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# A Long-Term Follow-Up Of The STABILITY Study: Multicenter RCT Comparing Anterior Cruciate Ligament Reconstruction With And Without Lateral Extra-Articular Tenodesis In Individuals At High Risk Of Graft Failure

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Health and Rehabilitation Sciences

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## Abstract

One hundred and ninety-six patients at the Fowler Kennedy Sport Medicine Clinic (FKSMC) undergoing anterior cruciate ligament (ACL) reconstruction (ACLR) were randomized as part of the multi-center STABILITY study to receive either an isolated ACLR or ACLR with a lateral extra-articular tenodesis (LET). The STABILITY study followed these patients up to two years postoperative, and a long-term follow-up protocol was initiated afterwards. Eighty-two patients from this center were seen at three, five and seven years postoperative as part of a long-term follow-up. Our primary outcome was a composite outcome of instability and graft failure. Secondary outcomes included patient-reported outcome measures (PROMs), range of motion measurements, and adverse events. We found no statistically significant differences between groups for the composite outcome or the secondary outcomes, however there was a significant increase in graft rupture in the ACLR alone group. This thesis presents preliminary, single-center results of a long-term follow-up of the STABILITY study.

## Keywords

Anterior cruciate ligament reconstruction, anterior cruciate ligament, lateral extra-articular tenodesis, stability, long-term outcomes

## Summary for Lay Audience

Athletes participating in pivoting sports such as soccer and basketball have a high chance of injuring the anterior cruciate ligament (ACL) in their knees, leading to feelings of instability in the joint. The ACL is responsible for stabilizing the knee during movement, and ACL injuries are debilitating and can lead to long term consequences such as post-traumatic osteoarthritis (PTOA) if not treated properly. The standard approach to treat a torn ACL is an ACL reconstruction (ACLR) using one of the patient's own tendons as a graft to replace the torn ACL inside the knee. However, previous research has shown high ACL re-tear rates in patients that return to pivoting sports after undergoing an ACLR. Clinicians began to explore other surgical techniques in an attempt to further reduce risk of re-injury and investigated the possibility of adding an extra procedure called a lateral extra-articular tenodesis (LET) to the ACL reconstruction. In order to determine if the extra procedure provided any benefits, the STABILITY study was conducted as a randomized clinical trial (RCT), where patients were randomized to receive either the ACLR alone, or ACLR with LET. Patients involved in this study were followed up to two years postoperatively.

The purpose of this thesis was to perform a long-term follow-up of patients involved in the STABILITY study (three, five and seven years postoperative). We asked patients to complete questionnaires about their knee function, and surgeons assessed their knee during a clinical examination. We did not find statistically significant differences between the groups for the outcome measures, however more patients in the ACLR alone group re-tore their ACL, compared to the ACLR with LET group. Long term outcomes are critical to understanding the benefits and consequences of surgical approaches for ACL reconstructions and can inform us of ways to improve techniques for the future.

## Co-Authorship Statement

The long-term follow-up protocol was designed by Dr. Alan Getgood and Dr. Dianne Bryant, after completion of the original STABILITY study two years postoperative. I was responsible for contacting patients that had participated in the original study at the Fowler Kennedy Sport Medicine Clinic to ask them to participate in long-term follow-up. After confirming interest in participation from the patient, I was then responsible for obtaining informed consent, scheduling clinical appointments at FKSMC with the patient's respective surgeon (Dr. Getgood, Dr. Litchfield, or Dr. Willits), and collecting data during follow-up visits.

For this thesis, I wrote the original draft of the manuscript and performed the data analysis. Dr. Bryant, Dr. Getgood, Andrew Firth and Hana Marmura provided feedback including comments and suggestions before submission of the final manuscript.

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# Chapter 1

## 1 Introduction

The anterior cruciate ligament (ACL) is considered one of the main stabilizers of the knee joint, and as a result, ACL injuries are one of the most common knee injuries, especially in athletes (1–4). Surgical reconstruction of the ACL is commonly sought out to restore stability and normal function to the knee joint (4–6), especially by athletes aspiring to return to pre-injury levels of sports and activities (4–6). As this type of injury is so prevalent, the number of surgical reconstructions performed continues to increase, with an estimated cost of almost one billion dollars per year (7).

Earlier approaches to ACL reconstruction included isolated extra-articular procedures, such as a lateral extra-articular tenodesis (LET). There are different variations of this technique (8–12), however postoperative results were generally poor (8,13–18). ACL reconstruction techniques have evolved over the years, with the most common technique being an intra-articular reconstruction using an autograft (graft harvested from the patient) or an allograft (graft harvested from a cadaver) to reconstruct and replicate the function of the native ACL (6,19). Unfortunately, even with advanced reconstruction techniques, there is a small subset of patients that continue to suffer with instability in their affected knee after surgery (4,20–23).

Within the last decade, after biomechanical studies found that it contributed to rotational stability of the knee (14,24–27) more emphasis has been placed on the ‘rediscovery’ of the anterolateral ligament (ALL) and its implications in ACL deficiency (14,24–27). More recently, surgeons have started to combine an intra-articular ACL reconstruction with an extra-articular procedure, and most studies have shown promising results in favour of this combination (22,28–36). However, a systematic review performed by Hewison and colleagues found a lack of well-controlled randomized trials comparing isolated ACL reconstruction to ACL reconstruction with an extra-articular procedure (36). The STABILITY study was the first methodologically rigorous, adequately powered randomized, multi-center clinical trial that definitively compared ACL reconstruction to ACL reconstruction with LET, and the two-year outcomes favoured the addition of the LET (15). The purpose of this thesis is to investigate long-term outcomes of the

STABILITY study, at least three years postoperative, to determine if the results still favour the addition of a LET to ACLR.

## Chapter 2

### 2 Literature Review

#### 2.1 Anatomy

##### 2.1.1 The Knee Joint

The knee is a gliding hinge joint that allows ranges of motion including flexion-extension and internal-external rotation, composed of the medial tibiofemoral, lateral tibiofemoral, patellofemoral, and proximal tibiofibular joint (6,37). Rolling, gliding and rotation are key principles of knee joint kinematics. There are two bony articulations in the knee; the articulation between the femur and the tibia, and the articulation between the patella and the femur (6,38).

Surrounding and reinforcing the knee are extra-capsular ligaments; including two collateral ligaments (medial collateral ligament (MCL) and lateral collateral ligament (LCL)), the patellar ligament, the oblique popliteal ligament (OPL), and the arcuate popliteal ligament (APL) (38). The MCL and LCL provide stability to the medial and lateral aspects of the knee respectively, against varus-valgus stress during external and internal rotation (37). The patellar ligament attaches to the apex of the patella and to the tibial tuberosity and is the continuation of the quadriceps femoris tendon. Its role is to help stabilize the patella, and forms part of the extensor mechanism of the lower limb (39). The OPL is a flat ligament that diagonally crosses the posterior aspect of the knee joint and reinforces the posterior knee capsule. This ligament adds stability to the knee by helping to prevent excessive external rotation and hyperextension (40). The APL is a structure of the posterolateral corner (PLC) and forms an arch-like appearance across the posterior aspect of the knee. The APL also contributes to knee stability by restricting excessive external rotation (41). While the ligaments in the knee are the primary source of stabilization, the surrounding muscles act as the secondary source, and both work together to keep the knee in working order (38).

The medial and lateral menisci are fibrocartilaginous structures positioned between the medial and lateral femoral condyles respectively, and the tibia (38,42). The meniscal surfaces follow the contours of the tibia and femur and increase the congruence between the femoral condyle and

tibial plateau (37,42). They act as shock absorbers for the body during loading and dynamic movements (5,38).

The anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL) are intra-articular ligaments located between the tibia and femur that form a cross (or an “x”) to prevent excessive displacement of the tibia anteriorly, posteriorly and rotationally with respect to the femur (38,42–44).

## 2.1.2 The Anterior Cruciate Ligament (ACL)

### 2.1.2.1 Anatomy

The anterior cruciate ligament (ACL) travels posteriorly to anteriorly, originating on the posteromedial side of the lateral femoral condyle, and inserting anterior to the intercondylar tibial eminence (3–6,44,45). On average, the ACL measures approximately 31-38 mm in length (42,44), with a width between 10-12 mm (4,20,42,44). It is widely accepted that there are two bundles that form the ACL: the anteromedial (AM) and posterolateral (PL) bundle, named according to their respective insertions on the tibia (3–5,20,37,38,42,44,46–50). However, some studies suggest a flat ribbon-like shape to the ligament with no clear separation into bundles (20,46,51).

### 2.1.2.2 Function

In the ACL, the AM and PL bundles each contribute differently to the transfer of loading when the knee flexes and extends through its normal range of motion (4,20). For example, the fibers of the AM bundle are tense during flexion while the fibers of the PL bundle are relaxed, and the fibers of the PL bundle are taut during extension while the fibers of the AM bundle are more lax (3,37,42,44,47). The primary function of the ACL is to resist anterior translation of the tibia relative to the femur (3–6,20,30,38,42,44,45,47,50,52). In addition to resisting anterior translation, the ACL also stabilizes the knee against internal rotation of the tibia (3,5,20,30,38,42,50).

The presence of mechanoreceptors in the ACL has been reported in numerous studies, and it has been suggested that these mechanoreceptors play a role in proprioception, as well as initiating

the stabilizing muscular reflexes (4,53). Multiple studies have proposed that persistent instability after an ACL rupture can be attributed partly to the loss of proprioceptive feedback from the injury (53).

## 2.2 Mechanism of Injury

An injury to the ACL is one of the most common knee ligament injuries (1–4,54). Most ACL ruptures occur when there is little or no contact at the moment of injury, known as a noncontact injury (1,4–6,45,50,52,55). A noncontact injury is often reported when there is a change in velocity and force across the knee joint, commonly occurring through sudden deceleration while changing direction, jumping, twisting, and pivoting when participating in sport-related activities (1,3,4,52,55). During sidestepping and crossover cutting motions, the load on the ACL increases due to an increase in varus/valgus and internal/external rotational movements, thus increasing the risk of injury due to the added stress on the ligament (4,52).

A contact ACL injury consists of an external force that generally causes a sudden deceleration or change in knee direction (3,52). The most common mechanisms for a contact injury include a blow to the lateral aspect of the leg causing valgus collapse, a blow to the medial aspect of the leg causing varus collapse, or an anterior blow to the leg causing hyperextension (1,52). These injuries tend to result from higher energy mechanisms, and patients often report feeling or hearing a ‘pop’ in their knee (3,4,52).

There are multiple factors that contribute to an increased risk of ACL rupture which can be divided generally into intrinsic and extrinsic factors (1,4,5,52). Intrinsic risk factors include anatomical features such as increased generalized joint laxity, body mass index, posterior tibial slope, decreased size and strength of the ACL, malalignment of the lower extremities, and a narrow intercondylar notch, along with hormonal influences (1,3–5,47,52). Studies have shown an increased risk of ACL tear in women compared to men, and that most ACL injuries occur beginning in late adolescence (5). There is also evidence to suggest that genetic factors can contribute to excessive joint laxity, also known as joint hypermobility (56). Extrinsic risk factors include the relative strength and interaction between the quadriceps and the hamstrings, decreased neuromuscular control, footwear, the playing surface, and the playing style of the



athlete (1,4,5,52,55). The type of sport also contributes to the risk of ACL tear. Sports that involve pivoting, cutting and jumping motions such as soccer, football and basketball are also considered a risk factor for ACL tears (1,3,4).

### 2.2.1 Associated Injuries

While ACL tears can occur alone, in most cases they occur along with other ligamentous injuries in the knee and associated osseous structures (3,50,54). During a contact mechanism of injury, if the force applied to the knee causes the femur to externally rotate with a valgus force at the knee, an injury known as the O'Donoghue "unhappy" triad may occur: a tear of the ACL, MCL, and medial meniscus (3). However, lateral meniscal tears tend to occur more frequently than medial meniscal tears, making this injury pattern uncommon (3). If the knee internally rotates because of an applied force, an ACL tear can occur along with a lateral meniscus tear and injury to the posterolateral corner structures (3). During a noncontact mechanism of injury, excessive anterior translation of the tibia and internal rotation with respect to the femur can occur when an athlete is trying to decelerate and change directions quickly, which often results in a combined injury of the ACL and MCL (3).

The posterolateral corner (PLC) structures of the knee, which help to stabilize the knee joint, can be injured in conjunction with the ACL and PCL as well, most often by mechanisms that cause hyperextension and impose a varus force to the knee (3). Reconstructions to the cruciate ligaments may eventually fail causing chronic knee instability if injuries to the posterolateral corner go untreated. In patients with chronic ACL deficiency, medial meniscal tears tend to occur more frequently, most likely because of chronic knee instability (3).

Contusions of the bone (more commonly known as bone bruises) often go hand-in-hand with ACL tears as a result of the impact force between the articular cartilage of the femur and tibia (57). This impact force then transfers to the bone, causing trabecular microfracture and osteochondral lesions (3,57). In particular, the "kissing contusions" are a well-known contusion pattern highly associated with ACL injuries that can be identified using magnetic resonance imaging (MRI) (3). The Segond fracture is another osseous injury that is highly associated with ACL rupture and consists of an avulsion fracture of the proximal lateral tibia (3,58). Bone

contusions or edema were found in more than 80% of subjects with an ACL rupture in studies investigating MRIs of acute ACL injuries (57).

## 2.3 Epidemiology

The incidence of ACL injuries continues to increase throughout the years, with more than 120,000 ACL injuries occurring every year in the United States alone, most likely due to an increase in sports participation during adolescent years (4,7,21,45,49,52,55,59–61). It is estimated that approximately 50% of sport-related knee injuries are specific to the ACL (55), with most ACL injuries sustained through noncontact mechanisms (52,55,59).

Several studies have noted that the risk of ACL injury is higher in female athletes, likely due to multiple factors such as hormone levels, a smaller intercondylar notch width, valgus alignment of the lower limbs, and neuromuscular imbalances (3–6,52,55,57,59,60,62). In a systematic review and meta-analysis published by Gornitzky and colleagues in 2016, it was estimated using data from large samples of high school athletes that the risk of ACL injury in female athletes was increased by a factor of 2.1-3.4 compared to males (60). Similarly, a systematic review and meta-analysis published by Bram and colleagues in 2021 noted almost a 1.4-fold increased risk of ACL injury in females compared to males (59).

Current ACL injury research is mostly centered on determining specific sports that put an athlete at the highest risk of experiencing an ACL injury, as well as investigating the difference in injury incidence rates between males and females participating in comparable sports (45). Gornitzky and colleagues reported an overall incidence rate (IR) of 0.081 ACL injuries per 1000 exposures in female high school athletes for all sports combined, compared to high school male athletes with an overall IR of 0.052 per 1000 exposures (55,60). The relative risk (RR) was also calculated to compare the rate of ACL injury per exposure between female and male athletes, and was found to be 1.57, indicating that females had a significantly higher rate of injury per exposure (55,60). Soccer, football, basketball, and lacrosse were the sports found to have the highest injury rate, with female soccer having the highest injury rate per exposure compared to males (IR 0.148 and 0.040 respectively), and football having the highest number of ACL injuries (273 injuries in 3,056,431 exposures) (55,60). In the systematic review and meta-analysis

performed by Bram and colleagues, the incidence rate of ACL injury across 18 studies was 0.069, with a significantly higher rate of injury in females compared to males with a calculated RR of 1.40 and IRs of 0.084 and 0.060 respectively (59). Soccer and gymnastics were found to have the highest rates of ACL injury in female athletes (IR 0.166 and 0.114 respectively), and football was found to have the highest rate of ACL injury in male athletes (IR 0.101) (59).

While most current research focuses on the incidence of ACL injuries in various sports and comparisons between sex, there are a few established ACL registries that exist internationally to report the incidence of ACL injuries in the general population (45). ACL registries were established in Norway, Denmark, and Sweden in the years 2004 and 2005 respectively, and in 2006, a law passed in Denmark that mandated all public and private hospitals and clinics to report ACL injuries to the national database (45,63). In Norway, the annual incidence of primary ACL reconstructions was 34 per 100,000 people, while in Sweden, the annual incidence was 32 per 100,000 people, and in Denmark the incidence was 38 per 100,000 (45,63). A national population-based study published by Gianotti and colleagues described the epidemiology of knee ligament injury in New Zealand (64). In this study, there were 238,488 knee ligament injuries reported over a 5-year period, with 7,375 (80%) identified as ACL injuries (64).

## 2.4 Diagnosis

To correctly diagnose an ACL tear, a patient needs to be assessed physically in a clinical setting, and also needs to provide details about the history of the injury (3–5,7,55,65). A study published in 2015 by Geraets and colleagues concluded that when performed by an orthopaedic surgeon, the combination of a thorough medical history and physical examination had high ACL rupture diagnostic value (65). If the initial diagnosis based on these assessments is still inconclusive, MRI diagnostics can be used in addition, when accessible (3–5,7,55,65).

### 2.4.1 Patient History

After an acute injury involving the ACL, patients will often report hearing or feeling a ‘pop’ in the knee, followed by swelling and pain (3–5,55,65). Patients may also describe feeling limited with respect to participation in various activities due to feelings of instability or ‘giving-way’ episodes in the affected knee (5,65). As mentioned previously, the most common mechanism of

injury that patients describe in their history is noncontact in nature, such as a deceleration, jumping, pivoting, or cutting action (1,3–5,55).

## 2.4.2 Clinical Examination

During a physical examination, there are three main diagnostic assessments that clinicians use to assess for an ACL injury: (1) the Lachman test; (2) the anterior drawer test; and (3) the pivot shift test (3–5,7,55,65).

The Lachman test is known to be the most sensitive test used to determine ACL tears (3–5,7,55). A systematic review and meta-analysis published by Huang and colleagues in 2016 found the overall sensitivity and specificity to be 0.87 and 0.97 respectively (7). To perform the Lachman test, the patient lies supine on the examination table with their affected knee flexed between 15 and 30 degrees, ensuring neutral rotation. The clinician uses one hand to stabilize the distal femur, and the other hand to apply force to the proximal tibia to assess the degree of anterior translation relative to the femur (3,4). A positive Lachman test is concluded when there is increased laxity or excessive anterior translation of the tibia compared to the contralateral side (3,4).

The anterior drawer test is generally considered to be less sensitive for ACL ruptures compared to the Lachman test (3,5,7,55). However, this can depend on the timing of assessment after the initial injury. False-negative results can occur more often in acute injuries compared to chronic injuries due to factors such as hemarthrosis, reactive synovitis, and protective hamstring muscle action due to pain (7,55). Huang and colleagues found that the overall sensitivity of anterior drawer test was 0.72, with an overall specificity of 0.93 (7). Kaeding and colleagues noted the sensitivity and specificity of the anterior drawer test to be 49% and 58% respectively in acute injuries, and 92% and 91% respectively in chronic injuries (55). To perform the anterior drawer test, the patient lies supine on the examination table with their affected knee flexed to 90 degrees. The examiner sits on the foot to stabilize the leg and to prevent motion and will then pull the proximal tibia forward with both hands. The focus of this test is to evaluate the anteromedial bundle of the ACL. A positive anterior drawer test is concluded when there is excessive anterior translation of the tibia compared to the contralateral side (3).

The pivot shift test is known to be the most specific test to aid in the diagnosis of an ACL tear, however, has a lower sensitivity due to the level of difficulty in performing the maneuver as a result of patient discomfort and guarding (3,7,55). Huang and colleagues found the overall sensitivity of the pivot shift test to be lower than the other two diagnostic tests, with a value of 0.490. However, the overall specificity was found to be 0.97 making it the most specific out of the three diagnostic tests (7). The pivot shift test consists of two main components: (1) subluxation (anterior tibial translation and internal rotation), and (2) reduction (posterior tibial translation and external rotation) (7,66). To perform the pivot shift test, the patient lies supine on the examination table with their affected knee extended. The examiner supports the patient's foot between their elbow and flank and grasps the proximal tibia. The examiner then will rotate the tibia internally, and then apply a valgus stress while flexing the knee slowly. A positive pivot shift test is concluded if there is forward subluxation of the tibia between 20 and 40 degrees of flexion. When the knee is flexed greater than 40 degrees, the iliotibial (IT) band will aid in the reduction of the tibia back under the femur, which produces the 'clunk' (3).

### 2.4.3 Imaging

Plain radiographs (X-rays) can be helpful when initially evaluating a patient with an ACL tear. Although the radiographs may look normal most of the time, they may reveal associated injuries or fractures (3–5,55). Anteroposterior and lateral radiographs are most visualized and can indicate the presence of joint effusion, femoral condyle irregularities, and associated fractures such as the Segond fracture, which is usually pathognomonic for an ACL tear (3–5,55).

Magnetic resonance imaging (MRI), when available, is the primary method used to diagnose ACL injuries in the United States (5,55). MRI has a sensitivity of 86% and a specificity of 95% for diagnosing ACL injuries and is able to visualize the two bundles of the ACL, which is important when considering surgical reconstruction (3–5,55). Associated injuries that can be visualized via MRI include bone contusions, meniscal injuries, and collateral ligament tears (3,5,57). An ACL tear can be correctly diagnosed from a clinical history and physical examination in most cases. Since MRI scans often increase treatment wait times for patients and come at a high cost, the history and examination alone may be sufficient (7). However, MRI is

helpful to rule out associated injuries, which may alter the plan of management and acuity of surgery (3).

## 2.5 Treatment

### 2.5.1 Non-operative vs. Surgical Treatment

After a suspected ACL injury, all patients are encouraged to use ice, compression, and to elevate the knee as soon as possible to limit the use of the injured knee and prevent further injury (4). Active, early range of motion should be encouraged to limit stiffness. The decision to undergo non-operative treatment versus surgical treatment depends on a number of factors, and each patient's case is different. Factors that influence the management of ACL tears include the degree to which a patient is experiencing instability in the knee, the degree of ACL disruption (partial versus complete tear), injuries to associated structures, and the age and activity level of the patient (3–5). In a systematic review published by Krause and colleagues in 2018, it could not be concluded based on two randomized trials whether non-operative or surgical management of ACL rupture yielded better outcomes (67). However, in the observational studies analyzed, they found that there tended to be better functional outcomes after ACL reconstruction, compared to non-operative treatment (67).

After an initial evaluation, if an ACL tear is still suspected, it is important for patients to be referred for physical therapy to strengthen their leg muscles and maintain range of motion of the knee, regardless of the method of treatment they may decide to eventually undergo (5).

### 2.5.2 Non-operative Treatment

Non-operative treatment of an ACL tear includes methods such as bracing and physical therapy with a focus on increasing strength in the quadriceps and hamstring muscles (3–5). Patients with serious comorbidities precluding them from undergoing surgery, older patients, and patients who are not active or do not wish to commence or return to participating in demanding physical activities and sports will often opt to treat their ACL injury conservatively, if they are not experiencing frequent episodes of instability (3–5). However, delaying surgical repair in some

cases can leave the knee prone to further injury such as meniscal tears and injury to articular cartilage due to the persistent instability (3,4).

### 2.5.3 Surgical Treatment

Younger, more active patients seeking to return to a high level of physical activity or higher risk pivoting sports may seek surgical options from an orthopaedic surgeon (4–6). In addition, patients who have frequent ‘giving-way’ episodes, or those with concomitant meniscal or ligamentous injuries (such as PCL, MCL or LCL tears) are also encouraged to pursue surgical evaluation (3–5). The goal of the ACL reconstruction is to replace the torn ligament with a graft to restore the kinematic, biologic, and anatomic function of the native ACL, thus reducing instability in the joint (4,13,19,20,26,37,49,54,58,62,68).

There are three types of grafts that can be used during reconstruction: (1) autografts, tissue harvested from the patient’s own tendon; (2) allografts, tissue harvested from human cadavers; and (3) synthetic grafts (6). Autografts and allografts are the most used grafts, and there are pros and cons in both instances (6,19).

There are different types of autografts that can be harvested from the patient at the time of surgery, with the most common being the bone-patellar-tendon bone (BPTB), quadriceps tendon (QT), and hamstring tendon (HT) (semitendinosus-gracilis) (4,6,19,58,61). Using an autograft decreases the risk of foreign body rejections, disease transmission, and potential allergic reactions. However, the length of surgical procedure and subsequent recovery period is increased due to the additional incision to harvest the graft. Other negative effects include graft site (donor) morbidity from where the graft was harvested, and potential reduced muscle strength and endurance in the hamstrings in the case of the HT autograft (4,6). In 2019, Mouarbes and colleagues published a systematic review and meta-analysis investigating outcomes for QT, BPTB and HT autografts (61). A total of 27 articles met the eligibility criteria, including 15 articles reporting outcomes after QT autograft, 7 articles comparing outcomes of QT versus BPTB autograft, and 5 articles comparing QT versus HT autograft. Analysis showed comparable clinical and functional outcomes between QT, BPTB and HT autografts, however, patients reported less pain from the QT graft harvest site compared to the BPTB autograft, and better

functional outcome scores (Lysholm scale) compared to the HT autograft. Of note, the authors did mention difficulty comparing graft choices due to heterogeneity in surgical techniques and rehabilitation protocols, which may have contributed to lowering the power of the meta-analysis (60)

Similarly, different types of allografts can be obtained from human cadavers, such as Achilles tendon, hamstring tendon, and anterior/posterior tibialis (4,6). Using an allograft reduces the time needed for the surgical procedure and subsequent recovery and eliminates the potential for graft site morbidity. However, there is still a risk of disease transmission and immune reactions such as rejection despite sterilization. It has also been hypothesized that sterilization processes may alter the biomechanical properties of the graft (4,6,23). In a systematic review and meta-analysis of five studies, Cruz and colleagues found a significantly higher failure rate after reconstruction using allograft compared with autograft in pediatric/adolescent populations (Odds ratio (OR) 3.87) (23). Data on allograft reconstructions were pooled due to variability of allograft type used in the individual studies, and therefore no comments could be made regarding which allograft type was more desirable in this population. In addition, no adjustment was made for autograft type (BPTB versus HT). The authors did use a validated bias-assessment tool to evaluate the included studies and found a low risk of bias (23).

#### 2.5.4 Results of Anterior Cruciate Ligament Reconstruction

Due to the frequent failure of non-operative treatment approaches to ACL injuries, especially in younger patients aspiring to return to an active lifestyle, surgical reconstruction remains the most common option pursued (4). However, there are many factors that can influence the surgical outcome and the risk of graft failure. Surgery-related risk factors for ACL graft failure include technical errors such as nonanatomic tunnel placement (placement of the graft does not imitate histological and biomechanical features of the native ligament), inadequate graft fixation, improper tensioning of the graft, graft impingement on the intercondylar roof, and insufficient graft material (4,20). Other risk factors indicated for ACL graft failure do not relate to the surgical performance and include higher levels of activity, younger age, the use of allograft versus autograft, and an increased lateral tibial posterior slope (20–23).



A systematic review published in 2021 by Haybäck and colleagues investigated failure rates of common grafts used in ACL reconstruction and included 194 studies of varying study types and different evidence levels from the last decade (21). They hypothesized there to be no statistically significant difference in graft failure rates within the different types of autografts, and when comparing autografts and allografts. There are many factors that are important when considering a successful ACL reconstruction, however the indication of graft failure remains one of the most important indicators (21). HT autografts, BPTB autografts, QT autografts, and a group consisting of allografts were included in the analysis. Differences in yearly failure rates between graft groups were calculated, and after statistical analysis, the authors concluded that there were no significant differences in yearly graft failure rates (21).

In 2020, members of the MOON (Multicenter Orthopaedic Outcomes Network) Group published results from a prospective longitudinal cohort study (69). This study investigated the incidence of ACL revision reconstruction rates, and contralateral ACL tears after primary ACL reconstruction resulting in the need for contralateral ACL reconstruction in a specific cohort of high-school and college-aged athletes. The authors hypothesized there to be no differences in rate of failure between HT and BPTB autografts at six years postoperative. It is important to note that when focusing on a specific cohort of patients, such as young, active patients, differences in failure rates of graft type are more easily distinguished compared to systematic reviews that investigate all patients. Using predictive modeling, the authors found that patients in this cohort who had received the HT autograft were more likely to experience a graft failure leading to subsequent ACL revision reconstruction. Specifically, results showed that the odds of revision reconstruction on the ipsilateral knee in HT autograft patients were 2.1 times higher than the odds in BPTB autograft patients. However, there was no significant difference in the incidence of ACL reconstruction of the contralateral knee (69).

Mohtadi and Chan published 5-year postoperative results in 2019 from a randomized clinical trial comparing patient-reported and clinical outcomes of patients randomized to receive either a BPTB autograft, single-bundle HT autograft, or double-bundle HT autograft (70). The outcomes of interest included the ACL Quality of Life Questionnaire (ACL-QOL), Tegner activity index, International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form and

Objective scores, the Cincinnati Occupational Rating Scale, single leg hop test, and clinical outcomes such as the anterior drawer test, Lachman test, and pivot-shift test, as well as range-of-motion assessments and kneeling pain. The authors were also interested in proportions of graft failure and contralateral ACL rupture. At five years postoperative, the authors found no significant difference in ACL-QOL scores among the three groups, however, there were significantly more traumatic reinjuries in both HT groups compared to the BPTB group (70).

### 2.5.5 Double-Bundle vs. Single-Bundle ACL Reconstruction

The difference in kinematics and tensile properties between the AM and PL bundles of the ACL throughout varying degrees of flexion means that the ACL is not a purely isometric ligament (37,68). Up until recently, single-bundle reconstructions were standard, with the surgeon placing the graft isometrically to prevent irreversible graft elongation due to repetitive stretching (37,48,68). Single-bundle reconstructions can restore anterior-posterior knee stability because they reconstruct the AM bundle, but lack in the ability to restore normal rotational kinematics, which the PL bundle is primarily responsible for. It has been shown that between 10% and 30% of patients were still reporting persistent symptoms of instability in their knee after a single-bundle reconstruction technique was performed (4). In biomechanical and clinical studies conducted recently, grafts placed isometrically were not able to restore normal knee kinematics and had a persistent positive pivot-shift, compared to anatomical grafts placed in the footprint of the native ACL (68). Anatomic reconstruction is defined as the proper placement of tunnels in the native footprint of the ACL after accurate visualization of anatomic landmarks (48). The lack of rotational stability in a single-bundle reconstruction eventually led to the development of the double-bundle reconstruction, where the goal was to reconstruct the AM and PL bundles separately but position them as close as possible in the centers of the tibial and femoral footprints to resemble the native bundles of the ACL more accurately (4,31,37,48,49,58,68). Clinical and biomechanical studies have shown promising results of the double-bundle technique thus far in terms of re-establishing rotational stability however this technique is difficult and demands a high level of technical skill from the surgeon (4,48,50,68).

Numerous systematic reviews and meta-analyses have been conducted to investigate outcomes from single-bundle versus double-bundle reconstructions. In 2014, Desai and colleagues

performed a meta-analysis of studies comparing single-bundle and double-bundle ACL reconstructions, with a strict inclusion criteria of only anatomical primary ACL reconstructions versus non-anatomical reconstructions (68). A total of 15 studies were included in the meta-analysis. Anterior knee laxity was measured using the KT-1000 arthrometer in three of the studies, which showed a significant difference in favour of the double-bundle reconstruction. Graft failures were reported in six of the studies, although statistical analysis was only performed in one study, which showed statistical significance favouring the double-bundle reconstruction as well. Two of the studies reported a significant difference in the pivot-shift test, also in favour of the double-bundle reconstruction. The overall meta-analysis was not statistically significant in terms of measuring differences in rotational laxity in the pivot-shift test. The authors' assessment of bias revealed some studies with unclear methods, and prospective studies were evaluated alongside randomized trials which increased the risk of selection bias. However, the strict inclusion criteria of evaluating only anatomical reconstructions did increase the quality of the results, but the authors noted investigation of long-term outcomes is still needed (68).

In 2015, Mascarenhas and colleagues performed a systematic review of overlapping meta-analyses investigating postoperative stability differences in single-bundle and double-bundle reconstructions (49). Nine meta-analyses were included in the analysis, and of the nine studies, eight performed an analysis of heterogeneity. Patient reported outcome measures (PROMs) included the IKDC score, Lysholm knee score, and Tegner activity index, along with the pivot-shift test, KT arthrometry, Lachman testing, and the anterior drawer test to assess knee stability. In order to assess the quality of the meta-analyses, the authors used the Quality of Reporting of Meta-analyses (QUOREM) system, the Oxman-Guyatt quality appraisal tool, and the Modified Coleman Methodology Score. The authors used the Jadad decision algorithm to interpret discordant meta-analyses. In terms of patient reported outcomes, the authors found higher IKDC scores reported in one study, favouring the double-bundle group, compared to four other studies that indicated no difference. There were no significant differences in Lysholm or Tegner scores between single-bundle and double-bundle groups in any studies. Seven of the studies reported superior pivot-shift test results in the double-bundle group, while two studies did not find any significant differences. In addition, eight studies found the double-bundle technique favourable in terms of KT arthrometry results, while one study did not find a significant difference. Superior

results for Lachman testing were found in the double-bundle group in three studies, with no significant difference found in two other studies. The authors concluded the possibility that the double-bundle technique can provide better stability in the knee postoperatively in terms of functional outcomes such as KT arthrometry and pivot-shift testing when compared with the single-bundle technique, however it is not clear if there is a significant effect on clinical outcomes and patient reported outcomes. The authors mentioned that substantial differences that may only present in longer-term follow-up would potentially be overlooked in this study since most of the literature comparing these techniques consisted of short-term follow-up periods (49).

In 2019, Dong and colleagues performed a meta-analysis of randomized controlled trials investigating long term results associated with single-bundle and double-bundle reconstructions (50). Five studies were included in the meta-analysis, with a minimum follow-up of five years. Outcome measures included the Lysholm knee score (four studies), IKDC score (four studies), the pivot-shift test (three studies), side-to-side differences measured by KT-1000/2000 (four studies), and osteoarthritic changes (two studies). The authors found no statistically or clinically significant difference between the single-bundle and double-bundle groups in any of the outcome measures at a minimum follow-up of five years, and all pooled analyses had low or no heterogeneity. The authors did note a few limitations, including the small sample size due to the inclusion of only five studies. Variables that could potentially act as confounders such as graft type, fixation methods, or anatomic versus non-anatomic reconstruction were not accounted for in the analysis due to insufficient data (50).

### 2.5.6 The Anterolateral Ligament (ALL)

In 1879, Paul Segond was responsible for the discovery of the avulsion fracture highly associated with ACL injuries at the proximal lateral tibia, known today as the Segond fracture. At the same time, he visualized a fibrous band at the location of the fracture that appeared to be under tension when the knee was internally rotated (13,14,26,27,37). This structure has had different names over the years, but in 2012, Vincent and colleagues began referring to it as the ‘anterolateral ligament’ (ALL) (14,27).

Based on anatomic investigations on cadavers, histologic analyses, and findings during knee surgery, it is generally accepted that the ALL originates on the lateral femoral condyle and travels distally, attaching to the proximal tibia near Gerdy's tubercle (14,25–27,37).

Biomechanical analyses have demonstrated that the ALL does contribute to rotational stability of the knee (14,24–27). Sonnery-Cottet and colleagues performed a biomechanical analysis comparing results of rotational tests on isolated ACLs as well as ACLs with the addition of the ALL section and found an increase in the test results when the ALL was added (24). They also found that a tear of the ALL increased rotational laxity in the knee when combined with an ACL tear, demonstrating that the ALL and ACL are highly synergistic (24). Kennedy and colleagues (26) found that the ALL was able to withstand a mean maximum load of 175 N, whereas Helito and colleagues found the maximum mean strength of the ALL to be 204.8 N (25). ALL ruptures are frequently accompanied by a Segond fracture in addition to an ACL rupture, although they may not always occur concomitantly (14,24–27). More recently recognizing the importance of the ALL as an additional stabilizer to the ACL, surgeons consider a combination of ACL reconstruction with ALL reconstruction to restore native knee kinematics (14,24–26,29,32,34,58).

### 2.5.7 Extra-Articular Reconstruction

Early attempts to restore stability in an ACL-deficient knee are linked with a history of ALL reconstruction. Before arthroscopic ACL reconstructions became the standard, extra-articular procedures were performed with the goal of treating and minimizing rotational instability and anterior subluxations (13–15,17,36). The first common approach to extra-articular reconstruction was a lateral extra-articular tenodesis (LET), which involves harvesting a strip of the patient's iliotibial (IT) band, tunneling it over or under the LCL, and anchoring it on the lateral femoral condyle (13–15). Different methods of performing extra-articular reconstructions have been developed over the years, such as the MacIntosh procedure (8), Losee's 'sling and reef' operation (9), Ellison's distal ITT transfer (10), the Lemaire operation (11), and the Andrews operation (12). Most of these techniques are similar in that they all involve the use of a strip of the IT band, which is then tunneled under or over the LCL, and anchored at different spots along the lateral femoral condyle (13,58).

Results of extra-articular reconstruction as an isolated procedure are variable, with most outcomes reported as poor. A systematic review performed by Slette and colleagues in 2016 investigating biomechanical results of LET procedures in the knee found that isolated LET procedures were unable to restore normal anterior stability to the knee, and reduced internal rotation of the tibia to levels considered less than normal in varying angles of flexion of an ACL-deficient knee (18). Neyret and colleagues reported a positive pivot-shift test at one-year post-op in four out of 11 successful knees, and five out of seven knees; all having undergone an isolated LET Lemaire operation. The operation was considered successful for 68% of the patients over 35 years of age, but success was considerably reduced for patients under age 35 (21% success rate). When an intra-articular reconstruction was performed in addition to the Lemaire operation, the success rate was 83% (17). Between December 1974 and July 1976, Kennedy and colleagues performed an LET using the Ellison procedure in patients with anterolateral rotatory instability, and results were found to be unpredictable. They were unable to eliminate a positive anterior drawer test in any knee, and when this procedure was performed in isolation, only 46% of patients reported good or excellent results (16). Fifty patients that underwent a MacIntosh LET procedure between 1973 and 1978 were reviewed by Ireland and Trickey (8), and out of 14 'excellent' and 23 'good' results, less than half of the patients were able to return to their sport at a pre-injury level. Due to the frequency of failure and recurrent instability of isolated extra-articular reconstructions, more advanced intra-articular techniques were developed (13,14,18,32,36,58). Despite the advancements and refinement in surgical technique allowing surgeons to perform an intra-articular ACL reconstruction, rotational instability and graft failure are still seen in approximately 1.7% to 7.7% of patients (14). These findings have led to the investigation of extra-articular reconstruction in combination with intra-articular reconstruction, where a systematic review performed by Hewison and colleagues in 2015 reported a statistically significant reduction in rotational laxity measured by the pivot-shift test when an LET was added to the intra-articular ACL reconstruction (36). Another systematic review and meta-analysis performed by Beckers and colleagues in 2021 investigating the addition of lateral augmentation techniques to a primary ACL reconstruction reported similar findings, with a significant reduction in graft failure and persistent rotatory laxity after addition of a lateral augmentation (71).

### 2.5.7.1 Non-randomized Studies

In 2013, Dejour and colleagues published results of a comparative study between ACL reconstructions consisting of single-bundle BPTB grafts, double-bundle HT grafts, and single-bundle BPTB grafts combined with a modified Lemaire LET (28). They hypothesized that out of the three different techniques, the double-bundle HT reconstruction and the BPTB + LET reconstruction would be superior in terms of restoring knee stability, measured by postoperative anterior tibial translation (ATT) values. They also hypothesized that IKDC scores would be similar between the groups, but there would be increased anterior knee pain and postoperative sensory deficits in the groups with the BPTB grafts. Seventy-five patients were recruited from a total of 196 ACL reconstructions that were performed by one surgeon in 2005, with 25 patients in each of the three reconstruction technique groups. Patients determined to have more knee laxity were allocated to receive the BPTB + LET reconstruction. The primary outcome of this study was postoperative ATT, and this was measured by obtaining Telos™ stress radiographs. Other outcome measures were also collected, such as the IKDC objective and subjective forms, absence of knee pain and sensory deficits, pivot-shift testing, and return to sports. The authors found that ATT significantly improved in all three groups postoperatively in both the internal and external compartment ( $p=0.0001$ ). There was no significant difference between the correction of ATT in the medial compartment between the three groups, but the correction of ATT in the lateral compartment was found to be superior in the BPTB + LET group compared to the other two groups ( $p=0.0001$ ). There was no statistically significant difference between IKDC subjective and objective scores, pivot-shift test scores, and ability to return to sports. Six patients in the double-bundle HT group reported anterior knee pain, compared to nine in the BPTB and nine in the BPTB + LET groups, however, this was not found to be statistically significant. The authors concluded that adding an extra-articular procedure in combination with an ACL reconstruction can add superior stability in patients who have increased knee laxity. This study is considered a prospective cohort study, and due to the lack of randomization and therefore absence of allocation concealment, there is a higher potential for selection bias. Specifically, the surgeon chose group allocation based on individual patient characteristics; for example, patients with greater laxity were always allocated to receive the BPTB + LET reconstruction, and the remaining grafts were assigned based on sports participation. Since the reason for group

allocation was based on potential prognostic factors, this puts the study at high risk of selection bias. There was also a clear predominance of men (51 males vs. 24 females), which meant the groups were not balanced. The authors noted an identical rehabilitation protocol was prescribed to each group, and an independent orthopaedic surgeon performed clinical and radiographic evaluations, however it is not known if the surgeon was blinded to group allocation. If the surgeon performing the assessments was not blinded to group allocation (i.e., the patient wears an opaque sleeve around the operated knee), they would be able to visualize the additional incision of the LET, potentially increasing the risk of detection and performance bias. All patients evaluated were included in the analysis as there was no loss to follow-up, therefore there was a low potential of attrition bias. No sample size calculation was provided, and no power analysis was performed to our knowledge. The authors used confidence intervals when interpreting the mean paired difference in ATT, and these were fairly narrow indicating higher precision.

Sonnery-Cottet and colleagues conducted a prospective comparative study of 502 patients that received either: (1) isolated BPTB autograft reconstruction (n=105); (2) isolated HT autograft reconstruction (n=176); or (3) combined HT autograft + ALL reconstruction (n=221) and published their findings in 2017 (29). A subset of patients between the ages of 16 and 30 were selected from a population of 1346 patients that underwent ACL reconstruction by a single surgeon between January 2012 and May 2014. The authors hypothesized that there would be a decreased rate of graft failure and increased rate of return to sport in the combined procedure, compared to the isolated procedures. The IKDC form, Lysholm knee score, Tegner activity index, range of motion, Lachman testing, and laxity testing with a Rolimeter arthrometer comprised the outcome measures. At baseline, there were significant differences between groups with respect to sex ( $p < 0.0001$ , higher percentage of male patients), age ( $p = 0.0004$ ) and sport participation ( $p < 0.0001$ , higher percentage of contact sports). The authors accounted for these differences through multivariate analyses. At a mean follow-up period of 38.4 months, there were no significant differences found between groups with respect to mean subjective IKDC score, laxity, Lysholm score, and Tegner score. Graft failure rate was found to be 3.1 times less in the HT + ALL reconstruction group compared to the isolated HT group (hazard ratio [HR], 0.327; 95% CI, 0.130-0.758) and 2.5 times less compared to the isolated BPTB group (HR,



0.393; 95% CI, 0.153-0.953), and this was the key finding of the study. There was no significant difference in graft failure rate of the isolated BPTB group compared to the isolated HT group (HR, 1.204; 95% CI, 0.555-2.663). The authors concluded that the addition of ALL reconstruction with intra-articular ACL reconstruction is safe and reduces the rate of graft failure. This study is also considered a prospective cohort study, so due to the lack of randomization and therefore absence of allocation concealment, there is a higher potential for selection bias. The authors noted that the graft chosen was based on patient preference, as well as the opinion of the surgeon based on patient characteristics and potential risk factors for graft failure. Therefore, since the graft choice was partially influenced by the surgeon's assessment of prognostic factors, this puts the study at high risk of selection bias. The authors also noted a trend toward more frequent use of the HT + ALL reconstruction technique due to the presence of excellent clinical outcomes over time at follow-up. All patients regardless of group allocation were provided with a standardized rehabilitation protocol, and clinical assessments were performed by an independent surgeon. It is not known whether the independent surgeon was blinded to group allocation or not, therefore there is a higher potential for detection and performance bias since they would be able to see the incisions of the ALL reconstruction. Thirty-nine patients (7.2%) were lost to follow-up due to the inability to reach patients despite attempts to communicate. This data can be considered missing completely at random (MCAR) since it does not depend on the outcome of the study and does not bias the results. There was no sample size calculation or power analysis provided in the results. The authors presented 95% confidence intervals to interpret results of adjusted hazard ratios of the predictive factors of graft failure. All confidence intervals were narrow and therefore had higher precision, with the exception of age and type of sport.

In 2019, Rowan and colleagues published their results from a retrospective review of a database that collected prospective clinical outcomes of patients that underwent isolated HT ACL reconstructions, and HT ACL reconstructions with the addition of a modified Lemaire LET (30). The main objective of this study was to compare PROMs (Lysholm knee score and Tegner activity index), re-injury, re-operation, and return to sport between the two groups. They hypothesized that the addition of the LET to the ACL reconstruction would influence the clinical outcomes. A series of patients who had an isolated HT ACL reconstruction were compared with

a subsequent series of patients who had the HT ACL reconstruction + LET, with all surgeries performed by a single surgeon at a single center. Propensity matching was performed to minimize baseline differences between the treatment groups, and after analysis, there were  $n=125$  and  $n=46$  patients in the isolated HT ACL and HT ACL + LET group, respectively. LET was performed in combination with ACL reconstruction in patients that met certain criteria, such as having a high-grade pivot-shift test. The median follow-up was 52 months (range 24-96) and 27 months (range 24-45) in the HT ACL group versus the HT ACL + LET group respectively. The authors found a statistically significant difference in postoperative Lysholm and Tegner scores in favour of the HT ACL + LET technique ( $p=0.005$  and  $p=0.003$  respectively), as well as a significant reduction in time in months to return to sport favouring the HT ACL + LET technique ( $p<0.001$ ). They also reported no graft failures in the HT ACL + LET group, whereas 5.9% of patients in the HT ACL group did, however, this was not statistically significant. The authors noted that confounding due to more elite athletes in the HT ACL + LET group could affect the comparison between groups, however, results showed that clinical outcomes favoured the addition of the LET to the ACL reconstruction, when certain criteria are applied to patients. This study is considered a retrospective review of a prospective cohort study with historical control, and due to the lack of randomization and therefore absence of allocation concealment, there is a higher potential for selection bias. The LET was not added as the treatment group until after a cohort of patients who underwent isolated ACL reconstruction was established, therefore the research question came after one cohort's data was collected, and before the implementation of the additional LET for patients meeting certain criteria. As the indication for the addition of LET was based on prognostic factors such as a high-grade pivot-shift, this puts the study at high risk of selection bias. All patients were provided with a standardized physiotherapy protocol, and since the outcome measures were PROMs as part of a patient database, there was no clinician to perform and report clinical findings. Before performing propensity matching, there were significant differences in demographics between groups. Since this was a retrospective review, the authors were limited to the outcome measures contained within the standard prospective patient database managed at that center before the research question was addressed.

In 2021, Ahn and colleagues conducted a retrospective study investigating differences in postoperative knee stability and clinical outcomes between double-bundle ACL reconstruction

and single-bundle ACL reconstruction with the addition of the LET (31). They hypothesized that the addition of the LET to the single-bundle reconstruction would provide superior outcomes compared to the double-bundle reconstruction. Between January 2014 and January 2017, 171 consecutive patients had an ACL reconstruction performed by one surgeon, at one center. Of these 171 patients, 95 were ultimately enrolled in the study after meeting inclusion criteria, with 48 patients having the HT autograft double-bundle reconstruction, and the remaining 47 patients having the HT autograft single-bundle reconstruction plus LET. The primary outcome was postoperative knee laxity, quantified by the pivot-shift test, and clinical outcomes measured by the IKDC examination form (72) at the patient's most recent follow-up. Secondary outcomes included postoperative Kellgren-Lawrence grade (73), and if surgery was warranted to remove the tibial fixation screw after reconstruction, a second-look arthroscopy was performed to visualize graft maturation at least one-year post-reconstruction. The single-bundle + LET group showed significantly better pivot-shift test results and an IKDC objective grade compared to the double-bundle group. There was no statistical difference between subjective functional IKDC scores between both groups ( $p=0.83$ ) and Kellgren-Lawrence grade of knee radiographs ( $p=0.872$ ). Although there were several limitations to this study including potential confounders not adjusted for, and potential patient selection bias due to the retrospective nature of the study, the authors suggested that surgeons should consider adding an extra-articular procedure when performing an intra-articular ACL reconstruction. As this study is considered a retrospective review, due to the lack of randomization and therefore absence of allocation concealment, there is a higher potential for selection bias. The surgeon chose the group allocation of the patient based on the pivot-shift test and the presence or absence of meniscal tears. Since these can be considered prognostic factors, this puts the study at high risk of selection bias. The postoperative clinical evaluations were performed by the same surgeon that performed the surgeries, increasing the potential of detection and performance bias since the surgeon would be unblinded to group allocation. To mitigate the risk of confirmation bias, an orthopaedic surgery resident was present with the surgeon at follow-up to observe the evaluations and provide feedback. Two orthopaedic surgery residents were blinded to IKDC grade and group allocation in order to evaluate preoperative and postoperative laxity observed on stress radiographs, which decreased the potential for detection and performance bias in this case. The same rehabilitation protocol was

provided for both groups, and there were no significant differences in demographic characteristics of the patients between groups. No sample size calculation was provided, however the authors performed a post hoc power analysis for the primary outcome. Confidence intervals were not reported in order to interpret the results.

Mahmoud and colleagues published a matched cohort study in 2022 to investigate potential differences in PROMs and graft survival between patients who underwent ACL reconstruction with LET versus patients who underwent ACL reconstruction alone (22). They hypothesized that the PROMs would be equivalent in both groups, and graft failure rate would be lower in the ACL + LET group. In this retrospective case-control study, 72 patients that had undergone an ACL reconstruction with HT autograft and LET and 72 patients who only had an ACL reconstruction with HT autograft were recruited from a single surgeon from 1996 to 2015. The patients were matched based on age, gender, and year of operation. The primary outcomes were PROMs – specifically the Lysholm knee score, Tegner activity index, Oxford Knee score, and IKDC subjective knee form. Medical charts were also reviewed to record ACL graft failure and postoperative complications. The authors found the graft failure rate to be 5% in the ACL + LET cohort, and 11% in the ACL cohort. However, the authors also noted that this study was not adequately powered to detect differences in graft failure to reach statistical significance, so no definitive conclusions could be made on that basis. They did find that ACL + LET cohort was associated with an improvement in PROMs, equivalent to the ACL cohort. Since the graft failure for the ACL + LET was lower than the ACL group, although the study was not powered enough to draw a conclusion about the significance of the difference, the ACL + LET cohort was considered biased and higher-risk, which indicates that the LET is a safe addition to ACL reconstruction. To determine any statistical significance in graft failure between techniques, the authors noted further investigation would be required. As this study is considered a retrospective case-control study, due to the lack of randomization and therefore absence of allocation concealment, there is a higher potential for selection bias. Since the surgeon only performed the LET on patients with increased risk factors for graft failure, it is clear that the reason for allocation was based on patient characteristics, which puts this study at high risk of selection bias. Since the outcome measures PROMs, there was no clinician to perform and report clinical findings other than those found in the patient's medical chart after review. The authors

performed a power analysis to determine the number of patients needed to detect a minimal clinically important difference (MCID) of 10 points. Seventy-two ACL + LET patients were included in the graft survival analysis, however only 70% (n=50) completed the PROMs. The authors did not provide an explanation for the missing data, and therefore the type of missing data cannot be determined and accounted for in analysis. The authors provided confidence intervals to aid in the interpretation of the PROMs, however the intervals were fairly wide and showed a lack of precision.

Earlier this year, Viglietta and colleagues published long-term results after conducting a retrospective analysis of patients who underwent ACL reconstruction with HT autograft between January 2002 and November 2003 at a single center (32). Their primary goal was to determine whether there were differences in the development of osteoarthritis after ACL reconstruction versus ACL reconstruction and LET (Arnold-Coker modification of the MacIntosh LET technique) during a long-term follow-up. They also sought to determine whether the combination of ACL reconstruction and LET was associated with better stability of the knee, function, and decreased rates of graft failure. To assess the level of osteoarthritis (OA), weightbearing radiographs were obtained and evaluated using the Fairbank scale (74), the Kellgren-Lawrence scale (73), and the IKDC grading system (72). PROMs included the Tegner activity index, Lysholm knee score, and the IKDC rating system was used to assess clinical outcomes. In the isolated ACL reconstruction group, 79 patients were assessed, and in the ACL reconstruction + LET group, 76 patients were assessed. Results showed no statistically significant differences in Lysholm and Tegner scores between the groups. Patients in the isolated ACL group had a significantly higher grade of OA according to the IKDC radiographic score ( $p=0.01$ ) and the Kellgren-Lawrence score ( $p=0.04$ ), while there was no significant difference between groups in terms of the Fairbank score. The Fairbank classification is another measure used to assess the level of OA in the knee, like the Kellgren-Lawrence grading scale. However, each change in grade of severity requires the patient to have one symptom, two or three changes, or all four changes in the knee (spurring of tibial spines, marginal osteophytes, flattening of femur/tibia, and narrowing of joint space) to be considered grade I, II, III or IV. In comparison, the Kellgren-Lawrence classification focuses on minute changes more specifically in joint spacing and the presence of osteophytes (54). It is likely significant differences were not noticed in the Fairbank

scores because most patients may not satisfy the criteria to move up a degree in severity compared to the Kellgren-Lawrence grading scale. In the lateral compartment of the knee, patients in the isolated ACL group also had a significantly higher grade of OA according to the IKDC radiographic score ( $p=0.03$ ) and Kellgren-Lawrence score ( $p=0.04$ ), while there was no significant difference between groups in terms of the Fairbank score. In the medial compartment of the knee, there were no statistically significant differences between the isolated ACL group and the ACL + LET group. It was also noted that patients in both groups that had undergone a partial meniscectomy had higher grades of OA than patients who did not undergo a meniscectomy. Overall, the authors' main finding was a significantly lower incidence of OA in the tibiofemoral joint and lateral compartment of the knee in patients who had the combined ACL reconstruction and LET. The authors concluded that patients who undergo an isolated ACL reconstruction are at higher risk of developing OA after a minimum follow-up of 15 years, compared to patients who receive the LET with the ACL reconstruction. As this study is considered a retrospective review, due to the lack of randomization and therefore absence of allocation concealment, there is a higher potential for selection bias. The indications at the time to perform the LET in conjunction with the ACL reconstruction were the presence of a high-grade pivot-shift test or involvement in high-risk sports. This puts the study at high risk of selection bias since the group allocation was decided by the senior surgeon based on the characteristics of the patient. Both groups received the same rehabilitation protocol to minimize differences in recovery. The authors noted that follow-up evaluations were performed by an independent surgeon, however they were not blinded to group allocation as they were able to visualize the extra incision of the LET, potentially increasing the risk of detection and performance bias. The authors provided an explanation of their sample size calculation to detect differing degrees of OA in the groups. Overall, 35 patients were lost to follow-up because they were unreachable, and one patient was excluded because they underwent a revision ACL reconstruction during the period of follow-up. The unreachable patients can be considered MCAR, however it is unclear whether it was appropriate to exclude the patient with the revision surgery. The authors did not report confidence intervals to aid in the interpretation of their results.

### 2.5.7.2 Randomized Studies – ACLR alone vs. ACLR + LET

In 2001, Anderson and colleagues published results of a randomized trial comparing three different surgical methods to reconstruct the ACL (19). Between 1991 and 1993, 105 patients were randomized to (1) isolated BPTB autograft reconstruction (n=35); (2) HT autograft reconstruction with a Losee extra-articular tenodesis (n=35); or (3) isolated HT autograft reconstruction (n=35). At baseline, there were no significant differences among the three groups. Outcome measures included a physical examination, joint laxity assessed by the KT-1000 arthrometer, quadriceps and hamstring muscle strength assessed with a dynamometer, radiographs, and the IKDC knee evaluation form. At a mean follow-up of 35.4 months, the authors found no statistical differences in range of motion, patellofemoral crepitation, mean quadriceps and hamstring muscle strength, IKDC subjective assessment or symptoms, and degenerative changes noted on radiographs. They did however find that there was statistically significant stability in favour of the BPTB group compared to the isolated HT group after evaluation with the KT-1000 ( $p < 0.05$ ). Patients that had the BPTB reconstruction had a significantly better overall knee rating according to the IKDC scale compared with the HT + LET group ( $p < 0.02$ ), however, the authors noted that the presence of multiple categories can cause difficulty in interpretation of statistical significance. The results of this study showed no improvement in outcomes when LET is added, and the authors concluded no benefit to the combined procedure. It is not clear whether the authors used a specific randomization process (ie stratified, blocked), however allocation concealment was maintained as participants were not randomized until after confirming the inclusion criteria, using a randomized list generated by a computer. There was no mention of blinding of study participants, and all preoperative and postoperative examinations were performed by the senior author, therefore increasing the risk of performance and detection bias due to the obvious extra incision from the extra-articular tenodesis. To decrease the risk of performance and detection bias, study team members blinded to group allocation could have performed the assessments. Three patients were lost to follow-up, of which the authors did not provide a reason, therefore increasing attrition bias. They were subsequently excluded from the analysis, which does not follow the intention-to-treat principle. The authors also did not include confidence intervals to interpret their results.

Zaffagnini and colleagues published 5-year results in 2006 of a randomized trial that also compared three different ACL reconstruction techniques (33). A total of 75 patients were recruited, with 25 patients randomized to each group using alternate systematic sampling. The authors proposed a strict inclusion criteria, and all patients were required to be involved in cutting sports at a competitive level. The three reconstruction techniques were: (1) BPTB autograft; (2) HT autograft; and (3) HT autograft with a lateral extra-articular plasty using an over-the-top technique. There were no significant differences between the three groups at baseline assessments, and all reconstructions were performed by a single surgeon. Outcomes collected at follow-up included IKDC scores, Tegner scores, thigh circumference, anterior knee and kneeling pain, pivot-shift testing, Lachman testing, KT-2000 arthrometer testing, range of motion measurements, time to return to sport, and radiographs to assess for OA. At five years postoperative, all 75 patients were available for follow-up. The authors found no significant difference between IKDC scores and Tegner scores. Significantly higher scores for the subjective IKDC form in both the BPTB and HT + lateral plasty group were reported, compared to the isolated HT group ( $p=0.04$ ). Reports of anterior knee pain and kneeling pain were significantly higher in the BPTB group, compared to both HT groups ( $p=0.0001$ ). Negative pivot-shift test results were reported in 88% of patients in the BPTB group and 92% of patients in the HT + extra-articular plasty group, and this was a statistically significant difference with respect to the isolated HT group, with 64% of patients having a negative pivot-shift score ( $p=0.03$ ). Similarly, results of the KT-2000 arthrometer showed significantly more laxity in the isolated HT group compared to the other groups ( $p=0.05$ ). After Lachman testing, 88% of patients in the BPTB group had no laxity, 78% of patients in the isolated HT group had no laxity, and 92% of patients in the combined HT + lateral plasty group had no laxity, however this was not considered statistically significant. Patients in the HT + lateral plasty group were also able to return to sports after a shorter period of time compared to the other groups ( $p=0.05$ ). Only one patient was found to have degenerative changes after radiographic evaluation, and they had received the isolated HT reconstruction. The authors noted the small sample size and subsequent decreased power as a potential limitation, however they concluded that adding an extra-articular plasty could enhance successful postoperative outcomes. As decisions about eligibility were made before randomization via alternate systematic sampling, allocation concealment was



maintained to reduce the risk of selection bias. Two independent surgeons that did not perform the surgery executed the evaluations, however it is not clear whether they were blinded which could increase the risk of performance and detection bias since they would be able to visualize the extra incision on the knee from the extra-articular plasty. All patients received the same post-operative protocol to help decrease the risk that differences are due to rehabilitation. There were no patients reported lost to follow-up, however there were only 25 patients in each group to begin the study, so the sample size was fairly small, and no sample size calculation was provided.

In 2017, Ibrahim and colleagues published their results after conducting a randomized controlled trial comparing isolated HT ACL reconstruction to HT reconstruction with the addition of an ALL reconstruction (34). They hypothesized that the addition of the ALL reconstruction would provide more knee stability and better functional recovery. Between January and June of 2014, 110 male patients were quasi-randomized based on birth dates to group A (n=56) and group B (n=54). Patients born on an odd-numbered day were randomized to group A (combined ACL reconstruction and ALL reconstruction), and patients born on an even-numbered day were randomized to group B (isolated ACL reconstruction). There were no significant differences in patient characteristics between groups at baseline. One surgeon performed all surgeries, and the operated knees were covered to ensure outcome assessors were blinded to surgical allocation. Outcomes included a clinical examination, where the pivot-shift test, Lachman test, and anterior drawer test were performed. Joint laxity was assessed using the KT-1000 arthrometer. Functional outcomes such as the Lysholm knee score, Tegner activity score, and IKDC score were also recorded. After analysis, the authors found no statistically significant differences between groups for any of the clinical examination findings, Lysholm, Tegner and IKDC scores at a mean follow-up of 27 months. However, KT-1000 scores were significantly better ( $p < 0.001$ ) in that received the ALL reconstruction. The authors noted limitations to this study, including the absence of female patients, and the lack of power. They concluded that the addition of the ALL reconstruction did improve subjective and objective outcomes, however the findings were not statistically significant. Since patients were randomized by birth date, it is possible that there is a higher risk of selection bias because the surgeon would be able to tell the group allocation sequence based on looking at the patient's birth date. Only one surgeon performed all of the

operations, but in order to reduce performance and detection bias, preoperative and postoperative assessments were performed by different surgeons, where the operated knees were covered with an opaque sleeve to ensure blinding of the examiner. Otherwise, the examiners would be able to distinguish the group allocation of the patient due to extra incisions in the ALL reconstruction group. Seven patients were lost to follow-up, and the authors chose to exclude them from the analysis, which generally threatens internal validity and does not follow the intention-to-treat principle. However, the authors noted the reason for loss to follow-up was due to all seven patients leaving the country, so this would be considered data missing completely at random (MCAR). Only male athletes were included in this study, which decreases the generalizability of the results to a larger population, since females athletes are more likely to sustain an ACL injury. The authors used a Fisher exact test to report p-values of preoperative pivot-shift results, and postoperative pivot-shift, Lachman, and anterior drawer results. A Mann-Whitney *U* test was used to report p-values of preoperative and postoperative KT-1000 arthrometer results. No confidence intervals were reported, and there was no sample size calculation or power analysis.

In 2020, Castoldi and colleagues published results of a long-term follow-up from a single-center randomized study to determine differences in clinical and radiological outcomes between patients randomized to receive an isolated BPTB autograft ACL reconstruction (n=61) or BPTB autograft + LET (modified Lemaire) (n=60) (2). Patients were consecutively recruited between January 1998 and September 1999, and subsequently underwent unblinded block randomization. There were no significant differences in baseline characteristics and demographics between groups at the time of surgery. The authors hypothesized that the addition of the LET would improve PROMs and graft-survival over a longer period of time without an increased risk of developing OA. The primary outcome measure was the IKDC subjective knee form. Secondary outcomes included the Lysholm knee score, the “forgotten knee” score (75), graft failure, and presence of OA. Eighty patients (81 knees, 67%) were available for follow-up at a mean of 19.4 years (range 19, 20.2 years) post-reconstruction. There were no significant differences between groups in the IKDC subjective knee form, the Lysholm score, or the forgotten knee score. This study was underpowered to detect a clinically important difference in graft failure, however, the authors noted a trend toward a decreased risk of graft failure in the BPTB + LET group versus the isolated BPTB group (13% versus 29% respectively, p=0.1). There was a significant increase

in risk of lateral compartment OA in the BPTB + LET group ( $p=0.02$ ), although the authors were unable to make any definite conclusions due to the increased number of lateral meniscectomies performed that acted as a confounder. Castoldi and colleagues concluded no difference in PROMs between the two groups, and that the LET could potentially increase the risk of lateral compartment OA development over a longer-term follow-up period. The authors maintained allocation concealment by ensuring inclusion criteria was met and confirmed via MRI before inclusion in the study, and subsequent block randomization. This study was performed at a single center, however it is not clear if more than one surgeon performed the surgeries. The authors did mention that there was a study team member independent from the surgeon that recorded PROMs. It is unclear who performed the postoperative clinical examinations, and there was no mention of the blinding of the examiner(s), which could increase the risk of performance and detection bias by visualizing the extra incision from the LET. Loss to follow-up was an issue in this study, as a total of 41 patients (34%) were lost to follow-up, with no reasons provided other than one patient undergoing a total knee replacement, excluding them from analysis. This puts the study at a higher risk of attrition bias and can threaten the precision due to the smaller sample size and an imbalance of prognostic factors. Excluding these patients, especially the patient that received the knee replacement, does not follow the intention-to-treat principle. A sample size calculation and power analysis was provided for the primary outcome, but the authors did not report any confidence intervals in the interpretation of their results.

Porter and Shadbolt published 2-year outcomes in 2020 of a randomized controlled trial comparing a group of patients who received an isolated HT autograft reconstruction to a group of patients who received HT autograft reconstruction with a modified LET (35). Their objective was to see if adding the LET would improve clinical outcomes and/or lower the risk of ACL graft failure in patients whose pivot-shift test results showed inability to restore anterolateral stability at the time of ACL surgery. Between July 2014 and January 2017, 55 patients were recruited and underwent isolated hamstring tendon ACL reconstruction. On the operating table, if their post-procedure pivot-shift test results were still positive, they were then randomized using a computer-generated number to either receive the additional LET ( $n=28$ ), or not ( $n=27$ ). There were no significant differences between baseline characteristics and baseline PROMs. Primary outcomes of interest included subjective IKDC score, Knee Injury and Osteoarthritis Outcome

Score (KOOS) quality of life (QoL) and sport/recreation (Sport/Rec) subscales, the Lysholm knee score, the Tegner activity scale, and reports of graft failure. Secondary outcomes included reports of contralateral ACL tears and other knee-related complications. There were no significant differences between groups for the IKDC score, the KOOS QoL score, the occurrence of meniscal tears, or risk of contralateral ACL rupture. The LET group did however have significantly higher KOOS Sport/Rec scores, Lysholm scores, and Tegner scores ( $p=0.02$ ,  $p=0.004$ ,  $p=0.03$  respectively) compared to the isolated reconstruction group. Both groups were found to have a similar risk of contralateral ACL rupture. The authors noted a few limitations of the study, including the small sample size, and only having one surgeon to perform the surgeries. However, it was concluded that the addition of the LET decreased the risk of graft failure in patients with a residual positive pivot-shift result. Since patients were not randomized until after inclusion criteria were fulfilled and after the isolated reconstruction, allocation concealment was maintained in order to reduce the probability of selection bias. One aspect of the inclusion criteria to note was that the patients were only eligible if they sustained an ACL tear via a noncontact mechanism. Although noncontact injuries are more common, contact injuries do occur in sports, which could affect the generalizability of the results to the population. Patients requiring repair of their meniscus at the time of surgery were also excluded due to differences in rehabilitation protocol, however many ACL injuries occur concomitantly to meniscal injuries, so generalizability of the results to the population should be interpreted with caution. One surgeon performed the surgeries, and there is no mention of blinded outcome assessors at the follow-ups, which could increase performance and detection bias upon visualizing the extra incision of the LET. There were no patients lost to follow-up, however four patients were excluded from analysis due to graft rupture relating to low PROM scores. The authors did not perform a sensitivity analysis including these values, therefore it is not certain whether removing the values was appropriate. The authors did not perform a sample size calculation or pre hoc power analysis, but did perform a post hoc power analysis, where they were underpowered with regard to the IKDC score and meniscal tears. No confidence intervals were reported to aid in the interpretation of precision.

Getgood, Bryant and colleagues reported the absence of adequately powered studies investigating outcomes of isolated intra-articular ACL reconstruction versus intra-articular

reconstruction with the addition of LET (15). In 2020, they published 2-year outcomes of the STABILITY study: a pragmatic, multicenter, randomized clinical trial investigating isolated HT autograft ACL reconstruction versus HT autograft ACL reconstruction with a modified Lemaire LET. Their goal was to determine whether the HT reconstruction with LET showed a lower rate of graft failure in young patients at a higher risk of a failed reconstruction. Between January 2014 and March 2017, 618 patients across seven centers in Canada and two centers in Europe were randomized at the time of surgery. Randomization occurred via telephone or a computer software in a 1:1 ratio, stratified by surgeon, sex and meniscal repair. There were no statistical differences found between groups at baseline. The primary outcome of interest was ACL reconstruction clinical failure, with secondary outcomes consisting of PROMs such as the Four-Item Pain Intensity Measure (P4), Marx Activity Rating Scale, ACL-QOL, IKDC score, and the KOOS. All patients were analyzed using the intention to treat principle, and were evaluated at 3, 6, 12, and 24 months postoperative. 40% of patients in the isolated ACL reconstruction group experienced the primary outcome of clinical failure, compared to 25% of patients in the ACL + LET group ( $p < 0.0001$ ). Pain was noted to be significantly less in the isolated ACL group ( $p = 0.003$ ) at 3 months, but this difference resolved over time. At 24 months, the Marx Activity Rating Scale, ACL-QOL, IKDC, and KOOS scores were not statistically different between groups. This study also showed a significant decrease in clinical failure of ACL reconstruction when LET is added. This study was the first adequately powered study that showed a significant reduction in graft failure rates when comparing surgical techniques. In this cohort of patients, 34 of 298 (11%) in the isolated ACL reconstruction group sustained a graft failure, compared to 11 of 291 (4%) in the ACL + LET group ( $p < 0.001$ ). The addition of the LET was found to be protective for both groups, however graft failure was more commonly seen in patients under the age of 20. The authors concluded that adding the LET to ACL reconstruction reduces graft failure and persistent rotatory laxity. As patients were randomized by telephone or web-based software at the time of surgery and after confirming eligibility, allocation concealment was properly implemented and maintained to reduce selection bias. The authors included the presence of meniscal repair (as well as surgeon and sex) in the stratified randomization to ensure balanced prognostic factors, since rehabilitation would be altered. To ensure standardization across centers, all patients received the same instructions for rehabilitation. A clinician who was

not part of the surgical team was blinded to group allocation via an opaque elastic bandage around the knee in order to perform the assessment of the primary outcome, the pivot-shift test, and to reduce the risk that selection and detection bias would affect the internal validity. A sample size was calculated taking into consideration a relative risk reduction in ACLR of at least 40%. Eighteen patients were lost to follow-up, with an additional 11 withdrawals from the study (5% attrition rate). However, it was not clear what the reasons for withdrawal or loss to follow-up were. To decrease the risk of attrition bias, the authors performed a sensitivity analysis using a multiple imputation function to compute missing data. The authors also reported 95% confidence intervals for the adjusted mean difference of the PROMs and range of motion measurements for interpretation of the results.

### 2.5.8 Summary

The ACL is an important ligament in the knee and adds crucial stability to the joint by resisting excessive anterior translation and internal rotation. ACL injuries are one of the most common knee injuries, and often occur in young, active athletes. Varying intrinsic and extrinsic factors may put a patient at higher risk of ACL injury, and in most athletes, injury occurs through noncontact mechanisms. Conservative management may be adequate for a subset of patients, but ACL reconstruction is usually necessary if patients have a desire to return to activities including pivoting sports, which are deemed higher-risk for ACL injury and re-injury.

Earlier surgical techniques to address ACL injury and rupture focused on lateral extra-articular procedures such as the LET. Poor outcomes led to the development of more refined intra-articular procedures using various autografts or allografts.

The “re-discovery” of the ALL has led surgeons to consider a combination of intra-articular and extra-articular reconstructions to address residual instability after ACL reconstruction. The majority of non-randomized and randomized studies show promising results in favour of combined intra- and extra-articular reconstruction. However, with small sample sizes and inadequate power as important limitations, authors were unable to firmly draw conclusions. The STABILITY study was the first adequately powered randomized clinical trial that investigated

the addition of the LET to an intra-articular ACL reconstruction, and showed results that favoured this addition.

## Chapter 3

### 3 Objectives and Methodology

#### 3.1 Objectives

Our primary objective was to conduct a long-term follow-up of the STABILITY study: the multicenter, prospective, randomized clinical trial that compared single-bundle HT autograft ACLR with or without the addition of a modified Lemaire LET. Our primary outcome was ACLR clinical failure, defined as the composite outcome including either (1) symptomatic instability requiring a revision ACL reconstruction, (2) symptomatic instability associated with a positive pivot shift or an asymmetrical pivot shift greater than the contralateral side, or (3) a graft rupture. Secondary outcome measures were the ACL Quality of Life Questionnaire (ACL-QOL), Knee Injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee Subjective Knee Form (IKDC), Marx Activity Rating Scale, range of motion, and adverse events.

We hypothesized that there would be no difference in ACL-QOL, KOOS, IKDC and Marx scores between patients who had the ACL reconstruction with LET and those who had the ACL reconstruction alone. However, we hypothesized that there would be a decrease in the composite outcome of ACL clinical failure in the patients who received the ACL reconstruction with LET. We did not expect to see many differences in adverse events between groups, other than for ACL graft rupture, and no significant differences in side-to-side difference for flexion and extension range of motion.

#### 3.2 Trial Design

The current study was a long-term follow-up of a pragmatic, multicenter, randomized clinical trial, STABILITY, involving seven centers in Canada and two centers in Europe. The long-term follow-up was conducted only at one center - the Fowler Kennedy Sport Medicine Clinic in London, Ontario, and this is where the 3-, 5- and 7-year post-op appointments took place. Local recruitment for these follow-ups began September 2020.



### 3.3 Institutional Approval

Local ethics approval for the original STABILITY study was obtained from the Health Sciences Research Ethics Board (HSREB) at Western University. (REB file number: 104524) (Appendix A). Approval was obtained from Lawson Health Research Institute's Clinical Research Impact Committee and Lawson Administration (Lawson Approval Number: R-14-059). The trial was also registered on clinicaltrials.gov (NCT02018354).

### 3.4 Eligibility Requirements

Patients were eligible to participate in the long-term follow-up portion of the study if they had participated in the original STABILITY study conducted from January 2014 to March 2019 and provided informed consent.

To be eligible for the original STABILITY study, patients had to: (A) have an ACL deficient knee; (B) be skeletally mature to 25 years of age at the time of surgery; and (C) have two or more of the following: (1) participated in a competitive pivoting sport; (2) have a pivot shift of grade two or higher; or (3) have generalized ligamentous laxity (Beighton (76) score of 4 or greater) or (4) genu recurvatum (knee hyperextension) greater than 10 degrees.

Patients were ineligible for the original STABILITY study if they: (1) had a previous ACL reconstruction on either knee; (2) required a bilateral ACL reconstruction; (3) had a multi-ligament injury (two or more ligaments requiring surgical attention – ie, PCL, MCL, LCL, or PLC); (4) had a symptomatic articular cartilage defect requiring treatment other than debridement; (5) had greater than three degrees of asymmetric varus or valgus alignment; (6) had a past or present history of metabolic bone, collagen, crystalline, degenerative joint or neoplastic disease; (7) had a femoral, tibial or patellar fracture (other than Segond fractures); (8) had a cognitive impairment or psychiatric illness that precluded informed consent or rendered the patient unable to complete questionnaires; (9) had a major medical illness where life expectancy was less than two years; (10) did not read, speak or understand English, French or Dutch; or (11) had no fixed address and no means of contact or were not available for the original two year follow up period.

## 3.5 Subject Recruitment

Local subjects from the Fowler Kennedy Sport Medicine Clinic that had previously consented to take part in the original STABILITY study were contacted consecutively according to their ACL surgery date in the study, to recruit them for a 3-, 5- or 7-year postoperative appointment. All patients provided informed consent in the form of an updated letter of information (Appendix B).

## 3.6 Randomization

In the original STABILITY study, after ensuring informed consent was obtained, a diagnostic knee arthroscopy was performed to confirm patients met the study eligibility criteria. If the patient was confirmed to be eligible, the randomization was performed by either the research staff or nursing staff in the operating theatre. The patients were randomized in a one-to-one ratio via telephone or a web-based service (EmPower Inc.), in permuted block sizes of two and four, into one of two groups: (1) ACL reconstruction alone (control) or (2) ACL reconstruction with lateral extra-articular tenodesis (experimental). The randomization was stratified by surgeon, sex, and meniscal tear status, since the presence or absence of a meniscal tear would alter post-operative rehabilitation.

## 3.7 Interventions

### 3.7.1 Anterior Cruciate Ligament Reconstruction (Active Comparator)

All study patients, regardless of treatment group, received a standard anatomic ACL reconstruction using a four-strand autologous hamstring graft. This procedure was performed in a standardized manner across all study sites. If the diameter of the graft was found to be less than 7.5 millimeters, the semitendinosus was tripled or quadrupled in order to provide a greater graft diameter. Femoral tunnels were drilled using an anteromedial portal technique, with femoral fixation provided by an Endobutton or equivalent. Tibial fixation was provided by an interference screw. Of the 196 patients recruited from the Fowler Kennedy Sport Medicine Clinic, 99 patients were randomized to receive the standard anatomic ACL reconstruction only.

### 3.7.2 Lateral Extra-Articular Tenodesis (Experimental)

A modification of the Lemaire technique (77) was used to perform the LET procedure for the patients randomized to this intervention and was standardized across all study centers. An oblique skin incision measuring approximately five centimeters was made between the lateral femoral epicondyle and Gerdy's tubercle. A one-centimeter wide by eight-centimeter long strip was harvested from the iliotibial band, leaving the Gerdy's tubercle attachment intact. Using a No. 1 Vicryl suture, the proximal end of the iliotibial band graft was whipstitched. The graft was then tunneled under the lateral collateral ligament (LCL) and attached to the distal femur with a Richards Staple (Smith & Nephew) anterior to the intermuscular septum and proximal to the femoral insertion of the LCL. Fixation of the knee was performed at 60° to 70° of flexion and the tibia at 0° of rotation. There was minimal tension applied to the graft, and the free end of the graft was looped back onto itself and then sutured using the No. 1 Vicryl suture. Of the 196 patients recruited from the Fowler Kennedy Sport Medicine Clinic, 97 patients were randomized to receive the standard anatomic ACL reconstruction with the added LET.

A postoperative rehabilitation protocol created by the Fowler Kennedy Sport Medicine Clinic Physical Therapy Department was given to all patients and was standardized across all study centers.

## 3.8 Outcome Measures

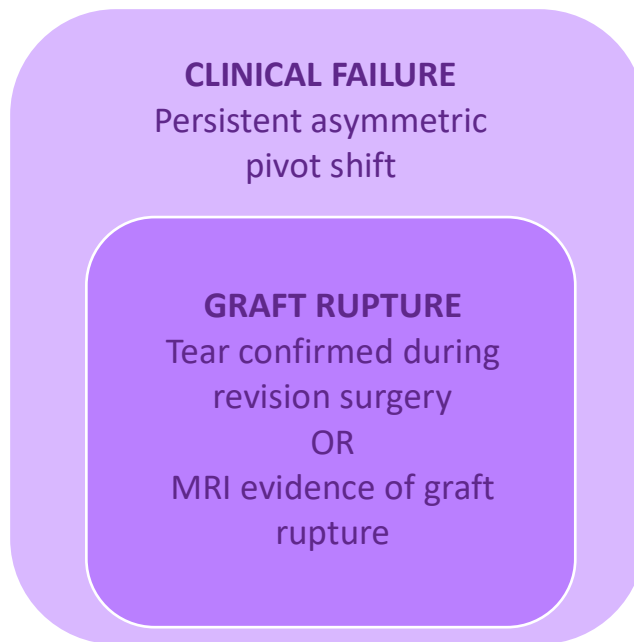
In the original study, all patients were assessed preoperatively and at 3, 6, 12, and 24 months postoperatively. In the long-term follow-up portion of the study, patients were assessed at the 3-year, 5-year, 7-year, and 10-year mark postoperatively. Currently, no patients have reached the 10-year mark. For the purposes of this thesis, we analyzed data from the 3-, 5- and 7-year follow-up period.

### 3.8.1 Primary Outcome Measure

#### 3.8.1.1 ACLR Clinical Failure

Our primary outcome was determining ACLR clinical failure (Figure 1), a composite measure of rotatory laxity defined as one or more of a persistent (detected at  $\geq 2$  visits) mild asymmetric

pivot shift (grade 1), a moderate or severe (grade 2 or 3) asymmetric pivot shift at any follow-up visit, or a graft rupture. Graft rupture was defined as a tear of the graft confirmed by either magnetic resonance imaging or arthroscopic examination (15).



**Figure 1: Diagram of the composite primary outcome of ACLR clinical failure.**

The pivot shift test is a diagnostic tool used to assess anterolateral rotatory instability in an ACL deficient knee (66). This test consists of two phases: (1) subluxation and (2) reduction. In an ACL deficient knee, the reduction event can be observed and graded as a glide (grade 1), clunk (grade 2), or gross reduction (grade 3). Evidence suggests that the pivot shift test is the most specific diagnostic test used for diagnosing ACL deficiency, with a specificity ranging from 0.97 to 0.99 (7). An unblinded surgeon performed the assessment of the primary outcome at the 3-, 5- and 7-year clinical assessment. A positive pivot shift was defined as having a persistent (identified at more than 2 visits) mild asymmetric pivot shift (grade 1), or a moderate or severe (grade 2 or 3) asymmetric pivot shift at any follow-up visit.

## 3.8.2 Secondary Outcome Measures

### 3.8.2.1 ACL Quality of Life Questionnaire (ACL-QOL)

The ACL Quality of Life Questionnaire (ACL-QOL) is a disease-specific patient-reported 32-item questionnaire scored using a visual analog scale (VAS) from 0 mm (ie. extremely difficult) to 100 mm (ie. not difficult at all) developed by Mohtadi (78). There are five domains that comprise the questionnaire: (1) symptoms and physical complaints; (2) work-related concerns; (3) recreation and sport concerns; (4) lifestyle concerns; and (5) social and emotional concerns. Scores are calculated by converting the average of each of the five domains to a total average score out of 100%, where 100% represents the best possible score. The ACL-QOL has shown a test-retest reliability with an ICC of 0.60 and a Cronbach's alpha ranging from 0.93-0.98 indicating unidimensionality of the questionnaire (79).

### 3.8.2.2 Knee Injury and Osteoarthritis Outcome Score (KOOS)

The Knee Injury and Osteoarthritis Outcome Score (KOOS) is a knee-specific, patient-reported, 42-item questionnaire developed by Roos and colleagues (80). This outcome measure is intended to be used by those that have experienced a knee injury that can eventually result in post-traumatic OA or primary OA (81), and covers five domains that are reported separately: (1) pain (nine items); (2) other symptoms (seven items); (3) activities of daily living (seventeen items); (4) sport and recreation function (five items); and (5) knee-related quality of life (four items). The five domains are scored separately, with each item in the domain ranging from zero to four based on a 5-point Likert scale system. The items in each domain are then summed, averaged, and standardized to a score from zero (extreme knee problems) to 100 (no knee problems) to give the overall domain score. The KOOS has demonstrated a test-retest reliability of 0.75 to 0.93 across the five domains, as well as construct validity, and high effect sizes (>0.8) six months postoperatively across the five domains, and has been validated in subjects undergoing ACL reconstructions (80).

### 3.8.2.3 International Knee Documentation Committee Subjective Knee Form (IKDC)

The International Knee Documentation Committee (IKDC) Subjective Knee Form is a patient-reported, 18-item, knee-specific questionnaire developed by the IKDC in order to measure symptoms, function and sports activity (82). This instrument was designed to detect the improvement or the deterioration of symptoms, function, and sport activity in patients with a range of knee conditions, including ligament injuries. To assess symptoms, patients are asked about pain, stiffness, swelling, joint locking and instability. Response types of this measure include 5-point Likert scales, 11-point Likert scales, and dichotomous “yes or no” responses, resulting in a total score ranging from 0 to 100, where 100 indicates no impairment and a high level of participation (83). The IKDC has evidence to suggest a positive test-retest reliability, with an ICC ranging from 0.87 to 0.98, and demonstrates good internal consistency and responsiveness (83).

### 3.8.2.4 Marx Activity Rating Scale

The Marx Activity Rating Scale (Marx) is a patient-reported, four-item rating scale used to assess patients' activity levels, developed by Marx and colleagues (84). Instead of asking patients about their participation in specific sports, they are asked about how often they perform certain components of physical function such as: (1) running; (2) cutting; (3) decelerating; and (4) pivoting. Within each component of physical function, the patient is asked to indicate on a 5-point scale of frequency ranging from less than one time in a month to four or more times in a week, how often they performed each of the activities. One point is allocated for each category of frequency, adding up to a maximum of sixteen points total across the four categories. The Marx Activity Rating Scale emphasizes activities that are difficult for patients with conditions of the knee such as ACL insufficiency, and has demonstrated a test-retest reliability of 0.97 at one week and was significantly correlated with other activity rating scales studied (84).

### 3.8.2.5 Range of Motion (Passive knee extension and active-assisted knee flexion)

Range of motion was assessed by measuring passive knee extension as well as active-assisted knee flexion. A universal Goniometer was used for all range of motion measurements, measured

in degrees. The Goniometer axis was placed over the lateral epicondyle of the femur. The stationary arm was aligned parallel to the longitudinal axis of the femur, while the movable arm was aligned parallel to the longitudinal axis of the lateral malleolus. To measure passive knee extension, the patient sat with both legs extended on a table, with the heels propped up on a foam roller to ensure that the calf and upper thigh cleared the treatment table. The patient was instructed to relax both quadriceps and hamstrings to assure a passive measurement. To measure active-assisted knee flexion, the patient was seated on the treatment table, and was instructed to perform active-assisted knee flexion by placing one hand under their thigh to commence flexion, and then clasp their hands just below the tibial tuberosity, sliding their foot on the table and bringing the knee as far into flexion as possible.

### 3.8.2.6 Adverse Events

At the follow-up visits, patients were asked whether they had experienced any recent injuries or adverse events since the time of previous follow-up. If there were adverse events to report, the date of onset, description of event, actions taken, and date of resolution were recorded for each event. Adverse events were considered minor medical adverse events if the event resolved on its own or with minimal management. Adverse events were considered minor surgical events if the patient required surgical intervention not involving an ACL tear (such as meniscal repairs, surgical washout, manipulation under anesthesia (MUA) or hardware removal). Proportions of contralateral ACL tears were reported, as well as instances of graft failure.

## 3.9 Statistical Analysis

All analyses of data were performed using the program IBM SPSS Statistics version 28.0.1 (85). We presented demographic characteristics of study subjects by group using descriptive characteristics. To compare continuous variables, we used the independent-samples t-test for normally distributed outcomes, and the Mann-Whitney U test for non-normally distributed ones. To compare categorical variables, we used the Chi-square test for homogeneity for outcomes with a sufficiently large sample size, and the Fisher's exact test for outcomes where less than five observations were found in any category.

We presented unadjusted means and standard deviations for continuous variables (ACL-QOL, KOOS, IKDC, Marx and range of motion measurements of the surgical knee at the time of long-term follow-up).

For the primary outcome, we calculated the relative risk reduction (RRR) and risk difference (RD) of clinical failure for each group with 95% confidence intervals.

For the PROMs (ACL-QOL, KOOS, IKDC and Marx) we conducted an analysis of covariance (ANCOVA). The preoperative scores and time from surgery to follow-up served as the covariates, the 3-, 5- and 7-year postoperative scores served as the dependent variable, and the study group (ACLR or ACLR + LET) served as the independent variable.

For range of motion measurements for mean extension and flexion between groups, we also conducted an ANCOVA. The baseline contralateral limb measurements in extension and flexion respectively, as well as time from surgery to follow-up served as the covariates. Surgical limb extension and flexion at follow-up respectively served as the dependent variable, and the study group served as the independent variable. The adjusted mean difference with a 95% confidence interval was presented. The side-to-side differences (SSDs) in range of motion for flexion and extension were also calculated using the ANCOVA and presented as adjusted means and adjusted mean differences with 95% confidence intervals. For the SSD in flexion, the interaction term between group and time from surgery to follow-up was statistically significant and therefore we were unable to perform the parametric ANCOVA. We opted to perform the non-parametric Quade's rank ANCOVA, and presented medians with interquartile ranges (IQRs).

Descriptive information of adverse events were reported, separated by group up to 24 months postoperative, and greater than 24 months postoperative (number and proportion of patients) for specific adverse events (general, related to ACLR, related to LET). Levels of adverse events were categorized into four groups: (1) none (no adverse event); (2) minor medical (event that resolved spontaneously or with minimum medical management); (3) minor surgical (event such as a meniscal tear or stiffness requiring surgical intervention); and (4) ipsilateral graft rupture and contralateral ACL rupture. The proportions within each group were reported.



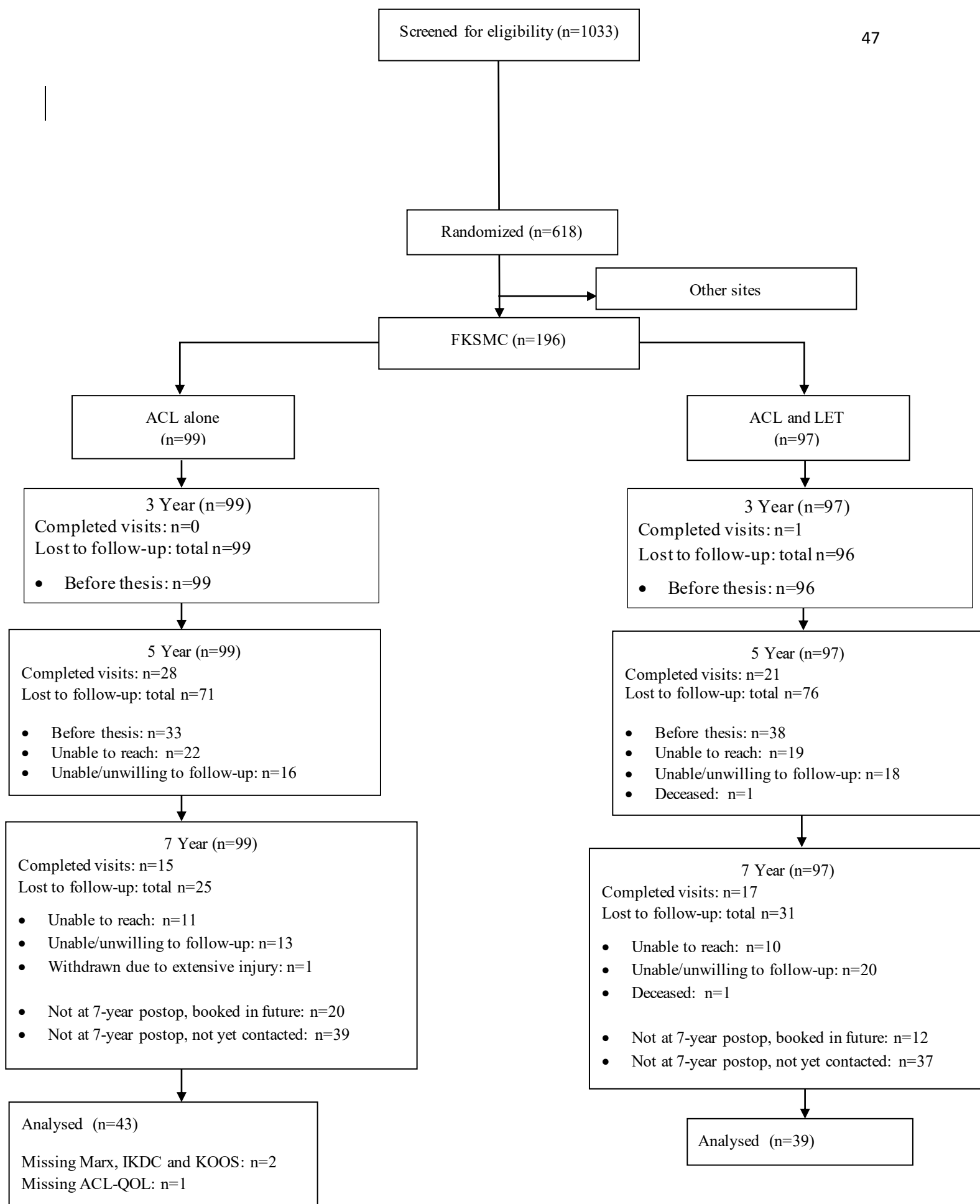
## Chapter 4

### 4 Results

#### 4.1 Participant Flow

The flow of patients through each follow-up period is outlined in Figure 1. Across all study centers, 1033 patients were screened for eligibility. Of these, 618 patients consented and were randomized into the study, including 196 (32%) at the Fowler Kennedy Sport Medicine Clinic (FKSMC) in London, Ontario.

From September 2020 to June 2022, multiple attempts were made to contact all 196 patients randomized at FKSMC to ask them to participate in the long-term follow-up. In total, 82 patients (n= 43 ACL alone, n=39 ACL + LET) agreed to complete PROMs, a clinical assessment, and a range of motion measurement at FKSMC. One patient was assessed at three years postoperative, 49 patients were assessed at five years postoperative, and 32 patients were assessed at seven years postoperative. One patient was withdrawn from the long-term follow-up per the primary investigator, as they had sustained an ipsilateral Knee Dislocation-3L in 2021 (multiligamentous knee injury involving the ACL, PCL and LCL) with associated popliteal artery injury and peroneal nerve palsy requiring extensive surgical intervention. One patient was withdrawn after a family member indicated that they had passed away.



**Figure 2: Participant flow through the trial.**

## 4.2 Demographic Information

Patient demographics were similar between the two groups at baseline for all patients included in the long-term follow-up portion of the study at FKSMC (Table 1).

**Table 1: Baseline demographics for patients undergoing anterior cruciate ligament (ACL) reconstruction alone or with a lateral extra-articular tenodesis (LET).**

Demographic Characteristics	ACLR alone (n=43)	ACLR + LET (n=39)	P-value
Sex, n males (%)	21 (49)	15 (39)	0.34
Age, years (mean $\pm$ SD)	19 $\pm$ 3	18 $\pm$ 3	0.47
Height, cm (mean $\pm$ SD)	174 $\pm$ 10.5	171 $\pm$ 8.2	0.11
Weight, kg (mean $\pm$ SD)	73 $\pm$ 17.2	71 $\pm$ 13.6	0.44
BMI, kg/m <sup>2</sup> (mean $\pm$ SD)	24 $\pm$ 4	24 $\pm$ 3.4	0.91
Beighton score, 0-9 (mean $\pm$ SD)	3.3 $\pm$ 2.5	2.8 $\pm$ 2.8	0.46
Time from injury to surgery, months, median (IQR)	3 (3)	4 (6)	0.18
Operative limb, n dominant (%)	23 (54)	19 (49)	0.67
Mechanism of injury, n non-contact (%)	35 (81)	27 (69)	0.20
Sport played at time of injury, n (%)			0.32
Soccer	17 (41)	21 (55)	
Basketball	9 (21)	3 (8)	
Football or Rugby	2 (5)	4 (11)	
Downhill skiing	0	1 (3)	
Volleyball	1 (2)	2 (5)	
Other	6 (14)	3 (8)	

Smoking status, n (%)			
Smoker	0	1 (3)	0.48
Non-smoker	43 (100)	38 (97)	
Graft source, n (%)			
Semitendinosus and gracilis	43 (100)	38 (97)	0.48
Semitendinosus	0	1 (3)	
Graft diameter, mm, median (min, max)	8 (7, 9)	8 (7, 8.5)	0.92
Meniscectomy, n (%)			
Medial	0	1 (3)	0.12
Lateral	9 (21)	3 (8)	
Both	0	0	
Meniscal repair, n (%)			
Medial	19 (44)	12 (31)	0.35
Lateral	5 (12)	4 (10)	
Both	1 (2)	4 (10)	
Change in rehab due to meniscus repair, n (%)	7 (23)	7 (27)	0.70
Chondral defect, ICRS >3 any compartment, n (%)	1 (2)	1 (3)	1.0

*Abbreviations: ACLR = Anterior cruciate ligament reconstruction, LET = Lateral extra-articular tenodesis, SD = standard deviation, BMI = Body mass index, IQR = Interquartile range, ICRS = International Cartilage Repair Society*

### 4.3 Primary Outcome Measure

At long-term follow-up, 28 of 43 (65%) patients in the ACLR alone group, had sustained the primary outcome of clinical failure, compared to 19 of 39 (49%) patients in the ACLR + LET group (relative risk reduction (RRR), 0.25; 95% CI, -0.10 to 0.49;  $p=0.14$ ). The risk difference (RD) was 16% (95% CI, -7% to 40%).

Not all patients that sustained the primary outcome of ACLR clinical failure experienced a graft failure. At long-term follow-up, 9 of 43 (21%) patients in the ACLR alone group experienced a graft failure, compared to 1 of 39 (3%) patients in the ACLR + LET group (RRR, 0.88; 95% CI, 0.08 to 0.98;  $p=0.04$ ). The RD was 18% (95% CI, 3% to 34%).

### 4.4 Secondary Outcome Measures

The means and standard deviations for continuous variables (ACL-QOL, KOOS, IKDC, Marx and range of motion measurements at the time of long-term follow-up) are presented in Table 2. Total KOOS and IKDC scores for each group are presented in Figure 2 as a boxplot for each visit starting at the baseline visit and ending at the long-term follow-up visit (either three, five or seven years postoperative),

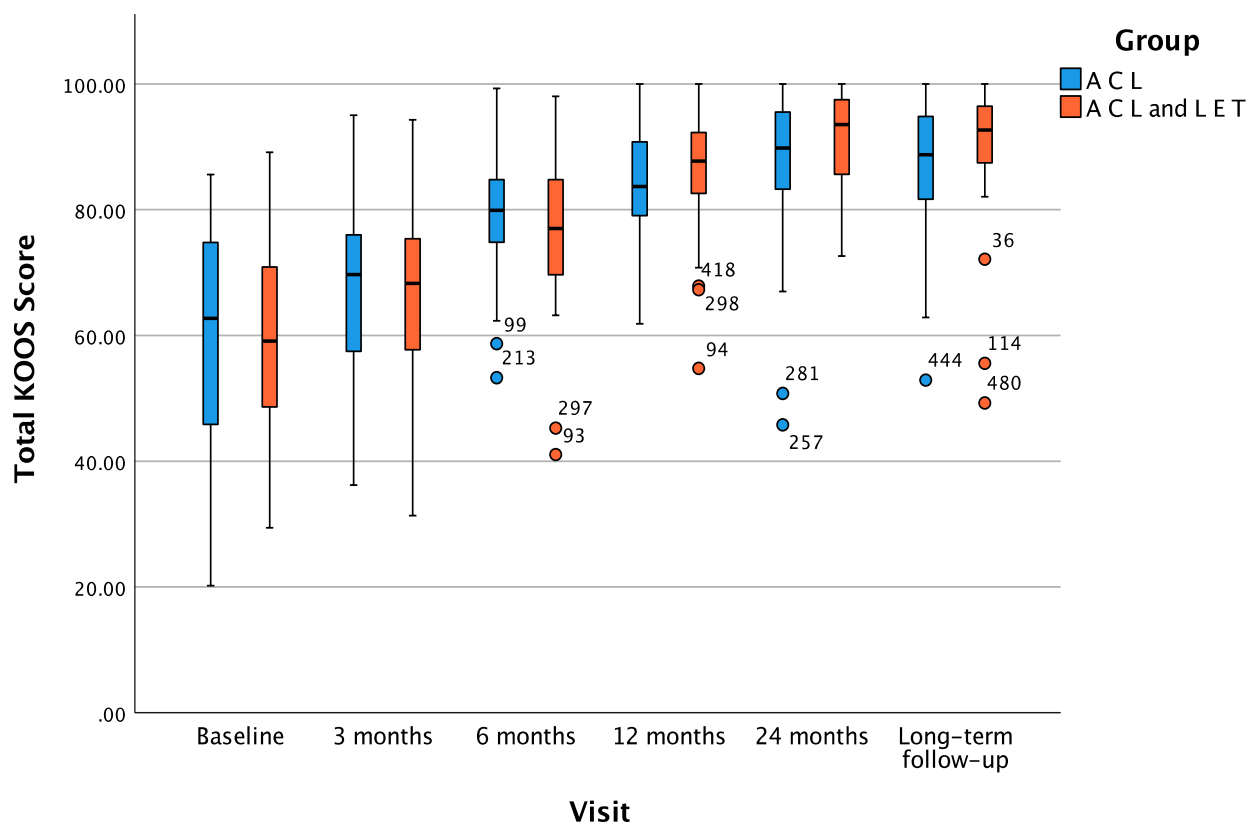
**Table 2: PROMs and range of motion measurements (unadjusted) with adjusted mean differences of patients that participated in the long-term follow-up at the Fowler Kennedy Sport Medicine Clinic.**

	ACLR alone (n=43)	ACLR + LET (n=39)	Adjusted Mean Difference (95% CI)	P-value
Postoperative ACL-QOL (mean $\pm$ SD) (median, IQR)	75.7 $\pm$ 17.2 80.1 (23.6)	78.3 $\pm$ 18.9 83.9 (19.2)	2.2 (-5.9 to 10.3)	0.34
Postoperative KOOS (mean $\pm$ SD) (median, IQR)	86.7 $\pm$ 10.6 88.7 (14.1)	89.8 $\pm$ 10.8 92.7 (9.3)	3.2 (-1.6 to 7.9)	0.08

Postoperative IKDC (mean $\pm$ SD) (median, IQR)	86.8 $\pm$ 10.9 89.7 (17.2)	89.7 $\pm$ 13.4 94.3 (8.1)	3.2 (-2.4 to 8.7)	0.09
Postoperative Marx (mean $\pm$ SD)	8.9 $\pm$ 4.8	8.2 $\pm$ 5.1	-1.0 (-3.1 to 1.2)	0.37
Surgical Knee ROM (degrees) (mean $\pm$ SD) Passive extension Active flexion	-0.5 $\pm$ 2.6 139.8 $\pm$ 9.8	-1.4 $\pm$ 2.9 144.4 $\pm$ 7.3	-0.5 (-1.6 to 0.6) 4.1 (1.2 to 7.0)	0.33 0.006
Side-to-side difference (degrees)  (Operative – contralateral)  Passive extension (mean $\pm$ SE) (median, IQR)  Active flexion (median, IQR)	0.5 $\pm$ 0.2 0 (1)  -1 (4)	0.5 $\pm$ 0.2 0 (1)  -1 (3)	-0.02 (-0.6 to 0.5)	0.52  0.80

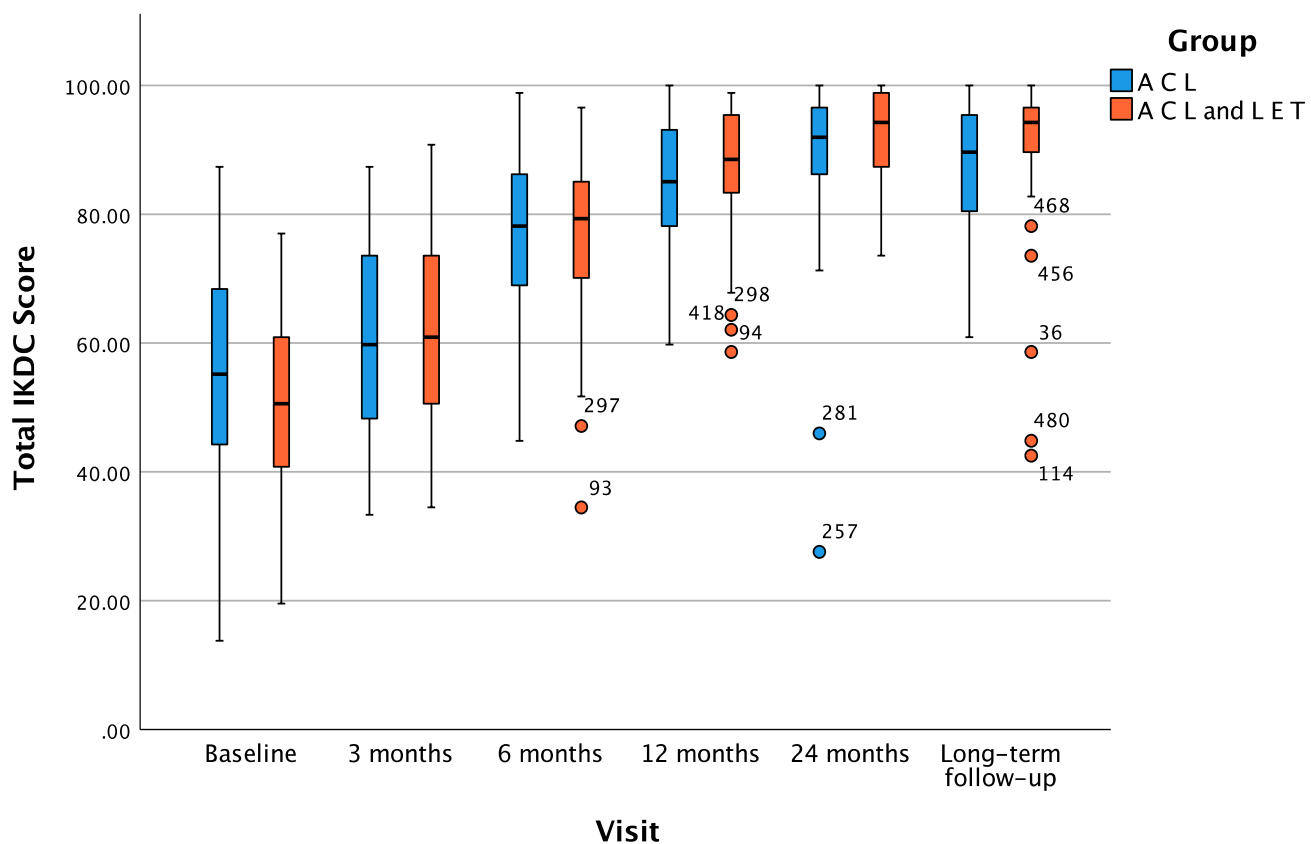
*Abbreviations: ACLR = Anterior cruciate ligament reconstruction, LET = Lateral extra-articular tenodesis, SD = standard deviation, ACL-QOL = ACL Quality of Life Questionnaire, KOOS = Knee Injury and Osteoarthritis Outcome Score, Marx = Marx Activity Rating Scale, IKDC = International Knee Documentation Committee Subjective Knee Form, ROM = Range of motion*

**Note:** Negative values for ROM measurements indicate hyperextension. Positive values for the SSDs in extension indicate a loss of extension on the operative limb. Negative values for the SSDs in flexion indicate a loss of flexion on the operative limb. Mean differences of the PROMs are adjusted for their respective baseline scores and days from surgery to follow-up. Mean differences of range of motion measurements are adjusted for their respective contralateral measurements at baseline and days from surgery to follow-up. The mean and standard error for the SSD in extension as well as the mean difference of SSD in extension are adjusted for contralateral extension measurements at baseline and days from surgery to follow-up. The medians and interquartile ranges are presented for postoperative ACL-QOL, KOOS, and IKDC scores in addition to the SSDs in extension and flexion due to violations of the ANCOVA assumptions.



*Abbreviations: ACL = Anterior cruciate ligament, LET = Lateral extra-articular tenodesis, KOOS = Knee Injury and Osteoarthritis Outcome Score*

**Figure 3: Boxplot of total Knee Injury and Osteoarthritis Outcome Score (KOOS) scores by visit for patients undergoing ACLR with or without LET. Solid black lines represent group median, the coloured boxes represent the IQR, whiskers represent the minimum and maximum values (excluding outliers), and the solid dots represent outliers.**



*Abbreviations: ACL = Anterior cruciate ligament, LET = Lateral extra-articular tenodesis, IKDC = International Knee Documentation Committee Subjective Knee Form*

**Figure 4: Boxplot of total International Knee Documentation Committee Subjective Knee Form (IKDC) scores by visit for patients undergoing ACLR with or without LET. Solid black lines represent group median, the coloured boxes represent the IQR, whiskers represent the minimum and maximum values (excluding outliers), and the solid dots represent outliers.**



#### 4.4.1 ACL Quality of Life Questionnaire (ACL-QOL)

We identified one outlier in the data, as there was one case with a standardized residual greater than  $\pm 3$  standard deviations. The outlier was associated with a 3-year follow-up, and was -3.16 standard deviations, indicating a low total ACL-QOL score. At this visit, the patient also reported an adverse event consisting of graft failure of a contralateral ACL reconstruction, which may have affected the score.

After adjustment for baseline ACL-QOL scores and days from surgery to follow-up, there was no statistically significant difference in postoperative ACL-QOL scores between the interventions, with the outlier included,  $p=0.59$ .

As the outlier was not a result of data entry error or measurement error, we performed a sensitivity analysis to determine any differences after removal of the outlier. After the outlier was removed, there was still no statistically significant difference in postoperative ACL-QOL scores between the interventions,  $p=0.28$ .

We also used the non-parametric Quade's rank ANCOVA as this test is less sensitive to outliers in the data, and there was no statistically significant difference in postoperative ACL-QOL scores,  $p=0.34$  (Table 2).

#### 4.4.2 Knee Injury and Osteoarthritis Outcome Score (KOOS)

There were three outliers with a standardized residual greater than  $\pm 3$  standard deviations. The first case occurred at the time of five-year follow-up, where the patient reported increased pain, and MRI findings showed a potential meniscal tear. The second case occurred at the time of seven-year follow-up, where the patient had a diagnosed new ipsilateral meniscal tear requiring surgical intervention. The third case is the same case described in the ACL-QOL results, where the patient reported graft failure of their contralateral ACL reconstruction.

After adjustment for baseline KOOS scores and days from surgery to follow-up, there was no statistically significant difference in postoperative KOOS scores between the interventions,  $p=0.19$ .

As the outliers were not a result of data entry error or measurement error, we performed a sensitivity analysis to determine any differences after removal of the outliers. After the outliers were removed, we found a statistically significant difference in postoperative KOOS scores between the interventions, favouring the ACLR + LET group (adjusted mean difference, 4.6 (95% CI 1.1 to 8.1),  $p=0.01$ ).

We also used the non-parametric Quade's rank ANCOVA as this test is less sensitive to outliers in the data, and there was no statistically significant difference in postoperative KOOS scores,  $p=0.08$  (Table 2).

#### 4.4.3 International Knee Documentation Committee Subjective Knee Form (IKDC)

We found two outliers with a standardized residual greater than  $\pm 3$  standard deviations. The first case is the case described in the KOOS results, where the patient had a diagnosed new ipsilateral meniscal tear requiring surgical intervention. The second case is the case described in both the ACL-QOL and KOOS results, where the patient reported graft failure of their contralateral ACL reconstruction.

After adjustment for baseline IKDC scores and days from surgery to follow-up, there was no statistically significant difference in postoperative IKDC scores between the interventions,  $p=0.26$ .

As the outliers were not a result of data entry error or measurement error, we performed a sensitivity analysis to determine any differences after removal of the outliers. After the outliers were removed, we found a statistically significant difference in postoperative IKDC scores between the interventions, favouring the ACLR + LET group (adjusted mean difference, 5.8 (95% CI 1.3 to 10.3),  $p=0.011$ ).

We also used the non-parametric Quade's rank ANCOVA as this test is less sensitive to outliers in the data, and there was no statistically significant difference in postoperative IKDC scores,  $p=0.09$  (Table 2).

#### 4.4.4 Marx Activity Rating Scale

After adjustment for baseline Marx scores and days from surgery to follow-up, there was no statistically significant difference in postoperative Marx scores between the interventions,  $p=0.37$  (Table 2).

#### 4.4.5 Range of Motion (Passive knee extension and active-assisted knee flexion)

We used a one-way ANCOVA to present adjusted means and mean differences in passive knee extension and active-assisted knee flexion for the surgical limb (Table 2). For extension, after adjustment for days from surgery to follow-up and contralateral extension at baseline, there was one outlier with a larger degree of hyperextension. We did not believe the result of the ANCOVA would be materially affected, and therefore we opted to continue the analysis. There was no significant difference in extension between groups ( $p=0.33$ ). For flexion, after adjustment for days from surgery to follow-up and contralateral flexion at baseline, we found no outliers. There was a significant difference in flexion between groups ( $p=0.006$ ), with patients in the ACLR + LET group achieving greater flexion.

We used a one-way ANCOVA to compare side-to-side differences (SSDs) in passive extension and active-assisted flexion between the ACLR alone group and the ACLR with LET group, adjusting for days from surgery to follow-up and baseline contralateral passive extension and flexion, respectively. After calculating SSDs in extension, there were two outliers with a standardized residual greater than  $\pm 3$  standard deviations. The first case was described in the KOOS and IKDC section, where the patient had a diagnosed new ipsilateral meniscal tear requiring surgical intervention causing a loss of extension on the operative limb. The second case had experienced a sport injury and was diagnosed with a graft failure upon examination, and was also unable to reach full extension.

As the outliers were not a result of data entry error or measurement error, we performed a sensitivity analysis to determine any differences after removal of the outliers. After removal of the outliers, the assumption of equality of variances was violated, and therefore we were unable

to continue with the parametric ANCOVA without outliers. We used the non-parametric Quade's rank ANCOVA as this test is less sensitive to outliers in the data, and there was no statistically significant difference in SSDs for extension,  $p=0.52$ .

After calculating SSDs in flexion, there were no outliers, however the assumption of homogeneity of regression slopes was violated as the interaction term between group and days from surgery to follow-up was statistically significant. Therefore, we were unable to continue with a parametric ANCOVA. To continue with the analysis, we used the non-parametric Quade's rank ANCOVA, and there was no statistically significant difference in SSDs for flexion,  $p=0.80$ .

#### 4.4.6 Adverse Events

47 of 82 (57%) patients seen at long-term follow-up experienced at least one adverse event from the time of surgery to most recent follow-up. Table 3 shows the distribution of various adverse events reported, divided by events that occurred within the first 24 months after surgery, to events that occurred greater than 24 months after surgery.

**Table 3: Adverse events by surgical group.**

	Up to 24 months postoperative		>24 months postoperative	
	ACLR alone (n=43)	ACLR + LET (n=39)	ACLR alone (n=43)	ACLR + LET (n=39)
<b>General</b>				
Persistent effusion Aspiration	3 (7%) 1 (2%)	1 (3%)	0	0
Deep infection	1 (2%)	0	0	0
Hematoma	0	1 (3%)	0	0
Crepitation (new or increased)	0	0	1 (2%)	0
<b>Related to ACLR</b>	ACLR alone	ACLR + LET	ACLR alone	ACLR + LET
Graft failure	3 (7%)	1 (3%)	6 (14%)	0
Contralateral ACL rupture	1 (2%)	4 (10%)	4 (9%)	5 (13%)

Excessive pain Intra-articular injection	5 (12%) 1 (2%)	1 (3%)	3 (7%) 1 (2%)	2 (5%)
Excessive stiffness MUA	1 (2%) 1 (2%)	1 (3%)	0	0
Locking	0	0	1 (2%)	0
Chondral defect (lateral femoral condyle) Intra-articular injection	1 (2%) 1 (2%)	0	0	0
Giving-way episode	0	1 (3%)	0	0
ACL hardware symptoms Hardware removal	1 (2%)	0	3 (7%) 1 (2%)	0
Hamstring strain/tear	3 (7%)	0	1 (2%)	0
Retear meniscal tear (unrelated to graft)	1 (2%)	4 (10%)	3 (7%)	3 (8%)
New meniscal tear (unrelated to graft rupture)	0	1 (3%)	4 (9%)	1 (3%)
<b>Related to LET</b>		ACLR + LET		ACLR+ LET
Intraoperative Damage to LCL attachment (repaired)		1 (3%) 1 (3%)		
Postoperative		0		0

*Abbreviations: ACLR = Anterior cruciate ligament reconstruction, LET = Lateral extra-articular tenodesis, MUA = Manipulation under anesthesia, LCL = Lateral collateral ligament*

Adverse events by category are presented in Table 4. The ACLR alone group experienced more graft failures than the ACLR + LET group (21% vs 4%).

**Table 4: Categories of adverse events by surgical group.**

Adverse Event Category, n (%)	ACLR alone	ACLR + LET
	Total n=43	Total n=27
Minor medical adverse events	25 (58)	7 (26)
Minor surgical events (excluding ACL tears)	4 (9)	10 (37)
Contralateral ACL rupture	5 (12)	9 (33)
Graft failure	9 (21)	1 (4)

*Abbreviations: ACLR = Anterior cruciate ligament reconstruction, LET = Lateral extra-articular tenodesis, ACL = Anterior cruciate ligament*

**Note:** Total numbers for each category do not match the total number of patients that experienced at least one adverse event (n=47), because some patients experienced more than one adverse event (ie; if one patient experienced a minor medical adverse event and a graft failure, both were counted in this table). Percentages are reported as event divided by total number of adverse events in each group.

## Chapter 5

### 5 Discussion and Future Direction

#### 5.1 Discussion

The purpose of the follow-up of the STABILITY randomized clinical trial was to compare long-term outcomes for patients who underwent ACL reconstruction surgery after injuring their ACL, randomized either to receive the ACL reconstruction alone, or with the addition of the LET. At three, five and seven years postoperative, patients were contacted to return to FKSMC for a long-term follow-up. Patients completed a range of PROMs such as the ACL-QOL, KOOS, IKDC and Marx, and the laxity of their knee was assessed via the pivot-shift test, through a clinical assessment with their surgeon. Patients were also asked about adverse events, and range of motion measurements were performed on the surgical and contralateral limbs. The composite primary outcome measure of clinical failure was not statistically significantly different between groups (65% ACLR alone vs 49% ACLR + LET,  $p=0.14$ ), however the ACLR alone group experienced significantly more graft failures than the ACLR + LET group (21% ACLR alone vs 3% ACLR + LET,  $p=0.04$ ).

Overall, 47 of 82 (57%) patients seen for long-term follow-up reported at least one adverse event from the time of surgery to most recent follow-up, which is a high number. The high rate of adverse events could potentially be explained due to the original cohort including only young, active patients wanting to return to sport after surgery. According to a systematic review performed by Barber-Westin and Noyes, one in five athletes suffers a re-injury to either knee after returning to sport (86). Patients in the ACLR + LET group reported more minor surgical adverse events, and contralateral ACL ruptures compared to the ACLR alone group, however patients in the ACLR alone group reported more minor medical adverse events. At two years postoperative, out of the 618 patients originally randomized in the STABILITY study, 12 patients (4%) in the ACLR alone group and seven patients (2%) in the ACLR + LET group experienced a contralateral ACL rupture, and this was not a statistically significant difference between groups,  $p=0.26$ . It is possible that patients who experienced an adverse event, even a small one, early during their recovery after surgery may be more likely to seek long-term follow-

up with their clinician. Along the same line, it is likely that patients who experienced an adverse event within the last year or two were more likely to come in when contacted and offered a follow-up appointment as part of the study, which would increase the number of adverse events reported in this sample. This would increase the risk of selection bias and attrition bias because the missing data could potentially be related to how well patients recover after surgery. This sample of patients may not be representative of the entire STABILITY cohort, anecdotally patients who were doing well were less inclined to be followed than those experiencing events, especially contralateral ACL tears and ipsilateral graft failures.

At long-term follow-up, we did not expect to find significant differences in the scores of the PROMs between groups, and the results of each PROM were consistent with our hypotheses. Previously published randomized studies comparing ACLR alone to ACL + LET report similar findings in terms of PROMs (2,19,34,35). In our analysis of the PROMs, we used days from surgery to follow-up as a covariate. The time to follow-up between three, five and seven years was not associated with the scores of the PROMs, indicating that a standard study endpoint of two years may be appropriate if differences are not seen long-term. This could be particularly appealing for centers with limited resources and time who do not have the capacity to follow up with patients at three, five or seven years. Although there were more graft failures in the ACLR alone group, it is likely that the lack of difference between groups was because a sufficient amount of time had passed from their revision reconstruction surgery to the date of long-term follow-up, and they were likely back to their pre-revision function. It is also possible that the priorities of these patients have changed since their surgery and subsequent recovery period. This could contribute to response shift bias, where over time there is a change in how a patient may view or interpret a subjective outcome measure, such as a PROM (87). Response shift can occur due to (1) recalibration (changes in the internal standard of measurement of the patient); (2) reprioritization (changes in importance of different domains measured in the PROM); or (3) reconceptualization (the PROM is redefined) (87).

During this follow-up period, we also did not expect to find significant differences in side-to-side difference for flexion and extension range of motion, and this was found to be true after analysis. We did not expect to find significant differences because with proper rehabilitation after surgery,



any differences in flexion and extension resolve quickly. In addition, joint diseases such as osteoarthritis (OA) in the knee that may limit range of motion would not be expected so soon after ACL reconstruction. Studies investigating the incidence of OA after ACL reconstruction do not report clinically detectable osteoarthritic findings until at least ten years postoperative (62). In this long-term follow-up, it is too early to detect OA, since we have no patients at ten years postoperative. Other randomized studies comparing ACLR alone to ACL + LET also reported no statistical differences in range of motion (19,33).

Although the composite primary outcome was not considered statistically significant, it is important to note that there was a discernible difference between groups, with more patients sustaining ACLR clinical failure in the ACLR alone group (65% vs 49%; RRR, 0.25; 95% CI, -0.10 to 0.49;  $p=0.14$ ). If we look further at patients who specifically experienced a graft failure, an important finding is that the ACLR + LET group experienced significantly less graft failures than the ACLR alone group, which is similar to the results of the two-year STABILITY outcomes. It is likely that ACLR regardless of LET is unable to completely restore native knee kinematics, although a LET may add greater stability.

Overall, out of 196 patients randomized at FKSMC, 82 patients (42%) were seen for long-term follow-up over a period of approximately one-and-a-half years. There were several barriers during attempts to recruit patients back to clinic, such as outdated contact information, and geographic distance. To improve the number of patients recruited, in the future, we could plan for long-term follow-up in the original study so that patients are aware of potential study expectations. We could also follow up with patients on a yearly basis for the purposes of keeping contact information accurate and updated if they are not regularly being seen in clinic. Many patients had indicated that they were too far away to commute to FKSMC for clinical examination, and some even reported that they were living in a different province, or even a different country. However, we are proud of the number we were able to recruit back to clinic, as this study was originally only designed with a two-year postoperative endpoint in mind. More patients at their 7-year postoperative mark have been scheduled to come to clinic in the following months as well, noted in Figure 1, and we will continue recruitment to include patients

at 10 years postoperative when the time comes. Now, we have longer term data including clinical examination findings, PROMs, and imaging outcomes.

## 5.2 Limitations

The original STABILITY study was a multicenter study, consisting of seven centers in Canada and two centers in Europe. However, the long-term follow-up was only performed at our center (FKSMC), indicating a lack of power. In addition, many patients had passed their 3- or 5-year postoperative timepoint by the time the long-term follow-up protocol was established, noted as ‘Before thesis’ in Figure 1, contributing to the loss to follow-up.

At the time of long-term follow-up, patients were in their early to late twenties, and many that were contacted had started their careers, families and adult lives, and were no longer local or available for follow-up. When performing a long-term follow-up of a study, contact information can be a barrier. In this case, many patients had changed their contact information, and were unreachable via phone numbers and emails. Fortunately, electronic medical records (EMRs) include contact information for patients’ relatives, so in the cases where the patient’s number was incorrect, a family member would be contacted to update the patient’s contact information. To improve long-term follow-up, patient contact information needs to always be accurate and updated in a central system accessible for all clinics (ie; Cerner PowerChart). Unfortunately, different clinics use different EMR systems, so updated contact information may be difficult to find if it is inaccessible to the research assistant responsible for recruitment.

Our results showed differences in proportions of patients that sustained a contralateral rupture of the ACL, while the two-year postoperative results do not. This could be due to the small sample of patients at long-term follow-up, compared to the 618 patients randomized across all study sites. Higher rates of contralateral ACL ruptures in the LET group at long-term follow-up could potentially be explained because this group of patients experienced fewer ipsilateral graft failures and therefore would be more likely to continue with sport. We would only be able to draw this conclusion if we followed all patients at all study sites.

The STABILITY study utilized blinded assessors to reduce the chance that selection or detection bias would affect the results due to the additional incision needed for the LET. In our long-term

follow-up, the surgeons performing the clinical assessments were not blinded to group allocation, and therefore this may have increased the risk that selection and detection bias were present, reducing the internal validity.

### 5.3 Strengths

The original STABILITY study found clinically significant findings at an endpoint of two years postoperative, however no long-term follow-up was planned at commencement of the study. Our work contacting the cohort of patients from FKSMC that participated in the STABILITY study, consenting them for further follow-up, and scheduling clinical visits has made it possible to determine whether the shorter-term benefits of the LET in conjunction with the ACLR persist over longer periods of time.

Our statistical analysis was strengthened through our willingness to use a mixed-effects model adjusted for days from surgery to follow-up. This reduced the impact of patients being outside the study visit window at each timepoint when they were available to come to clinic for an assessment.

We were also able to collect a wide range of outcomes, as we were able to recruit patients for a clinical assessment rather than completing PROMs remotely. Patients seen in clinic also underwent radiographic assessment (X-rays), and the patients at seven years postoperative underwent MRI, completed isokinetic strength testing using a Biodex dynamometer, and performed the Drop Vertical Jump test. These outcomes were not included in this thesis but will allow investigators to assess joint changes and development of OA longitudinally between two years postoperative, and long-term.

### 5.4 Future Direction

For this long-term follow-up, we will continue recruiting patients to include 10-year postoperative outcomes, including radiographic analysis of OA. Patients in the STABILITY cohort at FKSMC are also being recruited for a study investigating genetic markers associated with OA, and how these genetic factors may predispose patients with a knee injury to develop OA in the future. The goal of that study is to evaluate whether genetic screening could help

researchers and clinicians understand why some patients may be more at risk of developing OA after joint injury (in this case, the ACL). At their seven-year postoperative appointment, the STABILITY patients at FKSMC are also given the opportunity to participate in a sub-study of the long-term follow-up, investigating the addition of a one-year physical activity intervention and whether this can delay or prevent the onset of early-stage knee OA. This study includes more outcomes including a physical activity app to measure physical activity levels, a motion-capture gait analysis, and ultrasound imaging.

Future directions should continue to facilitate interventions such as physical activity and physiotherapy to delay, prevent, or reduce OA after ACL injury rather than just observing. The genetic marker study and the physical activity intervention sub-study results will help to determine whether there is a genetic component to OA that can potentially be targeted, and the effectiveness of physical activity to delay onset of OA.

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# Appendices

## Appendix A: UWO REB Approval



Research Ethics

Use of Human Participants - Initial Ethics Approval Notice

Principal Investigator: Dr. Alan Getgood  
 File Number: 104524  
 Review Level: Full Board  
 Protocol Title: Multicenter Randomized Clinical Trial comparing Anterior Cruciate Ligament Reconstruction With and Without Lateral Extra-articular Tenodesis in Individuals Who Are At High Risk of Graft Failure.  
 Department & Institution: Schulich School of Medicine and Dentistry/Surgery, Western University  
 Sponsor:  
 Ethics Approval Date: February 07, 2014  
 Ethics Expiry Date: September 30, 2023

### Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Other	12 Month Clinical Assessment (Received Oct.11/13)	
Other	24 Month Clinical Assessment (Received Oct.11/13)	
Other	3 Month Clinical Assessment (Received Oct.11/13)	
Other	6 Month Clinical Assessment (Received Oct.11/13)	
Other	Baseline Clinical Assessment (Received Oct.11/13)	
Instruments	International Knee Documentation Committee (IKDC) Subjective (Received Oct.11/13)	
Instruments	Lower Extremity Functional Scale (LEFS)(Received Oct.11/13)	
Instruments	4-Item Pain Intensity Measure (P4)(Received Oct.11/13)	
Instruments	Return to Sport (Received Oct.11/13)	
Instruments	EQ-5D VAS (Received Oct.11/13)	
Instruments	Hop Testing (Received Oct.11/13)	
Instruments	Range of Motion (Received Oct.11/13)	
Instruments	Strength (Received Oct.11/13)	
Instruments	SF-12 Health Survey (Received Oct.11/13)	
Instruments	Knee Injury and Osteoarthritis Outcome Score (Received Oct.11/13)	
Instruments	MARK Activity Rating Scale (Received Oct.11/13)	
Instruments	Mohrads Anterior Cruciate Ligament Quality of Life Questionnaire (Received Oct.11/13)	
Western University Protocol	Original (received Oct.11/13)	
Letter of Information & Consent	Clean updated LOI and Consent	2013/11/30
Recruitment Items	Poster	

This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number 00B 00000340.

Signature

Ethics Officer to Contact for Further Information

This is an official document. Please retain the original in your files.

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## Appendix I: Letter of Information and Consent



### LETTER OF INFORMATION

**Title of Research:**

Multicenter Randomized Clinical Trial comparing Anterior Cruciate Ligament Reconstruction With and Without Lateral Extra-articular Tenodesis in Individuals Who Are At High Risk of Graft Failure.

**Lead Researchers:**

Dr. Alan Getgood  
Fowler Kennedy Sport Medicine Clinic, Western University  
London, Ontario, [REDACTED]

Dr. Dianne Bryant  
Elborn College, Western University  
London, Ontario, [REDACTED]

**Study Sponsors:**

International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS)  
Orthopaedic Research and Education Foundation (OREF)

**Information:**

You are being invited to participate in a research study because your surgeon has determined that you have a torn anterior cruciate ligament (ACL) and you have elected to undergo surgery to reconstruct this ligament. The purpose of this letter is to provide you with information required for you to make an informed decision regarding participation in this research.

The purpose of this study is to compare outcomes (function, strength, range of motion and quality of life) between patients who receive the usual anterior cruciate ligament (ACL) reconstructive surgery to patients who receive anterior cruciate ligament reconstructive surgery with a lateral extra-articular tenodesis. A lateral extra-articular tenodesis is the creation of a new ligament-like structure using a piece of the Iliotibial (IT) band on the outside of the knee. The usual standard of care for an ACL tear is ACL reconstruction without this lateral extra-articular tenodesis (new ligament-like structure). Some studies have shown high graft failure rates (ACL re-tear) in young individuals who return to pivoting contact sports following ACL reconstruction. This study is designed to look at whether or not adding this extra structure reduces the risk of graft failure in this population. To determine whether one procedure is better than the other, we must randomize (like flipping a coin) you into one of the surgery groups. Six hundred (600) patients will take part in this study at different centres around the world. This centre will recruit two hundred (200) patients; approximately 100 per group.

**Eligibility:**

To participate in this study you must be 25 years of age or younger. You cannot have had previous



ACL reconstruction on either knee. You cannot have a multi-ligament injury (two or more ligaments requiring surgery). If you are currently participating in another research study, you must inform your surgeon and the research assistant.

**Explanation of the Study Procedures:**

The goal of anterior cruciate ligament reconstruction surgery is to replace the torn ACL with a tissue graft to provide stability to the knee. This is done through a surgical procedure that is performed arthroscopically (with a camera). Either spinal or general anesthesia is used. Small screws are placed into the bone to hold the tissue graft in place.

If, during the surgery, your surgeon determines that your knee does not meet the requirements for the study i.e. other ligaments are found to be torn, or it cannot be treated using the surgical procedure defined in the study protocol, he/she will withdraw you from the study and you will be treated according to standard practice of your surgeon.

**Description of the Study:**

The total time commitment of the study is ten years. Visits for this study will coincide with follow-up visits that you would already attend with your surgeon after your surgery. Each visit with the surgeon will take approximately 40 minutes of your time. Before your surgery, you will be asked to complete ten questionnaires along with a strength assessment, hop test and range of motion measurement. Following your surgery you will receive instructions to undergo standardized physical therapy. You will be given a Rehabilitation Guide to give to your physical therapist.

After surgery, you will come in for an appointment with your surgeon at 3 months, 6 months, 1 year, 2 years, 3 years, 5 years, 7 years and 10 years where you will be asked to complete a clinical assessment, and the same nine questionnaires. You will be asked if any adverse events have occurred since your last visit and asked to provide details. We will ask for an update at each follow-up visit until the event has resolved. At that time, we will also take an x-ray and measure your range of motion. Completing these questionnaires will take approximately 15 - 20 minutes of your time and the x-ray and collection of range of motion measurements will take approximately 15 minutes. Hop testing will occur at the 6 month, 1 year and 2 year visits and strength testing will occur at the 6 month, 1 year, 2 year and 7 year visits. The hop and strength testing will take approximately 45 minutes.

At 6 months, 1 year, 2 years and 7 years post - surgery, we will measure your strength and assess your ability to perform a series of simple jumping tasks. Strength tests will be performed by bending and extending your knee 3 times to measure your strength against resistance. This is done using a computerized machine called an isokinetic dynamometer. During each test session, you will be seated with your back against a backrest with a seat belt securing you into place.

We will schedule 100 patients (50 from each group) for Magnetic Resonance Imaging (MRI) at or after your 2 year, 7 year and 10 year appointment. MRI is a common medical diagnostic tool that

uses a strong magnetic field, a low frequency magnetic field and a radio frequency field. The purpose of the MRI is to evaluate the lateral compartment of your knee following your ACL reconstruction. The MRI will take approximately 2 hours of your time and we will schedule and confirm the time and location with you beforehand.

If you have undergone a posterior meniscal root repair we will schedule you for MRI testing at or after your 1 year appointment. The purpose of the MRI is to evaluate the healing of your meniscus following its repair. The MRI will take approximately 2 hours of your time and we will schedule and confirm the time and location with you beforehand.

The jumping tests are subdivided into functional tests and biomechanical assessment. The functional tests include a single hop for distance, a timed 6 metre hop test, a triple hop for distance and a crossover hop for distance. The biomechanical assessment will use motion analysis equipment and a clinician rated scale to look at the mechanics of your knee as you perform a vertical jumping task.

The single hop for distance test is performed by having you stand on your leg to be tested, and hop forward on the same leg. The timed 6 metre hop test is performed by having you perform large one - legged hops in series over the 6 metres. The triple hops for distance test is performed by having you stand on one leg and perform three hops in a row on the same leg, landing as far away as possible. The crossover hop for distance is performed by having you hop forward three times while making a "Z" pattern.

The biomechanical assessment will take place in the Wolf Orthopaedic Biomechanics Laboratory (WOBL) at the Fowler Kennedy Sports Medicine Clinic. The task will require you to jump onto a force plate while sensors monitor your movements and muscle activity. These sensors will be placed on your skin over your feet, knees, hips, arms and shoulders using double-sided tape. You will be asked to wear dark (black or navy) shorts and a dark (black or navy) T-shirt or tank top to limit identifiable features and assist with the placement of the sensors. Although the sensors are easily removed, the tape may cause some pulling of hair therefore we may ask to shave some areas with a plastic disposable razor in order to limit discomfort.

After becoming familiarized with the instrumentation we will ask you to perform a double leg drop vertical jump. This task will require you to drop/hop off a box (at an elevated height of 31cm) and land with both legs on a force plate outlined on the ground, following which you will immediately jump vertically as high as you can, as if rebounding a basketball. As you are performing this task, a clinician and a researcher will use a Clinician Rated Drop Vertical Jump Scale to evaluate your landing. Additionally, we will videotape your jump so that the same clinician and researcher can later review the video and re-rate your jump, which will help us determine whether the evaluation of your landing is similar whether it is done in-person or using a video. Only your torso and lower body will be visible in the video.

**Alternatives to Participation:**

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Patient Initials: \_\_\_\_\_

Version: December 1, 2021

If you do not choose to participate in this study, you will receive the usual ACL reconstructive surgery provided by your surgeon.

**Risks:**

You could fall, injure or re - injure yourself while performing tests, however, the risks are no greater than those encountered with typical postoperative rehab protocols.

Your participation in this study may involve an MRI. No X-rays are used. As with any technology there is a risk of death or injury. For MRI the risk of death is less than 1 in 10 million and the risk of injury is less than 1 in 100,000. These risks do not arise from the MRI process itself but from a failure to disclose or detect MRI incompatible objects in or around the body of the subject or scanner room. It is therefore very important that you answer all questions honestly and fully on the MRI screening questionnaire.

Almost all the deaths and injuries related to MRI scans have occurred because the MRI operator did not know that surgically implanted metal hardware (such as a cardiac pacemaker) was present inside the subject during the MRI scan. Other Remote risks involve temporary hearing loss from the loud noise inside the magnet. This can be avoided with ear headphone protection that also allows continuous communication between the subject and staff during the scan. For comparison, the risk of death in an MRI is similar to travelling 10 miles by car, while the risk of injury during an MRI is much less than the risks associated with normal daily activities for 1 hour.

If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop or been a soldier, if you have some type of implanted electrical device (such as a cardiac pacemaker), if you have severe heart disease (including susceptibility to arrhythmias), if you are wearing metal braces on your teeth, or [for women] if you could be pregnant, or have an intrauterine device, you should not have an MRI scan.

If you undergo a posterior meniscus root repair and are unable to have an MRI scan you will still be allowed to continue participating in the rest of this study.

There are no other known health risks associated with this study.

**Benefits:**

There are no direct benefits to you for participating in this study; however your participation will help inform surgeons and physiotherapists as to which surgical procedure offers patients who undergo ACL reconstruction the best outcome.

**Cost/Compensation:**

You will not be compensated for your participation in this study. You will be responsible for the cost of parking.

**Voluntary Participation:**

Your participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future care. Should you choose to withdraw from this study, we will keep all data obtained up to the point that you chose to withdraw.

Participation in this study does not prevent you from participating in any other research studies at the present time or future. If you are participating in another research study, we ask that you please inform of us of your participation. You do not waive any legal rights by signing the consent form.

**Request for Study Results:**

Should you decide to participate and want to receive a copy of the study results, please provide your contact information on a separate piece of paper. Once the study has been published, a copy will be mailed to you. Please note that the results of this study are not expected for at least 5 years. Should your mailing information change, please let us know.

**Confidentiality:**

All information will be kept confidential to the best of our ability. The company that takes care of the research database is EmPower Health Research. Your identifying information (name, mailing address, phone number, email address, date of birth) is being collected as part of your participation in this study. Your data is protected by a username and password. It travels in a scrambled format to a server (storage computer) that is located in Montreal, Quebec, Canada. The company that houses the server is a professional company (Netelligent) with extremely high standards of physical and virtual security. We want to let you know however, that even with this high level of security, there is always a remote chance that your information could be accessed or “hacked” by someone who is not supposed to have your information. The chance that this information will be accidentally released is small. In any publication, presentation or report, your name will not be used and any information that discloses your identity will not be released or published.

We wish to also make you aware that Dr. Bryant, who is one of this study's investigators, is the Owner and Director of EmPower Health Research Inc. However, Dr. Bryant does not receive any personal gain or compensation of any kind due to the use of EmPower services on this study.

Study data will be kept for 15 years as per Lawson’s data retention policy. Representatives of the University of Western Ontario Health Sciences Research Ethics Board may require access to your study-related records or follow-up with you to monitor the conduct of this research. Representatives of Lawson Quality Assurance (QA) Education Program may look at study data for QA purposes.

**Questions:**

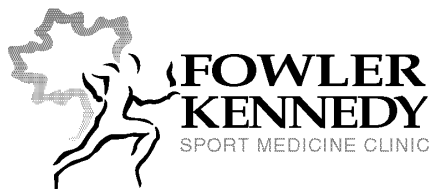
If you have any questions about your rights as a research participant or the conduct of this study, you may contact the Patient Relations Office at LHSC at (519) 685-8500 ext. 52036 or access the online form at: <https://apps.lhsc.on.ca/?q=forms/patient-relations-contact-form>.

If you have questions or concerns about your surgery or physiotherapy, please contact your orthopaedic surgeon or physiotherapist. If you have any questions about this research, please contact one of our Research Manager, Stacey Wanlin at [REDACTED] or your orthopaedic surgeon.

This letter is yours to keep.

Sincerely,

Dr. Alan Getgood, MD  
Dr. Dianne Bryant, PhD  
Stacey Wanlin



### CONSENT FORM

**Title of Research:**

Multicenter Randomized Clinical Trial comparing Anterior Cruciate Ligament Reconstruction With and Without Lateral Extra-articular Tenodesis in Individuals Who Are At High Risk of Graft Failure.

I have read the letter of information, have had the nature of the study explained to me, and I agree to participate in the study. All questions have been answered to my satisfaction. I will receive a copy of the Letter of Information and this signed consent form.

Printed Name of the Participant	Signature of the Participant	Date
Printed Name of the Parent or Substitute Decision Maker (if required)	Signature of the Parent or Substitute Decision Maker (if required)	Date
Printed Name of the Person Responsible for Obtaining Informed Consent	Signature of the Person Person Responsible for Obtaining Informed Consent	Date



- I would like to receive a copy of the results of this study.  
Please mail to:

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Please check the appropriate box below and initial:

- I agree to be contacted for future research studies
- I do NOT agree to be contacted for future research studies

## Curriculum Vitae

**Name:** Katelyn Inch

**Post-secondary Education and Degrees:** Western University  
London, Ontario, Canada  
2020-2023 M.Sc.  
Health and Rehabilitation Sciences, Measurement and Methods  
*Collaborative Specialization in Musculoskeletal Health Research*

Western University  
London, Ontario, Canada  
2016-2020 B.Sc., *Honours*

**Honours and Awards:** Dean's Honour List  
2020

Western Scholarship of Excellence  
2016

**Related Work Experience** Teaching Assistant, Clinical Consolidation – Wound Healing  
Western University  
2021-2022

Teaching Assistant, Advanced Health Care Practice Clinical Mentorship  
Western University  
2020-2022

Orthopaedic Sport Medicine Research Assistant  
Fowler Kennedy Sport Medicine Clinic  
2021-Present

**Publications:**  
Inch, Katelyn M., "Investigating Long-term Outcomes of ACL Repair Techniques: A Follow-up of the Stability Study" (2021). Inspiring Minds – Showcasing Western's Graduate Research, Scholarship and Creative Activity. 33.