was attached to the lever arm of the dynamometer at the level proximal to the malleoli. The participant’s dominant leg was determined as the preferred leg used to kicking a ball. Both legs were tested during (i) concentric quadriceps and concentric hamstrings contractions at an angular velocity of 60°/s and 120°/s and (ii) eccentric hamstrings contractions at an angular velocity of 60°/s and 120°/s. This allowed calculation of the so-called conventional (Hcon:Qcon) and functional (Hecc:Qcon) HQ ratios. Testing at 120°/s is considered a safe and reliable velocity to test fast actions although with the limitation of not representing actual sports play which tends to involve faster joint angular rotations (Delextrat et al. 2013a, Delextrat et al. 2010). Participants were given a familiarization trial (sub-maximal) before engaging in a maximal trial of five repetitions for each speed and each mode for both legs.

4.3.5 Electromyography (EMG) placement

Preparation and placement of electrodes for EMG was conducted following the SENIAM guidelines (Stegeman and Hermens 2007). Participants were shaved if the skin surface at which the electrodes have to be placed was covered with hair. Then the skin was cleaned with an alcohol swab and allowed to vaporize so that the skin is dry before electrodes were placed. Electrodes were placed over four muscles of each upper leg, i.e. the vastus lateralis (VL), vastus medialis (VM), biceps femoris (BF) and semitendinosus (ST) as shown in figure 4.1. For VL and VM the participants were required to extend their knees. VL electrodes were placed 60% along the line from the anterior superior iliac spine (ASIS) to the lateral side of the patella while VM electrodes were placed 80% along the line between the ASIS and medial epicondyle of the knee. For BF and ST, participants were instructed to flex their knees while the investigator provided a small resistance. BF electrodes were placed at 50% on the line between the ischial tuberosity and the lateral epicondyle of the tibia. ST electrodes were placed at 50% along the line between the ischial tuberosity and the medial epicondyle of the tibia. Electrodes were placed carefully to align with the striation of the muscle fibers. The inter-electrode distance was 2cm.

4.3.6 Dynamic Tasks

The EMG system was comprised of a Direct Transmission System (DTS) Belt Receiver (Noraxon, Model 580, Arizona, USA) and eight EMG sensors (Noraxon, Model 546 DTS Belt Receiver EMG Sensor, Arizona, USA) that were synchronised with the motion capture system with ten infrared cameras sampling at 250 Hz (Oqus Cameras Qualisys, Gothenburg, Sweden) and a force platform (Kistler Type 9281E, Winterthur, Switzerland) sampling at 1500 Hz during assessment of the dynamic tasks. Participants were required to perform a series of dynamic tasks, which were randomly sequenced and were familiarized prior to testing. Five dynamic trials were recorded for both dominant and non-dominant leg for each task.

4.3.6.1 Drop vertical jump

A study by Hewett (2005) suggested that valgus knee loading predicted ACL injury in a drop vertical jump task. To reproduce this task a 31cm box was placed 30cm away from the centre of the force platform. Prior to testing, the subject was given instructions and the task was demonstrated. The participant was instructed to stand on the box with feet positioned 35cm apart before jumping off. Once the subject landed on the ground, they were required to immediately do a maximal vertical jump while raising both arms up in the air. Upon testing, participants were given two to three trials to ensure that they were sufficiently familiarized with the task.

4.3.6.2 Single-legged drop jump

The single-legged drop jump is used to assess dynamic valgus and is considered to have a higher possibility of measuring undesirable behaviours compared to a double-leg drop landing task (Wang 2011). The procedures of this task are almost similar to those of the drop vertical jump where in this specific task instead of standing on two legs, participants were instructed to stand on one leg on the box prior to jumping and were required to immediately do a maximal vertical jump on one leg as soon as they land on the ground. Participants were given two to three practice trials to ensure that they were sufficiently familiarized with the task (Brazen et al. 2010).

4.3.6.3 Single-legged hop for distance

A study by Boden (2000) discovered that rapid braking which usually occurs in dynamic sports could lead to an ACL injury. To replicate this sudden deceleration, a single leg hop test was used. Participants were required to perform a single leg hop task that consisted of a take-off and landing task. Participants had to jump forward and land on the force platform and were tested on both their dominant and non-dominant legs. The starting distance from the single leg hop landing was determined by the length of the subject’s leg; measured from the greater trochanter to the lateral malleolus (Webster et al. 2004). To ensure maximal muscle forces were used, participants were instructed to jump as high as possible during the hop for distance whilst landing within the allocated horizontal distance. Participants were given two to three trials to ensure that they were sufficiently familiarized with the task.

4.3.6.4 Side-cutting manoeuvre

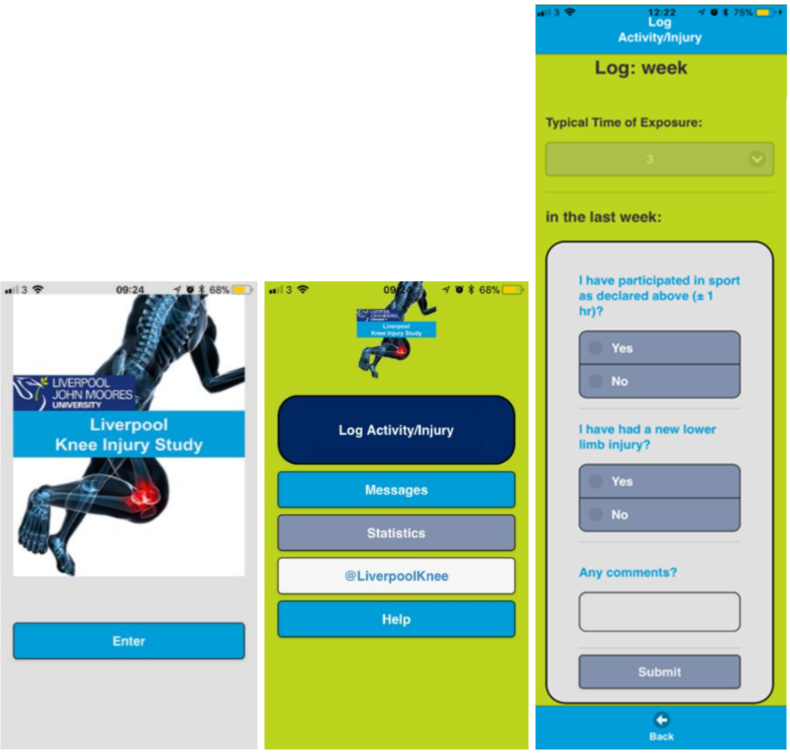
The side-cutting manoeuvre is a movement that sports players perform in match situations when time for decision making about posture correction is extremely limited. The purpose of the side-cutting manoeuvre is typically to avoid a defensive player by suddenly changing direction (Zebis et al. 2009). Originally, unanticipated side-cutting manoeuvres would have been preferred for the prospective study, but this was changed to anticipated side-cutting for time limitations of data collection. During unanticipated manoeuvres participants often shortened their steps, take hops, or even miss the platform, which contributed to an average of 3-8 error trials, adding too much additional time to the protocol. Approach speeds were recorded with timing gates placed 2 m apart and 2 m from the point where the side-cut is executed. To limit inter-trial variability, a successful trial was only valid if the approach speed was between 4.3 ms^{-1} and 4.7 ms^{-1}, and the stance foot was entirely on the force plate (Vanrenterghem et al. 2012). Participants were asked to cut at 45° with the dominant foot landing on the force plate. Participants were given two to three trials to ensure that they were sufficiently familiarized with the task.

Overall, the four dynamic tasks selected for the prospective study had in some ways been used previously to assess individuals at risk of sustaining non-contact ACL injury as described in Chapter 3. In fact only for drop vertical jump and side-cutting manoeuvre, had potential at-risk neuromuscular strategies been demonstrated in previous prospective work (Smeets et al. 2019, Zebis et al. 2009). Due to the limited number of prospective studies, we decided to incorporate all four dynamic tasks rather than selecting one over the other. This had no substantial impact on the overall duration of the test session. This was to ensure that the prospective study comprehensively captured any relevant neuromuscular activation strategies, possibly across tasks.

4.3.7 Monitoring App

In order to ease the follow-up procedure, a mobile application was developed by colleagues in the School of Computing and Mathematical Sciences under instruction from the research team to monitor participants' activity and injury exposure. The online injury registration system was an application designed for smartphones or computer, which consisted of two primary questions concerning sporting exposure and injury status (Figure 4.1). The mobile application sent notifications to the participants once a week for 36 weeks (1 season). If participants missed the first notification, another alert for the week was sent automatically the next day. The incoming data from the mobile application was stored in an allocated server and checked weekly by the researcher

(Figure 4.2). For participants who did not own a smart phone, the injury monitoring procedure were done through e-mail.



Log: week

Typical Time of Exposure: 3

in the last week:

I have participated in sport as declared above (± 1 hr)?
○ Yes
○ No

I have had a new lower limb injury?
○ Yes
○ No

Any comments?

Figure 4.1 (Left to right) LKIS mobile application welcome page, menu page and activity / injury log page.

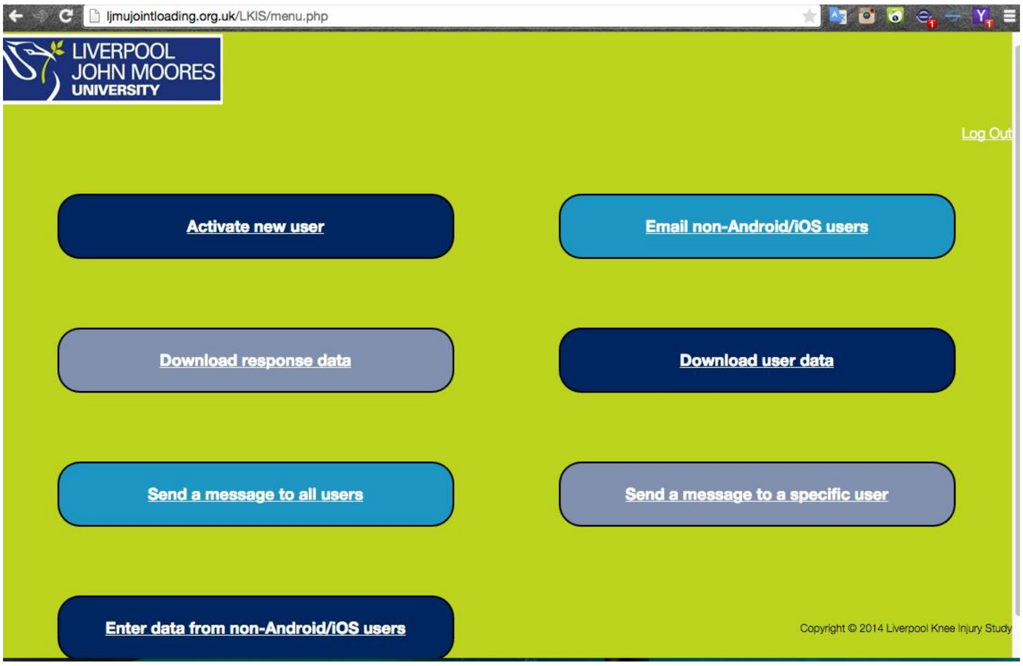


Figure 4.2 Monitoring server page

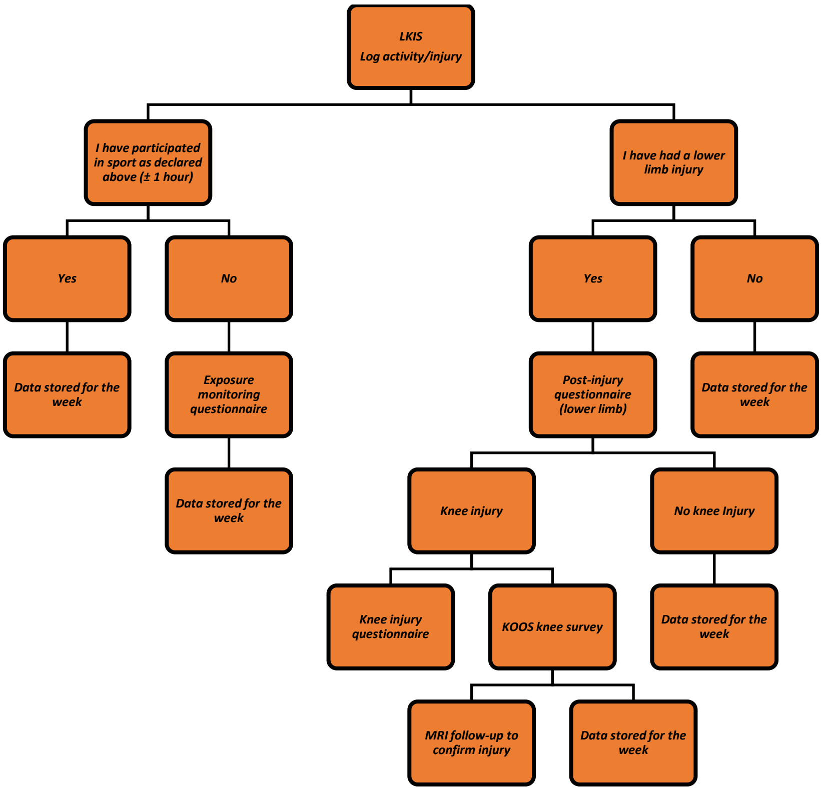


Figure 4.3 Flow chart of the follow-up process and questionnaires completed when relevant

4.4 Results

We were able to recruit a total of 104 recreational athletes. Fifty-five male recreational athletes (age: 21.3 ± 3.4 years, stature: 175.6 ± 8.1 cm, mass: 75 ± 11.7 kg) and 49 female recreational athletes (age: 22.3 ± 3.8 years, stature: 164.1 ± 7.8 cm, mass: 64.3 ± 10.4 kg) volunteered to participate in the study.

Out of the 104 participants, 11 participants had already been recruited prior to the LKIS mobile application being available so no exposure and injury data was registered for these participants. The compliance of all other participants in reporting their activities and injury through the LKIS mobile application is illustrated in Figure 4.4. Out of the 93 participants, 51% of the participants finished the monitoring requirement of 36 weeks. Only 14% of the participants managed to comply for 0 to 4 weeks. The highest hours of exposure were 20 hours per week and the lowest registered hours of exposure was 2 hours as shown in Figure 4.5. Most of the participants had 6-7 hours of exposure per week while only 3 participants registered 20 hours of exposure per week (the median of participants' declared exposure was 6 hours per week; IQR = 5-10). No non-contact ACL injuries were recorded during the 9 months monitoring period. There was a total of 18 injuries that were recorded consisting of hamstring or quadriceps strain/pull (n=7), lateral collateral ligament strain (n=1), ankle sprain (n=4) and muscle/ligament soreness around the foot and knee (n=6).

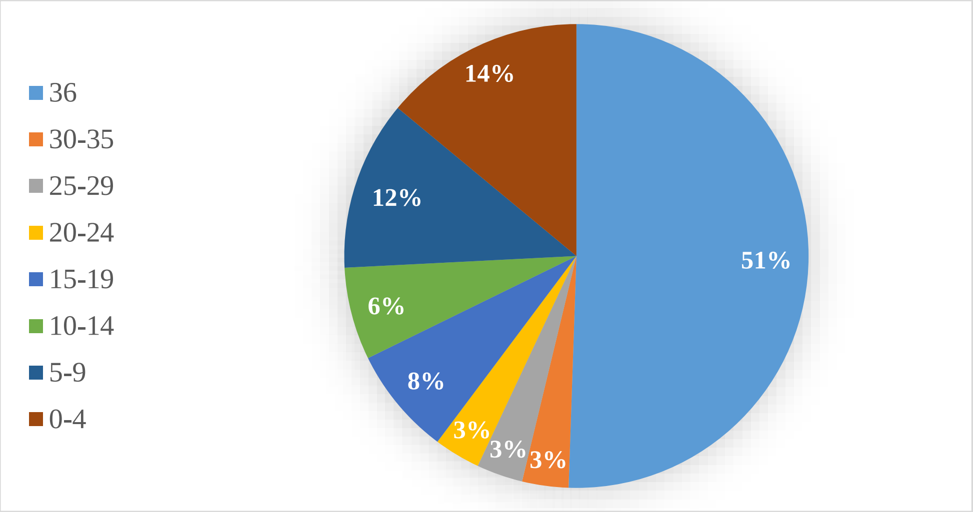


Figure 4.4 Participants' compliance rate (%) on the number of weeks (0-36) through self-reporting on the LKIS mobile application (n=93)

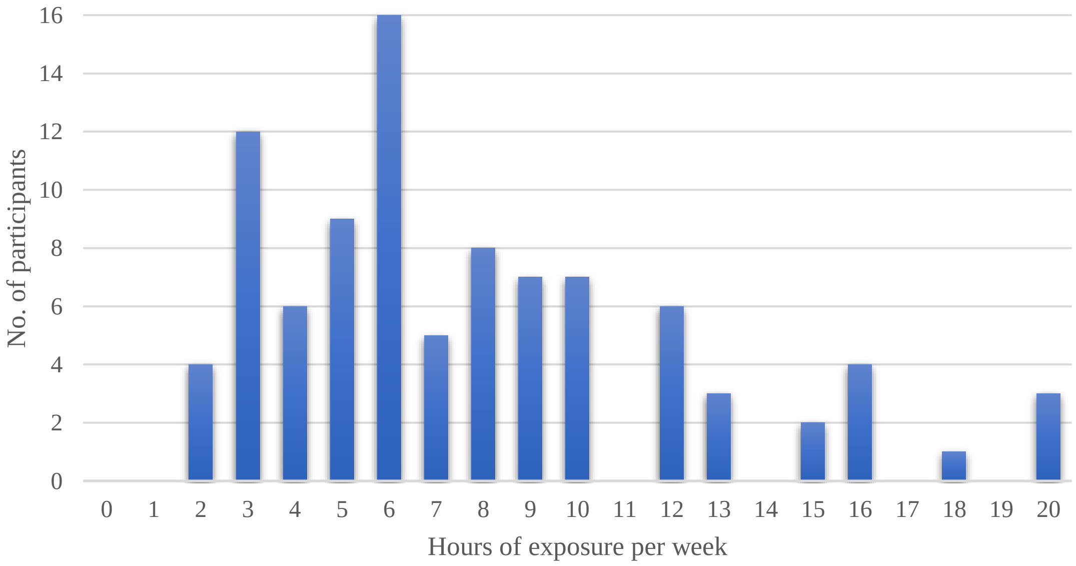


Figure 4.5 The median of participants' declared exposure was 6 hours per week (IQR = 5-10)

4.5 Discussion

Methods of monitoring injury using different methods have been observed in several investigations (Ekegren et al. 2014, Moller et al. 2012, Nilstad et al. 2014) though none have reported on using a bespoke mobile application. Having a full compliance of 51% was considered positive, but there is still considerable improvement possible. Due to the mobile application being a self-reported monitoring system, it is likely that participants did not feel the need to register their weekly exposure when there was no supervision. Even though regular messages and notifications were sent through the application server to remind all participants to register their weekly exposure and injuries, the fact that this is less personal than follow-up phone calls such as often done in previous studies, may have desensitized participants and been less effective. The mobile application was developed to ease the participant's effort for registering injury and weekly exposure, and feedback from some participants confirmed that it typically took just one minute to register if there were no injuries. Accordingly, previous studies have seen high response rates in novel injury surveillance methods (Ekegren et al. 2014, Moller et al. 2012). Overall, the increased ease of use may have been confounded by desensitization from a lack of personal involvement.

4.6 Transition towards contingency plan

We had expected to monitor at least 2-5% of non-contact ACL injuries based on the current epidemiology. In the first two years of data collection, no ACL injuries were recorded. The risk of registering too few injuries for minimal analysis in the third year was too high, so therefore the decision was made to stop recruiting and utilize the obtained database for further analysis according to a prior established contingency plan.

This study therefore continued with two further aims which was (i) to critically evaluate HQRs as indicator of muscular strength imbalance (Chapter 5) and (ii) to observe if neuromuscular (co-)activation patterns are associated with muscular strength or muscular strength imbalance (Chapter 6).

Chapter 5 Scaling Issues in the Assessment of Hamstring and Quadriceps Ratio (HQR): Should HQR be Allometrically Scaled?

5.1 Abstract

The currently available evidence concerning hamstring-quadriceps ratios (HQR) as a risk factor for non-contact ACL injuries is contradictory. All studies evaluating HQR assume that greater quadriceps strength is compensated proportionally by greater hamstring strength, yet this is not considering allometric principles. The aim of this study was to investigate the proportionality in HQR in several athlete populations. Data was collected both in an elite football club and for recreational team sport athletes in a laboratory setting**.** Seventy-one (71) male elite football athletes (mean ± SD age: 22.59 ± 4.8 years; stature: 181.7 ± 6.3 cm; mass: 78.4 ± 8.3 kg), 55 male recreational athletes (age: 21.3 ± 3.4 years, stature: 175.6 ± 8.1 cm, mass: 75 ± 11.7 kg) and 49 female recreational athletes (age: 22.3 ± 3.8 years, stature: 164.1 ± 7.8 cm, mass: 64.3 ± 10.4 kg) participated in the study. Concentric hamstring and quadriceps strength (Hcon and Qcon), and eccentric hamstring strength (Hecc) were tested in participants' dominant and non-dominant limbs using isokinetic dynamometry at 60°/s of isokinetic velocity. Linear regression analyses showed that the Hcon:Qcon and Hecc:Qcon relationships were systematically non-proportional. Correcting HQRs based on an average allometric exponent (0.65 for Hcon:Qcon and 0.78 for Hecc:Qcon) successfully removed bias from quadriceps strength and significantly altered population rankings. Therefore, quadriceps strength meaningfully affects HQRs, and unless if quadriceps strength itself would be under investigation, allometrically scaled HQRs are proposed as a superior representation of strength (im)balance than the default HQR.

5.2 Introduction

There is a general concern over the balance between hamstring and quadriceps strength in the prevention and treatment of lower extremity musculoskeletal injuries. Strong quadriceps muscles allow one to forcefully extend the knee joint during highly dynamic sporting activities such as landing, jumping, sprinting or kicking, which is considered a key performance indicator for many sports. High quadriceps muscle forces also result in high anterior tibial shear forces (ATSF) from the patellar tendon, which is a knee destabilizing side effect (Brown et al. 2014, Levine et al. 2013, Bennett et al. 2008, Cowling and Steele 2001). To counter ATSF and help stabilize the knee joint, adequate hamstring co-contractions are deemed necessary. The measurement of the equilibrium between hamstring and quadriceps strength is therefore frequently used by researchers and practitioners to determine whether the hamstring muscles are sufficiently trained so they can provide sufficient stabilization to the knee joint during dynamic activities. The most common method of assessing the balance between hamstring and quadriceps capacity has been the calculation of the ratio between hamstring over quadriceps strength (HQR) under isovelocity conditions as measured with an isokinetic dynamometer (Hislop and Perrine, 1967). In an effort to identify those who may struggle with knee stabilization and are therefore at greater risk of an injury, researchers have tried to identify cutoff values for HQR (Manson et al. 2014, Delextrat et al. 2013b, Zebis et al. 2011a, Fousekis et al. 2011, Aagaard et al. 2002, Aagaard et al. 1998). However, despite extensive efforts in the past few decades in associating HQR with the risk of acquiring an injury, we found conflicting evidence of HQR as a risk factor for ACL injuries (see Chapter 3).

The relationship between hamstring and quadriceps strength is traditionally expressed as a simple 1:1 ratio (i.e. H^1/Q^1 or $H^1.Q^{-1}$). This means that hamstring strength is assumed to vary in direct proportion to quadriceps strength. Nevertheless, a ratio is only one of several approaches for normalising the magnitude of one variable for another variable. In fact, ratios have been found in many other fields, e.g. morphological evolution, to not size-scale accurately and uniformly across the measurement range. Such variations in size-scaling is known as allometry. In the allometric literature, there are two types of scaling that have been expressed in terms of growth; i) proportional scaling (1:1 or sometimes known as iso-metric scaling) and ii) allometric scaling (not proportional). In proportional scaling, relationships are constant throughout size changes during growth or during evolution, for example frogs' legs and body length retain an isometrically scaled relationship even if the frog itself increases in size tremendously (Emerson 1978). Conversely, allometric scaling involves variations in a relationship across the measurement range. For example, in monitor lizards the limbs are relatively longer in larger-bodied species (Christian and Garland 1996). It is conceivable therefore that these scaling principles could be relevant to the hamstrings and quadriceps because of their different anatomical structure and function. The quadriceps are knee extensors and predominantly single joint muscles whereas the hamstrings are bi-articular muscles contributing to hip extension and knee flexion. These morphological and functional differences may well mean that their strength scales non-proportionally between individuals. As such, investigating of whether the relationship between hamstring and quadriceps is indeed proportional (1:1) is can reveal whether the traditional HQR is good candidate as injury risk factor, or whether an allometrically scaled HQR may be better suited.

Therefore, the aim of this study was twofold:

i) to identify whether the relationship between hamstring and quadriceps strength is proportional and if not,

ii) to identify whether an unbiased estimate of the balance between hamstring and quadriceps strength could be proposed using allometric scaling principles.

5.3 Methods

5.3.1 Participants

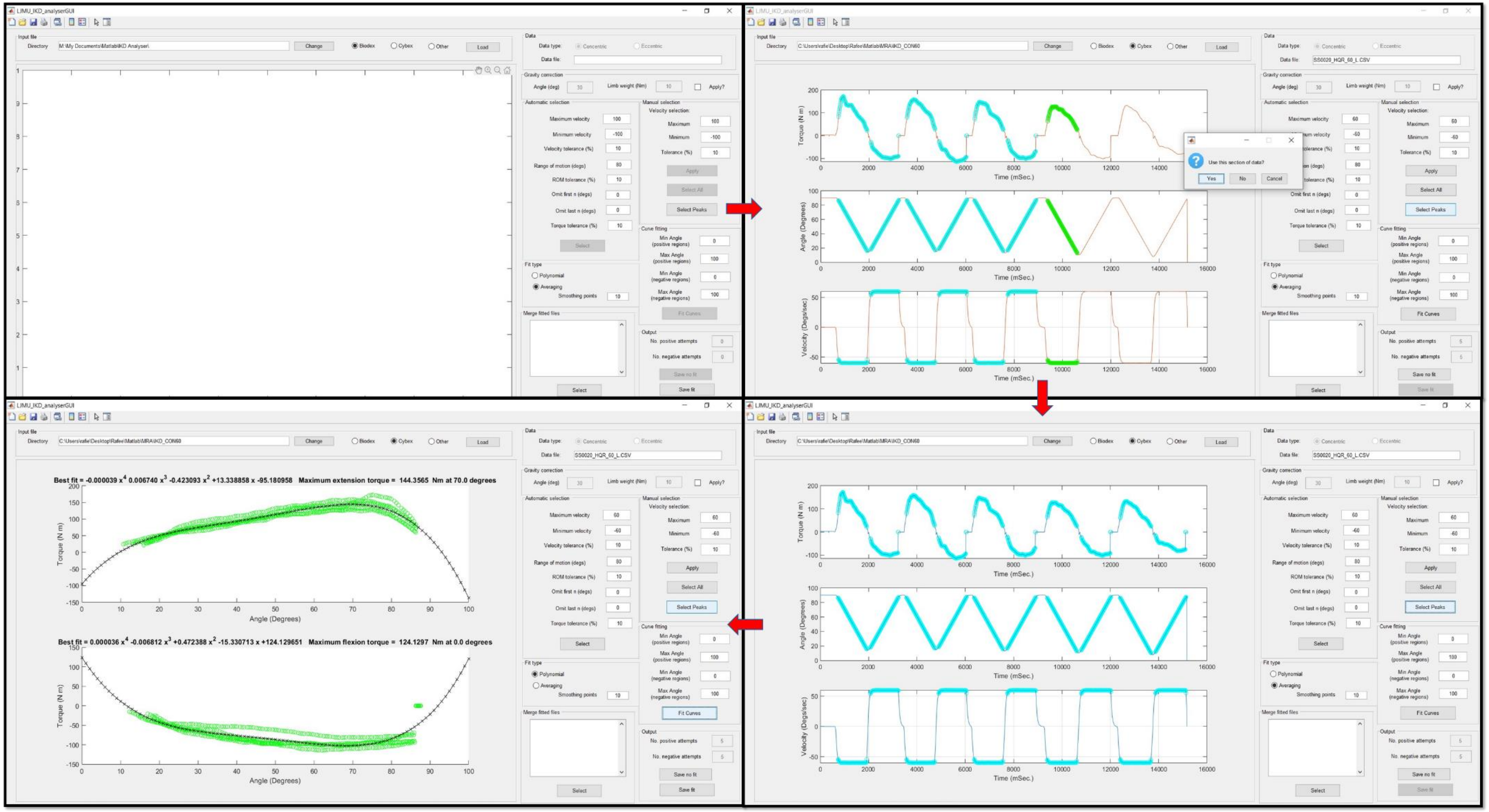
Three groups of participants were recruited for this study to observe if the proportionality problem is similar across populations or population specific. Seventy-one (71) male elite football athletes (MEFA) (mean ± SD age: 22.59 ± 4.8 years; stature: 181.7 ± 6.3 cm; mass: 78.4 ± 8.3 kg), fifty-five (55) male recreational athletes (MRA) (age: 21.3 ± 3.4 years, stature: 175.6 ± 8.1 cm, mass: 75 ± 11.7 kg) and forty-eight (48) female recreational athletes or FRA (age: 22.3 ± 3.8 years, stature: 164.1 ± 7.8 cm, mass: 64.3 ± 10.4 kg) volunteered to participate in the study. Participants were given a questionnaire on their injury history and none had a recent (< 12 month) major lower limb injury. Written consent was obtained from all the participants and the study was performed in accordance with the university ethics committee guidelines (14/SPS/032).

5.3.2 Isokinetic Dynamometer Assessment

Isokinetic dynamometry (Biodex System 3, Shirley, NY) was used for the assessment of hamstrings and quadriceps strength in both dominant (defined as the preferred leg when kicking a ball) and non-dominant legs. Participants were seated on the dynamometer chair and a fixation girdle was placed around the thigh, pelvis and chest whilst arms were folded. The axis of rotation of the dynamometer was aligned with the knee joint axis defined as the most prominent point on the lateral epicondyle of the femur as palpated externally on the lateral surface of the knee joint. The dynamometer's shin brace was placed 2 cm above the medial malleolus while being tightly secured to the already adjusted dynamometer lever arm where a pad with 2 mm of high-density foam was secured tightly to the tibia to avoid any discomfort. Range of motion was set with participant's maximum extension and flexion movements where they felt comfortable and without excessive stretch of their hamstrings. Anatomical zero was set at the most extended position on an individual basis. Gravity correction for limb weight was implemented using the manufacturer protocol. Instructions were given to the participants to produce maximum muscular effort throughout the range of motion for both knee extensors and knee flexors, at a constant angular velocity of 60°/s. For familiarization trials, 3-5 sub maximal level repetitions were included before 5 maximal effort trials. Concentric trials were included to calculate Hcon:Qcon for all populations, and also eccentric trials to calculate Hecc:Qcon for the male and female recreational athletes. However, eccentric hamstrings data were not possible with the elite male footballers.

5.3.3 Data reduction

The raw data were analysed with the open-source analysis software IKD1D (www.ikd1d.org) to acquire the peak torque values (Vanrenterghem 2016). This process involves averaging the peak torque values of the five maximum effort trials. Trials were included i) if they were within 10% of the chosen isokinetic velocity, ii) if they were within 10% of the maximum peak torque across trials and iii) if no substantial abnormalities (fluctuation/oscillation) were observed in the trials. As a consequence of the stringent trial selection criteria, eccentric hamstrings data from two MRA and two FRA had to be excluded.



Use this section of data?

Directory: C:\Users\rafie\Desktop\Rafee\Matlab\MRA\IKD_CON60

Data file: SS0020_HQR_60_L.CSV

Best fit = -0.000039 x^4 0.006740 x^3 -0.423093 x^2 +13.338858 x -95.180958 Maximum extension torque = 144.3565 Nm at 70.0 degrees

Best fit = 0.000036 x^4 -0.006812 x^3 +0.472388 x^2 -15.330713 x +124.129651 Maximum flexion torque = 124.1297 Nm at 0.0 degrees

Data type: ● Concentric ○ Eccentric
Gravity correction: Angle (deg) 30, Limb weight (Nm) 10, ☐ Apply?
Automatic selection: Maximum velocity 60; Minimum velocity -60; Velocity tolerance (%) 10; Range of motion (degs) 80; ROM tolerance (%) 10; Omit first n (degs) 0; Omit last n (degs) 0; Torque tolerance (%) 10
Manual selection – Velocity selection: Maximum 60; Minimum -60; Tolerance (%) 10
Curve fitting: Min Angle (positive regions) 0; Max Angle (positive regions) 100; Min Angle (negative regions) 0; Max Angle (negative regions) 100
Fit type: ● Polynomial ○ Averaging; Smoothing points 10
Output: No. positive attempts 5; No. negative attempts 5

Figure 5.1 IKD1D Analysis Software (Vanrenterghem 2016)

5.3.4 Comparison between populations

One-way ANOVA was used to compare quadriceps peak torque, hamstrings peak torque, and HQR (conventional) between MEFA, MRA and FRA while independent t-test was used to compare hamstring eccentric peak torque and DHQR (functional) between MRA and FRA. Fisher’s LSD was also used to compare significance of the ANOVA groups.

5.3.5 Evaluation of allometric scaling

A linear regression analysis was undertaken to identify the characteristics of the relationship between HQRs and quadriceps strength within each population. The allometric exponent can be determined by the beta coefficient (β) of the regression equation. The ‘allometric exponent’ was calculated for hamstring strength relative to quadriceps strength to determine proportionality. A log-log (natural logarithmic) approach to deriving the exponent was used, as is standard practice in allometry (Albrecht et al. 1993). If the exponent is near to 1 (i.e. $H^1.Q^{-1}$), one can assume that the 1:1 ratio relationship is appropriate. Deviation from this can be used to establish a more suitable allometrically scaled HQR.

5.3.6 Identification of misclassification of subjects using rank analysis and cross-tabs

HQR ratios were calculated both proportionally and allometrically and these were ranked into quartiles with 1 being the lowest and 4 the highest. To identify if individuals maintained or changed their position in a quartile depending on HQR method, cross-tabulation was used to identify levels of misclassification between the 1:1 (proportional) and allometrically scaled HQR. Specifically, a Chi-squared test was conducted in SPSS (version 21, SPSS Inc., USA).

5.4 Results

5.4.1 Isokinetic quadriceps, hamstrings and hamstrings eccentric peak torque with HQR (conventional) and DHQR (functional)

Results showed a significantly larger torque in MEFA for hamstring and quadriceps compared to MRA and FRA and a significantly larger hamstrings and quadriceps torque for MRA compared to FRA (table 5.1). FRA has the lowest peak torque for all the groups. MRA also showed a larger hamstrings eccentric torque compared to FRA. HQR (MEFA, MRA and FRA) and DHQR (MRA and FRA) were not significantly different between groups.

5.4.2 Does quadriceps strength influences HQR?

The regression analysis for MEFA, MRA and FRA populations showed a consistent pattern of HQR and DHQR whereby as quadriceps strength increases, HQR value decreases as shown in Figure 5.2.

5.4.3 Log transformation of Hamstring and Quadriceps Strength

From figure 5.3, HQR shows a) $\beta = 0.61$, 95% CI (0.45, 0.77) in MEFA; b) $\beta = 0.63$, 95% CI (0.48, 0.77) in MRA; and c) $\beta = 0.72$, 95% CI (0.55, 0.89) in FRA; which is lower than the expected 1. The DHQR were also below 1 with a) $\beta = 0.72$, 95% CI (0.56, 0.87) in MRA and b) $\beta = 0.84$, 95% CI (0.69, 0.99) in FRA.

5.4.4 Scaled HQR based on the identified exponent

The scaling of HQR and DHQR were calculated based on the population’s respective allometric exponent extracted from the log transformation, as shown in Table 5.2 (HQR) and Table 5.3 (DHQR). The consequent allometrically scaled HQRs were no longer affected by quadriceps strength (Figure 5.4).

Table 5.1 Quadriceps/hamstring peak torque and HQR

Variables	Population	N	Mean ± SD Nm	P	
Quadriceps Concentric Torque	MEFA	142 (71 subjects on both legs)	220.87 ± 46.58	MRA FRA	<0.006 <0.001
	MRA	110 (55 subjects on both legs)	205.75 ± 46.77	MEFA FRA	<0.006 <0.001
	FRA	96 (48 subjects on both legs)	139.46 ± 30.11	MEFA MRA	<0.001 <0.001
Hamstrings Concentric Torque	MEFA	142 (71 subjects on both legs)	113.44 ± 26.15	MRA FRA	<0.005 <0.001
	MRA	110 (55 subjects on both legs)	105.05 ± 23.71	MEFA FRA	<0.005 <0.001
	FRA	96 (48 subjects on both legs)	72.29 ± 17.20	MEFA MRA	<0.001 <0.001
Hamstrings Eccentric Torque	MRA	106 (53 subjects on both legs)	140.83 ± 34.03	<0.001	
	FRA	92 (46 subjects on both legs)	99.40 ± 24.71		
Conventional HQR	MEFA	142 (71 subjects on both legs)	0.52 ± 0.12	MRA FRA	0.859 0.856
	MRA	110 (55 subjects on both legs)	0.52 ± 0.11	MEFA FRA	0.859 0.738
	FRA	96 (48 subjects on both legs)	0.53 ± 0.11	MEFA MRA	0.856 0.738
Dynamic HQR	MRA	106 (53 subjects on both legs)	0.70 ± 0.13	0.184	
	FRA	92 (46 subjects on both legs)	0.72 ± 0.12		

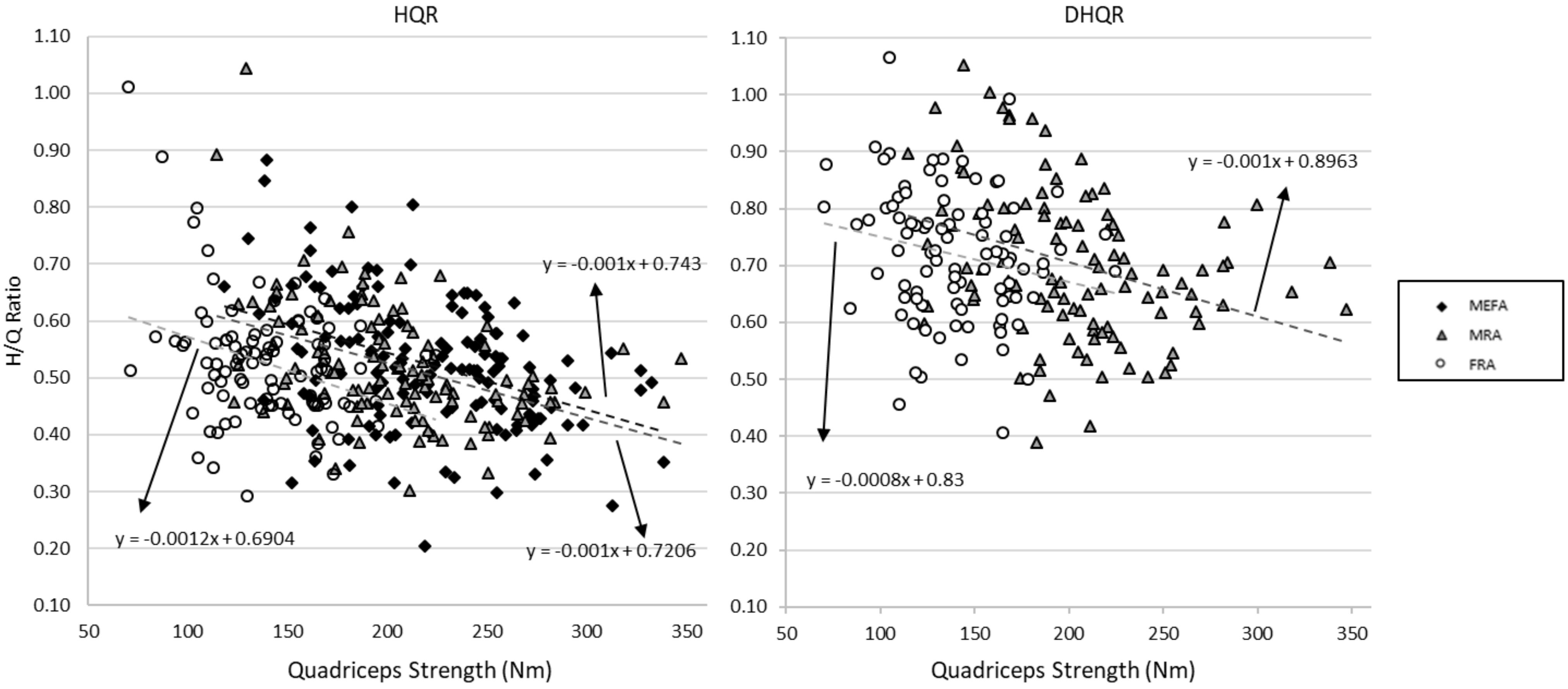


Figure 5.2 Regression analyses for Quadriceps Strength versus HQR (left) and Dynamic HQR (DHQR, right) for all groups. The linear regression equation for each group is shown.

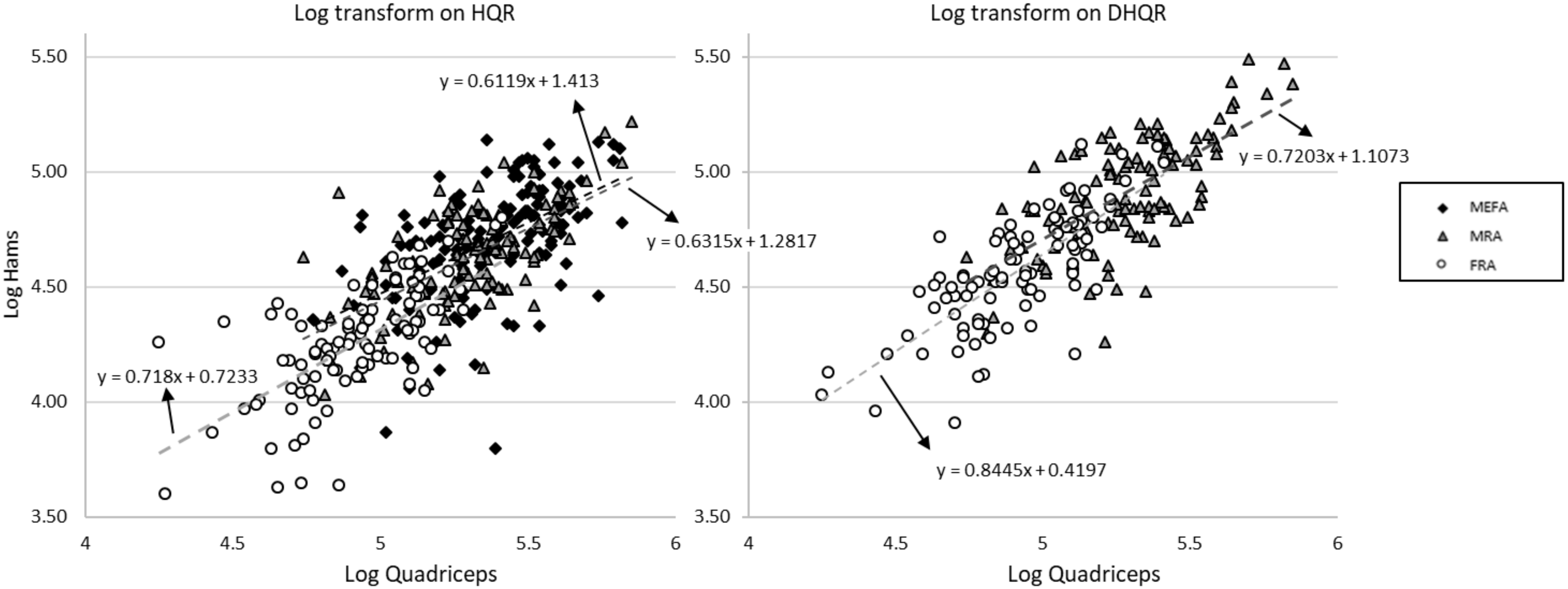


Figure 5.3 Log transformed Quadriceps and Hamstrings strength data for the HQR (left) and DHQR (right).

Table 5.2 Allometric exponent in HQR

Population	Scaled HQR
MEFA	$\text{Hamstrings/Quadriceps}^{0.61}$
MRA	$\text{Hamstrings/Quadriceps}^{0.63}$
FRA	$\text{Hamstrings/Quadriceps}^{0.72}$

Table 5.3 Allometric exponent in DHQR

Population	Scaled DHQR
MRA	$\text{Hamstrings/Quadriceps}^{0.72}$
FRA	$\text{Hamstrings/Quadriceps}^{0.84}$

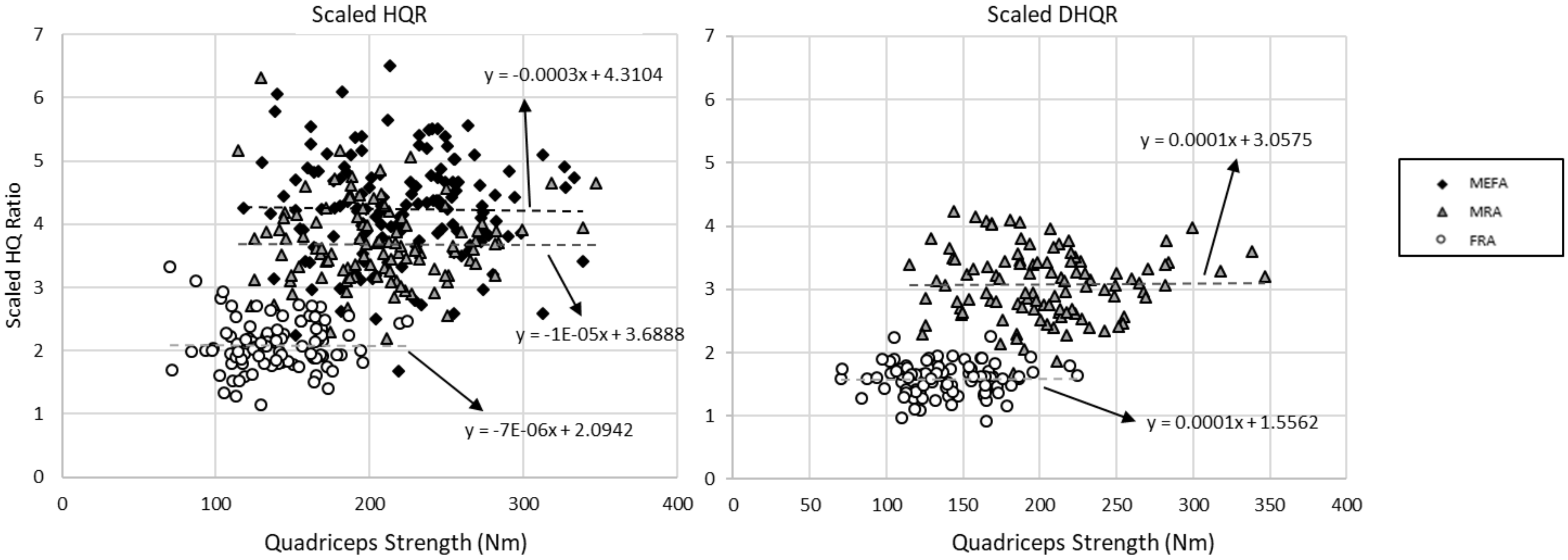


Figure 5.4 Scaled HQR (left) and scaled DHQR (right) on quadriceps strength

5.4.5 Identifying misclassification of subjects using rank analysis and cross-tabs

The outcome of the rank analysis – the data is segregated into quartiles where quartile 1 contains the lowest values of HQR and quartile 4 the highest - with cross tabulation to identify the misclassifications between traditional and scaled HQR is shown in Table 5.4.

Table 5.4 Cross-tabs report on misclassification between traditional HQR and Scaled HQR. Data in the principal diagonal (highlighted cells) shows the number of individuals with agreement on classification between traditional and scaled HQRs, whereas all other cells shows a number of misclassifications, with cells further away from the principal diagonal showing the worst misclassification.

Missclassifications between traditional and scaled HQR in MEFA (Coventional)						
Quartile		Scaled HQR				
		1	2	3	4	Total
HQR	1	27	6	0	0	33
	2	8	19	11	1	39
	3	0	8	20	6	34
	4	0	3	5	28	36
Total		35	36	36	35	142

Chi-square and P values		
▨	$MEFA\ (conventional)$ $x^2(9) = 157.65, p < 0.05$	▨
	$MRA\ (conventional)$ $x^2(9) = 127.16, p < 0.05$	$MRA\ (functional)$ $x^2(9) = 158.15, p < 0.05$
	$FRA\ (conventional)$ $x^2(9) = 102.91, p < 0.05$	$FRA\ (functional)$ $x^2(9) = 156.35, p < 0.05$

Missclassifications between traditional and scaled HQR in MRA (Conventional)						
Quartile		Scaled HQR				
		1	2	3	4	Total
HQR	1	22	5	0	0	27
	2	3	15	10	0	28
	3	2	8	13	5	28
	4	0	0	5	22	27
Total		27	28	28	27	110

Missclassifications between traditional and scaled DHQR in MRA (Funtional)						
Quartile		Scaled DHQR				
		1	2	3	4	Total
DHQR	1	23	3	0	0	26
	2	3	19	5	0	27
	3	0	5	17	5	27
	4	0	0	5	21	26
Total		26	27	27	26	106

Missclassifications between traditional and scaled HQR in FRA (Conventional)						
Quartile		Scaled HQR				
		1	2	3	4	Total
HQR	1	19	3	0	0	22
	2	5	14	5	2	26
	3	0	6	12	4	22
	4	0	1	7	18	26
Total		24	24	24	24	96

Missclassifications between traditional and scaled DHQR in FRA (Functional)						
Quartile		Scaled DHQR				
		1	2	3	4	
DHQR	1	22	1	0	0	23
	2	1	17	5	0	23
	3	0	4	15	4	23
	4	0	1	3	19	23
Total		23	23	23	23	92

There was a significant association in classification between HQRs and DHQRs and their scaled versions for all three groups (P < 0.001).

5.5 Discussion

This study aimed to examine whether the proportional (1:1) ratio between the hamstring and quadriceps strength capacity as a representation of muscle imbalance is independent of quadriceps strength. This study found that quadriceps biased HQR exists across 3 specific populations with the conventional and dynamic allometric exponents lower than 1 for all 3 groups. We demonstrated that an alternative to address this bias is to undergo a scaling process based on the allometric exponent of the specific population. Applying appropriately allometrically scaled HQR/DHQR helped remove the quadriceps bias. This allometric scaling procedure might help increase the chances of success in future work concerning HQR/DHQR as a risk factor of injury.

The allometric exponents differed slightly between the 3 groups. This variability in exponents across populations demonstrated that HQR/DHQR exponents moves further away from the proportional line (i.e., reduce) as one has increased muscular strength, but also as one has a higher level of play (elite athletes showed a more disproportionate HQR/DHQR compared to recreational). The HQR is more affected than the DHQR, indicating that eccentric strength of the hamstrings can ‘keep up relatively better’ with quadriceps strength than concentric hamstring strength. Overall though, the usage of proportional calculations should be used with care. Especially when developing an injury threshold. Many studies have described a nominal threshold based on normative cutoff values for the HQR (Manson et al. 2014, Delextrat et al. 2013b, Zebis et al. 2011a, Fousekis et al. 2011, Aagaard et al. 2002, Aagaard et al. 1998). However, our results demonstrate that all these proportional HQR thresholds can lead to potential misclassifications of individuals, with false positives primarily for individuals with high quadriceps strength.

The question remains whether it is necessary to calculate a new allometric exponent for every new sub-population tested (e.g. different sporting disciplines, playing levels, ages and gender). Differences between our subpopulations suggest that if sub-populations show similar strength one may not need to recalculate the allometric exponent. Only if sub-populations are considerably different in their actual (quadriceps) strength levels, further study to identify the true magnitude of the allometric exponent would be needed before implementing the allometric scaled HQR into risk factor studies. Alternatively, one could incorporate an allometric recalculation of the HQR within the studied population prior to subjecting it to the risk analysis. In daily practice, the use of either traditional or scaled HQRs depends on one's objective. For example, physiotherapists or physical trainers who wishes to use HQR to assess the individual's capacity to stabilise their knee joint in general, then the use of the traditional HQR may well be appropriate. However, if one wishes to predict injury risk based on HQR, then the use of allometrically scaled HQRs may be advised, but future research still needs to confirm this based on direct/indirect observations.

5.6 Limitations

A first limitation in this study is that we assumed that neither quadriceps nor hamstrings strength independently are considered a risk factor for ACL injury. In risk analyses one should not forget that the strength capacity of either of these muscles alone could be a risk factor in their own right, as has been considered in previous research (Ahmad et al. 2006, Bennell et al. 1998, Bowerman et al. 2006, Carvalho et al. 2016, Dauty et al. 2016, de Lira et al. 2017, Grygorowicz et al. 2010, Grygorowicz et al. 2017a, Holcomb et al. 2007, Kim and Hong 2011, Nunes et al. 2018, Risberg et al. 2018, Söderman et al. 2001, Uhorchak et al. 2003, Xaverova et al. 2015). So far, strength capacity of the individual muscle groups are not seen as a risk factor for ACL injury. A second limitation, as already stated above, is that the allometric exponents observed in the current study may still not be representative for other subpopulations, for example in other sporting environments (types of sports played/athletes’ status: elite or recreational). For example, elite rugby players or bodybuilders could show a different allometric exponent than that of elite football players or elite hockey players. Also, one should be prudent extrapolating our findings to sub-populations where individuals do not participate in organized sports. For future work, investigation in other populations such as non-athletes or populations of different ages might be of interest. Finally, all our results were obtained at 60°/s of joint rotation velocity. Other modalities of assessment would require separate identification of the applicable allometric exponents.

5.7 Conclusion

Quadriceps strength substantially biases traditional HQR. By identifying the allometric exponent of the relationship between hamstring and quadriceps, this bias can be removed. This systematic correction appears to be applicable across a diverse range of sporting populations. If in the future researchers would want to be successful in identifying whether (low) HQR/DHQR is a risk factor for injury, then there is the potential to use allometrically scaled HQR/DHQR. However, the use of allometrically scaled HQRs should be tested to see if they predict injury better than non-scaled HQRs which can only be confirmed through prospective work.

Chapter 6 Associating Muscular Strength Imbalance to Dynamic Function

6.1 Abstract

The aim of this study was to reveal whether there is an association between muscular strength imbalance of the quadriceps and hamstrings (represented by 4 types of HQRs) and the neuromuscular activation patterns during a single-legged hop. The study was conducted in a biomechanics laboratory setting**.** Twenty-seven male recreational athletes (age: 21.3 ± 3.4 years, height: 175.6 ± 8.1 cm, mass: 75 ± 11.7 kg) volunteered to participate in the study. Concentric hamstring and quadriceps strength (Hcon and Qcon), and eccentric hamstring strength (Hecc) were tested in participants' dominant and non-dominant limbs using isokinetic dynamometry at 60°/s, to calculate the conventional Hamstring/Quadriceps ratio (Hcon/Qcon = HQR) and dynamic Hamstring/Quadriceps ratio (Hecc/Qcon = DHQR), and both ratios were allometrically scaled to account for quadriceps strength bias (SHQR and SDHQR). A single-legged hop was used for the dynamic assessment with four EMG electrodes attached to the VL, VM, BF and ST for both dominant and non-dominant leg. Using Statistical Parametric Mapping (SPM) the study found i) no significant correlations between HQR, DHQR, SHQR and SDHQR and muscular activation vectors of the knee flexors and extensors during a single-legged hop task and ii) no significant differences in muscular activation vectors between low and high ratio groups. Muscular strength imbalance therefore appears unrelated to neuromuscular activation. Future research should cautiously associate muscular strength imbalance with dynamic function and injuries obtained during dynamic activities. Until otherwise proven, our results suggest that muscular strength imbalances do not provide an insight into how an individual performs those tasks in which the risk of injury occurs, and that for the time being the observation of both is justified in research to identify neuromuscular risk factors.

6.2 Introduction

In Chapter 3 (the systematic review) contradictory evidence relating to isokinetic testing outcomes (particularly HQR) were found as a means to reveal heightened ACL injury risk (Uhorchak et al. 2003, Söderman et al. 2001, Steffen et al. 2016). A possible reason for this inconsistency was that there was no clear understanding of whether muscular strength imbalance of the lower extremity is related to dynamic function (refers to the neuromuscular activation pattern during dynamic tasks). In this chapter we will focus explicitly on this relationship.

Dynamic function and muscular strength imbalance are observed in different ways. The dynamic function of muscles is usually observed by examining neuromuscular activation patterns during dynamic activities using electromyography. Muscular strength imbalance is usually measured in a controlled isokinetic or isometric environment (not in dynamic or game-like situations). Nonetheless, in the literature findings on muscular strength imbalance are often interpreted in the context of expected dynamic function during dynamic tasks (Carvalho et al. 2016, Dauty et al. 2016, Dellagrana et al. 2015, Grygorowicz et al. 2010, Grygorowicz et al. 2017a, Holcomb et al. 2007, Kabacinski et al. 2018, Kim and Hong 2011, Nunes et al. 2018, Risberg et al. 2018, Söderman et al. 2001, Xaverova et al. 2015). To date, there are only two studies that have looked into linking muscular strength assessments and dynamic functions (Husted et al. 2018, Shultz et al. 2009). The study by Shultz (2009) found lower thigh muscle strength was a weak (males) to moderate (females) predictor of greater quadriceps activation amplitudes. This was not supported in the study by Husted (2018) where no relationship was observed between maximal lower extremity isometric muscle strength (hip extensor, hip abductor and knee flexor) and lower extremity muscle pre-activation levels (gluteus maximus, gluteus medius, BF and ST) during side-cutting.

Athletes with an imbalance in muscle strength, may not necessarily demonstrate higher muscular activation to compensate for the weakness.

Quantifying the relationship between muscular strength and dynamic function is not a trivial task. In the abovementioned studies, the observation of dynamic function was usually reduced to EMG activations at predefined time points only. It would be better if there is no need for such data reduction, which is possible through the statistical method that was relatively recently introduced in the biomechanical field, that is, Statistical Parametric Mapping (SPM). With SPM it is possible to examine the multi-muscle EMG signal, subsequently referred to as the EMG vector-field, where using this as the sole unit of observation allows both time dependence and inter-muscle dependence to be incorporated directly into the statistical testing (Pataky et al. 2013, Robinson et al. 2015).

The aim of the study was therefore to investigate the association between muscular strength imbalance (HQRs) and dynamic function (neuromuscular activation magnitudes – multi-muscle time-series) in a dynamic hop task. Specifically, 4 types of HQRs will be associated with a multi-muscle EMG vector during a single-legged hop task. As this approach investigates the existence of linear relationships, we will also observe if any differences exist in neuromuscular patterns between those with low versus those with high muscular strength ratios, this to test the existence of possibly non-linear relationships.

6.3 Methods

6.3.1 Participants

Datasets from only twenty-seven male recreational athletes (age: 21.3 ± 3.4 years, height: 175.6 ± 8.1 cm, mass: 75 ± 11.7 kg) out of 104 (55 males and 49 females) and limited to a single-legged hop task were eligible for analysis after quality checking. This considerable reduction in data was primarily due to loss of signal or undesirable artefacts in the EMG signals. Participants were given a questionnaire on their injury history and none had a recent (< 12 month) major lower limb injury. Written consent was obtained from all participants and the study was performed in accordance with the university ethics committee guidelines (14/SPS/032).

6.3.2 Isokinetic Dynamometer Assessment

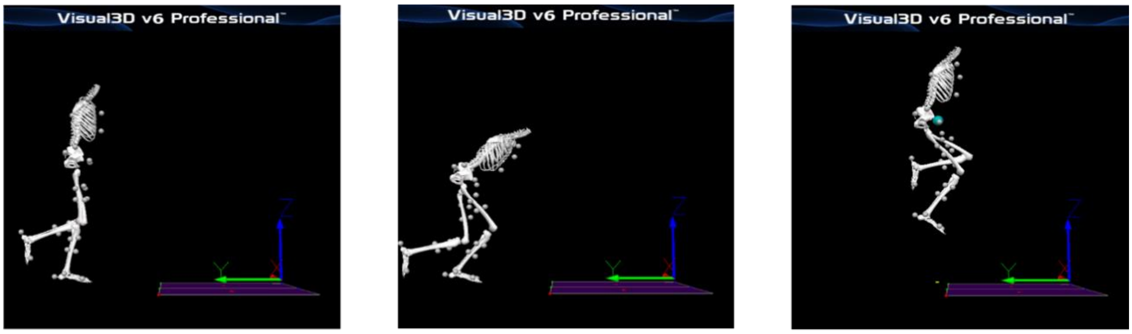
Assessment of muscular strength of the hamstrings and quadriceps was conducted as described in detail in Chapter 5 section 5.3.2

The peak torques for knee flexors and extensors were averaged for the five trials for both the dominant and non-dominant leg. Peak torques were then computed into 4 ratios; conventional HQR (HQR), functional or dynamic HQR (DHQR), allometrically scaled HQR (SHQR) and allometrically scaled DHQR (SDHQR). Quantification of allometrically scaled ratios is described in Chapter 5 section 5.3.4. The group was then divided into quartiles (independently for each ratio), ranked from 1-4 with 1 being the lowest and 4 the highest. This allowed to compare the two extreme groups that were ranked 1 (lowest HQR) and 4 (Highest HQR), excluding those ranked 2 and 3. The highest and lowest ranked groups were used to evaluate any between-group differences in neuromuscular activation patterns across time.

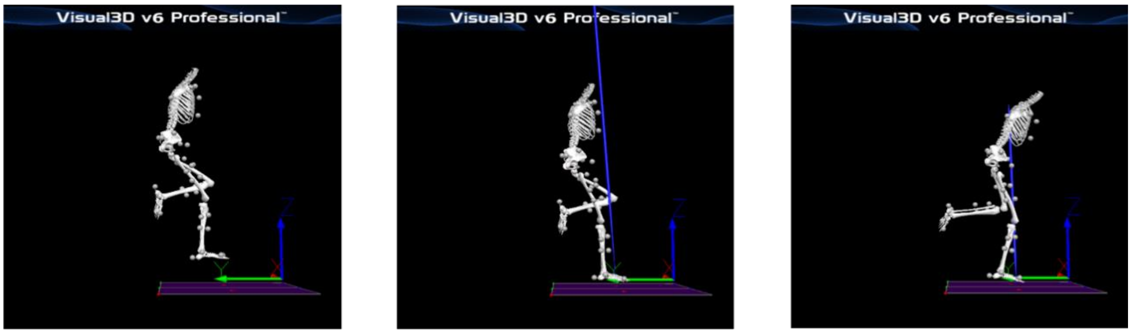
6.3.3 Electromyography (EMG) placement

Eight EMG sensors (Noraxon, Model 546 DTS Belt Receiver EMG Sensor, Arizona, USA) and 8 dual EMG electrodes (Noraxon dual EMG electrode) were placed on both the dominant and non-dominant legs. The dual EMG electrodes were self-adhesive and made from silver chloride (Ag/AgCl) with dimensions of the figure 8-shaped adhesive is 4cm x 2.2cm, diameter of the two circular adhesives is 1cm and Inter-electrode distance is 1.75cm. Preparation and placement of electrodes for EMG were done following the Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles guidelines (Stegeman and Hermens 2007). Subjects were shaved if the skin surface at which the electrodes had to be placed was covered with hair. The skin was then cleaned with an alcohol swab and dried before electrodes were placed. Sensors and electrodes were placed on four muscles of each upper leg; the vastus lateralis (VL), vastus medialis (VM), biceps femoris (BF) and semitendinosus (ST). For VL and VM the subjects were required to extend their knees and the VL electrode was placed 2/3rd distance on the line from ASIS to the lateral side of the patella while VM electrodes were placed 80% on the line between ASIS and medial ligament of the knee. For BF and ST, subjects were instructed to flex their knees while the investigator added a small resistance. BF electrodes were placed at 50% on the line between the ischial tuberosity and the lateral epicondyle of the tibia. ST electrodes are placed at 50% on the line between the ischial tuberosity and the medial epicondyle of the tibia. Electrode placement was aligned with the striation of the muscle fibers as best as possible.

6.3.4 Single-legged hop



Start/Eccentric Concentric Highest COM



Pre-activation Landing End/LDPLUS1

Figure 6.1 Phases of single-legged hop

This task was chosen to imitate an acceleration and rapid deceleration movement in a sports setting (Boden et al. 2000). The task consisted of a start/eccentric phase (muscles are relaxed and lengthened) followed by concentric phase (shortening of muscles), pre-activation (50ms before initial contact) as done by Zebis (2009), landing (initial contact with the force platform) and end/LDPLUS1 (1 second after initial contact). Participants had to jump forward and land on the force platform and were tested on both their dominant and non-dominant legs. The starting distance for the single leg hop landing was determined by the length of the subject’s leg; measured from the greater trochanter to the lateral malleolus (Webster et al. 2004). Subjects were given 2-3 trials to ensure that they were sufficiently familiarized with the task. Five dynamic trials were recorded for both legs.

6.3.5 Data collection and processing

6.3.5.1 EMG measurement

The EMG system was comprised of a Direct Transmission System (DTS) belt receiver (Noraxon, Model 580, Arizona, USA) and EMG sensors at a sampling frequency of 1500 Hz which was also synchronized with motion capture software with 10 infrared cameras at sampling frequency of 250 Hz (Proreflex Qualisys, Gothenburg, Sweden) and a force platform (Kistler Type 9281E, Winterthur, Switzerland) at a sampling frequency of 1500 Hz. All EMG signals were pre-processed according to manufacturer recommendations (Konrad 2005). Signals were then full-wave rectified, high-pass filtered at 20 Hz and low-pass filtered at 500 Hz. Commonly for normalization, maximum voluntary isometric contraction (MVIC) is used in the area of comparing neuromuscular activation levels. However, we were unable to use MVIC as a method of normalization due to pragmatic constraints such as managing time efficiency. Our data collection procedure took 2-3 hours with tests that included isokinetic strength measurement (8 tests of isokinetic strength), 4 dynamic tasks pre-test (Bilateral drop max vertical jump, unilateral drop max vertical jump, max single legged hop for distance and side-cutting), a fatigue simulation, and post-test of all the dynamic tasks mentioned. Therefore, we considered an alternative means of normalization which uses a compromise of within task normalization – the peak dynamic method for its reliability to reduce inter-individual variability (Burden et al. 2003, Yang and Winter 1984). Specifically, we took the reference activation value as the highest activation value obtained during the push-off that precedes the observed landing phase (taking from start of the push-off until the highest position of the center of mass). This reference value is expected to come from a contraction phase where maximum effort of the muscles is used to perform the single-legged hop. The EMG data were normalized for each individual trial. Filtered signals were smoothed by calculating the root mean square

(RMS) value within a 100 ms moving average window. All signals were processed using Visual3D (version 6.00.24, C-Motion, Germantown, MD, USA).

6.3.6 Statistical analysis

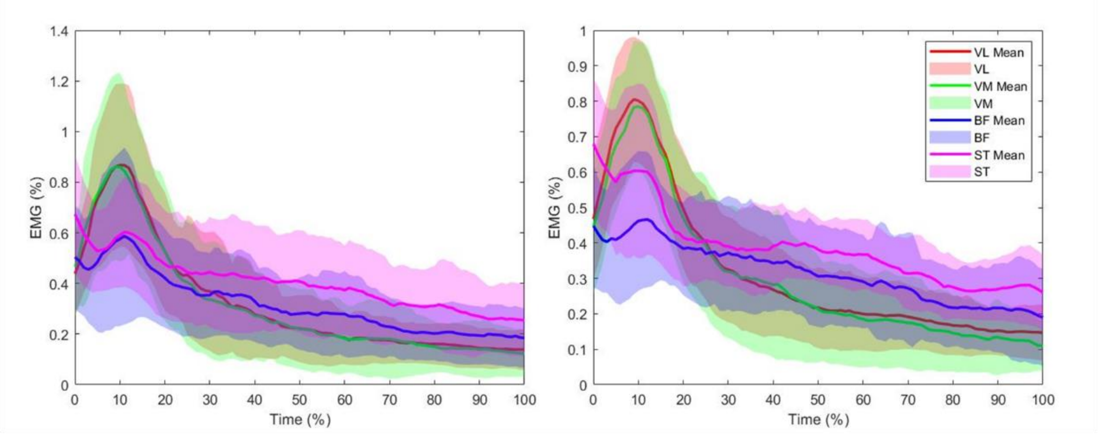
Mean EMG vectors were formed by arranging each neuromuscular EMG signal (VL, VM, BF and ST) cropped between movement start and end, as a four-component vector-field. Associations for individual muscles were not lost by using the multi-vector analysis. If significant relationships were observed in the vector analysis, SPM allows the data to be analysed (post-hoc) either in pairs (paired vectors) or at individual muscular level to observe the muscle pairs/muscle responsible for significant regions of the (i) CCA analysis and (ii) Hotellings T2 test.

Canonical Correlation Analysis was then used to correlate the four types of HQRs (HQR, DHQR, SHQR and SDHQR) which are discrete variables, to the time-series EMG vector, for which alpha was set at 0.05. Canonical correlation analysis (CCA) is the vector-field equivalent of regression (Pataky et al. 2013). The CCA analysis was implemented in the SPM1D Statistical Parametric Mapping package (Pataky 2012) in Matlab **(**MATLAB Release 2015a, The MathWorks, Inc., Natick, Massachusetts, United States)**.** If significant relationships were observed, post-hoc analyses were conducted at a paired and singular muscular level, observing correlations of quadriceps, hamstrings and hamstrings eccentric strength with their respective muscular activation profiles (i.e. VL and VM for quadriceps and BF and ST for hamstrings).

For the second part of the analysis the study compared the mean EMG activation vectors from the extreme groups of low and high HQRS and SHQRs (rank 1 and 4). This was done using a Hotellings T2 test (vector-field equivalent of independent t-test), for which Alpha was also set at 0.05. Also, if significant relationships were observed, post-hoc analyses were conducted at a paired and singular muscular level, observing correlations of quadriceps, hamstrings and hamstrings eccentric strength with their respective muscular activation profiles (i.e. VL and VM for quadriceps and BF and ST for hamstrings).

6.4 Results

6.4.1 EMG data of VL, VM, BF and ST after processing and normalization.



Dominant

Non-Dominant

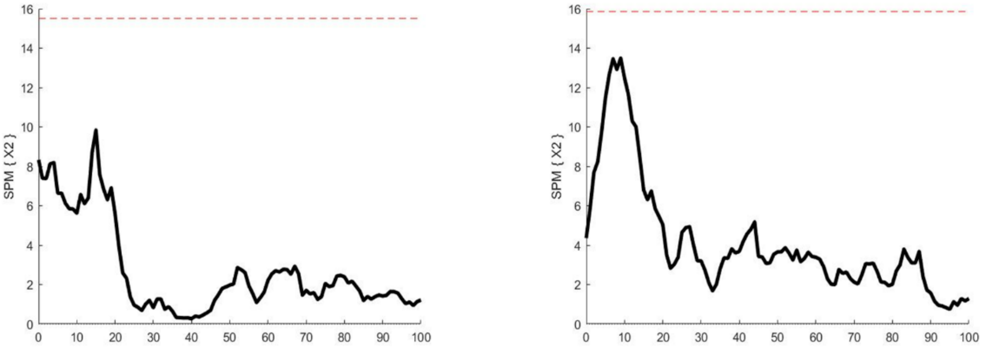
Figure 6.2 EMG data means (+/- standard deviations) for the 4 muscles (VL, VM, BF and ST) for all 27 subjects after processing and normalization. Time 0 - 4.58 % were defined as the pre-activation phase (50 ms before initial contact/landing) and 4.58-100% were initial contact/landing to the end phase of the single-legged hop task.

6.4.2 Correlations between the HQRs and muscular activation vector over time (within-group analysis).

There was no significant relationship recorded between the EMG vector-field (of VL, VM, BF and ST) and the HQRs (HQR, DHQR, SHQR and SDHQR) over time (P>0.05) as shown in Figure 6.3.

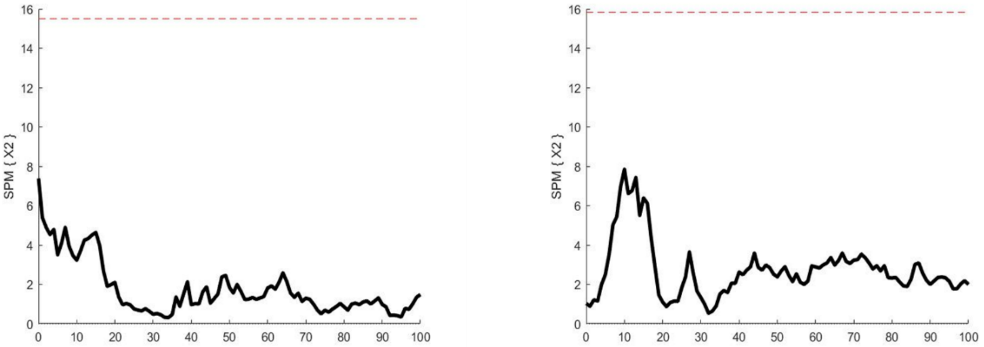
6.4.3 Muscular activation vector of four muscles (VL, VM, BF and ST) over time between groups of low and high HQRs (between-group analysis).

There was also no significant difference recorded between the EMG vector-field (of VL, VM, BF and ST) and the HQRs (HQR, DHQR, SHQR and SDHQR) between low and high HQRs over time (P>0.05) as shown in Figure 6.4. Therefore, post-hoc analysis was not pursued for both observations.



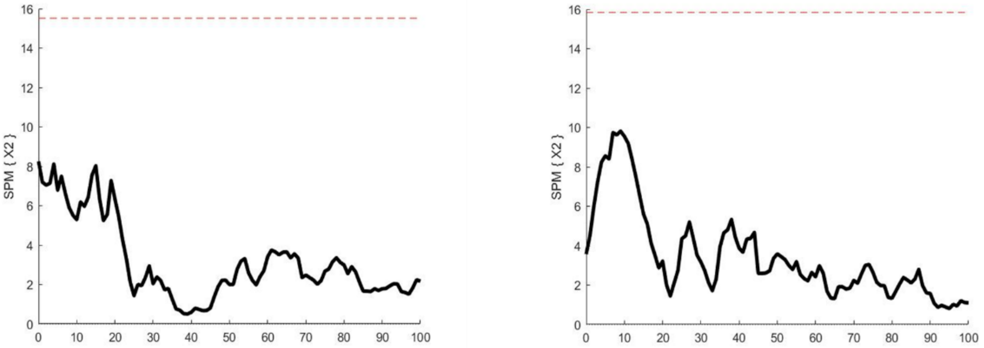
Male Dominant HQR

Male Non-Dominant HQR



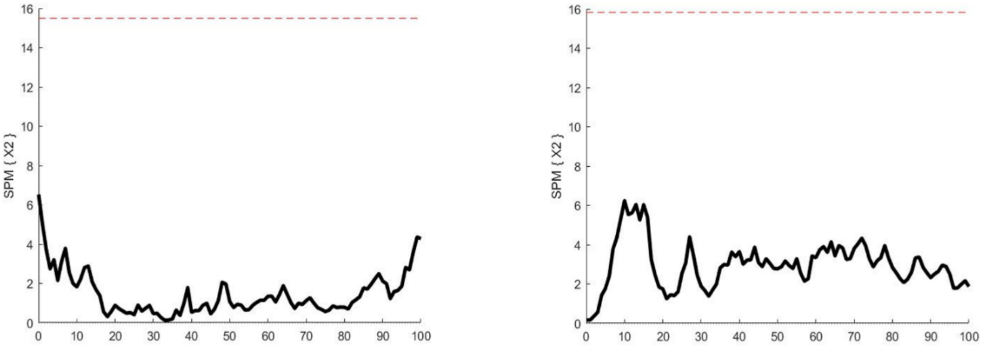
Male Dominant DHQR

Male Non-Dominant DHQR



Male Dominant SHQR

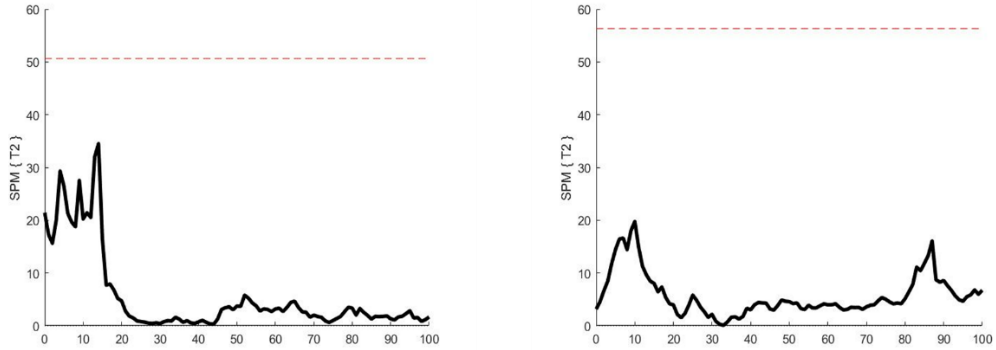
Male Non-Dominant SHQR



Male Dominant SDHQR

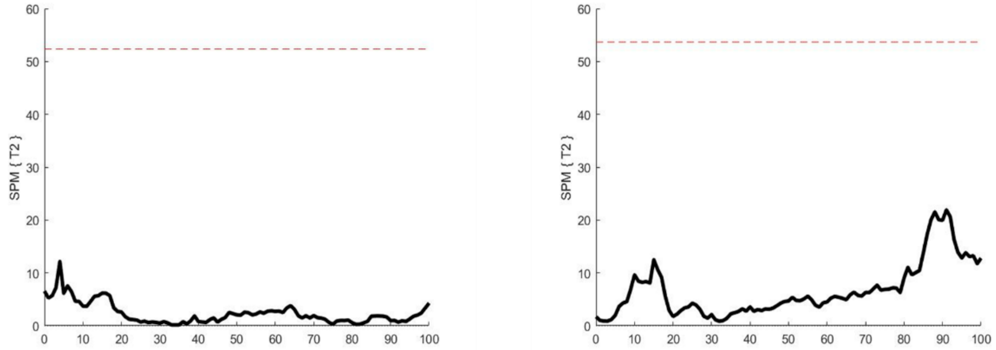
Male Non-Dominant SDHQR

Figure 6.3 CCA inference profiles of the relationship between neuromuscular activation vector of the 4 muscles (VL, VM, BF and ST) and the 4 HQRs (HQR, DHQR, SHQR or SDHQR) for both dominant and non-dominant side.



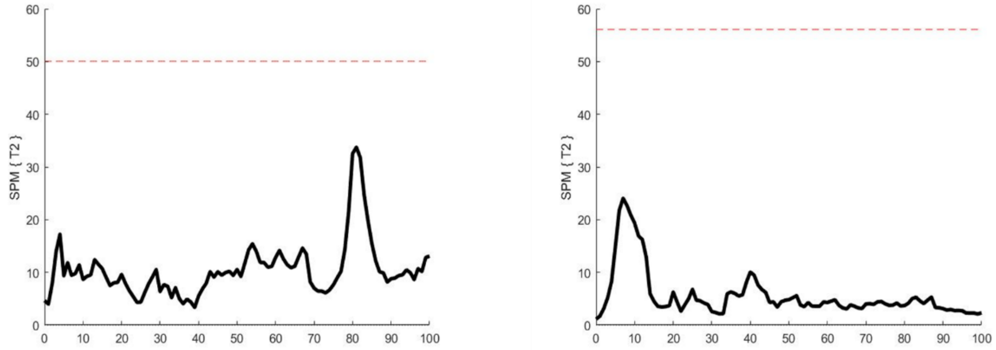
Male Dominant HQR

Male Non-Dominant HQR



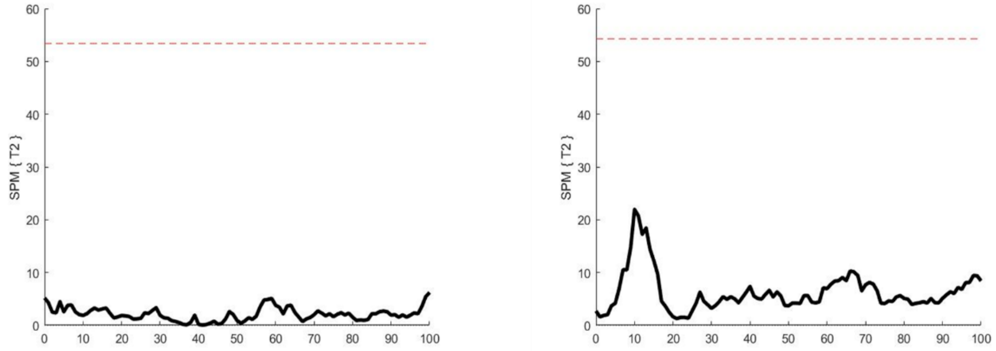
Male Dominant DHQR

Male Non-Dominant DHQR



Male Dominant SHQR

Male Non-Dominant SHQR



Male Dominant SDHQR

Male Non-Dominant SDHQR

Figure 6.4 Hotelling's T^2 Test inference profiles comparing the neuromuscular activation vector of the 4 muscles (VL, VM, BF and ST) between groups of low and high HQRs of all 4 HQRs (HQR, DHQR, SHQR or SDHQR) for both dominant and non-dominant sides.

6.5 Discussion

The aim of this study was to investigate any associations between muscular strength imbalance and dynamic function of the quadriceps and hamstring muscles. This study found that muscular strength imbalance and dynamic function were not associated. Further analysis of neuromuscular activation vectors between low and high HQRs also did not find any significant difference in their activation patterns.

In the past, high muscular strength imbalances have been assumed to translate to the imbalances of co-activation or poor function of the knee musculature during dynamic activities that contribute to injuries (Carvalho et al. 2016, Dauty et al. 2016, Dellagrana et al. 2015, Grygorowicz et al. 2017a, Holcomb et al. 2007, Kabacinski et al. 2018, Kim and Hong 2011, Lyons 2006, Nunes et al. 2018, Risberg et al. 2018, Söderman et al. 2001, Xaverova et al. 2015). Surprisingly, these studies did not necessarily measure the relationship between muscular strength imbalance with the functional aspect of the movement. The assumption that muscle strength imbalance influences dynamic function needs to be clarified by observing the relationship between them. Our study however, showed no significant relationships between muscular strength imbalance (HQRs) and dynamic function. This aligns with observations from a recent study (Husted et al. 2018) where they found that isometric maximal strength of the knee flexors was not related to the pre-activation of the BF and ST muscles during a side-cutting manoeuvre in adolescent female handball and soccer elite athletes. The fact that neither muscular strength nor muscular imbalance demonstrates a clear relationship with muscular activation levels raises an important question that perhaps muscular strength is not necessarily accompanied by compensatory higher muscle activation during dynamic activities. To date, we are not aware of any other studies that have investigated the relationship between muscular strength imbalance and neuromuscular activation/functions, so interpreting both facets interchangeably should be avoided.

The concern with the available muscular strength imbalance literature in assuming its contributive effect on dynamic function is that future prevention programs might focus predominantly on strength training to decrease strength imbalances (Freeman et al. 2019, Milanese and Eston 2019, van der Horst et al. 2015, van Dyk et al. 2019, Whyte et al. 2019) and less on neuromuscular techniques and strategies that promote neuromuscular co-activation balance. Resistance training to improve muscular strength imbalance may not necessarily result in adopting a better motor pattern, and probably still needs to be combined with other neuromuscular training modalities such as involving balance/coordination exercises and specific jump training and sports specific technical training. Studies have found that plyometric exercises (Hewett et al. 1996) and balance/coordination (Holm et al. 2004, Zebis et al. 2008) exercises are well associated with improvements in functional performance. As explained by Husted (2018), the fact that plyometric and balance/coordination exercises seem poorly integrated in daily training among adolescent female athletes seems alarming bearing in mind the high risk of non-contact ACL injury in this particular population. Furthermore, a recent study by Weir et al. (2019) showed that biomechanically informed injury prevention training was effective in reducing ACL and lower limb injury incidence and demonstrated improvements in desirable muscle activation strategies. Perhaps this ‘technique correction approach’ is better suited to improve neuromuscular activation strategies rather than assuming that strength training alone would be able to correct this. From these evidences, future preventive efforts should focus on implementing all types of neuromuscular training in their daily training routines, i.e. exercise programs featuring training drills that target muscle strength, plyometric, balance/coordination, core exercises and biomechanically cued instructions and not just solely or predominantly resistance training. To note, this study was a cross-sectional comparison, and does not involve any training modalities. We are therefore not certain that if increased muscular capacity or decreased muscular strength imbalances by itself would not be able to lead to important neuromuscular activation changes.

6.6 Limitations

The study only focused on one task which is the single-legged hop. Future prospective studies could include the side-stepping/cutting task and drop vertical jumps (Smeets et al. 2019, Zebis et al. 2009). Another limitation is that despite its benefits of incorporating time-dependent and multi-muscle evaluations, SPM does not evaluate associations with time shifts in activations. That would require other approaches, such as PCA (Cappellini et al. 2006, O'Connor and Bottum 2009). By not using MVCs to normalize the study’s EMG data, it is prone to overestimations. Although modifications were made by normalizing dynamically by setting the reference activation value as the highest activation value during the phases between start of the push-off until the highest position of the center of mass (to simulate contraction phase where maximum effort of the muscles is thought to be used), there were still overestimations as shown in figure 6.2 which shows that there is a possibility that the muscles’ maximum effort could vary within the phase (Burden 2010, Burden et al. 2003). However as mentioned before in the thesis, we were not able to use MVCs due to time efficiency in incorporating tests within a 2-3 hour protocol.

6.7 Conclusion

The study observed the association between muscular strength imbalance and dynamic function across all phases of the single-legged hop. Muscular strength imbalance of the quadriceps and hamstrings was not related to neuromuscular activation vectors during single-legged hops. Neuromuscular activation vectors of individuals with low muscle strength ratios were also not distinguishable from individuals with high muscle strength ratios. Future research should use caution when associating individual’s muscular strength imbalance measurements with dynamic function, and this relationship should still be thoroughly investigated.

Chapter 7 General Discussion

7.1 Summary

The key findings from this thesis revealed that (i) weak prospective evidence exists for neuromuscular predictors of a primary non-contact ACL injury despite a substantial body of research that has studied various neuromuscular risk factors for ACL injury. Current evidence is contradictory, and studies are limited largely to case-control and associative investigations; (ii) traditional HQRs were found to be biased by quadriceps strength and by applying allometric scaling principles, this bias could be removed; (iii) low and high HQRs were not associated with altered neuromuscular activation during dynamic tasks. Therefore, assumptions that a low HQR can be a predictor of neuromuscular deficits in performing dynamic tasks, or the associated injury risk, are questionable.

7.2 An update on the systematic review

Since the final date for which studies were included in the systematic review in Chapter 3 (July 2015), the systematic literature search was re-run on the 5 electronic databases from PubMed, Scopus, Web of Science, CINAHL and SPORTDiscus, i.e. between July 2015 and December 2019. This was to further explore the developments in the literature on neuromuscular risk factors of non-contact ACL injuries. The new search revealed the recent publication of 5 review papers (2 narrative reviews and 3 systematic reviews), an exponential growth in associative studies, little addition of studies on neuromuscular activation, and only one prospective study associating neuromuscular activation with non-contact ACL injury risk.

Table 7.1 Updated studies on non-contact ACL injuries (May 2015 – Dec 2019)

	Reviews	Prospective Studies	Associative Studies
Muscular Strength Imbalance (HQR)	(Bencke et al. 2018, Hewett et al. 2016, Monajati et al. 2016, Read et al. 2016)	N/A	(Carvalho et al. 2016, Croix et al. 2018, de Lira et al. 2017, Dellagrana et al. 2015, Grygorowicz et al. 2017a, Grygorowicz et al. 2017b, Kabacinski et al. 2018, Lehnert et al. 2018, Liporaci et al. 2018, Nunes et al. 2018, Risberg et al. 2018, Xaverova et al. 2015)
Neuromuscular Activation (EMG)	(Bencke et al. 2018, Dedinsky et al. 2017, Hewett et al. 2016, Read et al. 2016)	(Smeets et al. 2019)	(Husted et al. 2018, Malfait et al. 2016, Shibata et al. 2018)

The last 4 years showed that the trend of limited prospective investigation which we had revealed remains, and that there is very little high-quality (level 1) evidence being added to the current knowledge on risk factors. Therefore, tendency of biased reporting around poorly evidenced risk factors can be observed in associative studies. Moreover, there seemed to be a trend on the importance of prevention programs observed by the sprouting growth of studies which have been highlighted by the 3 reviews papers (Dedinsky et al. 2017, Hewett et al. 2016, Monajati et al. 2016). To add in concordance with the message of our systematic review, 2 review papers highlighted that the literature surrounding neuromuscular risk factors are still to date strikingly sparse in associating with non-contact ACL injuries, indicating that there is a growing perception of a need to generate new higher quality evidence (Bencke et al. 2018, Read et al. 2016).

7.3 Critical reflections on muscular strength imbalance as risk factor

Few experts will doubt that an imbalance of strength in the knee musculature is a potential risk factor for injury. Strong quadriceps during concentric actions together with weak hamstrings is expected to decrease the stability of the knee by increasing anterior tibial shear force and deliver stress on the ACL. It may even lead to increased risk of hamstring tears (Orchard et al. 1997). Therefore, the assessment of muscle strength imbalance in the form of HQR has received considerable attention in the literature.

In Chapter 5 we discovered that if one wishes to assess imbalance unbiased for quadriceps strength, an allometric scaling to the calculation of HQR should be applied. If this bias was not acknowledged in HQR calculations as done in the traditional way of calculating HQRs, there is a high probability of misclassifications as reported in our study. These misclassifications as a result from the biased HQRs, may have led to the inconsistent findings with poor predictive power seen in our systematic review (Chapter 3). However, before implementing the allometric scaling technique, it must first be justified through prospective work to directly assessed its relationship with non-contact

ACL injuries. Although this allometric scaling is a step forward to remove the bias observed in traditional HQRs, the chances of it being established as a strong predictor of injury with high sensitivity and specificity remains slim (Bahr 2016).

Besides these limitations in terms of predictive statistics, our research has also pointed out that the steps of data collection, processing, and analysis to a great extent determine the reliability and validity of the outcome measures. During our study we encountered several critical choices on these aspects, shown in table 7.2. We noticed that often (some of) these aspects are not reported. In order to increase our chances of being able to observe in future prospective cohort studies whether or not HQR is a risk factor of injury, it is advisable that all procedures are described in as much as possible detail to ensure replication potential. In fact, if one were to consider running multi-centre studies to increase participant numbers, then this is of particular concern.

Table 7.2 Steps of ensuring reliable and valid parameters of muscular strength imbalance assessments

Data Collection	Data Processing	Data Analyses	Confounding Factors Leading to Injuries
• Concentric and Eccentric? • Angular velocity? • How many repetitions? - Consecutively or with breaks? • Gravity correction?	• Normalize to body weight? • Normalize to height? • Normalize to tibia length? • Range of motion of data reported? – Are extreme ranges removed?	• Only peak torques? • Angle-specific torques?	• Are trainings given equally across subjects? • Environmental factors played any role? i.e.: weather, footwear etc. • Status of the individual on the day of injury?

7.4 Critical reflections on neuromuscular behaviours as risk factor

Neuromuscular behaviours or patterns have been observed for a few decades now and seem to demonstrate similar alterations in individuals who go on to suffer ACL injuries. Currently, 2 prospective studies found that having low medial-to-lateral-co-activation where individuals tend to activate the lateral part of the knee musculature are associated with acquiring an ACL injury (Smeets et al. 2019, Zebis et al. 2009). Although a significant observation, both studies used different tasks (drop vertical jump and side-cutting). Perhaps, if more prospective work is done in the near future observing this pattern in different tasks, as well as adding to the literature using the same tasks, we might come closer towards having a better understanding of the knee musculature and its relationship with non-contact ACL injuries during dynamic activities.

In relation to muscular strength imbalance as observed in chapter 6, we have extensively elaborated on the common assumption that muscle strength imbalance reveals something about neuromuscular function during the execution of dynamic tasks. We did not find any relationships between these variables and there were no significant discrepancies between neuromuscular activation patterns of individuals with low versus high muscle strength imbalance. Nonetheless, future studies should remain critical and continue to explore this relationship. The relationship between neuromuscular strength imbalance of the quadriceps and hamstring muscles and its neuromuscular activation was explored through SPM to avoid unnecessary data reduction in terms of observing activation patterns. Whilst this approach has the benefit of being more comprehensive, it still comes with the limitation that it does not directly evaluate temporal differences within those activation patterns. Past studies have for example shown that observing timing shifts through the use of Principal Component Analysis (PCA) can reveal important alterations in neuromuscular behaviour (Cappellini et al. 2006, O'Connor and Bottum 2009). It may be advised in the future work to progress towards methods such as PCA to evaluate all potentially critical features of neuromuscular behaviour, but this was beyond the scope of this project.

Through this work it has become clear that there remains limited evidence on neuromuscular activation patterns as a risk factor for non-contact ACL injury. Part of this may be caused by the fact that EMG recordings are not easy to acquire even in a controlled lab environment, and that they are not easily interpreted for quantifying deficits in neuromuscular behaviour. Most likely this explains why studies on neuromuscular activation are scarce compared to studies on kinetics and kinematics.

7.5 Implications for practitioners

To date, both quantity and quality of evidence revolving around neuromuscular markers associated with non-contact ACL injury (muscular strength imbalance and neuromuscular activation pattern) are very limited and contradictory and should be interpreted with care. With the growing rate of prevention programs and associative studies, it is imperative that future work is emphasized on contributing towards more prospective evidence that enables strengthening of the core foundation where this research question is built upon. A stronger foundation will directly/indirectly improve the quality of the observed marker and will aid in leading to a consistent direction (quality-focused objective) of the literature.

If practitioners wish to use muscle strength imbalance measurement or HQRs, using an allometric scaling as described in chapter 5 would help in removing quadriceps strength bias calculations as demonstrated when measuring using traditional HQRs. Particularly for very strong athletes this would have a tangible impact. However, to increase the probability of observing associations between HQRs and non-contact ACL injury, this HQR modification still needs further justification, and can only be confirmed through prospective work. Our findings also suggested that dynamic function and muscular capacity should both be observed in search of injury risk. As far as this thesis was able to observe, we found that the associations between muscular strength imbalance and dynamic function were not obvious. It is recommended that researchers keep in mind that both observations appear to have independent value.

7.6 Limitations

Scientific experimentation inherently comes with limitations. One overarching limitation of the experimental work presented in this thesis is that it reports on observations in a lab-based and not in a real-world environment. The findings associated with this study may or may not translate to what really occurs in the real-world environment. Perhaps with technological advancements we may one day be able to measure these risk factors on field which will be a better representation and thereby increasing the chances of acquiring a meaningful observation for predicting injury. In the future, we hope to gradually shift from lab-based experiments to field-based observations. Another limitation is that we did not succeed in obtaining true prospective evidence. Even with all the considerations in increasing the probability to observe participants who will potentially acquire an ACL injury (by recruiting athletes from ACL risk sports with a constant monitoring over 9 months) we were not able to record any incident. The contingency study’s narrative could have been different if we were able to acquire individuals with ACL injuries. Therefore, observations made by the study are only cross-sectional and act as surrogate measurements (based on risk markers of prospective work) that could not be translated or associated directly with neuromuscular risk factors of ACL injury.

7.7 Future research/directions

For future examination of ACL injury risk, one approach would be to move beyond simple associations between two variables and to encourage a more multi-factorial or “complex” approach (Bittencourt et al. 2016). But before we combine the different disciplines in the area (e.g. anatomical, hormonal, biomechanical and etc.), the multiple factors in the neuromuscular field will need to be addressed first. Finding the association between muscular strength imbalance and neuromuscular control through prospective work could branch a novel approach in catering for injury profiling. Essentially, if muscular strength imbalance and neuromuscular control are not linked, they should still be paired (as one is a representative of neuromuscular capacity and the other, during dynamic bouts) but then be interpreted separately. For instance, having both a bad HQR and neuromuscular activation may signify an individual with a potential risk of injury. Also, for future research to focus on neuromuscular activation parameters such as the medial-to-lateral-coactivation of hamstrings and quadriceps, could increase potential associations between injury risk as in recent work this variable has seen consistent findings in two prospective studies (Zebis et al. 2009, Smeets et al. 2019).

To date within the context of the non-contact ACL injury prevention framework (Donnelly et al. 2012), we remain stagnant at stage 2 in the effort to find relevant variables as observed through our contingency studies of allometric scaling and association between muscular strength imbalance and dynamic function. Moreover, as the results in this thesis were cross-sectional, future validation is needed through prospective work to further evaluate these associations. To promote feasibility in prospective practice, one viable approach is establishing a multicentre experiment, where data can be shared across multiple research centres, adding up the samples of monitored subjects. However, we do acknowledge that although this effort is in reality hard as venues and equipment need to be accurately aligned across centres but it is certainly possible (Myer et al. 2014). Another alternative is to work alongside federations by promoting test-batteries that allow key markers of most acquired injuries within the related sport. This will open up opportunities for more researchers to make prospective work a good practice in an effort to get stronger evidence in this field.

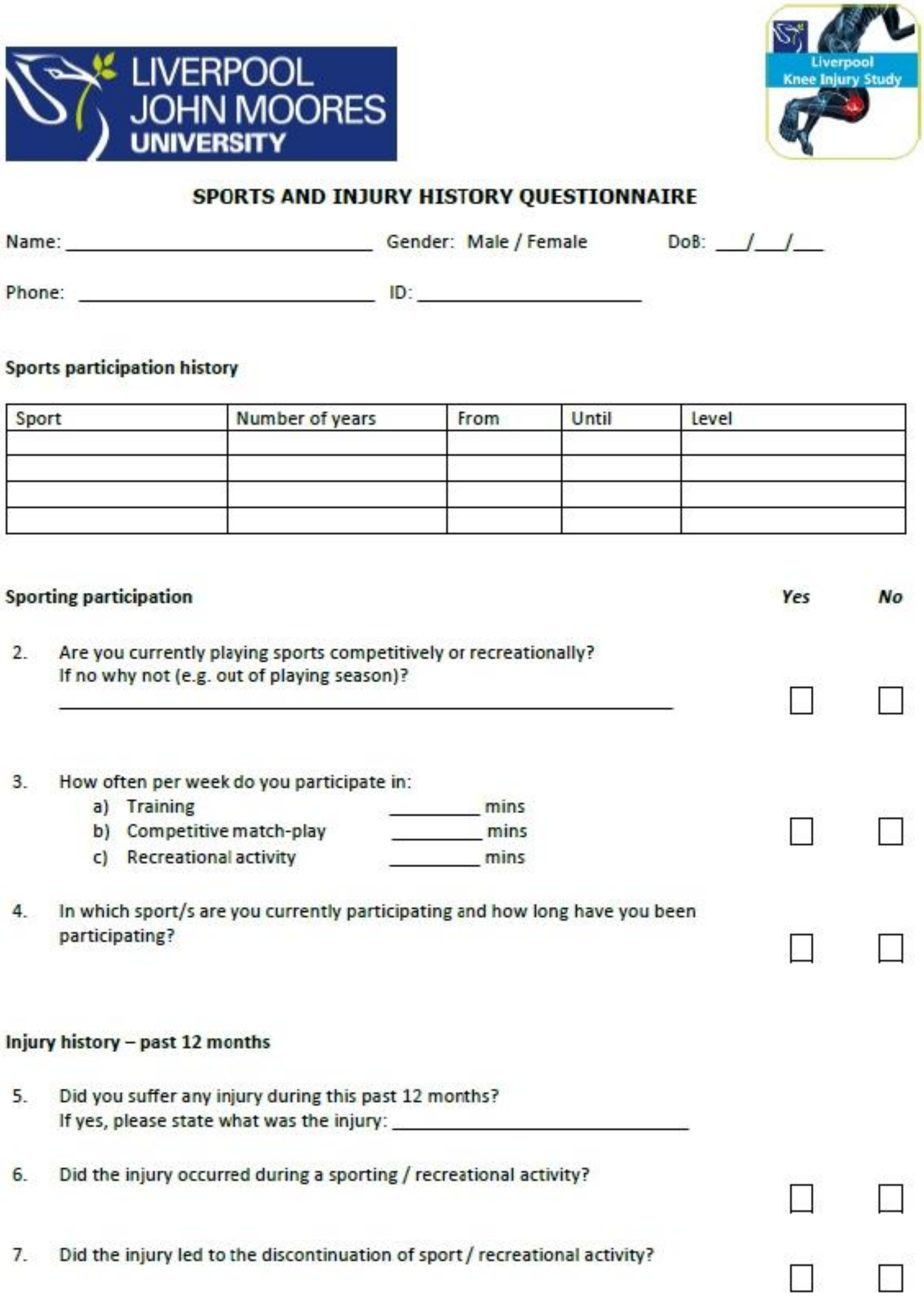
Another opportunity is to venture into real-world observation for example with new advancement in technologies such as the myontec EMG shorts or EMG sensors (Bengs et al. 2017) and full body inertial and magnetic system by Xsens (Mecheri et al. 2016) that might make EMG measurement more practical in field settings.

7.8 General Conclusion

This thesis found that prospective evidence of neuromuscular risk factors is scarce, very limited and is contradictory. However, to date, a growing trend of studies associating neuromuscular risk factors and injuries from case control and associative studies have been observed. This trend of building evidence on a very inconsistent and limited prospective foundation should be interpreted with caution and focus should be emphasized on generating more prospective work. The relevance of observing muscular strength imbalance using allometric scaling was demonstrated as a novel analysis technique to eliminate the quadriceps bias which is present in the traditional way of calculating HQRs. This thesis also was the first to explore the relationship between muscular strength imbalance and neuromuscular function which is predominantly assumed to be related. The study did not find any significant relationship between muscular strength imbalance and neuromuscular function nor distinguish patterns of neuromuscular activation between low and high HQRs. Ultimately, the outcome of this thesis critically reviewed the quality of the research evidence, provides a new perspective on how to observe HQRs and a better understanding at the assumed relationship between muscular strength imbalance and neuromuscular function.

Chapter 8 Appendices

8.1 Appendix A. Sport and Injury History Questionnaire



LIVERPOOL JOHN MOORES UNIVERSITY

Liverpool Knee Injury Study

SPORTS AND INJURY HISTORY QUESTIONNAIRE

Name: ______________________ Gender: Male / Female DoB: ___/___/___

Phone: ______________________ ID: ____________________

Sports participation history

Sport	Number of years	From	Until	Level

Sporting participation ***Yes*** ***No***

2. Are you currently playing sports competitively or recreationally? If no why not (e.g. out of playing season)? ______________________ ☐ ☐

3. How often per week do you participate in: ☐ ☐
    a) Training _________ mins
    b) Competitive match-play _________ mins
    c) Recreational activity _________ mins

4. In which sport/s are you currently participating and how long have you been participating? ☐ ☐

Injury history – past 12 months

5. Did you suffer any injury during this past 12 months? If yes, please state what was the injury: ______________________

6. Did the injury occurred during a sporting / recreational activity? ☐ ☐

7. Did the injury led to the discontinuation of sport / recreational activity? ☐ ☐

Extended Injury history

8. Have you ever fractured or broken any bones in your body? Bone Fractured and Date: ____________________ ☐ ☐

9. Have you ever dislocated any joint in your body?
Joint Dislocated and Date: ____________________ ☐ ☐

10. Have you ever had surgery done as a direct result of a fracture or dislocation? ☐ ☐

11. Do you have a pin, wire, plate, or screw in your body as a result of surgery?
Where? ____________________________ ☐ ☐

12. Have you ever had an injury to your back for which you sought medical attention? ☐ ☐

13. Do you continue to experience back pain?
If yes please specify ____ ☐ ☐

14. Have you ever injured ligaments, cartilage, or any other structures in your knee or ankle? ☐ ☐

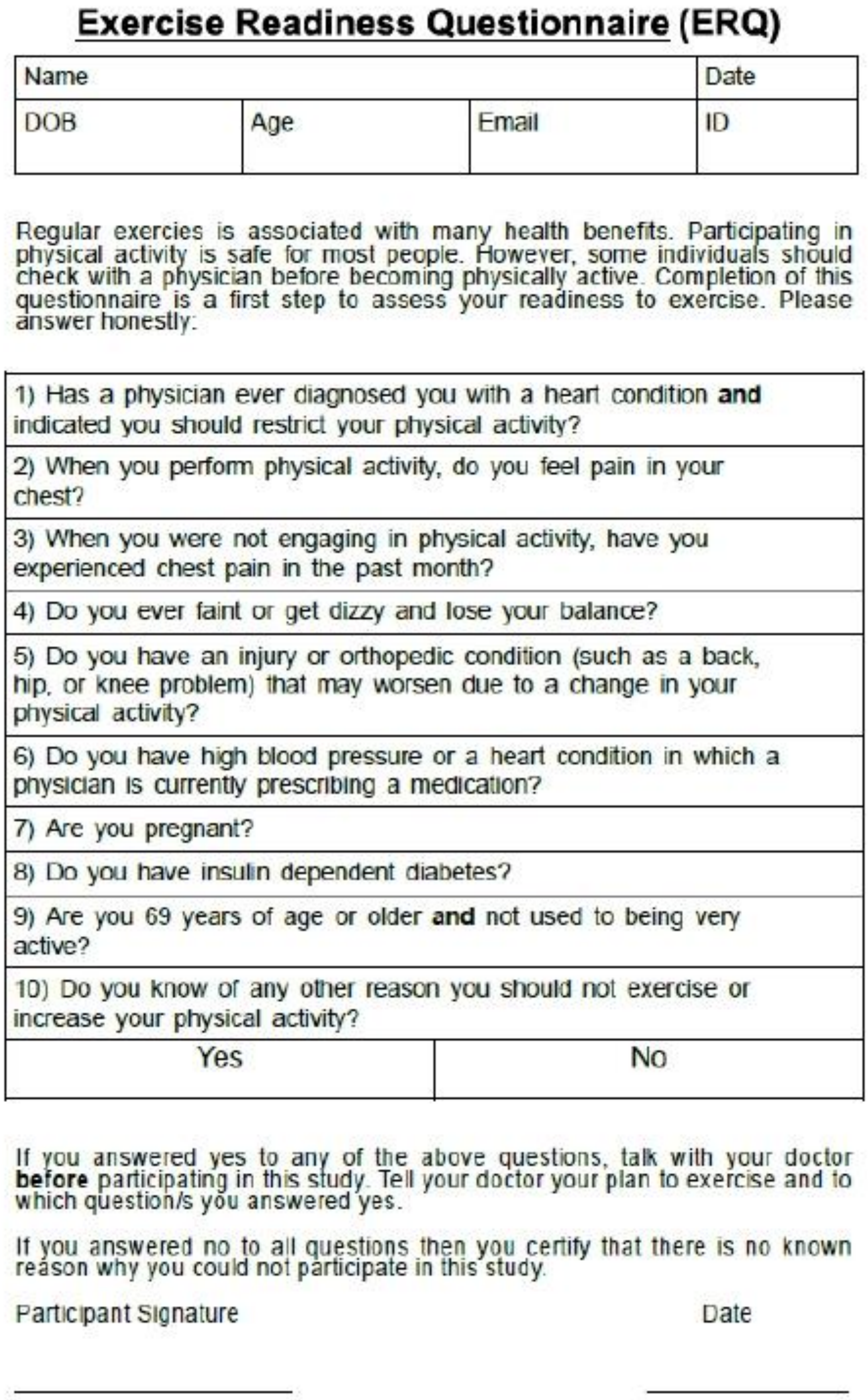
15. Does your knee or ankle hurt after vigorous physical activity? ☐ ☐

16. Have you ever had surgery to the lower limb?
If YES, please specify the type and approximate date
____ ☐ ☐

Risk takers

17. A risk taker can be defined as someone who risks loss or injury in hope of gain or excitement. Do you consider yourself as a risk taker? ☐ ☐

8.2 Appendix B. Exercise Readiness Questionnaire



Exercise Readiness Questionnaire (ERQ)

Name			Date
DOB	Age	Email	ID

Regular exercies is associated with many health benefits. Participating in physical activity is safe for most people. However, some individuals should check with a physician before becoming physically active. Completion of this questionnaire is a first step to assess your readiness to exercise. Please answer honestly:

1) Has a physician ever diagnosed you with a heart condition **and** indicated you should restrict your physical activity?
2) When you perform physical activity, do you feel pain in your chest?
3) When you were not engaging in physical activity, have you experienced chest pain in the past month?
4) Do you ever faint or get dizzy and lose your balance?
5) Do you have an injury or orthopedic condition (such as a back, hip, or knee problem) that may worsen due to a change in your physical activity?
6) Do you have high blood pressure or a heart condition in which a physician is currently prescribing a medication?
7) Are you pregnant?
8) Do you have insulin dependent diabetes?
9) Are you 69 years of age or older **and** not used to being very active?
10) Do you know of any other reason you should not exercise or increase your physical activity?

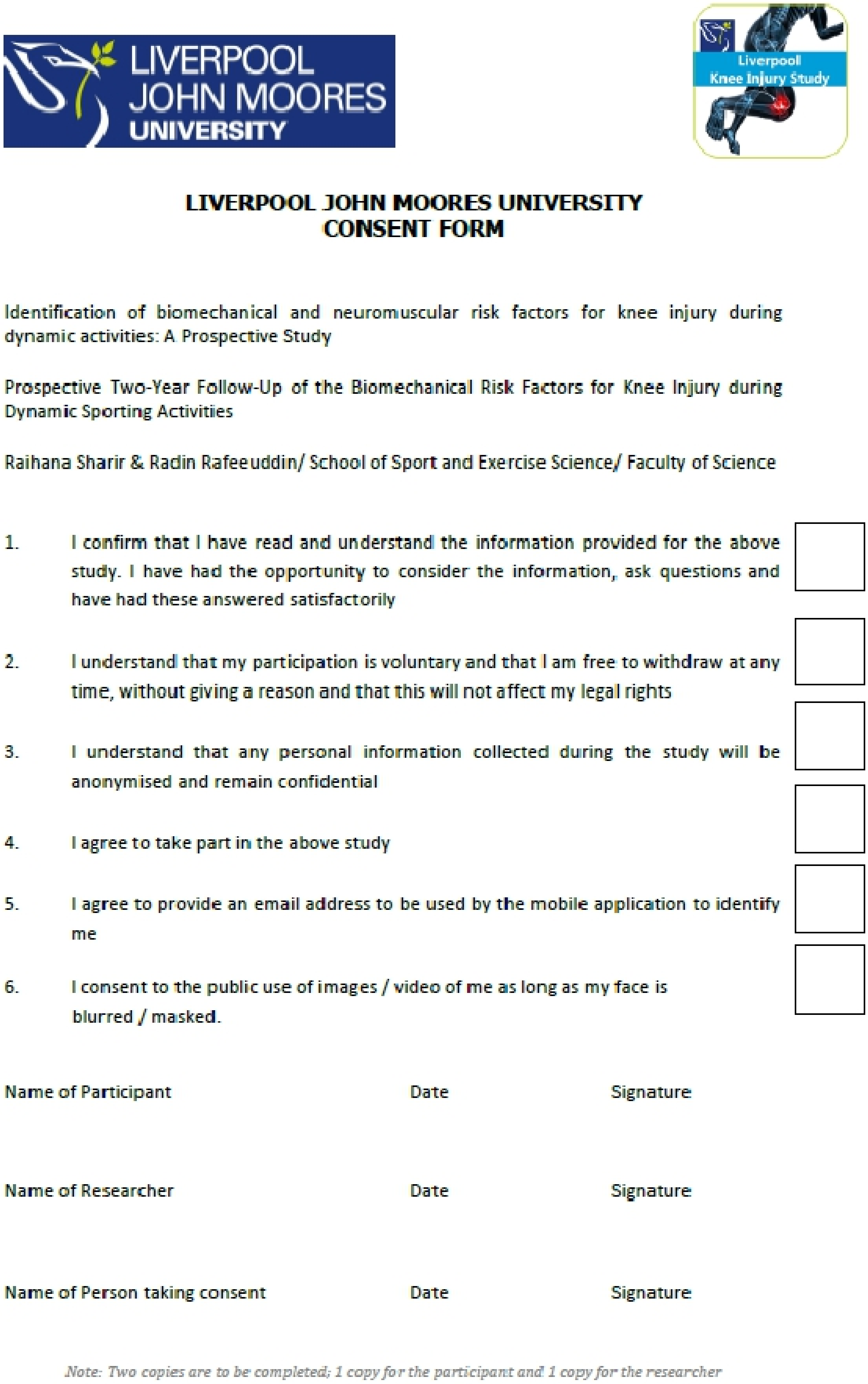
Yes	No

If you answered yes to any of the above questions, talk with your doctor **before** participating in this study. Tell your doctor your plan to exercise and to which question/s you answered yes.

If you answered no to all questions then you certify that there is no known reason why you could not participate in this study.

Participant Signature Date

8.3 Appendix C. Inform Consent Form



LIVERPOOL JOHN MOORES UNIVERSITY
CONSENT FORM

Identification of biomechanical and neuromuscular risk factors for knee injury during dynamic activities: A Prospective Study

Prospective Two-Year Follow-Up of the Biomechanical Risk Factors for Knee Injury during Dynamic Sporting Activities

Raihana Sharir & Radin Rafeeuddin/ School of Sport and Exercise Science/ Faculty of Science

1. I confirm that I have read and understand the information provided for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and that this will not affect my legal rights ☐
3. I understand that any personal information collected during the study will be anonymised and remain confidential ☐
4. I agree to take part in the above study ☐
5. I agree to provide an email address to be used by the mobile application to identify me ☐
6. I consent to the public use of images / video of me as long as my face is blurred / masked. ☐

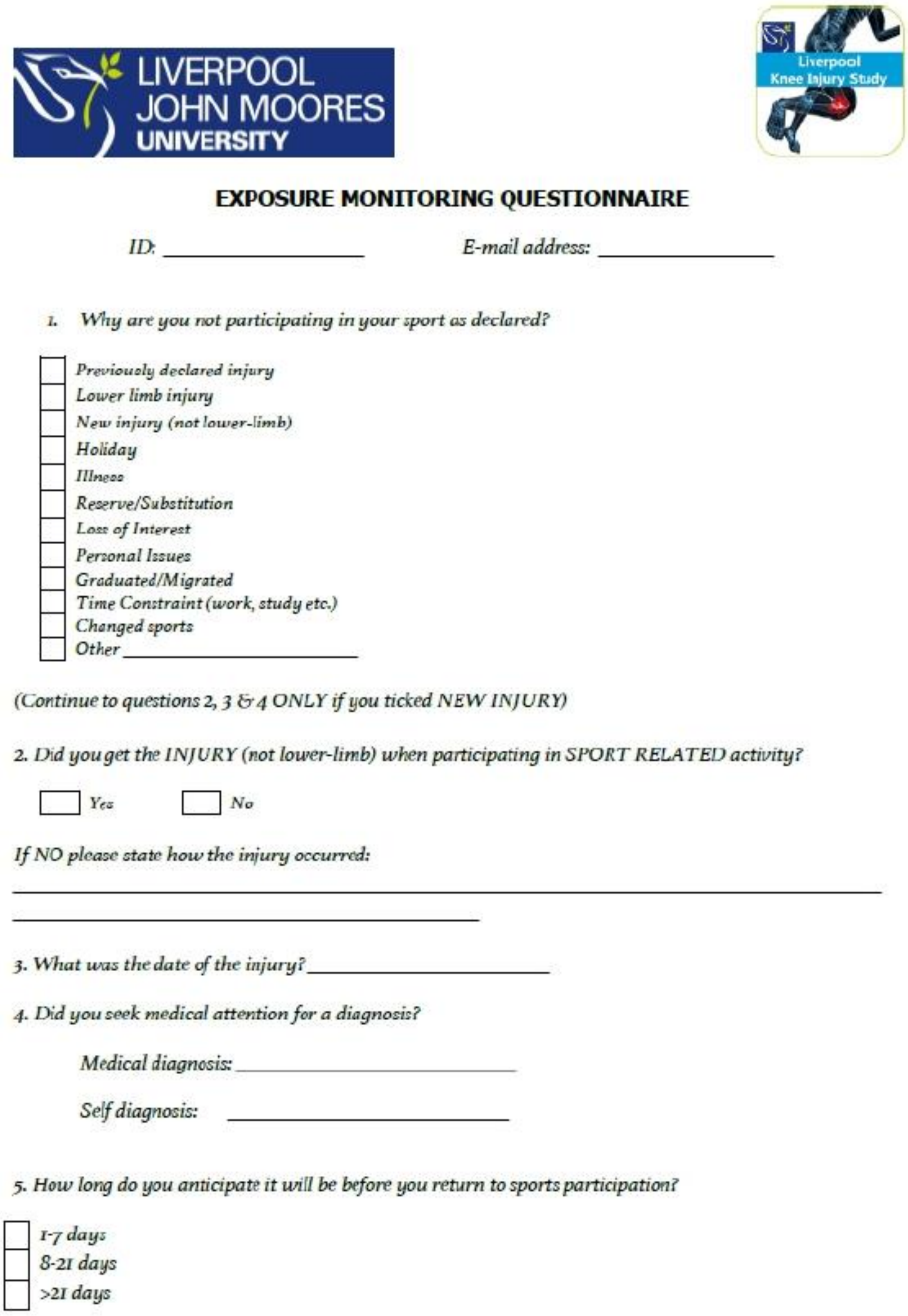
Name of Participant Date Signature

Name of Researcher Date Signature

Name of Person taking consent Date Signature

Note: Two copies are to be completed; 1 copy for the participant and 1 copy for the researcher

8.4 Appendix D. Exposure Monitoring Questionnaire



LIVERPOOL JOHN MOORES UNIVERSITY

Liverpool Knee Injury Study

EXPOSURE MONITORING QUESTIONNAIRE

ID: ____________________ *E-mail address:* ________________

1. *Why are you not participating in your sport as declared?*

☐ *Previously declared injury*
☐ *Lower limb injury*
☐ *New injury (not lower-limb)*
☐ *Holiday*
☐ *Illness*
☐ *Reserve/Substitution*
☐ *Loss of Interest*
☐ *Personal Issues*
☐ *Graduated/Migrated*
☐ *Time Constraint (work, study etc.)*
☐ *Changed sports*
☐ *Other* ______________________

(Continue to questions 2, 3 & 4 ONLY if you ticked NEW INJURY)

2. Did you get the INJURY (not lower-limb) when participating in SPORT RELATED activity?

☐ *Yes* ☐ *No*

If NO please state how the injury occurred:

____

____

3. What was the date of the injury? ______________________

4. Did you seek medical attention for a diagnosis?

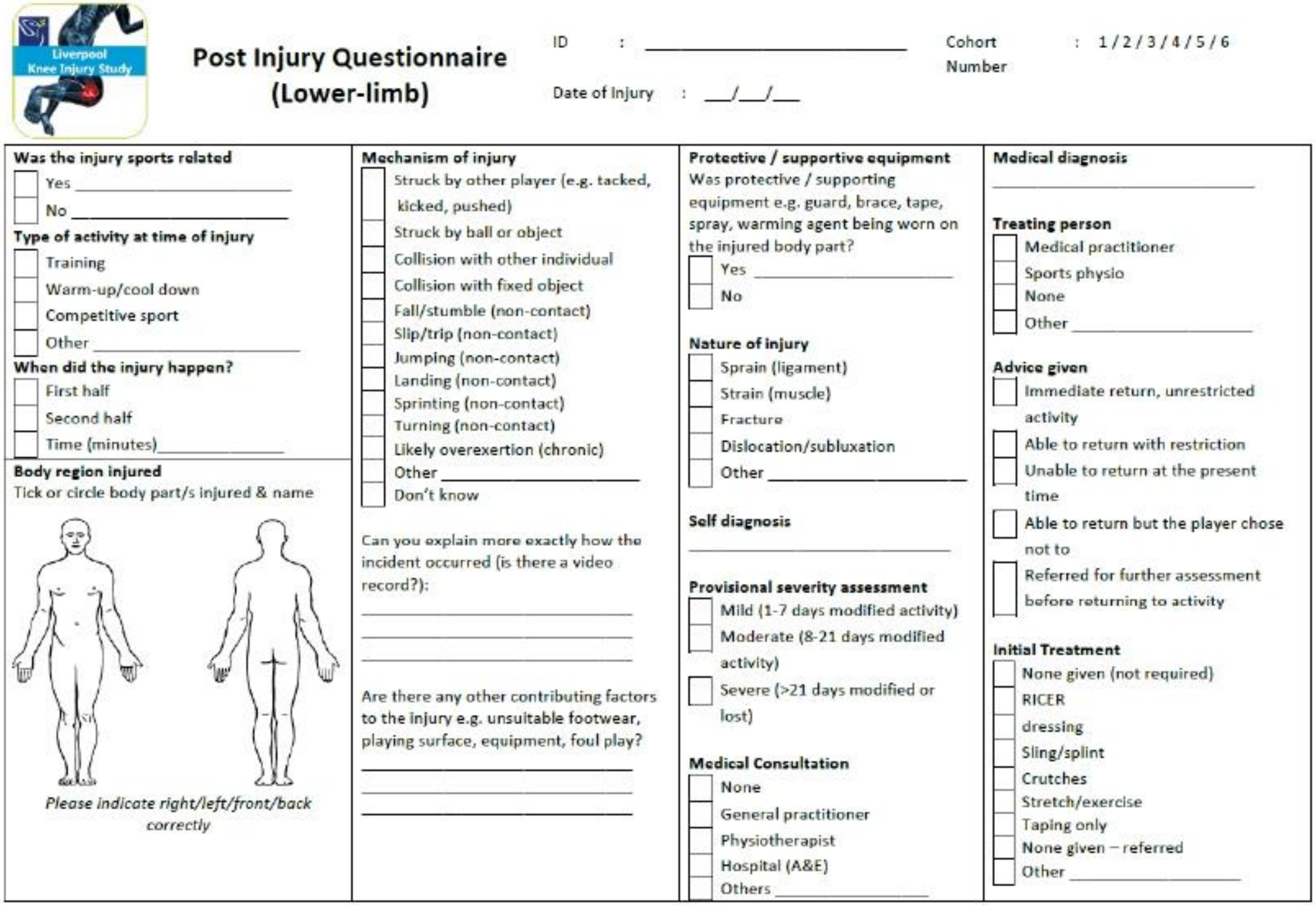
Medical diagnosis: ___________________________

Self diagnosis: ___________________________

5. How long do you anticipate it will be before you return to sports participation?

☐ *1-7 days*
☐ *8-21 days*
☐ *>21 days*

8.5 Appendix E. Post-Injury Questionnaire (lower limb)



Liverpool Knee Injury Study

Post Injury Questionnaire (Lower-limb)

ID : ____________________

Date of Injury : ___/___/___

Cohort Number : 1 / 2 / 3 / 4 / 5 / 6

Was the injury sports related

- ☐ Yes ____________
- ☐ No ____________

Type of activity at time of injury

- ☐ Training
- ☐ Warm-up/cool down
- ☐ Competitive sport
- ☐ Other ____________

When did the injury happen?

- ☐ First half
- ☐ Second half
- ☐ Time (minutes)____________

Body region injured

Tick or circle body part/s injured & name

Please indicate right/left/front/back correctly

Mechanism of injury

- ☐ Struck by other player (e.g. tacked, kicked, pushed)
- ☐ Struck by ball or object
- ☐ Collision with other individual
- ☐ Collision with fixed object
- ☐ Fall/stumble (non-contact)
- ☐ Slip/trip (non-contact)
- ☐ Jumping (non-contact)
- ☐ Landing (non-contact)
- ☐ Sprinting (non-contact)
- ☐ Turning (non-contact)
- ☐ Likely overexertion (chronic)
- ☐ Other ____________
- ☐ Don't know

Can you explain more exactly how the incident occurred (is there a video record?):

____

____

____

Are there any other contributing factors to the injury e.g. unsuitable footwear, playing surface, equipment, foul play?

____

____

____

Protective / supportive equipment

Was protective / supporting equipment e.g. guard, brace, tape, spray, warming agent being worn on the injured body part?

- ☐ Yes ____________
- ☐ No

Nature of injury

- ☐ Sprain (ligament)
- ☐ Strain (muscle)
- ☐ Fracture
- ☐ Dislocation/subluxation
- ☐ Other ____________

Self diagnosis

____

Provisional severity assessment

- ☐ Mild (1-7 days modified activity)
- ☐ Moderate (8-21 days modified activity)
- ☐ Severe (>21 days modified or lost)

Medical Consultation

- ☐ None
- ☐ General practitioner
- ☐ Physiotherapist
- ☐ Hospital (A&E)
- ☐ Others ____________

Medical diagnosis

____

Treating person

- ☐ Medical practitioner
- ☐ Sports physio
- ☐ None
- ☐ Other ____________

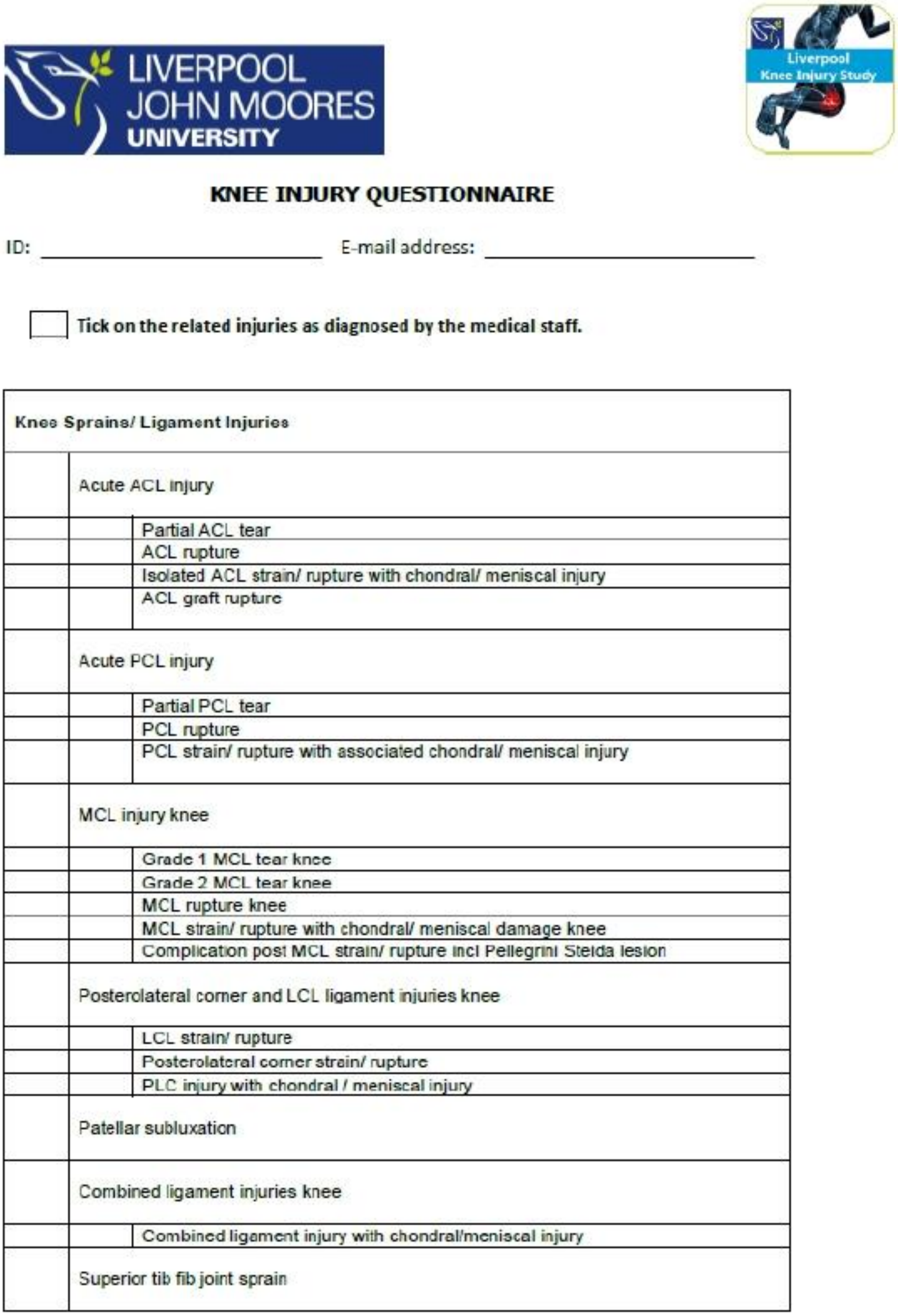
Advice given

- ☐ Immediate return, unrestricted activity
- ☐ Able to return with restriction
- ☐ Unable to return at the present time
- ☐ Able to return but the player chose not to
- ☐ Referred for further assessment before returning to activity

Initial Treatment

- ☐ None given (not required)
- ☐ RICER
- ☐ dressing
- ☐ Sling/splint
- ☐ Crutches
- ☐ Stretch/exercise
- ☐ Taping only
- ☐ None given – referred
- ☐ Other ____________

8.6 Appendix F. Knee Injury Questionnaire



LIVERPOOL JOHN MOORES UNIVERSITY

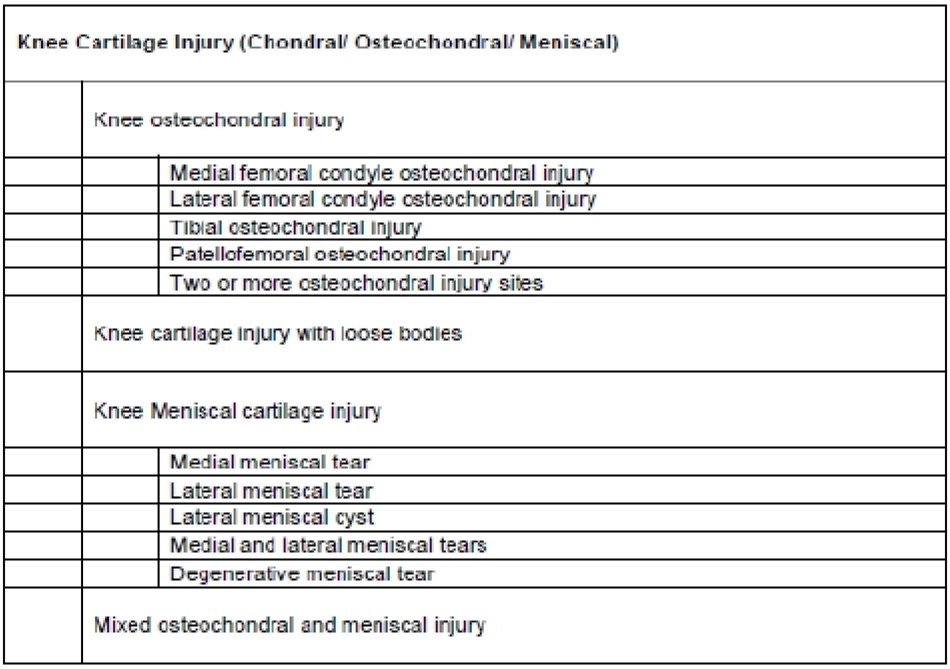
Liverpool Knee Injury Study

KNEE INJURY QUESTIONNAIRE

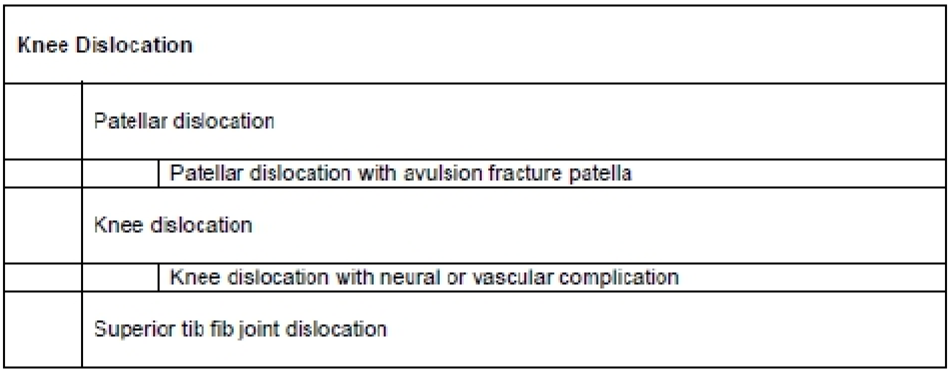
ID: ______________________ E-mail address: ______________________

☐ **Tick on the related injuries as diagnosed by the medical staff.**

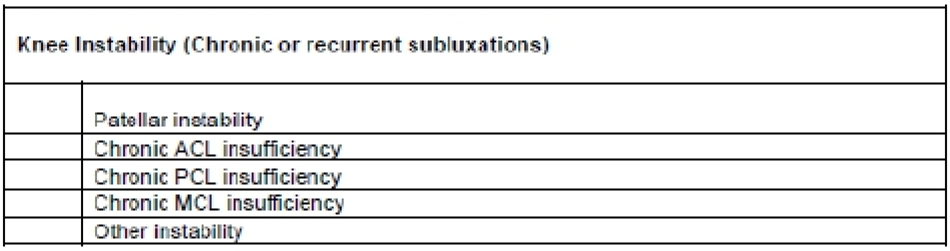
Knee Sprains/ Ligament Injuries		
	Acute ACL injury	
		Partial ACL tear
		ACL rupture
		Isolated ACL strain/ rupture with chondral/ meniscal injury
		ACL graft rupture
	Acute PCL injury	
		Partial PCL tear
		PCL rupture
		PCL strain/ rupture with associated chondral/ meniscal injury
	MCL injury knee	
		Grade 1 MCL tear knee
		Grade 2 MCL tear knee
		MCL rupture knee
		MCL strain/ rupture with chondral/ meniscal damage knee
		Complication post MCL strain/ rupture incl Pellegrini Steida lesion
	Posterolateral corner and LCL ligament injuries knee	
		LCL strain/ rupture
		Posterolateral corner strain/ rupture
		PLC injury with chondral / meniscal injury
	Patellar subluxation	
	Combined ligament injuries knee	
		Combined ligament injury with chondral/meniscal injury
	Superior tib fib joint sprain	



Knee Cartilage Injury (Chondral/ Osteochondral/ Meniscal)		
	Knee osteochondral injury	
		Medial femoral condyle osteochondral injury
		Lateral femoral condyle osteochondral injury
		Tibial osteochondral injury
		Patellofemoral osteochondral injury
		Two or more osteochondral injury sites
	Knee cartilage injury with loose bodies	
	Knee Meniscal cartilage injury	
		Medial meniscal tear
		Lateral meniscal tear
		Lateral meniscal cyst
		Medial and lateral meniscal tears
		Degenerative meniscal tear
	Mixed osteochondral and meniscal injury	



Knee Dislocation		
	Patellar dislocation	
		Patellar dislocation with avulsion fracture patella
	Knee dislocation	
		Knee dislocation with neural or vascular complication
	Superior tib fib joint dislocation	



Knee Instability (Chronic or recurrent subluxations)	
	Patellar instability
	Chronic ACL insufficiency
	Chronic PCL insufficiency
	Chronic MCL insufficiency
	Other instability

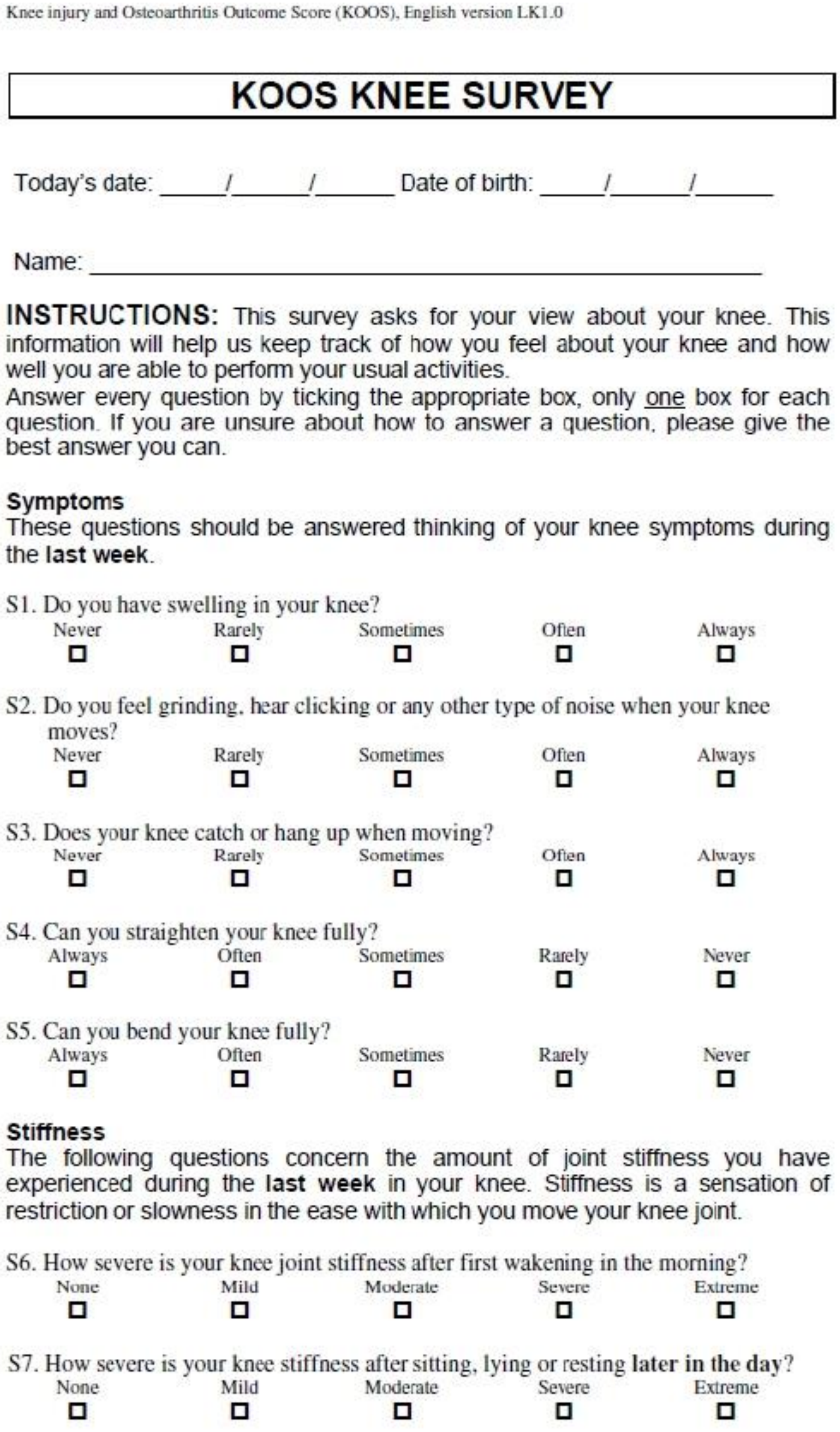
Knee Impingement/ Synovitis/ Biomechanical Lesion not associated with other conditions		
	Patellofemoral pain	
		Patellofemoral pain with patellar tendinopathy
		Excess lateral pressure syndrome
		Hoffa's fat pad impingement
		PFS related to bipartite patella
	ITB friction syndrome	
	Knee joint synovitis	
		Synovial plica of knee
	Bakers Cyst	
		Ruptured Bakers Cyst

Knee Fractures		
	Patellar fracture	
	Distal femoral fracture	
		Intraarticular femoral fracture
	Proximal tibial fracture	
		Intraarticular tibial fracture

Knee Stress Fracture	
	Patellar stress fracture
	Distal femoral stress fracture
	Proximal tibial stress fracture

Knee Osteoarthritis	
	Patellofemoral osteoarthritis
	Medial compartment osteoarthritis knee
	Lateral compartment osteoarthritis knee
	Bi or tri-comparmental osteoarthritis

8.7 Appendix G. KOOS Knee Survey



Knee injury and Osteoarthritis Outcome Score (KOOS), English version LK1.0

KOOS KNEE SURVEY

Today's date: _____/_____/_____ Date of birth: _____/_____/_____

Name: ____

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

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

S1. Do you have swelling in your knee?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

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

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

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

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S4. Can you straighten your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

S5. Can you bend your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

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

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Pain

P1. How often do you experience knee pain?

Never	Monthly	Weekly	Daily	Always
☐	☐	☐	☐	☐

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

P2. Twisting/pivoting on your knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P3. Straightening knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P4. Bending knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P5. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P6. Going up or down stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P7. At night while in bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P8. Sitting or lying

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P9. Standing upright

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, daily living

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

A1. Descending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A2. Ascending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

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

A3. Rising from sitting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A4. Standing
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A5. Bending to floor/pick up an object
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A6. Walking on flat surface
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A7. Getting in/out of car
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A8. Going shopping
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A9. Putting on socks/stockings
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A10. Rising from bed
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A11. Taking off socks/stockings
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A12. Lying in bed (turning over, maintaining knee position)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A13. Getting in/out of bath
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A14. Sitting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

A15. Getting on/off toilet
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, sports and recreational activities

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

SP1. Squatting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP2. Running

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP3. Jumping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP4. Twisting/pivoting on your injured knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP5. Kneeling

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Quality of Life

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

Never	Monthly	Weekly	Daily	Constantly
☐	☐	☐	☐	☐

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

Not at all	Mildly	Moderately	Severely	Totally
☐	☐	☐	☐	☐

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

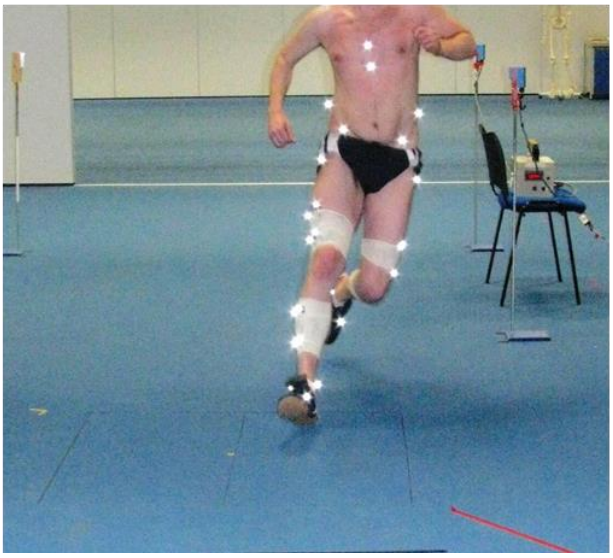
Not at all	Mildly	Moderately	Severely	Extremely
☐	☐	☐	☐	☐

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

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

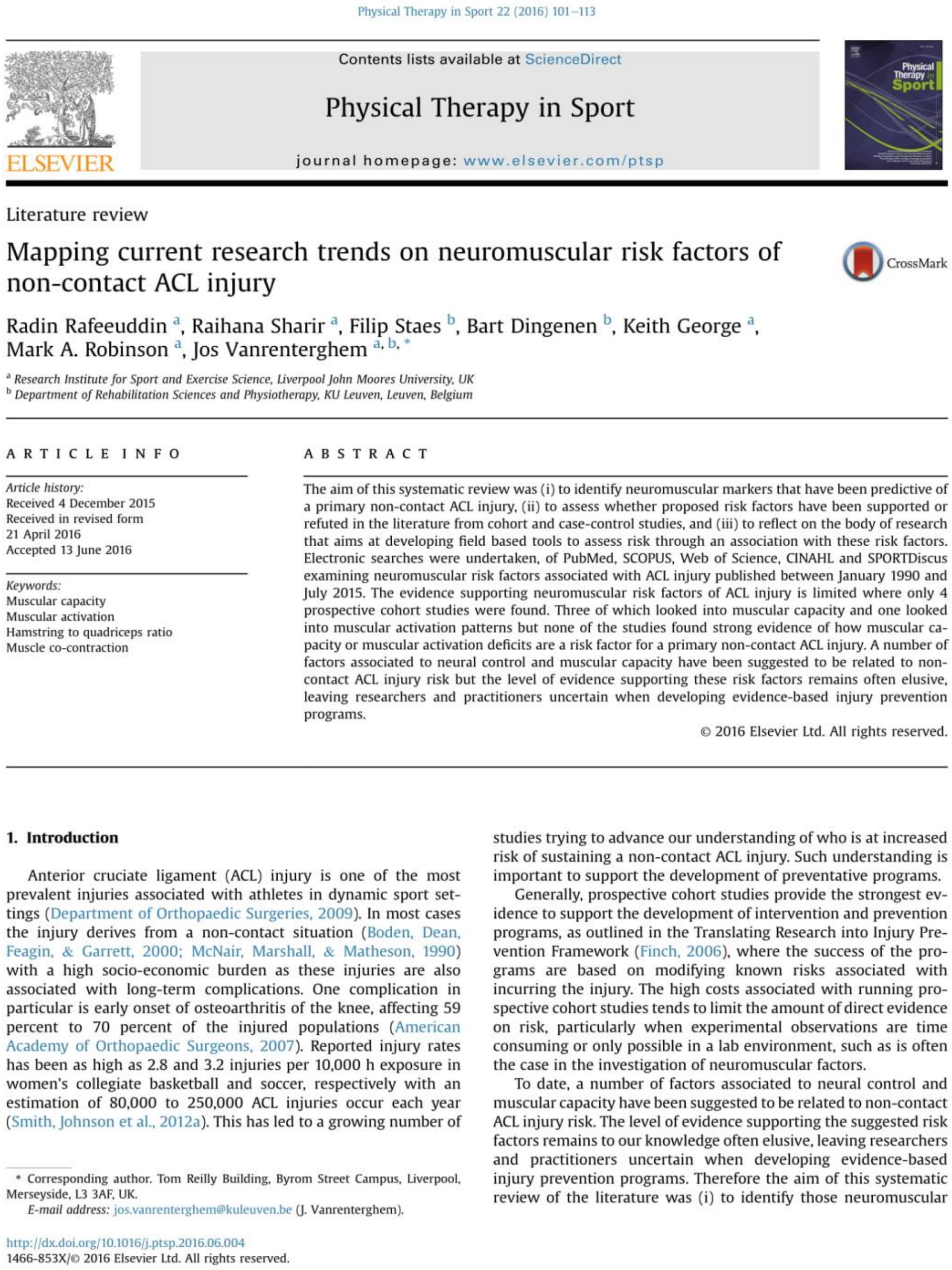
Thank you very much for completing all the questions in this questionnaire.

8.8 Appendix H. Securing EMG with flexible tapes



Chapter 9 Publications

9.1 Publication i.



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Literature review

Mapping current research trends on neuromuscular risk factors of non-contact ACL injury

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ABSTRACT

The aim of this systematic review was (i) to identify neuromuscular markers that have been predictive of a primary non-contact ACL injury, (ii) to assess whether proposed risk factors have been supported or refuted in the literature from cohort and case-control studies, and (iii) to reflect on the body of research that aims at developing field based tools to assess risk through an association with these risk factors. Electronic searches were undertaken, of PubMed, SCOPUS, Web of Science, CINAHL and SPORTDiscus examining neuromuscular risk factors associated with ACL injury published between January 1990 and July 2015. The evidence supporting neuromuscular risk factors of ACL injury is limited where only 4 prospective cohort studies were found. Three of which looked into muscular capacity and one looked into muscular activation patterns but none of the studies found strong evidence of how muscular capacity or muscular activation deficits are a risk factor for a primary non-contact ACL injury. A number of factors associated to neural control and muscular capacity have been suggested to be related to non-contact ACL injury risk but the level of evidence supporting these risk factors remains often elusive, leaving researchers and practitioners uncertain when developing evidence-based injury prevention programs.

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1. Introduction

Anterior cruciate ligament (ACL) injury is one of the most prevalent injuries associated with athletes in dynamic sport settings (Department of Orthopaedic Surgeries, 2009). In most cases the injury derives from a non-contact situation (Boden, Dean, Feagin, & Garrett, 2000; McNair, Marshall, & Matheson, 1990) with a high socio-economic burden as these injuries are also associated with long-term complications. One complication in particular is early onset of osteoarthritis of the knee, affecting 59 percent to 70 percent of the injured populations (American Academy of Orthopaedic Surgeons, 2007). Reported injury rates has been as high as 2.8 and 3.2 injuries per 10,000 h exposure in women's collegiate basketball and soccer, respectively with an estimation of 80,000 to 250,000 ACL injuries occur each year (Smith, Johnson et al., 2012a). This has led to a growing number of studies trying to advance our understanding of who is at increased risk of sustaining a non-contact ACL injury. Such understanding is important to support the development of preventative programs.

Generally, prospective cohort studies provide the strongest evidence to support the development of intervention and prevention programs, as outlined in the Translating Research into Injury Prevention Framework (Finch, 2006), where the success of the programs are based on modifying known risks associated with incurring the injury. The high costs associated with running prospective cohort studies tends to limit the amount of direct evidence on risk, particularly when experimental observations are time consuming or only possible in a lab environment, such as is often the case in the investigation of neuromuscular factors.

To date, a number of factors associated to neural control and muscular capacity have been suggested to be related to non-contact ACL injury risk. The level of evidence supporting the suggested risk factors remains to our knowledge often elusive, leaving researchers and practitioners uncertain when developing evidence-based injury prevention programs. Therefore the aim of this systematic review of the literature was (i) to identify those neuromuscular

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markers that have been predictive of a primary non-contact ACL injury, (ii) to assess whether the identified risk factors have seen supportive evidence from cohort and case-control studies, and (iii) to reflect on the body of research that aims at developing field based tools to assess risk through an association with these risk factors.

2. Method

The Cochrane Handbook (Higgins & Green, 2009) and the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) (Liberati, Altman, & Tetzlaff) guidelines were used in conducting this systematic review.

2.1. Electronic literature search

The literature selection process consisted of exploring electronic databases from PubMed, Scopus, Web of Science, CINAHL and SPORTDiscus between January 1990 and July 2015. The search terms were constructed and tested prior to the initial search so that the key terms cover as much as possible the existing literature of neuromuscular risk factors for non-contact ACL injury. In addition, a hand search was done on the reference lists of included articles. The search terms were divided into four groups. Between groups, the search terms were connected with AND, and within groups the search terms were connected with OR. Depending on the search database, the appropriate search term notation technique was applied. The result of this search strategy is described in Table 1.

2.2. Literature selection

From the titles and abstracts (first stage), two authors (R.S. and M.R.) independently identified potentially relevant papers for full review to avoid bias. If there were any disagreements between the two reviewers, consensus was sought through discussion between them. If no consensus was reached, a moderator (J.V.) was consulted to reach a final consensus. Selection based on full text assessment (second stage) was done by two other reviewers (R.R. and J.V.) and if there were any disagreements between the two reviewers, consensus was sought through discussion between them. If no consensus was reached, a moderator (M.R.) was consulted to reach a final consensus. For these titles, categorization as well as inclusion and exclusion criteria were implemented in a study classification system using EndNote® (version X7.0.1, Thomson Reuters) to select the relevant titles. Inclusion criteria across studies were as follows: (i) studies that measure neuromuscular variables (e.g.: isokinetic dynamometry, isometric strength, electromyography or EMG); and (ii) studies measuring other variables (e.g.: biomechanical or physiological variables) but still containing neuromuscular assessments. Classification of included studies is described in Table 2. Exclusion criteria were (i) studies without abstracts; (ii) invited reviews or systematic reviews; (iii) studies that focused on the effect and impact of treatment/training; (iv) studies that only looked into orthopaedic and rehabilitative aspects of ACL reconstruction; (v) in-vitro studies; (vi) studies on non-team sports (such as golf, walking, etc); (vii) technical studies and (viii) studies that were not in English.

2.3. Data extraction

The first author (R.R.) extracted data from each included article based on their respective study designs. For prospective cohort studies, data supporting the strength of the prospective evidence (e.g.; number of subjects, monitoring/follow-up period and injury rate) and the neuromuscular variables measured were extracted. For retrospective and case-control studies the assessed task, neuromuscular variable measured, and findings were extracted. For associative studies (see Table 2), data that were extracted provided an insight to enable reflection on the amount of ongoing research that takes prospectively identified ACL injury risk factors as a foundation for their experimental research paradigm(s).

2.4. Methodological quality assessment

The first author (R.R.) assessed the methodological quality of the studies based on the Risk of Bias Tool by the Cochrane Bias Methods Group (Group) for prospective cohort, case-control studies, evaluating criteria associated to several factors (e.g., cohort selection, exposure assessment; see full list at bottom of Table 3). For each item, one point could be scored and the total score of the methodological quality ranged between 0 and 7 (prospective cohort) and 0–6 (case-control studies). If an item was not present, not reported or insufficient information was given, 0 points were scored. Some items were not applicable, depending on the study design of the included studies, and then these items were excluded from calculation of the quality scores.

3. Results

3.1. Search findings

Table 1 shows the overall process and outcome of keyword searches. The initial search retrieved a total number of 2260 studies: PubMed (696), Scopus (99), Web of Science (712), CINAHL (409) and SPORTDiscus (344) (see Fig. 1). Removing duplicates between database searches resulted in a total of 2204 titles. From the title and abstract assessment (1st stage), 269 studies were retrieved and eligible for full text assessment. From full text review

Table 1
Search strategy.

Step	Strategy	PubMed	Scopus	Web of science	CINAHL	SPORTDiscus
#1	Search "ACL injur*" OR "anterior cruciate ligament injur*"	9626	4159	22,358	4632	2022
#2	Search neuromuscular OR musc* OR timing OR activation OR isokinetic dynam* OR EMG OR electromyography	1,406,853	167,905	17,061,970	145,331	112,873
#3	Search#1 AND#2	1809	383	9703	1165	733
#4	Search jump* OR land* OR run* OR sprint* OR side* OR cut* OR crossover OR hop* OR one-leg* OR one leg* OR single-leg OR single leg OR isokinetic OR isometric OR isotonic OR flexion OR extension OR contraction*	1,336,769	78,845	6,538,119	171,728	223,533
#5	Search#3 AND#4	1171	130	2658	695	463
#6	Search risk OR prevent* OR predict* OR screening OR associat* OR sensitivity OR specificity OR reproducibility OR reliability OR validity	8,354,639	11,308,360	23,799,549	1,322,386	354,238
#7	Search#5 AND#6	696	99	712	409	344

Table 2
Classification of studies for risk factor studies.

Classification	Description
Prospective cohort studies	Study designs in which neuromuscular characteristics of one or more samples (called cohorts) are assessed and the occurrence of a non-contact ACL injury is followed prospectively to determine which initial participants' characteristics (risk factors) are associated with increased risk of incurring an ACL injury.
Case-control studies	Study designs that compared people who have suffered a non-contact ACL injury ('cases') with people from the same source population but without significant knee injury ('healthy controls'), to examine changes in neuromuscular characteristics after injury. Whilst these changes may reflect person-specific differences prior to injury, they also reflect post-injury adaptations due to prolonged deficiency (ACL-D) or reconstruction (ACL-R).
Associative studies	Study designs that used previously suggested risk factors in their work to establish associations with (a combination of) other characteristics of that population sample, typically to detect surrogate observations that are easier/cheaper when screening for non-contact ACL injury risk on a large scale or in the field.

Table 3
Methodological quality of studies (detail of items A–I are described in the footnote).

	Study	Quality score	A	B	C	D	E	F	G	H	I
Prospective cohort	Myer et al. [10]	6/7	Y	Y	Y	N/A	N/A	N	Y	Y	Y
	Söderman et al. [11]	6/7	Y	Y	Y	N/A	N/A	Y	N	Y	Y
	Uhorchak et al. [12]	7/7	Y	Y	Y	N/A	N/A	Y	Y	Y	Y
	Zebis et al. [13]	4/7	Y	NR	Y	N/A	N/A	Y	N	N	Y
Case-control studies	Hsiao et al. [14]	3/6	N/A	N	Y	Y	N	Y	N	N/A	N/A
	Konishi et al. [15]	2/6	N/A	N	N	Y	N	Y	N	N/A	N/A
	Swanik et al. [16]	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	Tsepis et al. [17]	4/6	N/A	Y	N	Y	Y	Y	N	N/A	N/A
	Urbach et al. [18]	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	Holsgaard-Larsen et al. [19]	3/6	N/A	Y	N	Y	N	Y	N	N/A	N/A
	Xergia et al. [20]	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	Drechsler et al. [21]	2/6	N/A	N	N	Y	N	Y	N	N/A	N/A
	Aalbersberg et al. [22]	3/6	N/A	Y	Y	N	N	Y	N	N/A	N/A
	DeMont et al. [23]	3/6	N/A	Y	N	Y	N	Y	N	N/A	N/A
	Steele et al. [24]	3/6	N/A	Y	N	N	Y	Y	N	N/A	N/A
	Swanik et al. [25]	3/6	N/A	Y	Y	Y	N	N	N	N/A	N/A
	Ortiz et al. [26]	2/6	N/A	N	N	N	Y	Y	N	N/A	N/A
	Ortiz et al. [27]	2/6	N/A	N	N	N	Y	Y	N	N/A	N/A

NA not applicable, N no or insufficient information, NR not reported, Y yes.
A. Was selection of the prospective cohorts drawn from the same population.
B. Can we be confident in the assessment of activity exposure in subjects.
C. Can we be confident that any injury was not present at start of the study (prospective) or had suffered from ACL injury and controls had not (case-control).
D. Were the cases (those who acquired ACL injury) appropriately selected.
E. Were the controls appropriately selected.
F. Did the study match injured and uninjured subjects (prospective) or cases and controls (case-control) for all variables that are associated with the potential risk factor or did the statistical analysis adjust for these prognostic variables.
G. Was the nature/cause of the ACL injury well defined.
H. Can we be confident in the assessment of the ACL injury.
I. Was the follow up of cohorts adequate.

(2nd stage), a further 221 papers were excluded retaining 4 prospective studies, 14 case-control studies and 30 associative studies. The mean methodological quality score for prospective studies was 5.75 (range 4–7) and for case-control studies was 3.21 (range 2–5).

3.2. *Prospective studies*

Of the 4 prospective studies observing the neuromuscular markers of ACL injury, 3 evaluated muscular capacity (comprising of isokinetic knee strength and H/Q ratio) as risk factor of non-contact ACL injury (Myer, et al., 2009; Söderman, Alfredson, Pietilä, & Werner, 2001; Uhorchak, Scoville, Williams, Arciero, St. Pierre, & Taylor, 2003), and 1 study evaluated muscular activation patterns (Mette K. Zebis, Andersen, Bencke, Kjær, & Aagaard, 2009) (see Table 4).

3.2.1. *Muscular capacity*

Myer et al (Myer et al., 2009). found that females who went on to suffer an ACL injury had decreased hamstring strength compared to male controls whereas matched female healthy controls who did not suffer from ACL injury had decreased quadriceps strength compared to male controls. Soderman et al (Söderman et al., 2001). found that an imbalance of the hamstrings to quadriceps ratio (H/Q ratio) between legs in female athletes was predictive of players who suffered an ACL injury, with a lower H/Q ratio on the side that would become injured (Söderman et al., 2001). On the contrary, Uhorchak et al (Uhorchak et al., 2003). did not find differences in H/Q ratios for males and females who go on to suffer ACL injury.

3.2.2. *Muscular activation pattern*

Zebis et al., 2009 (Mette K. Zebis et al., 2009) focused on muscle co-activation patterns during side cutting in elite female athletes and found that reduced pre-activity of the semitendinosus (ST) combined with increased pre-activity of the vastus lateralis (VL) indicates an increased risk of future non-contact ACL injury.

3.3. *Case-control studies*

Fourteen studies were included in the review to assess the consistency of findings of the identified neuromuscular risk factors

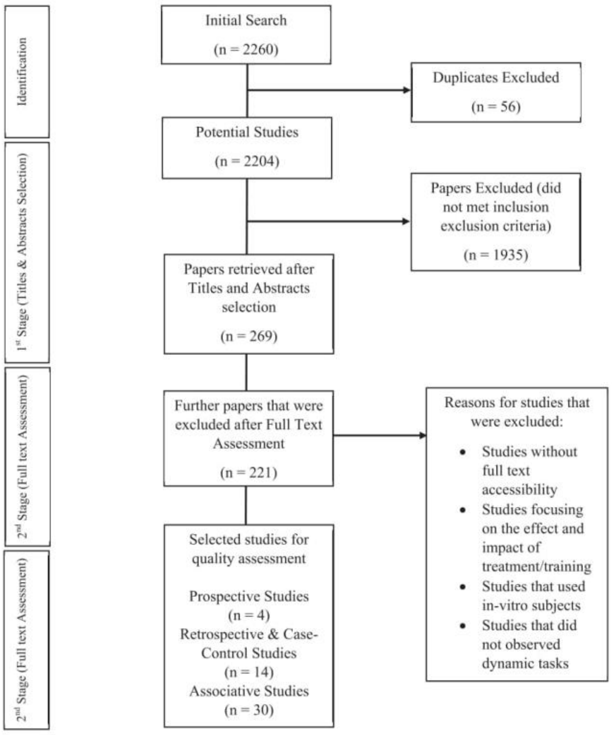

Fig. 1. Flow diagram of the overall selection and exclusion process.

associated with non-contact ACL injury from the prospective studies (see Table 5). In this section studies were further separated based on whether the study observed differences between participants with ACL deficiency (ACL-D) and healthy controls, or differences between ACL reconstructed participants (ACL-R) and healthy controls.

3.3.1. *Muscular capacity*

Five case-control studies analyzed deficits in muscular capacity in ACL-D subjects compared to healthy controls (Hsiao, Chou, Hsu, & Lue, 2014; Konishi, Oda, Tsukazaki, Kinugasa, Hirose, & Fukubayashi, 2011; Swanik, Lephart, Swanik, Stone, & Fu, 2004; Tsepis, Vagenas, Giakas, & Georgoulis, 2004; Urbach, Nebelung, Becker, & Awiszus, 2001). ACL-D subjects showed a deficit of the peak quadriceps torque in both isometric testing in males (Urbach et al., 2001) and isokinetic testing (Konishi et al., 2011; Tsepis et al., 2004) in males and females. Another study found quadriceps and hamstring deficits for isometric and isokinetic tests in male and females (Hsiao et al., 2014). In contrast, one study found greater isokinetic hamstring strength in ACL-D females (Swanik et al., 2004). Finally, one study found no difference in quadriceps strength between ACL-D and healthy controls.

Five case-control studies investigated muscular capacity deficits of ACL-R compared to healthy controls (Drechsler, Cramp, & Scott, 2006; Holsgaard-Larsen, Jensen, Mortensen, & Aagaard, 2013; Hsiao et al., 2014; Urbach et al., 2001; Xergia, Pappas, Zampeli, Georgiou, & Georgoulis, 2013). Two studies demonstrated weaknesses in quadriceps strength that were still present at both 1 and 3 months after injury in males and females during isometric and isokinetic contraction (Drechsler et al., 2006; Hsiao et al., 2014). Another study also found a decrement of isokinetic strength in the quadriceps in males (Xergia et al., 2013). One study that found a deficit in peak quadriceps torque in isometric contraction in males after ACL-R went on to observe that this deficit had disappeared two years after reconstruction (Urbach et al., 2001). Another study also found a reduced function of the operated leg, 2 years post ACL-reconstruction, for hamstring isometric contraction where asymmetry in hamstring strength was greater after ACL-R (Holsgaard-Larsen et al., 2013).

3.3.2. *Muscular activation patterns*

Five case-control studies examined deficits in muscular activation pattern between ACL-D and healthy controls (Aalbersberg, Kingma, & van Dieën, 2009; DeMont, Lephart, Giraldo, Swanik, & Fu, 1999; Steele & Brown, 1999; Swanik, Lephart, Giraldo, DeMont, & Fu, 1999; Swanik et al., 2004). One study found that the hamstrings were activated more in ACL-D subjects and this increased activation was more apparent in extended than in flexed

Table 4
Study characteristics and outcomes (Prospective Studies).

Author	Subjects characteristics	Monitoring/Follow up period	Neuromuscular measurement	Injury rate (%)	Objective	Results/Findings
(Myer et al., 2009)	Females = 1692 19 Postpubertal and 3 pubertal (only on injured subjects) High school and collegiate soccer and basketball players	5 years	Isokinetic Knee Strength	22 non-contact ACL injuries (1.3%)	To determine the association of quadriceps and hamstrings strength to anterior cruciate ligament (ACL) injury risk in female athletes.	Female ACL subjects had decreased hamstrings strength compared to MC (15%; 95% CI, 1–27%; P = 0.04). FC were not different from MC in hamstrings strength. Conversely, Female ACL subjects did not differ compared to the MC in quadriceps strength, and the FC demonstrated decreased quadriceps strength relative to MC (10%; 95% CI, 3–18%; P = 0.01).
(Söderman et al., 2001)	Female = 221 146 (75 dropouts) 20.6 ± 4.7 years Soccer players from 13 teams of 2nd and 3rd Swedish division	6 months (1 out-door season)	Isokinetic Knee Strength	5 ACL injuries-did not mentioned contact or non-contact (2.3%)	To study possible risk factors for leg injuries in female soccer players.	Multivariate logistic regression showed hyperextension of the knee joint, a low postural sway, reduced H/Q ratio during concentric action, and a higher exposure to soccer to significantly increase the risk of traumatic leg injury. All five players who suffered an anterior cruciate ligament injury during the study period had a lower hamstring to quadriceps ratio during concentric action on the injured side than on their non-injured side. Three of them had a H/Q ratio lower than 50%, and the other two had a H/Q ratio of 52% and 53% on the injured side.
(Uhorchak et al., 2003)	1198 Male = 1021 Female = 177 18.4 years (ranged from 17 to 23) Military cadets playing in competitive club and varsity sports	4 years	Isokinetic Knee Strength	24 non-contact ACL injuries (16 Males with 1.56% and 8 Females, with 4.52%)	To prospectively evaluate risk factors for noncontact anterior cruciate ligament injuries in a large population of young athletic people.	Men - Knee extensor and flexor strength ratios, including the eccentric hamstring muscles to concentric quadriceps muscles and end-range of motion ratios (P = 0.353 to 0.961) were not significantly different between the groups. Women – The strength ratios evaluating relationships between the quadriceps and hamstring muscle groups as well as strength in the end-range of motion (P = 0.424 to 0.700) were not significantly different between groups.
(Mette K. Zebis et al., 2009)	Female = 55 24 ± 5 years Elite female handball and soccer athletes	2 years (2 subsequent season)	Muscle Activation (vastus lateralis & medialis, rectus femoris, semitendinosus and bicep femoris) during side cutting.	5 non-contact ACL injuries-did not mentioned contact or non-contact (9.0%)	To identify risk factors that have high clinical relevance in the prevention of ACL rupture.	In the present study, currently non-injured female athletes with reduced EMG pre-activity of the ST and increased EMG pre-activity of the VL during side cutting were at increased risk of future noncontact ACL rupture. The study's data indicate that a high-risk zone can be used to identify non-injured players at high risk of future ACL rupture. Consequently, individual preventive efforts can be introduced in time. However, large prospective studies are needed to confirm this finding before definitive clinical recommendations can be made.

knee angles (Aalbersberg et al., 2009). Another study focusing on a deceleration task found delayed biceps femoris (BF) and semimembranosus (SM) activation (Steele & Brown, 1999). Further studies observed muscle activations in ACL-D females (DeMont et al., 1999; Swanik et al., 1999; Swanik et al., 2004). Muscle pre-activity strategies appeared to be different depending on the task being done with vastus lateralis (VL) activation being higher during hopping and vastus medialis obliquus (VMO) activation being lower during downhill walking (DeMont et al., 1999). Reactive muscle activity (after ground contact) during running was seen to be greater when observing peak activity in the BF and vastus medialis (VM), but smaller when observing overall EMG activity (Swanik et al., 1999). During landing, the ACL-D group demonstrated significantly less overall activity in the vastus lateralis (VL) (Swanik et al., 1999). ACL-D females had significantly increased preparatory muscle activity in the BF before landing, but no differences in reactive muscle activity during landing or reflex latency after joint perturbations were observed (Swanik et al., 2004).

Two case-control studies described differences in muscular activation patterns between ACL-R and healthy controls (Ortiz et al., 2008; Ortiz, Olson, Trudelle-Jackson, Rosario, & Venegas, 2011). One study demonstrated co-contraction ratios between normalised hamstring and quadriceps activations that were significantly closer to 1 in the ACL-R group during drop jumps, and greater gluteus maximus (Gmax) and rectus femoris (RF) activations (Ortiz et al., 2008). Another study from the same research group showed that neuromuscular recruitment strategies during two side hopping tasks in ACL-R females did not differ from healthy controls (Ortiz et al., 2011).

3.4. Associative studies

Thirty associative studies were retained (see Table 6). Out of these studies, 11 studies investigated associations with muscular capacity as a risk factor. Five of the studies assessed isokinetic and

Table 5
Study characteristics and outcomes (Retrospective and Case-Control Studies).

Author/Year	Subjects characteristics	Methodology of data collection	Dependent variable – test procedure	Results/Findings
(Hsiao et al., 2014)	12 ACL-D to ACL-R subjects (9 Males & 3 Females) 25.7 ± 9.3 years Non-active participants except for 3 subjects 15 Healthy Controls (11 Males & 4 Females) 23.0 ± 3.3 years Did not report control subjects sports participation	KIN-COM Isokinetic Dynamometer	Isokinetic knee strength – a series of contractions of the quadriceps and hamstrings over a knee joint range between 10 and 90° of flexion, in the form of 3 reciprocal concentric–concentric cycles with a 15-s rest in between. Contractions were performed in a random order at angular velocities of 50, 100, 150, 200, and $250^{\circ}.s^{-1}$. In each case, the highest force of contraction among 3 attempts was measured.	***Before Reconstruction*** Both quadriceps and hamstrings of the uninjured knees showed similar isometric performance to the control subjects; there was no significant difference between the uninjured and control groups at all testing knee angles in isometric MVCs. Compared with the uninjured knees, the injured knees showed significant weakness in both quadriceps and hamstrings ($p < 0.05$) across the whole range of knee angles tested. Before the reconstruction, there was no significant difference in the isokinetic force production in uninjured knees when comparing with the control group in all testing velocities for both quadriceps and hamstrings. The isokinetic MVCs from both quadriceps and hamstrings of the injured knees before reconstruction showed significant weakness at all movement velocities ($p < 0.05$) ***After Reconstruction*** There was no significant difference among the isometric MVCs produced by the uninjured knees preoperatively, 3 and 6 months after the ACL reconstruction, for both quadriceps and hamstrings. The isokinetic performance of the quadriceps and hamstrings also showed no significant change throughout the follow-up period at all testing movement velocities. Compared with the preoperative stage, isometric MVCs of the quadriceps at the 3-month follow-up was significantly weaker especially at positions that were more flexed ($p < 0.005$ at 90 and 70° of knee flexion). Unlike the quadriceps, there were no significant changes in isometric hamstrings MVCs of the injured knee at the 3 or 6-month follow-up. Quadriceps showed a more profound weakness during isokinetic contractions at the 3-month follow-up, with a diminished pattern of force: velocity relationship. There was a slight return of force and pattern of force production at 6-month follow-up when compared with that in the preoperative stage. Hamstrings showed slight though non-significant improvement in the isokinetic force production continuing through- out the 6-month follow-up period
(Konishi et al., 2011)	22 ACLD (11 Males & 11 Women) 24.7 ± 5.3 years 10 competitive, 10 recreational and 2 occasional sports participation 22 Healthy Controls (13 Males & 9 Women) 24.3 ± 5.7 years Various levels of sports activity were reported	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength – All subjects performed maximum concentric knee extensions ranging from 90-degree knee flexion to full extension. Isokinetic knee extension torque at preset angle velocities of 60 and 180°/s and were performed 5 times by each subject for each velocity. Patients with ACL injury were measured starting from the uninjured side and then continued on the injured side. Each trial was separated by a rest period of 2 min.	The mean torque values for knee extension of the injured and uninjured sides analyzed using a paired t-test indicated that mean torque values of the injured side at both 60 and 180°/s were significantly lower than those of the uninjured side ($p < 0.01$ at 60°/s, $p < 0.01$ at 180°/s). Peak torque for the groups at 60°/s and 180°/s were, injured side (134 ± 45, 97 ± 33), uninjured side (171 ± 46, 113 ± 28) and Control group (182 ± 46, 125 ± 42) respectively.
(Swanik et al., 2004)	12 ACLD 25.2 ± 7.3 years 17 Healthy Controls 22.7 ± 4.0 years Tegner activity score with an average of 5.4 All Females	Surface EMG (Noraxon) were placed on the VM, VL, Medial Hamstrings & Lateral Hamstrings. Biodex 2 Isokinetic Dynamometer	Muscular activation – The subject stood on a 20-cm step, balanced momentarily on the test limb, and hopped to a target (x) placed 30 cm horizontally. The subject did 2 practice attempts followed by 3 test trials and the ensemble peak was used for amplitude normalization. EMG preparatory muscle activity was represented by a 150-ms period before landing and reactive muscle activity was described by a 250-ms period after ground contact. Isokinetic knee strength – a standardized knee position was assumed and testing was done at speeds of 60°/second with torque values automatically adjusted for	Females with anterior cruciate ligament deficiencies had significantly increased preparatory muscle activity in the lateral hamstring before landing, but no differences in reactive muscle activity during landing or reflex latency after joint perturbation. Female ACLD also had greater peak torque and torque development for knee flexion.

Table 5 (*continued*)

Author/Year	Subjects characteristics	Methodology of data collection	Dependent variable – test procedure	Results/Findings
			gravity. Warm-up procedures consisted of two submaximal (50% and 75%), and one maximal repetition followed by data collection during five reciprocal maximum repetitions.	
(Tsepis et al., 2004)	32 ACLD (3 groups of knee function High, Intermediate and Low) 27.7 ± 7.3 years 12 Healthy Control 22.1 ± 2.9 Amateur soccer players All Males	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength – A warm up on the dynamometer consisted of five repetitions of incremental intensity from 50% to 100% of each subject's estimated maximal effort. After one minute of complete rest, 5 maximal repetitions of concentric extensions and flexions were performed at 60°/s. The testing order of the knees was randomized.	The average peak torque (APT) of the quadriceps of the injured knee was significantly lower than the APT of the intact knee in all-experimental groups (lowest $F = 6.8$; $P < 0.001$). Regarding the hamstrings, the APT in the injured knee was significantly lower than the APT of the intact knee in the low knee function (L3) group only ($F = 11.08$, $P < 0.001$).
(Urbach et al., 2001)	12 ACL-D to ACL-R subjects 26.9 years (ranged from 14.9 to 43.5) 12 Healthy Controls 26.4 years (ranged from 15.3 to 42.3) Tegner activity score with an average of 7.9 only on injured subjects were reported All Males	Purpose-built Chair (Urbach et al., 2001)	Isometric knee strength – Patients were seated in an upright position on a purpose-built chair. For electrical stimulation of the muscle aluminium-plate electrodes were strapped to the quadriceps and a constant current was applied (Dantec Counterpoint K II, Skovlunde, Denmark). The subjects were instructed to extend their knee fully for 5 s to determine the force at maximum voluntary contraction (MVC) measured as extension torque and for maximal potentiation of the twitch response. Immediately after twitch potentiation, the subjects performed isometric contractions with 90%, 75%, 50% and 100% of their MVC force by matching the visualized torque level on the monitor with the desired torque. When the torque was stable three single stimuli were applied to the muscle.	Before operation we found a deficit of voluntary activation of the quadriceps on both the injured (mean ± SEM 74.9± 3.5%) and the uninjured side (74.6± 3.0%) in comparison with the control group (91± 0.9%). Two years after reconstruction of the ACL the voluntary activation of the quadriceps improved significantly on both sides but remained less than that of the controls.
(Holsgaard-Larsen et al., 2013)	23 ACL-R 27.2 ± 7.5 years 25 Healthy Controls 27.2 ± 5.4 years MET score with an average of 36 All Males	Stabilized Dynamometry	Isometric knee strength & H:Q ratio – For each muscle group, 3 trials of approximately 4-s duration were performed and the trial with highest isometric strength (joint moment) was selected for further analysis. All contractions were performed in the sitting position with 90° of knee flexion. Pauses between successive contractions were 20–30 s. To stabilize the body, subjects were secured with a waist strap positioned across the proximal part of the thigh and participants were allowed to hold on to the construction for further support.	Maximal hamstring voluntary contraction was reduced by 0.22 Nm kg^{-1} in the operated versus non-operated limb in patients, resulting in a greater (p b 0.001) asymmetry in ACL-patients (77.4%) than controls (101.3%). In contrast, no limb-to-limb asymmetry was detected for maximal quadriceps strength. An 11.1% reduction in H/Q-ratio was observed in the ACL-patients on the operated side while no difference (0.5%) between legs was observed in controls, leading to greater ($p < 0.001$) asymmetry in ACL-patients (85.7% vs. 103.4%).
(Xergia et al., 2013)	22 ACL-R 28.8 ± 11.2 years 22 Healthy Controls 24.8 ± 9.1 years Tegner activity score with an average of 6.5 All Males	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength – The range of motion was set from 90° of flexion to full extension (0°) and was performed at 120°/s, 180°/s, and 300°/s. All tests were first performed on the intact lower extremity, followed by the involved lower extremity. For the control group, the dominant lower extremity was tested first. The test consists of 5 repetitions with a 1-min rest period in between.	Compared to the control group, the ACLR group had greater isokinetic knee extension torque deficits at all speeds ($P < 0.001$) When averaged across speeds, the ACLR group had a lower Limb Symmetry Index (LSI) compared to the control group (76.9% versus 98.2%).
(Drechsler et al., 2006)	31 ACLR (25 Males & 6 Females) 30.0 ± 8.0 years	Purpose Built Chair (refer to Drechsler et al., 2006)	Isometric knee strength and muscular activation – Subjects performed 3 or more MVCs (5-s	There were no significant differences in mean isometric MVC of the quadriceps femoris of uninjured limbs of the

(*continued on next page*)

Table 5 (*continued*)

Author/Year	Subjects characteristics	Methodology of data collection	Dependent variable – test procedure	Results/Findings
	20 Inactive Healthy Controls – RC (10 Males & 10 Females) 24.0 ± 4.0 years 5 Active Healthy Controls – SC (2 Males & 3 Females) 28.0 ± 3.0 High performance sporting activities	Surface EMG were placed on the RF. Digitizer DS7 current stimulator	duration) of quadriceps femoris, with a 2 min rest period between each MVC. The first 2 MVCs acted as trial attempts and were undertaken without stimulation. On the third occasion, the stimulator delivered 1 Hz stimuli for 5-s to the relaxed muscle. If the subject was unable to activate fully (i.e. the twitch augmented the MVC by more than 5%), MVC testing with twitch superimposition was repeated up to two additional times.	ACLR group, one month after surgery and of the RC and SC groups. In contrast the mean isometric MVC of quadriceps of the injured limbs of the ACLR group was significantly less (P = 0.0001) than that of the uninjured limb at both 1 and 3 months after surgery despite increases of I/U% from 1 to 3 months of 23± 3% and 16± 4% for male and female subjects, respectively.
(Aalbersberg et al., 2009)	11 ACL-D (4 Males & 7 Females) 35.0 years (ranged from 20.0 to 46.0) 15 Healthy Controls (10 Males & 5 Females) 23.0 years (ranged from 18.0 to 51.0) Did not report subjects sport participation	Custom-build seat (Aalbersberg et al., 2009) Kistler Force Plate Surface EMG were placed on the VM, RF, VL, SM, ST, BF & MG muscles.	Muscular activation – Subjects performed 3 maximum voluntary isometric contractions (MVIC) for both the quadriceps and the hamstrings at 90° of knee flexion in 3 positions (knee behind, over and in front of the ankle). Another series of 3 MVIC was performed for the GM muscle at 90° of ankle flexion.	No significance in muscle activation variables nor the moments between ACL-deficient and control subjects during knee behind the ankle position In postures with the knee in front of the ankle, ACL-deficient subjects showed, averaged over three force levels and three knee angles, a median activation level of 6.6% MVC (range 3.2–12.3) hamstrings activation, against 4.2% (range 1.8 –17.4) in control subjects. In postures with the knee over the ankle hamstrings activation were 9.1% MVC (range 2.0 –29.0) for ACL-deficient and 4.0% MVC (range 2.2–35.7) for control subjects. The differences between ACL-deficient and control subjects (2.4% MVC for postures with the knee in front of the ankle and 5.1% MVC for postures with the knee over the ankle) were significant.
(DeMont et al., 1999)	6 ACL-D 12 ACL-R 6 Healthy Controls 29.4 ± 10.4 years (all subjects) Tegner activity score with an average of 6.8 ± 1.5 (All Females)	Integrated EMG on the VMO, VL, MH, LH, MG and LG.	Muscular activation- Subjects performed 4 dynamic activities for IEMG assessment of downhill walking at 0.92 m/s, running at 2.08 m/s, 10 step hopping task and jump-landing task from a 20.3 cm step.	Side-side differences. Landing – ACLD shows side-to-side differences between the LG (involved 36.4% ± 19.7% and uninvolved 60.1% ± 23.6%, P < 0.05).], Running – ACLD shows side differences in the VMO (involved 11.4% ± 3.8%, uninvolved 7.2% ± 3.1%, P < 0.05) and VL (involved 13.3% ± 2.7%, uninvolved 8.9% ± 1.9%, P < 0.05) and Downhill Walking – ACL shows side differences between the VMO (involved 9.2% ± 4.2%, uninvolved 19.5% ± 7.3%, P < 0.05). Mean amplitude of IEMG. Running – ACLD differences between the VMO (involved 78.2% ± 23.2%, uninvolved 45.8% ± 18.9%, P < 0.05), Downhill Walking – ACLD shows differences between the LG (involved 79.7% ± 30.3% and uninvolved 122.3% ± 34.9%, P < 0.05) and Hopping – ACLR shows a side-to-side differences on the LG Landing – ACLD shows differences between the LG (involved 74.7% ± 40.0% and uninvolved 52.8% ± 14.3%, P < 0.05). ANOVA revealed group differences on the involved VL during hop and the VMO when walking downhill. ACLD had significantly higher IEMG area than controls in VL (ACLD 12.9% ± 5.8% and Controls 7.1% ± 3.9%, P < 0.05) but lower in VMO (ACLD 9.2% ± 4.2% and Controls 15.7% ± 3.6%, P < 0.05). The side-to-side differences of the ACLD and ACLR groups, as well as the group differences between ACL-D and control, suggest that different muscle activation strategies are used by females when performing different dynamic activities. Therefore, muscle unit differentiation may be the cause of our results. These changes appear to be reversed through surgery or the associated postoperative rehabilitation.
(Steele & Brown, 1999)	11 ACL-D (8 Males & 3 Females) 31.6 ± 7.6 years 11 Healthy Controls (8 Males & 3 Females) 30.4 ± 8.3 years Did not report subjects sport participation	Surface EMG (Noraxon) were placed on the VM, RF, VL, SM, BF & MG muscles.	Muscular activation – Subjects performed 5 trials of a dynamic and abrupt deceleration task in which they accelerated forward for three steps to receive a chest level pass, landed on the test limb in single-limb stance, and stabilized their position without raising the landing foot.	Peak BF & SM activity displayed by the control subjects' involved limbs occurred earlier than that for their non-involved limbs while the ACLD subjects displayed the reverse trend.
(Swanik et al., 1999)	6 ACL-D 12 ACL-R 6 Healthy Controls 29.4 ± 10.4 years (all subjects) Tegner activity score with an average of 6.8 ± 1.5	Integrated EMG (Noraxon) were placed on the VM, VL, Medial Hamstrings & Lateral Hamstrings.	Muscular activation- Subjects performed 4 dynamic activities for IEMG assessment of downhill walking at 0.92 m/s, running at 2.08 m/s, 10 step hopping task and	During running, the ACLD group demonstrated significantly greater area and peak IEMG activity in the MH in comparison with the ACLR group (30.3 ± 5.7, P < 0.05, CI = 19.1 to 41.5 and 365.4 ± 123.3, P < 0.05, CI = 123.7 to 607.1 respectively) and greater peak activity in the LH when

Table 5 (*continued*)

Author/Year	Subjects characteristics	Methodology of data collection	Dependent variable – test procedure	Results/Findings
	(All Females)		jump-landing task from a 20.3 cm step.	compared with the control group (379.5 ± 105.5, $P < 0.05$, CI = 172.7 to 586.3). The ACLD group also demonstrated greater peak activity in the VM (428.2 ± 110.2, $P < 0.05$, CI = 212.2 to 644.2) and less area of IEMG activity in the LH than the control group (30.1 ± 6.9, $P < 0.05$, CI = 16.57 to 43.6) during running. During landing, the ACLD group demonstrated significantly less area of IEMG activity in the VL when compared with the control group (109.7 ± 50.3, $P < 0.05$, CI = 11.1 to 208.3)
(Ortiz et al., 2008)	13 ACL-R 25.4 ± 3.1 years 15 Healthy Controls 24.6 ± 2.6 years Recreational fitness activities (All Females)	Surface EMG were placed on GMax, RF, LH and MH.	Muscular activation – 5 trials of a 40-cm single-legged drop jump and a 20-cm up down hop task. These tasks were randomly ordered. Each participant was allowed to rest as much as she wanted to prevent fatigue. No participant was allowed to rest less than 1 min between trials.	Multivariate analysis for EMG variables showed statistically significant differences between groups ($F_{4,23} = 6.47$, $P = 0.001$; ES = 0.53, β = 0.97) during drop jumps. Follow-up analyses of variance on each EMG variable showed significantly greater co-contraction ratios ($F_{1,26} = 8.83$, $P = 0.006$; ES = 0.25, β = 0.82), greater gluteus maximus full-wave rectified normalized EMG (F1,26 = 10.64, $P = 0.003$; ES = 0.29, β = 0.88), and greater rectus femoris full-wave rectified normalized EMG (F1,26 = 14.73, $P = 0.001$; ES = 0.36, β = 0.96) in the group with ACL reconstruction.
(Ortiz et al., 2011)	14 ACL-R 25.4 ± 3.1 years 15 Healthy Controls 24.6 ± 2.6 years Recreational fitness activities (All Females)	Surface EMG were placed on GMax, RF, LH and MH.	Muscular activation – The participant stood on the force plate of her preference and started jumping single-legged from one force plate to another for 10 consecutive times across the marked lines. One jump was defined as jumping away and back to the same force plate. A side-hopping maneuver was defined as the direction of movement to the opposite side of the weight- bearing leg whereas a crossover hop was defined as the direction of movement toward the same side of the weight-bearing leg	In neither group did group × maneuver interaction ($F_{4,22} = 1.05$; $P = 0.402$; effect size: 0.16; power: 0.28), group main effect ($F_{4,22} = 2.05$; $P = 0.12$; effect size: 0.27; power: 0.52), or maneuver main effect ($F_{4,22} = 2.20$; $P = 0.10$; effect size: 0.29; power: 0.55) in the gluteus, rectus femoris, and hamstrings muscles or the co-contraction ratios reach statistical significance. Electromyographic data revealed no statistically significantly differences between the groups.

VL vastus lateralis ***VM*** vastus medialis ***VMO*** vastus medialis obliquus ***RF*** rectus femoris ***LH*** lateral hamstring ***MH*** medial hamstring ***BF*** biceps femoris ***ST*** semitendinosus ***LG*** lateral gastrocnemius ***MG*** medial gastrocnemius ***Gmax*** gluteus maximus ***ACLD*** anterior cruciate ligament deficiency ***ACLR*** anterior cruciate ligament reconstructed ***MVC*** maximum voluntary contraction ***MVIC*** maximum voluntary isometric contraction ***RC*** inactive controls ***SC*** active controls ***H/Q*** hamstring/quadriceps ***EMG*** electromyography ***IEMG*** integrated electromyography.

isometric peak torques where 4 of the studies observed deficits in quadriceps and hamstring strength and 1 study focused on increments of isokinetic strength from an intervention to prevent ACL injury. The other 6 studies assessed H:Q ratios in a variety of ways.

Twenty studies investigated associations between muscular activation patterns as risk of ACL injury. Five of the 20 studies looked into an intervention to improve on quadriceps and hamstring activation or co-activation, 3 studies focused on pre-activation of the lower limbs in different tasks, 1 study investigated detraining effects on lower extremity EMG, 1 study assessed

Table 6
Associative studies.

Neuromuscular Risk Factor	Papers	Variables Observed
Muscular capacity	Hiemstra et al., 2007; Mattacola et al., 2002; Roberts et al., 2007; Wilkerson et al., 2004; M. K.; Zebis et al., 2011.	Isokinetic and isometric peak torques
	Ahmad et al., 2006; Bee-Oh et al., 2009; Bowerman et al., 2006; Grygorowicz et al., 2010; Holcomb et al., 2007; Hosokawa et al., 2011.	H:Q ratio
Muscular activation	Begalle et al., 2012; Elias et al., 2015; Nagano et al., 2011; R.; Shultz et al., 2015; Wilderman et al., 2009.	Intervention to improve on quadriceps and hamstring activation or co-activation
	Bencke & Zebis, 2011; Hannah et al., 2015; McLean et al., 2010.	Pre-activation of the lower limbs in different tasks
	Dai et al., 2012.	Detraining effects on lower extremity EMG
	Greska, 2012.	Lower extremity neuromechanics relative to leg dominance during an unanticipated sidestep cutting task, with differing states of fatigue and training
	Hughes & Daily, 2015; Kipp et al., 2014; Landry et al., 2009; Lategan, 2012; Liebensteiner et al., 2012; Palmieri-Smith et al., 2009.	Differences in muscle synergy strategy between gender
	Podraza & White, 2010; Walsh et al., 2012.	Relationship between muscle co-contraction and knee flexion angle
	Xie et al., 2013.	Phases of sidestep cutting that may place athletes at a greater risk for ACL injuries
	M. K. Zebis et al., 2011.	Muscle fatigue on neuromuscular strategy during a functional side cutting movement

lower extremity neuromechanics relative to leg dominance during an unanticipated sidestep cutting task, with differing states of fatigue and training, 6 studies investigated the differences in muscle synergy strategy between gender, 2 studies observed the relationship between muscle co-contraction and knee flexion angle 1 study identified the phases of sidestep cutting that may place athletes at a greater risk for ACL injuries and 1 study investigated the effect of muscle fatigue on neuromuscular strategy during a functional side cutting movement.

4. Discussion

4.1. Prospective evidence

The evidence supporting risk factors of ACL injury associated with muscular capacity or muscular activation patterns is limited. This systematic review found only four prospective studies of which three studies looked into muscular capacity (Myer et al., 2009; Söderman et al., 2001; Uhorchak et al., 2003) and only one study into muscular activation patterns (Mette K. Zebis et al., 2009). From the studied cohorts, there were only a small number of individuals who incurred an injury with injury rates ranging from 1.3% to 9.0%. The small percentages of injuries in the prospective cohorts were due to infrequent of acquiring a non-contact ACL injury, even though there is a high case rate for ACL injury. In prospective risk factor studies, the power of the study is determined by (i) the association strength of the risk factor and injury risk (the stronger the association, the fewer cases are needed), (ii) the rate of injury (the more frequent the injury, the fewer cases are needed), and (iii) the chosen significance level (Bahr & Holme, 2003). With low rates of injury, suggestions for future work have been that risk of ACL injury would need to be studied in substantially larger cohorts than typically done but the cost associated to that is simply too high. The relatively higher incidence of injury in females has led to most cohort studies only involving females (Myer et al., 2009; Söderman et al., 2001; Mette K.; Zebis et al., 2009). Considering the knowledge that injury mechanisms in females are different than in males and other risk factors such as laxity and hormonal factors may also differ between males and females (Smith, Vacek, et al., 2012b), this makes translating the risk factors to male populations highly ambiguous. Differences between injured and non-injured individuals were small, providing relatively low sensitivity and specificity of the measure to predict injury (Myer et al., 2009; Söderman et al., 2001; Uhorchak et al., 2003; Mette K.; Zebis et al., 2009). The value of the risk factors for targeted screening with a focus on differentiating interventions based on risk is therefore limited. Particularly, good research practice would require proposed risk factors to be confirmed in an independent study with an independent cohort, yet no risk factors have been independently confirmed to date. Altogether, whilst one may advise future research to involve greater cohorts, for example through multi-centre studies, such efforts should probably focus on multi-factorial risk. Particularly concerning neuromuscular factors, the link between muscular activation patterns and muscles' capacity to generate torque is often referred to when interpreting findings of one or the other (Myer et al., 2009; Söderman et al., 2001; Uhorchak et al., 2003; Mette K.; Zebis et al., 2009), but whether this link holds true in the context of ACL injury risk remains unknown. Also, muscular capacity as well as muscular activation patterns at the knee are related to capacity and activation patterns at the ankle and probably at hip and abdominal musculature (S. J. Shultz, Schmitz, Benjaminse, Chaudhari, Collins, & Padua, 2012; Zazulak, Ponce, Straub, Medvecky, Avedisian, & Hewett, 2005; Zeller, McCrory, Kibler, & Uhl, 2003). No papers on this topic fit our inclusion and exclusion criteria, but the focus on knee musculature based on the premise that this is the closest evidence to predicting ACL injury may well not hold true. Another approach may still be suggested based on a recent systematic literature review on the effectiveness of prevention programmes (Grimm, Jacobs, Kim, Denney, & Shea, 2015). This review revealed that the prevention of ACL injury has until now mostly been ineffective, yet the prevention of knee injuries in general has seen more success. Considering some suggestions that non-contact lower limb injuries can have similar causality, a potentially viable approach to making prospective studies more cost-effective may be to explore risk factors of any knee injury rather than only ACL injury.

4.2. Post-injury case-control evidence

Whilst one may focus on the fact that sample characteristics of the various studies were diffuse, the overarching message concerning post-injury supportive evidence to risk factors is that the effect of injury is greater than any remaining person-specific effects of risk prior to the injury. Clear and often long-term reductions in muscular capacity were found for quadriceps muscles in ACL-D (Hsiao et al., 2014; Konishi et al., 2011; Tsepis et al., 2004; Urbach et al., 2001) and ACL-R (Drechsler et al., 2006; Hsiao et al., 2014; Xergia et al., 2013) patients compared to healthy controls suggesting substantial consequences of post-injury inactivity, detrimental effects of kinesiophobia (Drechsler et al., 2006), autograft repair (Hiemstra, Webber, MacDonald, & Kriellaars, 2004), and potentially lack of rehabilitation compliance. These considerable changes in muscular capacity and likely alterations in muscular activation patterns altogether suggest that risk of re-injury is based on very different factors than risk of primary injury. Rather than hamstring weakness combined with high quadriceps strength (low H/Q ratios), re-injury risk may need to be explored through the consequences of quadriceps weakness and/or lack of quadriceps activation in the injured leg, particularly in the context of compensation mechanisms in the contralateral leg where re-injury is most prevalent (Wright, Magnussen, Dunn, & Spindler, 2011). Hamstring weakness was in most post-injury case-control studies not an indication of risk, with hamstring strength being the same between injured and non-injured limb, and between injured and healthy controls (Drechsler et al., 2006; Swanik et al., 2004; Tsepis et al., 2004; Xergia et al., 2013). This may reflect the effectiveness of many ACL rehabilitation protocols that focus on strengthening the hamstrings as an ACL protective measure. The evidence on hamstring weakness as a risk factor for primary ACL injury remains poor, and is confounded by many other factors, including the fact that hamstring inadequacy may well be joint-angle and joint-angular velocity specific, or as mentioned above, that muscular capacity may well be dissociated from risk inducing activation patterns. In muscular activation pattern assessment, only two case-control studies (Swanik et al., 1999; Swanik et al., 2004) found reduced activation of the semitendinosus combined with increased activation of the vastus lateralis during dynamic tasks as was found through prospective work (Mette K. Zebis et al., 2009). These observations again suggest discrepancies between risk factors of a primary injury versus re-injury. Changes observed in muscular activation patterns post ACL injury likely also result from adaptations associated with protective behaviour when performing selected tasks and/or as a result of rehabilitation focus.

4.3. Reflection on associative studies

The last decade has seen a substantial increase in studies that aim at translating evidence on risk into field-based screening tools through associating observations that are easy to assess in a clinical or field context with previously identified risk factors. For muscular capacity, 11 studies have looked into its association with sustaining a non-contact ACL injury (Ahmad, Clark, Heilmann, Schoeb, Gardner, & Levine, 2006; Bee-Oh, Yong Seuk, Jin Goo, Keun Ok, Jin, & Young Hoo, 2009; Bowerman, Smith, Carlson, & King, 2006; Grygorowicz, Kubacki, Pilis, Gieremek, & Rzepka, 2010; Hiemstra, Webber, MacDonald, & Kriellaars, 2007; Holcomb, Rubley, Lee, & Guadagnoli, 2007; Hosokawa et al., 2011; Mattacola, Perrin, Gansneder, Gieck, Saliba, & Iii, 2002; Roberts, Ageberg, Andersson, & Fridén, 2007; Wilkerson, Colston, Short, Neal, Hoewischer, & Pixley, 2004; M. K.; Zebis et al., 2011). These studies have associated muscular capacity with risks of acquiring ACL injury, validating ACL screening tools to be used in intervention programs to prevent ACL injury. Considering that the 3 prospective studies (Myer et al., 2009; Söderman et al., 2001; Uhorchak et al., 2003) did not find strong evidence of how muscular capacity deficits are a potential risk factor for non-contact ACL injury, the actual predictive value of screening tools with a moderately strong association to the actual risk factor is potentially very weak. The same case applies to screening for muscular activation deficits. There were 20 studies in the last 5 years that addressed an association with motion pattern deficits, seeking opportunities to observe risk from motion analysis (Begalle, Distefano, Blackburn, & Padua, 2012; Bencke & Zebis, 2011; Dai, Sorensen, Derrick, & Gillette, 2012; Elias, Hammill, & Mizner, 2015; Greska, 2012; Hannah, Folland, Smith, & Minshull, 2015; Hughes & Daily, 2015; Kipp et al., 2014; Landry, McKean, Hubley-Kozey, Stanish, & Deluzio, 2009; Lategan, 2012; Liebensteiner, Platzer, Burtscher, Hanser, & Raschner, 2012; McLean, Borotikar, & Lucey, 2010; Nagano, Ida, Akai, & Fukubayashi, 2011; Palmieri-Smith, McLean, Ashton-Miller, & Wojtys, 2009; Podraza & White, 2010; R.; Shultz, Silder, Malone, Braun, & Dragoo, 2015; Walsh, Boling, McGrath, Blackburn, & Padua, 2012; Wilderman, Ross, & Padua, 2009; Xie, Urabe, Ochiai, Kobayashi, & Maeda, 2013; M. K.; Zebis et al., 2011). Whilst there is value in understanding how motion patterns relate to the underlying activation of muscles, it is important to keep in mind that the proposed risk due to imbalance in activation between medial hamstring and lateral quadriceps muscles was based on a limited sample (5 injuries), one particular task (side cut), and a very small window of pre-activity observation (10 ms before touchdown) (Mette K. Zebis et al., 2009), and that this has until now not been confirmed independently. With none of the associative studies strictly adhering to these criteria when measuring muscle activation patterns, any subsequent suggestions made around risk of ACL injury through a screening tool that is based on associations with the suggested muscle activation deficit should be interpreted with great care.

5. Limitations

This review was bound by the chosen search terms and may still not have captured all studies identifying neuromuscular risk factors associated with non-contact ACL injury. We undertook careful hand-searching to detect masquerading articles (articles that were not properly indexed) in an attempt to ensure that all relevant studies were included. Also, the neuromuscular risk factors observed in this systematic review were solely based on attributes of muscular capacity and muscular activation patterns, whereas the term 'neuromuscular' has in the past been used to cover a broader grouping of observations, for example including kinematic (motion) and kinetic (force) observations. Our review was based on published and accessible work only (articles that may have been relevant but were not available for access were excluded from the study), whereas we are aware of more recent unpublished prospective work. To our knowledge, none of that unpublished work seems to direct towards any convincing evidence for neuromuscular risk factors of primary ACL injury.

The sample demographics in the prospective studies varied across studies with respect to age, sex, playing level and type of sport, therefore different risk factors may apply to different subject characteristics as been observed in the ACL prognostic literature.

6. Conclusion

To date, (i) the neuromuscular markers that have been predictive of a primary non-contact ACL injury from prospective evidence are weak, (ii) post-injury case-control studies cannot be used as support for pre-injury risk and (iii) despite a substantial body of research that has studied various neuromuscular risk factors for ACL injury, current evidence is contradictory and ongoing efforts are limited largely to case-control and associative investigations. This means that the evidence-base for the development of field-based and/or large scale screening, as well as the development of prevention programmes, is currently weak. With high costs involved in prospective cohort studies, a change in approach to create stronger evidence may well be necessary.

Conflict of interest

None declared.

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9.2 Publication ii.

233 ALLOMETRICALLY SCALED H:Q RATIOS: TIME TO SHARPEN OUR VISION CONCERNING STRENGTH RATIOS AS INJURY RISK FACTOR!

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Background Our recent systematic review showed that prospective studies found contradicting results concerning hamstring-quadriceps (H:Q) strength ratios as a risk factor for ACL injuries. All studies that express hamstring relative to quadriceps strength assume a proportional relationship yet this is not likely.
Objective i) To investigate if the H:Q strength relationship is proportional in athlete populations and ii) To evaluate the differences in participant rankings between the traditional way of calculating H:Q ratios and allometrically scaled H:Q ratios.
Design Controlled laboratory study.
Setting The study was conducted both in a club and biomechanics laboratory setting.
Participants 71 male elite football athletes, 55 male recreational athletes and 48 female recreational athletes participated in the study.
Assessment of Risk Factors Concentric hamstring and quadriceps strength (Hcon and Qcon), and eccentric hamstring strength (Hecc) were tested in participants' dominant and non-dominant limbs using isokinetic dynamometry at an angular velocity of 60°/s.
Main Outcome Measurements i) Allometric exponents (AE) of the Hcon:Qcon and Hecc:Qcon relationships and ii) Chi-square relationships between population rankings based on the traditional H:Q ratios and the allometrically scaled H:Q ratios.
Results i) Linear regression analyses showed that the Hcon:Qcon and Hecc:Qcon relationships were systematically non-proportional (AE ranged between 0.61 and 0.84) and ii) correcting H:Q ratios based on an average allometric exponent (0.65 for Hcon:Qcon and 0.78 for Hecc:Qcon) successfully removed bias from quadriceps strength, and significantly altered population rankings.
Conclusions Quadriceps strength meaningfully affects H:Q ratios, causing bias in proportionally scaled H:Q ratios. Unless if quadriceps strength itself is a risk factor, allometrically scaled H:Q ratios are a superior measure of H:Q strength (im)balance for injury risk analyses in athlete populations.

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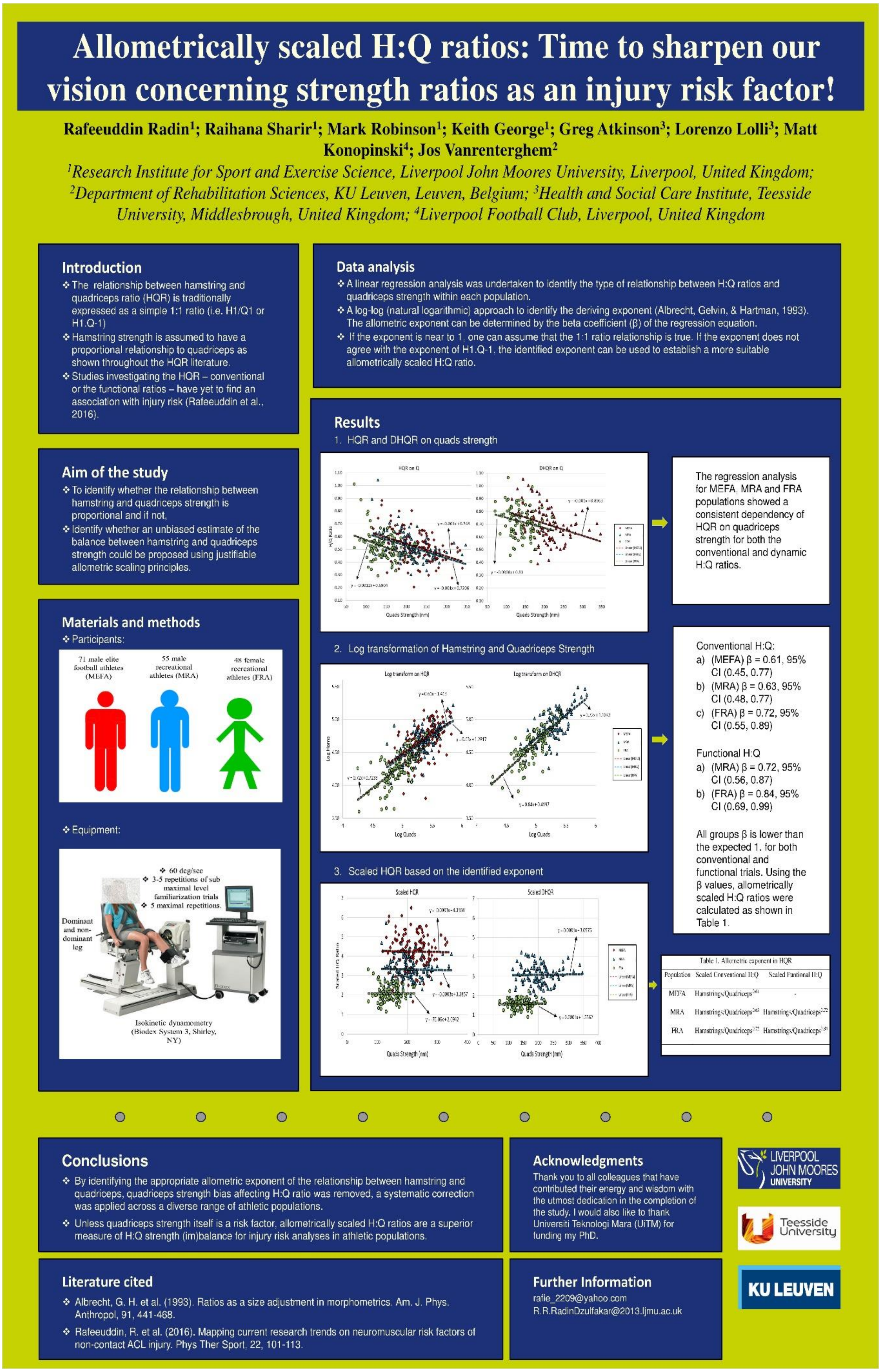

Allometrically scaled H:Q ratios: Time to sharpen our vision concerning strength ratios as an injury risk factor!

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Introduction

- The relationship between hamstring and quadriceps ratio (HQR) is traditionally expressed as a simple 1:1 ratio (i.e. H1/Q1 or H1.Q-1)
- Hamstring strength is assumed to have a proportional relationship to quadriceps as shown throughout the HQR literature.
- Studies investigating the HQR – conventional or the functional ratios – have yet to find an association with injury risk (Rafeeuddin et al., 2016).

Aim of the study

- To identify whether the relationship between hamstring and quadriceps strength is proportional and if not,
- Identify whether an unbiased estimate of the balance between hamstring and quadriceps strength could be proposed using justifiable allometric scaling principles.

Materials and methods

- Participants:

- Equipment:

Data analysis

- A linear regression analysis was undertaken to identify the type of relationship between H:Q ratios and quadriceps strength within each population.
- A log-log (natural logarithmic) approach to identify the deriving exponent (Albrecht, Gelvin, & Hartman, 1993). The allometric exponent can be determined by the beta coefficient (β) of the regression equation.
- If the exponent is near to 1, one can assume that the 1:1 ratio relationship is true. If the exponent does not agree with the exponent of H1.Q-1, the identified exponent can be used to establish a more suitable allometrically scaled H:Q ratio.

Results

1. HQR and DHQR on quads strength

The regression analysis for MEFA, MRA and FRA populations showed a consistent dependency of HQR on quadriceps strength for both the conventional and dynamic H:Q ratios.

2. Log transformation of Hamstring and Quadriceps Strength

Conventional H:Q:

a) (MEFA) β = 0.61, 95% CI (0.45, 0.77)
b) (MRA) β = 0.63, 95% CI (0.48, 0.77)
c) (FRA) β = 0.72, 95% CI (0.55, 0.89)

Functional H:Q

a) (MRA) β = 0.72, 95% CI (0.56, 0.87)
b) (FRA) β = 0.84, 95% CI (0.69, 0.99)

All groups β is lower than the expected 1. for both conventional and functional trials. Using the β values, allometrically scaled H:Q ratios were calculated as shown in Table 1.

3. Scaled HQR based on the identified exponent

Table 1. Allometric exponent in HQR

Population	Scaled Conventional H:Q	Scaled Funtional H:Q
MEFA	$\text{Hamstrings/Quadriceps}^{0.61}$	-
MRA	$\text{Hamstrings/Quadriceps}^{0.63}$	$\text{Hamstrings/Quadriceps}^{0.72}$
FRA	$\text{Hamstrings/Quadriceps}^{0.72}$	$\text{Hamstrings/Quadriceps}^{0.84}$

Conclusions

- By identifying the appropriate allometric exponent of the relationship between hamstring and quadriceps, quadriceps strength bias affecting H:Q ratio was removed, a systematic correction was applied across a diverse range of athletic populations.
- Unless quadriceps strength itself is a risk factor, allometrically scaled H:Q ratios are a superior measure of H:Q strength (im)balance for injury risk analyses in athletic populations.

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Further Information

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