LONGER-TERM QUALITY OF LIFE FOLLOWING ANTERIOR CRUCIATE LIGAMENT INJURY AND RECONSTRUCTION

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Bachelor of Physiotherapy (Hons)

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School of Health and Rehabilitation Sciences
The anterior cruciate ligament (ACL) serves to stabilise the knee complex and prevent intra-articular knee structures from sustaining damage during multiaxial, high impact movement. An ACL rupture most commonly occurs in adolescents and young adults taking part in competitive sports and causes substantial disruption to the knee joint. Anterior cruciate ligament reconstruction (ACLR) is the most common treatment offered to ACL-ruptured individuals worldwide. Individuals undergoing this surgery often have high expectations that rarely match surgical outcomes. Return to sport rates are low, re-injury fears are widespread and many individuals develop knee osteoarthritis within ten years of ACLR. This mismatch between expectations and actual outcomes has great potential to impact longer-term quality of life (QOL). The primary aims of this thesis were to: (i) generate a detailed picture of longer-term QOL following ACLR, and (ii) identify factors related to longer-term QOL in people with knee pain, symptoms or functional limitations following ACLR.

The first study in this thesis is a systematic review that revealed impaired knee-related QOL at 5 to 20 years after ACLR. However, it became evident that research into factors impacting upon QOL in this population was scarce. The systematic review found that having a subsequent knee injury, an additional knee surgery after ACLR, and developing severe radiographic osteoarthritis were associated with worse QOL outcomes. The second study in this thesis is a systematic review that investigated QOL more than five years after ACL rupture in individuals who remained ACL-deficient (did not undergo ACLR) and compared QOL between ACL-deficient and ACL-reconstructed groups. This systematic review found that ACL-deficient individuals reported comparable QOL outcomes to those who underwent ACLR 5 to 25 years previously. All studies that reported QOL after ACLR included asymptomatic participants without knee difficulties, which may underestimate the degree of QOL impairment experienced by people with ongoing knee difficulties.
The third study in this thesis used a cross-sectional design to describe QOL outcomes in 162 individuals with knee pain, symptoms or functional limitations 5 to 20 years following ACLR. It showed that individuals who did not return to sport after ACLR reported poorer knee-related and health-related QOL, compared to people who returned to pre-injury levels of sport. Higher body mass index (BMI) and subsequent surgery were also related to worse QOL after ACLR. This was the first study to show that return to sport was associated with QOL impairment more than five years after ACLR. However, quantitative assessment of QOL may overlook important considerations with regard to an individual’s life priorities, expectations, values and concerns.

To provide a detailed understanding of QOL following ACLR, qualitative interviews were performed with 17 individuals with knee difficulties 5 to 20 years following ACLR. This was the first qualitative study to explore QOL following ACLR. In these individuals, maintaining a physically active lifestyle was a critical feature of a satisfactory QOL and individuals with a strong preference for competitive sport who did not enjoy recreational exercise appeared to be at risk of experiencing prolonged periods of poor QOL. Fear of re-injury and lifestyle modifications following ACLR were also strong determinants of QOL. Furthermore, exploring personal perspectives of QOL following ACLR provided unique insights into the trajectory of QOL over time that had not been addressed in previous ACLR studies. This allowed identification of key points of transition, where intervention to facilitate positive lifestyle modifications could be most beneficial.

The high rates of early knee osteoarthritis after ACLR are alarming considering the young, active population in which ACLR is most prevalent. The impact of living with symptomatic radiographic osteoarthritis on the QOL of ACL-reconstructed individuals is poorly understood. The fifth study in this thesis explored the relationship between radiographic osteoarthritis and QOL, psychological factors, participant characteristics, work limitations, return to sport and knee symptoms in 81 ACL-reconstructed individuals with knee difficulties. This study found five factors that were strongly associated with increased odds of having radiographic knee osteoarthritis: knee-related QOL impairment, dissatisfaction with knee function, having an ACLR more than six months after ACL injury (compared to less than six months), a non-
contact mechanism of ACL rupture and receiving at least one additional surgery since ACLR.

In summary, this thesis identified key factors associated with longer-term QOL impairment in people with knee difficulties after ACLR. However, not all individuals with persistent knee symptoms and difficulties after ACLR were dissatisfied with their current knee function. Achieving satisfactory knee-related QOL appears achievable for some individuals irrespective of the presence of knee pain, osteoarthritis and reduced participation in high-level activities. By identifying specific factors related to unsatisfactory QOL following ACLR, this research has provided valuable information that may facilitate a greater clinical and research focus on improving longer-term QOL following ACLR.
DECLARATION BY AUTHOR

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

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PUBLICATIONS DURING CANDIDATURE

Peer-reviewed papers


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Kay Crossley and Ilana Ackerman made large contributions to the design and content of this thesis. They provided feedback for the entire thesis content and made additional contributions to each individual chapter including study design, interpretation of data, and editing of manuscripts/chapters.

Trevor Russell assisted in multiple aspects of this thesis. This included study design of various chapters, online questionnaire design, interpretation of data, and editing of manuscripts/chapters.

Erin Macri contributed to the systematic review comprising Chapter 4, including the quality appraisal, data extraction and editing the published manuscript.

Adam Culvenor contributed to the systematic review comprising Chapter 5, including the quality appraisal, data extraction, meta-analysis, and editing the published manuscript.

Susan Keays assisted with recruitment for the cross-sectional study (Chapter 6).

Sanjay Dhupelia graded all knee radiographs included in Chapter 8.

Kate Croft assisted with payment of radiographic invoices, contacting radiology clinics and participant recruitment for knee radiographs (Chapter 8).

Peter Baker provided statistical advice and assisted with data pooling for the systematic review comprising Chapter 3.

STATEMENT OF PARTS OF THE THESIS SUBMITTED TO QUALIFY FOR THE AWARD OF ANOTHER DEGREE

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<td>ACL</td>
<td>anterior cruciate ligament</td>
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<td>ACL-QOL</td>
<td>Quality of Life Outcome Measure (Questionnaire) for Chronic Anterior Cruciate Ligament Deficiency</td>
</tr>
<tr>
<td>ACLD*</td>
<td>anterior cruciate ligament deficient</td>
</tr>
<tr>
<td>ACLR</td>
<td>anterior cruciate ligament reconstruction</td>
</tr>
<tr>
<td>ADL</td>
<td>function in Activities of Daily Living</td>
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<tr>
<td>AQoL-8D</td>
<td>Assessment of Quality of Life 8D Utility Instrument</td>
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<tr>
<td>Beta (β)</td>
<td>standardized coefficient</td>
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<td>B</td>
<td>unstandardized coefficient</td>
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<td>BMI</td>
<td>body mass index</td>
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<td>BP</td>
<td>Bodily Pain</td>
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<td>CI</td>
<td>confidence interval</td>
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<tr>
<td>CS*</td>
<td>cross-sectional</td>
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<td>E.M</td>
<td>Erin Macri</td>
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<td>EQ-5D</td>
<td>Euro-QoL 5D</td>
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<td>HADS</td>
<td>Hospital Anxiety and Depression Scale</td>
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<td>I.A</td>
<td>Ilana Ackerman</td>
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<td>IQR</td>
<td>inter-quartile range</td>
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<td>K.C</td>
<td>Kay Crossley</td>
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<tr>
<td>KANON</td>
<td>the Knee Anterior Cruciate Ligament, Nonsurgical versus Surgical Treatment Trial</td>
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<tr>
<td>KOOS</td>
<td>Knee injury and Osteoarthritis Outcome Score</td>
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</table>
LARS  Ligament Augmentation Reinforcement System
MCID  minimal clinically important difference
MCII  minimal clinically important improvement
MCS  Mental Component Score
MH  Mental Health
MRI  magnetic resonance imaging
NR*  not reported
OA*  osteoarthritis
OR  odds ratio
PASS  patient acceptable symptomatic state
PCS  Physical Component Score
PF  Physical Function
PFJ*  patellofemoral joint
PRISMA  Preferred Reporting Items for Systematic Reviews and Meta-Analyses
Prosp*  prospective
PTSD*  post-traumatic stress disorder
QOL  quality of life
$r$  Pearson’s correlation coefficient
$R^2$  the proportion of variance in the dependent variable that can be accounted for by the independent variables in combination
RCT  randomised controlled trial
RE  Role Emotional
Retro*  retrospective
rho  two-tailed Spearman’s rank correlation coefficient
RTS*  return to sport
RP  Role Physical
S.D    Sanjay Dhupelia
S.F    Stephanie Filbay
SD (±)  standard deviation
SF    Social Function
SF-36  Short-Form 36
Sport/Rec  function in Sport and Recreation
T.R    Trevor Russell
TFJ*  tibiofemoral joint
V    Vitality
VIF    variance inflation factor
WALS  Workplace Activity Limitations Scale

*abbreviation appears in tables and figures only
PART A
BACKGROUND AND LITERATURE REVIEW
AN INTRODUCTION TO ANTERIOR CRUCIATE LIGAMENT INJURY

Anterior cruciate ligament rupture

For some individuals, an anterior cruciate ligament (ACL) rupture will alter the quality and course of their life. A fundamental understanding of the functional and structural properties of an intact ACL may assist in comprehending how an ACL rupture could have such a profound impact. The ACL plays a pivotal role in maintaining multiaxial knee stability between the articulating surfaces of the tibia and femur (Ardern, Matsumoto et al. 2001). The ACL medially rotates and tracks posteriorly, laterally and superiorly from its origin on the anterior tibial spine to its insertion on the posterior medial lateral femoral condyle (Dodds & Arnoczky, 1994). The ACL is comprised of two distinct bundles (the anteromedial bundle and posterolateral band), which function cohesively by interchanging between a lengthened and shortened state to assure some fibres of the ACL are under tension throughout full knee range of movement (Bach, Hull, & Patterson, 1997; Dodds & Arnoczky, 1994). The ACL also features unique structural properties and contains multiple collagen fibre types arranged amongst an intricate matrix with elastic and tensile properties that resist high-impact multiaxial strain (Duthon et al., 2006). The ACL is also believed to contain proprioceptive fibers that communicate with the cerebral cortex; disruption of these fibers may contribute to the pertinent instability resulting from ACL rupture (Pitman, Nainzadeh, Menche, Gasalberti, & Eun Kyoo, 1992). ACL rupture typically occurs while participating in high-impact competitive sport where individuals are commonly faced with high functional demands and exposed to large multiaxial loads (Gianotti, Marshall, Hume, & Bunt, 2009; Hewett, Ford, Hoogenboom, & Myer, 2010; Joseph et al., 2013). While a partial ACL tear may have some healing capacity, ACL rupture results in a complete
separation of the ligament into two distinct remnants (or separation from the bone), inhibiting healing of the ligament. An ACL-deficient knee that remains unstable may be at heightened risk of further trauma to other knee structures including the cartilage, meniscus, and other ligaments when faced with high demands like those occurring during competitive sport participation (Lohmander, Englund, Dahl, & Roos, 2007; Øiestad, Engebretsen, Storheim, & Risberg, 2009). Additional ramifications of sustaining an ACL rupture can include persistent knee pain, swelling, instability, activity restrictions, knee-related fears, reduced knee confidence and impaired quality of life (QOL) (Ardern, Taylor, Feller, & Webster, 2014b; Lohmander, Östenberg, Englund, & Roos, 2004; Øiestad et al., 2009).

**Anterior cruciate ligament reconstruction**

To minimise the likelihood of chronic knee instability and activity limitations, ACL reconstruction (ACLR) surgery is often performed whereby the torn remnants of the ACL are removed and replaced with a ligament graft. A number of different materials have been trialled in attempt to form a ligament graft that resembles the properties of the native ACL. Currently, the gold-standard and most commonly used techniques are the hamstring and patellar tendon autograft (Ahlden et al., 2012; Chechik et al., 2013; Delay, Smolinski, Wind, & Bowman, 2001; Maletis, Granan, Inacio, Funahashi, & Engebretsen, 2011), although there is little consensus regarding the most preferable method (Chechik et al., 2013; Marx, Jones, Angel, Wickiewicz, & Warren, 2003; Mirza, Mai, Kirkley, Fowler, & Amendola, 2000). Common variations include double-bundle and single-bundle techniques, contrasting graft fixation sites and devices, fixing the graft in varying degrees of tension, use of patellar tendon bone plugs, and performing additional extra-articular lateral stabilisation in attempt to enhance rotational stability (Abdelkafy, 2015; Alentorn-Geli, Samitier, Álvarez, Steinbacher, & Cugat, 2010; Arifeen et al., 2015; Arneja et al., 2009; Björnsson et al., 2015; Eriksson, 2007; Fleming et al., 2013; Foster, 2010; Marcacci, 2009; Ochiai, Hagino, Senga, Saito, & Haro, 2012; Song et al., 2013). A shared feature of all ACLR techniques is the potential damage to additional knee structures which may impact on knee symptoms and function. This trauma may include
complete or partial rupture of tendons during graft harvesting, bone drilling resulting in fracture of subchondral tibial and femoral bone, and potential damage to tissue through surgical excisions (including superficial nerves, fat pad, synovium, retinaculum, skin and bursa). Damage to these structures may result in persistent problems such as numbness and altered sensation, patellofemoral pain and difficulty kneeling (Ahn, Kim, Wang, Jung, & Lim, 2012; Culvenor et al., 2015; Kartus, Movin, & Karlsson, 2001). Although the overall ACLR surgical procedure has vastly reduced in invasiveness with the adoption of arthroscopic surgery and the cessation of open surgical techniques, a patient undergoing an ACLR can expect at least a short-term period of moderate to severe pain and joint inflammation and a prolonged period of altered weight bearing and limited function. Despite these post-operative difficulties, a common rationale for undergoing ACLR is that the procedure will improve knee stability, enabling an eventual return to unrestricted sport, and reducing the risk of additional knee injury and subsequent knee osteoarthritis (Feucht et al., 2014; Marx et al., 2003; Matava, Howard, Polakof, & Brophy, 2014).

Epidemiology of anterior cruciate ligament reconstruction

Rates of ACLR have been reported in several countries, most notably in Scandinavia, facilitated by nation-wide ACL registries that collect data on all ACLR procedures. A review of these registries reported an annual incidence of primary ACLR in Denmark of 38 per 100,000 inhabitants (Lind, Menhert, & Pedersen, 2009), 34 per 100,000 inhabitants in Norway (Granan, Bahr, Steindal, Furnes, & Engebretsen, 2008) and 32 per 100,000 inhabitants in Sweden (Granan, Forssblad, Lind, & Engebretsen, 2009). In the United States, the incidence of ACLR has been estimated at 30 per 100,000 inhabitants (Csintalan, 2008). In Australia, the estimated incidence rate of ACLR is higher at 52 per 100,000 inhabitants, using data from a national hospital administrative database (Janssen, Orchard, Driscoll, & van Mechelen, 2012). International data show that the incidence of ACLR is over twice as high in adolescents and adults younger than 39 years and female athletes experience higher rates of ACL rupture than their male counterparts (Granan et al., 2008; Granan et al., 2009; Janssen et al., 2012; Joseph
et al., 2013; Lind et al., 2009).

Research is scarce regarding population estimates for the incidence of non-operatively managed ACL ruptures. New Zealand utilises a tax-payer funded universal sports injury insurance scheme that funds health-care costs associated with sports injuries, resulting in the collection of incidence data for most sporting injuries (Gianotti et al., 2009). The incidence rate of non-surgically managed knee ligament injuries over a 5 year period in New Zealand was 1147 (95% confidence interval (CI) 1142 to 1158) per 100,000 person-years, and the incidence of ACLR was 37 (95% CI 36 to 38) per 100,000 person-years (Gianotti et al., 2009). These findings highlight the concerning prevalence of knee injury in the general population; unfortunately incidence data were not reported specifically for non-surgically managed ACL injuries. A large study investigating the epidemiology of ACL injury in high-school athletes participating in 5 male and 4 female sports estimated the national rate of ACL injury within these sports to be 215,628 ACL injuries over the 2007/08–2011/12 academic years, which equates to a rate of 6.5 per 100,000 athlete exposures (one athlete exposure is defined as one game or practice where an athlete is susceptible to injury) (Joseph et al., 2013). This study also reported that 77% of all ACL injuries were surgically reconstructed (Joseph et al., 2013). Despite the high prevalence of ACLR world-wide, the true incidence of ACL rupture remains unknown since rates of ACL injuries have only been reported within specific population subgroups and non-surgically managed ACL injuries are rarely reported and may go undiagnosed or misdiagnosed.

**Outcomes of anterior cruciate ligament reconstruction**

Anecdotally, the primary aims of ACLR are to restore knee joint biomechanics, enable resumption of desired sport and activities, minimise the likelihood for persistent pain and knee symptoms, reduce the risk of subsequent injury and early-onset osteoarthritis, and optimise long-term QOL. In recent years, new evidence has challenged these goals, reporting low return to sport rates after ACLR (Ardern et al., 2014b), persistent knee symptoms including pain and swelling (Lohmander et al., 2004), subsequent knee trauma and rupture of the ACL graft
(Hettrich, Dunn, Reinke, Spindler, & Group, 2013; Lyman et al., 2009; Shelbourne, 2009; Wright, 2014), high rates of early onset osteoarthritis (Øiestad et al., 2009) and a high prevalence of ongoing psychological issues, most notably fear of re-injury and poor knee confidence (Langford, Webster, & Feller, 2009; Wierike, Sluis, Akker-Scheek, Elferink-Gemser, & Visscher, 2013). To optimise the likelihood of a satisfactory outcome after ACLR, post-operative rehabilitation including early weight bearing, range of motion, neuromuscular and strengthening exercises is recommended (Kruse, Gray, & Wright, 2012; van Grinsven, van Cingel, Holla, & van Loon, 2010; Wright et al., 2008).

**Return to pre-injury sport**

A primary reason for performing ACLR is to enable a return to competitive sport following ACL injury (Marx et al., 2003). However, a recent meta-analysis pooled return to pre-injury sport rates from 69 studies at an average 40 (range 12-156) months following ACLR, and found that 65% (95% CI 59% to 72%) of participants returned to their pre-injury sport after ACLR, 55% (95% CI 46% to 63%) returned to competitive sport and only 42% (95% CI 33% to 49%) of individuals returned to non-elite competitive sport (Ardern et al., 2014b). Return to sport rates are higher in elite athletes, as demonstrated by a pooled estimate of 79% (95% CI 70% to 86%) return to pre-injury level of sport (Ardern et al., 2014b). Of those who returned to pre-injury level sport, only 44% described normal knee function, and those with abnormal or severally abnormal knee function experienced similar return to sport rates as those with normal or nearly abnormal knee function (Ardern et al., 2014b). Factors associated with a reduced likelihood of returning to sport included older age at the time of ACLR, female sex, participating in non-elite sport, a high fear of re-injury, low psychological readiness to return to sport and negative emotional responses to ACLR (Ardern, Taylor, Feller, & Webster, 2012a; Ardern et al., 2014b). Despite the low rates of return to sport reported in the literature, as many as 91% of patients expect to return to pre-injury sport within one year of ACLR (Feucht et al., 2014). This mismatch between return to sport expectations and actual return to sport rates could negatively impact on QOL and postoperative satisfaction.
**Concomitant joint injury**

Due to the high forces acting on the knee joint at the time of ACL rupture, concurrent damage to other structures in the knee is common (Noyes, Bassett, Grood, & Butler, 1980). As a consequence of knee trauma at the time of ACL rupture, bone marrow lesions (also known as ‘bone bruises’) occur in approximately 70% of knees (Papalia et al., 2015; Yu & Cook, 1996). Bone marrow lesions can persist more than 12 months after injury and are associated with a greater severity of acute knee pain (Frobell et al., 2009; Papalia et al., 2015). Despite a relationship with knee pain, bone marrow lesions are not associated with knee function during the first two years following ACL injury (Papalia et al., 2015). Further research is required to determine whether bone marrow lesions influence longer-term joint function, symptoms or rates of osteoarthritis development (Papalia et al., 2015).

Damage to the articular cartilage can also occur at the time of ACL rupture; full thickness cartilage lesions have been associated with more knee pain and symptoms, poorer function and reduced QOL at two years following surgery (Røtterud, Risberg, Engebretsen, & Årøen, 2012; Røtterud, Sivertsen, Forssblad, Engebretsen, & Aroen, 2013). Concomitant cartilage and meniscus injury with or without surgical repair has also been associated with higher rates of early-onset knee osteoarthritis compared with an isolated ACL rupture (Claes, Hermie, Verdonk, Bellemans, & Verdonk, 2013; Keays, 2010; Magnussen, Mansour, Carey, & Spindler, 2009; Murray et al., 2012; Øiestad et al., 2009; van Meer et al., 2015). Additionally, worse outcomes (reduced physical activity level and knee function, more pain and symptoms) were reported 16 years following ACLR in individuals with baseline meniscal damage compared to people with an isolated ACL rupture (Gerhard et al., 2012). More than 60% of all ACLR surgeries performed in the state of New York between 1997 and 2006 (total of 70,547 procedures) were performed with a concomitant surgery, and one in every two ACLRs involved concurrent surgery to the meniscus (Lyman et al., 2009). Receiving concomitant meniscus surgery at the time of ACLR is associated with worse outcomes between 2 and 15 years after surgery (including more knee symptoms, pain, worse knee function and QOL), compared to people who do not receive meniscus surgery (Barenius, Nordlander, Ponzer,
Tidermark, & Eriksson, 2010; Cox et al., 2014; Dunn et al., 2015; Neuman et al., 2008). These relationships suggest individuals who sustain associated or additional injuries may be at a heightened risk of poor QOL outcomes following ACLR.

Subsequent injury and revision surgery

More pain, symptoms, poorer function and worse QOL have been reported in individuals who experience a subsequent knee injury after ACLR (Swirtun & Renström, 2008). Subsequent surgery following ACLR is not uncommon, with as many as 7% of patients receiving a subsequent knee surgery to either knee within 1 year (Lyman et al., 2009) and 19% undergoing a subsequent surgery to their ACL-reconstructed knee within 6 years of ACLR (Hettrich et al., 2013). Additionally, a proportion of individuals who receive an ACLR will suffer a re-rupture of the ACL graft, or a rupture of the contralateral ACL. Rates of revision ACLR vary, with larger studies reporting a revision rate of two per-cent at two year follow-up (Andernord et al., 2015; Bjornsson et al., 2015), and four to five per-cent at five years following primary ACLR (Lind, Menhert, & Pedersen, 2012; Persson et al., 2014; Webster, Feller, Leigh, & Richmond, 2014). Revision rates are higher in young adults and adolescents and those returning to high-impact sports after primary ACLR (Andernord et al., 2015; Lind et al., 2012; Persson et al., 2014). Adolescents who undergo ACLR are also at greater risk of sustaining a contralateral ACL rupture compared to their adult counterparts (Leroux et al., 2014; Webster et al., 2014). An Australian study reported a contralateral ACL injury rate of 8% at an average 5 years after primary ACLR, which increased to an alarming 29% for people aged under 20 years (Webster et al., 2014). Overall, rates of sustaining a graft re-rupture or contralateral ACL rupture 15 years after primary ACLR are as high as one in every four individuals (Bourke, Salmon, Waller, Patterson, & Pinczewski, 2012). Additionally, reported rates of re-revision ACLR at an average five years after revision ACLR range from four to five per-cent (Leroux et al., 2014; Lind et al., 2012). Individuals having a re-revision procedure have lower activity levels and more cartilage injuries than those having their first revision surgery (Leroux et al., 2014). The true rate of ACL graft re-ruptures cannot be determined as an unknown proportion of graft ruptures
go undiagnosed or are not surgically reconstructed.

People presenting for revision ACLR are more likely to have concurrent meniscal and chondral damage than those undergoing a primary ACLR (Ahn, Lee, & Ha, 2008; Brophy, Haas, Huston, Nwosu, & Wright, 2015; Kievit, Jonkers, Barentsz, & Blankevoort, 2013; Thomas, Kankate, Wandless, & Pandit, 2005; Widener, Wilson, Galvin, Marchant, & Arrington, 2015). Furthermore, inferior outcomes are consistently reported following revision surgery compared with primary ACLR, including greater rates of osteoarthritis development, more pain and symptoms, lower activity levels, poorer function and worse QOL (Gifstad, Drogset, Viset, Grøntvedt, & Hortemo, 2012a; Kievit et al., 2013; Lind et al., 2012). The high rates of chondral lesions observed at the time of revision ACLR may be associated with the high rates of osteoarthritis development following revision ACLR (Salmon, Pinczewski, Russell, & Refshauge, 2006). Despite an overall reduction in patient expectations for revision ACLR compared to the very high expectations reported prior to primary ACLR, 96% of patients expect no risk or a slightly increased risk of developing osteoarthritis (compared to a healthy knee) 10 years following revision ACLR, 88% percent expect to return to the same level of sport, and all patients expect to have a normal or nearly normal knee after revision surgery (Feucht et al., 2014). In contrast to these expectations, only one in every two patients return to pre-injury sport following revision ACLR (Grassi et al., 2015) and reported rates of knee osteoarthritis four to eight years after revision ACLR range from 37% to 80% (Kamath, 2011). Considering on average, revision ACLR results in poorer outcomes compared with primary ACLR despite high expectations, re-injury and revision surgery have great potential to negatively impact longer-term psychological wellbeing and QOL.

**Knee osteoarthritis**

Osteoarthritis is a progressive synovial joint disease characterised by changes to subchondral bone, synovium, peri-articular muscles, meniscus, ligaments, and articular cartilage (Lane et al., 2011). Osteoarthritis remains a leading cause of global disability (Cross et al., 2014).
impacting one in three individuals over the age of 60 years (Felson, 2004). With no known curative treatment, total knee arthroplasty is commonly used to alleviate pain and improve function for people with end-stage knee osteoarthritis. Rupture of the ACL is associated with an increased risk of knee osteoarthritis, and possible explanations for this include alterations in knee biomechanics, modified joint loading and a cascade of intra-articular pathogenic processes commencing at the time of ACL rupture (Lohmander et al., 2007). This risk is heightened in individuals who suffer concomitant injury at the time of ACL rupture, one in two of whom will develop knee osteoarthritis 10 to 20 years following ACL injury (Øiestad et al., 2009). This short period of time between ACL injury and osteoarthritis development is alarming considering the high prevalence of ACL injury in adolescents, and the active demographic that commonly undergo ACLR (Renstrom et al., 2008). Young and middle aged adults with knee osteoarthritis report markedly reduced health-related QOL, more psychological distress and greater work impairment than age-matched population norms (Ackerman et al., 2015). The impact of symptomatic early knee osteoarthritis on sports participation and QOL among ACL-reconstructed individuals has not been investigated.

**Psychological outcomes**

Psychological impacts of ACL rupture and subsequent reconstructive surgery are heightened during the acute postoperative period (Brewer et al., 2007; Heijne, Axelsson, Werner, & Biguet, 2008; Langford et al., 2009; Tripp, Stanish, Ebel-Lam, Brewer, & Birchard, 2007) and may persist for years following ACLR with potential to influence longer-term outcomes (Ardern et al., 2012a; Wierike et al., 2013). Studies have found that patients who do not return to pre-injury sport at one year after ACLR, and three to four years later, report more fear of re-injury, negative emotions and lower confidence than those who do return to sport (Kvist, Ek, Sporrsedt, & Good, 2005; Webster, Feller, & Lambros, 2008). Furthermore, emotional disturbances were reported by individuals who had not returned to sport at 6 and 12 months after ACLR, compared to those who had returned to sport, despite no differences in knee function and symptoms (Langford et al., 2009). Fear of re-injury is a very common
psychological manifestation experienced by individuals after ACLR (Ardern et al., 2014a; Gignac et al., 2015; Kvist et al., 2005; Tripp et al., 2007) and higher levels of fear of re-injury have been associated with worse knee-related QOL (Kvist et al., 2005). Additionally, psychological factors assessed prior to undergoing ACLR are predictive of postoperative outcomes (Everhart, Best, & Flanigan, 2015). Specifically, pessimism (Swirtun & Renström, 2008) and low pre-operative predictions of future knee self-efficacy (Thomeé et al., 2008) have been shown to predict poor postoperative patient-reported outcomes. Having a more external locus of control (where individuals do not perceive to be in control of their own health state) has been associated with worse self-perceived function prior to ACLR (Nyland, Johnson, Caborn, & Brindle, 2002), lower knee self-efficacy one year after ACL injury (Thomeé et al., 2007), as well as worse functional outcomes and health-related QOL two years after ACLR (Nyland, Cottrell, Harreld, & Caborn, 2006). Taken together, these findings suggest that ACL injury and subsequent reconstructive surgery may have long-lasting psychological impacts with potential to influence knee function, return to sport and QOL. Quality of life outcomes after ACLR will be discussed in Chapter 2.

Non-operative management of anterior cruciate ligament rupture

Thirty-three years ago, a review article outlining future directions for ACL management concluded that “in the future, we hope to be able to discern more accurately which acute ACL ruptures need surgical treatment” (Clancy, 1983). Today, despite over 20,000 publications surrounding ACL injury management, only a very small number have focused on answering this question. Through use of exercise and rehabilitation strategies, some ACL-deficient individuals develop an ability to dynamically stabilize their knee, allowing full participation in pivoting sports and avoiding the need for an ACLR (Fitzgerald, Axe, & Snyder-Mackler, 2000; Frobell et al., 2013; Grindem, Eitzen, Moksnes, Snyder-Mackler, & Risberg, 2012; Johnson, Maffulli, King, & Shelbourne, 2003; Kaplan, 2011). Despite the high incidence of ACLR and the potential for poor long-term outcomes, there has been a notable shortage of high quality
studies investigating outcomes after non-operative management of ACL rupture (Luc, Gribble, & Pietrosimone, 2014; Smith, Postle, Penny, McNamara, & Mann, 2014). The first study to break this trend was a randomised controlled trial (RCT) (the Knee Anterior Cruciate Ligament, Nonsurgical versus Surgical Treatment (KANON) Trial) comparing outcomes between individuals randomised to receive either early ACLR followed by exercise therapy, or exercise therapy alone with an optional delayed ACLR if required and/or desired (Frobell, Roos, Roos, Ranstam, & Lohmander, 2010). The high methodological quality of the KANON trial minimised bias that had been evident in previous studies and found no differences in physical activity levels, rates of subsequent meniscus surgery, pain, symptoms, radiographic joint changes and QOL at two and five year follow-up between as-treated groups (early ACLR vs. exercise therapy alone vs. optional delayed ACLR) or randomised groups (early ACLR vs. exercise therapy alone with optional delayed ACLR) (Frobell et al., 2010; Frobell et al., 2013).

These results sparked heated debate leading to several opinion pieces, commentaries and editorials (Ardern, 2013; Aspdenberg, 2010; Harris, Driban, Sitler, Cattano, & Hootman, 2015a; Khan, 2010; Krogsgaard, Brodersen, & Comins, 2011; Levy, 2010; Løken, Årøen, & Engebretsen, 2011; Richmond, Lubowitz, & Poehling, 2011; Van de Velde & Gill, 2010). Such debate may have triggered a number of ensuing literature reviews that compared outcomes after ACLR and non-operative management. Although none of these reviews investigated QOL outcomes, similar rates of osteoarthritis development and physical activity levels were reported in ACL-reconstructed and non-operatively managed groups (Chalmers et al., 2014; Luc et al., 2014; Smith et al., 2014). One systematic review pooled results from prospective studies of 15 non-operatively managed cohorts, and found that on average individuals reported good function and activity levels and performed well in one-leg-hop for distance tests (Muaidi, Nicholson, Refshauge, Herbert, & Maher, 2007). Between group differences identified through meta-analysis included a greater likelihood of reduced knee range of motion or reduced knee extension one to four years following ACLR compared to the non-operatively managed groups (Smith et al., 2014) and a higher rate of subsequent meniscus injury in ACL-deficient groups (Chalmers et al., 2014; Smith et al., 2014).
On the other hand, contrasting conclusions were made on the rates of subsequent surgical procedures and passive knee laxity (Chalmers et al., 2014; Smith et al., 2014). The term knee laxity refers to passive instability (such as increased anterior-posterior translation measured by a mechanical devise or a clinician) whereas instability refers to a self-reported feeling of knee instability (Johnson et al., 2003). Articles dating back to the 1970’s and 1980’s highlighted the importance in differentiating between these two concepts and emphasised a need to operate on knees with instability as opposed to knee laxity (Clancy, 1983; Hughston, Andrews, Cross, & Moschi, 1976). The clinical relevance of potential differences in knee laxity between treatment groups is unclear, since the same studies report no differences in functional outcomes, physical activity levels or subjective knee instability between groups (Smith et al., 2014). Further discordance has been reported between passive knee laxity and functional measures in ACL-deficient individuals (Snyder-Mackler, Fitzgerald, Bartolozzi, & Ciccotti, 1997). A recent systematic review found that knee joint laxity, body mass index (BMI), sex, quadriceps strength, hop tests, and concomitant joint injury do not predict a need for undergoing ACLR after trialling non-operative management for ACL rupture, and conflicting associations were reported for pre-injury activity level and age (Eggerding, Meuffels, Bierma-Zeinstra, Verhaar, & Reijman, 2015). In contrast, a narrative literature review described differences between people who were perceived to have experienced worse outcomes following non-operative management of ACL rupture (described as ‘non-copers’) compared to those perceived to have had better outcomes (described as ‘copers’). While some differences were observed in knee kinematics, gait patterns and quadriceps strength between ‘copers’ and ‘non-copers,’ it is not known whether these factors were clinically relevant, or if they impacted the QOL of these ACL-deficient individuals (Kaplan, 2011). Moreover, research suggests that these categories are by no means fixed, with time or through rehabilitation, patients who were perceived as non-copers can develop adaptive strategies to improve their outcomes and knee function (Moksnes, Snyder-Mackler, & Risberg, 2008).

In summary, there is a shortage of high quality studies comparing longer-term outcomes following ACLR and non-operative management (Delincé & Ghafil, 2012; Smith et al., 2014). A proportion of individuals will do well with non-operative management, however to date there
is no clear criteria to identify who will benefit most without ACLR. There is no strong evidence to support favourable outcomes following ACLR compared to non-operative management, although differences in QOL and patient satisfaction between treatment strategies remain unclear. Furthermore, undergoing a period of prehabilitation (rehabilitation prior to ACLR) has been associated with better post-operative patient-reported knee scores and better knee function (Grindem et al., 2015; Shaarani et al., 2013). This suggests that initiating exercise therapy after ACL rupture may be beneficial irrespective of whether an individual elects to undergo ACLR in the future. Considering the additional trauma to intra-articular structures associated with undergoing ACLR, the prolonged period of debilitation that follows ACLR, the large financial cost to society and the individual, and the potential psychological consequences of undergoing surgery at a young age, longer-term QOL outcomes following conservative management of ACL rupture warrants consideration and further investigation.
What is quality of life?

Although a multitude of QOL definitions have been proposed, no consensus has been reached regarding an ideal classification (Barcaccia et al., 2013; Gill & Feinstein, 1994; Post, 2014). The World Health Organisation has defined QOL as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (The World Health Organization Group, 1995). A more succinct definition that has been proposed defines QOL as “the satisfaction of an individual’s values, goals and needs through the actualisation of their abilities or lifestyle” (Emerson, 1985, p. 282). Furthermore, self-reported QOL has been referred to as the congruence between an individual’s expectations, hopes or aspirations and their accomplishments or present experiences (Post, 2014). Due to the multiplicity of QOL definitions, a common recommendation in the literature is for authors to clearly define any QOL related terms used in their study at the outset (Barcaccia et al., 2013; Post, 2014). The concept of QOL as referred to in this thesis encompasses the following three principles:
• Quality of life reflects an individual’s perceived concordance between their ideal or expected state and their current state and abilities.

• Quality of life is a subjective multidimensional concept; interpretation is specific to the individual and dependent on a wide range of personal factors including cultural, behavioural, psychological, environmental and societal influences.

• Quality of life is a dynamic construct, which may change over time, in line with an individual’s expectations, beliefs, circumstances, knowledge and experiences.

Health-related quality of life

Health-related QOL has been referred to as one specific domain of the broad concept that encapsulates QOL (Dijkers, 1997; Torrance, 1987). Specifically, health-related QOL has been defined as the discord between health expectations and current health experience (Carr, Gibson, & Robinson, 2001; Post, 2014). Instruments that measure health-related QOL typically address several domains of health that are relevant to many health problems and populations. Common domains include functional health, social health, physical health and mental health (Post, 2014). Not surprisingly given the breadth of QOL definitions, there is large variation in the content of questionnaires designed to evaluate health-related QOL (Post, 2014). Some health-related QOL measures assess factors such as biological function, physical symptoms and functional status (Cleary & Wilson, 1995). One drawback in including domains such as these in health-related QOL measures is that they do not address the importance of biological, physical or functional impairment to the individual. Indeed, reported participation restrictions do not always coincide with satisfaction with participation (van der Zee, Post, Brinkhof, & Wagenaar, 2014) and good or excellent health is often reported by individuals with moderate to serious physical disabilities (Albrecht & Devlieger, 1999). Consequently, some classifications of health-related QOL have highlighted the importance of differentiating between health satisfaction and physical function, recognising that health-related QOL can differ amongst individuals with longstanding physical impairments or disabilities (Johnson & Wolinsky, 1993; Krahn, Fujiura, Drum, Cardinal, & Nosek, 2009; Schwartz et al., 2007). The concept of health-related QOL used throughout this thesis denotes the impact of all health-
related factors on an individual’s QOL.

Knee-related quality of life

The term ‘knee-related QOL’ used throughout this thesis, will refer to the influence of an individual’s knee upon their life quality. Thus, knee-related QOL is one specific component of the broader concept of health-related QOL. Following ACLR, assessment of knee-related QOL evaluates the impact of the knee upon an individual’s ability to achieve their desires, goals and ambitions, and may be influenced by a person’s surgical expectations and beliefs. The impact of an individual’s ACL-reconstructed knee upon their QOL should be interpreted independently from the presence or severity of physical or functional knee impairments.

Why measure quality of life in anterior cruciate ligament-reconstructed individuals?

“Really effective and humane medicine, the critic emphasises, must understand and care about a person as an integrated, feeling and active being. It is the quality of such an integrated person's life that we should care about, not primarily the person as a biological organism” (Nordenfelt, 1993) pp13.

Arguably, improving a patient’s knee-related QOL should be the overarching rationale for ACLR. Every ACL-reconstructed individual has unique beliefs, ambitions, experiences, goals and personal attributes. Such factors may largely explain variation in surgical outcomes and provide a rationale to shift toward more individualised, personalised patient-centred care. Patient-centred QOL measures can give context and meaning to objective measures that are commonly used to assess outcomes of ACLR (Carr & Higginson, 2001). However, the patient-reported measures frequently used to guide clinical management may not be of importance or relevance to the ACL-ruptured or reconstructed individual (Tanner, Dainty, Marx, & Kirkley, 2007) Knee-specific measures of physical function were amongst those rated of low
importance by ACL-ruptured individuals (Tanner et al., 2007). Information assessing the impact of specific physical symptoms or impairments upon the QOL of the individual could be used to guide individualised management strategies to optimise post-operative outcomes. An ACLR can have long-lasting physical and psychological ramifications and has associated costs, risks and potential complications (Ahn et al., 2012; Ardern et al., 2012a; Christino, Fantry, & Vopat, 2015; Culvenor et al., 2015; Everhart et al., 2015; Kartus et al., 2001; Mather et al., 2013). In order to weigh-up the risks, costs and benefits, surgeons and patients may attempt to predict the likely impact that undergoing an ACLR may have on future QOL. To facilitate such judgements, information on longer-term QOL following ACL-rupture and identification of factors with potential to impact future QOL is of great value to both health-care professionals and ACL-ruptured individuals.

**What quality of life measures are available?**

Patient-reported outcome measures are commonly used to measure QOL before and after ACLR. These measures can be generic (non-disease specific), knee specific or ACL specific. Generic health-related QOL measures do not include knee-specific questions and have been used in a range of populations with population norms available for comparison (Brazier, Roberts, Tsuchiya, & Busschbach, 2004; Garratt, Schmidt, Mackintosh, & Fitzpatrick, 2002; Hawthorne & Osborne, 2005; Hawthorne, Osborne, Taylor, & Sansoni, 2007; Ware, 1993). Knee-related QOL measures contain items pertaining specifically to the knee, but may not be specific to an ACL-ruptured population (e.g. they may have been validated for use in ACL, knee osteoarthritis and meniscal pathology populations) (Roos, Roos, Lohmander, Ekdahl, & Beynnon, 1998). In comparison, an ACL-specific QOL measure contains questions pertaining to the ACL-ruptured knee, and was devised with the purpose of addressing issues of interest to an ACL-ruptured population (Mohtadi, 1998). Table 2.1 and 2.2 outline the most common patient-reported questionnaires used to measure QOL in ACL-reconstructed populations.
**Table 2.1** Commonly used patient-reported measures of knee-related QOL in ACL-ruptured populations

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Items/domains</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Knee-related quality of life</strong></td>
<td>Knee injury and Osteoarthritis Outcome Score (KOOS) QOL subscale (Roos et al., 1998)</td>
<td>Comprises four questions addressing knee awareness, knee-related lifestyle modifications, knee confidence, and knee-related difficulties.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Has been used extensively in ACL-ruptured populations and published data are available for comparison</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quick and easy to complete</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The Minimal Detectable Change in patients with knee injury is 21.1 points (Collins et al., 2011).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The only measure devised for the purpose of assessing QOL in an ACL-ruptured population</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Includes items most relevant and important to ACL-ruptured individuals compared with other knee-related measures (Tanner et al., 2007).</td>
</tr>
</tbody>
</table>
**Table 2.2** Commonly used patient-reported measures of health-related QOL in ACL-ruptured populations

<table>
<thead>
<tr>
<th>Health-related quality of life</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Form 36 (SF-36)</strong> (Ware, 1993)</td>
<td>Comprises 36 questions across 8 health domains: Bodily Pain; General Health; Mental Health; Physical Function; Role Emotional; Role Physical; Social Function; Vitality. Valid for use in ACL-ruptured individuals (Shapiro, Richmond, Rockett, McGrath, &amp; Donaldson, 1996) but may be subject to floor and ceiling effects in ACL populations (Busija, Osborne, Nilsdotter, Buchbinder, &amp; Roos, 2008). The SF-36 is useful for measuring group changes over time after ACLR (Dunn et al., 2015), however, SF-36 subscales have low sensitivity to individual change after orthopaedic surgery (Busija et al., 2008). Extensive population norms are available from multiple countries and specific populations, including athletic populations. Can calculate a physical and mental summary component score.</td>
</tr>
<tr>
<td><strong>Euro-QoL 5D (EQ-5D)</strong> (Williams, 1990)</td>
<td>Contains five questions addressing mobility, self-care, usual activities, pain/discomfort and anxiety/depression. May not measure items of relevance or importance to ACL groups, potential for ceiling effect due to two of five items addressing self-care and walking mobility, and no reference to high level activities. Produces a utility score, allowing economic evaluation (Williams, 1990). Features an additional question addressing perceived overall health status measured on a visual analogue scale.</td>
</tr>
<tr>
<td><strong>Assessment of Quality of Life (AQoL-8D)</strong> (Richardson &amp; Osborne, 1999)</td>
<td>The AQoL-8D includes eight dimensions (Independent Living, Happiness, Mental Health, Coping, Relationships, Self-worth, Pain, Senses). Age- and gender-based population norms, strong psychometric properties and content validity, and strong construct and discriminative validity in osteoarthritis populations (Hawthorne &amp; Osborne, 2005; Richardson, Iezzi, Khan, &amp; Maxwell, 2014; Richardson &amp; Osborne, 1999; Whitfield, Buchbinder, Segal, &amp; Osborne, 2006). Produces a utility score, allowing economic evaluation (Richardson &amp; Osborne, 1999).</td>
</tr>
</tbody>
</table>
What is known about quality of life following anterior cruciate ligament reconstruction?

Quality of life within five years of anterior cruciate ligament reconstruction

Quality of life is usually impaired in the acute injury and early postoperative periods, and this impairment may persist until pre-injury knee function is restored or until the patient reaches a state of satisfaction or acceptance with their knee abilities. Most ACLRs aim to restore pain-free knee function, swelling, or movement restrictions, allowing unrestricted participation in desired activities (Lynch et al., 2013). As described in the previous chapter, some individuals experience persistent knee difficulties or fear of re-injury that can impact on their ability to return to desired activities (Ardern et al., 2014b). Several studies have investigated the impact of specific factors on health-related and knee-related QOL within five years of ACLR.

Not returning to pre-injury sport after ACLR has been associated with worse knee-related QOL two years (McCullough et al., 2012) and one to seven years (Ardern et al., 2014a) after ACLR. The presence of a full thickness cartilage lesion at the time of ACLR has also been associated with lower Knee injury and Osteoarthritis Outcome Score (KOOS) QOL scores at two years (Røtterud et al., 2013) and two to five years following ACLR (Røtterud et al., 2012). Likewise, worse Short-Form 36 (SF-36) scores have been reported at two year follow-up in individuals who had concomitant chondromalacia of the lateral tibial plateau at the time of ACLR (Dunn et al., 2015). Undergoing a revision ACLR has also been related to worse knee-related and health-related QOL outcomes within five years of surgery compared to primary ACLR (Bjornsson et al., 2015; Dunn et al., 2015; Kievit et al., 2013; Lind et al., 2009, 2012). Other factors that have been related to poorer knee-related or health-related QOL following ACLR include a high fear of re-injury (Kvist et al., 2005) and poor performance on a single-leg triple-leg hop test (Reinke et al., 2011).
A range of demographic factors have also been related to worse health-related QOL outcomes within five years of ACLR, these include being a current or previous tobacco smoker (Dunn et al., 2015; Kvist, Kartus, Karlsson, & Forssblad, 2014) having an older age, an increased BMI or having had fewer years of education at the time of ACLR (Dunn et al., 2015). Reporting lower pre-operative knee-related and health-related QOL scores has been associated with reporting lower scores on the same measures postoperatively (Bryant, Stratford, Marx, Walter, & Guyatt, 2008; Dunn et al., 2015). Worse self-predicted future knee self-efficacy measured pre-operatively was also predictive of lower knee-related QOL one year following ACLR (Thomeé et al., 2008). Other pre-operative factors related to worse postoperative QOL outcomes include lower physical activity levels (Dunn et al., 2015; Månsson, Kartus, & Sernert, 2013) and reporting more anterior knee pain prior to ACLR (Heijne, Ång, & Werner, 2009).

Other studies found no influence of ACL autograft type (patellar tendon vs. quadruple-stranded vs. double-bundle hamstring tendon) on Quality of Life Outcome Measure (Questionnaire) for Chronic Anterior Cruciate Ligament Deficiency (ACL-QOL) scores at 2 years (Mohtadi, Chan, Barber, & Oddone Paolucci, 2014); KOOS-QOL or Euro-QoL 5D (EQ-5D) scores at 1 and 2 years (single vs. double bundle hamstring autografts) (Bjornsson et al., 2015); or SF-36 scores at 6, 12 and 24 months following ACLR (single vs. double-bundle) (Núñez et al., 2012; Ochiai et al., 2012). Similarly, differences in graft tension (low graft tension vs. high graft tension) did not impact knee-related or health-related QOL scores at three year follow-up (Fleming et al., 2013). The presence of a concomitant meniscal lesion or partial-thickness cartilage lesion was not associated with KOOS-QOL scores at 2 years in 3476 patients from the Norwegian and Swedish Registries (Røtterud et al., 2013). Moreover, receiving an early ACLR within four weeks of injury compared to an optional delayed ACLR after structured exercise, resulted in similar SF-36 and KOOS-QOL scores at two and five years following ACL rupture (Frobell et al., 2010; Frobell et al., 2013).
Quality of life more than five years after anterior cruciate ligament injury and reconstruction

Few studies have evaluated longer-term QOL following ACLR, in comparison to the large number of studies investigating QOL outcomes within two years of ACLR. There is also a scarcity of studies evaluating QOL outcomes more than five years following non-operative management of ACL rupture. Although some studies used the KOOS outcome measure, not all papers report the KOOS-QOL subscale score and even fewer explore associations between QOL and other variables more than five years following ACL injury. As a result, the impact of ACL injury and reconstruction on longer-term QOL is poorly understood. Considering the potential for osteoarthritis development and persistent knee pain and symptoms more than five years after ACL injury, further research investigating longer-term QOL after ACL injury is warranted. Investigation into longer-term QOL impairment following ACL injury and reconstruction may provide information to guide targeted interventions to improve QOL and satisfaction following ACL rupture. A systematic review of longer-term QOL after ACLR will be reported in Chapter 4, followed by a systematic review of longer-term QOL following non-operative management for ACL rupture in Chapter 5.
SUMMARY AND THESIS AIMS

The ramifications of sustaining an ACL rupture and undergoing subsequent reconstructive surgery can include persistent knee pain, swelling, instability, activity restrictions, knee-related fears, reduced knee confidence and the early onset of post-traumatic osteoarthritis (Ardern et al., 2014b; Lohmander et al., 2004; Øiestad et al., 2009). The primary treatment for ACL rupture offered to people who wish to return to sport is a surgical reconstruction of the ACL (Marx et al., 2003), with the majority of patients expecting to return to sport within one year of surgery (Feucht et al., 2014). Many individuals do not return to competitive sport after ACLR (Ardern et al., 2014b) despite most ACL ruptures occurring during competitive sport participation (Gianotti et al., 2009). This has further implications for the psychological wellbeing of individuals who place great importance on continuing sport participation. Of further importance is that ACL rupture commonly occurs in adolescents and young adults, placing these active individuals at risk of experiencing limitations in partaking in occupational, parental and recreational activities, with further potential to impact negatively upon QOL. Despite the large potential for QOL impairment in this population, the impact of living with ongoing knee difficulties more than five years after ACLR and factors related to poor QOL outcomes are poorly understood.

The aims of this thesis were to:

(i) evaluate longer-term QOL outcomes and identify factors that may affect QOL after ACLR by pooling results from previous studies;

(ii) evaluate longer-term QOL in ACL-deficient individuals and compare longer-term QOL outcomes in ACL-deficient and ACL-reconstructed groups using a systematic review and meta-analysis;
(iii) identify factors related to variability in longer-term QOL outcomes following ACLR in individuals with knee pain, symptoms or functional limitations;

(iv) explore personal perspectives on QOL following ACLR in individuals with knee pain, symptoms or functional limitations using qualitative methodologies;

(v) explore relationships between radiographic osteoarthritis, QOL, participant characteristics, and psychological factors in individuals with knee pain, symptoms or functional limitations more than five years after ACLR.
QUALITY OF LIFE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: A SYSTEMATIC REVIEW


INTRODUCTION

Anterior cruciate ligament rupture and subsequent reconstructive surgery can lead to ongoing knee symptoms with associated impairments, participation restrictions and related psychosocial implications (Ardern et al., 2012a; Kvist et al., 2005). Anterior cruciate ligament reconstruction is a common procedure in sports medicine, with estimated surgical rates of 52 per 100,000 inhabitants in Australia (Janssen et al., 2012), 30 per 100,000 in the United States (Csintalan, 2008) and 32 per 100,000 in Sweden (Granan et al., 2009). The overall aim of ACLR is to restore knee biomechanics, allow resumption of pre-injury activities, and optimise QOL. However, a recent systematic review involving 5770 patients found that only 44% of competitive athletes returned to their pre-injury level of sport at three years following ACLR (Ardern, Webster, Taylor, & Feller, 2011a). Psychological factors, such as fear of injury, can contribute to participation restrictions and have been associated with poor QOL outcomes two to four years following ACLR (Kvist et al., 2005; McCullough et al., 2012). Other factors, such as persistent pain (Lohmander et al., 2004) and post-traumatic osteoarthritis (Øiestad et al., 2009), may be inter-related and could impact on QOL after ACLR.
Of most concern is research showing that up to 13% of people with isolated ACL rupture and up to 48% with concomitant meniscal injury will develop knee osteoarthritis as early as ten years following ACLR, irrespective of surgical or conservative management (Øiestad et al., 2009). The personal impact of osteoarthritis following ACLR is heightened by the age of those undergoing this procedure, since the majority of ACL ruptures occur in adolescents and young adults (Granan et al., 2009; Renstrom et al., 2008). Younger adults with osteoarthritis can face a range of challenges not typically associated with an older osteoarthritis population, including work responsibilities, parental roles and competitive sports. Research has found that younger adults with osteoarthritis experience greater psychological distress then their older counterparts (Gignac et al., 2006). Additionally, teenagers who rupture their ACL are three times more likely to undergo a revision ACLR, and revision surgeries are associated with poorer QOL outcomes (Lind et al., 2012).

Health-related QOL fundamentally refers to the influence of a person’s health status on their perceived wellbeing and life quality. It is a multifaceted construct that encompasses physical, social, emotional and psychological components, and considers one’s goals, values and priorities in life (Edlund & Tancredi, 1985; Gill & Feinstein, 1994; Revicki, 1989). The impact of ACLR on health-related QOL could be exacerbated by limitations in participation in high-functioning activities such as competitive sports and through difficulty in meeting occupational demands. Patient-reported outcomes are commonly used to assess health-related QOL. The SF-36 is a generic health status measure designed for use in any population (Ware, 1993), while the KOOS-QOL subscale measures knee-related QOL (Roos et al., 1998). Both measures have been shown to be valid and reliable in ACL and osteoarthritis populations (Roos, Roos, & Lohmander, 1999; Shapiro et al., 1996; Ware, 1999). Despite the high prevalence of ACLR internationally and the potential longer-term implications for young, active populations, no systematic reviews have focussed on QOL following ACLR. The aims of this systematic review are: (i) to report QOL outcomes in people, on average, five years or more following ACLR; (ii) to compare QOL outcomes with available population norms; and (iii) to explore the relationship between QOL and participant factors (follow-up duration, sex, graft type).
METHODS

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2010).

Eligibility criteria

To be eligible for inclusion, studies were required to report generic health-related or knee-related QOL outcomes from arthroscopic hamstring or patellar tendon autograft ACLR at a minimum five year follow-up. Studies were excluded from the review if: (i) all ACLRs were performed with polyester ligament scaffold, synthetic ligament grafts or reinforced with LARS artificial ligament; (ii) all ACLRs were performed using an open surgical or robot-assisted operative technique; (iii) all surgeries involved primary repair of the ACL; (iv) all ACLR were revision surgeries; (v) all patients had meniscal or concomitant ligament repairs in addition to ACLR; or (vi) the paper was published in a language other than English.

Studies involving patients who underwent ACLR using an eligible autograft technique and patients whose surgeries utilised techniques mentioned in the exclusion criteria (allografts, open procedures, primary repair etc.) were eligible for inclusion in the review only if they reported (or the authors provided on request) separate QOL data for the eligible patients. Where papers utilised an outcome measure with a QOL component (such as the KOOS) but did not report data for the QOL subscale, these data were requested from the authors. If these data were not provided within four weeks, the paper was deemed to be ineligible for the purposes of this review. Where multiple publications reported outcomes at various time-points from the same study population, only the most recent publication was included in the review. A QOL instrument was defined as any patient-reported outcome measure (generic or knee specific) that primarily assesses QOL or features a QOL component or subscale.
Search strategy

A systematic search was undertaken in June 2012 to identify all relevant articles using the following five databases: Medline, CINAHL, Web of Knowledge, Scopus, and Sports Discus. The search strategy involved screening titles, abstracts and keywords for the terms “anterior cruciate ligament” or “ACL” AND “quality of life” or “QOL” or a range of relevant outcome measures such as the KOOS (see Appendix 4.1 for full search strategy). The search was performed independently by two of the authors (S.F, K.C). We reviewed all titles and abstracts and excluded clearly ineligible publications from further screening (Figure 4.1). Any disagreements regarding eligibility were resolved by an independent arbitrator (T.R). The full text versions of identified studies were reviewed for final eligibility screening. Reference lists of key papers were cross-checked to ensure all relevant studies were included in the final yield. Finally, the search was repeated in October 2012 prior to data analysis to ensure all eligible publications had been included.
Figure 4.1 Search strategy

n: sample size; QOL: quality of life

Quality appraisal

The methodological quality of the included studies was appraised using a 21-item checklist adapted from the Downs and Black criteria (Downs & Black, 1998). The Downs and Black tool has been identified as a useful tool for assessing both randomised and non-randomised studies (Deeks et al., 2003). Some items on the tool were deemed not applicable to the study aims and designs of papers included in this review. As the intervention was interpreted as ACLR surgery, items such as ‘blinding of participants to intervention’ and ‘compliance with intervention’ were excluded from the check-list (a total of six items were excluded – see

30
Appendix 4.2). Additionally, some items were slightly modified to capture all areas relevant to this review. The last item on the scale was modified to a dichotomous score of zero or one, where zero was allocated to studies with no sample-size calculation or reporting of insufficient power, and a score of one was given for sample-size calculations and sufficient power to detect a clinically significant difference in the primary outcome(s). All modifications and explanations for each item are listed in Appendix 4.2. Items scored one point for satisfaction of the criterion, and zero points for not satisfying the criterion or if it was unable to be determined. The maximum quality score was 21, with higher scores indicating greater methodological quality. The quality of all articles was evaluated by two independent assessors (S.F, E.M); where agreement was not achieved, an independent arbitrator (K.C) was utilised to reach consensus.

**Data management**

All data were extracted and collated by two independent reviewers (S.F, E.M), including patient demographics (for example age, gender and time from injury to surgery), surgical details (graft type, concomitant injuries), outcome measures and adverse events (re-rupture, additional injuries, subsequent surgeries, rates of osteoarthritis). Means and standard deviations (SDs) were extracted for each patient-reported outcome measure. Where only mean and p-values were reported, SDs and standard error values were estimated by using the mean difference between groups and converting p-values to t-scores (The Cochrane Collaboration, 2009). Where QOL data were reported in graph form only, mean values were estimated from the graph (Table 4.1) when such data could be clearly ascertained (e.g. full scale visible). Additionally, if a study characteristic was reported for two separate eligible subgroups (e.g. age at follow-up reported separately for males and females) the subgroups were combined using a formula from The Cochrane Handbook for Systematic Reviews of Interventions (The Cochrane Collaboration, 2009) to obtain mean and SD estimates for the combined cohort. If sufficient data were not reported, the corresponding author was contacted to request further data.
Statistical analysis

The mean difference and associated 95% CI were calculated for KOOS-QOL data. Using a random effects model meta-analysis, studies were weighted according to variance within and between studies. The random effects model accounts for heterogeneity in covariates between studies which may influence QOL. Combining SF-36 data for meta-analysis was deemed inappropriate due to the small number of studies reporting this outcome. To provide context for interpreting QOL outcomes following ACLR, QOL scores were compared with previously published population norms from similar age groups where possible. Two-tailed Spearman’s rank correlation coefficient (rho) was used to explore correlations between potential predictive variables (graft choice (% patella tendon), gender (% female), follow-up duration) and QOL outcomes. Additionally, this test was used to identify relationships between outcome measure subscales.

RESULTS

Search strategy

The systematic search strategy initially yielded 552 studies. Following the removal of 180 duplicate papers and the exclusion of 319 ineligible studies, the full text of 53 papers were obtained and reviewed (Figure 4.1). Of these, 37 papers did not meet the inclusion criteria. Due to heterogeneity in data reporting methods or insufficient descriptions of surgical techniques, additional data or surgical details from 11 authors (for 13 studies) were requested. Of these, seven authors (for eight studies) replied, and provided data for six studies (Barenius et al., 2010; Gifstad et al., 2012b; Mascarenhas et al., 2010; Mascarenhas, Tranovich, Kropf, Fu, & Harner, 2011; Neuman et al., 2008; Sajovic, Strahovnik, Dernovsek, & Skaza, 2011). Six studies were subsequently excluded due to not providing details or data necessary for inclusion, or confirming ineligibility by correspondence. This resulted in the quality appraisal of 16 papers.
Methodological appraisal

Quality appraisal scores ranged from 4 to 18. Two studies did not satisfy more than 10 of the criteria and were therefore excluded from the review (Arbes, Resinger, Vécsei, & Nau, 2007; Faber et al., 1999). The mean modified Downs and Black score for included studies was 14 (SD 2). When evaluated according to study design, prospective studies achieved a higher mean quality score (16 versus 13 for retrospective studies). The quality appraisal scores for each of the included studies are presented in Table 4.1.

Study characteristics

The 14 studies included reported QOL outcomes for a total of 2493 participants at a mean 9 (range 5-16) years following ACLR. The mean age of all participants at follow-up was 34 (range 18-42) years. The most commonly used QOL measure was the KOOS-QOL subscale, which was used in nine studies. The only generic (non-disease-specific) health-related QOL measures used were the SF-36 version one (used in five studies) and the SF-36 version two (used in one study). An ACL-specific knee-related QOL measure, the ACL-QOL (Mohtadi, 1998), was used in one study (Table 4.1). Aside from QOL, other commonly utilised outcome measures included the Tegner activity score (Tegner, Lysholm, Lysholm, & Gillquist, 1986) (used in 10 studies), the Lysholm knee scoring scale (Lysholm & Gillquist, 1982) (seven studies), the KT-1000 arthrometer (Daniel, Stone, Sachs, & Malcom, 1985) for assessing anterior/posterior tibio-femoral displacement (eight studies) and the Kellgren and Lawrence tool (Kellgren & Lawrence, 1957) for classifying radiographic osteoarthritis (six studies).

Knee injury and Osteoarthritis Outcome Scores

Mean KOOS-QOL scores were available from nine studies (Ahlden et al., 2012; Barenius et al., 2010; Gerhard et al., 2012; Gifstad et al., 2012b; Hoffelner et al., 2012; Möller, Weidenhielm, & Werner, 2009; Neuman et al., 2008; Øiestad, Holm, Engebretsen, & Risberg, 2011; Swirtun & Renström, 2008) and ranged from 63 to 83 out of a possible 100 (Figure 4.2).
Analysis of the relationship between KOOS-QOL and other KOOS subscales revealed a strong, positive correlation between the KOOS-QOL and KOOS-Pain subscales (rho = 0.85, p = 0.003), and the KOOS function in Sport/Recreation (Sport/Rec) subscales (rho = 0.70, p = 0.04). In comparison, there appeared to be a moderate correlation with KOOS Activity of Daily Living (ADL) subscales (rho = 0.66, p = 0.05) and little relationship with the KOOS-Symptoms scores (rho = 0.08, p = 0.70). Follow-up duration (p = 0.19) was not significantly associated with KOOS-QOL scores. Random effects meta-analysis resulted in a pooled KOOS-QOL summary effect of 74.5 (95% CI: 68.3 to 80.7). Comparison of pooled KOOS-QOL values with previously published population norms showed that ACLR populations reported poorer KOOS-QOL compared with healthy population norms with no knee symptoms (mean 90; 95% CI: 83.7 to 96.3) (Roos et al., 1998) and with general population norms (mean 82.4; 95% CI: 79.9 to 84.9) (Paradowski, Bergman, Sundén-Lundius, Lohmander, & Roos, 2006) (Figure 4.3).
Table 4.1 Study characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality</th>
<th>N</th>
<th>N eligible</th>
<th>Follow-up (years)</th>
<th>HT (%)</th>
<th>PT (%)</th>
<th>Age at follow-up (years)</th>
<th>Sex</th>
<th>Time from injury to surgery (months)</th>
<th>RCT</th>
<th>Pro / Ret</th>
<th>QOL measure(s)</th>
</tr>
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<tbody>
<tr>
<td>Ahlden 2012</td>
<td>16</td>
<td>10473</td>
<td>1452</td>
<td>5.4</td>
<td>82</td>
<td>18</td>
<td>NR</td>
<td>NR</td>
<td>24</td>
<td>no</td>
<td>Pro</td>
<td>KOOS</td>
</tr>
<tr>
<td>Barenius 2010</td>
<td>17</td>
<td>153</td>
<td>153</td>
<td>8.4 ± 0.98</td>
<td>49</td>
<td>51</td>
<td>34.0 ± 15.0</td>
<td>42</td>
<td>16.0 ± 24.2</td>
<td>yes</td>
<td>Pro</td>
<td>KOOS, SF36</td>
</tr>
<tr>
<td>Ferrari 2001</td>
<td>12</td>
<td>200</td>
<td>137</td>
<td>5.0 ± 25.4</td>
<td>0</td>
<td>100</td>
<td>35.25</td>
<td>0</td>
<td>1.3 ± 1.8</td>
<td>no</td>
<td>Ret</td>
<td>SF36</td>
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<tr>
<td>Gerhard 2012</td>
<td>12</td>
<td>63</td>
<td>63</td>
<td>16 ± 1</td>
<td>0</td>
<td>100</td>
<td>43</td>
<td>14</td>
<td>11 ± 23</td>
<td>no</td>
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<td>Gifstad 2012</td>
<td>13</td>
<td>93</td>
<td>93</td>
<td>7 (5.3-7.8)</td>
<td>49</td>
<td>51</td>
<td>34</td>
<td>37</td>
<td>NR</td>
<td>yes</td>
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</tr>
<tr>
<td>Hoffelner 2012</td>
<td>13</td>
<td>28</td>
<td>28</td>
<td>10</td>
<td>0</td>
<td>100</td>
<td>32.2 ± 6.4</td>
<td>25</td>
<td>5 ± 6</td>
<td>no</td>
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<tr>
<td>Mascarenhas 2011</td>
<td>12</td>
<td>38</td>
<td>19</td>
<td>9.1 ± 2.7</td>
<td>0</td>
<td>100</td>
<td>27.9 ± 8.1</td>
<td>37</td>
<td>NR</td>
<td>no</td>
<td>Ret</td>
<td>SF36</td>
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<tr>
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<td>12</td>
<td>46</td>
<td>23</td>
<td>5 ± 2</td>
<td>0</td>
<td>100</td>
<td>18 ± 3</td>
<td>57</td>
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<td>no</td>
<td>Ret</td>
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<td>18</td>
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<td>56</td>
<td>11.5 (11-12)</td>
<td>49</td>
<td>51</td>
<td>39</td>
<td>52</td>
<td>6 (2-240)</td>
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<td>Pro</td>
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<td>12.8 ± 3.5</td>
<td>0</td>
<td>100</td>
<td>NR</td>
<td>36</td>
<td>48</td>
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<td>13</td>
<td>151</td>
<td>151</td>
<td>5</td>
<td>0</td>
<td>100</td>
<td>27.6 F, 32.5 M</td>
<td>51</td>
<td>1.3 E, 37.3 L (0.2-209)</td>
<td>no</td>
<td>Ret</td>
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<td>Øiestad 2011</td>
<td>16</td>
<td>210</td>
<td>210</td>
<td>13.7 ± 4.4</td>
<td>14</td>
<td>86</td>
<td>39.1 ± 8.7</td>
<td>43</td>
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<td>16</td>
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<td>64</td>
<td>11</td>
<td>50</td>
<td>50</td>
<td>36 HT, 38 PT</td>
<td>42</td>
<td>25 HT, 23 PT (1-84)</td>
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<td>Pro</td>
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<tr>
<td>Swirtun 2008</td>
<td>13</td>
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<td>5.6 ± 0.52</td>
<td>32</td>
<td>68</td>
<td>32 ± 8.1</td>
<td>48</td>
<td>9</td>
<td>no</td>
<td>Pro</td>
<td>KOOS</td>
</tr>
</tbody>
</table>

aN number of participants for which data is reported (excluding all non-eligible participants) | b data from group of participants with less than 5 year follow-up were excluded | c data was provided through personal correspondence with author | d data from group of participants who did not undergo autograft ACLR were excluded | e age at follow-up calculated from age at surgery and time to follow-up data | f data extracted from graph | g did not report data for each SF-36 domain | N: sample size | HT: hamstring tendon autograft | PT: patella tendon autograft | RCT: randomised controlled trial | Pro: prospective | Ret: retrospective | KOOS: Knee injury and Osteoarthritis Outcome Score | SF36: Short-Form 36 (version 1) | SF36 v2: Short-Form 36 (version 2) | QOL: quality of life | NR: not reported | F: females | M: males | E: early ACLR group | L: late ACLR group | all data is mean ± SD or median (range)
Figure 4.2 KOOS values for individual studies

All values are mean ± standard deviation; lower score indicates poorer outcomes in all domains.
Figure 4.3 Forest plot of random-effects meta-analysis of KOOS-QOL mean, standard error (box) and 95% CI (whiskers) data from individual studies in addition to pooled summary mean and 95% CI

Population normative values are reported vertically; a: normative data extracted from Paradowski et al (2006), n = 291, age 18-54 years, mean (solid line “a”) 95% CI (dashed lines); b: normative data extracted from Roos et al (1998), n = 25, age 37-50 years, mean (solid line “b”) 95% CI (dotted lines); lower score indicates poorer outcomes.
Short-Form 36 (SF-36) scores

The SF-36 measure comprises eight individual health-related domains. For the SF-36 version one, the Role Emotional (RE) domain demonstrated the greatest variation, with mean scores ranging from 85 to 100 (Figure 4.4). In contrast, mean scores for the Social Functioning (SF) domain were fairly consistent across all studies. All ACLR studies reported higher mean SF-36 values in six domains than previously published population norms (n=2323) (Loge, Foss Abrahamsen, Ekeberg, & Kaasa, 1999), indicating better health-related QOL (Figure 4.4).

![Figure 4.4 SF-36 version one results for individual studies and normative population](image)

All values are mean ± standard deviation; lower SF-36 score indicates poorer outcome in all domains; PF: Physical Function, RP: Role Physical, BP: Bodily Pain, GH: General Health, V: Vitality, SF: Social Function, RE: Role Emotional, MH: Mental Health; a Normative data from Norwegian population n = 2323, age 44.9 ± 16.5 (Loge et al., 1999); Results from Sajovic et
al (2011) are not featured in this graph as SF-36 version 2 was used in this study and standardised scores are not directly comparable.

**ACL-QOL scores**

The ACL-QOL outcome measure was used to measure knee-related QOL in only one study (Ott, Ireland, Ballantyne, Willson, & McClay Davis, 2003). As the primary aim of this study was to compare outcomes between men and women following ACLR, separate ACL-QOL mean values were reported according to sex. No significant differences were found in ACL-QOL scores (mean for men 80.2; mean for women 76.3) at mean five year follow-up. Population norms for this instrument were not available for comparison.

**Factors potentially influencing quality of life after anterior cruciate ligament reconstruction**

**Sex and age**

The effect of sex on QOL outcomes after ACLR was investigated in five studies (Ferrari, Bach, Bush-Joseph, Wang, & Bojchuk, 2001; Möller et al., 2009; Øiestad et al., 2011; Ott et al., 2003; Swirtun & Renström, 2008). The majority of these studies found no significant differences in respect of sex for SF-36, KOOS-QOL or ACL-QOL outcomes (Möller et al., 2009; Øiestad et al., 2011; Ott et al., 2003; Swirtun & Renström, 2008). There was a non-significant trend observed towards studies with a higher portion of women reporting lower KOOS-QOL (rho = -0.63, p = 0.07) scores and no significant correlations between sex and SF-36 scores (p > 0.10 for all domains).
The relationship between age at ACL surgery and QOL was investigated in four studies (Hoffelner et al., 2012; Möller et al., 2009; Ott et al., 2003; Swirtun & Renström, 2008). Participant age did not influence QOL outcomes measured with the KOOS (Hoffelner et al., 2012; Möller et al., 2009; Swirtun & Renström, 2008) or SF-36 (Möller et al., 2009). Ott et al (2003) categorised participants by age and sex, and found the greatest discrepancy in ACL-QOL values in 12 to 18 year old women, who scored 15 points lower than their male counterparts (93 versus 78). Ahlden et al (2012) reported a significantly higher rate of revision surgeries (12%) in a similar aged female subgroup (15 to 18 years) compared with all patients (4%, p < 0.001) and age matched males (5%, p = 0.02).

Revision anterior cruciate ligament reconstruction

The reported rates of ACL re-rupture ranged from 1% (Ott et al., 2003) to 9% (Sajovic et al., 2011). Only two studies analysed QOL outcomes in those who underwent revision ACLR, and these studies found significantly poorer QOL outcomes post-revision surgery, compared with primary ACLR (Ahlden et al., 2012; Möller et al., 2009). Notably, a large Swedish ACL register study found participants who underwent revision ACLR (n = 194) scored worse in all KOOS subscales at five year follow-up (p < 0.001) compared with those who underwent primary reconstructions (n = 1258). It should also be noted that the studies that reported the highest KOOS-QOL scores excluded patients who had revision surgeries, concomitant injuries at baseline or subsequent injuries or complications (Gifstad et al., 2012b; Hoffelner et al., 2012). Likewise, one of two studies which excluded revision surgeries from their cohorts scored highest in each of the SF-36 domains, indicating a higher health-related QOL (Mascarenhas et al., 2010; Mascarenhas et al., 2011).
Meniscal or cartilage injury

The impact of sustaining concomitant meniscal or cartilage injury prior to ACLR on QOL outcomes at follow-up was investigated in five studies (Ahlden et al., 2012; Barenius et al., 2010; Gerhard et al., 2012; Möller et al., 2009; Swirtun & Renström, 2008). Meniscal injury (treated surgically at the time of ACLR) was associated with lower KOOS-QOL and SF-36 scores at greater than 10 years follow-up (Gerhard et al., 2012; Möller et al., 2009). In contrast, studies with follow-up periods of five, six and eight years found no significant differences in KOOS-QOL (Ahlden et al., 2012; Barenius et al., 2010; Swirtun & Renström, 2008) or SF-36 scores (Barenius et al., 2010) in those with and those without associated intra-articular injuries. However, these studies found significantly worse KOOS-QOL scores in those who underwent concomitant medial meniscus surgery (p = 0.035) (Barenius et al., 2010) or sustained subsequent trauma following ACLR (p = 0.002) (Swirtun & Renström, 2008) at eight and six year follow-up.

Time from injury to surgery

Time from injury to surgery was reported in 11 of the 14 studies reviewed, with mean times ranging from five months to two years (Table 4.1). Of these, three studies further investigated the relationship between time from injury to surgery and QOL outcomes. Two studies found no correlation between time from injury to surgery and KOOS and SF-36 scores (Øiestad et al., 2011) or ACL-QOL outcomes (Sajovic et al., 2011). In contrast, Barenius et al. (2010) found that participants who waited less than five months to have surgery had significantly better SF-36 scores in three subscales (PF: p = 0.014, BP: p = 0.013, SF: p = 0.037) and better KOOS-QOL scores (p = 0.059) at eight year follow-up, which may have been related to the fewer meniscal injuries (37% versus 62%, p = 0.008) at the time of ACLR.
**Graft type**

Four studies investigated differences in QOL outcomes between a bone-patellar-tendon-bone (BPTB) autograft and a double or single looped hamstring autograft (Barenius et al., 2010; Gifstad et al., 2012b; Mascarenhas et al., 2011; Sajovic et al., 2011). All of these studies found no significant differences in KOOS or SF-36 scores between groups at five, seven, eight, and eleven year follow-ups. Similarly, there were no significant correlations between graft type and KOOS-QOL (p = 0.33) or SF-36 (p > 0.44 for all domains) outcomes.

**Radiographic osteoarthritis**

Despite eight studies reporting the prevalence of radiographic osteoarthritis following ACLR, only two studies compared QOL in those with and those without osteoarthritis (Neuman et al., 2008; Øiestad et al., 2011). Øiestad et al. (2011) found that the presence of ‘any’ osteoarthritis (≥ grade 2) was not associated with KOOS-QOL scores, however those with ‘severe’ osteoarthritis (grade 4) reported significantly poorer KOOS-QOL subscale scores (p = 0.002). Neuman et al. (2008) reported a trend towards lower scores in all subscales of the KOOS in patients with radiographic osteoarthritis compared with those without osteoarthritis.

**DISCUSSION**

This systematic review presents a clear overview of longer-term QOL after ACLR and has shown that these outcomes were associated with several factors. First, the choice of patient-reported outcome measure used to assess QOL can impact on the interpretation of results. Studies that used the knee-specific KOOS reported poorer knee-related QOL, compared with published population norms (Ilich et al., 2012; Roos et al., 1999). In contrast, studies utilising the generic SF-36 questionnaire commonly reported similar or higher health-related QOL...
scores than age-equivalent population norms (Hopman et al., 2000; Loge et al., 1999). Second, various factors that may be associated with poorer QOL following ACLR were identified including concomitant or subsequent meniscal injury, revision ACLR surgery, and the presence of severe radiographic osteoarthritis. Participant sex, graft type, age at surgery and time from injury to surgery were not significantly associated with QOL outcomes.

Overall, studies that used a generic health status measure, the SF-36, reported similar or better health-related QOL outcomes, compared to previously published population norms (Hopman et al., 2009; Hopman et al., 2000; Loge et al., 1999; Ware, 2000). Visual comparison of SF-36 means between studies and population normative data (Loge et al., 1999), revealed a similar pattern of scores across all domains (Figure 4.4). The SF-36 is a generic measure of health-related QOL and features 36 items over 8 defined domains covering physical, mental and social health. Unlike the KOOS, the SF-36 addresses topics such as tiredness, sadness and nervousness, which are relevant to many patient populations. Considering the majority of ACL injuries occur in a young sporting population (Renstrom et al., 2008), it is possible that this patient group scored more highly than aged-matched less active counterparts. This may explain the similarities between SF-36 values for all ACLR studies and SF-36 values obtained from a healthy population of American college athletes aged 17 to 23 years (n = 696) (Huffman et al., 2008). These college athletes scored significantly better in all SF-36 domains (p < 0.01) except for Bodily Pain (p = 0.05) than an age-matched sample of the general population. Also, it is important to note that SF-36 normative data used for comparison in this review included older adults up to 80 years old, which may also partly explain the differences in health-related QOL scores among these studies.

Pooled results from studies using the knee-specific KOOS indicate significantly poorer KOOS-QOL compared with a healthy population with no history of ACL or meniscal injury, and no radiographic osteoarthritis. Comparison between pooled KOOS-QOL results and general population norms showed a statistically insignificant difference, however this difference may be of clinical importance due to the small degree of overlap in 95% CI between ACLR and
population norms (mean 75; 95% CI: 68.3 to 80.7 versus mean 82; 95% CI: 79.9 to 84.9) (Paradowski et al., 2006). This result could reflect the nature of the questionnaire, which is intended to assess knee injuries with the potential of causing post-traumatic osteoarthritis (Roos et al., 1998). The knee-related QOL subscale of the KOOS comprises four questions, which address knee awareness, knee-related lifestyle modification, lack of knee confidence and knee-related difficulties. It is therefore not surprising that medium to long term follow-up of ACLR patients revealed poorer KOOS-QOL than for controls without knee symptoms (Roos et al., 1999). None of the reviewed studies specifically reported KOOS-QOL in a subgroup of participants who were clinically symptomatic or had knee difficulties. Considering the positive relationship observed between KOOS-Pain and KOOS-QOL subscale scores, this may underestimate impairment in knee-related QOL.

The relationship between baseline meniscal injury and QOL may be at least partly mitigated by follow up duration. The two studies in this review that reported significantly poorer QOL outcomes in those with surgically treated meniscal injuries had follow-up durations of 11.5 years (Möller et al., 2009) and 16 years (Gerhard et al., 2012) following ACLR. In comparison, studies reporting no significant influence of concomitant intra-articular injuries on QOL outcome did so at five (Ahlden et al., 2012), six (Swirtun & Renström, 2008) and eight year (Barenius et al., 2010) follow-ups. These data suggest that the negative consequences of concomitant meniscal injury may develop over time, becoming most apparent after 10 years. This is in line with a systematic review that reported low osteoarthritis prevalence following isolated ACL injuries (0-13%) and higher prevalence of osteoarthritis in those with additional meniscal injuries (21-48%) at a minimum 10 years following ACL injury (Øiestad et al., 2009). Concomitant articular injury may also contribute to poor QOL outcomes following ACLR revision (Ahlden et al., 2012; Möller et al., 2009). A literature review on revision ACLR identified a trend for higher rates of chondral and meniscal injuries in those having revision surgeries (Kamath, 2011). Similarly, a single study reported significantly poorer KOOS-QOL in those who sustained subsequent knee trauma (Swirtun & Renström, 2008), which may be related to the acceleration of osteoarthritis progression (Chu, Williams, Coyle, & Bowers,
The temporal relationship between meniscal and other concomitant injury, osteoarthritis development and QOL after ACLR is not well understood and requires further investigation.

Although this review is the first to evaluate QOL after ACLR, there are several limitations of this research. Due to the small number of studies reporting SF-36 and ACL-QOL outcomes, meta-analysis and estimation of effect sizes were not appropriate for these measures. Although all studies reported QOL outcomes, on average, 5 to 20 years following ACLR, we acknowledge that some studies included participants who had an ACLR within the past five years. It is also important to acknowledge that due to the long follow-up period, impaired QOL may also be related to other factors aside from past ACL injury and reconstruction. Additionally, the relationship between follow-up duration and QOL may have been impacted by the wide range of follow-up times reported in some studies. The correlation analyses between KOOS subscales were limited to published mean group values rather than individual participant data. When comparing values to population reference groups, we chose reference groups of a similar age and from a similar geographical location where possible. However, since the demographic characteristics of participants varied between studies the chosen reference groups may have been less appropriate for some studies. As the majority of studies did not evaluate QOL outcomes as their primary aim, data were often reported separately for subgroups and only a small number of studies investigated the impact of specific demographic and surgical factors on QOL outcomes. This limited the ability to draw strong conclusions regarding factors which may predict poor QOL outcomes and highlights the need for further research in these areas.
CONCLUSION

This systematic review has shown that knee-related QOL is impaired at a minimum of five years after ACLR, compared to population norms for those without knee pain or injury. Impairment in knee-related QOL was less apparent when compared to normative data for the general population. In contrast, studies using the generic SF-36 measure reported health-related QOL outcomes that were similar to or better than population norms. Revision surgery, subsequent injuries following ACLR and the presence of severe radiographic osteoarthritis were associated with poorer QOL at a minimum five years following ACLR. Meniscal injuries had a negative impact on QOL 10 years or more following ACLR; however, graft type, sex, age at surgery and time from injury to surgery were not associated with QOL outcomes. A caveat to these findings is that only a limited number of studies investigated these factors, although the evidence to support these relationships was consistent. No research into the influence of psychological factors on longer-term QOL was identified and this would be a valuable direction for future research.
QUALITY OF LIFE AFTER NON-OPERATIVE MANAGEMENT OF ANTERIOR CRUCIATE LIGAMENT RUPTURE: A SYSTEMATIC REVIEW & META-ANALYSIS


INTRODUCTION

Over 127,000 ACL reconstructive surgeries are performed annually in the United States (Kim, Bosque, Meehan, Jamali, & Marder, 2011), most commonly in active adolescents and young adults. Rationales for performing an ACLR include facilitating a return to competitive sport (Marx et al., 2003; McRae, Chahal, Leiter, Marx, & MacDonald, 2011) and minimising the risk of post-traumatic knee osteoarthritis (Richmond et al., 2011). However, many ACL-reconstructed individuals cease sports participation (Ardern et al., 2014b), develop accelerated knee osteoarthritis (Øiestad et al., 2009), or experience ongoing fear of re-injury (Ardern et al., 2012a) and poor knee-related QOL (Chapter 4). This highlights the need to explore longer-
term outcomes following non-operative management of ACL rupture. Rehabilitation alone may be a successful alternative to ACLR for many individuals (Ericsson, Roos, & Frobell, 2013; Frobell et al., 2013).

A recent meta-analysis found that the rate of return to non-elite competitive sport following ACLR was surprisingly low (42%) (Ardern et al., 2014b). Emerging evidence suggests that this rate is no higher than that achieved by individuals managed with rehabilitation alone (Frobell et al., 2013; Grindem et al., 2012; Smith et al., 2014). Several systematic reviews have also revealed either no significant difference in radiographic osteoarthritis rates between groups of ACL-reconstructed and non-operatively managed individuals (Chalmers et al., 2014), or a slightly higher prevalence of osteoarthritis following ACLR (Harris et al., 2015b; Luc et al., 2014; Smith et al., 2014). The low return to sport rates and presence of osteoarthritis following ACLR may contribute to the impaired knee-related QOL identified in this population (compared to general population norms) 5 to 20 years after ACL rupture (Chapter 4). However, little is known about the long-term QOL of individuals following non-operative management of an ACL rupture, and how this compares with the QOL of individuals who undergo ACLR.

This systematic review is the first to investigate QOL in ACL-deficient individuals, enabling QOL comparisons between management approaches. Undergoing knee surgery may expose an individual to additional physical and psychological trauma, which could facilitate fear-avoidance behaviours (Leeuw et al., 2007), impact future participation in desired activities (Ardern et al., 2014b) and impair QOL. On the other hand, individuals who choose not to undergo surgery for ACL rupture may be more likely to experience limitations due to increased passive knee laxity (Grindem et al., 2012; Smith et al., 2014). Considering the increasing frequency of ACLR procedures (Csintalan, 2008; Lyman et al., 2009), reported knee-related QOL impairments more than five years after surgery (Chapter 4), and the ongoing debate regarding the optimal management of an ACL-ruptured knee, investigation into long-term QOL in ACL-deficient individuals is warranted.
Specific factors (revision surgery, concomitant meniscus surgery, subsequent injury, and severe osteoarthritis) have been associated with poor longer-term QOL in individuals who choose to undergo ACLR (Chapter 4). However, it is not known whether such factors are associated with QOL outcomes in individuals who remain ACL-deficient. Exploring potential predictors of low QOL in ACL-deficient people may assist clinical decision making by helping to identify patient subgroups most likely to benefit from non-operative management. This will also facilitate the development of evidence based treatment guidelines and recommendations.

The primary aim of this study was to report QOL outcomes in ACL-deficient individuals, 5 to 25 years following ACL rupture. The secondary aims were to: i) compare QOL in ACL-deficient individuals with published population norms; ii) compare QOL in ACL-deficient and ACL-reconstructed populations; and iii) investigate relationships between relevant participant characteristics and QOL outcomes in ACL-deficient individuals.

METHODS

This systematic review used the PRISMA guidelines for conducting and reporting systematic reviews (Moher et al., 2010) and the protocol for this review was prospectively registered on PROSPERO (CRD42014007499, 21/02/2014).

Search strategy

A search was performed on seven electronic databases in January 2014 to retrieve all relevant articles: Scopus, MEDLINE, Web of Knowledge (Web of Science), The Cochrane Library,
PubMed, CINAHL and SPORTDiscus. The search strategy retrieved articles that contained the term 'anterio\text{r cruciate ligament}' or the abbreviation 'ACL' in the title or abstract, as well as at least one key word relevant to QOL outcomes (see appendix 5.1 for full search strategy). This search was undertaken independently by two of the authors (S.F, A.C) who screened titles and abstracts for eligibility, and reviewed the references of relevant articles for any additional publications. If eligibility could not be ascertained from the abstract, the full text was retrieved. Any contrasting opinions in determining eligibility were resolved by an independent researcher (K.C). The searches were repeated in June 2014 to identify any further publications of relevance.

**Selection criteria**

Articles were considered eligible for inclusion in the review if they met the following criteria:

(i) study participants completed a health-related QOL or knee-related QOL outcome measure on average 5 to 25 years following ACL rupture;

(ii) all participants or a subgroup of participants had not received an ACLR, repair or augmentation at the time of follow-up; and

(iii) participants had a mean age between 18 and 55 years at the time of follow-up.

Articles including participants with partial ACL rupture, and articles published in languages other than English were excluded. Articles including both ACL-deficient and ACL-reconstructed participants were included only if they reported separate knee-related QOL or health-related QOL outcomes for non-operative participants, or if the authors provided these data on request. We did not exclude studies that reported data from participants who sustained a concomitant or subsequent meniscal or collateral ligament injury; were aged less than 18 years at the time of ACL injury; or had radiographic or clinical signs of osteoarthritis, as these were identified as variables with a potential to impact upon QOL. If multiple publications
featuring data from the same study cohort were retrieved, the article reporting outcomes of interest for the greatest number of eligible participants was included in the review.

**Methodological appraisal**

A modified version of the Downs and Black’s Checklist for the Assessment of Methodological Quality of Randomised and Non-Randomised Studies (Downs & Black, 1998) was used to appraise the quality of eligible articles. This tool is appropriate for methodological appraisal of a variety of study designs; however, some items were not applicable to the aims of this review and were consequently excluded or modified. In total, six items were excluded and additional items were modified or clarified, which resulted in modified Downs and Black criteria as described previously (Chapter 4). The methodological score ranged from 0 (lowest methodological quality) to 21 (highest quality), where randomised and prospective studies score more highly than retrospective or case studies. As studies of low methodological quality may be subject to greater bias (Van Tulder, Suttorp, Morton, Bouter, & Shekelle, 2009), articles achieving less than 50% of the total possible methodological appraisal score were excluded from the review.

**Patient-reported outcomes**

Self-administered questionnaires are commonly used to assess knee-related QOL and overall health-related QOL. Knee-related QOL refers to the impact of one’s knee status on their wellbeing and life satisfaction, and is commonly assessed in ACL-ruptured populations using questionnaires containing a knee-specific QOL subscale, such as the KOOS (Roos et al., 1998). The KOOS contains a subscale addressing QOL, in addition to Pain, Symptoms, ADL, and Sport/Rec subscales. Knee-related QOL can also be assessed using an ACL-specific questionnaire devised with the primary purpose of assessing QOL in an ACL-ruptured population, the only measure developed to date with this intention is the ACL-QOL (Mohtadi,
The ACL-QOL contains 31 items, across 5 subscales (Symptoms and Physical Complaints, Work-Related Concerns, Sports/Recreation, Lifestyle, Social and Emotional).

Health-related QOL refers to the influence of one’s health status on their wellbeing and life satisfaction and has been described as the discordance between an individual’s expectations of health and their current health experience (Carr et al., 2001). Health-related QOL can be assessed with non-disease-specific patient-reported outcomes, such as the SF-36 (Ware, 1993) which is commonly used in studies of ACL-ruptured individuals (Chapter 4) and assesses the influence of an individual’s health status on their overall life quality. The SF-36 is comprised of eight domains (Bodily Pain (BP); General Health (GH); Mental Health (MH); Physical Function (PF); Role Emotional (RE); Role Physical (RP); Social Function (SF); and Vitality (V)). All three measures (SF-36, KOOS, ACL-QOL) are valid for use in ACL-ruptured individuals (Collins et al., 2011; Mohtadi, 1998; Shapiro et al., 1996) and are measured on 0 to 100 scales, where 0 represents the poorest possible outcome, and 100 represents the best possible score. Separate scores can be calculated for individual domains or subscales, in addition to an overall score for each measure.

**Data extraction**

Study characteristics and participant demographics were extracted independently by two of the authors (S.F, A.C). These data were cross-checked and any discrepancies resolved through discussion. Data extracted included knee-related QOL and health-related QOL scores, participant characteristics (age, BMI, sex, time since ACL injury, proportion undergoing a delayed ACLR), as well as factors that could potentially influence QOL outcomes (concomitant and subsequent injuries, prevalence of tibiofemoral and patellofemoral osteoarthritis, activity levels and return to sport data).
Statistical analysis

Primary outcomes included all knee-related QOL and health-related QOL scores. The 2-tailed Spearman rank correlation coefficient (rho) was used to explore potential relationships between knee-related QOL scores, participant demographics and study characteristics (follow-up duration, sex (% female), quality appraisal score, mean age), as well as relationships between subscales of the primary knee-related outcome measure. Random-effects meta-analysis was used to produce forest plots for primary outcomes displaying mean differences and 95% CIs between ACL-deficient and ACL-reconstructed subgroups from individual studies, and pooled mean differences (95% CIs) for combined studies. Where only domain scores were presented for a given outcome measure, component scores were calculated using reported mean values from each domain. Where only 95% CIs were reported for a primary outcome, SDs were estimated using the square root of the sample size and corresponding t scores (The Cochrane Collaboration, 2009). If population norms were reported separately for males and females (Cameron et al., 2013; Paradowski et al., 2006), or for two separate age groups within a more appropriate age range (Tengman et al., 2014), the two groups were combined using a formula from The Cochrane Handbook for Systematic Reviews of Interventions (The Cochrane Collaboration, 2009) to obtain mean and SD estimates for the combined groups.

RESULTS

Literature search

The systematic search yielded a total of 1172 studies. After removal of 549 duplicate articles, a further 555 papers were excluded through screening of titles and abstracts, resulting in the full text retrieval of 68 studies. Of these, 56 papers did not meet the eligibility criteria and were excluded (Figure 5.1). Additional data from the authors of six papers with insufficient reporting of outcomes for the purposes of this review were requested. Five authors provided data required
to meet the eligibility criteria (Frobell et al., 2013; Lohmander et al., 2004; Meunier, Odensten, & Good, 2007; Neuman et al., 2008; Potter et al., 2012) and one study was subsequently excluded as no further data was provided by the authors (McAllister et al., 2003). Eleven papers were included in the initial appraisal of methodological quality, and an additional eligible paper was identified in the June 2014 searches (Tengman et al., 2014).

**Figure 5.1** Search strategy

n: sample size; QOL: Health-related quality of life.
Quality appraisal

Quality appraisal scores for the reviewed studies ranged from 4 to 21. The study with the lowest quality was excluded due to satisfying less than 10 (4 of 21) of the quality appraisal criteria (Arbes et al., 2007). The quality appraisal scores for the remaining 11 studies are presented in Table 5.1.

Study and participant characteristics

Quality of life outcomes were reported for a total of 473 ACL-deficient participants from 11 studies at a mean 10 years (range 5 to 23 years) following ACL rupture. Study and participant characteristics are presented in Table 5.1. Knee-related QOL was measured with the KOOS-QOL subscale in eight studies (Frobell et al., 2013; Lohmander et al., 2004; Meunier et al., 2007; Michalitsis, Vlychou, Malizos, Thriskos, & Hantes, 2013; Neuman et al., 2008; Swirtun & Renström, 2008; Tengman et al., 2014; von Porat, Roos, & Roos, 2004) and the ACL-QOL in one study (Hartwick, Meeuwisse, Vandertuin, & Maitland, 2003). Health-related QOL was measured with the SF-36 in five studies (Fithian et al., 2005; Frobell et al., 2013; Lohmander et al., 2004; Potter et al., 2012; von Porat et al., 2004), and three studies included both a knee-related QOL and a health-related QOL measure (Frobell et al., 2013; Lohmander et al., 2004; von Porat et al., 2004). Six studies used a prospective study design; however, only one was a RCT (Frobell et al., 2013). Nine studies reported outcomes for both ACL-deficient and ACL-reconstructed subgroups, or provided these data on request.
<table>
<thead>
<tr>
<th>Study</th>
<th>Quality¹</th>
<th>Country</th>
<th>n=ACLD/ACLR²</th>
<th>Follow-up (years)</th>
<th>BMI (kg/m²)</th>
<th>Mean age at follow-up (years)</th>
<th>Sex (% women)</th>
<th>Study design</th>
<th>QOL measure(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fithian et al 2005</td>
<td>13</td>
<td>America</td>
<td>113/96</td>
<td>7 (3-10)</td>
<td>NR</td>
<td>45±11, 38±14, 37±14⁴</td>
<td>54, 61, 46⁴</td>
<td>Prosp</td>
<td>SF-36</td>
</tr>
<tr>
<td>Frobell et al 2013</td>
<td>21</td>
<td>Sweden</td>
<td>29/59</td>
<td>5</td>
<td>24±3⁵</td>
<td>31±5⁵</td>
<td>31</td>
<td>RCT</td>
<td>KOOS, SF-36</td>
</tr>
<tr>
<td>Hartwick et al 2003</td>
<td>11</td>
<td>Canada</td>
<td>17/0</td>
<td>12 (1-26)</td>
<td>27</td>
<td>40±8</td>
<td>47</td>
<td>CS</td>
<td>ACL-QOL</td>
</tr>
<tr>
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<td>15</td>
<td>Sweden</td>
<td>32/52</td>
<td>12</td>
<td>23 (18-40)</td>
<td>31 (26-40)</td>
<td>100</td>
<td>Retro</td>
<td>KOOS, SF-36</td>
</tr>
<tr>
<td>Meunier et al 2007</td>
<td>13</td>
<td>Sweden</td>
<td>36/0⁶</td>
<td>15±1</td>
<td>NR</td>
<td>36 (29-45)⁺³,⁵</td>
<td>38</td>
<td>Prosp</td>
<td>KOOS</td>
</tr>
<tr>
<td>Michalitsis et al 2013</td>
<td>14</td>
<td>Greece</td>
<td>32/7/0</td>
<td>5±5</td>
<td>26</td>
<td>30</td>
<td>11</td>
<td>CS</td>
<td>KOOS</td>
</tr>
<tr>
<td>Neunman et al 2008</td>
<td>18</td>
<td>Sweden</td>
<td>71/22⁺⁸</td>
<td>16±1³</td>
<td>26±4³</td>
<td>42±7³</td>
<td>39¹</td>
<td>Prosp</td>
<td>KOOS</td>
</tr>
<tr>
<td>Potter et al 2012</td>
<td>12</td>
<td>America</td>
<td>7/12⁺⁷</td>
<td>7-11</td>
<td>NR</td>
<td>42±10⁺⁵</td>
<td>77</td>
<td>Prosp</td>
<td>SF-36</td>
</tr>
<tr>
<td>Swirtun &amp; Renstrom 2008</td>
<td>13</td>
<td>Sweden</td>
<td>24/22</td>
<td>6±1</td>
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<td>48</td>
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<td>KOOS</td>
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<tr>
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<td>37/33</td>
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<td>KOOS</td>
</tr>
<tr>
<td>Von Porat et al 2004</td>
<td>14</td>
<td>Sweden</td>
<td>65/89</td>
<td>14</td>
<td>26±2</td>
<td>40±6</td>
<td>0</td>
<td>CS</td>
<td>KOOS, SF-36</td>
</tr>
</tbody>
</table>

¹ quality appraisal scores range from 0 (worst) to 21 (best); ² number of eligible participants reporting QOL outcomes; ³ included delayed ACLR patients; ⁴ Data reported separately for ACL-deficient patients grouped by risk level (low, moderate, high) based on baseline knee stability and sports participation; ⁵ Estimated using mean age from baseline and mean follow-up; ⁶ n=42 had a surgical ACL repair, as opposed to ACLR; ⁷ QOL data provided for a portion of total sample with >5 year follow-up; ⁸ All n=22 were delayed ACLR; ACLD: anterior cruciate ligament deficient; ACLR: anterior cruciate ligament reconstructed; BMI: body mass index; QOL: quality of life; NR: not reported; Prosp: prospective; RCT: randomised controlled trial; CS: cross-sectional; Retro: retrospective; KOOS: Knee injury and Osteoarthritis Score; SF-36: Short-Form 36; All data are reported as range only, mean only, mean ± standard deviation, or mean (range).
Knee-related quality of life in anterior cruciate ligament deficient individuals

A total of five studies reported KOOS-QOL data for ACL-deficient participants (Frobell et al., 2013; Meunier et al., 2007; Swirtun & Renström, 2008; Tengman et al., 2014; von Porat et al., 2004) and a further three studies provided these data on request (Lohmander et al., 2004; Michalitsis et al., 2013; Neuman et al., 2008). Mean KOOS-QOL values ranged from 54 (Lohmander et al., 2004; Michalitsis et al., 2013) to 77 (Swirtun & Renström, 2008) out of a maximum of 100 (best possible score). Strong positive relationships were identified between KOOS-QOL and all subscales of the KOOS (Pain: \( \rho = 0.86, p = 0.01 \); Symptoms: \( \rho = 0.79, p = 0.02 \); ADL: \( \rho = 0.79, p = 0.02 \); and Sport/Rec: \( \rho = 0.74, p = 0.04 \)) (Frobell et al., 2013; Lohmander et al., 2004; Meunier et al., 2007; Michalitsis et al., 2013; Swirtun & Renström, 2008; Tengman et al., 2014; von Porat et al., 2004). KOOS-QOL scores were not significantly related to follow-up duration (\( \rho = 0.25, \rho = 0.55 \)), sex (\( \rho = 0.28, p = 0.51 \)), age (\( \rho = 0.42, p = 0.31 \)), sample size (\( \rho = 0.35, p = 0.40 \)) or quality appraisal scores (\( \rho = 0.13, p = 0.76 \)).

Only one study used the ACL-QOL to report knee-related QOL in ACL-deficient individuals (Hartwick et al., 2003). This study evaluated knee-related QOL in 17 people with knee osteoarthritis at an average 9 years following ACL rupture. These participants reported a mean ± SD ACL-QOL score of 39 ± 19 indicating very low QOL (score of 100 indicates optimal QOL). Total ACL-QOL scores were correlated to the level of pain reported during isometric knee extension (Pearson’s \( r = -0.56; p = 0.016 \)).
Figure 5.2 KOOS values for individual studies from ACL-deficient cohorts

All subscale scores represent means; a lower score indicates poorer outcomes in all subscales; ADL: Activities of Daily Living; Sport/Rec: function in Sport and Recreation; QOL: Quality of Life; KOOS: Knee injury and Osteoarthritis Outcome Score.

Comparison to normative populations

KOOS-QOL scores in ACL-deficient individuals ranged from 54 ± 17 (Lohmander et al., 2004) to 77 ± 22 (Swirtun & Renström, 2008) (mean ± SD), these were impaired compared to Swedish general population norms (81 ± 24) (Paradowski et al., 2006), Swedish amateur soccer players with minor (14%), severe (23%) or no history (63%) of knee injury (88 ± 17) (Frobell, Svensson, Gothrick, & Roos, 2008) and a population of military recruits (92 ± 28) (Cameron et al., 2013). The other KOOS subscale scores reported by ACL-deficient groups were similar to those reported by the general Swedish population (Frobell et al., 2008). In contrast, all ACL-deficient groups reported more knee pain and worse function in sport and recreation compared to amateur soccer players and military recruits (Figure 5.3).
Blue squares: mean values from military recruits with no history of knee ligament injury (aged 19 ± 1 years, n = 1005) (Cameron et al., 2013); Green diamonds: mean values from amateur Swedish soccer players with minor (14%), severe (23%), or no (63%) history of knee injury (aged 22 ± 4 years; n = 188) (Frobell et al., 2008); Red triangles: mean values from the Swedish general population (aged 18 to 54 years; n = 291) (Paradowski et al., 2006); All normative populations include men and women; a lower score indicates poorer outcomes in all subscales; ADL: function in Activity of Daily Living; Sport/Rec: function in Sport and Recreation; QOL: Quality of Life; KOOS: Knee injury and Osteoarthritis Outcome Score.

Knee-related quality of life comparisons between anterior cruciate ligament deficient and anterior cruciate ligament reconstructed groups

Pooling of KOOS-QOL data extracted from the studies reporting separate scores for ACL-deficient and ACL-reconstructed groups (Frobell et al., 2013; Lohmander et al., 2004; Neuman et al., 2008; Swirtun & Renström, 2008; Tengman et al., 2014; von Porat et al., 2004) revealed no significant
difference in knee-related QOL between groups (mean difference: 2.9, 95% CI: -3.3 to 9.1) (Figure 5.4). Of these studies, 3 found no difference in KOOS-QOL between ACL-deficient and ACL-reconstructed groups at 5, 12, and 14 year follow-up (Frobell et al., 2013; Lohmander et al., 2004; von Porat et al., 2004), or no difference in KOOS-QOL between ACL-deficient and delayed ACL-reconstructed groups (all ACL-reconstructed individuals in this study initially received non-operative management) (Neuman et al., 2008). The remaining two studies reported better KOOS-QOL scores in ACL-deficient participants at 6 and 23 year follow-up, respectively (Swirtun & Renström, 2008; Tengman et al., 2014). Meunier et al (2007) initially allocated participants to surgical repair (not reconstruction) of the torn ACL or non-operative management, and reported no between-group differences in KOOS-QOL scores.

![Figure 5.4](image)

**Figure 5.4** Forest plot of random-effects meta-analysis of KOOS-QOL scores

Mean differences (boxes) and 95% CIs (whiskers) are presented for individual studies reporting data for ACL-deficient and ACL-reconstructed subgroups; The pooled mean difference and 95% CI are represented by the diamond; A negative mean difference indicates a favourable knee-related QOL outcome for ACL-reconstructed participants; ACLR: anterior cruciate ligament reconstruction; ACLD: anterior cruciate ligament deficient.
Health-related quality of life

Health-related quality of life in anterior cruciate ligament deficient individuals

The only health-related QOL measure used in the included studies was the SF-36. Two studies reported SF-36 scores for all domains for ACL-deficient participants (Fithian et al., 2005; von Porat et al., 2004), and a further two studies provided these data on request (Frobell et al., 2013; Lohmander et al., 2004). One additional study provided SF-36 physical and mental component scores, but did not report data for individual SF-36 domains (Potter et al., 2012). Comparison of SF-36 domain scores revealed similarities in reported mean values across all studies, with the exception of the low Bodily Pain domain score reported by Fithian et al. (2005) and the low physical and mental component scores reported by Potter et al (2012) (Figure 5.5).

Comparison to normative populations

Health-related QOL scores, measured with the SF-36, were similar or slightly higher in ACL-deficient individuals compared to a population based sample from Norway (n = 2323; aged 45 ± 17 years) (Loge et al., 1999) (Figure 5.6). Specifically, similar scores were reported for the four physical health domains (PF, RP, BP and GH) addressing activity limitations due to physical health, bodily pain, self-rated health and future health expectations. The four SF-36 mental health domain scores reported by ACL-deficient groups in each study were similar or higher than those reported from Norwegian population norms (Figure 5.6) (Loge et al., 1999). These four domains (V, SF, RE and MH) address energy and fatigue, the influence of emotional health on activity participation and social activities, anxiety and depression. Considering ACL rupture commonly occurs during participation in competitive sport, SF-36 scores in ACL-deficient groups were compared with norms available from a more active population of 696 college athletes (n=696: mean age 19, range 17 to 23 years) (Huffman et al., 2008), over half of these athletes reported previous sporting injuries. Lower mean SF-36 scores were observed for all ACL-deficient groups compared with this active population (Figure 5.6).
**Figure 5.5** SF-36 results for individual studies

All scores represent mean values; a lower SF-36 score indicates poorer outcome on each domain; PF: Physical Function; RP: Role Physical; BP: Bodily Pain; GH: General Health; PCS: Physical Component Score (the aggregate mean score of PF, RP, BP and GH domains); V: Vitality; SF: Social Function; RE: Role Emotional; MH: Mental Health; MCS: Mental Component Score (the aggregate mean score of V, SF, RE and MH domains); only component scores were reported by Potter et al. (2012).
**Figure 5.6** SF-36 scores for individual studies (grey lines) compared with sporting and general population-based normative data

Green line: mean scores from college athletes (n = 696; mean age 19, range 17 to 23 years) (Huffman et al., 2008); Red line: normative data from the Norwegian general population (n = 2323; aged 45 ± 17 years) (Loge et al., 1999); All scores are mean values; a lower SF-36 score indicates poorer outcomes in all domains; PF: Physical Function; RP: Role Physical; BP: Bodily Pain; GH: General Health; PCS: Physical Component Score (the aggregate mean score of PF, RP, BP and GH domains); V: Vitality; SF: Social Function; RE: Role Emotional; MH: Mental Health; MCS: Mental Component Score (the aggregate mean score of V, SF, RE and MH domains); only component scores were reported by Potter et al. (2012).

**Health-related quality of life comparisons between anterior cruciate ligament deficient and anterior cruciate ligament reconstructed groups**

Pooling of mean SF-36 domain scores from individual studies identified no significant differences
between ACL-deficient and ACL-reconstructed groups for seven of the eight domains (Figure 5.7 and 8). However, there was a significant difference for the SF-36 Vitality domain, favouring the ACL-reconstructed group (mean difference: -4.3, 95% CI: -7.6 to -1.0) (Figure 5.8). Three out of four studies reporting SF-36 scores found no differences between ACL-deficient and ACL-reconstructed groups (Frobell et al., 2013; Potter et al., 2012; von Porat et al., 2004). The only study to report between-group differences in SF-36 scores, reported increased PF, RP, BP, V, SF and RE scores in participants who underwent ACLR (Fithian et al., 2005).

**Figure 5.7** Forest plot of random-effects meta-analysis of SF-36 domains contributing to the Physical Component Score

Mean differences (boxes) and 95% CIs (whiskers) are presented for individual studies reporting data for ACL-deficient and ACL-reconstructed subgroups, in addition to the pooled mean difference and 95% CI (diamond); A negative mean difference indicates a favourable QOL outcome for ACL-reconstructed participants; Data from Potter et al. (2012) was not included in this meta-analysis as SF-36 domain scores were not reported; ACLR: anterior cruciate ligament reconstruction; ACLD: anterior cruciate ligament deficient.
Figure 5.8 Forest plot of random-effects meta-analysis of SF-36 domains contributing to the Mental Component Score

Mean differences (boxes) and 95% CIs (whiskers) are presented for individual studies reporting data for ACL-deficient and ACL-reconstructed subgroups, in addition to the pooled mean difference and 95% CI (diamond); A negative mean difference indicates a favourable QOL outcome for ACL-reconstructed participants; Data from Potter et al. (2012) was not included in this meta-analysis as SF-36 domain scores were not reported; ACLR: anterior cruciate ligament reconstruction; ACLD: anterior cruciate ligament deficient.

Factors that may influence quality of life

Tibiofemoral osteoarthritis and cartilage pathology

Three studies reported no difference in knee-related QOL between individuals with tibiofemoral radiographic osteoarthritis and those without osteoarthritis (Lohmander et al., 2004; Meunier et al.,
2007; von Porat et al., 2004). However, only one study reported knee-related QOL scores separately for ACL-deficient and ACL-reconstructed participants with and without tibiofemoral osteoarthritis (Tengman et al., 2014). This study reported higher KOOS-QOL scores in ACL-deficient individuals with osteoarthritis (Kellgren and Lawrence ≥ grade 2; n = 25; KOOS-QOL 59 ± 27) compared with ACL-reconstructed individuals with osteoarthritis (n = 26; mean KOOS-QOL 48 ± 22). However, a between-group statistical analysis was not reported. No studies investigated differences in QOL based on the presence of tibiofemoral cartilage pathology.

Patellofemoral osteoarthritis and cartilage pathology

Four studies reported rates of patellofemoral osteoarthritis or patellofemoral cartilage lesions in ACL-deficient participants more than five years following ACL rupture (Fithian et al., 2005; Frobell et al., 2013; Lohmander et al., 2004; Michalitis et al., 2013). These studies found lower rates of patellofemoral degenerative changes (58% v 76%, p = 0.02) (Fithian et al., 2005), lower rates of patellofemoral osteoarthritis (28% v 61%, p = 0.01, OR 5.8) (Lohmander et al., 2004) or a trend toward less patellofemoral osteoarthritis (p = 0.08) (Frobell et al., 2013) in ACL-deficient participants compared with those managed with ACLR. The fourth study included only ACL-deficient participants, and found no patellofemoral cartilage lesions among the sample at an average five years after ACL rupture (Michalitis et al., 2013). However, the relationship between patellofemoral changes and QOL scores was not investigated.

Concomitant and subsequent injuries

Two studies found that subsequent meniscus injury (Michalitis et al., 2013) and meniscal repair (von Porat et al., 2004) were not related to KOOS-QOL or SF-36 outcomes at an average 5 and 14 years after ACL rupture. In contrast, Swirtun & Renström (2008) reported a relationship between subsequent trauma (described as subsequent meniscus, cartilage or medial collateral ligament injury, patella subluxation or fracture, or arthroscopic debridement) to the ACL-injured knee and poorer KOOS-QOL scores (p = 0.002). While increased rates of osteoarthritis were reported in those with baseline meniscectomy or meniscal repair (Lohmander et al., 2004; Meunier et al., 2007; Neuman et
al., 2008), the influence of meniscus surgery or subsequent trauma on QOL outcomes was not evaluated specifically for ACL-deficient individuals.

**Delayed anterior cruciate ligament reconstruction**

Three studies reported no significant difference in KOOS-QOL scores between ACL-deficient participants, and those who were initially managed non-operatively but had a delayed ACLR prior to 5, 15 and 16 year follow-up (Frobell et al., 2013; Meunier et al., 2007; Neuman et al., 2008). The proportion of participants deciding to have an ACLR despite undergoing initial non-operative management ranged from 23% (Fithian et al., 2005) to 51% (Frobell et al., 2013) across the included studies. Participants in the study by Michalitsis et al. (2013) differed from those in other studies in that all participants completed questionnaires one day prior to undergoing a delayed ACLR, at a mean five years post-injury. These participants reported the poorest knee-related QOL (Figure 5.2).

**Activity level**

Five studies compared return to sport rates or activity level between ACL-deficient and ACL-reconstructed groups. There were no reported differences in return to pre-injury sport or activity level at follow-up between non-surgical and surgical groups (Fithian et al., 2005; Frobell et al., 2013; Lohmander et al., 2004; Meunier et al., 2007; Swirtun & Renström, 2008). No study compared QOL between those who returned to the same level of sport and those who did not in ACL-deficient individuals more than five years following ACL rupture.
DISCUSSION

This systematic review shows that knee-related QOL is impaired 5 to 25 years following ACL rupture in ACL-deficient individuals, compared to population-based normative data. Meta-analyses using pooled data from multiple studies revealed no difference in knee-related QOL between patients who underwent ACLR and those who did not. All of the included studies reported similar (Frobell et al., 2013; Lohmander et al., 2004; von Porat et al., 2004) or better (Swirtun & Renström, 2008; Tengman et al., 2014) knee-related QOL 5 to 25 years following ACL rupture in people who remain ACL-deficient, compared to those managed with surgical reconstruction. In contrast, health-related QOL in ACL-deficient groups was similar to general population norms but impaired compared to more active populations. Data pooling revealed no health-related QOL differences between ACL-deficient and ACL-reconstructed groups for seven of the eight SF-36 domains.

Knee-related quality of life

Knee-related QOL scores in ACL-deficient individuals were impaired compared to general population norms (Paradowski et al., 2006). Greater knee-related QOL impairments were observed when ACL-deficient patients were compared to Swedish amateur soccer players (Frobell et al., 2008) and military recruits (Cameron et al., 2013); these populations are likely to be more active than the general population. The magnitude of difference is consistent with the minimal clinically important change (the smallest change required for an effect to be considered clinically relevant) for the KOOS (8 to 10 points) (Roos et al., 1998). Notably, ACL-ruptured individuals are typically active in competitive sports at the time of injury (Ahlden et al., 2012) and may have a higher pre-injury QOL compared with the general population. This should be considered when making QOL comparisons following ACL rupture. Two of the lowest KOOS-QOL scores were reported in studies including all male (von Porat et al., 2004) and all female (Lohmander et al., 2004) Swedish soccer players at a mean 12 years and 14 years following ACL rupture, respectively. These ACL-deficient groups reported markedly impaired KOOS-QOL scores in contrast to a comparable sample of Swedish amateur male and female soccer players (Frobell et al., 2008). The KOOS-QOL subscale is comprised of four questions, one of these questions addresses knee-related lifestyle modifications. This may
partly explain the impaired KOOS-QOL scores reported in ACL-deficient soccer players (30% of male soccer players reported severe lifestyle change (von Porat et al., 2004) and 50% of female soccer players reported lifestyle changes) (Lohmander et al., 2004). Anterior cruciate ligament-deficient individuals may benefit from targeted support to return to their desired activity level, or encouragement to adopt an active lifestyle if ceasing sport participation.

The meta-analyses revealed similar knee-related QOL between individuals who received an ACLR and those who remained ACL-deficient. Notably, the highest quality paper and only RCT included in meta-analysis found no difference in KOOS-QOL scores between treatment groups (Frobell et al., 2013). There is also substantial overlap between the knee-related QOL scores reported in ACL-deficient populations (ranging from 54±17 to 77±22) and those reported in a recent systematic review looking at health-related QOL in ACL-reconstructed individuals 5 to 20 years after surgery (range of KOOS-QOL scores for ACL-reconstructed populations 63±22 to 83±18; pooled mean 75, 95% CI: 68 to 81) (Chapter 4). The results of both systematic reviews therefore suggest that ACL-ruptured individuals are at risk of long-term QOL impairments, irrespective of surgical or non-surgical management. Strategies to improve knee-related QOL following ACL rupture are important to incorporate into standard rehabilitation regimes. Such approaches could address knee confidence and assist individuals to make healthy lifestyle modifications or resume pre-injury activities. Most importantly, an individualised approach is required, as QOL is an individual construct (Carr & Higginson, 2001) and should be taken in the context of one’s goals, expectations, standards and concerns (The World Health Organization Group, 1995). To date, no studies have trialled interventions targeting QOL impairments after ACL rupture, this review indicates that such research is warranted.

**Health-related quality of life**

Health-related QOL measured with the SF-36 was similar or better compared with data from the Norwegian general population (Loge et al., 1999), but worse compared to college athletes (Huffman et al., 2008). The study of college athletes reported significantly higher health-related QOL scores for athletes compared to an age-matched general population cohort. Additionally, higher QOL was
observed in athletes without a history of injury, compared to those with a past history of injury (Huffman et al., 2008). This highlights the importance of considering pre-injury activity levels when evaluating health-related QOL. We found no significant pooled mean difference between ACL-deficient and ACL-reconstructed subgroups for seven of the eight SF-36 domains. There was a significant between-group difference for the SF-36 Vitality domain (which assesses levels of energy and fatigue), where ACL-reconstructed individuals demonstrated more favourable outcomes. However, this difference of four SF-36 points is smaller than the estimated minimal detectable change of five points (Busija et al., 2008), and largely attributable to results from one larger, moderate quality study (Fithian et al., 2005) (Figure 5.8). The other three studies reporting SF-36 Vitality scores (including the only high quality RCT) found no significant difference between groups. Importantly, the observed pooled mean difference for the SF-36 Vitality domain is unlikely to be of clinical significance. Notably, participants in this study who received conservative management reported lower SF-36 scores on all domains compared with reconstructed participants and lower SF-36 bodily pain scores compared with other samples of ACL-deficient participants (Figure 5.5) (Fithian et al., 2005). Although it is not apparent why these participants reported greater levels of bodily pain, increased pain levels provide one potential explanation for the reduced SF-36 domain scores reported in this group.

**Concomitant injuries and osteoarthritis**

No studies investigated associations between concomitant or subsequent meniscal and cartilage injury or surgery on QOL outcomes for ACL-deficient participants specifically. Although the systematic review in Chapter 4 identified relationships between concomitant meniscal surgery at the time of ACLR and poorer KOOS-QOL and SF-36 scores more than 10 years following surgery (Gifstad et al., 2012b; Øiestad et al., 2011), similar analyses could not be performed for ACL-deficient cohorts.

Limited research has shown that radiographic osteoarthritis severity is associated with knee-related QOL 14 years following ACLR (Øiestad et al., 2010). The only study reporting KOOS-QOL scores according to osteoarthritis severity and treatment groups found better knee-related QOL in ACL-deficient participants with osteoarthritis compared to ACL-reconstructed participants with
osteoarthritis (mean 59 vs. 48) (Tengman et al., 2014). This difference is greater than the minimal clinically important change for the KOOS (Roos et al., 1998) and is likely to be of clinical relevance.

While studies identified differences in rates of patellofemoral osteoarthritis (Lohmander et al., 2004) or degenerative changes (Fithian et al., 2005) between ACL-deficient and ACL-reconstructed groups, the influence of patellofemoral changes on QOL in ACL-deficient individuals was not explored in the included studies. Patellofemoral osteoarthritis may contribute to pain, symptoms and activity restrictions following ACL rupture (Culvenor, Cook, Collins, & Crossley, 2013).

**Considerations for quality of life comparisons between anterior cruciate ligament deficient and anterior cruciate ligament reconstructed groups**

A range of potential biases were identified in the included studies that could result in the underestimation or overestimation of QOL in these patient populations. These include advice regarding activity modification, study designs that may result in surgical bias, and the surgical treatment of baseline meniscal injuries in non-reconstructed individuals. Several studies purposefully selected individuals with a low pre-injury activity level for non-operative management or strongly advised non-operatively managed participants against returning to high impact sports (Fithian et al., 2005; Neuman et al., 2008; Potter et al., 2012; Swirtun & Renström, 2008; Tengman et al., 2014). This could potentially influence KOOS-QOL scores, where one of four questions addresses lifestyle modifications. Advice to patients that ACLR is required for return to sport may result in a surgical bias, and could increase the likelihood of ACL-deficient participants adopting a less active lifestyle, or experiencing reduced confidence taking part in future activities. Increased lifestyle modifications and reduced knee confidence is likely to translate into a poor KOOS-QOL score.

The impact of meniscal injury and subsequent surgery on QOL in ACL-deficient participants is difficult to determine. Meniscal injuries occurring at the time of ACL rupture may go undiagnosed in non-operatively managed patients who do not receive magnetic resonance imaging (MRI) or diagnostic arthroscopy. This may result in mislabelling some concomitant meniscal injuries as new subsequent meniscal injuries in ACL-deficient groups, making interpretation of the influence of
concomitant and subsequent meniscal injuries on QOL in these individuals more difficult than ACL-reconstructed groups. Where studies did perform baseline MRI or diagnostic arthroscopies, baseline meniscal surgery was frequently performed in patients managed without ACLR. Undergoing any form of knee surgery may have psychological consequences, such as increased fear of re-injury and poor knee confidence, potentially negatively impacting QOL. It is also possible that for some individuals, undergoing knee surgery positively influences outcome through placebo mechanisms, especially if an individual holds strong beliefs or expectations that the surgery will be effective (Flood, Lorence, Ding, McPherson, & Black, 1993; Sihvonen et al., 2013).

Limitations and strengths

An ACL specific QOL instrument (ACL-QOL) was only used in one study, precluding between-study comparisons for this measure. As most studies did not evaluate QOL as their primary objective, potential influences on QOL were rarely explored for ACL-deficient participants, limiting conclusions about factors impacting on QOL. Furthermore, patient-reported QOL measures often fail to address patient-perceived important and relevant factors (Carr & Higginson, 2001). The KOOS-QOL is a valid measure of knee-related QOL and the most commonly used QOL measure 5 to 20 years after ACLR (Chapter 4). However, specific items (knee-related lifestyle modification and knee awareness) may not accurately reflect QOL in ACL-ruptured individuals. Heightened knee awareness has the potential to facilitate positive lifestyle modifications that result in a satisfactory QOL (Österberg, Kvist, & Dahlgren, 2013). We recommend that future studies measuring knee-related QOL as a primary outcome in ACL-deficient participants include the ACL-QOL questionnaire. We also recommend comparisons with active reference groups to enhance interpretability of findings.

Rehabilitation has potential to improve QOL, but only four studies included in this review described a standardised rehabilitation program for non-operative patients (Fithian et al., 2005; Frobell et al., 2013; Neuman et al., 2008; Tengman et al., 2014). Rehabilitation strategies varied between studies (physiotherapist supervised neuromuscular training or a strategy of self-monitored training that commonly resulted in poor joint mobility and muscle atrophy (Neuman et al., 2008); a goal oriented physiotherapist led progressive program focusing on functional stability training and activity modification (Tengman et al., 2014); an unmonitored rehabilitation program consisting of non-impact
closed chain strengthening and range of motion exercises (Fithian et al., 2005); and a standardised evidence-based goal-oriented rehabilitation program described in great detail (Frobell et al., 2013)). Consequently, the influence of specific rehabilitation strategies on QOL outcomes could not be evaluated. Long-term QOL outcomes reported by participants in other studies may have been influenced by ineffective post-injury management and better outcomes might have been obtained from evidence-based rehabilitation programs.

Additionally, ACLR studies with long-term follow-up may have used surgical procedures that are now outdated and not comparable to modern day techniques. There is also a need for high quality RCTs investigating longer-term QOL as a primary outcome between ACL-reconstructed and ACL-deficient groups, since other study designs are more susceptible to bias. Finally, all included articles were published in English, 7 of 11 eligible studies were performed in Sweden and 2 were performed in the United States. This potentially limits the generalisability of findings to other populations. The main strengths of this review were the systematic approach to literature searching, study selection and data extraction, the inclusion of both knee-specific QOL and health-related QOL data, and access to unpublished data that enabled pooling of key outcomes for meta-analysis. The availability of normative QOL data enhanced the interpretation of results and enabled the evaluation of findings within a broader population context.

**SUMMARY & CONCLUSION**

This systematic review has shown that knee-related QOL is impaired 5 to 25 years following ACL rupture in ACL-deficient individuals compared to population norms, and to an even greater degree when compared to young, active adults. Meta-analysis identified no significant differences in knee-related QOL between ACL-deficient and ACL-reconstructed groups. Average health-related QOL scores in ACL-deficient people were similar to those reported in a general population, but impaired compared to more active populations. The only difference between ACL-deficient and ACL-reconstructed groups for health-related QOL outcomes was a favourable SF-36 Vitality score for ACL-reconstructed participants; however this is unlikely to be of clinical significance. These findings
indicate that longer-term impairments in knee-related QOL are evident after ACL rupture, irrespective of operative or non-operative management. There is a need for strategies to improve longer-term QOL after ACL injury and a greater focus on reducing the incidence of ACL injury through primary prevention is warranted.
PART B

EXPLORATION OF LONGER-TERM QUALITY OF LIFE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN PEOPLE WITH KNEE DIFFICULTIES
RETURN TO SPORT MATTERS: LONGER-TERM QUALITY OF LIFE AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN PEOPLE WITH KNEE DIFFICULTIES

The ensuing chapter has been published in its entirety: Filbay SR, Ackerman IN, Russell TG, Crossley KM. Return to sport matters: longer-term quality of life after anterior cruciate ligament reconstruction in people with knee difficulties. Scandinavian Journal of Medicine & Science in Sports (published online first, 11th May 2016)

INTRODUCTION

Anterior cruciate ligament rupture and subsequent reconstructive surgery can result in persistent knee pain, symptoms, physical activity restrictions and psychological issues (Ardern et al., 2012a; Ardern, Taylor, Feller, & Webster, 2014b; Lohmander et al., 2004; Wasserstein, Huston, Nwosu, & Spindler, 2015). The systematic review in Chapter 4 revealed impaired knee-related QOL in people 5 to 20 years following ACLR. However, few studies have focused on QOL as a primary outcome and consequently, research investigating factors related to longer-term QOL after ACLR is scarce. Furthermore, no studies to date have explored longer-term QOL or psychological health specifically in individuals with knee difficulties after ACLR (Filbay, Ackerman, Russell, Macri, & Crossley, 2014). The impact of living with knee
difficulties on the QOL of previously active ACL-reconstructed individuals is poorly understood. Considering ACLR is most prevalent in adolescents and young adults (Granan et al., 2008; Granan et al., 2009; Janssen et al., 2012; Joseph et al., 2013; Lind et al., 2009) persistent knee difficulties could impede on work responsibilities, sporting desires and parenting roles with great potential to impact upon QOL and psychological health.

A recent study found that all individuals undergoing ACLR expected to have normal or almost normal knee function within one year of ACLR, and 91% expected to return to their pre-injury level of sport (Feucht et al., 2014). Despite these high expectations, a large study of 1761 young ACL-reconstructed individuals found that over one in three reported knee difficulties six years following primary ACLR (Wasserstein et al., 2015). Additionally, a recent meta-analysis found that as many as one in two ACL-reconstructed individuals do not return to non-elite sport (Ardern et al., 2014b). A mismatch between an individual’s desires or expectations and their perceived abilities may impact negatively on their QOL (Carr et al., 2001; Ruta, Garratt, Leng, Russell, & MacDonald, 1994). Investigating factors related to longer-term QOL and psychological health in people with knee difficulties following ACLR could assist in developing strategies to optimise longer-term outcomes after ACLR (Filbay, 2015; Filbay et al., 2014). The purpose of this study was to (i) describe QOL and psychological health outcomes and; (ii) identify factors related to variability in QOL and psychological health outcomes, in people with knee difficulties (pain, symptoms or functional limitations) 5 to 20 years following ACLR.
METHODS

Study design

A cross-sectional study design was used. Ethical approval for this study was obtained from The University of Queensland Medical Research Ethics Committee (approval number 2012001240, Appendix 6.1). Funding for this study was obtained from the Physiotherapy Research Foundation (PRF) (Seeding Grant number: S13-004).

Setting and participant recruitment

All individuals who had undergone a hamstring or patellar tendon autograft ACLR 5 to 20 years previously were identified from the surgical records of four orthopaedic surgeons (based in Melbourne, Brisbane, Toowomba and Nambour, Australia) and invited by letter to participate in the study (Appendix 6.2). Between June 2013 and February 2014, 2391 letters of invitation were sent to archived postal addresses of potentially eligible patients. In total, 346 individuals responded to this invitation. Since only eligible individuals were asked to respond to the invitation and many archived postal addresses were outdated, the exact number of letters received remains unknown, precluding calculation of a response rate. Over this eight month period, participants were also recruited from the general community through advertisements in public places and online (online Arthritis and Sports Medicine newsletters and social media sites). People having revision or contralateral ACLR more than 5 years ago, concomitant or subsequent surgery (meniscal, cartilage or other ligamentous repair) were eligible for the study. Individuals were considered ineligible if they: (i) reported a comorbidity likely to impact QOL (e.g. chronic back pain, cancer, acute injury); (ii) were aged under 18 years or over 55 years at the time of recruitment; (iii) underwent an ACLR (primary or revision) within the past five years; (iv) were not fluent in written English; (v) were asymptomatic according to predefined KOOS cut-off criteria (as outlined below).
Symptomatic cut-off criteria

To ensure all participants experienced a degree of knee difficulties (knee pain, symptoms or functional limitations) we modified previously published KOOS criteria that were devised to identify individuals symptomatic enough to seek medical care (Englund, Roos, & Lohmander, 2003). The published criteria required reporting a suboptimal score (any score other than the best possible response on a 5-point Likert scale) on at least 50% of questions for the KOOS-QOL and two of the additional four KOOS subscales (corresponding to cut-off values of ≤86.1 (Pain), ≤85.7 (Symptoms), ≤86.8 (ADL), ≤85.0 (Sport/Rec), and ≤87.5 (QOL)). We modified these criteria to include individuals reporting impairment in any two KOOS subscales. The rationale for this modification was to allow for the inclusion of individuals reporting high KOOS-QOL scores despite knee difficulties, since a primary aim of this study was to explore QOL variability in people with knee difficulties after ACLR.

Defining knee difficulties

For the purpose of this study, knee difficulties were defined as self-reported knee pain, symptoms or functional limitations determined by reporting less than optimal scores on at least 50% of questions on the KOOS-Pain, KOOS-Symptoms, KOOS-ADL or KOOS-Sport/Rec subscale.

Defining quality of life

Due to the multiplicity of QOL definitions, it is recommended that researchers be as clear as possible in defining the concept of QOL to enable interpretation and comparisons between studies (Post, 2014). Quality of life has been defined by the World Health Organisation as ‘an individual’s perceptions of their position in life taken in the context of the culture and value systems where they live and in relation to their goals, expectations, standards and concerns’
One aspect of QOL is the concept of health-related QOL (Barcaccia et al., 2013), which refers to the discordance between an individual’s health expectations or desires, and their current health experience (Carr et al., 2001). For this research, we have used the term ‘knee-related QOL’ to refer to the degree that an individual’s QOL is impacted by knee-related factors.

**Procedure**

All participants completed the KOOS, the Assessment of Quality of Life 8D Utility Instrument (AQol-8D), the ACL-QOL, the Workplace Activity Limitations Scale (WALS), the Hospital Anxiety and Depression Scale (HADS) and a questionnaire collecting participant characteristics and additional information (all study questionnaires are included in Appendix 6.3). Participants elected to complete questionnaires either online or in paper form. Online questionnaires were completed by participants following an email link to a custom built online questionnaire system (Mark-Rite PROMS, University of Queensland, Brisbane). All participants provided informed consent prior to commencing questionnaires. Paper versions of the questionnaire were sent to participants if requested, with a postage paid reply envelope. All participants received a follow-up reminder if the questionnaires were not completed within eight weeks. Questionnaire responses were screened for age, comorbidities, time since surgery and application of the KOOS symptomatic cut-off criteria to confirm participant eligibility.

**Patient reported outcomes**

**Participant demographics and characteristics**

Information collected included age, BMI, work status, time since most recent ACLR, time from injury to ACLR, mechanism of injury, postoperative symptoms, subsequent surgery, current treatment and osteoarthritis knowledge (Appendix 6.3). Where there was potential for recall bias, participants were given an ‘unsure’ option. To evaluate return to sport, participants responded to the following question ‘please tick the most appropriate statement regarding your
level of sport participation after injuring your ACL’ by selecting one of the following three options: ‘I returned to competitive sport at the same or higher level than before ACL injury’, ‘I returned to competitive sport at a lower level than before ACL injury’ or ‘I did not return to competitive sport after my ACL reconstruction.’ Individuals who did not return to the same or higher level of sport were then asked if this was because of their knee (‘If you did not return to competitive sport, or returned to competitive sport at a lower level than prior to your ACL reconstruction, was this because of your knee?’). Participants were asked what sports they were participating in at the time of ACL injury, if they were not participating in a competitive sport when they ruptured their ACL, a ‘not applicable’ response was given to the return to sport question. Participants were also requested to nominate which of the following activities they would prefer to participate in, in the absence of knee pain or impairment: ‘family duties’, ‘social activities’, ‘work-related activities’, ‘sport’ or ‘exercise.’

**Knee-related QOL**

Three measures were selected to provide a comprehensive overview of knee-related QOL; the KOOS (the most commonly used measure of knee-related QOL more than five years following ACLR (Filbay et al., 2014; Filbay, Culvenor, Ackerman, Russell, & Crossley, 2015)) the ACL-QOL (contains items of high importance to ACL-reconstructed individuals compared to other knee-related measures (Tanner et al., 2007)) and a custom QOL question (allows the individual to provide an overall assessment of the impact of their knee on their QOL considering all important and relevant influences).

The KOOS is a patient reported questionnaire developed to assess an individual’s opinion about their knee and associated problems (Roos, 2003), it contains five subscales: Pain, Symptoms, ADL, Sport/Rec and QOL. The KOOS-QOL subscale contains four questions addressing knee awareness, knee-related lifestyle modification, knee confidence and knee-related difficulties. The KOOS is valid and reliable for use in ACLR and knee osteoarthritis populations (Collins et al., 2011; Roos & Lohmander, 2003; Salavati, Akhbari, Mohammadi, Mazaheri, & Khorrami, 2011). The QOL and Sport/Rec subscales are more valid than other KOOS subscales for use within one year of ACLR (Comins, Brodersen, Krogsgaard, & Beyer, 2008). An
individual score for each subscale can be calculated where 0 represents no impairment and 100 represents extreme impairment.

The ACL-QOL is the only patient administered QOL measure specific to an ACL population and is valid, reliable and responsive to change (Mohtadi, 1998). The ACL-QOL contains 32-items and five domains (Symptoms/Physical, Work-Related, Sport/Rec, Lifestyle, Social/Emotional). Each ACL-QOL item is measured on a visual analogue scale from 0 (severe impairment) to 100 (no impairment). Domain scores are averages of all items in each domain and an overall ACL-QOL score represents the average of all domains.

We also included a custom ‘knee impact question’ that allowed individuals to evaluate the impact of their knee on their QOL in line with their expectations, priorities and values. Participants responded to the question: ‘do you believe that your knee is impacting on your quality of life?’ with one of four responses; ‘not at all’, ‘slightly’, ‘moderately’ and ‘significantly’.

Health-related QOL

The AQoL-8D is a multi-attribute generic (non-disease-specific) measure of health-related QOL and comprises eight dimensions (Independent Living, Happiness, Mental Health, Coping, Relationships, Self-worth, Pain, Senses). The AQoL-8D has demonstrated strong psychometric properties including content validity (Hawthorne & Osborne, 2005; Richardson et al., 2014), construct validity and discriminative validity in osteoarthritis (Whitfield et al., 2006). An AQoL utility value is calculated where 1.00 and 0.00 represent full health and worst possible health, respectively. Summary scores can also be calculated, the ‘Physical super-dimension’ (covering independent living, pain and senses) and the ‘Mental super-dimension’ covering mental health, happiness, coping, relationships and self-worth. The minimal important difference in AQoL scores is considered to be 0.06 utility points (Hawthorne & Osborne, 2005).
**Psychological health**

The HADS is comprised of 14 questions, 7 that evaluate depression, and 7 that evaluate anxiety. Higher scores indicate greater impairment, with a maximum anxiety or depression score of 21. Scores of 0 to 7 indicate no impairment, 8 to 10 a borderline case, and 11 or greater suggest the responder has depression or anxiety (Snaith, 2003). The HADS has demonstrated strong internal consistency, concurrent validity, sensitivity and specificity in assessing the symptom severity and presence of depression and anxiety disorders in a range of disease-specific patient groups and in the general population (Bjelland, Dahl, Haug, & Neckelmann, 2002).

**Work Limitations**

The WALS is the preferred instrument for measuring productivity in workers with osteoarthritis and is highly responsive to change in work ability over time (Tang et al., 2013). The WALS is comprised of 12 questions; each question addresses activity specific work-related difficulties. Responses range from ‘no difficulty’ to ‘not able to do’ and higher scores indicate greater impairment.

**Data and statistical analysis**

All variables were normally distributed and independent t-tests were conducted to examine differences in demographic characteristics between participants and ineligible asymptomatic individuals. For the multivariable analyses, to avoid unnecessary adjustment of variables and potential over-adjustment bias (Schisterman, Cole, & Platt, 2009) direct acyclic diagrams (featuring hypothesised causal relationships between variables) were used to identify covariates for inclusion in regression analysis (Shrier & Platt, 2008). In line with the study aims, we focused on identifying variables that may be assessed at any time after ACLR (such as return to sport and surgical delay) rather than patient reported outcomes measured at the same time as QOL. The reasoning for this was that strong associations between patient reported outcomes assessed concurrently are expected and of limited clinical importance due to
overlapping constructs in measures. Justification and selection of potential explanatory variables for use in causal diagrams were based upon current literature findings and clinical reasoning, whereby all variables with a potential to impact on longer-term QOL or psychological health were included. This resulted in the inclusion of theoretically meaningful variables in the absence of statistical significance exploration (Shmueli, 2010). Any variables that were not a direct or indirect cause of an exposure, outcome or covariate were excluded from further analyses (Shrier & Platt, 2008). This process resulted in the identification of six explanatory variables (years since ACLR, time from ACL injury to ACLR, revision ACLR, contralateral ACLR, subsequent surgery, return to sport) and three demographic variables (BMI, age, sex) for use in multivariable analyses. These variables were assessed for collinearity, multicollinearity, univariate and multivariate outliers. Additionally, the normality, homoscedasticity and linearity of residuals were assessed.

To estimate the proportion of variance in QOL and psychological health scores that were accounted for by the explanatory variables, standard linear multiple regression analysis was performed. A sample size of 162 is greater than the minimal sample size recommended to assume a medium sized effect with 10 explanatory variables in multivariable analysis (Tabachnick & Fidell, 2007). We present the unstandardized (B (95% CI)) and standardised coefficients (Beta (β)) for the multivariable analyses. Our recent systematic review found that the KOOS-Pain subscale was closely related to KOOS-QOL scores 5 to 20 years after ACLR (Filbay et al., 2014). We performed a sensitivity analysis adjusting for KOOS-Pain scores (in addition to other explanatory variables) to determine if any relationships remained between explanatory variables and QOL outcomes after accounting for knee pain severity. The results of this sensitivity analysis are reported descriptively and presented in Appendices 6.4 to 6.6.
RESULTS

Recruitment

In total, 212 individuals consented to participate and completed questionnaires (Figure 6.1). Of these, 50 were excluded due to co-morbidities, not completing the KOOS or not meeting the predefined KOOS cut-off criteria (Figure 6.1). KOOS subscale scores are reported in Figure 6.2. Asymptomatic individuals did not differ in age, follow-up duration, BMI, or gender from eligible participants (p > 0.16 for all analyses). Data were available for analysis from 162 eligible participants, of which 83% were recruited from the records of four orthopaedic knee surgeons and 17% recruited through community advertisements.

Figure 6.1 Recruitment flow chart
Participant characteristics

Questionnaires were completed on average 9 ± 4 years (range 5 to 20 years) following participants’ most recent ACLR. The mean age of participants at the time of questionnaire completion was 38 ± 9 (range 20 to 55) years and 54% were male. The majority of participants were in paid employment (91%) and over half had children (56%). Twenty-three participants (14%) had a revision ACLR more than 5 years ago, and 18 individuals (11%) reported having a previous ACLR on the contralateral knee; these individuals answered questions regarding their most symptomatic knee. One in two participants (48%) had received at least one additional knee surgery (not including revision ACLR or concomitant surgery performed at the time of primary or revision ACLR). Collectively, participants reported playing 26 different sports at the time of ACL rupture, the most common were netball (20%), rugby (11%), Australian rules football (11%), soccer/futsal (16%) basketball (9%), snow/water skiing (8%), and touch football (6%). Only one participant was not taking part in competitive sport at the time of ACL injury. Sixty-three (39%) participants returned to competitive sport after ACLR, 46 (28%) returned at a lower level of competition and 52 (32%) did not return to competitive sport following ACLR. One in two participants nominated sport as the activity they would prefer to participate in, in the absence of knee pain or impairment (n=80, 49%). On average, low WALS scores were reported, suggesting few work limitations in this sample (3.9 ± 2.8).

Full participant characteristics are provided in Table 6.1.
<table>
<thead>
<tr>
<th>Table 6.1 Participant characteristics (n=162)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at follow-up (years)</td>
</tr>
<tr>
<td>Gender (% female)</td>
</tr>
<tr>
<td>Follow-up duration (years)</td>
</tr>
<tr>
<td>Body mass index (National Heart Lung and Blood Institute, 1998)</td>
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<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Percentage with children</td>
</tr>
<tr>
<td>Time from injury to surgery</td>
</tr>
<tr>
<td>&lt; 6 months</td>
</tr>
<tr>
<td>&gt; 6 months</td>
</tr>
<tr>
<td>unsure</td>
</tr>
<tr>
<td>Revision ACLR</td>
</tr>
<tr>
<td>Left ACLR</td>
</tr>
<tr>
<td>Right ACLR</td>
</tr>
<tr>
<td>Bilateral ACLR</td>
</tr>
<tr>
<td>Subsequent surgery</td>
</tr>
<tr>
<td>Contact injury</td>
</tr>
<tr>
<td>Return to sport rates</td>
</tr>
<tr>
<td>same or higher level than before ACL injury</td>
</tr>
<tr>
<td>lower level than before ACL injury</td>
</tr>
<tr>
<td>did not return to sport after ACLR</td>
</tr>
<tr>
<td>not applicable</td>
</tr>
<tr>
<td>Return to sport at lower level or not at all due to knee</td>
</tr>
<tr>
<td>Currently receives knee treatment</td>
</tr>
<tr>
<td>Pain/impairment free participation preference (%)</td>
</tr>
<tr>
<td>family duties</td>
</tr>
<tr>
<td>social activities</td>
</tr>
<tr>
<td>work</td>
</tr>
<tr>
<td>sport</td>
</tr>
<tr>
<td>exercise</td>
</tr>
<tr>
<td>Current work status (%)</td>
</tr>
<tr>
<td>full-time</td>
</tr>
<tr>
<td>part-time/casual</td>
</tr>
<tr>
<td>student</td>
</tr>
<tr>
<td>stay at home parent/carer</td>
</tr>
<tr>
<td>unemployed</td>
</tr>
<tr>
<td>Work Activity Limitation Scale score</td>
</tr>
</tbody>
</table>

ACLR: anterior cruciate ligament reconstruction; Revision ACLR: percent having one or more revision ACLR; Bilateral ACLR: percent having at least one ACLR on each knee; Subsequent surgery: percent having at least one additional knee surgery to an ACL-reconstructed knee (excluding revision ACLR or concomitant surgery performed at the time of primary or revision.
All results are reported as mean ± standard deviation, or percentage and corresponding number of participants reporting each response.

Patient-reported outcomes

Knee-related QOL

Participants reported a mean KOOS-QOL score of 55 ± 20, indicating impaired knee-related QOL (Figure 6.2). A mean ACL-QOL score of 57 ± 21 was reported, further indicative of impaired knee-related QOL; the domain with greatest impairment was sport and recreational function (41 ± 28) and the least impaired domain was work-related concerns (78 ± 21) (Figure 6.3). The single-item knee-related QOL question showed that 17% of participants did not perceive their knee as having an impact on their current QOL, 45% reported a slight impact, 28% a moderate impact and 10% reported that their knee significantly impacted their QOL.

Figure 6.2 KOOS mean scores (boxes) and SDs (whiskers)
n=162; a lower score indicates poorer outcomes in all subscales; SD: standard deviation; ADL: Activities of Daily Living; Sport/Rec: function in Sport and Recreation; QOL: Quality of Life; KOOS: Knee Injury and Osteoarthritis Outcome Score

Figure 6.3 ACL-QOL mean domain scores (bars) and SDs (whiskers)

n=161; SD: standard deviation; a lower score indicates poorer outcomes in all domains; ACL-QOL: Quality of Life Assessment in Anterior Cruciate Ligament Deficiency questionnaire; Sport/Rec: function in Sport and Recreation

**Health-related QOL**

Participants reported an average AQoL-8D utility score of $0.80 \pm 0.14$, super dimension mental score of $0.50 \pm 0.19$ and super dimension physical score of $0.76 \pm 0.14$ (Figure 6.4).
Figure 6.4 AQoL-8D mean dimension scores and utility scores (bars) and SDs (whiskers)

n=161; AQoL-8D: Assessment of Quality of Life 8D Utility Instrument; SD: standard deviation; utility scores of 1.0 represent full health and 0.0 worst possible health

Psychological health

Participants reported an average HADS anxiety score of $5.5 \pm 3.7$ and HADS depression score of $2.7 \pm 2.6$. According to published criteria (Snaith, 2003) 93% of participants did not have scores indicative of depression, 10 people (6%) had scores indicating borderline depression, and 2 people (1%) had scores corresponding to symptoms of clinical depression. For items pertaining to anxiety, 73% of participants reported scores reflecting no anxiety, 19% reported scores corresponding to borderline anxiety and 4 people (2%) could be considered likely to have anxiety (Snaith, 2003).
Explaining variability in quality of life and psychological health outcomes

Knee-related QOL

Multivariable analysis showed that non-return to sport (compared with returning to sport at the same or higher level), higher BMI and subsequent surgery were independently associated with poorer KOOS-QOL scores. Together, all variables accounted for an estimated 24% of the variability in KOOS-QOL scores (Table 6.2). Return to sport explained the greatest proportion of variance in KOOS-QOL scores ($\beta = .29$, $p = 0.001$) where returning to sport at the same or higher level predicted an estimated 12 points higher KOOS-QOL score, compared to not returning to sport after ACLR. All three variables remained significant explanatory factors after adjusting for KOOS-Pain scores, even though pain explained a large amount of variance in KOOS-QOL scores (Appendix 6.4).

Non-return to sport (compared with return to sport at any level), higher BMI, subsequent knee surgery and contralateral ACLR were independently associated with worse ACL-QOL scores. Specifically, all variables in combination accounted for 36% of the variability in ACL-QOL scores (Table 6.2). Return to sport (at the same or higher level) explained the greatest proportion of variance in ACL-QOL scores ($\beta = .48$, $p < 0.001$), where returning to sport predicted an estimated 21 point higher ACL-QOL score, compared to those who did not return to sport. After adjustment for KOOS-Pain scores, BMI no longer explained ACL-QOL scores ($\beta = -.11$, $p = 0.06$), and waiting greater than six months from injury to surgery was found to be significantly associated with worse ACL-QOL scores ($\beta = -.13$, $p = 0.03$). Return to sport, subsequent surgery and contralateral injury remained significant explanatory factors after adjustment for KOOS-Pain (Appendix 6.4). Time since ACLR, revision surgery, age and sex were not significantly associated with knee-related QOL outcomes.
### Table 6.2 Knee-related QOL linear regression multivariable analyses

<table>
<thead>
<tr>
<th>Explanatory variables:</th>
<th>KOOS-QOL (n=159)</th>
<th>ACL-QOL (n=158)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI)</td>
<td>Beta (β) p value</td>
</tr>
<tr>
<td>Years since ACLR</td>
<td>-0.3 (-1.1 to 0.6)</td>
<td>-0.05 0.54</td>
</tr>
<tr>
<td>Injury to ACLR</td>
<td>-4.4 (-11.1 to 2.2)</td>
<td>-0.10 0.19</td>
</tr>
<tr>
<td>Revision ACLR</td>
<td>-4.7 (-13.3 to 3.9)</td>
<td>-0.08 0.28</td>
</tr>
<tr>
<td>Contralateral ACLR</td>
<td>-7.4 (-16.3 to 1.6)</td>
<td>-0.12 0.11</td>
</tr>
<tr>
<td>Subsequent surgery</td>
<td>-7.6 (-13.8 to -1.5)</td>
<td>-0.19 0.02</td>
</tr>
<tr>
<td>RTS same/higher level*</td>
<td>12.0 (4.8 to 19.1)</td>
<td>0.29 0.001</td>
</tr>
<tr>
<td>RTS lower level*</td>
<td>0.3 (-7.3 to 7.8)</td>
<td>0.01 0.94</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.9 (-1.4 to -0.3)</td>
<td>-0.24 0.002</td>
</tr>
<tr>
<td>Age</td>
<td>0.1 (-0.2 to 0.5)</td>
<td>0.06 0.45</td>
</tr>
<tr>
<td>Sex</td>
<td>4.7 (-1.1 to 10.5)</td>
<td>0.12 0.11</td>
</tr>
</tbody>
</table>

R² (p value) | 0.24 (p<0.001) | 0.36 (p<0.001)

B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised coefficient; Subsequent surgery: at least one additional knee surgery to an ACL-reconstructed knee (excluding revision ACLR or concomitant surgery performed at the time of primary or revision ACLR); RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; KOOS: Knee Injury and Osteoarthritis Outcome score; ACLQOL: Anterior Cruciate Ligament Quality of Life questionnaire; * Did not return to sport = reference category; Sample size does not equal 162 for these analyses due to n=1 not participating in sport at the time of injury, n=2 selected ‘unsure’ options, and n=1 did not complete the ACLQOL; injury to ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as no=0, yes=1; Sex was coded as male=0, female=1; Years since surgery, BMI and age were continuous variables.

### Health-related quality of life

All explanatory variables in combination explained approximately 19% of the variability in AQoL-8D scores. Return to sport at the same or higher level (compared to not returning to sport at all) and BMI significantly explained the greatest proportion of variance in health-related quality of life.
related QOL scores, where returning to sport predicted an estimated .06 higher AQoL-8D scores compared to those who did not return to sport (Table 6.3). These relationships remained after adjustment for KOOS-Pain (Appendix 6.5).

Table 6.3 Health-related QOL linear regression multivariable analyses

<table>
<thead>
<tr>
<th>Explanatory variables:</th>
<th>B (95% CI)</th>
<th>Beta (β)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years since ACLR</td>
<td>0.00 (-0.0 to 0.0)</td>
<td>-0.05</td>
<td>0.55</td>
</tr>
<tr>
<td>Injury to ACLR</td>
<td>-0.03 (-0.1 to 0.0)</td>
<td>-0.09</td>
<td>0.25</td>
</tr>
<tr>
<td>Revision ACLR</td>
<td>0.05 (0.0 to 0.1)</td>
<td>0.12</td>
<td>0.13</td>
</tr>
<tr>
<td>Contralateral ACLR</td>
<td>0.00 (-0.1 to 0.1)</td>
<td>0.01</td>
<td>0.90</td>
</tr>
<tr>
<td>Subsequent surgery</td>
<td>-0.01 (-0.1 to 0.0)</td>
<td>-0.05</td>
<td>0.54</td>
</tr>
<tr>
<td>RTS same/higher level*</td>
<td>0.06 (0.0 to 0.1)</td>
<td>0.22</td>
<td>0.02</td>
</tr>
<tr>
<td>RTS lower level*</td>
<td>0.00 (-0.1 to 0.1)</td>
<td>0.00</td>
<td>0.96</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.01 (0.0 to 0.0)</td>
<td>-0.24</td>
<td>0.002</td>
</tr>
<tr>
<td>Age</td>
<td>0.00 (0.0 to 0.0)</td>
<td>-0.11</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex</td>
<td>0.01 (0.0 to 0.0)</td>
<td>0.02</td>
<td>0.79</td>
</tr>
</tbody>
</table>

| R² (p value)           | 0.19 (p<0.001) |

B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised coefficient; RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; Subsequent surgery: at least one additional knee surgery to an ACL-reconstructed knee (excluding revision ACLR or concomitant surgery performed at the time of primary or revision ACLR); * Did not return to sport = reference category; Sample size does not equal 162 for these analyses due to n=1 was not participating in sport at the time of injury, n=2 selected ‘unsure’ options, and n=1 did not complete the AQoL-8D; injury to ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as no=0, yes=1; Sex was coded as male=0, female=1; Years since surgery, BMI and age were continuous variables.
Psychological health

In combination, all variables accounted for 18% of variability in HADS depression scores; specifically, male sex and greater BMI were associated with more depressive symptoms, before and after adjustment for KOOS-Pain scores. There was a trend for return to sport at the same or higher level to be associated with less depressive symptoms (p = 0.058). In contrast, none of the included variables significantly explained the variability in HADS anxiety scores (Table 6.4). KOOS-Pain did not explain a significant proportion of variance in HADS anxiety or depression scores in a multivariable model (Appendix 6.6).

Table 6.4 Psychological health linear regression multivariable analyses

<table>
<thead>
<tr>
<th>Explanatory variables:</th>
<th>HADS Depression (n=158)</th>
<th></th>
<th>HADS Anxiety (n=158)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI)</td>
<td>Beta (β)</td>
<td>p value</td>
<td>B (95% CI)</td>
</tr>
<tr>
<td>Years since ACLR</td>
<td>0.07 (-0.1 to 0.2)</td>
<td>0.10</td>
<td>0.24</td>
<td>0.06 (-0.1 to 0.2)</td>
</tr>
<tr>
<td>Injury to ACLR</td>
<td>0.68 (-0.2 to 1.6)</td>
<td>0.12</td>
<td>0.14</td>
<td>0.29 (-1.1 to 1.6)</td>
</tr>
<tr>
<td>Revision ACLR</td>
<td>-0.30 (-1.5 to 0.9)</td>
<td>-0.04</td>
<td>0.62</td>
<td>0.36 (-1.4 to 2.2)</td>
</tr>
<tr>
<td>Contralateral ACLR</td>
<td>0.16 (-1.0 to 1.4)</td>
<td>0.02</td>
<td>0.79</td>
<td>-1.32 (-3.1 to 0.5)</td>
</tr>
<tr>
<td>Subsequent surgery</td>
<td>0.34 (-0.5 to 1.2)</td>
<td>0.06</td>
<td>0.43</td>
<td>-0.62 (-1.9 to 0.6)</td>
</tr>
<tr>
<td>RTS same/higher level*</td>
<td>-0.94 (-1.9 to 0.0)</td>
<td>-0.18</td>
<td>0.06</td>
<td>-0.65 (-2.1 to 0.8)</td>
</tr>
<tr>
<td>RTS lower level*</td>
<td>-0.68 (-1.7 to 0.3)</td>
<td>-0.12</td>
<td>0.19</td>
<td>0.44 (-1.1 to 2.0)</td>
</tr>
<tr>
<td>BMI</td>
<td><strong>0.11 (-0.4 to 0.2)</strong></td>
<td><strong>0.24</strong></td>
<td><strong>0.003</strong></td>
<td>0.06 (-0.5 to 0.2)</td>
</tr>
<tr>
<td>Age</td>
<td>0.01 (-0.0 to 0.1)</td>
<td>0.02</td>
<td>0.77</td>
<td>-0.05 (-0.1 to 0.0)</td>
</tr>
<tr>
<td>Sex</td>
<td><strong>-0.94 (-1.7 to -0.2)</strong></td>
<td><strong>-0.18</strong></td>
<td><strong>0.02</strong></td>
<td>0.24 (-1.0 to 1.4)</td>
</tr>
</tbody>
</table>

R² (p value) | 0.18 (p=0.001) | 0.07 (p=0.39)

B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised coefficient; Subsequent surgery: at least one additional knee surgery to an ACL-reconstructed knee (excluding revision ACLR or concomitant surgery performed at the time of primary or revision ACLR); RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; HADS: Hospital Anxiety and Depression Scale. * Did not return to
sport = reference category; Sample size does not equal 162 for these analyses due to n=1 was not participating in sport at the time of injury, n=2 selected ‘unsure’ options, and n=1 did not complete the HADS; injury to ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as no=0, yes=1; Sex was coded as male=0, female=1; Years since surgery, BMI and age were continuous variables.

DISCUSSION

Returning to sport at the same or higher level was related to better knee-related and general health-related QOL in people with knee difficulties 5 to 20 years after ACLR. This relationship remained after adjusting for KOOS-Pain scores despite a clear relationship between knee pain and QOL. We also found that few participants reported work limitations or depressive symptoms and these are positive findings considering all participants experienced some degree of knee difficulties. Subsequent surgery, increased BMI and contralateral ACLR were associated with poorer scores on one or more QOL measures. Higher BMI and male sex were associated with more depressive symptoms. Age, gender, time since surgery and revision ACLR were not associated with QOL or psychological health outcomes in individuals with knee difficulties after ACLR.

KOOS-QOL scores in individuals with knee difficulties more than five years following ACLR were impaired compared with Swedish population norms aged 18 to 54 years (Paradowski et al., 2006), amateur soccer players with minor (14%), severe (23%), or no (63%) history of knee injury (Frobell et al., 2008), and U.S military recruits with no history of knee ligament injury (Cameron et al., 2013). A mean AQOL-8D utility score of 0.80 ± 0.14 reported by participants in this study is similar to the mean score reported by Australians who rated their health status as ‘good’ (mean 0.81 ± 0.19) as opposed to ‘excellent’ (0.91 ± 0.14), ‘very good’ (0.88 ± 0.14), ‘fair’ (0.68 ± 0.23), or ‘poor’ (0.42 ± 0.30) in an earlier population-based study (Hawthorne & Osborne, 2005). Unfortunately no physically active reference groups, who are likely to report
higher health-related QOL than less active counterparts (Huffman et al., 2008) were available for comparison.

This is the first study to evaluate the relationship between return to sport and longer-term QOL after ACLR. We did not expect to find such consistent relationships between return to sport and QOL outcomes 5 to 20 years after ACLR in people with knee difficulties. Although return to sport was associated with better QOL, the longer-term impact of returning to sport with knee difficulties on future joint health should be considered (Culvenor & Crossley, 2015). The high rate of participants reporting a preference to take part in sport in the absence of knee difficulties, over and above other activities including family or occupational duties, suggests that sport participation remains a priority for many individuals. Despite this, one in three participants did not return to any level of competitive sport after ACLR and 79% of individuals reported their knee as the reason for not returning to pre-injury sport. This potential mismatch between sporting desires and outcomes in people with knee difficulties may have contributed to the observed impairment in QOL. A study exploring pre-operative expectations of ACLR found that 91% of participants expected to return to sport one year following surgery with no or slight restrictions (Feucht et al., 2014). This contrasts with the actual return to sport rates in our cohort and findings from a recent literature review (Ardern et al., 2014b). Notably, health-related QOL has been described as ‘the gap between our expectations of health and our experience of it’ (Carr et al., 2001) and discordance between surgical expectations and actual outcomes may have contributed to the identified impairments in QOL.

Average HADS depression scores for this sample were less impaired than published population norms (Breeman, Cotton, Fielding, & Jones, 2015; Mutrie & Hannah, 2007). The low rates of depression in this sample of individuals living with knee difficulties might reflect a response shift and accommodation to knee difficulties overtime. Lower rates of depressive symptoms have been associated with higher rates of moderate-to-vigorous physical activity and sports participation (Brunet et al., 2013; Mutrie & Hannah, 2007; Pinto Pereira, Geoffroy, & Power, 2014; Sabiston et al., 2013). We found that people with knee difficulties who returned to the same or higher level of sport after ACLR tended to report less depressive symptoms compared
with those who did not return to sport (B (95% CI) -0.94 (-1.9 to 0.0), p = 0.06). Furthermore, a large study of similarly aged participants identified physical activity as a key factor contributing to the observed relationship between obesity and increased rates of depression (de Wit, Fokkema, van Straten, & Lamers, 2010). It is possible that for some individuals, ceasing sport resulted in reduced levels of moderate-to-vigorous physical activity, which could be associated with weight gain, depressive symptoms and reduced QOL. Further research is needed to explore these relationships as we did not collect longitudinal data on physical activity levels, dietary intake or pre-injury BMI. Of concern is that over half the study participants were overweight or obese at the time of questionnaire completion and higher BMI was associated with worse QOL. Management strategies aimed at improving QOL following ACLR could include weight maintenance strategies, addressing barriers to returning to sport or facilitating a transition to a healthy lifestyle incorporating regular moderate-to-vigorous physical activity when ceasing sport participation.

A key strength of this study was the use of patient-reported measures and the inclusion of knee-specific, ACL-specific and generic (non-disease-specific) health-related QOL measures that provided complementary information and enabled a comprehensive picture of QOL to be generated. We also included a custom QOL question that enabled each individual to evaluate the impact of their knee on their QOL in the context of their personal goals, priorities and values. To minimise selection bias, we included recruitment of participants from community advertisements and these participants did not differ in age, gender, BMI or follow-up duration to participants recruited through orthopaedic surgeons’ records. Nevertheless, as most participants were recruited through orthopaedic surgeons, a degree of selection bias may exist. These surgeons worked in the private health care system and consequently, these findings may not be generalisable to people undergoing ACLR in public hospital settings. Furthermore, the results of this study are not generalisable to all ACL-reconstructed individuals, as we only included individuals reporting knee pain, symptoms or activity limitations. This was the first study to explore QOL in people with knee difficulties after ACLR, enabling the identification of relationships that may not have been evident in previous studies and potential targets for clinical management.
We acknowledge the potential for recall bias relating to questions that required participants to answer retrospectively (for example, mechanism of injury, time from injury to surgery). We sought to minimise the likelihood of recall error by including an ‘unsure’ response option for these items. We collected limited information regarding return to sport, consequently, details of return to sport including duration of sport participation after ACLR and whether the individual returned to training or match play remain unknown. Due to the cross-sectional study design, we were unable to make any causal inferences and due to the nature of recruitment, we could not collect detailed data for all participants on surgical techniques or concomitant surgeries. However, all participants recruited through orthopaedic surgeons underwent a hamstring or patellar tendon autograft ACLR, and no differences in QOL have been reported between these techniques 5 to 20 years following ACLR (Filbay et al., 2014). We also acknowledge that KOOS-QOL and ACL-QOL scores may be negatively biased by sport-related lifestyle modifications or difficulty participating in sport. Due to the nature of questions in these measures, sport-related limitations would result in reduced QOL scores irrespective of the importance that each individual places on sport participation.

CONCLUSION

Poorer longer-term QOL outcomes were related to not returning to sport, higher BMI, contralateral ACLR and subsequent knee surgery in people with knee difficulties 5 to 20 years after ACLR, and return to sport explained the greatest variability in QOL. Individuals with knee difficulties who do not return to sport may benefit from targeted strategies to optimise longer-term QOL following ACLR.
PERSONAL PERSPECTIVES ON QUALITY OF LIFE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN PEOPLE WITH KNEE DIFFICULTIES: A QUALITATIVE STUDY


INTRODUCTION

Anterior cruciate ligament rupture most commonly occurs in adolescents and young adults during competitive sport participation (Granan et al., 2009; Janssen et al., 2012; Renstrom et al., 2008). Estimates of ACLR prevalence reveal an alarmingly high rate of ACLR in Australia, exceeding other countries with a rate of 52 per 100,000 inhabitants (Csintalan, 2008; Gianotti et al., 2009; Granan et al., 2008; Granan et al., 2009; Janssen et al., 2012; Lind et al., 2009). Optimising longer-term QOL following ACLR is important, considering the potential for persistent physical and psychological difficulties and the high rates of early-onset knee osteoarthritis after ACL injury (Ardern, Taylor, Feller, & Webster, 2012b; Arderen et al., 2014b; Kvist et al., 2005; Lohmander et al., 2004; Øiestad et al., 2009). Of further concern is that as many as 1 in 5 ACL-reconstructed individuals undergo subsequent knee surgery within 6 years.
of ACLR (Hettrich et al., 2013) and 1 in every 4 individuals may experience an ACL graft rupture or contralateral ACL rupture within 15 years of ACLR (Bourke et al., 2012). Subsequent knee surgery including revision ACLR and contralateral ACLR are associated with worse patient-reported outcomes including reduced longer-term QOL (Ahlden et al., 2012; Faltstrom, Hagglund, & Kvist, 2013; Gifstad et al., 2012a; Kievit et al., 2013; Lind et al., 2012; Möller et al., 2009; Wasserstein et al., 2015). Our systematic review reported impaired knee-related QOL 5 to 20 years after ACLR (Filbay et al., 2014), but we did not identify any studies investigating the impact of return to sport on longer-term QOL following ACLR. This is despite less than half of non-elite sports participants returning to competitive sport after ACLR (Ardern et al., 2014b), which contrasts most patients’ expectations of full return to sport within one year of surgery (Feucht et al., 2014). Young, active individuals undergoing ACLR commonly have unrealistic expectations (including a low likelihood of ongoing pain or instability and a low risk of developing post-traumatic osteoarthritis (Feucht et al., 2014)) and these may impact on their QOL outcomes.

Current patient-reported measures of QOL have limited ability to capture individual expectations, and do not specifically evaluate the importance of knee-related impairments to the individual (Carr & Higginson, 2001; Carr et al., 2001). Despite the breadth of quantitative ACL injury literature, qualitative studies exploring personal perspectives following ACLR are rare and no qualitative studies have investigated QOL following ACLR. Past qualitative studies have focused on return to sport following ACLR (Carson & Polman, 2012; Nordahl, Sjostrom, Westin, Werner, & Alricsson, 2014; Thing, 2006; Tjong, Murnagahan, Nyhof-Young, & Ogilvie-Harris, 2014). One study identified fear, a change in life priorities, and personality traits as factors that influenced an individual’s decision to return to sport after ACLR (Tjong et al., 2014). Two small studies of five rugby players (Carson & Polman, 2012) and five elite adolescent alpine skiers (Nordahl et al., 2014) identified high knee confidence as a key facilitator and low knee confidence as a key barrier to return to play (Carson & Polman, 2012; Nordahl et al., 2014). Similarly, a study interviewing 17 female handball players described confidence in the capabilities of one’s body as a key factor influencing decisions to return to sport after ACLR (Thing, 2006). While several qualitative studies have investigated factors influencing the decision to return to sport after ACLR, it is not clear how these factors impact...
longer-term QOL, particularly among people with ongoing knee symptoms or activity limitations (Carson & Polman, 2012; Nordahl et al., 2014; Thing, 2006; Tjong et al., 2014). Qualitative research could enhance our understanding of factors impacting negatively upon QOL after ACLR and provide information to guide management strategies for optimising outcomes following ACL injury.

The research questions for this study were:

1. How do individuals with knee difficulties describe their QOL and experiences 5 to 20 years after ACLR?

2. What factors impact upon QOL in people with knee difficulties 5 to 20 years following ACLR?
METHODS

Participants

Participants for qualitative interviews were purposively sampled from a larger cross-sectional study of 162 individuals who had undergone ACLR 5 to 20 years previously (Filbay, Ackerman, Russell, & Crossley, 2015). The eligibility criteria for this cross-sectional study required all participants to (i) be aged 18 to 55 years, (ii) have received an ACLR or revision surgery 5 to 20 years previously, and (iii) report knee symptoms or functional limitations on the KOOS, determined by predefined cut-off criteria (Chapter 6). This cut-off criteria required reporting less than optimal scores for at least 50% of questions on any two KOOS subscales (corresponding to cut-off values of ≤86.1 (Pain), ≤85.7 (Symptoms), ≤86.8 (ADL), ≤85.0 (Sport/Rec), and ≤87.5 (QOL)). Recruitment details and participant characteristics for the cross-sectional study have been described previously (Chapter 6). These 162 participants completed a battery of questionnaires including the KOOS and the ACL-QOL which are valid and reliable for use in ACL-reconstructed individuals (Mohtadi, 1998; Roos & Lohmander, 2003; Salavati et al., 2011). Demographic, lifestyle and return to sport data were also collected and relevant questionnaire responses from the cross-sectional study are presented for each interviewee (Table 7.1).
To enable comparisons between individuals with high and low knee-related QOL, we specifically sampled those with high or low ACL-QOL scores. Participant ACL-QOL scores were ranked and the first individuals selected for the qualitative study were those with ACL-QOL scores in the 10th and 90th percentiles, followed by those with the next highest and lowest ACL-QOL scores, respectively. In total, 16 people with high ACL-QOL scores (score range 82 to 92) and 14 people with low ACL-QOL scores (score range 25 to 30) were sent an email invitation to take part in a telephone interview. Of these, five declined due to other commitments (four with high ACL-QOL scores and one with a low ACL-QOL score) and eight did not respond (four from each group). All individuals who agreed to take part were interviewed for this study, resulting in 17 interviews (8 individuals with a high ACL-QOL score and 9 individuals with a low ACL-QOL score). To determine an appropriate sample size, we ceased recruitment when no new themes emerged over two consecutive interviews for participants with high ACL-QOL scores and for participants with low ACL-QOL scores.

**Design**

The interviews were conducted from August to October 2014, after obtaining informed verbal consent from each individual. Two pilot interviews were conducted to refine the broad areas to be covered, the structural order and outline of the interview. Semi-structured telephone interviews were performed and the audio recordings transcribed by a single investigator (S.F). The interviewer (S.F) had no involvement with the clinical care of any study participants. All transcripts were de-identified, and each interviewee was assigned an alias for use in data transcription and reporting. Interview duration ranged from 16 to 41 minutes.

A standardised semi-structured interview guide (Appendix 7.1) provided the framework for each interview, which covered four broad areas: (i) peri-operative experiences (including ACL injury and initial management; satisfaction with surgery and health-care providers; ACLR preparation, expectations and experience; and post-operative experiences); (ii) sport and exercise (including return to sport; experiences of sport and exercise participation; physical activity priorities, motives and importance across the lifespan); (iii) psychological impacts
(including emotions, fears and knee confidence); (iv) current experience (including current knee symptoms and function; lifestyle modifications; management strategies; knowledge and information). The semi-structured interviews were shaped by the responses provided by the interviewees, enabling the researcher to adapt the interview guide to elicit the most useful information from each respondent. This enabled omission of questions answered in a previous response and the addition of specific prompts, as required, to gain more detailed information (Jones, Brown, & Holloway, 2012). Participants were also given the opportunity to contribute any additional information at the end of the interview.

Data analysis

The first stage of data analysis involved general inductive thematic analysis, where multiple readings, reviewing and data interpretation was undertaken to identify themes arising from the data (Braun & Clarke, 2006; Thomas, 2006). Inductive coding was supported by NVivo version 10 software (Bazeley & Jackson, 2013). In line with an inductive thematic approach, coding was data-driven, performed without reference to a pre-existing coding structure (Braun & Clarke, 2006). Coding was performed diversely and inclusively, enabling exploration of all important themes relevant to the study aims (Braun & Clarke, 2006). The coding process resulted in the identification of key themes and sub-themes. The coding structure was revised and refined throughout the data interpretation process to reduce redundancy, identify new emerging sub-categories and incorporate new themes and insights. A hierarchical approach to coding was used, linking themes with a commonality or causal relationship to assist with pattern recognition (Bazeley & Jackson, 2013). During refinement, the prevalence of themes was considered with regard to the number of different participants who articulated a theme, although this was not a critical component of the analysis (Braun & Clarke, 2006). Following a minimum of two rounds of coding and analysis by a single investigator (S.F), a second investigator coded a random sample of six interview transcripts (I.A) and any contrasting opinions in identified themes were discussed. Where possible, conceptual maps were developed to assist with data interpretation and provide potential explanations for key themes.
RESULTS

Participants

Interview data were available from 17 participants. Individuals with low ACL-QOL scores had a mean age of 36 (SD 8, range 25 to 50) years, 56% were male, 78% were overweight or obese, and these participants had received their most recent ACLR an average of 10 (SD 5, range 6 to 18) years previously. In comparison, those reporting high ACL-QOL scores had a similar mean age of 37 (SD 10, range 23 to 50 years), 38% were male, fewer were classified as overweight or obese (38%), and a similar mean 9 years (SD 5, range 5 to 18 years) since ACLR was reported. Participant characteristics are reported in Table 7.1 and patient-reported outcomes are described in Table 7.2.
Table 7.1 Participant characteristics

<table>
<thead>
<tr>
<th>ID</th>
<th>ACL QOL</th>
<th>Age</th>
<th>Years since last ACLR</th>
<th>Sex</th>
<th>BMI</th>
<th>Return to sport</th>
<th>ACLR type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucy</td>
<td>25</td>
<td>33</td>
<td>6</td>
<td>F</td>
<td>normal</td>
<td>lower</td>
<td>primary</td>
</tr>
<tr>
<td>Flynn</td>
<td>26</td>
<td>44</td>
<td>16</td>
<td>M</td>
<td>obese</td>
<td>no</td>
<td>revision x 2</td>
</tr>
<tr>
<td>Sue</td>
<td>26</td>
<td>41</td>
<td>18</td>
<td>F</td>
<td>obese</td>
<td>no</td>
<td>primary</td>
</tr>
<tr>
<td>Claire</td>
<td>27</td>
<td>34</td>
<td>6</td>
<td>F</td>
<td>obese</td>
<td>no</td>
<td>primary</td>
</tr>
<tr>
<td>Will</td>
<td>27</td>
<td>50</td>
<td>12</td>
<td>M</td>
<td>normal</td>
<td>lower</td>
<td>primary</td>
</tr>
<tr>
<td>Kate</td>
<td>28</td>
<td>26</td>
<td>12</td>
<td>F</td>
<td>obese</td>
<td>lower</td>
<td>primary</td>
</tr>
<tr>
<td>Jack</td>
<td>29</td>
<td>41</td>
<td>11</td>
<td>M</td>
<td>overweight</td>
<td>lower</td>
<td>contra</td>
</tr>
<tr>
<td>Nick</td>
<td>29</td>
<td>25</td>
<td>6</td>
<td>M</td>
<td>obese</td>
<td>yes</td>
<td>contra</td>
</tr>
<tr>
<td>Hugh</td>
<td>30</td>
<td>32</td>
<td>6</td>
<td>M</td>
<td>overweight</td>
<td>lower</td>
<td>revision + contra</td>
</tr>
<tr>
<td>Zara</td>
<td>83</td>
<td>50</td>
<td>13</td>
<td>F</td>
<td>obese</td>
<td>yes</td>
<td>primary</td>
</tr>
<tr>
<td>Ross</td>
<td>83</td>
<td>35</td>
<td>6</td>
<td>M</td>
<td>overweight</td>
<td>yes</td>
<td>primary</td>
</tr>
<tr>
<td>Beth</td>
<td>86</td>
<td>49</td>
<td>5</td>
<td>F</td>
<td>normal</td>
<td>yes</td>
<td>primary</td>
</tr>
<tr>
<td>Amy</td>
<td>87</td>
<td>28</td>
<td>10</td>
<td>F</td>
<td>normal</td>
<td>lower</td>
<td>primary</td>
</tr>
<tr>
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ID: de-identified name; ACLQOL: ACL-QOL score (0 worst, 100 best); F: female; M: male; Return to sport: participants selected one of the following options - ‘I returned to competitive sport at the same or higher level than before ACL injury’ = Yes, ‘I returned to competitive sport at a lower level than before ACL injury’ = Lower, ‘I did not return to competitive sport after my ACLR’ = No; The horizontal line separates those with low ACL-QOL scores (above) from those with high ACL-QOL scores (below); ACLR: anterior cruciate ligament reconstruction; Contra: contralateral ACLR
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<th>Limitation in most important activity</th>
<th>Current knee satisfaction</th>
<th>KOOS Pain</th>
<th>KOOS Symptoms</th>
<th>KOOS QOL</th>
<th>Trouble with knee confidence</th>
<th>Lifestyle modification</th>
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<td>54</td>
<td>81</td>
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</table>

ID: de-identified name; Most important activity: ACL-QOL Q19 ‘the most important sport/recreational activity that you do or wish to do’; Limitation in most important activity: ‘how limited are you in playing that number one sport or activity?’ answers range from 0 (totally limited) to 100 (not limited); Current knee satisfaction: Taking into account your level of pain and also your functional impairment, if you were to remain for the next few months as you are today, would you consider that your current state is satisfactory?; KOOS: Knee-injury and Osteoarthritis Outcome Score (domain scores range 0 (worst) to 100 (best); Trouble with knee confidence: KOOS-QOL Q3: ‘How much are you troubled with lack of confidence in your knee?’ (not at all, mildly, moderately, severely or extremely); Lifestyle modifications: KOOS-QOL Q2: ‘Have you modified your lifestyle to avoid potentially damaging activities to your knee?’ (not at all, mildly, moderately, severely or totally); The horizontal line separates low ACL-QOL scores (above) from high ACL-QOL scores (below).
Key themes

Four key themes emerged from the interviews: physical activity preferences, lifestyle modifications, adaptation and acceptance, and fear of re-injury (Table 7.3). These themes and related sub-themes are described with supporting quotes from the interviews in the following sections.

Table 7.3 An overview of common themes related to QOL

<table>
<thead>
<tr>
<th>Theme</th>
<th>Sub-theme</th>
<th>Low ACLQOL</th>
<th>High ACLQOL</th>
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<tr>
<td>Physical activity preferences</td>
<td>Preference for competitive sport</td>
<td>n=9</td>
<td>n=2</td>
</tr>
<tr>
<td></td>
<td>Enjoys recreational exercise</td>
<td>n=6</td>
<td></td>
</tr>
<tr>
<td>Lifestyle modifications¹</td>
<td>Negative lifestyle modifications</td>
<td>n=6</td>
<td>n=1</td>
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<tr>
<td></td>
<td>Positive lifestyle modifications</td>
<td>n=3</td>
<td>n=7</td>
</tr>
<tr>
<td>Adaptation and acceptance</td>
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<td>n=7</td>
<td>n=5</td>
</tr>
<tr>
<td></td>
<td>Delayed adaptation</td>
<td>n=7</td>
<td>n=1</td>
</tr>
<tr>
<td></td>
<td>No adaptation</td>
<td>n=2</td>
<td>n=2</td>
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<tr>
<td>Fear of re-injury²</td>
<td>Fear accommodation</td>
<td>n=5</td>
<td>n=4</td>
</tr>
<tr>
<td></td>
<td>Fear suppression</td>
<td>n=4</td>
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</tr>
<tr>
<td></td>
<td>Fear avoidance</td>
<td>n=5</td>
<td>n=4</td>
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Note, some participants described transitioning between sub-themes overtime:
¹ Within the theme of lifestyle modifications: n=4 participants made negative lifestyle modifications for years but had made positive lifestyle modifications at the time of interview;
² Within the theme of fear of re-injury: n=6 described fear-suppression or avoidance behaviours for years but had developed fear-accommodation behaviours at the time of interview.
Physical activity preferences

Within the theme of physical activity preferences, two contrasting sub-themes were apparent from the interviews. The first involved 11 individuals who described a strong preference for participation in competitive sports in comparison to recreational exercise.

“I do love netball. I hate the gym. Absolutely hate it. It makes it pretty hard when you can’t play the sports that you love, which I don’t consider to really be exercise, and you’ve got to find alternatives to exercise which I can’t stand.” (Claire)

“I just stopped playing all sport and became a lot less physically active and was quite unfit as well, but about a year or two ago I decided to take some form of sport back up. I wouldn’t say I was playing very successfully, I was in a lot of pain and I wasn’t moving very well at all but it was better than not playing any sport.” (Hugh)

“Was competitive sport the easiest and the best way for you to exercise?” (Interviewer)

“Yep, yep, very much so. I couldn’t find gym work or cardio very enjoyable. There was only so much of it I could do… it was just tiring to get in there and do that, do things like that, over and over again, like the same exercises over and over again.” (Hugh)

The contrasting sub-theme comprised a group of six individuals who preferred, enjoyed or were satisfied taking part in non-competitive recreational exercise. While some of these individuals had participated in team sports in the past, they did not display a strong preference for returning to competitive sport and described satisfaction with being physically active through recreational exercise.

“Oh look I probably could have played, but to me that was a fairly major injury that had me off for a long time, from doing exercise, and the exercise that I like doing (recreational exercise), and I said I didn’t want to risk doing it a second time.” (Beth)
“I didn't actually do sport (at school). I was maybe a bit shy and you had to be pretty aggressive and competitive, and I, that's not really my personality. I have on and off done stuff and have been involved in aerobics a fair bit. I'd always gone to aerobics and done a fair bit of gym work. I liked doing aerobic activity.” (Zara)

**Lifestyle modifications**

Ten participants reported having modified their way of life because of their knee in ways that had improved their QOL (positive knee-related lifestyle modifications), while seven participants had made lifestyle modifications at some stage after ACLR that impacted negatively upon their QOL (negative knee-related lifestyle modifications) (Table 7.3).

A conceptual diagram summarising the concepts of activity preferences and lifestyle modifications with potential impacts on QOL is presented in Figure 7.1. Six individuals with a preference for competitive sport described transitioning to an inactive lifestyle after sport cessation. For several participants, this resulted in weight gain, exacerbation of knee symptoms and a reduced motivation to exercise with negative impacts on QOL.

“You know I'm disappointed that I didn't go back, and I'm disappointed that I swapped the lifestyle instead of keeping up with the sporting lifestyle, I went to a social lifestyle, and started putting the weight on, because now I'm at the stage where I've got too much weight. I've got worse knee issues. I'm not helping it by being overweight. It certainly made me change my lifestyle.” (Sue)

“What do you do now sport and exercise wise?” (Interviewer)

“Pretty much near nothing. Because I'm not playing sport I drink more and then obviously everything that goes with that, you know, you put on weight, you can't do this you can't do that, you know you've got to exercise and you go, if I do that I'm going in for more surgery.” (Claire)
In contrast, the six individuals who enjoyed recreational exercise were often able to make positive lifestyle modifications. This tended to manifest in a sense of satisfaction with their current knee function and QOL.

“I started doing dancing, that's helped a lot. Now I do Pilates regularly, so that's helped with the movement and kept it going, so I do have fairly good movement now, and I have a fairly active lifestyle.” (Zara)

“If I stick to my regular exercise, it helps me with my knee, in terms of, I don’t feel, I don’t notice any problems with my knee if I exercise regularly. If I have a big break in exercise and I don’t do anything then I do notice that the soreness and the swelling come back after a while.” (Tina)

**Figure 7.1** A conceptual diagram portraying common interactions between activity preferences, lifestyle modifications and quality of life

Red boxes and arrows: represent a current state with a tendency towards poor knee-related quality of life; Green boxes and arrows: represent a current state with a tendency towards
satisfactory knee-related quality of life; Orange arrows: represent periods of transition between green and red states. Note, arrows represent common paths of transition described by study participants; An individual may remain in a given state (box) without transitioning; The direction of arrows represent the most common pathways; ACL: anterior cruciate ligament; RTS: return to sport

**Adaptation and acceptance**

A strong theme of personal adaptation and acceptance also emerged from the interviews. Five individuals described having adapted their lifestyle with ease following ACLR, while eight individuals took years to adapt their lifestyle in line with their knee’s abilities. This delayed adaptation often resulted in a concurrent improvement in satisfaction and QOL. The remaining four individuals did not describe any knee-related lifestyle adaptations during their interview.

**Early adaptation**

A sub-group of five individuals described adapting their lifestyle within a short period of time following ACLR and attaining a state of satisfaction with their knee. For individuals with a preference for recreational exercise, a short transitional period (indicated by orange arrows in Figure 7.1) was more frequently described.
“I was quite happy to give up netball and touch football because I just was not going to go through that again and didn't want to do it again, and switched to cycling and running.” (Beth)

“I tried to get back into it all, but then I guess you just, your heart wasn’t in it anymore because you didn’t want to have to go through that again. I sort of tried to get back to the same level but I didn’t really try, I was going into grade 11 and 12 so I focused more on my school rather than my sport after that.” (Emma)

Delayed adaptation
Eight individuals described knee-related difficulties after surgery, but acknowledged they had grown to accept their current knee state having adapted their lifestyle over a period of years.

“I was about 90 kilos, I was very, very overweight, and like I'm 53kg now. I just started exercising again, and eating well. Since I lost weight, my knee has never locked again. I just decided one day that that was enough and I just started exercising. I've gone from what I feel like 10 per-cent quality of life, to 100% quality of life, for me, being active is everything.” (Lucy)

“I found ways to enjoy sport in a, in a very casual way and because I've lost a lot of weight recently and I've started getting fit again, I'm actually quite positive about my prospects of enjoying sport on a recreational basis over the next few years. Right now, I'm quite happy to be doing the things I'm doing, finding new activities that I can do that are within my capacities but are still enjoyable.” (Hugh)

Fear of re-injury
The final key theme related to a fear of re-injury, which all participants reported they had experienced at some point after ACLR. Participants described their knee-related fears, how
these fears changed over time, and how fear had impacted on their activity choices and QOL. Three common sub-themes emerged in relation to fear of re-injury: (i) fear accommodation (ii) fear suppression, and (iii) fear avoidance. Figure 7.2 provides a conceptual diagram summarising the most common fear of re-injury behaviours in the context of physical activity preferences, lifestyle modifications and potential impacts on QOL.

**Figure 7.2** A conceptual diagram portraying described experiences of fear of re-injury and relationships with lifestyle modifications and quality of life

Red boxes and arrows: represent a current state with a tendency towards poor knee-related quality of life; Green boxes and arrows: represent a current state with a tendency towards satisfactory knee-related quality of life; Note, arrows represent common paths of transition described by study participants; an individual may remain in a given state (box) without transitioning; ACL: anterior cruciate ligament.
**Fear accommodation**

There was a subgroup of participants who, over time, became mindful of their knee-related fears and modified their movement patterns or activity choices to minimise risk of subsequent knee injury. These accommodations enabled individuals to maintain an active lifestyle and participate in desired activities, resulting in satisfaction with current knee function and QOL (Figure 7.2). Three participants made early accommodations after ACLR, while others made delayed accommodations after years of fear-avoidance behaviour (n=3) or after experiencing subsequent knee trauma following return to competitive sport (n=3). This subsequent trauma resulted in increased fear of re-injury, which led to activity modifications that reduced perceived risk of re-injury.

“I had the opportunity to keep going through but then, I was just like well you know, I’ve already had 2, I’m 18 years of age, you know, what sort of future have I got if I blow it out again at 18. ...so I went yeah, no I’m just going to go play back at state level and leave it, and yeah, just walked away.” (Flynn)

“You really need to apply a lot more thought process to what you do rather than just, you know, you take it for granted that people have got good knees, they don’t even think twice about climbing up something, or jumping off something, whereas I look at things differently now and go, well, how do I get up there? Or how do I do that without putting myself in a position where I can hurt my knee? It’s yeah, just more of a thought process.” (Jack)

**Fear suppression**

Six participants with a strong desire to continue participating in high-impact competitive sport described an ability to overcome or suppress initial fear of re-injury in order to continue sport participation. While continuing sport participation, these individuals experienced a satisfactory QOL, irrespective of the presence of physical knee symptoms. However, participating in unrestrictive competitive sport often resulted in subsequent knee trauma, ACL re-rupture or a progressive exacerbation of knee symptoms. As outlined in Figure 7.2, this resulted in one of two transitions: increased knee awareness, delayed activity adaptation and satisfactory QOL (3
participants); or, reduced knee function and adoption of an inactive lifestyle with negative impacts on QOL (3 participants).

“"I adapted my game, I ran in straight lines. I played like that for a long time, for many years, until, umm, I couldn't really run at all, and I was having trouble just walking anywhere, so it had got quite bad."” (Will)

“"It's usually pretty good during the game, and during training and things, it's more, I suppose it doesn't recover very well, it just seems to constantly ache, I think, for a few days after a, after a hard run on it."” (Nick)

**Fear avoidance**

Nine individuals described ceasing sport participation due to a fear of re-injury. Of these, five individuals remained physically active in recreational exercise despite ceasing competitive sport and this had minimal impact on their QOL, while four individuals transitioned to an inactive lifestyle, with further negative impacts on their QOL (Figure 7.2). All individuals who described fear-avoidance behaviours and a strong preference for competitive sport over recreational exercise described a transition to an inactive lifestyle.

“"So what sport or exercise do you do now?” (Interviewer)

“"At the moment, pretty much, nothing. I’m always a bit cagey still, I’m always, it's always in the back of my mind, watch your knee, watch your knee."” (Sue)

"I'm still scared. I still don't even play in the backyard with my dogs."” (Lucy)
DISCUSSION

This is the first study to explore the impact of the ACL-reconstructed knee on longer-term QOL using a qualitative approach, and it highlights the contribution of physical activity preferences, lifestyle modification, and fear of re-injury to QOL and overall satisfaction in people with knee difficulties after ACLR. For many individuals ACL rupture marked the beginning of persistent knee difficulties that required ongoing self-management and consideration. A shift toward this realisation was accompanied by acceptance, adaptation and improvement in QOL. However, the period of transition was variable; while some individuals achieved this relatively quickly, others required more than a decade to do so and some participants remained dissatisfied with their knee state at the time of interview. We gained a unique perspective into the trajectories of QOL over time that has not been identified in previous ACLR studies. This allowed identification of key points of transition, where intervention to facilitate positive lifestyle modifications could be most beneficial.

Fear of re-injury and psychological readiness are common barriers to returning to pre-injury sport after ACLR (Ardern et al., 2012b; Ardern, Taylor, Feller, Whitehead, & Webster, 2013; Kvist et al., 2005; Lentz et al., 2015; McCullough et al., 2012; Tripp et al., 2007). In fact, the contribution of psychological factors to an individual’s decision to return to sport may be of greater importance than physical limitations, such as pain and instability (Ardern, Webster, Taylor, & Feller, 2011b; Gobbi & Francisco, 2006; Warner, Smith, Wright, Matava, & Brophy, 2011). Tanner et al (2007) investigated the importance of knee-specific questionnaire items to ACL-ruptured patients, and found that fear of re-injury was considered most important to patients before and after ACLR. Additionally, a recent qualitative study by Tjong et al (2014) interviewed 31 individuals who underwent ACLR at least 2 years previously and found that fear was the most commonly reported reason for patients not to return to sport. Furthermore, a sub-group of individuals in the study described overcoming initial fears in order to return to sport (Tjong et al., 2014). However, due to the shorter follow-up time, the study by Tjong and colleagues was not able to evaluate longer-term consequences and outcomes. Although fear of re-injury is commonly perceived as an unfavourable consequence of ACLR, being cautious...
and modifying behaviour to reduce risk of re-injury may be a rational response to ACL injury. Furthermore, the current study suggests that for some people this could actually serve as a protective mechanism for optimising future knee function. However, large longitudinal studies would be required to reliably test this hypothesis.

It is possible that the experience of undergoing ACLR and the subsequent postoperative period contributed to the fear of re-injury described by study participants. On average, similar knee-related QOL has been reported between ACL-reconstructed and non-operatively managed groups 5 to 20 years after ACL injury (Chapter 5). However, comparisons between psychological traits, behaviours and re-injury fears in those who report poor QOL after ACLR and non-operative management have not been performed and may prove a fruitful area for future research. The data in this study indicate that individuals with a strong preference for competitive sport who do not enjoy recreational exercise and display fear-avoidance behaviours may be at risk of poorer QOL outcomes. Negative impacts on QOL became apparent irrespective of physical activity preferences when fear-avoidance behaviours extended beyond sporting activity to recreational exercise and activities of daily living. These relationships are supported by quantitative study findings, where fear-avoidance beliefs were related to function in sport and activities of daily living (Ross, 2010) and a high fear of re-injury was associated with poor knee-related QOL after ACLR (Kvist et al., 2005). Identifying individuals with strong activity preferences displaying fear-related patterns following ACLR may enable clinicians to facilitate transition to a satisfying, physically active lifestyle, with potential to improve knee-related QOL. Irrespective of sport or recreational exercise preference, maintaining some form of enjoyable regular physical activity appears paramount in optimising QOL following ACLR. Further research is needed to develop and evaluate strategies that physiotherapists and other health care professionals can utilise to improve longer-term QOL following ACLR.

Participation in regular physical activity and sport is associated with less depressive symptoms, reduced rates of obesity and better health-related QOL (de Wit et al., 2010; Huffman et al., 2008; Mutrie & Hannah, 2007). Weight gain was described as a consequence of reduced
physical activity by 65% of participants and this became a key feature in a cycle involving exacerbation of knee symptoms, reduced motivation, increased fear of re-injury and poor QOL. Notably, some individuals reported being inactive and having impaired QOL for more than 10 years before reaching a state of acceptance and satisfactory QOL. Participants described a number of self-management strategies that facilitated their transition to a state of acceptance, the most common strategy involved reducing their expectations to allow participation in lower risk physical activity, adapting their goals to accommodate knee impairments, accepting a revised sporting role such as coaching or refereeing, or shifting focus to other aspects of life including work or family life. This state of acceptance and adaptation resulted in a satisfactory QOL irrespective of physical knee symptoms. Individuals who were able to transition reasonably quickly after ACLR to a satisfactory state were often those who enjoyed recreational exercise, or those who described early fear-accommodation behaviours. As depicted in Figure 7.1, there appear to be clear periods of transition where the implementation of management strategies could be beneficial for facilitating an active lifestyle with minimal impact on QOL.

Interestingly, 29% of participants were satisfied with their knee function despite reporting very low KOOS-QOL and ACL-QOL scores, high levels of pain and symptoms, moderate to severe trouble with knee confidence and extreme limitations taking part in their most important sport or activity (Table 7.2). This mismatch may reflect these individuals having reached a state of acceptance and adaptation irrespective of knee impairments. Considering the high rates of osteoarthritis development that have been reported as early as 10 years following ACLR (Øiestad et al., 2010) and the chronic nature of osteoarthritis, understanding ways of optimising QOL and satisfaction in people with knee symptoms after ACLR is of great value. Exploring differences between individuals who are satisfied and dissatisfied with their knee despite reporting impaired patient-reported outcomes could provide information that may be useful in developing strategies to optimise QOL in people with persistent knee symptoms after ACLR.

The purposive sampling strategy enabled the identification of common and contrasting experiences amongst individuals with high and low knee-related QOL scores. An additional
strength of this study was the ability to use multiple patient-reported outcome measures collected as part of a larger cross-sectional study (Chapter 6) to aid in the interpretation of findings. The semi-structured interviews were devised to capture the full array of personal experiences from ACL injury to the time of interview, providing insights into changes in QOL over time that have not previously been captured using traditional quantitative measures. We acknowledge the possibility of recall bias as a limitation in considering the time period since ACL injury. Additionally, a wide variety of factors can impact upon an individual’s QOL at a given point in time, and due to the focus on knee-related factors, other potential influences on QOL were not specifically explored. Similarly, factors unrelated to the knee may have contributed to periods of transition, adaptation and acceptance, most of which were not captured in this study. As all participants were English speaking Australians it is not known whether these findings are generalisable beyond this setting. As with all qualitative research, the study sample is unlikely to be representative of all ACL-reconstructed individuals, particularly given that study participants all experienced a degree of knee pain, symptoms or functional limitations and were specifically recruited with high or low QOL scores. Future quantitative research could assist in further exploring the themes identified and evaluating long-term (>20 year) QOL outcomes after ACLR.
INTRODUCTION

Osteoarthritis of the knee is a leading cause of disability world-wide (Cross et al., 2014). Although most prevalent in older adults, osteoarthritis also has a substantial impact on the lives of younger individuals (Ackerman et al., 2015; Institute for Health Metrics and Evaluation, 2015). Individuals who experience symptomatic osteoarthritis may endure chronic pain and physical activity limitations with potential to profoundly impact upon QOL (Ackerman, Graves, Wicks, Bennell, & Osborne, 2005; Covinsky, Lindquist, Dunlop, Gill, & Yelin, 2008; Cross et al., 2014; Mathers, Fat, & Boerma, 2008). Considering many ACL-reconstructed individuals develop knee osteoarthritis within 10 years of injury, and ACL injury is most common in adolescents and young adults, a proportion of ACL reconstructed individuals will experience worsening knee pain and symptoms with impacts on psychological health and QOL, which may lead to the need for total knee replacement surgery (Anderson, Browning, Urband, Kluczynski, & Bisson, 2016).

Despite the undisputable burden of osteoarthritis, not all individuals with radiographic osteoarthritis experience knee difficulties. There is discordance between radiographic signs of knee osteoarthritis and the presence and severity of knee pain (Bedson & Croft, 2008; Dieppe,
Cushnaghan, Tucker, Browning, & Shepstone; Hannan, Felson, & Pincus, 2000; Javaid et al., 2012; Lawrence, Bremner, & Bier, 1966; Phan et al., 2006). The reported proportions of people with radiographic knee osteoarthritis who experience knee pain range from 15% to 81% (Bedson & Croft, 2008). This mismatch between pain and radiographic signs of osteoarthritis may explain why the few studies investigating osteoarthritis and QOL after ACLR found no relationship between knee-related QOL scores and radiographic tibiofemoral osteoarthritis (using a conventional diagnostic criteria of Kellgren & Lawrence grade 2 or above) (Culvenor et al., 2014; Neuman et al., 2008; Øiestad et al., 2011) and inconsistent relationships with patellofemoral radiographic osteoarthritis (Culvenor et al., 2014; Neuman et al., 2009; Øiestad et al., 2012). Psychosocial factors including pain-related fear, self-efficacy, depression and anxiety may partly explain pain variation in individuals with knee osteoarthritis (Creamer & Hochberg, 1998; Sinikallio, Helminen, Valjakka, Vaisanen-Rouvali, & Arokoski, 2014; Sluka et al., 2012; Somers et al., 2009), although this has not been investigated in an ACL-reconstructed population. Exploring the relationship between QOL, satisfaction, psychological health and radiographic osteoarthritis within a sample of individuals who all experience knee difficulties after ACLR may provide new insights into this area.

Risk factors for incident knee osteoarthritis in the general population include obesity, previous knee injury, female gender, older age and a history of regular sports participation (Blagojevic, Jinks, Jeffery, & Jordan, 2010; Cooper et al., 2000). In a typical ACL-reconstructed population where risk factors including a history of knee trauma and sports participation are present, there is a need to identify others factors associated with an increased odds of developing symptomatic knee osteoarthritis. While some identified risk factors have been extensively studied (including meniscus or cartilage injury, subsequent surgery and revision ACLR) other potential risk factors have not been investigated or require further research (including return to sport and mechanism of ACL injury) (Ajuied et al., 2014; Øiestad et al., 2009). Very few studies exploring factors related to osteoarthritis after ACLR consider both the patellofemoral and tibiofemoral joint and most include asymptomatic participants (Culvenor et al., 2014; Hunter, March, & Sambrook; van Meer et al., 2015). There is a need to develop methods for early identification of individuals at heightened risk of developing symptomatic radiographic knee
osteoarthritis after ACLR. This may enable early intervention to prolong or prevent progression to end stage knee osteoarthritis and allow the individual to make informed decisions about physical activity and lifestyle choices. The aim of this study was to answer the following two questions:

1. What factors are related to the odds of having radiographic osteoarthritis in people with knee difficulties 5 to 20 years after ACLR?

2. Is there a relationship between radiographic osteoarthritis and QOL, satisfaction, anxiety or depression in people with knee difficulties 5 to 20 years after ACLR?

METHODS

Study design

A cross-sectional study design was used.

Ethics approval and funding

Ethical approval for this study was obtained from The University of Queensland Medical Research Ethics Committee (approval number 2012001240, Appendix 6.1). Funding for knee radiographs was awarded by the Physiotherapy Research Foundation (PRF) (Seeding Grant number: S13-004).
Participants

Knee radiographs were obtained for a subgroup of individuals from the larger cross-sectional study of 162 individuals with knee pain, symptoms or functional limitations 5 to 20 years following ACLR (Chapter 6). Details of the recruitment procedure and eligibility criteria for this study have been described previously (Chapter 6). In brief, to be eligible for the cross-sectional study all individuals reported a degree of knee pain, symptoms or functional limitations according to predefined KOOS cut-off criteria (Chapter 6). An individual with knee difficulties was defined as any participant reporting a less than optimal score for at least 50% of items in any two KOOS subscales subscales (corresponding to cut-off values of ≤86.1 (Pain), ≤85.7 (Symptoms), ≤86.8 (ADL), ≤85.0 (Sport/Rec), and ≤87.5 (QOL)). Study information, eligibility criteria and an invitation to receive a knee radiograph were sent to all study participants. Figure 8.1 describes the recruitment process which resulted in radiographs from 81 individuals that were available for grading and analysis.

![Participant recruitment flow chart](image)

**Figure 8.1** Participant recruitment flow chart
**Radiographic assessment**

All knee radiographs were performed between September 2014 and August 2015. Radiographic clinics across Australia were contacted prior to receiving a referral and were informed of the study protocol and procedure. Three views of the ACL-reconstructed knee(s) were requested to allow for radiographic grading of the tibiofemoral and patellofemoral joint: weight bearing postero-anterior (PA) erect in 15 degrees knee flexion, weight-bearing lateral in 30 degrees knee flexion, and non-weight bearing skyline in 45 degrees knee flexion. All radiographs were graded by an experienced radiologist (S.D) using the Kellgren & Lawrence criteria for defining radiographic osteoarthritis (Kellgren & Lawrence, 1957). Using these criteria, osteophytes, narrowing of joint cartilage, sclerotic or pseudocystic subchondral bone or an altered shape of the tibial or femoral condyles were considered radiographic signs of osteoarthritis. A Kellgren and Lawrence score of grade 0 represents no radiographic changes, grade 1 minimal changes, grade 2 definite but minimal changes, grade 3 moderate changes and grade 4 severe radiographic changes (Kellgren & Lawrence, 1957). A Kellgren and Lawrence score of ≥ grade 2 for the tibiofemoral or patellofemoral joint was used to define the presence of radiographic osteoarthritis (Kellgren & Lawrence, 1957). Radiographic osteoarthritis was further classified by the compartment(s) involved: ‘medial tibiofemoral’, ‘lateral tibiofemoral’ and ‘patellofemoral.’

**Exploratory factors**

All exploratory factors were derived from data collected as part of the larger cross-sectional study described in Chapter 6. Psychometric properties and scoring information for all patient-reported measures have been previously described (Chapter 6).

*(i) Participant characteristics and knee-related factors*

All demographic and participant characteristic data were collected previously, as described in
Chapter 6. Due to the small number of participants having had a revision ACLR, one new summary variable was created (‘additional knee surgery’) by combining two previously described variables, ‘subsequent surgery’ and ‘revision ACLR’ (Chapter 6). Knee pain and symptoms (measured using KOOS-Pain and KOOS-Symptoms subscales), work limitations (assessed using the WALS) and return to sport status (where participants selected one of three options) were described in detail in Chapter 6. For use in multivariable analysis, return to sport was converted to a dummy variable where non-return to sport was used as a reference category.

(ii) Quality of life and psychological factors

The ACL-QOL was chosen to evaluate knee-related QOL since this is the only ACL-specific QOL measure (Mohtadi, 1998) and contains items of high importance to ACL-injured individuals in comparison to other commonly used measures (Tanner et al., 2007). Satisfaction with current knee state was assessed using recommended wording for the Patient Acceptable Symptomatic State (PASS) (Kvien, Heiberg, & Hagen, 2007; Tubach et al., 2007) “Taking into account your level of pain and also your functional impairment, if you were to remain for the next few months as you are today, would you consider that your current state is satisfactory?” (yes/no) (Appendix 6.3). Anxiety and depression were measured using the HADS, as described in Chapter 6. Scoring and interpretation of these measures were also described in Chapter 6.

Statistical analysis

The Shapiro-Wilk statistic indicated the assumption of normality was not met for several variables, consequently non-parametric tests were chosen and data were reported as median and inter-quartile range (IQR) or frequency (percent) as appropriate. To compare participant characteristics between radiographed study participants and non-radiographed individuals from the parent study (Chapter 6), Mann-Whitney U tests for continuous data and chi-square tests for binary data were used. To address the aims of this study, binary logistic regression analysis was used to identify factors related to the odds of having radiographic osteoarthritis and to
investigate the relationship between radiographic osteoarthritis and QOL, satisfaction, anxiety or depression. Results were reported as odds ratios (OR) with 95% confidence intervals (95% CI), with and without adjustment for potential confounders. Potential confounders were identified from the literature as variables likely to be associated with radiographic osteoarthritis in people with knee difficulties (BMI, age and ‘time since ACLR surgery’). Consequently, no more than four variables were included in multivariable analyses. When assessing relationships between binary variables, ORs close to 1.0 were considered to represent a weak relationship and ORs over 3.0 for positive associations (or less than 0.3 for negative associations) were considered to represent a strong relationship (Haddock, Rindskopf, & Shadish, 1998). Underlying assumptions were tested prior to data analysis. Body mass index as a continuous variable violated the assumption of linearity (assessed by determining whether the interaction between the independent variables and the logit of the dependent variable was significant (Hosmer & Lemeshow, 2000)), consequently, BMI was converted to a binary variable (normal range vs. overweight or obese) with reference to international classification guidelines (normal weight: 18.9–24.9 kg/m², overweight: 25.0–29.9 kg/m², obese: ≥30.0 kg/m²) (National Heart Lung and Blood Institute, 1998). No variables violated the assumption of multicollinearity (assessed by examining variance inflation factor (VIF) and tolerance values where a VIF value greater than 10 (Myers, 1990) or a tolerance value < 0.1 (Menard, 1995) was considered an indication of multicollinearity). A p value <0.05 was considered to represent statistical significance and all statistical procedures were performed using SPSS version 22.
RESULTS

Sample characteristics

Knee radiographs were taken at a median 9 (IQR 8 to 11) months after questionnaire completion and participants had undergone their most recent ACLR a median 8 (IQR 7 to 12) years previously. Participant characteristics for the sample who had radiographs (n = 81) and comparisons with the 81 individuals who did not receive knee radiographs are presented in Table 8.1. The only variable that was significantly different between these groups was age, where individuals who underwent radiographs were younger than those who did not undergo a knee radiograph (median age 36 vs. 40 years, p = 0.01).

Table 8.1 Participant characteristics in people who did and did not undergo a knee radiograph

<table>
<thead>
<tr>
<th></th>
<th>Radiograph (n=81)</th>
<th>No radiograph (n=81)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (% overweight or obese)</td>
<td>49 (61%)</td>
<td>48 (59%)</td>
<td>.87</td>
</tr>
<tr>
<td>Additional knee surgery (%)</td>
<td>38 (47%)</td>
<td>47 (58%)</td>
<td>.16</td>
</tr>
<tr>
<td>Age in years</td>
<td>36 (29-44)</td>
<td>40 (34-48)</td>
<td>.01</td>
</tr>
<tr>
<td>Time since last ACLR (years)</td>
<td>8 (7-12)</td>
<td>8 (7-11)</td>
<td>.63</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>45 (56%)</td>
<td>42 (52%)</td>
<td>.64</td>
</tr>
<tr>
<td>KOOS-Pain score</td>
<td>83 (72-90)</td>
<td>83 (72-89)</td>
<td>.98</td>
</tr>
<tr>
<td>KOOS-Symptoms score</td>
<td>71 (57-79)</td>
<td>68 (57-82)</td>
<td>.82</td>
</tr>
<tr>
<td>ACL-QOL score</td>
<td>52 (39-75)</td>
<td>59 (45-73)</td>
<td>.33</td>
</tr>
<tr>
<td>Dissatisfied (%)</td>
<td>23 (28%)</td>
<td>18 (22%)</td>
<td>.37</td>
</tr>
</tbody>
</table>
All values are reported as median (IQR) for continuous variables or frequency (percent) for binary data; KOOS and ACL-QOL scores range from 0 (extreme impairment) to 100 (best possible score); BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; KOOS: Knee Injury and Osteoarthritis Outcome Score; ACL-QOL: Quality of Life Assessment in Anterior Cruciate Ligament Deficiency questionnaire.

The prevalence of radiographic osteoarthritis by compartment and radiographic severity scores are presented in Figure 8.2. When all compartments were considered, the highest grade of osteoarthritis for participants was: (no osteoarthritis) n=2, 2.5%; grade 1 (minimal osteoarthritis) n=29, 36%; grade 2 (definite osteoarthritis) n=28, 34.5%; grade 3 (moderate osteoarthritis) n=15, 18.5%; grade 4 (severe osteoarthritis) n=7, 8.5%. Moderate and severe osteoarthritis was most commonly observed in the medial tibiofemoral compartment (Figure 8.2). Of the 50 people with radiographic osteoarthritis, 38% had osteoarthritis in one compartment only, 34% had osteoarthritis in 2 compartments and 28% had radiographic osteoarthritis in all 3 knee compartments (Figure 8.3).
**Figure 8.2** Knee osteoarthritis prevalence by compartment and severity (n=81)

TFJ: tibiofemoral joint; PFJ: patellofemoral joint; All compartments: presents the highest grade of osteoarthritis from any compartment for each participant; A Kellgren and Lawrence score of grade 0 represents no radiographic changes, grade 1 = minimal changes, grade 2 = definite but minimal changes, grade 3 = moderate changes and grade 4 = severe radiographic changes (Kellgren & Lawrence, 1957); If bilateral radiographs were taken the highest severity was reported for each compartment.

![Venn Diagram](image)

**Figure 8.3** Knee osteoarthritis prevalence by compartment (n=50)

TFJ: tibiofemoral joint; PFJ: patellofemoral joint; OA: osteoarthritis; n = number of participants with a Kellgren and Lawrence score of ≥ grade 2 (Kellgren & Lawrence, 1957) in each compartment(s); If bilateral radiographs were taken the highest severity was reported for each compartment from one knee only.
Participant characteristics and knee-related factors

Crude analyses
There was a strong relationship between additional knee surgery and osteoarthritis, where the odds of someone who had at least one additional surgery to their ACL-reconstructed knee having radiographic osteoarthritis were 4.2 times higher than for people who did not have additional surgery. Similarly, there was a strong relationship between time from injury to surgery and radiographic osteoarthritis, where the odds of someone who had an ACLR more than 6 months after injury having osteoarthritis were 6.4 times greater than for someone who had an ACLR within 6 months of injury. Reporting a contact mechanism of injury reduced the odds of having osteoarthritis by 35% compared to reporting a non-contact mechanism of injury (Figure 8.4). Unadjusted analyses found an association between KOOS-Symptoms scores and osteoarthritis, where a 1-point worse KOOS-Symptoms score corresponded to a 4% reduction in the odds of having knee osteoarthritis (Figure 8.4). A similar relationship was observed between KOOS-Pain scores and radiographic osteoarthritis, although this did not achieve statistical significance (p=0.05). Work limitations were also associated with radiographic osteoarthritis; for every 1-point worse WALS score, the likelihood of having radiographic osteoarthritis increased by 23% (Figure 8.4).

Adjusted analyses
The relationship between additional surgery and osteoarthritis strengthened after adjustment for age, BMI and time since ACLR, where having at least one additional knee surgery since ACLR was associated with a 5.5 fold increased odds of having future knee osteoarthritis. Strong relationships remained between contact mechanism of injury and reduced osteoarthritis odds (OR 0.32, 95% CI 0.1 to 0.9) and a delay of > 6 months from injury to surgery and increased osteoarthritis odds (OR 6.9, 95% CI 1.4 to 22.3) (Figure 8.4). Pain, symptoms and work limitations were no longer associated with radiographic osteoarthritis after adjustment for confounders (Figure 8.4).
Figure 8.4 Participant characteristics, knee-related factors and the odds of having radiographic patellofemoral and/or tibiofemoral osteoarthritis

All values are reported as median (IQR) for continuous variables or frequency (percent) for binary data; * Adjusted: multivariable analysis adjusted for age, BMI, time since last ACLR; BMI: Return to sport was assessed using dummy variables where ‘did not return to sport’ was used as a reference category; ** ‘unsure’ responses were removed resulting in one missing response for ‘injury to surgery’; *** ‘unsure’ responses were removed resulting in two missing responses for ‘contact mechanism’
Quality of life and psychological factors

Crude analyses

People without radiographic knee osteoarthritis reported better ACL-QOL scores than those with radiographic osteoarthritis (a median difference of 15 points) where a 1-point better ACL-QOL score corresponded to a 3% decrease in the odds of having osteoarthritis (Figure 8.5). Individuals who rated their knee as having a moderate to significant impact on their QOL (in response to the single-item QOL question) had a 8.6 times greater odds of having knee osteoarthritis, compared to individuals reporting their knee as having slight or no impact on their QOL (OR 8.6, 95% CI 2.6 to 28.2). Participants who were dissatisfied with their knee function had a 4.4 times greater odds of having osteoarthritis than participants who were satisfied with their knee function (Figure 8.5). Radiographic osteoarthritis was not associated with anxiety or depression scores.

Adjusted analyses

Following adjustment for age, BMI and time since ACLR, the relationship between dissatisfaction with knee function and osteoarthritis remained (OR 4.5, 95% CI 1.1 to 18.8). Participants who reported a moderate to significant impact of their knee on their QOL had 8.8 times greater odds of having knee osteoarthritis, compared to participants reporting less impact on QOL (Figure 8.5). Similarly, lower ACL-QOL scores remained significantly associated with increased odds for osteoarthritis after adjustment for confounding factors.
Table 8.5. Quality of life and psychological factors and comparisons between participants with and without radiographic patellofemoral and/or tibiofemoral osteoarthritis

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OA (n=50)</td>
<td>No OA (n=31)</td>
</tr>
<tr>
<td>ACL-QOL</td>
<td>51 (37 to 71)</td>
<td>66 (50 to 82)</td>
</tr>
<tr>
<td>Single item QOL**</td>
<td>28 (56%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5 (2 to 8)</td>
<td>5 (3 to 7)</td>
</tr>
<tr>
<td>Depression</td>
<td>2 (1 to 4)</td>
<td>2 (0 to 3)</td>
</tr>
<tr>
<td>Dissatisfied (%)</td>
<td>16 (32%)</td>
<td>3 (10%)</td>
</tr>
</tbody>
</table>

Figure 8.5 Quality of life and psychological factors and comparisons between participants with and without radiographic patellofemoral and/or tibiofemoral osteoarthritis

All values are reported as median (IQR) for continuous variables or frequency (percent) for binary data; * Adjusted: multivariable analysis adjusted for age, BMI and time since last ACLR; ** Single item QOL: number of participants reporting their knee having a moderate or significant impact on their quality of life (as opposed to no or slight impact)
DISCUSSION

Undergoing additional knee surgery since ACLR, a non-contact mechanism of injury and waiting longer than six months from injury to undergo ACLR were all related to an increased odds of having radiographic knee osteoarthritis, after adjusting for confounding factors. On the other hand, knee symptoms, sex, pain severity, return to sport status and work limitations were not related to the odds of having osteoarthritis after adjustment for potential confounders. Reporting dissatisfaction with knee function or greater knee-related QOL impairment was related to the presence of radiographic osteoarthritis. Reporting anxiety or depressive symptoms was not related to radiographic osteoarthritis in people with knee difficulties 5 to 20 years after ACLR.

Participant characteristics and knee-related factors

Additional knee surgery

Individuals who underwent one or more additional knee surgery (on a previously ACL-reconstructed knee) had an increased odds of having radiographic osteoarthritis compared to people who had not received an additional surgery. The CIs for this effect were large (OR 5.5, 95% CI 1.7 to 15.4), indicating substantial variance that is probably related to the small sample size. Notably, 57% of participants in this study received at least one additional knee surgery on their ACL-reconstructed knee. Although this rate may be higher than expected for all ACL-reconstructed individuals (since this sample all experienced some degree of knee difficulties), as many as one in five individuals may be expected to undergo a subsequent knee surgery within six years of ACLR (Hettrich et al., 2013). Unfortunately no information regarding the type of surgery or subsequent injuries was collected. As highlighted in the systematic review in Chapter 4, one study found that subsequent trauma to the ACL-reconstructed knee was related to worse QOL, pain, symptoms and more functional limitations six years after ACLR (Swirtun & Renström, 2008). Intuitively, individuals who experience subsequent joint injury
would be more likely to undergo additional knee surgery.

Due to the small number of participants in this study undergoing revision ACLR, the variables ‘revision’ and ‘subsequent surgery’ were combined (the distinction between these variables was outlined in Chapter 6) to form one summary variable (‘additional knee surgery’). Revision surgery has been associated with increased rates of knee osteoarthritis, worse QOL, greater pain severity, more knee symptoms and poorer postoperative function compared with primary ACLR (Gifstad et al., 2012a; Kievit et al., 2013; Lind et al., 2012; Salmon et al., 2006). Combined, there is evidence that shows people who have a subsequent surgery after ACLR are at increased risk of experiencing poor long-term outcomes. What remains unclear, are the factors that contribute to the worse outcome in individuals who have additional knee surgery. Perhaps some individuals are dissatisfied with their knee function and undergo surgery in attempt to improve satisfaction and QOL, or perhaps repeated surgery can have negative impacts on future joint health and knee function. A recent systematic review found no benefit of arthroscopic surgery for knee pain and degenerative knee disease one to two years after arthroscopy, and considering potential harms associated with arthroscopic surgery, recommended against arthroscopic surgery for people with knee osteoarthritis (Thorlund, Juhl, Roos, & Lohmander, 2015). Due to the strong relationship between osteoarthritis and additional surgery, it is possible some of these surgeries were performed in attempt to alleviate knee symptoms affiliated with a degenerative joint. Additional knee surgery could be perceived as a form of additional trauma to the knee joint with psychological impacts, and if ineffective in relieving knee symptoms or pain, could have further negative impacts on an individual’s QOL. However, this is speculative and further research is needed to investigate the relationship between additional surgery and poorer longer-term outcomes after ACLR.
Mechanism of anterior cruciate ligament injury

A novel finding in the current study was the relationship between a non-contact mechanism of ACL injury and a heightened risk for future radiographic osteoarthritis. A search of the literature did not locate any studies directly exploring this relationship. However, a wealth of literature provides useful information to develop potential hypotheses for this finding. People who experience a non-contact ACL rupture may be more likely to have predisposing anatomical and biomechanical risk factors for ACL injury (including knee joint laxity, decreased hamstring strength and decreased proprioception, hip adduction coupled with dynamic knee valgus) compared to someone who ruptures their ACL following an external force (such as a collision, a tackle or foul play) (Alentorn-Geli et al., 2009a; Griffin et al., 2000; Renstrom et al., 2008). High-impact sports participation in individuals with these anatomical and biomechanical risk factors may expose the knee joint structures to repetitive micro-trauma that could accelerate the onset of osteoarthritis (Meyer, Villwock, & Haut, 2009; Seegmiller & McCaw, 2003; Yeow, 2009). Furthermore, the risk factors that predisposed an individual to non-contact ACL rupture may persist after ACLR, impacting on postoperative joint loading and knee stability with further potential to accelerate osteoarthritis development (Andriacchi, Briant, Bevill, & Koo, 2006). Individuals with these ongoing risk factors may be more likely to undergo revision ACLR or suffer a subsequent joint injury on return to high-impact sport, both revision ACLR and subsequent joint trauma are associated with an increased risk of osteoarthritis (Gifstad et al., 2012a; Kamath, 2011; Kievit et al., 2013; Lind et al., 2012). Considering the incidence of non-contact mechanisms of ACL rupture can be reduced with prevention programs (targeting biomechanical and neuromuscular risk factors) and individuals displaying predisposing risk factors for non-contact ACL injury are identifiable (Alentorn-Geli et al., 2009c; Griffin et al., 2000; Myklebust et al., 2003; Renstrom et al., 2008), further research exploring this relationship is warranted.

Time from injury to surgery

Another strong relationship identified was the association between a longer time from injury to ACLR (> 6 months vs. < 6 months) and higher odds of knee osteoarthritis. However, the
effect of time from injury to surgery on radiographic osteoarthritis had a wide 95% CI (OR 6.9, 95% CI 1.4 to 22.3) indicating uncertainty around this estimate. As outlined in Chapter 4, three studies have explored the relationship between time from injury to surgery and longer-term QOL outcomes. Two studies found no relationship between time from injury and knee-related or health-related QOL (Øiestad et al., 2011; Sajovic et al., 2011) and one study found worse SF-36 scores (for three domains: PF, BP, SF) and a trend for worse KOOS-QOL scores in those who underwent ACLR more than five months after ACLR (Barenius et al., 2010). Notably, in this study those who had ACLR more than five months after injury also reported higher rates of meniscal injuries (37% vs. 62%, p=0.008). This is in line with findings from a study of 616 participants that reported more meniscal injury in patients who underwent ACLR more than 3 months after injury and more cartilage injury in those who received ACLR more than 6 months from injury (Razi et al., 2013). Similarly, a large study of 1434 individuals found a relationship between an increased period of time from injury to surgery and higher rates of concomitant joint injury when presenting for ACLR, including injury to meniscus and joint surfaces (Ralles, Agel, Obermeier, & Tompkins, 2015). People with concomitant injury to other knee structures at the time of ACLR report higher rates of osteoarthritis 10 to 20 years later (Claes et al., 2013; Keays, 2010; Magnussen et al., 2009; Murray et al., 2012; Øiestad et al., 2009; van Meer et al., 2015) and poorer patient-reported outcomes after ACLR including more knee pain, symptoms, poorer function and reduced QOL (Barenius et al., 2010; Cox et al., 2014; Dunn et al., 2015; Gerhard et al., 2012; Neuman et al., 2008; Røtterud et al., 2012; Røtterud et al., 2013). Considering the consistent relationship between meniscal and cartilage injury and increased rates of osteoarthritis after ACLR, this could provide one potential explanation for the higher odds of osteoarthritis in those having ACLR more than six months after injury in the current study.

Pain and symptoms

Participants with osteoarthritis reported more knee pain and symptoms than those without, although this did not exceed the minimal clinically important difference (MCID) for the KOOS and became statistically non-significant following adjustment for age, BMI and time since surgery. One or more of these factors may be more closely related to variation in knee pain and
symptoms than structural changes on radiograph. In line with the eligibility criteria for recruitment into the cross-sectional study (Chapter 6), individuals without osteoarthritis also reported large amounts of knee pain and symptoms (median KOOS-Pain and KOOS symptom scores for individuals without osteoarthritis exceeded suggested cut-off values for identifying individuals symptomatic enough to seek medical care) (Englund et al., 2003). This is in line with previous research findings showing that as many as one in two individuals with pain and symptoms suggestive of osteoarthritis do not have radiographic signs of osteoarthritis and one in two individuals with definite radiographic osteoarthritis do not report knee pain (Lawrence et al., 1966). This suggests there is likely to be individual variation in experienced pain and symptoms following ACLR irrespective of osteoarthritis changes. Considering the close relationship between knee pain severity and QOL reported in Chapter 4 and 6, further investigations to provide insights into reasons for heightened or reduced pain levels following ACLR are warranted. Finan et al (2013) found that individuals who reported high levels of pain with few radiographic signs of knee osteoarthritis (Kellgren & Lawrence grade ≤ 2) displayed greater signs of central pain sensitization than their counterparts with low pain and moderate to severe osteoarthritic changes on radiograph (Kellgren & Lawrence grade 3-4) (Finan et al., 2013). Psychological factors are related to pain severity in individuals with knee osteoarthritis (Kittelson, Stevens-Lapsley, & Schmiege, 2015; Wideman et al., 2014) and psychosocial interventions have potential to reduce knee pain in the presence of radiographic osteoarthritis (Creamer & Hochberg, 1998). Had psychological factors (such as self-efficacy, pain catastrophising, fear-avoidance, locus of control and personality traits) been measured in the current study, they may have provided valuable information regarding the discord between knee pain and radiographic osteoarthritis.

Return to sport

A recent systematic review investigating factors related to osteoarthritis progression following ACLR concluded that it was not possible to determine the effect of return to sport due to a shortage of studies reporting on this relationship (Ajuied et al., 2014). The authors of this review hypothesised that a return to cutting and pivoting sports may play a role in the development and progression of osteoarthritis after ACLR, although they had no evidence to
support this hypothesis (Ajuied et al., 2014). Interestingly, the results of the present study found that return to sport status was not related to the presence of radiographic osteoarthritis in people with knee difficulties more than five years following ACLR. In Chapter 7, return to sport experiences were described in greater detail using personal perspectives from ACL-reconstructed individuals. Some participants who did not return to any sport adopted a physically active lifestyle participating in lower impact exercise. On the other hand, other individuals who did not return to sport became physically inactive and described experiencing weight gain and worsening knee symptoms (Chapter 7). Thus, within each return to sport category there may be subgroups of individuals with higher or lower risks of osteoarthritis development, which could partly explain the non-significant relationship between return to sport and radiographic osteoarthritis. Longer-term follow-up of study participants beyond 20 years may reveal new associations between sporting behaviours and osteoarthritis development following ACLR.

**Quality of life and psychological factors**

In this study, individuals with radiographic knee osteoarthritis reported a 15-point lower median ACL-QOL score compared to those without osteoarthritis. Knee-related QOL measured with a single item was strongly related to the odds of having knee osteoarthritis (moderate to significant impairment in QOL reported by 55% of participants with osteoarthritis vs. 16% without osteoarthritis). Notably, the 95% CI for the single-item QOL measure was very wide, indicating imprecision in this estimate, likely due to the limited sample size. Nevertheless, the relationship observed between knee-related QOL and radiographic osteoarthritis was consistent irrespective of measure. Considering all study participants reported a degree of knee difficulties regardless of radiographic findings, further research is needed to understand reasons for the lower QOL in people with knee osteoarthritis after ACLR. Investigating other variables not measured in the present study (including psychological variables) may assist in better understanding the relationship between QOL and radiographic osteoarthritis in people with knee difficulties after ACLR.
Furthermore, people with radiographic osteoarthritis were more dissatisfied with their knee function compared to those without osteoarthritis (32% vs. 10%). However, despite twice as many individuals being dissatisfied with their knee function in the osteoarthritis group, overall rates of satisfaction were high (68% of people with knee osteoarthritis were satisfied with their knee function). This could reflect a proportion of people being within the earlier stages of osteoarthritis development, since only 15 participants (18.5%) had moderate osteoarthritis changes and 7 individuals (8.5%) had severe osteoarthritis changes. The ability for people to be satisfied with their knee function despite experiencing knee difficulties (as described in Chapter 7) could partly explain the imprecision in this estimate indicated by a wide 95% CI (OR 4.5, 95% CI 1.1 to 18.8).

**Strengths and limitations**

The main limitation of this study was that only 50% of individuals from the parent study elected to undergo a knee radiograph. Despite this, the radiographed sample appeared to be broadly representative of the larger sample, as all characteristics were similar except median age. Considering radiographed participants were younger in age and older age is related to increased rates of osteoarthritis (Institute for Health Metrics and Evaluation, 2015), osteoarthritis might be even more prevalent among the 81 individuals who were not radiographed. Since this study did not aim to ascertain what proportion of ACL-reconstructed individuals develop osteoarthritis after ACLR, this is unlikely to impact upon the results of this study. However, there may have been a recruitment bias where individuals with specific personality traits or lifestyle characteristics may be more likely to choose to have a knee radiograph.
Another limitation of this study is the lack of detailed information on concomitant and subsequent injury and surgery, largely due to the cross-sectional study design. Additionally, the median time from questionnaire completion to knee radiography was nine months. Knee pain, symptoms and QOL may fluctuate over time and patient-reported measures completed nine months previously may not accurately reflect health status at the time of radiograph. Despite this limitation, several measures were related to the presence of radiographic osteoarthritis at an average of nine months following questionnaire completion. A single binary osteoarthritis outcome was used to account for participants with osteoarthritis in multiple compartments, as a result we were unable to evaluate relationships separately for the tibiofemoral and patellofemoral joint. Despite this, considering the prevalence of osteoarthritis in both the tibiofemoral and patellofemoral joint was a strength of this study since most previous studies considered only one of these joints. This is the first study to explore QOL and radiographic osteoarthritis changes specifically in people with knee pain, symptoms or functional limitations after ACLR, contributing new insights in this field.

CONCLUSION

This study identified five key factors that were strongly, but imprecisely, related to increased odds of radiographic osteoarthritis in individuals with knee difficulties at a median eight years following ACLR. Reporting more knee-related QOL impairment or dissatisfaction with knee function was associated with increased odds of having radiographic osteoarthritis. Receiving one or more additional knee surgeries since ACLR, reporting a non-contact mechanism of ACL injury and a delay longer than six months from injury to ACLR were all associated with increased odds of radiographic osteoarthritis. All these relationships remained significant after adjusting for potential confounding factors.
PART C
AN EXTENDED DISCUSSION OF QUALITY OF LIFE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION
This Chapter will provide an extended discussion of the thesis findings in the context of previous literature. Chapter 9 will conclude by suggesting directions for future research and proposing potential strategies to improve longer-term QOL following ACLR.

Sport-related aspects

Return to sport

Enabling return to competitive sport is a common reason for performing ACLR and most individuals electing to undergo surgery expect to return to pre-injury sport within one year (Feucht et al., 2014; Marx et al., 2003; McRae et al., 2011). Of concern is that more than 50% of non-elite sports participants do not return to pre-injury sport after ACLR (Ardern et al., 2014b), which was a critical determinant of longer-term QOL 5 to 20 years after ACLR in people with knee difficulties (Chapter 6). Prior to this research, only two studies had explored the relationship between return to sport and QOL outcomes (Ardern et al., 2014a; McCullough et al., 2012). One study reported lower KOOS-QOL scores in high school and college athletes who did not return to sport compared to those who returned to their pre-injury level of sport two years after ACLR (McCullough et al., 2012). In this study, high-school athletes who returned to sport reported a median KOOS-QOL score of 90 compared to 75 for those who did not return, and college athletes who returned to sport reported a median KOOS-QOL score of 94 compared to 72 for those who did not return. One in every two athletes (at both high-school and college level) reported fear as a factor affecting their decision to
return to sport (McCullough et al., 2012). Similarly, a Swedish study also reported worse KOOS-QOL scores in individuals who had not returned to pre-injury sport one to seven years after ACLR (mean KOOS-QOL score 70 vs. 57), and that distrust in the knee and fear of re-injury were the most commonly reported reasons for not returning to sport (Ardern et al., 2014a). Functional and objective knee measures have been found to be inaccurate predictors of return to sport following ACLR (Ardern et al., 2011a). On the other hand, psychological measures of fear of re-injury, mood and knee confidence are known to be related to an individual’s decision to return to sport following ACLR (Ardern et al., 2014b; Ardern et al., 2011a; Kvist et al., 2005; McCullough et al., 2012; Tripp et al., 2007). These study conclusions are in line with the key theme described in Chapter 7, where individuals with a high desire to return to sport who did not do so due to fear of re-injury described negative impacts on QOL. Early identification of this potentially at-risk subgroup could enable the implementation of early management strategies to minimise the impact of fear of re-injury on QOL and facilitate adoption of a sustainable and satisfying physically active lifestyle.

Additionally, there may be a perception that return to sport at a lower level after surgery (or non-return to pre-injury level of sport) constitutes an undesirable surgical outcome (Marx et al., 2003). However, results from qualitative interviews (Chapter 7) suggest that eliminating fear of re-injury and facilitating a return to sport may not be ideal for all individuals. There may be circumstances where return to sport is associated with exacerbation of knee symptoms, re-injury or worsening of QOL following sport cessation. On the contrary, other individuals successfully adapted their lifestyle, remained physically active and reduced their perceived risk of further injury. This strategy may produce a more desirable outcome for an individual who places great value on being physically active across their lifespan. For this reason, emphasis should be placed on tailoring management strategies to the individual after ACLR. Some people may benefit from assistance to reduce fear of re-injury and improve confidence to facilitate a return to sport, while others may be better suited to modify sporting choices to enable continued sport participation at an altered but satisfying level. Other individuals may benefit most from support to transition from competitive sport to a sustainable, recreationally active lifestyle with a lowered perceived risk of re-injury.
Athletic identity

Athletic identity refers to the degree that an individual identifies themselves with the athletic role (Brewer & Stephan, 2007; Sparkes, 1998). Individuals with a high athletic identity are more likely to be emotionally impacted by sporting injury than those with low athletic identity, who may be more likely to obtain enjoyment and a sense of wellbeing from alternative sources (Brewer, Mignano, Van Raalte, & Winter, 2006; Fuller, 2014; Schutte & McNeil, 2015). Although the concept of athletic identity was not formally evaluated in this research, previous studies in ACL-injured athletes have reported decreased mood, poorer coping and slower psychological recovery in competitive compared to recreational athletes at two and eight weeks following ACLR (Morrey, Stuart, Smith, & Wiese-Bjornstal, 1999). Greater levels of athletic identity and lower levels of acceptance following ACLR have also been associated with more depressive symptoms and negative mood during the early postoperative rehabilitation period (Baranoff, Hanrahan, & Connor, 2015; Brewer et al., 2007). Considering individuals with a strong athletic identity can have greater difficulty coping with retirement from competitive sport (Fuller, 2014; Lavallee, Grove, & Gordon, 1997), variation in athletic identity may explain some of the variability in the relationship between non-return to sport and poorer longer-term QOL outcomes (Chapter 7). Using validated measures of athletic identity may assist in early identification of individuals at risk of transitioning to an inactive (and potentially dissatisfying) lifestyle following sport cessation after ACLR.

Psychological aspects

Psychological readiness for surgery and postoperative expectations

Individual differences in expectations can contribute to variability in QOL in people with the same illness or condition (Carr et al., 2001; Rapkin & Schwartz, 2004). Individuals with unrealistic postoperative expectations who are not psychologically ready to undergo ACLR may experience less acceptance postoperatively. Low acceptance two weeks following ACLR was found to be predictive of increased depressive symptoms and increased alcohol and other substance use to cope with ACL injury at six months (Baranoff et al., 2015). Furthermore, feeling less psychologically prepared for
ACLR has been associated with reduced postoperative rehabilitation adherence and participation (Udry, Shelbourne, & Gray, 2003). Poor adherence to rehabilitation after ACLR was related to more patient-reported knee symptoms at six months (Corsetti et al., 2004) and higher rates of fear of re-injury at five months following ACLR (Pizzari, McBurney, Taylor, & Feller, 2002). However, no studies have explored the influence of psychological readiness or surgical expectations on longer-term QOL outcomes following ACLR. Enhanced post-injury education is a strategy that could assist patients in developing feasible/realistic expectations and hence, reduce the imbalance between expectation and experience that may contribute to poor QOL following ACLR. An Australian study of 222 people with knee or hip osteoarthritis presenting for an orthopaedic consultation at a large hospital found that only 1 in 5 felt they had received adequate education about their diagnosis, prognosis and treatment options (Haskins, Henderson, & Bogduk, 2014). To date, no studies have evaluated the quality of education and information provided to ACL-ruptured individuals. Further research is required to evaluate the impact of pre-operative readiness, education and expectations on post-operative experiences and longer-term QOL.

Psychological attributes related to post-operative outcomes

Psychological attributes including knee self-efficacy and locus of control have been related to QOL outcomes after ACLR (Mendonza, Patel, & Bassett, 2007; Nyland et al., 2006; Thomeé et al., 2007; Thomeé et al., 2008; Thomeé et al., 2006). Self-efficacy refers to an individual’s thoughts and judgements regarding their perceived ability to perform an action or execute a task to a particular standard (Bandura, 1977). Self-efficacy has been shown to be closely related to health-related QOL in individuals with chronic pain (Börsbo, Gerdle, & Peolsson, 2010). Anterior cruciate ligament-injured individuals with high levels of knee self-efficacy score favourably on a range of outcomes including knee-related QOL, rehabilitation compliance, single-leg hop test, physical activity levels and return to sport, compared to individuals with lower levels of knee self-efficacy (Mendonza et al., 2007; Thomeé et al., 2007; Thomeé et al., 2008; Thomeé et al., 2006). Locus of control refers to an individual’s belief that their actions have control over an outcome (Rotter, 1966). In an ACL-injured population, locus of control has been associated with a range of patient-reported outcomes, including self-rated knee function, mental health, satisfaction and return to sport (Ardern et al., 2011b; Nyland et al., 2006; Thomeé et al., 2008). Knee self-efficacy and locus of control are often inter-related in
ACL-injured individuals (Thomeé et al., 2007). As with many psychological factors, the influence of knee self-efficacy and locus of control on QOL outcomes beyond five years of ACLR has not been evaluated.

Pain catastrophising has been described as “an exaggerated negative ‘mental set’ brought to bear during actual or anticipated pain experience” (Sullivan et al., 2001) p. 53. Individuals who display greater signs of pain catastrophising two weeks after ACLR report more depressive symptoms and greater pain severity at six month follow-up (Baranoff et al., 2015). Catastrophising thoughts can lead to emotional disturbances and fear-avoidance behaviours (Tripp, Stanish, Coady, & Reardon, 2004). Although this was not explicitly assessed, catastrophising thoughts may have contributed to the fear-avoidance behaviours described by a subgroup of individuals participating in the qualitative study (Chapter 7). Pain catastrophising may become apparent prior to ACLR and can be measured with established patient-reported questionnaires, such as the Pain Catastrophising Scale (Sullivan, Bishop, & Pivik, 1995). Identifying psychological traits related to postoperative outcome (including self-efficacy, locus of control and pain catastrophising), in conjunction with injury-related risk factors (including meniscus or cartilage injury, revision ACLR and subsequent injury) may provide a means of screening for individuals at heightened risk of poor longer-term QOL following ACLR. These individuals may benefit from additional early intervention incorporating psychological support.

**Psychological interventions**

The limited number of studies that have investigated the influence of psychological interventions on outcomes following ACLR have reported promising findings (Wierike et al., 2013). A treatment strategy combining relaxation and guided imagery with a standard physiotherapy regime resulted in less fear of re-injury, less pain and improved knee strength at six months following ACLR, compared to physiotherapy alone or a placebo strategy of physiotherapy, encouragement, support and attention (Cupal & Brewer, 2001). A RCT performed in New Zealand found that patients who viewed two coping model DVDs reported lower levels of expected pain pre-operatively, greater self-efficacy for rehabilitation prior to discharge and better knee function scores at six weeks post-ACLR, compared with patients who did not view the videos (Maddison, Prapavessis, & Clatworthy, 2006). These DVDs
featured models performing rehabilitation tasks corresponding to expected milestones and interviews with ACL-reconstructed patients who disclosed their thoughts and feelings surrounding the injury and surgery, problems encountered and strategies used to overcome these, as well as their preoperative expectations and how these compared to their postoperative experiences. Such content may have generated more realistic expectations with potential to improve QOL outcomes, although QOL was not specifically measured in this study (Maddison et al., 2006).

An Italian study randomised 106 ACL-ruptured patients to view one of two videos 3 times a week for the first 8 weeks after ACLR while performing a standardised rehabilitation regime (Zaffagnini, Russo, Marcheggiani Muccioli, & Marcacci, 2013). These videos were very different from those utilised in Maddison et al (2006). They featured artistic images and film clips designed to elicit specific conscious and subconscious emotional responses. One group viewed an art video that aimed to produce positive and therapeutic insight, while the control group viewed a video with an insight that did not favour psychological recovery (Zaffagnini et al., 2013). Individuals viewing the more positive video reported better subjective knee function and less kinesiophobia (fear of movement and re-injury) at three months following ACLR and spent a shorter time on crutches than the control group (Zaffagnini et al., 2013). A small Australian study of ACL-reconstructed individuals 3 to 4 months post-surgery trialled an intervention comprising 3 sessions of 20 minute writing over a 3-day period designed to encourage athletes to disclose any negative emotions associated with ACL injury or rehabilitation (Mankad, Gordon, & Wallman, 2009). Emphasis was placed on disclosing emotions that had not been previously discussed with others. Despite a small sample size of 15 participants, this intervention resulted in reduced psychological stress, improved mood and impacts on immunological function measured through collection of blood samples (Mankad et al., 2009). Together these studies highlight the potential to improve ACLR outcomes when psychological aspects are addressed in interventions. These few studies also highlight an absence of research evaluating the impacts of psychological interventions on longer-term outcomes following ACLR including return to sport and QOL.
Fear of re-injury

As discussed previously, fear of re-injury is related to longer-term knee-related QOL in ACL-reconstructed individuals. Several hypothetical explanations could justify a persistent fear of re-injury after ACLR. For some individuals, a fear of re-injury could be an innate response to knee trauma experienced at the time of ACL-rupture and subsequent trauma incurred at the time of ACLR, resulting in a fear of the precipitating event, environment and circumstance in which ACL-rupture occurred. For most people, this event occurred during competitive sport participation, which could partly explain the relationship between fear of re-injury and return to sport. On the other hand, some individuals may fear repeat surgery and consequent pain, swelling and incapacitation. Individuals who have a negative peri-operative experience may have a greater desire to avoid undergoing a repeat surgery. A negative experience of ACLR may result in psychological distress, which is related to depression, anxiety, reduced pain tolerance, emotional disturbances and catastrophising in ACL-injured populations (Mainwaring, Hutchison, Bisschop, Comper, & Richards, 2010; Morrey et al., 1999; Tripp et al., 2004; Udry et al., 2003). Further studies that explore the reasons behind fear of re-injury and compare ACL-reconstructed and non-operatively managed individuals could provide valuable information to better understand fear of re-injury following ACLR. A recent study explored fear of re-injury after ACLR from the rehabilitation therapist’s perspective and found fear of re-injury was poorly recognized as a barrier to return to sport by therapists; none of the therapists interviewed believed that a patient they treated had failed to return to sport due to fear of re-injury (McVeigh & Pack, 2015). This suggests that there may be potential to improve identification and management of individuals with a heightened fear of re-injury after ACLR.
Physical aspects

Knee pain

The systematic review in Chapter 4 investigating QOL 5 to 20 years after ACLR found that knee pain was strongly correlated with knee-related QOL scores. Similarly, in a cohort of individuals with knee difficulties (Chapter 6) greater knee pain was strongly related to worse knee-related and health-related QOL scores (Appendix 6.4 and 6.5). Persistent knee pain is common following ACLR; a large study of 1761 young, ACL-reconstructed individuals (median age 23 years) found that one in three individuals experienced persistent knee pain at two year follow-up, and as many as one in two experienced knee pain six years following primary ACLR (Wasserstein et al., 2015). Although not specifically explored in an ACL-reconstructed population, experiencing a higher intensity of pain in the acute postoperative period is a strong predictor for developing persistent post-surgical pain following a variety of common surgical procedures (Kehlet, Jensen, & Woolf, 2006). Chimielewski et al. (2011) found that decreased knee pain at 12 weeks following ACLR was associated with increased self-efficacy for rehabilitation (Chmielewski et al., 2011). This study also found that preoperative psychological factors (kinesiophobia, pain catastrophising and self-efficacy for rehabilitation) were not related to knee pain intensity at 12 weeks following ACLR, however this study did not explore the relationship between preoperative psychological factors and pain that persists more than 3 months following ACLR (Chmielewski et al., 2011).

A large prospective study of 525 individuals found that bone bruising, meniscus injury and cartilage injury were not associated with knee pain severity at two years following ACLR, but female sex and higher BMI at the time of ACLR were (Dunn et al., 2010). Another large study of 1761 ACL-reconstructed individuals found that subsequent knee surgery was the strongest predictor of a painful knee at 2 and 6 years following ACLR, and lower activity levels at 2 years predicted more knee pain at 6 years post-ACLR (Wasserstein et al., 2015). Notably both of these studies explored a range of injury-related, surgery-related and patient demographic variables but the impact of psychological factors on longer-term knee pain after ACLR was not investigated (Dunn et al., 2010; Wasserstein et al., 2015). Studies investigating a greater variety of prognostic factors (including psychological
variables) for longer-term knee pain after ACLR may provide useful information for managing and preventing persistent knee pain following ACLR. Considering the close relationship between knee pain and QOL, improving the management and reducing the prevalence of persistent knee pain after ACLR has potential to improve longer-term QOL outcomes.

**Subsequent surgery**

The studies comprising this thesis found significant relationships between subsequent surgery and an increased odds of having radiographic osteoarthritis (Chapter 8) and worse knee-related QOL outcomes (Chapter 4 and 6). Receiving a subsequent knee surgery to the ACL-reconstructed knee has been identified as a strong predictor of increased knee pain at two and six years after ACLR (Wasserstein et al., 2015). Despite this, the association between subsequent surgery and poor knee-related QOL remained strong after adjustment for knee pain (Chapter 6). The reason for worse longer-term QOL in people having subsequent surgery after ACLR remains unclear. Subsequent surgery may have additive psychological consequences (such as a heightened fear of re-injury after additional surgery) with potential for negative impacts on satisfaction and QOL. It is also possible that poor QOL or persistent pain could precede additional surgery and contribute to the decision to undergo subsequent surgery after ACLR. Additional arthroscopic surgery may be ineffective in relieving pain or symptoms for some individuals, especially in the presence of degenerative knee changes (Thorlund et al., 2015). Further prospective research is needed to evaluate the effectiveness of subsequent surgeries for improving longer-term knee pain, function and QOL in ACL-reconstructed individuals.

Surprisingly, there was no relationship between revision ACLR and QOL outcomes in 162 ACL-reconstructed individuals with knee difficulties (Chapter 6). This finding contrasts previous studies that included participants without knee difficulties and found poorer outcomes after revision surgery compared with primary ACLR (Ahlden et al., 2012; Möller et al., 2009). Considering only 14% of individuals in the cross-sectional study had a revision ACLR, there was likely insufficient power to evaluate relationships between revision surgery and QOL outcomes. On the other hand, participants who received a contralateral ACLR in the cross-sectional study (Chapter 6) were more likely to report an impaired QOL score compared to people who had one ACL-intact knee. This is consistent with
previous research showing poorer ACL-QOL and KOOS-QOL scores two to five years following bilateral ACLR, compared with unilateral ACLR (Faltstrom et al., 2013). Another study found that individuals undergoing contralateral ACLR had a higher return to sport rate prior to their second surgery, compared to the average return to sport rate of individuals who received unilateral ACLR (Ardern et al., 2014b). It is intuitive that individuals who return to pre-injury competitive sport would be more likely to experience a contralateral ACL rupture, compared to someone who did not return to high impact sport. Therefore, individuals who undergo a contralateral ACLR may place greater importance on sport participation, and considering return to sport rates and satisfaction with activity levels are lower following contralateral ACLR compared to unilateral ACLR (Faltstrom et al., 2013), the greater mismatch between desires and outcomes could partly explain the lower QOL scores following contralateral ACLR.

**Time from injury to surgery**

In the cross-sectional study (Chapter 6) a trend was observed for worse ACL-QOL scores in people with a delay from ACL rupture to ACLR of more than six months, compared to less than six months. In Chapter 8, waiting longer than 6 months from injury to surgery was associated with increased odds of having radiographic osteoarthritis 5 to 20 years later in people with knee difficulties (compared to having ACLR within 6 months of ACL injury). The systematic review of longer-term QOL after ACLR (Chapter 4) did not find a consistent relationship between time from injury to surgery and QOL. However, one of three studies exploring this relationship reported better QOL in individuals who had ACLR within five months of ACL injury (Barenius et al., 2010). It is possible that studies using a dichotomous variable to measure time from injury to surgery, with a cut-off value around six months, may be more likely to observe relationships with outcomes compared to those measuring time from injury to surgery on a continuous scale.

One possible explanation for a potential relationship between a longer time from injury to ACLR and worse longer-term QOL is the increased likelihood for subsequent knee injury in those with a longer time to surgery. Barenius et al (2010) reported more meniscus injury in those who had ACLR more than five months from injury. This is in line with findings from a study of 616 participants that
reported more meniscal injury in patients who underwent ACLR after three months and more cartilage injury in those who received ACLR more than six months from injury (Razi et al., 2013). Similarly, a large study of 1434 patients found a relationship between an increased period of time from injury to surgery and higher rates of concomitant joint injury when presenting for ACLR, including injury to meniscus and joint surfaces (Ralles et al., 2015). Concomitant meniscus and cartilage injury have been associated with an increased likelihood for self-reported knee symptoms, pain, function and poorer QOL 2 to 16 years after ACLR (Barenius et al., 2010; Cox et al., 2014; Dunn et al., 2015; Gerhard et al., 2012; Neuman et al., 2008; Røtterud et al., 2012; Røtterud et al., 2013). Concomitant meniscus or cartilage injury or surgery have also been related to increased rates of post-traumatic knee osteoarthritis following ACLR (Claes et al., 2013; Keays, 2010; Magnussen et al., 2009; Murray et al., 2012; Øiestad et al., 2009; van Meer et al., 2015).

A common limitation of studies exploring the impact of time from injury to surgery on postoperative outcomes is the lack of standardisation or reporting on rehabilitation or physical activity levels during this pre-operative period. Individuals who are more physically active or those experiencing episodes of instability before undergoing ACLR appear to be at greater risk of joint injury with increased time from ACL rupture to ACLR (Kluczynski, Marzo, & Bisson, 2013; Ralles et al., 2015). However, these scenarios do not necessarily support an early ACLR over trialling conservative management. The only RCT comparing outcomes between individuals randomised to early ACLR (8 to 10 weeks after ACL rupture) or early rehabilitation and optional delayed ACLR, found no difference in the proportion of patients undergoing subsequent meniscus surgery, as well as similar physical activity levels, knee pain, symptoms and QOL at two and five year follow-up (Frobell et al., 2010; Frobell et al., 2013). Standardising rehabilitation and restricting physical activity levels within six months of ACL injury irrespective of ACL management strategy may play an important role in preventing further joint injury and optimising longer-term outcomes.
Directions for future research and strategies to improve quality of life in practice

Common practice for managing ACL-reconstructed individuals comprises a goal-oriented progressive exercise program focusing largely on strength and restoration of pain and symptom-free knee function (Adams, Logerstedt, Hunter-Giordano, Axe, & Snyder-Mackler, 2012). Multiple studies have identified relationships between psychological factors and post-operative outcomes following ACLR (Everhart et al., 2015; Nyland et al., 2006; Nyland et al., 2002; Swirtun & Renström, 2008; Thomeé et al., 2007; Thomeé et al., 2008). Preoperative identification of patients with psychological characteristics associated with an increased likelihood for poor QOL outcomes could allow for the implementation of early interventions to optimise longer-term outcomes following ACLR. Furthermore, a majority of ACLR rehabilitation programs cease within 12 months of surgery (Adams et al., 2012; Delay et al., 2001) and no studies have evaluated the efficacy of longer-term interventions to improve QOL more than five years after ACLR. Management strategies implemented beyond five years post ACLR that address both physical knee complaints and psychological knee difficulties may enhance QOL by improving concordance between knee desires and abilities.

There is also potential for both health-care providers and ACL-ruptured patients to learn from the experiences of long-term ACL-reconstructed individuals who have developed strategies to effectively manage their knee and achieve a satisfactory QOL despite experiencing knee difficulties (Chapter 7). For example, a group-based education and peer support program could be trialled, involving ACL-reconstructed individuals at various stages post-ACLR who meet and discuss self-management strategies, lifestyle modifications, fears, concerns and feelings surrounding their knee. Such an intervention could be moderated by a health-care professional who could provide education surrounding evidence-based exercise recommendations, osteoarthritis management, additional support when ceasing competitive sport and referral to appropriate health-care professionals if required. Additionally, an ACL-reconstructed individual may benefit from annual or bi-annual screening to identify and manage any knee-related physical or psychological difficulties or concerns. Periodic longer-term follow-up could reduce the likelihood of individuals experiencing prolonged
periods of poor knee-related QOL, fear of re-injury and physical inactivity.
A small proportion of text comprising this chapter was adapted from the following publication: SR Filbay & KM Crossley. Quality of life after anterior cruciate ligament reconstruction. *The Anterior Cruciate Ligament: Basic Science and Reconstruction 2e. Chapter 118* (In print, June 2016)

This thesis has reviewed the literature reporting QOL outcomes after ACLR and investigated QOL using quantitative and qualitative methodologies more than five years after ACLR. These investigations have provided valuable insights into longer-term QOL after ACL rupture and have enabled the identification of common issues and considerations in measuring QOL in this population. In this chapter, these issues and considerations will be discussed. Recommendations for measuring QOL in research and practice following ACLR will also be provided.

**Limitations of existing measures**

“Questions arise as to whether such measures are truly patient centred and to what extent they actually represent the quality of life of individual patients or groups of patients. Do they simply describe a patient's health in terms of what health professionals or society believe constitutes quality of life for people who are ill, something that may include factors that have little relevance to or importance for patients?” (Carr & Higginson, 2001) p. 1357
While providing useful information, it is important to acknowledge that standardised QOL instruments have several limitations. Most patient-reported outcomes used in ACL-reconstructed populations contain restricted responses, which do not allow patients to rate the importance or impact of a physical impairment or activity limitation on their life quality. These issues have been previously recognised when measuring health-related QOL in people with disabilities, where measures are often confounded with assessment of function, resulting in a negative bias where lower scores may incorrectly portray poorer health (Krahn et al., 2009). When health-related QOL measures are confounded by assessing function, they may lack sensitivity and risk important changes to the individual’s QOL going undetected due to unchanging or worsening physical function (Krahn et al., 2009).

Furthermore, most QOL questionnaires equally weight each item, which assumes that each item is of equal importance to the individual. However, a recent study found that commonly used knee-related patient-reported outcomes include many items that are of little or no importance to ACL-reconstructed individuals (Tanner et al., 2007). As a result, mean knee-related QOL scores may be influenced negatively by impairments of little importance to the respondent, and may inaccurately reflect the impact of the ACL-reconstructed knee on the respondent’s QOL.

“The challenge in measuring quality of life lies in its uniqueness to individuals. Many of the existing measures of quality of life fail to take account of this by imposing standardised models of quality of life and preselected domains; they are thus measures of general health status rather than quality of life” (Carr & Higginson, 2001) p. 1357

**Knee Injury and Osteoarthritis Outcome Score (KOOS)**

When the KOOS instrument was devised in 1998 it was the first knee-specific patient-reported outcome measure with a QOL component (Roos et al., 1998). Ground breaking at the time, it enabled clinicians to consider the QOL of the patient in clinical decision making and assessment of orthopaedic surgical outcomes. Since 1990, the KOOS has been used extensively in knee osteoarthritis and ACL research; a search in Scopus performed in April 2015 identified 674
publications with the keyword ‘KOOS’ in the abstract or title. Its popularity was confirmed in the two systematic reviews featured in this thesis (Chapter 4 and 5), where the KOOS-QOL subscale was the most frequently used longer-term QOL outcome measure in both ACL-reconstructed and ACL-deficient populations. However, the individual items of the KOOS-QOL are rarely reported or discussed in the literature.

Question one of the KOOS-QOL subscale asks ‘How often are you aware of your knee problem?’ The scoring for this item is structured in a way that results in a worse QOL score allocated to respondents who indicate increased states of knee awareness. On the contrary, personal perspectives on life after ACLR described in Chapter 7 highlight the possibility that for some individuals, increased knee awareness may actually facilitate an active lifestyle and positive lifestyle changes. Question two in the KOOS-QOL subscale asks ‘Have you modified your lifestyle to avoid potentially damaging activities to your knee?’ During the qualitative interviews (Chapter 7) it became evident that positive lifestyle modifications can occur following ACLR, resulting in QOL improvement and satisfaction irrespective of physical knee impairments. Österberg and colleagues described similar positive lifestyle modifications in ACL-deficient individuals associated with feelings of satisfaction (Österberg et al., 2013). The limitation with item two in the KOOS-QOL subscale is that a worse QOL score is given to individuals who have made knee-related lifestyle modifications. Considering these two items comprise 50% of the KOOS-QOL score, future studies using this measure should exercise caution when interpreting the clinical meaningfulness of KOOS-QOL findings. To counteract such pitfalls, a combination of generic (non-disease-specific), knee-specific, and ACL-specific QOL measures were used throughout this thesis in addition to a single-item QOL measure to generate a more accurate understanding of QOL in this population.

**ACL-QOL**

In 1998 another new patient-reported measure was published, this time with the primary purpose of measuring QOL in an ACL-ruptured population (Mohtadi, 1998). Tanner et al. (2007) investigated the perceived importance of knee-specific patient-reported outcomes to ACL-reconstructed individuals by asking individuals to rank whether they experience a particular impairment or not, and
if experienced, to what degree that impairment is important to them on a 5-point Likert scale (1 = experienced but not important, 5 = experienced and extremely important). Measures were then ranked according to frequency of items experienced and the number of items rated as high or low importance (Tanner et al., 2007). As a result, the ACL-QOL questionnaire was identified as containing items of highest relevance and importance to this patient population (Tanner et al., 2007). Despite this, 25 of 31 ACL-QOL items were deemed to be of little or no importance to ACL-ruptured individuals (this was favourable to 41 of 42 KOOS items that were rated of little or no importance). This suggests that even though the ACL-QOL was devised with the primary purpose of measuring QOL in an ACL-ruptured population it is still limited in its ability to accurately measure the impact of an individual’s knee upon their QOL.

Specifically, the impact of a respondent’s knee upon their QOL may be overestimated if that individual experiences knee symptoms or limitations in sporting activities. For example, the ACL-QOL Symptoms and Physical Complaints domain contains four questions. Two questions are worded in a way that allows the individual to evaluate the impact of knee symptoms upon their life quality (“..how troubled are you by giving way episodes..” and “..how much are you troubled by stiffness or loss of motion in your knee?”) However, the other two items are not worded in this way; instead they measure the severity of pain or degree of muscle weakness without evaluating whether the presence of pain or weakness is impacting the QOL of the individual (“..how much pain or discomfort do you have in your knee?” and “..how weak is your knee?”). The largest domain, ‘Recreational Activities and Sport Participation or Competition’ contains 12 questions, the majority of which relate to QOL, with the exception of only two items. These two items do not allow the respondent to express whether specific limitations in sporting activities impact upon their life quality. In cases where an individual is limited in their ability to participate in sport, but does not place importance on sporting abilities or performance, this might falsely translate into a poorer QOL score. Findings from qualitative interviews (Chapter 7) suggest that those individuals who prioritise and enjoy recreational activity may report limitations in competitive sport that do not impact on their life quality. Conversely, similar limitations can have a detrimental impact upon the QOL of other individuals. Four of the six items in the Life Style domain are worded appropriately for a QOL measure; the other two are identical to item one and two of the KOOS-QOL subscale, sharing the same aforementioned shortcomings. In contrast, all questions in the ‘Work-Related Concerns’ domain begin with “How much of a concern
is..” or “How much trouble do you have because of..” and therefore sufficiently address QOL, as do all questions comprising the Social and Emotional domain. In summary, although a majority of ACL-QOL items can give an accurate reflection of a person’s QOL following ACLR, 19% of ACL-QOL items may inaccurately reflect poor QOL for some individuals with potential to negatively bias the ACL-QOL score for individuals with functional impairments or physical symptoms.

Considerations

Comparison to population norms and reference groups

For most QOL measures, published population norms are available. However, a typical ACL-ruptured individual is more active than the general population at the time of injury. Higher physical activity levels and sports participation have been related to better health-related QOL scores (Huffman et al., 2008). Therefore, comparison to general population norms may underestimate the degree of QOL impairment in ACL-ruptured individuals who may have better QOL compared to the general population, but lower QOL compared with their team mates. The systematic review exploring QOL 5 to 20 years following ACLR (Chapter 4) found that studies using the KOOS-QOL tended to report worse QOL scores compared to population norms, whereas use of the SF-36 following ACLR resulted in similar or better scores than population averages. Some measures, such as the SF-36, have athletic population norms available for comparison, which can aid the interpretability of results. Knee-related QOL scores from healthy populations ‘free from knee pain or injury’ have potential to be misleading since greater impairment would be expected following ACL rupture compared with individuals with no knee problems.
The temporal trajectory of quality of life following anterior cruciate ligament reconstruction

Quality of life is a dynamic concept and QOL instruments are often used to assess changes over time. This is of particular relevance when determining the effectiveness of an intervention, including the efficacy of ACLR and postoperative rehabilitation strategies. When using QOL measures longitudinally, clinicians and researchers should be aware of fluctuations in QOL scores that can occur over time following ACLR. As eluded to in the qualitative study (Chapter 7), trajectories in QOL can vary greatly between individuals. As expectations change over time, so too may an individual’s perception of their knee upon their QOL (Carr et al., 2001). An example of a common trajectory of QOL experienced by participants (Chapter 7) included a prolonged period of poor QOL (often involving physical inactivity, fear of re-injury and dissatisfaction with knee function) until reaching a period of acceptance and adaptation (often involving a re-evaluation and lowering of expectations and resumption of physical activity at a modified level) after which an improvement in QOL was often described. In contrast, another common QOL trajectory involved a prolonged period of satisfactory QOL that was disrupted by periods of transition, instigated by subsequent knee injury or ceasing competitive sport (Chapter 7). Measuring QOL cross-sectionally does not provide any information about change over time and this was a key limitation of the cross-sectional study (Chapter 6). Although the potential for recall bias must be acknowledged, the qualitative study (Chapter 7) enabled participants to describe their QOL journey over time, providing novel information about influential experiences such as re-injury, acceptance and lifestyle modifications.

Discordance between satisfaction and quality of life scores

An interesting finding in the qualitative study (Chapter 7) was the reporting of knee satisfaction in individuals with very low knee-related QOL scores. This has important clinical implications; a clinician should be aware that an individual who scores poorly on a patient-reported QOL questionnaire may actually be satisfied with their current knee state. This disparity between QOL scores and satisfaction could be partly explained by the aforementioned limitations of available QOL measures.
Recommendations for quality of life assessment following anterior cruciate ligament reconstruction

Appropriate selection of quality of life measures

It is recommended that selection of an appropriate QOL measure be undertaken after careful review of questionnaire content and that a measure is selected to align with the purpose of a study or address areas important and relevant to the individual (Carr & Higginson, 2001; Fitzpatrick, Davey, Buxton, & Jones, 1998; Garratt et al., 2002; Post, 2014). Based on an in-depth literature review, the criteria proposed by Fitzpatrick and colleagues to assess the quality and appropriateness of QOL measures included: reliability, validity, responsiveness, feasibility, appropriateness, interpretability, precision, and acceptability (Fitzpatrick et al., 1998). Of particular importance is selecting a QOL measure that is responsive and sensitive to change over time in an ACL-ruptured population (Guyatt, Deyo, Charlson, Levine, & Mitchell, 1989). Additionally, published data on MCID, minimal clinically important improvement (MCII) or patient acceptable symptomatic state (PASS) can facilitate interpretation of scores and change in scores over time (Juniper, Guyatt, Willan, & Griffith, 1994; Kvien et al., 2007). Combining the aforementioned factors, an ideal QOL measure should have available MCID/MCII or PASS data, satisfy the majority of criteria recommended by Fitzpatrick and colleagues and address factors of importance and relevance to the individual. The ACL-QOL can be considered an appropriate tool for measuring QOL following ACL rupture, since this questionnaire contains more items of importance to ACL-ruptured individuals in comparison to other knee-specific measures (including the KOOS) (Tanner et al., 2007). The critical limitations in interpreting the meaningfulness of impairments in KOOS-QOL scores have been discussed earlier in this Chapter.
Health-related and knee-related QOL measures offer complimentary attributes, and value can be gained from using both a generic and a knee-specific measure. Generic health-related QOL or health-status measures such as the SF-36 and the AQoL-8D can provide complimentary information that would not be obtained from knee-specific QOL measures. Specifically, use of a generic health-related QOL measure would assist in determining the overall health status of the individual, addressing such aspects as sleep, fatigue, other bodily pain, comorbidities and mental and social health which may be of relevance to an ACL-reconstructed individual with potential to impact upon and interact with self-perceived knee-related QOL. However, health-related QOL measures are often confounded by assessment of physical function (Krahn et al., 2009). As a result, health-related QOL measures which differentiate physical function from health-status are recommended. Alternatively, when using a measure such as the SF-36 which contains a large physical function component, reporting of individual domain scores may enable the identification of improvements that may be important to the individual and facilitate a more accurate interpretation of high or low ‘health-related QOL’ scores (Krahn et al., 2009).

Flagging important items

A more patient-centred approach could involve flagging individual questionnaire items of greatest importance to the patient and specifically following these up at subsequent visits, although the responsiveness to change of individual items would be unknown for many QOL questionnaires. Methods recommended for incorporating patient input into QOL assessment include allowing the patient to rate the importance of each item, or enabling the patient to contribute to the measurement by mentioning any additional issues of importance that were not captured in the questionnaire (Gill & Feinstein, 1994). Notably, the KOOS-QOL and ACL-QOL address some topics of high importance to many ACL-reconstructed individuals including expectations, fears, knee difficulties and knee confidence which may provide valuable information when interpreted in isolation from summary scores. Due to limitations in current knee-related QOL measures, a new knee-related QOL questionnaire that takes into consideration the importance of each item to the individual may improve the measurement of knee-related QOL in ACL injured individuals.


**Further questioning**

Considering the limitations of commonly used QOL measures, the development of a new QOL measure for use in ACL-reconstructed individuals free from the biases that exist in currently used measures is warranted. In the meantime, patient-centred questions might be a valuable adjunct to standardised patient-reported measures for use pre and postoperatively, although these would require validation testing using patient samples. Table 10.1 provides some suggestions of patient-centred questions for use in clinical practice that may assist in bridging the gap between standardised patient-reported questionnaires and a patient’s personal attributes, life priorities, ambitions, goals, and values.

**Table 10.1** Example of patient-centred questions that may be used to accompany standardised QOL measures

<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘To what degree is your knee impacting on your quality of life?’</td>
</tr>
<tr>
<td>‘In what way is your knee impacting on your current happiness?’</td>
</tr>
<tr>
<td>‘What do you really want to be able to do, that you can’t do because of your knee?’</td>
</tr>
<tr>
<td>‘Is there anything that is important to you that was not covered in this questionnaire?’</td>
</tr>
<tr>
<td>‘Could knee difficulties prevent you from achieving your goals and ambitions?’</td>
</tr>
<tr>
<td>‘What do you expect to achieve from this ACL reconstruction?’</td>
</tr>
</tbody>
</table>

The previously described limitations in patient-reported QOL measures for use in ACL-ruptured populations prompted the inclusion of a single-item question in the cross-sectional study; “Do you believe that your knee is impacting on your QOL?” The advantage of using a single-item QOL question such as this is that it enables the individual to self-evaluate the influence of their knee upon their QOL in line with their own expectations. Considering QOL is a subjective concept and the interpretation and evaluation of QOL depends largely on an individual’s beliefs, goals and expectations, there may be added value in including a single-item QOL question in future research and clinical practice.
This thesis commenced by providing an overview of research surrounding ACL injury, management and longer-term outcomes. By summarising current evidence, it became apparent that many ACL-reconstructed individuals experience ongoing physical and psychological knee difficulties after ACLR. Despite potential for ongoing knee difficulties, the degree of longer-term QOL impairment and factors impacting longer-term QOL in these individuals remained unclear. This led to a systematic review pooling data from all published studies reporting QOL outcomes at least five years following ACLR. This review found that, on average, knee-related QOL was impaired 5 to 20 years following ACLR and several factors were associated with worse QOL outcomes. However, conclusions were limited by the small number of studies investigating QOL as a primary outcome and the absence of studies that had explored QOL specifically in people with knee difficulties. A second systematic review found that QOL outcomes were no better in ACL-reconstructed groups, compared to groups of individuals who did not undergo ACLR following ACL rupture. Taken together, these systematic review findings highlight that a proportion of individuals experience knee-related QOL impairment more than five years after ACLR, warranting further investigation into longer-term QOL outcomes following ACLR.

Using a mixed-methods approach (comprising quantitative and qualitative methodologies), a detailed investigation of QOL in people with knee difficulties after ACLR was performed and specific factors associated with worse longer-term QOL were identified. Factors associated with impaired QOL more than five years following ACLR in 162 people with knee difficulties included not returning to competitive sport, undergoing a subsequent knee surgery after ACLR and a high BMI. Findings from the qualitative study suggested that maintaining some form of satisfying physical activity may be a critical determinant of longer-term QOL following ACLR in people with knee difficulties. Further insight was gained into the relationship between return to sport and QOL, where people with a strong
preference for competitive sport over recreational exercise who cease competitive sport after ACLR, and individuals who are limited in physical activity participation due to fear of re-injury, may benefit from support to maintain a physically active lifestyle and prevent prolonged periods of poor QOL.

To further augment understanding of longer-term QOL following ACLR, the final study in this thesis explored the relationship between QOL and radiographic osteoarthritis in individuals with knee difficulties and additional factors associated with poor long-term outcomes in this population were identified. Given that radiographic osteoarthritis was related to worse knee-related QOL and dissatisfaction with knee function, risk factors for radiographic osteoarthritis may be considered together with predictors of poor QOL to recognise people at heightened risk of worse longer-term QOL outcomes after ACLR. These included a delay of greater than six months from injury to surgery, undergoing a subsequent knee surgery and a non-contact mechanism of ACL injury. Since these studies specifically involved individuals who experienced some form of knee difficulty, these findings may not be applicable to all ACL-reconstructed individuals. There is likely to be a subset of individuals who experience no QOL impairment or knee difficulties after ACLR.

From a clinical perspective, there is a clear need to develop and evaluate interventions aimed at improving longer-term QOL for those individuals who experience knee-related dissatisfaction or QOL impairment following ACLR. Strategies to address both physical and psychological knee difficulties may prove successful in improving longer-term QOL after ACLR. Despite potential for ongoing knee difficulties, it is common practice for an ACL-reconstructed individual to cease rehabilitation around one year following ACLR, and re-initiate management following subsequent knee injury or the development of symptomatic osteoarthritis. The gap between these events provides a great opportunity to implement strategies aimed at establishing achievable knee expectations, promoting an active lifestyle, improving knee function and facilitating sustainable self-management strategies. A positive finding of this thesis was that individuals can adapt to altered knee function and achieve satisfaction despite persistent knee pain and symptoms. However, the potential for positive adaptation is difficult to determine from the KOOS-QOL and ACL-QOL measures, where knee-related lifestyle modification is assumed to have a negative impact on QOL. Further research should capitalise on these findings by developing strategies to promote positive lifestyle adaptations in individuals with persistent knee difficulties after ACLR.
In summary, the results of the studies presented in this thesis highlight that QOL impairment is common 5 to 20 years following ACLR, despite this achieving a satisfactory QOL is possible even with persistent knee pain and symptoms. A greater focus on optimising longer-term QOL following ACLR is needed.


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Surgery, 21(3), 225.
# APPENDICES

## APPENDIX 4.1 SYSTEMATIC REVIEW SEARCH STRATEGY

<table>
<thead>
<tr>
<th>Database</th>
<th>Search Strategy</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinahl</td>
<td>(TITLE-ABS-KEY(“knee injury and osteoarthritis outcome score” OR SF-36 OR ”short form” OR short-form OR QOL OR HRQoL OR ”quality of life” OR ACL-QOL OR OR ”Lower Extremity Activity Profile” OR leap OR kqol OR AQoL-8D OR EQ5D OR EQ-5D OR WOMAC) AND TITLE-ABS-KEY(“anterior cruciate ligament” OR ACL))</td>
<td>52</td>
</tr>
<tr>
<td>Medline</td>
<td></td>
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<tr>
<td>SPORTDiscus</td>
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<td>21</td>
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<tr>
<td>Scopus</td>
<td></td>
<td>268</td>
</tr>
<tr>
<td>Web of Knowledge</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>552</td>
</tr>
</tbody>
</table>
# APPENDIX 4.2 MODIFIED DOWNS AND BLACK CRITERIA USED FOR QUALITY APPRAISAL

Scoring: **YES** = (1); **NO** = (0) Unable to determine: **UTD** = (0)

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>ADDITIONAL EXPLANATION/ MODIFICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the hypothesis/aim/objective of the study clearly described?</td>
<td><strong>Must be explicit</strong></td>
</tr>
</tbody>
</table>
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | **NO** = If a main outcome is first mentioned in the results section  
**YES** = if all primary outcomes are described in methods or introduction (i.e. reproducible) |
| 3. Are the characteristics of the patients included in the study clearly described? | **YES** = if clear inclusion and/or exclusion criteria given. |
| 4. Are the interventions of interest clearly described?                 | **YES** = The surgical ACL reconstructive technique should be clearly described (i.e., graft type, incision, allograph/autograft etc.) |
| 5. Are the distributions of principal confounders in each group of subjects to be compared clearly described? | **YES** = if age, gender and one or more confounder is described. |
| 6. Are the main findings of the study clearly described?                | **YES** = All major findings clearly described so that the reader can check the major analyses and conclusions. Simple outcome data (including denominators, numerators) should be reported for all major findings.  
**NO** = If only percentages or only p values are reported for main findings. |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported.  
**YES** = (mean + SD/SE/C) OR (median + range/IQR).  
**NO** = mean + range/IQR OR if variability not reported. |
| 8. Have all important adverse events that may be a consequence of the intervention been reported? | **NO** = If no adverse events reported.  
**UTD** = If one adverse event reported.  
**YES** = If more than one reported (i.e., re-rupture, subsequent surgeries, contralateral injury, meniscal damage). |
| 9. Have the characteristics of patients lost to follow-up been described? | **YES** = if no patients lost to follow-up; **or** <5% loss to follow-up; **or** tells us something about those lost to follow-up (such as age, gender, that they did not differ from the rest of the
<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Have actual probability values been reported (e.g. 0.035 rather than &lt;0.05) for the main outcomes except where the probability value is less than 0.001?</td>
<td>Additional explanation not necessary.</td>
<td></td>
</tr>
<tr>
<td>11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?</td>
<td>YES = if the source of the population (ie, hospital, surgeon) and how they were selected is stated; or if stated that all of a population were selected; or an unselected sample of consecutive patients were selected; or a random sample from an entire population were selected. UTD = If the study does not state what proportion that sample was from the source population. NO = if unable to answer yes to any of the above criteria set for YES or UTD.</td>
<td></td>
</tr>
<tr>
<td>12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?</td>
<td>YES = if the study reports how many agreed to participate and compares one or more confounder with those agreeing and those not agreeing to participate (ie, that they did not differ from the source population, or mean age, or gender etc.) OR YES = if all of a population were selected. UTD = if they did not state how many agreed to participate from the source population, or if they did not compare those agreeing with those not agreeing to participate. NO = if significant difference was reported in sample compared to population.</td>
<td></td>
</tr>
<tr>
<td>13. Was the study prospective?</td>
<td>YES = prospective studies</td>
<td>NO = retrospective studies</td>
</tr>
<tr>
<td>14. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?</td>
<td>YES = Where follow-up was the same for all study patients; or YES = acceptable range of difference between groups (1 year follow up = 1 month each way; 2 years follow up = 2 months; 3 years follow up = 3 months… ...10 years follow up = 10 months); or YES = if differences were adjusted by survival analysis etc. NO = if only one intervention group, and follow-up range greater than 5 years and no adjustments made; or NO = does not report mean follow-up time for each intervention group or cohort (however, if randomised to groups, at same time-point, assume no significant difference if not stated); or NO if unacceptable difference in follow-up between groups and no adjustments were made.</td>
<td></td>
</tr>
<tr>
<td>15. Were the main outcome measures used accurate (valid and reliable)?</td>
<td>YES = If outcome measures are clearly described, and references other article(s) which found outcome measure to be valid and reliable, or demonstrates the outcome measure(s)</td>
<td></td>
</tr>
</tbody>
</table>
16. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?

*YES* = Patients for all comparison groups should be selected from the same hospital(s) or surgeon(s); or *YES* = if only one intervention group and source of participants is described.

*UTD* = The question should be answered UTD for cohort and case control studies where there is no information concerning the source of patients.

17. Were study subjects randomised to intervention groups?

Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation.

18. Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?

*NO* = All non-randomised studies, or *NO* = If assignment was concealed from patients but not from staff.

19. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?

In non-randomised studies if the effect of the main confounders (gender, age + 1 more) was not investigated or no adjustment was made in the final analyses the question should be answered as = *NO*.

*YES* = If no significant difference in confounders (age, gender + 1 more) between groups stated/shown. *YES* = If adjustments were made for 1 or more confounders in the analysis.

20. Were losses of patients to follow-up taken into account?

*YES* = If 5% or less loss to follow-up, assume too small to effect main findings; *YES* = If >5% loss to follow-up and intention to treat analysis performed.

*UTD* = If the number of patients lost to follow-up are not reported.

*NO* = If >5% loss to follow-up, and no adjustments made.

21. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance <5%?

*YES* = If sample size was calculated and sample size was sufficient to detect a clinically important effect where the probability value for a difference being due to chance <5%.

*NO* = if no sample size calculation, or calculation found insufficient sample size to detect clinically important effect in primary outcome(s).
## APPENDIX 5.1 SYSTEMATIC REVIEW SEARCH STRATEGY

<table>
<thead>
<tr>
<th>Database</th>
<th>Date</th>
<th>Search Strategy</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scopus</td>
<td>30/01/2014</td>
<td>Your query: (TITLE-ABS-KEY(&quot;anterior cruciate ligament&quot; OR &quot;ACL&quot;) AND TITLE-ABS-KEY(KOOS OR &quot;knee injury and osteoarthritis outcome score&quot; OR SF-36 OR &quot;short form-36&quot; OR QOL OR &quot;quality of life&quot; OR ACL-QOL OR AQOL-8D* OR A-QOL OR ACLQOL OR ACL-QOL OR &quot;Lower extremity Activity Profile&quot; OR leap OR KQOL-26 OR womac OR EQ-5D OR HRQOL))</td>
<td>355</td>
</tr>
</tbody>
</table>
APPENDIX 6.1 ETHICS APPROVAL

THE UNIVERSITY OF QUEENSLAND
Institutional Human Research Ethics Approval

Project Title: Early-Onset Knee Osteoarthritis Following Anterior Cruciate Ligament Reconstruction: The Impact On Quality Of Life, Work Participation And Health Costs

Chief Investigator: Ms Stephanie Filbey

Supervisor: A/Prof Kay Crossley, Dr Ilana Ackerman, A/Prof Trevor Russell

Co-Investigator(s): None

School(s): School of Health and Rehabilitation Sciences, Department of Physiotherapy

Approval Number: 2012001240

Granting Agency/Degree: PhD

Duration: 31st December 2015

Comments:

Note: If this approval is for amendments to an already approved protocol for which an UQ Clinical Trials Protocol/Insurance Form was originally submitted, then the researchers must directly notify the UQ Insurance Office of any changes to their Form and Participant Information Sheets & Consent Forms as a result of the amendments, before action.

Name of responsible Committee:
Medical Research Ethics Committee
This project complies with the provisions contained in the National Statement on Ethical Conduct in Human Research and complies with the regulations governing experimentation on humans.

Name of Ethics Committee representative:
Professor Bill Vicenzino
Chairperson
Medical Research Ethics Committee

Signature [Signature] Date 30/11/2022
Early-onset knee osteoarthritis following anterior cruciate ligament reconstruction: the impact on quality of life

Study information sheet

We invite you to participate in our research project “Early-onset knee osteoarthritis following anterior cruciate ligament reconstruction: the impact on quality of life”. We would like to give you some background information on why we think this project is important and what we would like you to do if you decide to join us in this research.

What is the purpose of this study?

Anterior cruciate ligament reconstruction (ACLR) is a relatively common operation in young active people who have ruptured their ACL. The reconstructive surgery is normally aimed at restoring stability of the knee and to allow return to sports and other high impact activities. Although these aims are often achieved, it is known that people who have undergone an ACLR are at increased risk of developing knee osteoarthritis (OA) in the future.

What we want to know is how living with persistent pain or stiffness in your knee impacts your quality of life. We want to know whether your knee limits you from doing any of the things you would like to do, and how this makes you feel. Most research focuses on OA in older people, but younger and middle-aged adults get OA too, and face unique challenges like work commitments, sports, and child caring.
Who can participate in this study?

You can participate in this study if you can answer yes to these 4 questions:

- 1. Are you between 18 and 55 years of age?
- 2. Have you had an ACLR more than five years ago?
- 3. Have you either been told by a doctor that you have osteoarthritis of the knee or have you experienced knee pain, decreased knee function or stiffness on most days for more than 3 months?
- 4. Are you fluent in written English?

Who is not able to participate in this study?

Please note, if you answer yes to either of the following 2 questions you will not be able to take part in this study:

- 1. Do you have any illnesses or medical conditions (other than knee OA) which might impact on your function or quality of life? (examples include back pain, recent injury, cancer, lung conditions, infectious diseases etc.)
- 2. Have you had an ACLR within the last five years?

What will I be expected to do if I agree to participate?

If you agree to participate in the study we ask that you complete a questionnaire. You can choose to complete this online or have it mailed to you. If you have had an x-ray of your knee in the past 6 months, we may ask for a copy of these scans. If you have not had an x-ray within the last 6 months, we may ask you to get another x-ray of your knee. If required, we will pay for this x-ray and provide you with a summary of the x-ray findings.

What do I get if I agree to participate?

If you agree to participate, following study completion we will provide you with an overview of the study findings, information on knee OA and current research updates. If an x-ray is required, you will get a summary of your x-ray findings and the opportunity to discuss these findings with a physiotherapist if you like. Last but not least, you get the satisfaction of knowing you are helping improve the understanding and treatment of people like yourself, living with knee pain or stiffness following ACLR.

Are there any risks involved?

The process of having an x-ray involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The expected dose from an x-ray of your knee is around 0.03 mSv. At this dose level no harmful effects of radiation have been
demonstrated, as any effect is too small to measure. The risk is believed to be very low. If you are breastfeeding or could be pregnant you will not be eligible for an x-ray.

Can I withdraw from the study if I wish?

Yes. Although we encourage you to complete the study, your participation in this study is voluntary. If you do not wish to take part you are under no obligation to do so. Also, if you decide to take part but later change your mind, you are free to withdraw from the project at any stage. You may also withdraw any unprocessed data previously supplied by you.

Will my details be kept confidential?

Yes. The anonymity of your participation is assured by our procedure, in which a code number and not your name will identify you. No findings that could identify you will be published and access to individual results is restricted to the investigators. Coded data will be stored for at least 5 years. All data and results will be handled in a strictly confidential manner, under guidelines set out by the National Health and Medical Research Council. The principal investigator (Miss Stephanie Filbay) is responsible for maintaining this confidentiality. This project is subject to the requirements of the Human Research Ethics Committee of the University of Queensland.

Who can I contact if I have any questions?

This study has been cleared by one of the human ethics committees of the University of Queensland in accordance with the National Health and Medical Research Council’s guidelines. You are of course, free to discuss your participation in this study with project staff (contactable on +61 409 937 031). If you would like to speak to an officer of the University not involved in the study, you may contact the Ethics Officer on 3365 3924.

Who are the researchers conducting this study?

Miss Stephanie Filbay is a physiotherapist and a PhD Candidate in the Department of Physiotherapy at the University of Queensland.

Associate Professor Kay Crossley is a physiotherapist and Associate Professor in the Department of Physiotherapy at the University of Queensland.

Dr Ilana Ackerman is a physiotherapist and post-doctoral research fellow at the Melbourne EpiCentre, Department of Medicine (Royal Melbourne Hospital), The University of Melbourne.

Associate Professor Trevor Russell is a physiotherapist and Associate Professor in the Department of Physiotherapy at The University of Queensland.
What is the next step?

If you would like to participate in this study, please contact Stephanie by:

- **Phone or text**: on 0409937031 or
- **Email**: stephanie.filbay@uqconnect.edu.au or
- **Post**: by completing this sheet and posting in the reply paid envelope provided.

---

If you choose to respond to this letter via post, please tick all boxes that apply:

- ☐ I have had an ACLR more than 5 years ago
- ☐ I do not have any current injuries or chronic diseases (unrelated to the knee) which may impact on my function or quality of life
- ☐ I have been advised by a doctor that I have knee OA, or I experience knee stiffness, decreased knee function or persistent knee pain.

**How would you like to receive your questionnaire?**

- ☐ I would like to receive my questionnaire and any correspondence via email
  
  Email address: ___________________________________________________________

- ☐ I would prefer to receive my questionnaire via post

---

*We thank you for your time, and look forward to hearing from you, should you wish to participate.*
APPENDIX 6.3 CONSENT FORM AND STUDY QUESTIONNAIRE

Early-onset knee osteoarthritis following ACLR: the impact on quality of life

Study consent form

I, ________________________________ (participant’s full name), consent to participate in the above research project, on the basis that I:

1. Have read and understood the information sheet provided to me.
2. Have had the opportunity to clarify any aspect of my participation in the study with the investigators.
3. Understand participating in this study involves completing a questionnaire.
4. Have had all the foreseeable risks of participation in the study explained to me by way of the methods outlined in 1 and 2 above.
5. Understand that I may not benefit directly from participating in this study, although the results of this study and x-ray results will be made available to me.
6. Understand that all information provided by myself and the data collected from me is to be treated with the utmost confidentiality and that this data will be reported in a manner that does not identify me. On request, I may have access to my results.
7. Am free to withdraw from the study at any stage without providing a reason and without penalty.

Name of participant:

Signature of participant: ________________________________
Date: ________________________________

The following physiotherapists involved in this study, would like to kindly thank you for your participation:

Miss Stephanie Filbay: physiotherapist and PhD Candidate, Division of Physiotherapy, School of Health and Rehabilitation Sciences, The University of Queensland.

Associate Professor Kay Crossley: physiotherapist and Associate Professor, Division of Physiotherapy, School of Health and Rehabilitation Sciences, The University of Queensland.

Dr Ilana Ackerman: physiotherapist and post-doctoral research fellow at the Melbourne EpiCentre, Department of Medicine (Royal Melbourne Hospital), The University of Melbourne.

Associate Professor Trevor Russell: physiotherapist and Associate Professor in the Division of Physiotherapy, School of Health and Rehabilitation Sciences, The University of Queensland.
Participant Details

1. Date of birth: ______ / ______ / _____________

2. Gender:
   - Male
   - Female

3. Email address: ___________________________________________________________

4. Mobile number: __________________________________________________________

5. Postal address: __________________________________________________________

   __________________________________________________________
   __________________________________________________________

6. Date of your most recent ACLR (month/year):_______ / ___________
7. What type of ACL graft did your surgeon use during your most recent ACLR?

- □ Hamstring
- □ Patella tendon
- □ LARS
- □ Allograft (donor tissue)
- □ Other
- □ Unsure

8. Did you have any meniscus or cartilage damage at the time of surgery?

- □ Meniscus damage
- □ Cartilage damage
- □ Unsure
- □ No meniscus or cartilage damage

9. Did you damage any of the following ligaments at the time of your ACL injury? (tick all that apply)

- □ Posterior cruciate ligament (PCL)
- □ Medial collateral ligament (MCL)
- □ Lateral collateral ligament (LCL)
- □ Unsure
- □ No, I did not damage any of these ligaments
Early-onset knee osteoarthritis following anterior cruciate ligament reconstruction: the impact on quality of life

The following questionnaire will ask you a range of questions about your knee, and how your knee function impacts on your life. Please answer all questions accurately, and if you are confused about any of the questions or need to clarify anything, please contact Miss Stephanie Filbay on +61 409 937 031 or email stephanie.filbay@uq.net.au.

Once you complete the questionnaire, return it in the reply paid envelope provided. Please note; if we have not received the questionnaire in 2 weeks, or if there are any missing responses, you will receive a friendly reminder phone call from us. Once again, we thank-you kindly for taking part in this study, your participation is valued greatly.

Demographics

1. What is your height? ________________cm

2. What is your current weight? ________________kg

3. What has been your main occupation since your ACLR?

________________________________________________________
4. What is your current work status?

☐ Full-time  ☐ Part-time  ☐ Stay at home parent/carer

☐ Casual  ☐ Retired  ☐ Student  ☐ Unemployed

5a. Do you have children?

☐ Yes  ☐ No

5b. ...if yes, what age are your children (please tick all that apply)?

☐ 0-4 years  ☐ 5-9 years  ☐ 10-14 years

☐ 15-19 years  ☐ 20-24 years  ☐ 25+ years

6a. Do you have any illnesses/ medical conditions other than osteoarthritis of the knee?

☐ Yes  ☐ No

6 b. ...if yes, please specify:______________________________________________

______________________________________________

______________________________________________
7. How long did you wait from your time of injury until having ACL reconstructive surgery?

☐ Less than 1 month  ☐ 1-3 months  ☐ 4-6 months

☐ 6-12 months  ☐ 1-2 years  ☐ Greater than 2 years

☐ Unsure

8a. How many ACLRs have you had on your **left knee**?

☐ None  ☐ 1  ☐ 2  ☐ 3 or more

8b. How many other surgeries (not including ACLR) have you had on your **left knee**?

☐ None  ☐ 1  ☐ 2  ☐ 3 or more

9a. How many ACLRs have you had on your **right knee**?

☐ None  ☐ 1  ☐ 2  ☐ 3 or more
9b. How many other surgeries (not including ACLR) have you had on your right knee?

☐ None  ☐ 1  ☐ 2  ☐ 3 or more

10a. Were you playing sport when you injured your ACL?

☐ Yes  ☐ No

10b. ...if yes, which sport you were playing (please specify)?

________________________________________________________________________

11a. Please tick the most appropriate statement regarding your level of sport participation after injuring your ACL:

☐ I returned to competitive sport at the same or higher level than before ACL injury

☐ I returned to competitive sport at a lower level than before ACL injury

☐ I did not return to competitive sport after my ACLR

11b. If you did not return to competitive sport, or returned to competitive sport at a lower level than prior to your ACLR, was this because of your knee?

☐ Yes  ☐ No
12. Did your ACL injury involve contact with another player or object?

☐ Yes  ☐ No  ☐ Unsure

13. Did you experience any of the following problems one year after your ACLR (tick all that apply)?

☐ Difficulty straightening your knee  ☐ Persistent swelling

☐ Difficulty bending your knee  ☐ Instability or giving way

☐ Pain around the knee cap  ☐ Unsure

14. Do you consider yourself to have a higher than average pain tolerance?

☐ Yes  ☐ No

15. After rupturing your ACL, did anybody speak to you about the potential of getting osteoarthritis in the future?

☐ Yes  ☐ No  ☐ Unsure

16a. Do you currently receive treatment for your knee?

☐ Yes  ☐ No
16b. ... If yes, how satisfied are you with the treatment you receive?

☐ Very satisfied  ☐ Moderately satisfied  ☐ Somewhat satisfied  ☐ Unsatisfied

17. How would you rate your knowledge of osteoarthritis?

☐ Very good  ☐ Good  ☐ Average  ☐ Poor  ☐ Very poor

18. Do you believe that your knee is impacting on your quality of life?

☐ Not at all  ☐ Slightly  ☐ Moderately  ☐ Significantly

19. If you had to choose only one of the following activities to participate in free from knee pain or impairment, which of the following would you choose?

☐ Participation in exercise  ☐ Participation in sport

☐ Work related activities  ☐ Participation in social activities

☐ Family-responsibilities as a parent/spouse/sibling
20. Taking into account your level of pain and also your functional impairment, if you were to remain for the next few months as you are today, would you consider that your current state is satisfactory?

☐ Yes  ☐ No
ANTERIOR CRUCIATE LIGAMENT QUALITY OF LIFE ASSESSMENT

DIRECTIONS

Please answer each question with respect to the current status, function, circumstances and beliefs surrounding your knee anterior cruciate ligament (ACL) deficient knee. Please consider the last three months.

Indicate with a slash (/) on the line, the point ranging from 0 to 100 which most closely represents your situation.

For example, the following question:

Is this a good questionnaire?

0  [ ]  100
Useless  [ ]  Fantastic

If the slash is placed in the middle of the line, this indicates that the questionnaire is of average quality, or in other words, between the extremes of ‘useless’ and ‘fantastic’. It is important to put your slash at either end of the line if the extreme descriptions accurately reflect your situation.
SECTION A: SYMPTOMS & PHYSICAL COMPLAINTS

The first four questions are related to: SYMPTOMS & PHYSICAL COMPLAINTS.

1. With respect to your overall knee function. How troubled are you by “giving way” episodes?
(Make a slash at the extreme right if you are experiencing, no giving way episodes in your knee. Please note that this question has two parts. It is concerned with both, the severity (1a) and frequency (1b) of the giving way episodes.)

1a 0  Major giving way episodes  100  Minor giving way episodes

1b --------------------------  100
   0  Constantly giving way  Never giving way

2. With any kind of prolonged activity (i.e. greater than half an hour) how much pain or discomfort do you get in your knee?

----------  100
   0  Severe pain  No pain at all

3. With respect to your overall knee function, how much are you troubled by stiffness, or loss of motion in your knee?

----------  100
   0  Severely troubled  Not troubled at all

4. Consider the overall function of your knee and how it relates to the strength of your muscles: How weak is your knee?

----------  100
   0  Extremely weak  Not weak at all
SECTION B: WORK RELATED CONCERNS

The following questions are being asked with respect to your job or vocation (i.e., WORK RELATED CONCERNS). The questions are concerned with your ability to function at work and how your knee has affected your current work-related concerns. If you are a full-time student/home maker, then consider this and any part-time work together. Consider the last three months.

*** If you are CURRENTLY NOT EMPLOYED for reasons OTHER THAN YOUR KNEE then place a check on this line. _________

5. How much trouble do you have, because of your knee with turning or pivoting motions at work? (Make a slash at the extreme left if you are unable to work because of the knee.)

0 ................................................................. 100
Severely troubled No trouble at all

6. How much trouble do you have, because of your knee, with squatting motions at work?
(Make a slash at the extreme left if you are unable to work because of the knee.)

0 ................................................................. 100
Severely troubled No trouble at all

7. How much of a concern is it for you to miss days from work, due to problems or re-injury to your knee? (Make a slash at the extreme left if you are unable to work because of the knee.)

0 ................................................................. 100
An extremely significant concern No concern at all

8. How much of a concern is it for you to lose time from "school" or work because of the treatment of your ACL deficient knee?

0 ................................................................. 100
An extremely significant concern No concern at all
SECTION C: SPORT / RECREATION / COMPETITION

The following questions are being asked with respect to your RECREATIONAL ACTIVITIES, SPORT PARTICIPATION OR COMPETITION. The questions are concerned with your ability to function and participate in these activities as they relate to your knee problem. Consider the last three months.

9. How much limitation do you have with sudden twisting and pivoting movements or changes in direction?

0  100
Totally limited No limits

10. How much of a concern is it for you that your sporting/recreational activities may result in the status of your knee to worsen?

0  100
An extremely significant No concern at all concern

11. How does your current level of athletic or recreational performance, compare to your pre-injury level?

0  100
Totally limited No limitations

12. With respect to the activities or sports that you currently desire to be involved with, how much have your expectations changed because of the status of your knee?

0  100
Expectations totally lowered Expectations not lowered at all

13. Do you have to play your recreation/sport under caution? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0  100
Always play under caution Never play under caution

14. How fearful are you of your knee “giving way” when playing recreation/sport? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0  100
Extremely fearful No fear at all
15. Are you concerned about environmental conditions, such as a wet playing field, a hard court, or the type of gym floor when involved in your recreation or sport? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 100
Extremely concerned Not concerned at all

16. Do you find it frustrating to have to consider your knee with respect to your recreation/sport?

0 100
Extremely frustrated Not frustrated at all

17. How difficult is it for you to "go full out" at your recreation/sport? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 100
Extremely difficult Not difficult at all

18. Are you fearful of playing contact sports? (Circle the “N/A” at the right of the scale if you do not play contact sport for reasons other than the knee.)

0 100 N/A
Extremely fearful No fear at all

The following questions are specifically asking about the two most important sports or recreational activities that you do. Please write them in order of importance.

1. 

2. 

19. How limited are you in playing the number "1" sport/recreational activity? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 100
Extremely limited Not limited at all

20. How limited are you in playing the number "2" sport / recreational activity? (Make a slash at the extreme left i.e. 0, if you are unable to play recreation/sport because of your knee)

0 100
Extremely limited Not limited at all
SECTION D: LIFESTYLE

The following questions are concerned with your lifestyle in general and should be considered outside of your work and recreational/sport activities as they relate to your anterior cruciate ligament (ACL) deficient knee.

21. Do you have to concern yourself with general safety issues (e.g. carrying small children, working in the yard, etc.) with respect to your ACL deficient knee?

0 100
Extremely concerned No concern at all

22. How much has your ability to exercise and maintain fitness been limited by your knee problem?

0 100
Totally limited Not limited at all

23. How much has your enjoyment of life been limited by your knee problem?

0 100
Totally limited Not limited at all

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

0 100
All of the time None of the time

25. Are you concerned about your knee, with respect to lifestyle activities that you and your family do together?

0 100
Extremely concerned No concern at all

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

0 100
Totally modified No modifications
SECTION E: SOCIAL AND EMOTIONAL

The following questions are being asked regarding your attitudes and feelings as they relate to your anterior cruciate ligament deficient knee.

27. Does it concern you that your competitive needs are no longer being met because of your knee problem? (Make a slash at the extreme right i.e. 100, if your competitive needs are being met. Make a slash at the extreme left i.e. 0 if you do not have any competitive needs.)

0 100
Extremely concerned No concern at all

28. Have you had difficulty being able to psychologically "come to grips" with your knee problem?

0 100
Extremely difficult Not difficult at all

29. How often are you apprehensive about your knee?

0 100
All of the time None of the time

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

0 100
Severely troubled No trouble at all

31. How fearful are you of re-injuring your knee?

0 100
Extremely fearful No fear at all

Thank you for completing this questionnaire.
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 one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

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

<table>
<thead>
<tr>
<th>S1. Do you have swelling in your knee?</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
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<th>S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
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<th>S3. Does your knee catch or hang up when moving?</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
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<th>S4. Can you straighten your knee fully?</th>
<th>Always</th>
<th>Often</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
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<th>S5. Can you bend your knee fully?</th>
<th>Always</th>
<th>Often</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
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**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.

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<tr>
<th>S6. How severe is your knee joint stiffness after first wakening in the morning?</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>S7. How severe is your knee stiffness after sitting, lying or resting later in the day?</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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</table>
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.

<table>
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<tr>
<th>A3. Rising from sitting</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A4. Standing</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A5. Bending to floor/pick up an object</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A6. Walking on flat surface</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A7. Getting in/out of car</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A8. Going shopping</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A9. Putting on socks/stockings</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A10. Rising from bed</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
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<th>A11. Taking off socks/stockings</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A12. Lying in bed (turning over, maintaining knee position)</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
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<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A13. Getting in/out of bath</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A14. Sitting</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>A15. Getting on/off toilet</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</tr>
</tbody>
</table>
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.
AQOL-8D  (Data Collection Copy)

Tick the box that best describes your situation as it has been over the past week

Q1 Thinking about how much energy you have to do the things you want to do:
I am
- always full of energy
- usually full of energy
- occasionally energetic
- usually tired and lacking energy
- always tired and lacking energy

Q2 How often do you feel socially excluded or left out?
- never
- rarely
- sometimes
- often
- always

Q3 Thinking about how easy or difficult it is for you to get around by yourself outside your house (e.g., shopping, visiting):
- getting around is enjoyable and easy
- I have no difficulty getting around outside my house
- a little difficulty
- moderate difficulty
- a lot of difficulty
- I cannot get around unless somebody is there to help me

Q4 Thinking about your health and your role in your community (that is to say neighbourhood, sporting, work, church or cultural groups):
- my role in the community is unaffected by my health
- there are some parts of my community role I cannot carry out
- there are many parts of my community role I cannot carry out
- I cannot carry out any part of my community role

Q5 How often do you feel sad
- never
- rarely
- some of the time
- usually
- nearly all the time

Q6 Thinking about how often you experience serious pain:
I experience
- very rarely
- less than once a week
- three to four times a week
- most of the time

Q7 How much confidence do you have in yourself?
- Complete confidence
- A lot
- A moderate amount
- A little
- None at all

Q8 When you think about whether you are calm and tranquil or agitated:
I am
- always calm and tranquil
- usually calm and tranquil
- sometimes calm and tranquil, sometimes agitated
- usually agitated
- always agitated

Q9 Thinking about your health and your relationship with your family:
- my role in the family is unaffected by my health
- there are some parts of my family role I cannot carry out
- there are many parts of my family role I cannot carry out
- I cannot carry out any part of my family role

Q10 Your close relationships (family and friends) are:
- very satisfying
- satisfying
- neither satisfying nor dissatisfying
- dissatisfying
- unpleasant
- very unpleasant

Q11 When you communicate with others, e.g. by talking, listening, writing or signing:
- I have no trouble speaking to them or understanding what they are saying
- I have some difficulty being understood by people who do not know me. I have no trouble understanding what others are saying to me
- I am understood only by people who know me well. I have great trouble understanding what others are saying to me.
- I cannot adequately communicate with others
Tick the box that best describes your situation as it has been over the past week

Q12 How often do you have trouble sleeping?
☐ never
☐ almost never
☐ sometimes
☐ often
☐ all the time

Q13 How often do you feel worthless?
☐ never
☐ almost never
☐ sometimes
☐ usually
☐ always

Q14 How often do you feel angry?
☐ never
☐ almost never
☐ sometimes
☐ often
☐ all the time

Q15 Thinking about your mobility, including using any aids or equipment such as wheelchairs, frames, sticks:
☐ I am very mobile
☐ I have no difficulty with mobility
☐ I have some difficulty with mobility (for example, going uphill)
☐ I have difficulty with mobility. I can go short distances only.
☐ I have a lot of difficulty with mobility. I need someone to help me
☐ I am bedridden

Q16 Do you ever feel like hurting yourself?
☐ never
☐ rarely
☐ sometimes
☐ often
☐ all the time

Q17 How enthusiastic do you feel?
☐ extremely
☐ very
☐ somewhat
☐ not much
☐ not at all

Q18 And still thinking about the last seven days, how often did you feel worried?
☐ never
☐ occasionally
☐ sometimes
☐ often
☐ all the time

Q19 Thinking about washing yourself, toileting, dressing, eating or looking after your appearance:
☐ these tasks are very easy for me
☐ I have no real difficulty in carrying out these tasks
☐ I find some of these tasks difficult, but I manage to do them on my own
☐ many of these tasks are difficult, and I need help to do them
☐ I cannot do these tasks by myself at all

Q20 How often do you feel happy?
☐ all the time
☐ mostly
☐ sometimes
☐ almost never
☐ never

Q21 How much do you feel you can cope with life’s problems?
☐ completely
☐ mostly
☐ partly
☐ very little
☐ not at all

Q22 How much pain or discomfort do you experience:
☐ none at all
☐ I have moderate pain
☐ I suffer from severe pain
☐ I suffer unbearable pain

Q23 How much do you enjoy your close relationships (family and friends)?
☐ immensely
☐ a lot
☐ a little
☐ not much
☐ I hate it
Tick the box that best describes your situation as it has been over the past week

Q24 How often does pain interfere with your usual activities?
- never
- rarely
- sometimes
- often
- always

Q25 How often do you feel pleasure?
- always
- usually
- sometimes
- almost never
- never

Q26 How much of a burden do you feel you are to other people?
- Not at all
- A little
- A moderate amount
- A lot
- totally

Q27 How content are you with your life?
- extremely
- mainly
- moderately
- slightly
- not at all

Q28 Thinking about your vision (using your glasses or contact lenses if needed):
- I have excellent sight
- I see normally
- I have some difficulty focusing on things, or I do not see them sharply. E.g. small print, a newspaper or seeing objects in the distance.
- I have a lot of difficulty seeing things. My vision is blurred. I can see just enough to get by with.
- I only see general shapes. I need a guide to move around.
- I am completely blind

Q30 How much help do you need with jobs around the house (e.g. preparing food, cleaning the house or gardening):
- I can do all these tasks very quickly and efficiently without any help
- I can do these tasks relatively easily without help
- I can do these tasks only very slowly without help
- I cannot do most of these tasks unless I have help
- I can do none of these tasks by myself

Q31 How often do you feel socially isolated?
- never
- rarely
- sometimes
- often
- always

Q32 Thinking about your hearing (using your hearing aid if needed):
- I have excellent hearing
- I hear normally
- I have some difficulty hearing or I do not hear clearly. I have trouble hearing softly-spoken people or when there is background noise.
- I have difficulty hearing things clearly. Often I do not understand what is said. I usually do not take part in conversations because I cannot hear what is said.
- I hear very little indeed. I cannot fully understand loud voices speaking directly to me.
- I am completely deaf

Q33 How often do you feel depressed?
- never
- almost never
- sometimes
- often
- very often
- all the time

Q34 Your close and intimate relationships (including any sexual relationships) make you:
- very happy
- generally happy
- neither happy nor unhappy
- generally unhappy
- very unhappy

Q35 How often did you feel in despair over the last seven days?
- never
- occasionally
- sometimes
- often
- all the time
### Hospital Anxiety and Depression Score (HADS)

This questionnaire helps your physician to know how you are feeling. Read every sentence. Place an “X” on the answer that best describes how you have been feeling during the LAST WEEK. You do not have to think too much to answer. In this questionnaire, spontaneous answers are more important

<table>
<thead>
<tr>
<th>A</th>
<th>I feel tense or 'wound up':</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Most of the time:</td>
</tr>
<tr>
<td></td>
<td>A lot of the time:</td>
</tr>
<tr>
<td></td>
<td>From time to time (occ.):</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>I still enjoy the things I used to enjoy:</td>
</tr>
<tr>
<td></td>
<td>Definitely as much:</td>
</tr>
<tr>
<td></td>
<td>Not quite as much:</td>
</tr>
<tr>
<td></td>
<td>Only a little:</td>
</tr>
<tr>
<td></td>
<td>Hardly at all:</td>
</tr>
<tr>
<td>A</td>
<td>I get a sort of frightened feeling as if something awful is about to happen:</td>
</tr>
<tr>
<td></td>
<td>Very definitely and quite badly:</td>
</tr>
<tr>
<td></td>
<td>Yes, but not too badly:</td>
</tr>
<tr>
<td></td>
<td>A little, but it doesn't worry me:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td>D</td>
<td>I can laugh and see the funny side of things:</td>
</tr>
<tr>
<td></td>
<td>As much as I always could:</td>
</tr>
<tr>
<td></td>
<td>Not quite so much now:</td>
</tr>
<tr>
<td></td>
<td>Definitely not so much now:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td>A</td>
<td>Worrying thoughts go through my mind:</td>
</tr>
<tr>
<td></td>
<td>A great deal of the time:</td>
</tr>
<tr>
<td></td>
<td>A lot of the time:</td>
</tr>
<tr>
<td></td>
<td>From time to time, but not often:</td>
</tr>
<tr>
<td></td>
<td>Only occasionally:</td>
</tr>
<tr>
<td>D</td>
<td>I feel cheerful:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td></td>
<td>Not often:</td>
</tr>
<tr>
<td></td>
<td>Sometimes:</td>
</tr>
<tr>
<td></td>
<td>Most of the time:</td>
</tr>
<tr>
<td>A</td>
<td>I can sit at ease and feel relaxed:</td>
</tr>
<tr>
<td></td>
<td>Definitely:</td>
</tr>
<tr>
<td></td>
<td>Usually:</td>
</tr>
<tr>
<td></td>
<td>Not often:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td>D</td>
<td>I feel as if I am slowed down:</td>
</tr>
<tr>
<td></td>
<td>Nearly all the time:</td>
</tr>
<tr>
<td></td>
<td>Very often:</td>
</tr>
<tr>
<td></td>
<td>Sometimes:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td>A</td>
<td>I get a sort of frightened feeling like &quot;butterflies&quot; in the stomach:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td></td>
<td>Occasionally:</td>
</tr>
<tr>
<td></td>
<td>Quite often:</td>
</tr>
<tr>
<td></td>
<td>Very often:</td>
</tr>
<tr>
<td>D</td>
<td>I have lost interest in my appearance:</td>
</tr>
<tr>
<td></td>
<td>Definitely:</td>
</tr>
<tr>
<td></td>
<td>I don't take as much care as I should:</td>
</tr>
<tr>
<td></td>
<td>I may not take quite as much care:</td>
</tr>
<tr>
<td></td>
<td>I take just as much care:</td>
</tr>
<tr>
<td>A</td>
<td>I feel restless as I have to be on the move:</td>
</tr>
<tr>
<td></td>
<td>Very much indeed:</td>
</tr>
<tr>
<td></td>
<td>Quite a lot:</td>
</tr>
<tr>
<td></td>
<td>Not very much:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td>D</td>
<td>I look forward with enjoyment to things:</td>
</tr>
<tr>
<td></td>
<td>As much as I ever did:</td>
</tr>
<tr>
<td></td>
<td>Rather less than I used to:</td>
</tr>
<tr>
<td></td>
<td>Definitely less than I used to:</td>
</tr>
<tr>
<td></td>
<td>Hardly at all:</td>
</tr>
<tr>
<td>A</td>
<td>I get sudden feelings of panic:</td>
</tr>
<tr>
<td></td>
<td>Very often indeed:</td>
</tr>
<tr>
<td></td>
<td>Quite often:</td>
</tr>
<tr>
<td></td>
<td>Not very often:</td>
</tr>
<tr>
<td></td>
<td>Not at all:</td>
</tr>
<tr>
<td>D</td>
<td>I can enjoy a good book or radio/TV program:</td>
</tr>
<tr>
<td></td>
<td>Often:</td>
</tr>
<tr>
<td></td>
<td>Sometimes:</td>
</tr>
<tr>
<td></td>
<td>Not often:</td>
</tr>
<tr>
<td></td>
<td>Very seldom:</td>
</tr>
</tbody>
</table>

226
Workplace Activity Limitations Survey

These questions ask you about activities related to your job. When you think about how much difficulty you have with these activities, think about doing them **WITHOUT ANY HELP FROM ANOTHER PERSON OR WITHOUT THE HELP OF A SPECIAL GADGET OR PIECE OF EQUIPMENT**.

For each of the following questions, please TICK ☑ only ONE box that best applies to your work situation.

<table>
<thead>
<tr>
<th>No difficulty</th>
<th>Some difficulty</th>
<th>A lot of difficulty</th>
<th>Not able to do</th>
<th>Difficulty unrelated to arthritis</th>
<th>Not applicable to my job</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. How much difficulty do you have getting to and from work (e.g., subway, bus, car, walking) and getting to and from work on time?  
   - [ ] No difficulty  
   - [ ] Some difficulty  
   - [ ] A lot of difficulty  
   - [ ] Not able to do  
   - [ ] Difficulty unrelated to arthritis  
   - [ ] Not applicable to my job

2. How much difficulty do you have getting around the workplace (e.g., stairs, hallways, furniture)?  
   - [ ] No difficulty  
   - [ ] Some difficulty  
   - [ ] A lot of difficulty  
   - [ ] Not able to do  
   - [ ] Difficulty unrelated to arthritis  
   - [ ] Not applicable to my job

3. How much difficulty do you have sitting for long periods of time at your job (e.g., more than 20 minutes)?  
   - [ ] No difficulty  
   - [ ] Some difficulty  
   - [ ] A lot of difficulty  
   - [ ] Not able to do  
   - [ ] Difficulty unrelated to arthritis  
   - [ ] Not applicable to my job

4. How much difficulty do you have standing for long periods of time at your job (e.g., more than 20 minutes)?  
   - [ ] No difficulty  
   - [ ] Some difficulty  
   - [ ] A lot of difficulty  
   - [ ] Not able to do  
   - [ ] Difficulty unrelated to arthritis  
   - [ ] Not applicable to my job

5. How much difficulty do you have lifting, carrying or moving objects?  
   - [ ] No difficulty  
   - [ ] Some difficulty  
   - [ ] A lot of difficulty  
   - [ ] Not able to do  
   - [ ] Difficulty unrelated to arthritis  
   - [ ] Not applicable to my job
6. How much difficulty do you have working with your hands (e.g., writing, typing, grasping small objects, holding a phone)?

7. How much difficulty do you have crouching, bending, kneeling or working in awkward positions?

<table>
<thead>
<tr>
<th>No difficulty</th>
<th>Some difficulty</th>
<th>A lot of difficulty</th>
<th>Not able to do</th>
<th>Difficulty unrelated to arthritis</th>
<th>Not applicable to my job</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ]</td>
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<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
</tr>
</tbody>
</table>

8. How much difficulty do you have reaching?

9. How much difficulty do you have with the schedule or hours of work that your job requires?

10. How much difficulty do you have with the pace of work that your job requires?

11. Overall, how much difficulty do you have meeting your current job demands?

12. As a result of your arthritis, how much difficulty do you have concentrating or keeping your mind on your work?

<table>
<thead>
<tr>
<th>No difficulty</th>
<th>Some difficulty</th>
<th>A lot of difficulty</th>
<th>Not able to do</th>
<th>Difficulty unrelated to arthritis</th>
<th>Not applicable to my job</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>
APPENDIX 6.4 KNEE-RELATED QOL MULTIVARIABLE ANALYSES ADJUSTED FOR KOOS-PAIN

<table>
<thead>
<tr>
<th>Explanatory variables</th>
<th>KOOS-QOL</th>
<th>ACL-QOL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI)</td>
<td>Beta (p value)</td>
</tr>
<tr>
<td>Years since ACLR</td>
<td>-0.16 (-0.9, 0.6)</td>
<td>-0.03 (0.66)</td>
</tr>
<tr>
<td>Injury to surgery</td>
<td>-4.26 (-10.0, 1.5)</td>
<td>-0.09 (0.14)</td>
</tr>
<tr>
<td>Revision ACLR</td>
<td>-6.88 (-14.3, 0.5)</td>
<td>-0.12 (0.07)</td>
</tr>
<tr>
<td>Contralateral ACLR</td>
<td>-1.94 (-9.7, 5.9)</td>
<td>-0.03 (0.62)</td>
</tr>
<tr>
<td>Subsequent surgery</td>
<td>-5.94 (-11.2, -0.6)</td>
<td>-0.15 (0.03)</td>
</tr>
<tr>
<td>RTS same/higher level*</td>
<td>7.93 (1.7, 14.2)</td>
<td>0.19 (0.01)</td>
</tr>
<tr>
<td>RTS lower level*</td>
<td>2.58 (-4.0, 9.1)</td>
<td>0.06 (0.44)</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.51 (-1.0, 0.0)</td>
<td>-0.14 (0.04)</td>
</tr>
<tr>
<td>Age</td>
<td>0.23 (-0.1, 0.5)</td>
<td>0.11 (0.13)</td>
</tr>
<tr>
<td>Sex</td>
<td>2.74 (-2.3, 7.7)</td>
<td>0.07 (0.28)</td>
</tr>
<tr>
<td>KOOS-Pain</td>
<td>0.71 (0.5, 0.9)</td>
<td>0.50 (&lt;0.001)</td>
</tr>
</tbody>
</table>

R² (p value): 0.44 (<0.001) | 0.56 (<0.001)

B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised coefficient; R²: the proportion of variance in the dependent variable that can be accounted for by the independent variables in combination; RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; KOOS: Knee Injury and Osteoarthritis Outcome score; ACLQOL: Anterior Cruciate Ligament Quality of Life questionnaire; * Did not return to sport = reference category. Sample size does not equal 162 for these analyses due to n=1 not participating in sport at the time of injury, n=2 selected ‘unsure’ options, and n=1 did not complete the ACL-QOL; injury to ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as no=0, yes=1; Years since surgery, BMI, age and KOOS-Pain were continuous variables.
## APPENDIX 6.5 HEALTH-RELATED QOL MULTIVARIABLE ANALYSES ADJUSTED FOR KOOS-PAIN

<table>
<thead>
<tr>
<th>Explanatory variables</th>
<th>B</th>
<th>(95% CI)</th>
<th>Beta</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years since ACLR</td>
<td>0.00</td>
<td>-0.01</td>
<td>0.00</td>
<td>-0.04</td>
</tr>
<tr>
<td>Injury to surgery</td>
<td>-0.03</td>
<td>-0.08</td>
<td>0.02</td>
<td>-0.09</td>
</tr>
<tr>
<td>Revision ACLR</td>
<td>0.04</td>
<td>-0.02</td>
<td>0.10</td>
<td>0.11</td>
</tr>
<tr>
<td>Contralateral ACLR</td>
<td>0.02</td>
<td>-0.05</td>
<td>0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Subsequent surgery</td>
<td>-0.01</td>
<td>-0.05</td>
<td>0.03</td>
<td>-0.03</td>
</tr>
<tr>
<td>RTS same/higher level*</td>
<td>0.05</td>
<td>0.00</td>
<td>0.10</td>
<td>0.18</td>
</tr>
<tr>
<td>RTS lower level*</td>
<td>0.01</td>
<td>-0.05</td>
<td>0.06</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.01</td>
<td>-0.01</td>
<td>0.00</td>
<td>-0.21</td>
</tr>
<tr>
<td>Age</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.10</td>
</tr>
<tr>
<td>Sex</td>
<td>0.00</td>
<td>-0.04</td>
<td>0.04</td>
<td>0.00</td>
</tr>
<tr>
<td>KOOS-Pain</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.18</td>
</tr>
</tbody>
</table>

| R² (p value)               | .22 (≤0.001) |

AQoL-8D: Assessment of Quality of Life 8D Utility Instrument; B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised coefficient; R²: the proportion of variance in the dependent variable that can be accounted for by the independent variables in combination; RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; KOOS: Knee Injury and Osteoarthritis Outcome score; * Did not return to sport = reference category; Sample size does not equal 162 for these analyses due to n=1 was not participating in sport at the time of injury, n=2 selected ‘unsure’ options, and n=1 did not complete the AQoL-8D; injury to ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as no=0, yes=1; Years since surgery, BMI, age and KOOS-Pain were continuous variables.
## APPENDIX 6.6 PSYCHOLOGICAL HEALTH
### MULTIVARIABLE ANALYSES ADJUSTED FOR KOOS-PAIN

<table>
<thead>
<tr>
<th>Explanatory variables</th>
<th>B</th>
<th>(95% CI)</th>
<th>Beta</th>
<th>p value</th>
<th>B</th>
<th>(95% CI)</th>
<th>Beta</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years since ACLR</td>
<td>0.07</td>
<td>-0.1 - 0.2</td>
<td>0.26</td>
<td>0.06</td>
<td>0.06</td>
<td>-0.1 - 0.2</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Injury to surgery</td>
<td>0.68</td>
<td>-0.2 - 1.6</td>
<td>0.14</td>
<td>0.29</td>
<td>-1.1</td>
<td>1.6</td>
<td>0.03</td>
<td>0.68</td>
</tr>
<tr>
<td>Revision ACLR</td>
<td>-0.25</td>
<td>-1.4 - 0.9</td>
<td>-0.03</td>
<td>0.68</td>
<td>0.38</td>
<td>-1.4 - 2.2</td>
<td>0.04</td>
<td>0.67</td>
</tr>
<tr>
<td>Contralateral ACLR</td>
<td>0.04</td>
<td>-1.2 - 1.3</td>
<td>0.00</td>
<td>0.95</td>
<td>-1.37</td>
<td>-3.2 - 0.5</td>
<td>-0.12</td>
<td>0.15</td>
</tr>
<tr>
<td>Subsequent surgery</td>
<td>0.30</td>
<td>-0.5 - 1.1</td>
<td>0.06</td>
<td>0.48</td>
<td>-0.64</td>
<td>-1.9 - 0.6</td>
<td>-0.09</td>
<td>0.32</td>
</tr>
<tr>
<td>RTS same/higher level*</td>
<td>-0.85</td>
<td>-1.8 - 0.1</td>
<td>-0.16</td>
<td>0.09</td>
<td>-0.61</td>
<td>-2.1 - 0.9</td>
<td>-0.08</td>
<td>0.42</td>
</tr>
<tr>
<td>RTS lower level*</td>
<td>-0.74</td>
<td>-1.8 - 0.3</td>
<td>-0.13</td>
<td>0.16</td>
<td>0.42</td>
<td>-1.1 - 2.0</td>
<td>0.05</td>
<td>0.60</td>
</tr>
<tr>
<td>BMI</td>
<td>0.11</td>
<td>0.0 - 0.2</td>
<td>0.22</td>
<td>0.01</td>
<td>0.06</td>
<td>-0.1 - 0.2</td>
<td>0.09</td>
<td>0.30</td>
</tr>
<tr>
<td>Age</td>
<td>0.00</td>
<td>0.0 - 0.1</td>
<td>0.02</td>
<td>0.84</td>
<td>-0.05</td>
<td>-0.1 - 0.0</td>
<td>-0.13</td>
<td>0.14</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.89</td>
<td>-1.7 - 0.1</td>
<td>-0.17</td>
<td>0.03</td>
<td>0.26</td>
<td>-0.9 - 1.5</td>
<td>0.03</td>
<td>0.67</td>
</tr>
<tr>
<td>KOOS-Pain</td>
<td>-0.02</td>
<td>0.0 - 0.0</td>
<td>-0.09</td>
<td>0.29</td>
<td>0.06</td>
<td>-0.1 - 0.2</td>
<td>0.06</td>
<td>0.48</td>
</tr>
</tbody>
</table>

| R2 (p value)          | .19 (0.001) | .07 (0.47) |

B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised coefficient; R²: the proportion of variance in the dependent variable that can be accounted for by the independent variables in combination; RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament reconstruction; HADS: Hospital Anxiety and Depression Scale; KOOS: Knee Injury and Osteoarthritis Outcome score; * Did not return to sport = reference category; Sample size does not equal 162 for these analyses due to n=1 was not participating in sport at the time of injury, n=2 selected ‘unsure’ options, and n=1 did not complete the HADS; injury to ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as no=0, yes=1; Years since surgery, BMI, age and KOOS-Pain were continuous variables.
# APPENDIX 7.1 SEMI-STRUCTURED INTERVIEW GUIDE

## ACL injury, surgery and perioperative experiences

<table>
<thead>
<tr>
<th>Semi-structured interview questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can you tell me how you injured your ACL?</td>
</tr>
<tr>
<td>Can you tell me what happened after your injury?</td>
</tr>
<tr>
<td>Can you tell me about your ACL surgery? How was your experience of surgery?</td>
</tr>
<tr>
<td>Decision to have surgery? Did they give you other options?</td>
</tr>
<tr>
<td>Were you adequately prepared for surgery?</td>
</tr>
<tr>
<td>Was it what you expected?</td>
</tr>
<tr>
<td>Tell me a bit about your experience with life after surgery?</td>
</tr>
<tr>
<td>How did you cope psychologically and emotionally after surgery?</td>
</tr>
<tr>
<td>looking back, is there anything you would change about your surgery or your rehabilitation?</td>
</tr>
<tr>
<td>Can you tell me a bit about your experiences with health care professionals over the years?</td>
</tr>
</tbody>
</table>

## Sport, exercise and athletic identity

<table>
<thead>
<tr>
<th>Semi-structured interview questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before you injured your ACL, what did sport mean to you?</td>
</tr>
<tr>
<td>How important to you was returning to sport after your surgery?</td>
</tr>
<tr>
<td>Did you return to sport?</td>
</tr>
<tr>
<td>- (if no). Why not?</td>
</tr>
<tr>
<td>- (if yes). Did you have any difficulties or issues with getting back to sport after your ACLR?</td>
</tr>
<tr>
<td>What does sport and exercise mean to you now?</td>
</tr>
<tr>
<td>What sport/exercise do you participate in now?</td>
</tr>
<tr>
<td>Did you feel like you could reach your full sporting potential after surgery?</td>
</tr>
<tr>
<td>Does your knee impact on your current sporting or exercise capabilities?</td>
</tr>
<tr>
<td>(if yes) How does this make you feel?</td>
</tr>
</tbody>
</table>

## Psychological impacts

<table>
<thead>
<tr>
<th>Semi-structured interview questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>How much confidence do you have in your knee?</td>
</tr>
<tr>
<td>Do you have any fears in regards to your knee now?</td>
</tr>
<tr>
<td>How often do you think about your knee?</td>
</tr>
</tbody>
</table>
**Semi-structured interview questions**

**Current experience**

Tell me about your knee function today… (pain, swelling, stability?)

- Pain: where? How often? Duration? How would you describe this pain?

Is your knee impacting on your life? How so? (*work, family, social?*)

Is your knee limiting your ability to do anything you want to do? What things?

Have you modified your lifestyle because of your knee? If so, in what way?

Do you currently receive treatment for your knee?

- (if no).. Why not?
- (if yes).. What kind of treatment?

**Osteoarthritis**

What do you know about osteoarthritis?

Did anyone speak to you about the potential of getting osteoarthritis after surgery?

(Can go into detail if they ‘have osteoarthritis’).

- Who told you, you have osteoarthritis? How bad is it?
- Why do you think you got osteoarthritis?

**End of interview**

So that’s all the questions I have for you, is there anything else you would like to add that wasn’t covered, before we end the interview?