Psychological outcomes during rehabilitation after ACL reconstruction and implications for second ACL injury

RAMANA PIUSSI

Department of Health and Rehabilitation,
Institute of Neuroscience and Physiology,
Sahlgrenska Academy, University of Gothenburg

UNIVERSITY OF GOTHENBURG

2024

Layout:
Gudni Olafsson, GO Grafik AB, gudni@gografik.se

Illustrations:
Pontus Andersson, Pontus Art Production AB

Psychological outcomes during rehabilitation after ACL reconstruction

ramana.piussi@hotmail.com

978-91-8069-609-8 (Print)
978-91-8069-610-4 (PDF)
http://hdl.handle.net/2077/78559

Printed in Borås, Sweden 2024
Printed by Stema Specialtryck AB

”Volevi la bicicletta? Adesso pedala!”
“You wanted a bike? Now ride it!”

Contents

Abstract

An anterior cruciate ligament (ACL) injury is a common knee joint injury. An ACL injury is typically managed through surgical reconstruction of the ligament, followed by rehabilitation. For patients treated with ACL reconstruction and rehabilitation, during rehabilitation there is an ongoing interplay between the body and the mind, that is, physical and psychological factors. The purpose of this thesis was to investigate and better understand the psychological outcomes of patients after ACL reconstruction, and possible associations with a subsequent second ACL injury.

This thesis comprised six studies which covered the three pillars of evidence-based medicine (EBM): clinical expertise, best available evidence and patients' preferences.

Study I, for the clinical expertise pillar aimed to qualitatively explore sports physiotherapists' experiences of working with psychological impairments. Findings reveal that sport physiotherapists primarily rely on a blend of clinical experience, intuition, and peer discussions to navigate the psychological dimensions of rehabilitation and acknowledge a significant gap in formal training and knowledge.

Studies II, III, IV, and V focused on the best evidence pillar of EBM. Study II was a systematic review, while Study III, IV and V used data from a rehabilitation specific registry. Study II summarized the prevalence and severity of self-reported depression and anxiety symptoms. Study III examined differences in physical and psychological outcomes between patients who would and would not suffer a second ipsilateral ACL injury. Study IV aimed to incorporate results from psychological patient reported outcome measures (PROs) into assessment batteries, evaluating the risk of subsequent ACL injuries. Finally, Study V calculated cut-off scores on PROs to differentiate between patients likely and not likely to experience a second ACL injury. Results showed a large heterogeneity in how self-reported depression and anxiety symptoms are reported, and that the severity of symptoms peaked in the period around ACL reconstruction. Patients who would go on and suffer a second ipsilateral ACL injury scored higher on PROs. However, implementing PROs in test batteries did not affect the second ACL injury risk and the best scores to differentiate between patients likely and not likely to experience a second ACL injury were never better than the flip of a coin.

Study VI, for the patients' preference pillar, through interviews and qualitative content analysis addressed experiences of young active females who suffered two ACL injuries. In the young females' experiences,

the initial injury catalyzed a profound sense of loss, challenged their athletic identity and induced feelings of loneliness and despair. However, the journey from second ACL injury to the present day painted a picture of determination, support, hard work, and personal growth.

Sammanfattning på svenska

En främre korsbandsskada (ACL) är en allvarlig skada i knäleden. En ACL-skada behandlas vanligtvis med kirurgisk rekonstruktion av ligamentet och rehabilitering. För patienter behandlade med rekonstruktion och rehabilitering, under rehabiliteringen sker ett samspel mellan fysiska och psykologiska faktorer. Syftet med denna avhandling var att utforska psykologiska utfall hos patienter som behandlats med ACL-rekonstruktion, och att bedöma möjliga samband mellan psykologiska utfall efter ACL rekonstruktion och en andra ACL-skada.

Denna avhandling omfattade sex studier som täckte evidensbaserad medicins tre pelare: klinisk expertis, bästa tillgängliga evidens, och patienternas preferenser. Studie I, för klinisk expertis pelaren syftade till att kvalitativt utforska fysioterapeuters erfarenheter av att arbeta med psykologiska faktorer efter en ACL-rekonstruktion. Resultaten visar att fysioterapeuter i första hand förlitar sig på en blandning av klinisk erfarenhet, intuition och diskussioner med kollegor för att navigera psykologiska dimensionerna av rehabilitering och erkänner en betydande lucka i formell träning och kunskap.

Studier II, III, IV och V fokuserade på den bästa tillgängliga evidens pelaren. Studie II var en systematisk översikt, medan studie III, IV och V använde data från ett rehabiliteringsspecifikt register. Studie II sammanfattade prevalensen och allvar av självrapporterade depressions- och ångestsymtom. Studie III undersökte skillnader i fysiska och psykologiska utfall mellan patienter som skulle och inte skulle drabbas av en andra ipsilaterala ACL-skada. Studie IV syftade till att inkorporera resultat från psykologiska patientrapporterade utfall (PROs) i testbatterier för att bedöma risken för en andra ACL-skada. Slutligen beräknade studie V cut-offs på psykologiska PROs för att skilja mellan patienter som skulle och inte skulle drabbas av en andra ACL-skada. Resultaten visar en stor heterogenitet i hur självrapporterade depressions- och ångestsymtom rapporteras, och att symtomens allvar toppar under perioden kring ACL-rekonstruktion. Patienter som skulle drabbas av en andra ipsilaterala ACL-skada fick högre poäng i PROs. Implementering av PROs i testbatterier påverkade dock inte risken för en andra ACL-skada och bästa cut-offen för att skilja mellan patienter som skulle och inte skulle drabbas av en andra ACL-skada var aldrig bättre än att singla slant.

Studie VI, för patientens preferenspelare, utforskade genom intervjuer och kvalitativ innehållsanalys erfarenheter av unga aktiva kvinnor som drabbats av två ACL-skador. För unga aktiva kvinnornas erfarenheter, den initiala skadan gav av en djup känsla av förlust, utmanade deras atletiska identitet och framkallade känslor av ensamhet och förtvivlan. Men resan från den andra ACL-skadan till nutiden, målade en bild av beslutsamhet, stöd, hårt arbete och personlig tillväxt.

List of papers

This thesis is based on the following Studies, referred to in the text by roman numerals:

I. **Psychological impairments after ACL injury - Do we know what we are addressing? Experiences from sports physical therapists.**

Piussi R, Krupic F, Senorski C, Svantesson E, Sundemo D, Johnson U, Hamrin Senorski E.

SCANDINAVIAN JOURNAL OF MEDICINE AND SCIENCE IN SPORTS.

2021 JUL;31(7):1508-1517. DOI: 10.1111/SMS.13959.

II. **Self-Reported Symptoms of Depression and Anxiety After ACL Injury: A Systematic Review.**

Piussi R, Berghdal T, Sundemo D, Grassi A, Zaffagnini S, Sansone M, Samuelsson K, Hamrin Senorski E.

ORTHOPEDIC JOURNAL OF SPORTS MEDICINE.

2022 JAN 18;10(1):23259671211066493. DOI: 10.1177/23259671211066493.

III. **Greater Psychological Readiness to Return to Sport, as Well as Greater Present and Future Knee-Related Self-Efficacy, Can Increase the Risk for an Anterior Cruciate Ligament Re-Rupture: A Matched Cohort Study.**

Piussi R, Beischer S, Thomeé R, Thomeé C, Sansone M, Samuelsson K, Hamrin Senorski E.

ARTHROSCOPY.

2022 APR;38(4):1267-1276.E1. DOI: 10.1016/J.ARTHRO.2021.08.040.

IV. **No Effect of Return to Sport Test Batteries with and without Psychological PROs on the Risk of a Second ACL Injury: A Critical Assessment of Four Different Test Batteries.**

Piussi R, Simonson R, Högberg J, Thomeé R, Samuelsson K, Hamrin Senorski E.

INTERNATIONAL JOURNAL OF SPORTS PHYSICAL THERAPY.

2023 AUG 1;18(4):874-886. DOI: 10.26603/001C.81064

V. **Psychological Patient-reported Outcomes Cannot Predict a Second Anterior Cruciate Ligament Injury in Patients who Return to Sports after an Anterior Cruciate Ligament Reconstruction.**

Piussi R, Simonson R, Högberg J, Thomeé R, Samuelsson K, Hamrin Senorski E.

INTERNATIONAL JOURNAL OF SPORTS PHYSICAL THERAPY.

2022 DEC 1;17(7):1340-1350. DOI: 10.26603/001C.55544

VI. **'I was young, I wanted to return to sport, and re-ruptured my ACL' - young active female patients' voices on the experience of sustaining an ACL re-rupture, a qualitative study.**

Piussi R, Krupic F, Sundemo D, Svantesson E, Ivarsson A, Johnson U, Samuelsson K, Hamrin Senorski E.

BMC MUSCULOSKELET DISORD.

2022 AUG 9;23(1):760. DOI: 10.1186/S12891-022-05708-9.

Other publications by the same author not included in this thesis

1. **To achieve the unachievable-Patients' experiences of opting for delayed anterior cruciate ligament reconstruction after trying rehabilitation alone as primary treatment: A qualitative study**

   Rebecca Simonsson, Cajsa Magnusson, Ramana Piussi, Janina Kaarre, Roland Thomeé, Andreas Ivarsson, Kristian Samuelsson, Eric Hamrin Senorski.

   SCANDINAVIAN JOURNAL OF MEDICINE AND SCIENCE IN SPORTS.

   2024 FEB;34(2):E14569. DOI: 10.1111/SMS.14569.

2. **Comparison of knee flexor strength recovery between semitendinosus alone versus semitendinosus with gracilis autograft for ACL reconstruction: a systematic review and meta-analysis**

   Angelo Matteucci, Johan Högberg, Ramana Piussi, Mattias Wernbom, Edoardo Franceschetti, Umile Giuseppe Longo, Kristian Samuelsson, Johan Lövgren, Eric Hamrin Senorski.

   BMC MUSCULOSKELETAL DISORDERS.

   2024 FEB 12;25(1):136. DOI: 10.1186/S12891-024-07226-2..

3. **The NordBord test reveals persistent knee flexor strength asymmetry when assessed two and five years after ACL reconstruction with hamstring tendon autograft**

   Johan Högberg, Ramana Piussi, Rebecca Simonsson, Mattias Wernbom, Kristian Samuelsson, Roland Thomeé, Eric Hamrin Senorski.

   PHYSICAL THERAPY IN SPORTS.

   2024 MAR;66:53-60. DOI: 10.1016/J.PTSP.2024.01.008..

4. **Physical symptoms among professional gamers within eSports, a survey study.**

   Staffan Ekefjärd, Ramana Piussi, Eric Hamrin Senorski.

   BMC SPORTS SCIENCE, MEDICINE AND REHABILITATION.

   2024 JAN 15;16(1):18. DOI: 10.1186/S13102-024-00810-Y..

5. **The days of generalised joint hypermobility assessment in all patients with ACL injury are here.**

   Balint Zsidai, Janina Kaarre, Eleonor Svantesson, Ramana Piussi, Volker Musahl, Kristian Samuelsson, Eric Hamrin Senorski.

   BRITISH JOURNAL OF SPORTS MEDICINE.

   2024 JAN 12:BJSPORTS-2023-107188. DOI: 10.1136/BJSPORTS-2023-107188

6. **No Association Between Hamstrings-to-Quadriceps Strength Ratio and Second ACL Injuries After Accounting for Prognostic Factors: A Cohort Study of 574 Patients After ACL-Reconstruction.**

   Johan Högberg, Ramana Piussi, Mattias Wernbom, Francesco Della Villa, Rebecca Simonsson, Kristian Samuelsson, Roland Thomeé, Eric Hamrin Senorski.

   SPORTS MEDICINE OPEN.

   2024 JAN 12;10(1):7. DOI: 10.1186/S40798-023-00670-9.

7. **Restoring Knee Flexor Strength Symmetry Requires 2 Years After ACL Reconstruction, But Does It Matter for Second ACL Injuries? A Systematic Review and Meta-analysis.**

   Johan Högberg, Ramana Piussi, Johan Lövgren, Mattias Wernbom, Rebecca Simonsson, Kristian Samuelsson, Eric Hamrin Senorski.

   SPORTS MEDICINE OPEN.

   2024 JAN 5;10(1):2. DOI: 10.1186/S40798-023-00666-5.

8. **Psychological Factors in Sports Injury Rehabilitation: How Can a Sports Rehabilitation Practitioner Facilitate Communication?**

   Ramana Piussi, Andreas Ivarsson, Urban Johnson, Eric Hamrin Senorski.

   JOURNAL OF ORTHOPAEDIC AND SPORTS PHYSICAL THERAPY, OPEN.

   2023;1(2):1-3. DOI:10.2519/JOSPTOPEN.2023.0007

9. **Better safe than sorry? A systematic review and meta-analysis on time to return to sport after ACL reconstruction as a risk factor for second ACL injury.**

   Ramana Piussi, Rebecca Simonson, Balint Zsidai, Alberto Grassi, Jon Karlsson, Francesco Della Villa, Kristian Samuelsson, Eric Hamrin Senorski.

   JOURNAL OF ORTHOPAEDIC AND SPORTS PHYSICAL THERAPY,

   1–30. 2023 DOI.ORG/10.2519/JOSPT.2023.11977

10. **A comparison between physical therapy clinics with high and low rehabilitation volumes of patients with ACL reconstruction.**

    Rebecca Simonsson, Johan Högberg, Jakob Lindskog, Ramana Piussi, Axel Sundberg, Mikael Sansone, Kristian Samuelsson, Roland Thomeé & Eric Hamrin Senorski.

    JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH,

    2023 18(1), 842. DOI.ORG/10.1186/S13018-023-04304-4

11. **Greater self-efficacy, psychological readiness and return to sport amongst paediatric patients compared with adolescents and young adults, 8 and 12 months after ACL reconstruction.**

    Baldur Thorolfsson, Ramana Piussi, Thorkell Snaebjornsson, Jon Karlsson, Kristian Samuelsson, Susanne Beischer, Roland Thomeé & Eric Hamrin Senorski.

    KNEE SURGERY, SPORTS TRAUMATOLOGY, ARTHROSCOPY

    2023 DEC;31(12):5629-5640. DOI: 10.1007/S00167-023-07623-5.

12. **Lower rates of return to sport in patients with generalised joint hypermobility two years after ACL reconstruction: a prospective cohort study**

    Jakob Lindskog, Ramana Piussi, Rebecca Simonson, Johan Högberg, , Kristian Samuelsson, Roland Thomeé, David Sundemo, Eric Hamrin Senorski

    BMC SPORTS SCIENCE, MEDICINE AND REHABILITATION

    2023 AUG 12;15(1):100. DOI: 10.1186/S13102-023-00707-2

13. **Generalised joint hypermobility leads to increased odds of sustaining a second ACL injury within 12 months of return to sport after ACL reconstruction**

    Bálint Zsidai, Ramana Piussi, Roland Thomeé, David Sundemo, Volker Musahl, Kristian Samuelsson, Eric Hamrin Senorski

    BRITISH JOURNAL OF SPORTS MEDICINE.

    2023 MAY 16:BJSPORTS-2022-106183. DOI: 10.1136/BJSPORTS-2022-106183.

14. **Effect of Quadriceps and Hamstring Strength Relative to Body Weight on Risk of a Second ACL Injury: A Cohort Study of 835 Patients Who Returned to Sport After ACL Reconstruction**

    Rebecca Simonson, Ramana Piussi, Johan Högberg, Carl Senorski, Roland Thomeé, Kristian Samuelsson, Eric Hamrin Senorski

    ORTHOPEDIC JOURNAL OF SPORTS MEDICINE.

    2023 APR 28;11(4):23259671231157386. DOI: 10.1177/23259671231157386.

15. **When context creates uncertainty: experiences of patients who choose rehabilitation as a treatment after an ACL injury**

    Ramana Piussi, Rebecca Simonson, Moa Kjellander, Alice Jacobsson, Andreas Ivarsson, Jon Karlsson, Kristian Samuelsson, Eric Hamrin Senorski

    BMJ OPEN SPORT EXERCISE MEDICINE.

    2023 MAR 22;9(1):E001501. DOI: 10.1136/BMJSEM-2022-001501.

16. **Only 10% of Patients With a Concomitant MCL Injury Return to Their Preinjury Level of Sport 1 Year After ACL Reconstruction: A Matched Comparison With Isolated ACL Reconstruction**

    Eleonor Svantesson, Ramana Piussi, Susanne Beischer, Christoffer Thomeé, Kristian Samuelsson, Jón Karlsson, Roland Thomeé, Eric Hamrin Senorski

    SPORTS HEALTH.

    2023 MAR 10:19417381231157746. DOI: 10.1177/19417381231157746.

17. **Is absolute or relative knee flexor strength related to patient-reported outcomes in patients treated with ACL reconstruction with a hamstring tendon autograft? An analysis of eccentric Nordic hamstring strength and seated concentric isokinetic strength**

    Johan Högberg, Ramana Piussi, Rebecca Simonson, Axel Sundberg, Daniel Broman, Kristian Samuelsson, Roland Thomeé, Eric Hamrin Senorski

    KNEE.

    2023 MAR;41:161-170. DOI: 10.1016/J.KNEE.2023.01.010.

18. **A clinician-friendly test battery with a passing rate similar to a 'gold standard' return-to-sport test battery 1 year after ACL reconstruction: Results from a rehabilitation outcome registry**

    Daniel Broman, Ramana Piussi, Roland Thomeé, Eric Hamrin Senorski

    PHYSICAL THERAPY IN SPORTS.

    2023 JAN; 59:144-150. DOI: 10.1016/J.PTSP.2022.12.009.

19. **Some, but not all, patients experience full symptom resolution and a positive rehabilitation process after ACL reconstruction: an interview study**

    Ramana Piussi, Cajsa Magnusson, Sara Andersson, Kaisa Mannerkorpi, Roland Thomeé, Kristian Samuelsson, Eric Hamrin Senorski

    KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY.

    2022 DEC 9. DOI: 10.1007/S00167-022-07271-1.

20. **Persistent knee flexor strength deficits identified through the NordBord eccentric test not seen with "gold standard" isokinetic concentric testing during the first year after anterior cruciate ligament reconstruction with a hamstring tendon autograft**

    Johan Högberg, Emma Bergentoft, Ramana Piussi, Mathias Wernbom, Susanne Beischer, Rebecca Simonson, Carl Senorski, Roland Thomeé, Eric Hamrin Senorski

    PHYSICAL THERAPY IN SPORTS

    2022 MAY;55:119-124. DOI: 10.1016/J.PTSP.2022.03.004.

21. **Recovery of preoperative absolute knee extension and flexion strength after ACL reconstruction**

    Ramana Piussi, Daniel Broman, Erik Musslinder, Susanne Beischer, Roland Thomée, Eric Hamrin Senorski

    BMC SPORTS SCIENCE, MEDICINE AND REHABILITATION

    020 DEC 10;12(1):77. DOI: 10.1186/S13102-020-00222-8.

22. **Hop tests and psychological PROs provide a demanding and clinician-friendly RTS assessment of patients after ACL reconstruction**

    Ramana Piussi, Susanne Beischer, Roland Thomeé, Eric Hamrin Senorski

    BMC SPORTS SCIENCE, MEDICINE AND REHABILITATION

    2020 MAY 13;12:32. DOI: 10.1186/S13102-020-00182-Z.

23. **Superior knee self-efficacy and quality of life throughout the first year in patients who recover symmetrical strength after ACL reconstruction**

    Ramana Piussi, Susanne Beischer, Roland Thomeé, Eric Hamrin Senorski

    KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY

    2020 FEB;28(2):555-567. DOI: 10.1007/S00167-019-05703-Z.

Abbreviations

ACL:	Anterior Cruciate Ligament
ACL-RSI:	Anterior Cruciate Ligament Return to Sport after Injury scale
AIMS:	Athletic Identity Measurement Scale
AMED:	Allied and complementary MEdicine Database
AUC:	Area Under the Curve
BDI:	Beck Depression Inventory
BFR:	BloodFlow Restricted training
BMI:	Body Mass Index
BPTB:	Bone Patellar Tendon Bone
BSI:	Brief Symptom Inventory
CI:	Confidence Interval
CM:	Centimeters
COD:	Change Of Direction
COREQ:	COnsolidated criteria for REporting Qualitative research
CTT:	Classic Test Theory
DASS:	Depression Anxiety Stress Scale
DSM:	Diagnostic and Statistical Manual of mental disorders
EBM:	Evidence Based Medicine
GAD:	Generalized Anxiety Disorder
GRADE:	Grading of Recommendations Assessment Development and Evaluation
HADS:	Hospital Anxiety and Depression Score
HR:	Hazard Ratio
HT:	Hamstring Tendon
ICC:	Intraclass Correlation Coefficient
IKDC:	International Knee Documentation Committee
KG:	KiloGrams
K-SES:	Knee Self-Efficacy Scale
KOOS:	Knee injury and Osteoarthritis Outcome Score

LCL:	Lateral Collateral Ligament
LSI:	Limb Symmetry Index
MADRS:	Montgomery Åsberg Depression Rating Scale
MCL:	Medial Collateral Ligament
MeSH:	Medical Subject Heading
MINORS:	Methodological Index for Non-Randomized Studies
MMAT:	Mixed Methods Appraisal Tool
MTT:	Modern Test Theory
N:	Number
NM:	Newton Meter
NMES:	NeuroMuscular Electric Stimulation
PEDro:	Physiotherapy Evidence Database
PCL:	Posterior Cruciate Ligament
POMS:	Profile Of Mood States
POL:	Posterior Oblique Ligament
PRISMA:	Preferred Reporting Items for Systematic reviews and Meta-Analysis
PROSPERO:	international prospective register of systematic reviews
PROs:	Patient Reported Outcome measures
QoL:	Quality of Life
QT:	Quadriceps Tendon
QUIDS:	Quick Inventory of Depression Symptomatology
RCT:	Randomised Controlled Trial
RM:	Repetition Maximum
RoBANS:	Risk of Bias Assessment tool for Non-Randomized Studies
ROC:	Receiver Operating Curve
RPE:	Rate of Perceived Exertion
RTS:	Return To Sports
SF:	Short Form
SD:	Standard Deviation
STAI:	State and Trait Anxiety Inventory
STARD:	STAndards for Reporting Diagnostic accuracy
VAS:	Visual Analog Scale

Definitions

ACL reconstruction:
reconstruction of the native ACL using a graft

Allograft:
tissue from a genetically different donor of the same species

Area under the curve:
a way of assessing receiver operating curve. Represents the degree or measure of separability

Autograft:
tissue from one to another anatomical place of the same individual´s body

Bias:
systematic error

Case-control study:
controlled retrospective study in which exposures in a group with a given outcome (cases) is compared with exposure in a group without the outcome (controls)

Cohort study:
controlled prospective observational study in which outcomes in a group are compared with outcomes in a similar group

Confidence interval:
estimated range of values from a sample which includes the unknown target population parameter with a given probability

Confounding factor:
a factor that is associated with an exposure and has an impact on an outcome that is independent of the impact of the exposure

Constructionist theoretical framework:
framework that asserts that subjective experiences, including emotions, are variable and based on constructed interpretations

Content validity:
the extent to which a test covers all relevant parts of the construct it aims to measure

Contralateral:
belonging to the opposite side of the body

Discriminant validity:
the extent to which a test is not related to other tests that measure different constructs

Deductive approach:
approach which uses general premises from an existing theory to form a specific conclusion

Face validity:
the subjective degree to which an assessment appears effective in terms of its stated aims.

Graft failure:
Insufficiency of the reconstructed ACL graft

Incidence:
occurrence of new cases during a given period of time in a population at risk

Index:
epidemiologically, the first occurrence

Inductive approach:
approach which aims to move from specific observation to broad generalizations without using an existing theory

Injury to surgery:
time elapsing from ACL injury to ACL reconstruction

Ipsilateral:
belonging to the same side of the body

Levels of evidence:
a hierarchical system which aims to grade studies based on methodology

P-value:
the probability, under the assumption of the null hypothesis, of obtaining a result equal to or more extreme than what was actually observed

Power:
the test´s ability to correctly reject a null hypothesis that is indeed false

Prevalence:
the proportion of cases (both new and old) at a given time in relation to the population at risk

Randomized controlled trial:
controlled prospective interventional study in which trial participants are randomized to an intervention or a control and then compared over time

Recall bias:
the case in which participants in a study do not accurately remember a past event or experience or leave out details when reporting about them

Receiver operating characteristic curve:
a graphical plot that illustrates the diagnostic ability of a binary classifier system

Regression:
statistical model for the relationship between one or more explanatory variables and one or more dependent variables

Relative risk:
the ratio of the probability of an event occurring in a group with a given exposure to a group without the exposure

Relativist ontological position:
the belief that reality is a finite subjective experience

Reliability:
the extent to which an observation yields consistent results

Revision:
replacement of a previous ACL reconstruction

Risk:
the probability of the occurrence of new cases during a given time period in a population at risk

Semi-structured interview:
interview performed with a structured guide, and follow-up questions

Subjectivist/transactional epistemological standpoint:
standpoint inferring that knowledge is co-constructed through interaction between researcher and data

Systematic review:
a literature study in which an explicit and reproducible methodology is used to answer a specific question by analysis of evidence

Type 1 error:
incorrect rejection of a true null hypothesis

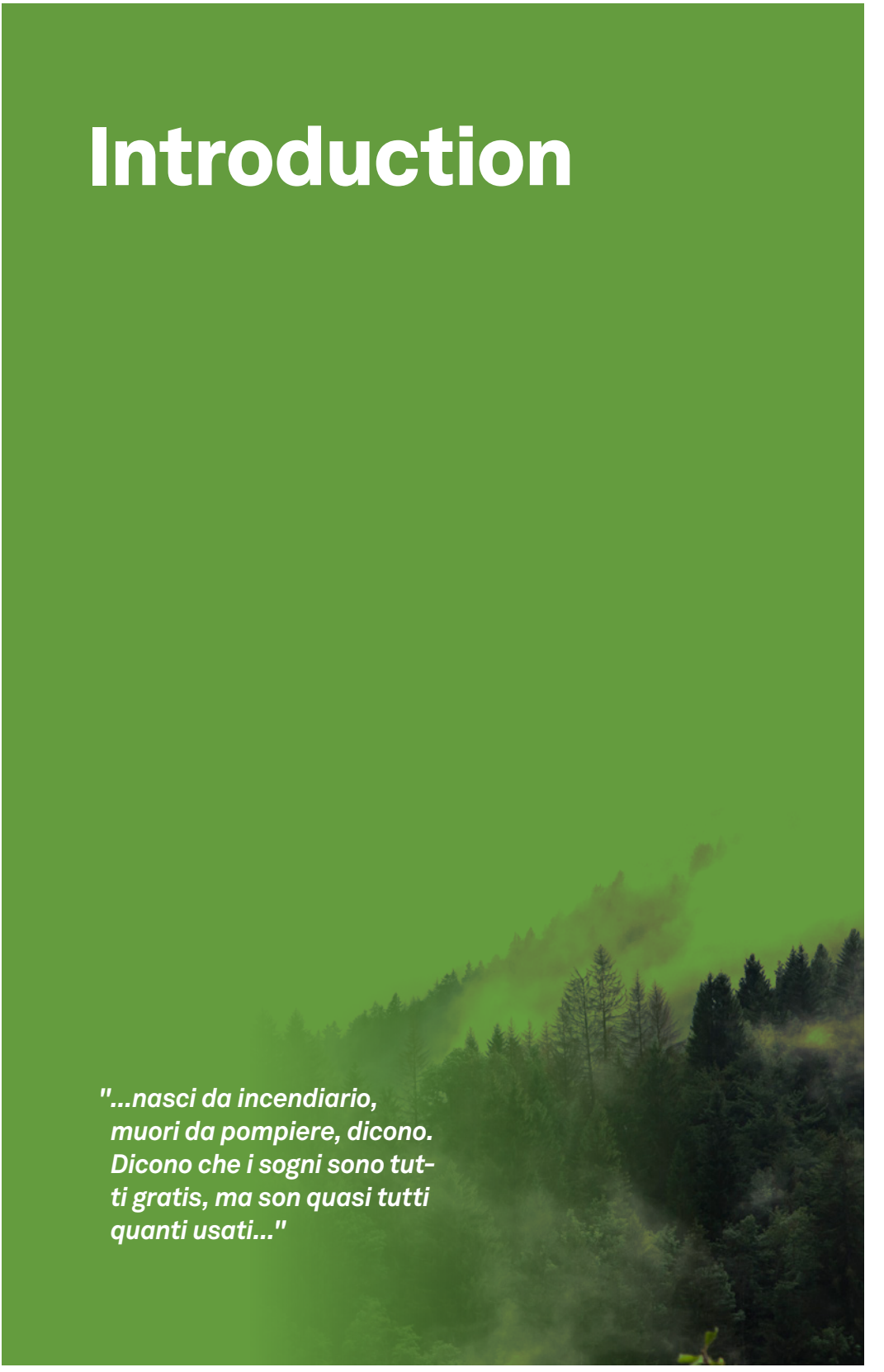
Type 2 error:
failure to reject a false null hypothesis

Validity:
the extent to which an observation is free from bias and thus reflects the construct

Variable:
an operationalized characteristic of a construct

Youden index:
a statistic test that captures the performance of a dichotomous diagnostic test. Derived by adding sensitivity and specificity -1.

Introduction



*"...nasci da incendiario,
muori da pompiere, dicono.
Dicono che i sogni sono tut-
ti gratis, ma son quasi tutti
quanti usati..."*

Anatomy

The knee joint

The knee, (Figure 1), serves as the connection between the thigh bone (femur) and the shin bone (tibia), and is the largest joint in the human body.

The knee joint main function is to support the body weight, and to allow movement of the legs. Almost any movement that uses the legs relies on the knees. The knee joint is formed by the distal part of the femur and the proximal part of the tibia. Furthermore, the distal extremity of the femur interacts with the body's largest sesamoid bone, the patella (kneecap), forming the patellofemoral joint.[1] During movement, the morphology of the knee joint allows the center of knee rotation to change during knee flexion.[2] The patellofemoral joint plays an essential role in the extension mechanism of the knee. One part of the patellofemoral joint, the patella, is embedded in the quadriceps tendon, which becomes the patellar tendon at the level of the patella, and then attaches to the tibial tuberosity. Consequently, as the moment arm is increased, the quadriceps muscle needs less force to extend the knee joint.[3] Other structures alongside bones form the knee joint: menisci, cartilage, joint capsule, and the ligaments.

The menisci

The menisci, two half-moon shaped fibrocartilage discs, reside between the femur and tibia within the knee's medial and lateral compartments (Figure 2).[4]

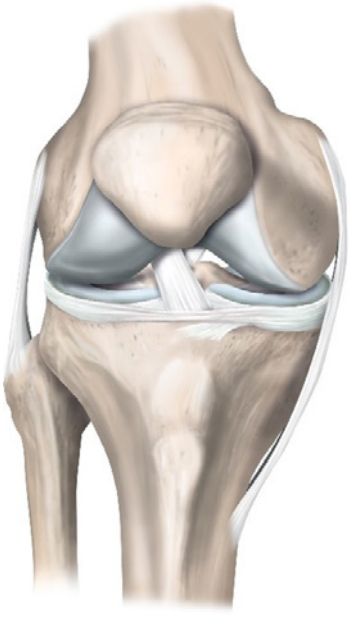


Figure 1: The knee joint.

Figure 2: The menisci.

The lateral part of each menisci is thicker compared with the medial part, creating a concave area in which the convex femur condyles can articulate with the tibial plateau.[4] Moving from the periphery to the central part of the menisci, the vascularization successively decreases, with only 10-25% of the peripheral part of the meniscus being vascularized in adults.[5] The menisci anchor to the tibial plateau through their anterior and posterior horns, and various ligaments link them together.[4] They are crucial for knee joint function, offering stability, distributing load, and facilitating load transmission across the joint.[6] The medial meniscus is connected to the medial collateral ligament (MCL), whereas the lateral meniscus lacks an attachment to the lateral collateral ligament (LCL).[6]

The articular cartilage

Hyaline cartilage covers the bony surfaces of both the femoro-tibial and patellofemoral joints. The role of the articular cartilage is to provide load transmission, and, in cooperation with the synovial fluid to provide friction-free surfaces for the joint to articulate.[7] Since the articular cartilage is not vascularized, it is dependent on the synovial fluid to receive needed nutrients.[8] The biomechanical properties of the articular cartilage allow it to be more elastic and tolerate more compression than bone.[8]

The Joint capsule

The joint capsule is a strong, fibrous structure that surrounds and encloses the knee joint. The joint capsule plays a crucial role in providing stability to the joint and protecting the internal structures. It is composed of two layers, one internal and one external.[9] The outer layer is made of dense connective tissue and protects the knee from external stress. The inner layer, called "synovial membrane" lines the joint cavity. The membrane secretes synovial fluid.[9] The space inside the knee created by the joint capsule is filled with synovial liquid, which is important for friction free movement and the nourishment of all structures within the joint. The capsule, along with other structures like ligaments and muscles, contributes to the overall stability and functionality of the knee.[9]

The collateral ligaments

The knee joint is stabilized by four primary ligaments, and the collateral ligaments are two of these essential structures (Figure 3). The collateral ligaments are located outside of the articulation and restrain excessive motion medially and laterally, respectively. The MCL is composed of superficial and deep layers, is eight to ten centimetres long, and attaches proximally on the medial femoral epicondyle.[10] Distally, the MCL attaches posterior to the medial condyle of the tibia and the pes anserinus, approximately five to seven centimetres distal to the joint line.[11 12] The MCL attaches medially to the medial meniscus. The MCL restrains valgus motion on the knee, medial, anterior and rotational movement of the tibia and knee hyperextension.[13] The posterior third of the MCL attaches to the posterior oblique ligament (POL), which is an important ligamentous structure which provides rotatory stability to the knee joint. The POL attaches proximally to the adductor tubercle of the femur and distally to the tibia and the posterior joint capsule. The POL controls anteromedial rotatory

laxity and aids the MCL to provide static resistance to valgus loads when the knee is fully extended.[14] Interestingly, the MCL ranks as the knee ligament most frequently injured.[15] The LCL starts at the lateral femoral epicondyle and connects near the biceps femoris tendon to the fibula's head.[16] The LCL´s primary function is to restrain varus and tibial external rotation. The LCL is seldomly injured alone, but rather as a concomitant injury after a major trauma to the knee.[17]

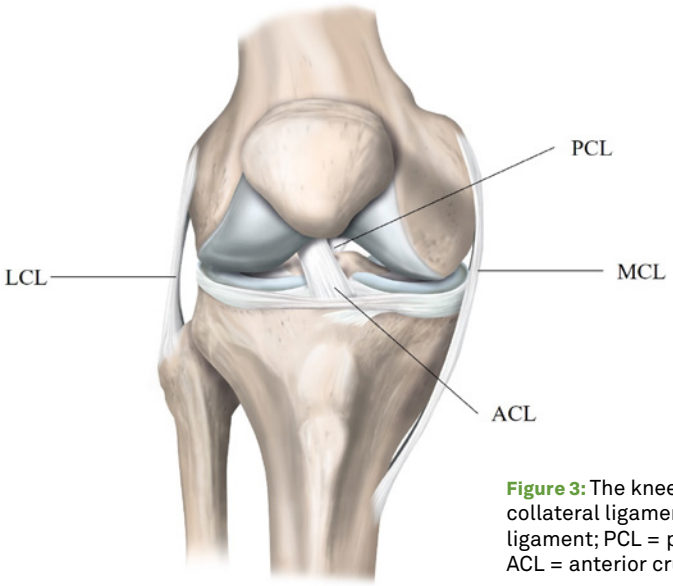


Figure 3: The knee joint ligaments; LCL = lateral collateral ligament; MCL = medial collateral ligament; PCL = posterior cruciate ligament; ACL = anterior cruciate ligament.

The cruciate ligaments

The cruciate ligaments are the two intra-articular ligaments of the knee joint. The anterior (ACL) and the posterior (PCL) cruciate ligament appear to form a cross inside the knee joint and are therefore named the cruciate ligaments.[18] The ACL and PCL are located on the dorsal area of the joint, and act in synergy to control the anteroposterior and rotational stability of the knee.[19] With the knee in flexion, the cruciate ligaments cross each other, while with the knee in extension, the ligaments are more parallel to each other.[19] The ACL and PCL ligaments are sometimes defined as the central pivot of the knee as opposed to the peripheral pivot (shattered red lines in Figure 4). As synthetized in Figure 4, biomechanically, the ACL and PCL should not be regarded as the sole rotational stabilizations for the knee joint. The central position of the ligaments implies a limited capacity of withstanding external pivoting forces.

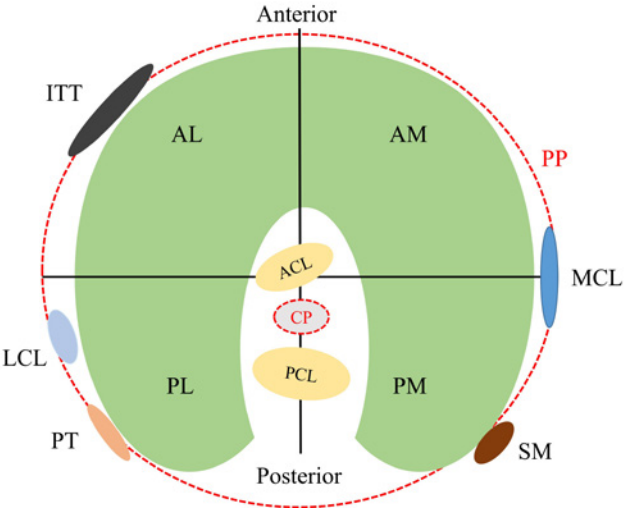


Figure 4: Illustration of knee stability structures with ACL and LCL grouped as central pivot. Division of tibial plateau into quadrants. AL: anterolateral; AM: anteromedial; PL: posterolateral; PM: posteromedial; ACL: anterior cruciate ligament; PCL: posterior cruciate ligament; CP: central pivot; PP: peripheral pivot; MCL: medial collateral ligament; SM: semimembranosus tendon; PT: popliteus tendon; LCL: lateral collateral ligament; ITT: iliotibial tract tendon.

The PCL, the knee joint's largest ligament, consists of two bundles—the anterolateral and the posteromedial—that work together. The PCL connects to the back of the lateral tibial plateau and the lateral side of the medial femoral condyle.[20] Thus, the PCL runs medially from the tibial to the femoral attachment, with a slight forward bend, and prevents the tibia to translate posteriorly.[20]

The ACL attaches to the anterior part of the medial tibial plateau and to the medial aspect of the lateral femur condyle.[21] The ACL has in earlier litterature been regarded as one ligament, but the insertion of the fibers creates in fact two bundles: the anteromedial and the posterolateral bundles.[22] The anteromedial bundle is more vertically oriented and twice as long as the posterolateral bundle. Consequently, the anteromedial bundle provides more antero-posterior stability, where the posterolateral bundle provides more rotatory stability. The ACL prevents the tibia from anterior translation and internal rotation.[23] Importantly, the fibers of the two cruciate ligaments are not straight but run in torsion.

The ACL injury

Etiology

An injury to the ACL (Figure 5) is a common sports-related injury and affects mostly people in late teenage and early twenties (Figure 6), and could potentially have an impact on injured individuals' future possibilities of being physically active.

Figure 5: Anterior Cruciate Ligament rupture.

An ACL injury is most often (nearly 75% of cases) sustained as a non-contact injury,[24] in sports characterized by quick accelerations, decelerations and changes of direction, so called pivoting sports. An ACL injury typically occurs when the knee is nearly fully extended, accompanied by slight knee abduction and external rotation of the tibia, during a sudden deceleration by the athlete before changing direction or executing a landing maneuver.[24] On the opposite, a contact injury is a result of external valgus force applied to the knee.[24] However, a variety of descriptions exist involving different combinations of knee extension, abduction and tibial rotation.[25] In video analysis, it has been shown that knee abduction and external tibial rotation are common mechanisms for ACL injuries.[26] Other body movements described in ACL injuries from video analysis include a flatfoot position at ground contact and lateral trunk lean.[27] Individuals suffering an ACL injury are often perturbed just before the injury.[26]

Epidemiology

Typically, individuals who suffer an ACL injury are young and active, where the mean age for an ACL reconstruction in Sweden is 27 years for females and 29 for males.[28] Females have shown greater injury rates in contact sports (1.88/10000 versus 0.87/10000 athlete-exposures) and in sports with high impact landing such as gymnastics (4.80/10000 versus 1.75/10000 athlete exposures).[29] In team sports, the overall rate of non-contact ACL injuries stands at 0.07 per 1000 player-hours and 0.05 per 1000 player-exposures.[30] The incidence rate among females is higher at 0.14 per 1000 player-hours compared to males at 0.05 per 1000 player-hours, with injuries occurring more frequently during competition than in training (0.48 per 1000 player-hours versus 0.04 per 1000 player-hours).[30] The greater frequency of injuries in females is attributed to differences in hormonal levels, anatomy, and neuromuscular factors between sexes. In Sweden, the incidence rate is around 80 new cases per 100,000 individuals annually,[28] while the United States records approximately 250,000 cases each year,[31] highlighting ACL injuries as among the most prevalent severe sports-related injuries.

Risk factors

Adolescent females who participate in sports suffer ACL injuries at a 2- to 10-fold greater risk compared with male counterparts active in the same sports, possibly due to the above mentioned hormonal, anatomical and neuromuscular differences.[32]

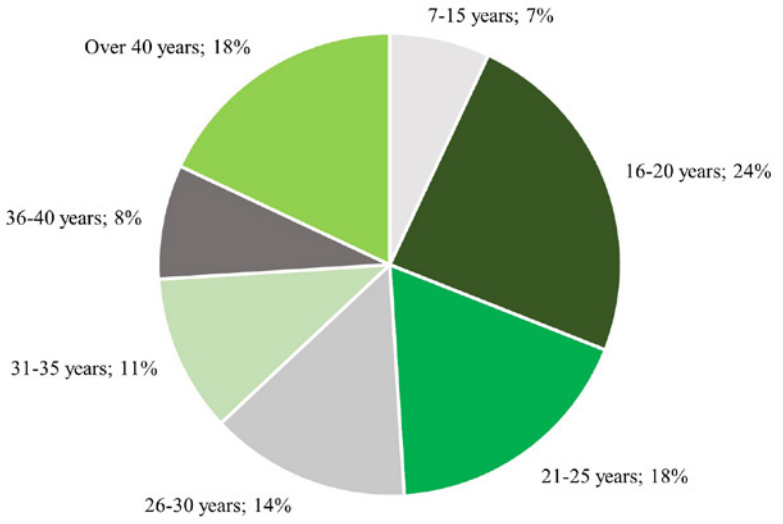


Figure 6: Primary ACL reconstruction rates (%) divided by patient age for year 2022. Data extracted from the Swedish National Knee Ligaments Registry (https://www.aclregister.nu/documents/).

Moreover, incidence depends on the type of activity. Within football and basketball, females displayed a roughly 3 times greater incidence risk of ACL injuries compared with males.[33] As a result, being female is identified as a risk factor for sustaining an ACL injury. In the early 2000s, the risk factors for an ACL injury were categorized into four groups: environmental, anatomical, hormonal, and biomechanical.[34]

- In terms of the environmental category, high friction between the shoe and the surface (foot gets stuck on the surface) has been identified as a risk factor,[35] but lately, the complex set of neurocognitive stimulus (team mates and opponents position and movements with an external object of focus, i.e. a boll) can be added to the environmental risk factors. A shortfall or lag in processing attentional information could lead to challenges in correcting coordination mistakes, potentially leaving the knee in vulnerable positions that elevate the risk of ACL injury.[36]

- In terms of the anatomical risk factors, knee laxity, (the combination of joint mobility and musculotendinous flexibility) has been identified as a risk factor, more common in females.[33] Other anatomical risk factors, more evident in females, are increased quadriceps angle, increased posterior tibial slope, and decreased notch width.[34 37] In addition, generalized joint hypermobility has been identified as perhaps one of the strongest risk factors for ACL injury.[38]

- In terms of the hormonal risk factors, studies have mentioned that female athletes may be more predisposed to

ACL injuries during the first half (preovulatory phase) of the menstrual cycle,[39] and that oral contraceptives may offer up to a 20% reduction in risk of injury.[40]

- In terms of the biomechanical risk factors, control and strength of the muscles surrounding the hip and the knee, where females showed inferior strength, have been suggested as risk factors.[34] Biomechanical risk factors also include the knee position when suffering an injury: knee extension, abduction and tibial rotation,[25] alongside poor trunk control.[27] As for neuromuscular activation, females have been reported to be slower compared with males in maximal muscular activation. This slower activation could delay the knee's readiness for physical tasks by hindering the ability to quickly generate muscle tension.[41]

Importantly, all categories interplay and different risk factors can have different importance in everyone.

The treatment

Following an ACL injury, patients have two treatment options: they can undergo rehabilitation alone or opt for surgical reconstruction of the injured ACL followed by subsequent rehabilitation. The surgical reconstruction can be performed early or delayed in case rehabilitation alone does not provide satisfactory results. A surgical reconstruction and subsequent rehabilitation are usually recommended for patients who wish to return to sport (RTS).[42-44] The choice of treatment is commonly influenced by several factors that have the potential to affect treatment outcomes.[42] Factors that impact treatment outcome encompass age, knee instability, knee laxity, symptoms of instability, level of physical activity, and concomitant injuries. It is important to note that knee "instability" is a spectrum, encompassing knee laxity, and symptoms of instability. In this context, instability refers to the subjective feeling of the knee not being stable, laxity refers to the objective looseness of the knee joint involving super-physiological movement, and symptoms of instability involve the knee "giving-way" and not supporting the patient's weight. Patients who are young, and who perceive the knee as greatly unstable, display objective knee laxity, have symptoms of functional instability, wish to return to knee demanding physical activity, and suffered concomitant injuries to cartilage and/or menisci, are generally believed to benefit from ACL reconstruction.[45 46]

Surgical reconstruction can utilize either a tendon from the patient's body (autograft) or a tendon donated from another person (allograft). Up to the early 1990s, the bone-patellar tendon-bone (BPTB) autograft was the predominant choice for initial ACL reconstruction. However, over the last three decades, the use of the hamstrings tendon (HT) autograft has become increasingly popular.[47] Quadriceps tendon (QT) autografts have become more common as reconstructive autografts after an ACL injury in the last 10 years.[47] In comparison to the HT tendon and the BPTB, the QT has shown similar functional outcomes in terms of objective laxity and self-reported knee function. Moreover, QT have displayed less

harvesting donor-site pain compared with BPTB, while survival rates for the QT are similar compared with the HT and BPTB.[48] The HT accounts for approximately 50% of primary reconstruction cases, followed by the BPTB (40%), and others (including the QT) in 10%.[47]

Although there is no unanimous agreement on the optimal timing for ACL reconstruction, it is generally advised to carry out the surgery between four to eight weeks after injury, provided there is no significant laxity, perceived instability, or symptoms of instability. However, within the Swedish National Health Service, the interval from injury to surgery often extends beyond eight weeks. Postponing ACL reconstruction allows for the reduction of inflammation, the resolution of knee joint effusion, and the enhancement of range of motion and muscle function.[49] Nonetheless, it is commonly observed that elite athletes, such as professional football players, frequently undergo ACL reconstruction shortly after injury to experience only one traumatic event to the knee, rather than two separated by several weeks. The actual timing of the surgery varies greatly, influenced by regional differences in healthcare provision. When ACL reconstruction is delayed beyond eight weeks, maintaining or increasing quadriceps strength becomes essential, as stronger pre-operative quadriceps are significantly associated with better knee function and a successful RTS after ACL reconstruction.[50] [51] A quadriceps strength deficit greater than 20% can last up to two years after reconstruction or even more.[50]

To date, three randomized controlled trials (RCTs) have compared the outcomes of patients who underwent ACL reconstruction versus those who received rehabilitation alone.[45] [52] [53] Frobell et al.[52] reported no differences between treatment groups in terms of patient-reported knee function measured by the Knee injury and Osteoarthritis Outcome Score (KOOS), including KOOS4, the Tegner activity scale, how many meniscus surgeries were required, or whether radiographic knee osteoarthritis developed.[52] The absence of differences between groups were reported to last at the 5 years follow-up as well.[54] Reijman et al[53] showed improved International Knee Documentation Committee (IKDC) scores during the first 12 months of follow-up in both the early ACL reconstruction and the rehabilitation groups. The early ACL reconstruction group, however, experienced significant improvements after three months and two years.[53] In contrast, Beard et al.[45] found that patients who underwent ACL reconstruction exhibited higher scores on both the KOOS4 and the Tegner activity scale compared to patients who were treated solely with rehabilitation. KOOS and KOOS4 have, however, been criticized for being inadequate (suboptimal content and structural validity) for evaluating ACL injuries.[55] [56] In addition, in the three RCTs, high percentages of patients who were randomly assigned to rehabilitation alone crossed-over to delayed reconstruction. A total of 38% [52], 50% [53] and 41% [45] of patients opted for late reconstruction, which indicates that rehabilitation alone is not suitable for all patients. In the five-years follow-up by Frobell et al.[54] 51% of patients opted for delayed reconstruction. Though, recent intriguing findings show that an injured ACL

can show signs of continuity on MRI without surgical reconstruction.[57] Eighty patients in an Australian cohort who suffered an ACL injury were treated with a standard brace locked at 90 degrees of knee flexion (to reduce the distance between ligament remnants) for 12 weeks (successively increased range of motion after week 4). Imaging of the knee taken with MRI at 3 and 6 months showed continuity of the ACL fibers in 90% of included patients.[57] Of the 80 included patients, only 2 (who did not suffer a second ACL injury) were then treated surgically, for a cyclops and a meniscal lesion. Findings are preliminary and need to be explored further. For instance, an interesting question would be the effect of 12 weeks of immobilization on the lower limb musculature, the length of the following recovery, and if an ACL that shows signs of continuity after injury on MRI, does stabilize the knee as effectively as a native ACL or an incorporated graft. Taken together, which individualized treatment, that is, rehabilitation alone or surgical reconstruction and subsequent rehabilitation, should be recommended after an ACL injury is still a matter of debate.

Symptoms following an ACL injury or reconstruction are hematoma (typical after injury), pain, inhibition of the quadriceps and hamstrings muscles, and reduced range of motion. In case of reconstructive surgery performed with an autograft, also possible donor-site morbidity such as pain and reduced function are present.[58] The quadriceps can suffer muscular hypotrophy leading to reduced function due to pain, hematoma and limited range of motion, which can lead to impairment of knee function.[59]

Rehabilitation

Early onset of rehabilitation after a trauma to the ACL, both in case of injury or reconstruction, is essential to manage early symptoms and properly restore knee function.

Following ACL reconstruction, rehabilitation extends over a considerable duration, typically ranging from 9 to 12 months,[60] with some guidelines proposing up to two years.[61] Patients have described this rehabilitation period as "tremendously" long in numerous qualitative studies.[62-65] The primary objectives of rehabilitation are to alleviate symptoms like pain, recover muscle strength and hop performance, enhance movement quality of the body and knee, and improve knee-related quality of life. For most individuals, the final aim is a safe RTS without the risk of a second ACL injury.[42]

Physiotherapeutic perspective

Physiotherapy is a health care profession. According to the "World Physiotherapy", "*physiotherapists provide services that develop, maintain, and restore people's maximum movement and functional ability. They can help people at any stage of life, when movement and function are threatened by ageing, injury, diseases, disorders, conditions, or environmental factors. Physiotherapists help people maximize their quality of life, looking at physical, psychological, emotional and social wellbeing. They work in the health spheres of promotion, prevention, treatment/intervention, and rehabilitation*" (https://world.physio/resources/what-is-physiotherapy; accessed 14/02/2024). In the realm of sport injuries, ACL injuries fit into the broader context of physiotherapy

by highlighting the profession's expertise in musculoskeletal rehabilitation. Physiotherapists specialize in the design and implementation of targeted interventions to enhance functional recovery. In the case of ACL reconstruction, physiotherapists work collaboratively with patients to optimize postoperative outcomes, and to facilitate a safe and effective return to normal activities, sports, or other physical goals. Physiotherapists´ holistic approach not only encompasses the restoration of functional recovery but also the psychological aspects of coping with the challenges of rehabilitation, fostering a comprehensive and patient-centered perspective. Thus, In the context of ACL reconstruction rehabilitation, the physiotherapeutic perspective is fundamental. Physiotherapists work closely with patients who have undergone ACL reconstruction surgery to guide patients through the comprehensive rehabilitation program. Physiotherapists tailor rehabilitation plans to the specific needs, wishes and abilities of each patient, considering factors such as age, fitness level, requirements and lifestyle. However, physiotherapists are not the only health care professionals who work with patients who rehabilitate after an ACL injury or reconstruction.

For illustration and comprehension, in this thesis rehabilitation after an ACL reconstruction will be dived into three stages: early, middle, and late. However, it should be mentioned that these stages are not entirely separated, can be different in length and may not apply to all patients. For some patients, "late stage" might not end, since some patients have defined rehabilitation after an ACL injury to be "lifelong".[64] Rehabilitation phases are briefly summarized in figure 7.

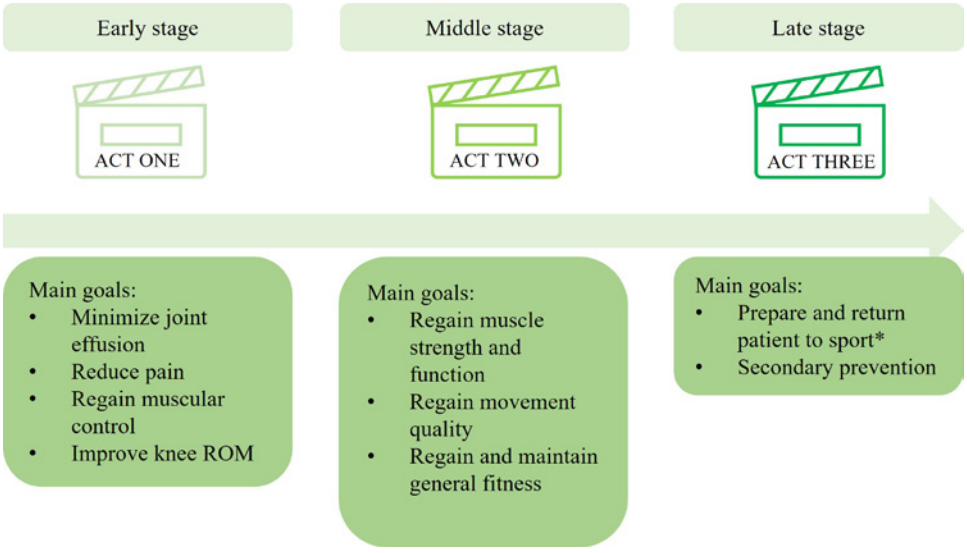


Figure 7: Brief illustration of possible rehabilitation stages for comprehension. ROM = range of motion; * = assuming this is the patient´s goal.

Early stage

In the first weeks after an ACL reconstruction, patients might present with significant impairments, such as limping due to pain, knee effusion, thigh muscular hypotrophy, and loss of neuromuscular control [66]. Patients might experience a wide range of psychological impairments in the period directly after ACL reconstruction, including depressed mood.[67] Symptoms might vary greatly from patient to patient, due to reasons including, but not limited to, choice of tendon to harvest for reconstruction. In this stage the rehabilitation goals are to minimize joint effusion, reduce pain, regain muscular control, and improve knee range of motion.

To improve knee range of motion and to reduce knee joint effusion, active exercises can be employed. Exercises such as unloaded knee flexion and extension sitting for instance on the floor where the heel can glide on the surface is an example. Such exercises should be performed several times a day. Patients who perform this kind of exercise should hold the maximal achieved flexion and extension several seconds before moving to the next repetition. While performing such exercises some level of pain can be tolerated but should not increase during exercises or after. Specifically, to reduce effusion, active muscular contractions are important to aid the venous system to pump the extra fluid to the lymphatic system. Exercises such as sitting knee extension, glute bridges (careful range of motion in case of hamstring graft harvesting) and continuous unloaded foot movements are examples of exercises that can be employed. Exercises for this purpose can be performed several times per day and ideally with large volumes. For instance, sitting knee extensions , which can be performed 30-35 repetitions in the currently available range of motion. As range of motion increases and swelling and pain decreases, active unloaded exercises can carefully be replaced by active loaded exercises with bodyweight or external weights. Examples of such exercises can be bodyweight squats, with eventually adapted range of motion, and/or leg press at a gym. When such exercises are implemented, exercise volume should be set low as to start with, for instance 2 sets of 8 repetitions. Pain and effusion need to be considered afterwards to ensure the affected knee can tolerate the new loading. In the improvement of knee range of motion, it is particularly important to focus on regaining full knee extension to allow for ambulation without limping.[66] To sit on the ground with as straight legs as possible (trying to extend the affected knee) with a pillow or a rolled blanket under the Achilles tendon can, thanks to gravitation, aid patients to regain extension quicker. However, in case of hamstring tendon harvest such position can stress the harvest site and should be performed carefully, for instance 3-4 sets of 2 minutes at the time with a rest of 2 minutes in between. In the past decades there has been a debate with regards to when it is safe to implement open kinetic chain exercises within rehabilitation after ACL reconstruction.[68] Some studies have suggested that to introduce open kinetic chain exercises too early might induce a graft elongation and consequently increased laxity later in rehabilitation.[69 70] However, the findings that open kinetic

chain exercises will lead to greater knee laxity have not been confirmed in a meta-analysis in 2018,[71] and were further refused in a cohort study in 2023.[72]

At clinical visits, for evaluation, range of motion can be assessed with a hand-held goniometer, swelling with the stroke tests, and pain with a scale such as the visual analog scale (VAS). On the VAS, on a 0-10 scale, pain during and/or after exercise should not exceed 5. (Figure 8).[73]

The stroke test (that is, brushing the patient´s knee on the medial side, distally to proximally a couple of times and then brushing laterally proximally to distally, in a downward motion to observe for waves of fluid) can be graded with 5 grades, and can aid to assess whether knee joint effusion has increased. The stroke test´s 5 grades[74] are:

- 0 – no wave produced with the lateral downward stroke
- Trace – small wave with the lateral downward stroke
- 1+ - large wave returns with lateral downward stroke
- 2+ - effusion spontaneously returns to medial side after upstroke (without lateral downward stroke)
- 3+ - so much fluid that it is impossible to move any of the effusion out of the medial aspect of the knee.

Another goal during the early stage is to re-gain muscular control. Muscular control is the voluntary ability to contract body muscles. Previously mentioned exercises performed as active exercises can aid for regaining muscular control as well. Further exercises that can be implemented are e.g. straight leg raises, side-lying hip abductions, prone hip extensions (careful range of motion in case of hamstring graft harvesting), or heel raises. Such exercises should be performed slowly, and patients should concentrate on muscular contraction while performing movements. Due to possible reduced neuromuscular control, and the low movement speed, these exercises can be challenging to perform. Accordingly, a lower training volume is a valuable option, for instance 3 sets of 6-8 repetitions, depending on each patient´s ability to perform the exercise.

Both the exercises used to minimize effusion, to regain range of motion and to regain muscular control, aid to reduce the pain, in absence of setbacks and in cases

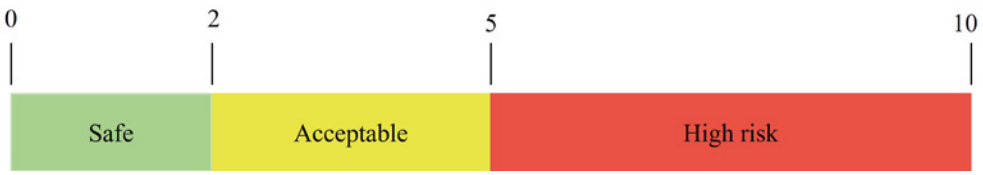


Figure 8: Pain monitoring model. Adapted from Thomeé el al.[73]

when pain increases. Further exercises that can be implemented to reduce pain in the early stage after an ACL reconstruction are isometric exercises. Exercises such as wall sit (with adapted range of motion), isometric glute bridges, and hold maximal achievable knee extension from a sitting position can be implemented. Ideally, holding position for 20-30 seconds can help to reduce pain, and 1-2 sets can be performed depending on patient´s ability.

In the early rehabilitation stage is very important not to increase symptoms such as pain or swelling. For the patient to train, without increased symptoms, the health care professional supervising rehabilitation needs to carefully plan the exercise volume. The goal is to achieve a "sweet spot" of training and rest that allows patients to perform exercises several times per day without increased symptoms.

However, there are cases in which active exercises cannot be performed due to the magnitude or exacerbation of symptoms. Moreover, some patients might struggle to activate lower limbs muscles after an ACL reconstruction due to "arthrogenic muscle inhibition".[75] Other types of treatment, such as aquatic treatment,[76] neuromuscular electrical stimulation (NMES),[77] or blood flow restricted training (BFR) can be employed in the early stage in patients who struggle to achieve progress. Aquatic treatment negates the effect of gravity and therefore can be implemented earlier than on land and allows the patient to perform movements in the water that would not be possible on land, and can for instance be important to aid patients in the recovery of normal gait. Additionally, if the water pressure is higher than the diastolic blood pressure, to immerge the body in water will aid to diminish knee joint effusion.[76] In patients who struggle to activate lower limb muscles NMES[77] can be used. The NMES involves using electrical stimulation to cause skeletal muscle contractions by directly stimulating peripheral nerves through the skin.[78] Protocols for the use of NMES vary,[77] but the treatment should comprise a frequency of 35-75 hertz, on intervals up to 15 second on, and up to 50 seconds off, several times a week for up to 6 weeks. Overall, NMES alongside with exercise might be more effective than exercises alone in improving quadriceps strength after ACL reconstruction.[77] Another treatment that can be used to achieve progression is BFR, which entails using an inflatable cuff or tourniquet positioned at the proximal end of an extremity, in this case the upper leg. The internal pressure of the cuff/tourniquet then is gradually increased, restricting arterial blood flow influx and venous efflux, usually at 80% arterial limb occlusion pressure.[79] Thus, BFR coupled with low-intensity resistance training can yield muscle adaptations as those observed in high-intensity resistance training.[80] To add BFR in early rehabilitation after ACL reconstruction has shown effects on muscle growth and strength comparable to heavy resistance training[81] This approach allows for training at a reduced intensity, minimizing stress, load, or discomfort on the knee joint, potentially leading to enhanced functional outcomes.[82] Training with BFR can already start in the first days after surgery. Published protocols vary greatly,[82] but a viable example can be that published by Lambert et al.,[83] where patients with BFR train 4 sets (30-15-

15-15 repetitions) with 30 seconds of rest between sets on several gym exercises such as knee extensions, curls and presses. BFR training can be performed for several weeks; for instance, 4-6 weeks. However, BFR does involve some potential side effects.[84] Tingling and delayed onset of muscle soreness have been reported to occur often, while rhabdomyolysis, fainting, and subcutaneous hemorrhaging less frequently.[84] Notably, rhabdomyolysis is the rapid break down of damaged skeletal muscles, and is a serious side effect.

During the early stage, core, hip and general strength exercises, such as push-ups, planks, sit-ups, rowing, pull-downs, shoulder press or interval training for arms on a stationary handcycle can be used to facilitate recovery and maintain general physical fitness. The eventual volume of such exercises should be adapted to the patient´s sport, pre-injury fitness level and goals. The healthy limb can be trained without restriction in order to achieve greater gains in the affected limb thanks to the cross-transfer phenomenon.[85]

During the early stage, not only pain, but range of motion and knee joint effusion should be considered. Continuous communication with the patient should be held to monitor for possible psychological impairment. Importantly, communication between the health care professional guiding rehabilitation and the patient should be performed in the best possible way,[86] as communication can affect treatment outcomes.[87] To communicate in the best possible way comprises several key components, such as: show respect and empathy, be genuine, be transparent, be concrete, check perceptions, have emotional intelligence, be specific, listen before you fix, value patient input, listen for the "but" and cooperate.[86 88] To show respect and empathy implies that the health care professional guiding rehabilitation needs to be open and welcome all possible questions. To do so, it is desirable to check patient´s perceptions, and to listen to those perceptions before important information are provided. Furthermore, by checking patient perceptions, the health care professional guiding rehabilitation can decide how and which information to provide to the specific patient, rather than to provide standard information. To decide what and how to say it, the health care professional guiding rehabilitation needs to have emotional intelligence, which then creates the base for a solid relationship with the patient. Then, when information is provided, the health care professional guiding rehabilitation should be specific, transparent, and genuine. This means to provide all information in a way that can be understood by the specific patient. In the communication, health care professional guiding rehabilitation should be open to welcome patient´s own input and cooperate with patients when the rehabilitation is outlined. Last, it is very important to listen for the "but". Be careful and listen if a patient says "I feel good, but…", and be ready to dig deeper in case this happens. An aid for the health care professional guiding rehabilitation to listen for the "but" are different questionnaires, where single questions might reveal some underlying psychological distress.[86 88] The key terms for good communication are summarized in a proposed "football team", where each term corresponds to a player position is outlined below (Figure 9).[86]

Figure 9: Key terms for communications, adapted from Piussi et al.[86]

Middle stage

Upon resolution of initial symptoms, patients move on to the middle stage of rehabilitation. Goals during this stage are to regain and eventually improve muscle strength, muscle function, muscle power, movement quality, and eventually general fitness, in case this is decreased after surgery.

To regain and improve muscle strength, function and power, a long period of strength training should be implemented. Concepts proper for strength training such as periodization and specificity can be adopted to tailor the strength training for every specific patient and situation, keeping in mind the pre-injury sport and trying to be as sport specific as possible.

Specificity in strength training refers to the principle that training should be closely aligned with the particular goals or activities an individual is aiming to improve. The concept of specificity is based on the idea that the body adapts to the specific demands placed upon it during exercise.[89] In other words, patients should train what it is aimed to be improved. Periodization in strength training refers to the systematic planning and organization of a training program into distinct phases or periods, each with specific goals and training parameters.[90] The aim is to help patients achieve quicker recover (compared with non-periodized strength training) by manipulating various training variables such as intensity, volume, and exercise selection throughout the training cycles. The different phases within a periodized program may include muscle hypertrophy, strength, power, and peaking phases, each tailored to address specific physiological adaptations. Common periodization models include linear periodization, where intensity increases and volume decreases over time, and undulating (non-linear) periodization, which

involves more frequent changes in intensity and volume within shorter time frames. The choice of periodization model depends on factors such as the athlete's experience, goals, and sport-specific requirements, as well as the prescribing health care professional guiding rehabilitation knowledge on the area. An example of linear periodization can be the following:

- A four-week cycle of hypertrophy. High training volume with sets and repetition around 3-4 x 12-15, ideally approximatively 50-60% of 1 repetition maximum (RM).

- A four-week cycle of strength. Training volume decreases, with sets and repetitions around 3-4 x 6-8, ideally approximatively 70-85% of 1 RM

- A three-week power cycle with a low volume and very high intensities. Training volume such as 4-5 sets x 2-4 repetitions, ideally in a pyramid manner: for instance, 2 sets of 4 repetitions, 2 sets of 3 repetitions, 2 sets of 2 repetitions and 1 set of 1 repetition with gradually increased weight when repetitions decrease.

Exercises such as front squats, back squats, Bulgarian split squats, lounges, leg extensions and leg curls, leg press, deadlifts and Nordic hamstring can be utilized. Importantly, all the mentioned exercises and periodization should be introduced and increased gradually. The main goal for rehabilitation is that the patient should recover, however, the main goal during rehabilitation is not to increase symptoms. Rapid increases in load and/or volume, that is, too much too soon, can increase symptoms such as knee effusion and pain. Thus, the health care professional guiding rehabilitation needs to carefully introduce new movements, gradually increase loads, and meticulously monitor symptoms such as pain and/or swelling. Another important aspect to consider for health care professionals guiding rehabilitation and patients is the between-sessions recovery. There is a relationship between overall training volume and risk for overuse and acute injuries.[91 92] Patients need to recover from the previous session before starting a new session, and pay attention to the fatigue that accumulates after several training sessions. If possible, 2-3 sessions a week of proper, dedicated strength training should be performed.

As defined by Buckthorpe,[93] movement quality is "the ability to control the limbs and achieve sufficient balance and kinematic alignment during functional activities, not displaying movement asymmetries or risk factors linked to ACL injuries". Patients who have undergone ACL reconstruction have demonstrated decreases in peak knee-flexion angle, external knee-flexion moment, and external knee-adduction moment during walking.[94] During jumping activities, individuals who have undergone ACL reconstruction exhibit a decrease in peak knee flexion angle and peak knee extensor moment, along with an increase in peak landing force asymmetry.[95 96] In particular, during vertical hops, these patients generate less force with the reconstructed leg compared to the uninjured leg.[97] Overall, individuals treated with ACL reconstruction display diminished movement quality, which

is influenced by a variety of factors such as personal attributes (e.g., sex and age), the specific task being performed, and environmental conditions (e.g., the type of surface, equipment used, and presence of obstacles).[98] To improve movement quality in patients who suffer an ACL injury, how complex a movement is should always be considered: a movement intended to increase movement quality needs to be challenging enough to stimulate motor learning, but not too challenging. As previously mentioned, training of movement quality should start at a basic level and successively increase. An example could be an exercise such as the lunge. Patients can be instructed to start performing lunges holding a stick behind the back with a relatively low speed and low volume, such as 2 sets of 10-12 repetitions. To increase difficulty, the same movement can be performed on an unstable surface. When this is tolerated by the knee, and the patient can properly perform the movement, a further increase could be to raise the training volume to 3 sets of 12 repetitions. Successively, a fourth set can be added, in which the patient must close his/her eyes. After a period of training, movement speed can be increased to raise the difficulty. Finally, after a strenuous 30-minute stationary bike session to induce fatigue, the lunge movement could be performed. Several factors can be manipulated to increase how challenging a movement is, including movement speed, surface, and fatigue. There is a lack of consensus with regards to how to evaluate movement quality after ACL reconstruction, both in terms of the specific tasks for assessment and the criteria that should be used to evaluate the quality of movement.[98] Moreover, the ideal standard for movement quality remains unknown, and it is uncertain whether there exists a universally accepted optimal movement pattern. Sometimes in patients treated with an ACL reconstruction, bad movement quality is visible: for instance, during a squat, as the knee flexion angle increases, patients might tend to shift the weight away from the injured leg, and accordingly the pelvis shifts laterally. In such cases, to film the patient performing the movement and then analyze the movement together can be a viable option for the patient to fully understand how to improve movement quality. The use of both verbal and visual feedback has been reported to improve the motor (re)learning experience.[99 100]

During the middle stage of rehabilitation, when patients approach symmetrical muscle strength, rehabilitation protocols should include exercises that prepare patients to run, such as small jumps and landing tasks, as well as repetitive low-load plyometric exercises such as jumping rope or step-up exercises. There are several proposed criteria that need to be achieved to allow patients to start running after an ACL reconstruction, including 70% quadriceps strength symmetry.[101] However, whenever a patient takes a running step, depending on the speed, the knee joint has to absorb a force equal to approximatively 5 times bodyweight.[102] Thus, if quadriceps has 70% of the possibility to help a knee absorb force, 70% symmetry can be questioned and may be regarded as too low. As for all other types of exercises and training, running needs to be successively introduced with very small volumes that successively increase as the knee joint, and the patients

appear to tolerate the new and increased load. This is especially true for running since running at low speed appears to result in a higher cumulative ground reaction force for the knees, compared with running at high speed.[103] Patients who resume running after ACL reconstruction are more likely to start run at low speeds. Intervals consisting of running and walking on a treadmill can be used to start. For example, 2 minutes running and 3 minutes walking times 4 would result in a cumulative 8 minutes running time.

In the middle stage of rehabilitation, if patients encounter difficulties training under high loads or face challenges in enhancing strength, like in the early stage, BFR training can assist. This method allows for training with lighter weights while still achieving adequate muscle activation. It facilitates more efficient motor neuron recruitment and the activation of type II muscle fibers.[104] Ideally, BFR training in the middle stage should be performed with more focus towards muscular exhaustion, that is, with higher volumes, compared with the early stage.

Overall, training during the middle stage should progressively increase demands on the knee joint and the muscles, in order to prompt an increase in strength and condition as an adaptation. Importantly, in the middle stage as well, knee symptoms such as pain and swelling should not increase. An increase in symptoms should be regarded as a set-back and rehabilitation should regress to find a proper training set-up and volume, which do not induce knee symptoms.

For evaluation, patients should be regularly evaluated with objective measures of muscle strength and muscle function. Commonly, isometric, or isokinetic tests are performed.[105-107] Results are generally presented as symmetry, with the Limb Symmetry Index (LSI), where a 90% has been proposed as successful outcome.[108] However, it is possible to achieve symmetry due to a loss of strength in the non-affected limb.[109 110] Consequently, absolute values should be taken into consideration as well, and whenever possible compared with pre-operative strength values.[106] Patient reported outcome measures (PROs), such as questionnaires can be employed to monitor patients´ self-reported knee function and psychological status. Out of 24 reported PROs in 2018,[55] the most common used in patients treated with ACL reconstruction were the IKDC and the KOOS. In the early stages, it is importnat to maintain open and honest communication, as previously mentioned, to guarantee that all factors significant to patients are assessed through the administered PROs or muscle function tests. To monitor patient´s recovery between sessions or within training periods, an adapted version of Borg´s rate of perceived exertion (RPE) scale can be used (Figure 10).[102] The adapted version is a scale where after a physical exertion, a person has to rate the exertion between 0 (rest; no exertion) to 10 (maximal exertion).[111] The RPE is a subjective measure used to gauge the intensity of physical activity. It is based on the sensations of efforts a person experiences during physical activity. The adapted RPE scale has shown good validity to measure training load, and correlates with other measures of training load such

as heart rate, VO_{2max} or lactate levels.[111] The adapted RPE scale has even been reported to be ecologically useful.[111] In this context, the term "ecological" is used in the sense of real-world, everyday situations as opposed to a controlled laboratory environment. In other words, how well the rating on a RPE scale aligns with the experiences of individuals in their day-to-day activities or specific contexts, and how applicable it is to real-world scenarios. Accordingly, the RPE scale covers factors other than the internal training load (lactate, VO_{2max}), but is even useful to monitor for external factors such as perceived stress. A patient who is stressed or anxious about his/her knee is therefore more likely to rate a high exertion for the same training load that would cause a medium exertion to a non-stressed or less anxious patient.

Rating	Description
0	Rest
1	Very, very easy
2	Easy
3	Moderate
4	Somewhat hard
5	Hard
6	
7	Very hard
8	
9	
10	Maximal

Figure 10: Adapted Borg Rate of Perceived Exertion scale. Visual representation altered from Foster et al.[102]

Late stage

Late-stage rehabilitation marks the culmination of a patient's journey post ACL reconstruction. The RTS stage (assumed this is the patients' goal), becomes the important point, emphasizing the significance of this transition in achieving full recovery. When strength values and movement quality are normalized, and repetitive plyometric movements such as running are well-tolerated by the knee, rehabilitation should focus on preparing patients to return to the pre-injury sport, and eventually return patients to sport. When patients RTS, this should be done with the lowest possible risk for a second ACL injury.

Exercises such as plyometrics (repetitive explosive resistance exercises which use the stretch-shortening cycle of the muscles and tendons fibers),[112] ballistics (exercises which accelerate a force through the entire range of motion),[112] change of direction, and exercises with external focus should be implemented for such aims. Merely engaging in strength training is insufficient for enhancing neuromuscular control in sports; instead, incorporating plyometric exercises is more applicable to athletic movements. Plyometric exercises, such as box jumps and lateral bounds, play a pivotal role in the late-stage rehabilitation. These dynamic movements enhance neuromuscular control, preparing individuals for the intricate demands of their specific sports. Rehabilitation protocols in this stage should incorporate both linear and multi-planar tasks.[113] Plyometric training involves the greatest external load for the specified task, along with joint-specific internal moments,

reactivity, muscle forces, and control challenges—each a vital component for active engagement in sports activities.[113] Examples of plyometric training are jumping circuits or several movements performed in quick succession, such as: running rush, a jump, and a running rush, performed as quickly as possible. Linear activities like sprinting build essential forward momentum, and additionally should be performed with focus on deceleration.[114] In fact, deceleration is very important in change of direction, and an inability to decelerate and reduce whole body momentum forward can have a major impact on the patient's performance,[114] and impact the risk of second knee injury.[115] Multi-planar tasks such as lateral shuffles, diagonal jumps and sudden changes of direction address the varied movements encountered in sports. Balancing these elements enhances overall agility and stability.

As described for the middle stage, exercises should progress in terms of how difficult they are, and accordingly limitations regress. In this stage it is important to adapt training to the specific sport requirements for each unique patient, in other words, individualize. One requirement in most sports is general fitness and condition. Several training variables such as volume and intensity can be modified to enhance general fitness and condition. Training sessions consisting of both some strength training, some condition training and some reaction training can be introduced to mirror the requirements of a sport situation e.g. a football match. An example of a training session comprising strength, condition and reaction can be:

1) A generic warm-up of 15 minutes
2) Strength: Superset of leg extensions and leg curls, 4 sets of 10 repetitions;
3) Strength: Plyometrics Bulgarian split squats in a smith machine, 3 sets of 30 second each leg.
4) Condition: Intervals on an assault bike: 30 seconds at very intensive level, 60 seconds' rest. 10 sets
5) Reaction: 2 sets of 5 minutes of quickly reacting to a verbal command and touching a marker on the floor (such as the "Blazepods"™)
6) Reaction: 2 sets of 5 minutes of a sport specific drill. For football, for instance: with a ball the patient receives a pass and a verbal command and must quickly turn and move towards a marker on the floor (specified in the verbal command).

While RTS has been described as a continuum starting the day of injury,[116] and not a specific dichotomous time point (Figure 11), patients can now be allowed to train the specific sport with certain limitations, depending on knee status and specific sport demands.

While some patients want to be a part of the team even when injured, not all patients might feel that way, and consequently, a judgement of when patients can start training with the team needs to be made in every specific case. In cases where patients resume training the sport they aim

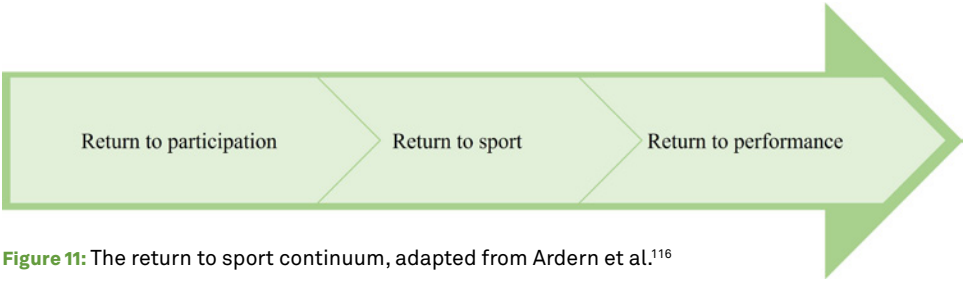


Figure 11: The return to sport continuum, adapted from Ardern et al.[116]

to return to with limitations (in football, only training passing drills but not situations where contact can occur), communication between the health care provider, and the staff responsible for the training is of primary importance. Professional football teams with perceived bad communication between medical staff and trainers suffer from significantly higher injury burden and therefore less player availability.[117] Accordingly, athletes caught between a medical staff and trainers that do not communicate well have impacted possibilities of recovery. One important aspect to consider when patients approach returning to the pre-injury sport is whether patients feel ready to do so. Patients might feel pressure and expectations to RTS from other people such as trainers, friends or family members, or economical pressure, in case of elite athletes or athletes with sponsorships. However, patients who RTS after an ACL reconstruction consistently report lack of confidence, self-limiting tendencies, and not to feel ready to RTS.[114 118] Patients who RTS without feeling prepared may, therefore, expose themselves to an increased risk of a second ACL injury.[114] As discussed in the early and middle stages of rehabilitation, open, clear and honest communication between the health care providers and patients is extremely important during rehabilitation and when about to resume the pre-injury activity.

In order to evaluate patients prior RTS, different criteria and tests have been proposed.[119] Despite no consensus on which criteria should be adopted, generally, different batteries of muscle function tests, PROs and scores on movement quality tasks are recommended,[120 121] but rarely used. In 2019 time from surgery and impairment-based measures were the most used RTS criteria.[122] To pass RTS test batteries has not been proven to lower the risk of a second ACL injury,[119] and consequently further research is needed to establish tests which can help clinicians reduce the risk of second ACL injury.

Inquiry:
The association between adding psychological questionnaires to RTS test batteries and the risk for second ACL injury

Inquiry:
The best cut-off values on questionnaires used to evaluate patients who suffer an ACL reconstruction that can differentiate patients who suffer a second ACL injury from patients who do not

A novel approach in the evaluation of patients following ACL reconstruction at the time of RTS involves on-field testing. One such example can be seen in football, where the evaluation of change of direction (COD) performances has gained some attention in the literature. It is noteworthy that within football, COD actions are commonly identified as the primary mechanisms leading to ACL injuries,[123] and accordingly, the assessment in RTS setting should be logical. The key to executing a COD maneuver without the risk of sustaining an ACL injury lies in the effective deceleration and reduction of horizontal body momentum during sprinting.[115] This critical skill is pivotal for athletes aiming to perform COD actions safely, that is, with minimal risk of an ACL injury.[115] Despite the importance of COD performance, there is currently limited evidence and few recommendations available.[124] Two recognized COD tests that aim to replicate on-field demands, including maximal linear sprinting, powerful horizontal deceleration, and COD ability, are the 505-agility test and the 90˚ cut test.[125 126] These tests offer valuable insights into an athlete's readiness to engage in activities involving dynamic movements, helping clinicians make informed decisions during the rehabilitation process. Unfortunately, one limitation relates to the clinical setting in which tests are performed. Not all health care professionals guiding rehabilitation have access to testing equipment and the space and conditions (such as non-slippery floor) required to perform the 505-agility test and the 90˚ cut test.

Psychology of injury

As the journey through the intricate web of rehabilitation unfolds, the recovery process extends beyond mere physiological adjustments. The meticulous focus on strengthening, movement quality, and general fitness lays the foundation for rebuilding the injured knee. Simultaneously there is an ongoing interplay between the body and mind. The interaction between the tangible aspects of recovery to the intangible terrain of psychological variables marks a pivotal juncture in the rehabilitation process. In the forthcoming exploration, the intricate connections between mental resilience, emotional well-being, and the ultimate restoration of holistic health after ACL reconstruction are discussed.

Practicing sports is a common way of being physically active. Sports injuries impact people's ability to be physically active and can have long term consequences if the injury is not properly treated. Within a bio-psycho-social perspective, a sport injury should not be seen only as a biological tissue damage. Patients' perceptions and experience of such damage can largely impact the recovery process. In fact, psychological and social/contextual factors are believed to impact rehabilitation outcomes, with inferior psychological results associated with less favourable rehabilitation outcomes following ACL reconstruction.[127]

Every sport injury has physical and psychological consequences for the injured individual. Psychological consequences include, but are not limited to, high stress level, perception of pain, sense of loss,

sadness, fear, anger, grief, frustration, anxiety,[128] and can lead to reduced levels of psychological wellbeing.[129] The ability of each unique individual to cope with psychological consequences of a sport injury will influence the likelihood of the injury and recovery experience to be perceived as positive (opportunity for growth and development) or negative.[130] To describe psychological response to a sport injury, several models have been developed. One example is Wiese-Bjornstal's[131] integrated model of psychological response to injury and rehabilitation (Figure 12). According to the model, psychological responses to a sport injury can be cognitive, emotional and behavioural.[131] Also, it is highlighted that the psychological responses to a sport injury are dynamic, change over time, and are individual, i.e. every person reacts differently. In the psychological response to a sport injury, each injured individuals personal and situational factor act as moderators.[131] Personal factors that act as moderators include personality traits, coping styles, and experiences of previous injury. While situational factors are the severity and type of injury, the social support received and the athletic identity. Wiese-Bjornstal's[131] model is circular and dynamic, where "*all [components of psychological response to injury] are inter-related, cyclic, spiralling, dynamic, and recursive in their influences on each other and on short- and long-term outcomes through biopsychosocial pathways*" [131].

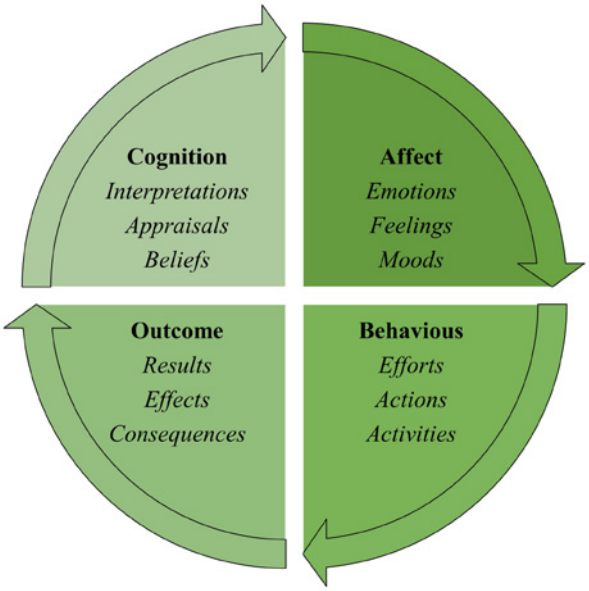


Figure 12: The integrated model of psychological response to injury and rehabilitation. Adapted from Wiese-Bjornstal's.[131]

Another example is the biopsychosocial model of sport injury rehabilitation, which focuses on the psychological aspects during sport injury rehabilitation as well.[127] Hence, the specifics of an injury, such as the severity and where it occurs, together with demographic details like age and sex, have the potential to influence biological processes (e.g., how tissues repair), psychological aspects (including personality traits, emotional states, and behaviours), and social or contextual dynamics (such as the strength of social connections or levels of life stress).

Psychological factors in the context of sports injury rehabilitation can be regarded as the emotional, mental, and behavioural aspects that can influence a patient's response to the injury and recovery process. Importantly, psychological factors are subjective, and have a wide spectrum: patients during rehabilitation after a sport injury such as an ACL injury may traverse a diverse range of psychological dimensions, from struggling with simple negative thoughts such as self-doubt and anxiety to navigating the challenges of lack of motivation and resilience. Moreover, the spectrum of psychological factors can extend beyond momentary struggles, potentially including issues such as identity crises, fear of movement or performance, and even clinical conditions like depression. A patient can be somewhat angry due to his/her knee injury or develop a serious depression with eating disorder. Some psychological factors that patients can experience after an ACL reconstruction include, but are not limited to, emotional responses; cognitions such as motivation, self-efficacy, and confidence; as well as locus of control; and behaviours such as coping.

After treatment with ACL reconstruction, patients can experience several different emotional responses. Commonly, emotional responses after the occurrence of an ACL injury are negatively loaded. Directly after an injury, patients have been reported to experience i.a. frustration, shock, tension and anger.[132] [133] During rehabilitation, fear and anxiety related to the injury, the consequences, and the potential re-injury[134] have been reported, alongside with frustration and anger: to deal with the limitations imposed by the injury can make patients feel frustrated about not being able to participate fully in their sport or angry about the circumstances of the injury.[135] As patients approach their RTS, many cite fear of re-injury as a primary factor deterring them from the resumption of athletic activities.[134] Patients treated with ACL reconstruction indicate that psychological hurdles outweigh physical challenges throughout the rehabilitation process.[118]

Inquiry:
Sport physiotherapists own experiences of addressing psychological factors during rehabilitation after an ACL reconstruction.

Further emotional responses experienced by patients after ACL reconstruction include feeling of uncertainty towards recovery,[136] and lack of confidence towards future sports.[137] Negative emotional responses tend to be associated with more negative outcomes after an ACL reconstruction, and conversely, more positive emotional

responses appear to be associated with a facilitation of recovery.[138] The psychological impact of an ACL injury has been reported both as an U-shaped curve: highest just after time of injury, and again around the time of RTS,[132] or as linearly increasing over time,[137 139] which is important because psychological factors are modifiable and have the potential to enhance rehabilitation outcomes after the ACL reconstruction.[140] In terms of the psychological impact an injury can have on a patient, athletic identity needs to be mentioned. Athletic identity is the degree of personal connection to the sport and is a personality trait. Higher levels of athletic identity can be protective of burnouts or increase motivation towards rehabilitation,[141] but might as well increase the risk of depression if an athlete suffers a injury.[142] Interestingly, individuals who have higher level of play in any sport during adolescence, tend to develop stronger senses of athletic identity.[142] Athletes derive a significant portion of their identity from their involvement in sports. An ACL injury can lead to a loss of the individual's active role within the team or sport, and a shift in how the individual perceive himself/herself. The loss of an active role can contribute to feelings of emptiness, a diminished sense of purpose, and challenges in reconciling the individual's identity beyond the athlete role.[143 144] In some cases, athletes may experience an identity crisis as they grapple with the shift from an active, competitive athlete to someone temporarily sidelined by injury. To cope with this identity crisis can be challenging, and athletes may need proper support to explore and redefine aspects of their identity. Moreover, limited participation in regular team activities, can lead to feelings of isolation. Patients may feel disconnected from their team and social circles, potentially leading to feelings of loneliness and withdrawal. This isolation can impact mood and contribute to mental health challenges.

Inquiry:
The prevalence and severity of negative psychological response following an ACL injury.

During rehabilitation it is important for patients to find the strength to carry out their rehabilitation and to put down all the effort needed to complete the entire process. Thus, patients need motivation, that is, the energizing of behaviours in pursuit of a goal.[145] A lack of motivation affects the possibility of fulfilling the rehabilitation.[146]

One important motivational theory that can aid health care professional guiding rehabilitation and healthcare professionals working with patients treated with ACL reconstruction is the Self-Determination Theory.[147] Self-Determination Theory is a psychological framework that explores human motivation and how individuals satisfy their basic psychological needs. The theory proposes that people are driven by three innate psychological needs: autonomy, competence, and relatedness.[147] In the context of sport injuries, Self-Determination Theory offers physiotherapists and healthcare professionals valuable insights, demonstrating how fulfilling basic psychological needs—namely autonomy, competence, and relatedness—can enhance intrinsic motivation. Intrinsic mo-

tivation, in turn, is associated with positive effects on behaviours, including improved performance, well-being, and the adoption of personally meaningful actions. Thus, by making sure patients who rehabilitate after ACL reconstruction satisfy their needs of autonomy competence and relatedness, physiotherapist, and health care professionals can enhance the experience of the rehabilitation process, and possibly achieve positive outcomes. Autonomy refers to the need to feel in control of both one's actions and decisions. In the context of sport injuries, autonomy involves giving patients the opportunity to make choices, involving patients in decision-making regarding their rehabilitation. Patients who feel they have control over their rehabilitation process are more likely to be motivated and engaged. Competence refers to the desire to feel proficient and skilled in engaging with one's surroundings. In terms of sports injury rehabilitation, competence involves setting but foremost achieving goals. As such, it is important to receive feedback on progress for the patients, and for the physiotherapists and health care professional guiding rehabilitation it is important to ensure that athletes experience success in their rehabilitation tasks. To enhance competence, a physiotherapist or health care professional guiding rehabilitation could provide a patient with a "simple" physical task as a goal. When the simple goal is achieved, the patient could experience a cascade of positive psychological responses. It should be kept in mind that the task needs to be somewhat challenging, and not too simple. If the task is too simple, the patient might not feel motivated to achieve the goal. Thus, creating rehabilitation plans that challenge patients but also acknowledge and celebrate incremental successes helps fulfil the patient´s competence needs. Relatedness is the need for social connections and a sense of belonging. In the context of sport injuries, relatedness involves maintaining positive relationships with teammates, coaches, and healthcare providers, and feeling supported throughout the rehabilitation process. To foster a supportive and connected environment is crucial. Social support, teamwork, and communication help fulfil the relatedness need, reducing feelings of isolation and contributing to the patient´s overall well-being. According to the Self-Determination Theory, motivation can be seen as both intrinsic and extrinsic [146], but the theory proposes a continuum of motivation, with intrinsic motivation at one end and extrinsic motivation at the other. The control and regulation of motivation is influenced by different factors or mechanisms explained by the theory.[148] Intrinsic motivation refers to the patient´s inherent desire to achieve personal goals, and it is a powerful psychological factor. Intrinsic motivation can drive commitment to the rehabilitation process. Extrinsic motivation refers to all the external sources, such as support from coaches, teammates, or family that can influence a patient´s motivation (Figure 13). Different factors and mechanisms that regulate motivation include external regulation, introjection, identification, and integration. Regarding external regulation, individuals participate in activities purely for the sake of external incentives or to evade penalties. In terms of introjection, motivation is driven by internal pressures proper for the individual, such as the desire for approval or avoiding guilt or

shame. Introjection involves internalizing external expectations or standards as one's own, leading individuals to engage in activities not necessarily for the activity´s intrinsic value, but to meet the internalized pressures. In terms of identification, the motivation is more autonomous, and individuals recognize the importance of an activity and willingly engage in it for personal values. When it comes to integration, which is the most autonomous form of extrinsic motivation, external activities are fully assimilated into an individual's sense of self (Figure 13). Within the Self-Determination Theory, the goal is to move individuals toward more autonomous forms of motivation, emphasizing intrinsic motivation when possible. The process of internalization involves individuals taking in external motivations and gradually integrating external motivations into individual´s sense of self.

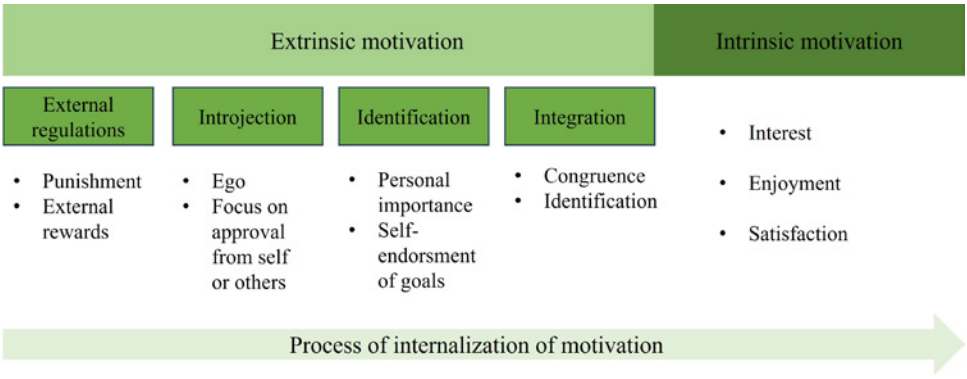


Figure 13: Intrinsic and extrinsic motivation. Adapted from Ryan and Deci.[148]

Taken together, understanding Self-Determination Theory in the context of sport injuries can contribute to a more holistic and athlete-centred approach to rehabilitation. By addressing the fundamental psychological needs of autonomy, competence, and relatedness, physiotherapists and health care providers can enhance intrinsic motivation, promote well-being, and optimize the rehabilitation experience for injured athletes. Consequently, a proper treatment should focus on the biological tissue damage, the psychological impact of the injury, and the injury's consequences in a social perspective.

Self-efficacy pertains to an individual's confidence in their ability to perform actions required to achieve specific outcomes.[149] In the context of rehabilitation following ACL reconstruction, self-efficacy plays a critical role, encompassing the patient's confidence both in their capability to successfully navigate the rehabilitation journey and in their ability to execute physical activities, such as jumping or running. Conversely, a deficiency

in self-efficacy can negatively influence the results of treatment.[150] Self-efficacy can sometimes be interchanged with confidence. Confidence refers to a retrospective meta-cognitive judgment, while self-efficacy refers to a prospective judgement of one's ability.[151] A meta-cognitive judgement refers to a reflective assessment or evaluation of one's own thought processes, knowledge, and abilities for a given situation. Therefore, when confidence is described as a retrospective meta-cognitive judgment, confidence is derived from looking back at past experiences and assessing one's own ability to have dealt with those situations successfully. For a patient who has been treated with ACL reconstruction, confidence is an important psychological factor alongside self-efficacy. Confidence, in the context of sports injury rehabilitation, relates to a patient´s trust or belief in the overall athletic abilities, including the ability to perform well in the sport despite the injury. Confidence extends beyond the specific tasks associated with rehabilitation, for which self-efficacy is important, to encompass a broader sense of competence.[151]

Locus of control has been defined as an individual's perception about the underlying main causes of events in his/her life,[152] and can be further divided intro internal or external locus of control. Patients who possess an internal locus of control attribute events to their own actions, whereas patients with an external locus of control attribute occurrences to factors like luck, chance, or the actions of others.[152] In terms of sports injury rehabilitation, the locus of control becomes relevant because it shapes an athlete's mindset and approach to the rehabilitation process. An internal locus of control is generally associated with a more proactive and determined attitude,[153] [154] contributing to better adherence to rehabilitation plans.[155] Conversely, an external locus of control may lead to a more passive or resigned attitude, potentially impacting an individual's commitment to the rehabilitation journey. Physiotherapists and other healthcare providers can work to foster an internal locus of control in patients by emphasizing their role in the rehabilitation process, providing education related to the benefits of adherence to protocols, and empowering patients to take an active role in their recovery.[156]

Coping can be defined as the use of cognitive, affective or behavioural efforts to effectively deal with imposed events that generate stress, such as an ACL injury.[157] Coping with the stress generated by an event such as the ACL injury is an important aspect of sports injury rehabilitation, and patients can employ various coping strategies to manage the physical, emotional, and psychological challenges associated with the injury. Techniques such as relaxation, visualization, coping modelling and goal-setting might help athletes manage stressors associated with the injury itself.[158] [159]

Social supports plays a fundamental role in how well a patient cope with a stressful situation, such as the ACL injury and rehabilitation process.[160] According to the American Psychological Association´s dictionary of psychology,[161] social support is "*the provision of assistance or comfort to others, typically to help them cope with biological, psychologi-*

cal, and social stressors. Support may arise from any interpersonal relationship in an individual's social network".[161] Social support can have many different dimensions, and different patients might need different kinds of social support.[162] Emotional support involves the provision of empathy, understanding, and encouragement. Teammates, friends, and family members can offer a listening ear, express empathy for the patient's challenges, and provide emotional reassurance during the rehabilitation journey. On the other hand, instrumental support involves tangible assistance or practical help. Friends or family members can for instance aid with daily tasks, transportation to medical appointments, or help with rehabilitation exercises. Within the realm of social support, it is important to understand that sports injuries can sometimes lead to feelings of isolation, especially if an athlete is temporarily removed from the team or training environment. Social support mitigates this isolation by maintaining social connections and preventing feelings of loneliness.[162-164] However, some patients have expressed their dislike for being injured and attending training with teammates, as it worsens the sense of injury and isolation.[114] Consequently, it is very important for health care providers to check patients perception and listen to what kind of support the individual patient needs, rather than to provide a standardized form of support.

Every person possesses distinct psychological characteristics that significantly influence their reaction to sports injuries. These factors act as moderators, determining the nature and intensity of psychological reactions following sport injuries such as ACL injury.[165] Different personality traits, coping strategies, feelings, and behaviours characterize individuals and profoundly shape how individuals perceive, interpret, and engage with the world around them. The influence of personality traits is profound, and various personality traits emerge as pivotal determinants. Traits such as optimism or pessimism, resilience, type A/B personality (A = aggressive, ambitious, competitive; B = relaxed, less stressed, laid-back), and introversion/extroversion significantly affect a patient's coping strategies, emotional responses, and overall adaptation to the rehabilitation process.[166-168] The dichotomy between optimistic and pessimistic traits, for instance, can sway the patient's outlook on the recovery journey, and influence motivation and perseverance. Different personality traits highlight the necessity for tailored approaches to social support, and necessitate varied forms of assistance, emphasizing the importance of understanding and catering to individual needs. Besides personality traits, several other factors can act as mediators in influencing how an individual experiences psychological factors after a sports injury, including nature and severity of the injury, expectations and beliefs, and cultural and social influences.

Taken together, psychological factors play an important role in the overall rehabilitation process, but are subjective, vary in intensity and time, and interplay with each other and with physical factors in a complicated manner. Each person's journey is unique, and a holistic approach to address the various factors is essential in promoting effective rehabilitation and recovery.

The second injury

Even with extensive research conducted on ACL injuries and their treatments, the rate of second ACL injuries following an initial ACL reconstruction remains alarmingly high, with reported prevalence ranging from 3-38% (Table 1). This variation is influenced by factors such as the patient's sex, age, level of activity, and whether the subsequent injury occurs on the same side (ipsilateral) or the opposite side (contralateral). The second injury occurs at a median time of 20 months after primary ACL reconstruction.[169] Table 1 summarizes several of the most recent studies reporting the prevalence of second ACL injury.

Table 1: Examples of studies reporting prevalence of second ACL injury. Where ipsilateral and contralateral is not specified, overall % rate is presented.

Author	Year	Details	n	Second ACL injury, %
Wright et al. [170]	2011	Systematic review	2026	Ipsilateral 5.8%; Contralateral 11.8%
Bourke et al. [171]	2012	Case series	673	23%
Wiggins et al.[172]	2016	Systematic review	72054	Overall 15% Ispilateral 7% Contralateral 8%
Nawasreh et al. [169]	2019	Systematic review	23579	Overall 6.11% Ipsilateral 3.29% Contralateral 2.82%
Webster et al.[173]	2021	Athletes younger than 20 years	128	34%
Patel et al.[73]	2021	Systematic review	2944	21.9%
Paterno et al.[174]	2022	Cohort study	159	22%
Van Melik et al.[175]	2022	Cohort study	144	5%
Fältström et al.[176]	2023	Cohort study	112	38%
Almeida et al.[177]	2023	Cohort study	88	14.9%
Di Zhao et al.[178]	2023	Systematic review	629219	3%
Zsidai et al.[179]	2023	Cohort study	153	7%
Marigi et al.[180]	2023	Cohort study	344	17%
Simonson et al. [181]	2023	Cohort study	835	8.3%

n = number

Risk factors for second ACL injury

The risk for second ACL injury is a complex equation that depends on many factors, which include genetic, physical, psychological, trauma, and surgical factors.[182-185] In each individual patient these factors may weigh differently, contributing to the complexity of the risk profile. Individual risk factors are disclosed in detail in the following paragraphs.

Biologic and intra-operative risk factors

Biological factors such as age matter for a second ACL injury risk: individuals under 18 [186] or under 25 [184] years of age face a higher risk. Patients sex is also a risk factor, as some studies suggest a higher risk for females [187], although the effect size is small,[73] and in some studies patients sex alone did not influence the second ACL injury risk.[188] The choice of graft material for reconstruction, such as HT autograft versus BPTB autograft, further adds to the complexity.[189 190] Inconsistencies arise as different studies report different outcomes in regard to graft survival and subsequent injury risk, where some studies report lower risk of revision with BPTB autografts compared with HT, but increased risk for contralateral ACL injury.[191 192] Body mass index (BMI) is another variable, with conflicting reports on its association with revision surgery.[193 194] The presence of cartilage injuries alongside the initial ACL injury might reduce the risk of sustaining a subsequent ACL injury.[188 195] In addition, joint hypermobility has recently been linked to a fourfold increase in the risk of a second ACL injury, regardless of graft choice.[179]

Rehabilitation-specific risk factors

The literature presents conflicting evidence regarding the link between physical variables, like muscle strength or hop performance, and the risk of a second ACL injury. No association between symmetrical muscle strength in quadriceps or hamstring and ipsilateral second ACL injury has been reported in several studies.[60 196-198] On the other hand, patients with higher absolute strength (measured as peak torque) in quadriceps, and patients not symmetrical in quadriceps and hamstring have been reported to be at higher risk in other studies.[105 180] A study found that increased relative quadriceps strength in the injured leg suggested a higher risk of a second ACL injury, although this risk diminished when patients achieved symmetrical muscle strength.[181] Simultaneously, it was noted that patients who experience a second ACL injury on the contralateral side exhibit lower quadriceps strength in that contralateral limb.[197] Executing an effective deceleration involves the application of high eccentric force in the knee extensor moment and rapid adjustments in movement speed. The combination of an eccentric knee extension moment with specific body positions, such as lateral trunk flexion, hip abduction with a wide foot-plant, rearfoot landing, and the knee close to full extension, amplifies the susceptibility to dynamic valgus and internal rotation. These biomechanical factors increase the risk of ACL strain and potential rupture.[199 200] Intense eccentric actions impose a considerable demand on the activation of high-threshold motor neurons.[201] After an ACL injury, negative alterations in the excitability of the spinal-reflex and corticospinal pathways occur,

which result in a diminished voluntary activation of high-threshold motor neurons. This reduction in activation contributes to a diminished ability to generate supramaximal eccentric actions.[202] In addition to diminished motor neuron activation and the contribution of anatomical, biomechanical, and environmental factors to the risk of a second ACL injury, it is crucial to acknowledge the impact of decreased capacity for force development (both concentric and eccentric) during COD movements, which are pivotal in sports with a high risk of ACL injuries, like football. A diminished capacity for quick force generation during COD movements can affect overall sports performance and significantly contribute to the increased likelihood of experiencing a second ACL injury following ACL reconstruction. This emphasizes the importance of comprehensive rehabilitation strategies that not only address structural considerations but also focus on optimizing neuromuscular function, particularly in scenarios requiring rapid force development.[203]

Psychological risk factors

Psychological factors are well-linked with risk of sustaining sports injuries, such as an ACL injury: how we perceive and react to stress has been shown to be associated with injury risk.[204] Research efforts have been made to explore the association between PROs and the occurrence of a second ACL injury, particularly among patients who have undergone ACL reconstruction. The ACL Return to Sport after Injury scale (ACL-RSI) is frequently employed to connect PROs to the risk of a second ACL injury, though the findings have yet to yield definitive conclusions. In 2019 McPherson et al.[205] observed that individuals who experienced a second ACL injury scored lower on the ACL-RSI. Conversely, different outcomes were observed among female athletes.[206]

Inquiry:
The association between psychological factors and second ACL injury risk

Contextual risk factors

Time intervals significantly influence the likelihood of experiencing a second ACL injury. The time between injury and reconstruction, specifically under 12 months, has repeatedly been linked to an increased risk for second ACL injury.[193 195 207] Furthermore, the time period from reconstruction to RTS may also impact the risk of incurring in a second ACL injury. However, the link between time between reconstruction and RTS is not well supported in the literature and a systematic review is needed. To RTS less than 9 months following ACL reconstruction has been linked to an increased risk of a second ACL injury, though these findings have not been consistently confirmed across studies.[60 105] Besides time to RTS, to actually RTS after ACL reconstruction has been linked to a higher second ACL injury risk, together with being active to a higher degree before index ACL injury (≥7 vs<7 on the Tegner Activity Scale) [208].

Numerous attempts to isolate individual risk factors have been made, without a conclusive result. Due to the complicated interplay of possible risk factors, a Swedish study aimed to identify a comprehensive clinical risk profile for a second ACL injury. The

results underline the intricate interaction between clinical, demographic, physical, and psychological factors which contribute to the overall risk. Notably, factors like hop length may exhibit varying associations, posing higher risks in some individuals and lower risks in others.[185]

Inquiry:
Experiences of patients who suffer two ACL injuries and are treated with two ACL reconstructions

Rationale for this thesis

The time required for the ACL to take load and eventually rupture varies between 0 and 61 milliseconds after initial contact.[209] As outlined in the introduction, the impact of an ACL tear, which occurs in a moment, can last a lifetime. Soon after the injury, patients—frequently young individuals at the peak of their physical activity—must confront significant challenges. These challenges include pain, fear, questioning personality, and sudden perceived weakness. Challenges can take a brutal amount of time to be dealt with and to resolve if they do. After these challenges, patients stand against a further massive confrontation: the risk for a second ACL injury. There is limited and conflicting findings on the association between psychological outcomes after ACL reconstruction and risk for second ACL injury. Thus, further research on the psychological impact of an ACL injury is needed, with particular emphasis on the possible link between the psychological impact of the first injury, and the risk for a second ACL injury.

Despite the extensive research dedicated to ACL injury and its treatment, the achievement of optimal outcomes for patients who experience a second ACL injury remains a challenge. Understanding the intricate puzzle of factors which all contribute in one way or another, to a second ACL injury, uniquely composed for each individual, is paramount. However, one crucial aspect that demands more attention is the psychological dimension. The current knowledge provides valuable insights into biological, biomechanical, and surgical factors associated with second ACL injuries. Yet, the psychological realm, a complex and influential aspect of an individual's response to injury and rehabilitation, remains relatively unexplored. Delving deeper into the psychological factors surrounding a first and a second ACL injury is an important part of the work needed to enhance care for affected patients. Researchers and health care providers, including physiotherapists, strive for comprehensive patient-centered care from a bio-psycho-social perspective. Therefore, recognizing the importance of mental factors in the realm of ACL injuries is crucial. Addressing psychological aspects following ACL reconstruction can play a key role in mitigating the risk of experiencing another ACL injury and could also aid to foster resilient and empowered individuals, which is one of the goals that physiotherapists and health care providers have with rehabilitation. In conclusion, a deeper dive into the psychological dimensions of primary and second ACL injuries is an opportunity for researchers, physiotherapists, and health care providers to improve patient care. The journey towards optimal outcomes for patients who suffer an ACL injury necessitates

a thorough exploration of the psychological landscape, shaping the future of ACL injury research and patient care.

The specific inquires highlighted in the introduction were:

- What do physiotherapists know about psychological factors during rehabilitation after an ACL reconstruction? (addressed in Study I)
- What is the prevalence and severity of negative psychological response following an ACL injury? (addressed in Study II)
- How are psychological factors related to a second ACL injury risk? (addressed in Study III)
- Can the adding of psychological questionnaires to RTS test batteries lower the risk for second ACL injury? (addressed in Study IV)
- Which cut-off values on the questionnaires used to evaluate patients who suffer an ACL reconstruction can differentiate patients who suffer a second ACL injury from those who do not? (addressed in Study V)
- What are the experiences of patients who suffer two ACL injuries and are treated with two ACL reconstructions? (addressed in Study VI)

Collectively, the purpose of this thesis was to investigate and better understand the psychological outcomes of patients after ACL reconstruction, and possible associations with a subsequent second ACL injury.

Aims

Overall objectives

The overall objective of this thesis was to investigate and better understand the psychological outcomes of patients after ACL reconstruction, and possible associations with a subsequent second ACL injury. Investigations covered understanding sports physiotherapists' experiences, exploration of self-reported psychological factors from the patients themselves, integration of psychological measures into return-to-sport assessments, differentiation of patient reported outcome measures in patients with and without second ACL injuries as well as patients´ own experiences.

Specific aims

Study I

The aim was to explore and gain a deeper understanding of sports physiotherapists' experiences of working with psychological impairments in patients treated with ACL reconstruction.

Study II

The aim was to investigate the prevalence of self-reported negative psychological factors, such as, symptoms of depression and anxiety in patients who suffered an ACL injury. A further aim was to investigate the severity of self-reported symptoms of depression and anxiety in the same patient population.

Study III

The aim was to study self-reported psychological outcomes and strength outcomes in patients treated with ACL reconstruction, prior to suffer a second ACL injury. A further aim was to compare self-reported psychological outcomes and strength outcomes with a matched cohort of patients who did not suffer a second ACL injury within the initial 2 years after primary ACL reconstruction.

Study IV

The aim was to integrate scores on psychological patient reported outcome measures into physical return to sport test batteries, and to determine if successfully completing tests that include both physical and psychological measures was linked to the risk of sustaining a second ACL injury.

Study V

The aim was to calculate which score on commonly used patient-reported outcome measures would best differentiate between patients who sustain a second ACL injury and patients who do not in the first 2 years after return to sport. A further aim was to perform the same assessment in patients who achieved symmetrical muscle function after ACL reconstruction.

Study VI

The aim was to explore and gain a deeper understanding of the experiences of young active women who wanted to return to sport and suffered a second ACL injury after treatment with ACL reconstruction.

Methods

"...cerco un centro di gravitá permanente, che non mi faccia mai cambiare idea sulle cose sulla gente..."

Method background

Theory of science

Science is a methodological and structured way of obtaining knowledge. There are two important concepts within science: ontology and epistemology. Ontology comes from the Greek word for "being" and "explanation" and means the explanation of being. In other words, ontology refers to what we know, how we perceive, and what is the world. Epistemology comes from the Greek word for "knowledge" and "explanation" and means the explanation of knowledge. In other words, the theory of knowledge: how do we know what we know. Two main approaches were derived in 1800 Europe within epistemology: empiricism and rationalism. Rationalism key concepts are that people can learn about the world around them through the use of rational thought. The famous "*cogito ergo sum*" (I think, therefore I am) was developed from that standpoint.[210] Empiricism is the theory that all knowledge is based on the experiences derived from the senses. Empiricists reject the thesis that the rational reason should be superior.[211] Rationalists might criticise empiricists and vice versa, while experiences can be of two types: the ones that involve our five senses and connect to the world around us, and the ones that involve rationale reason and are about what's happening in our minds. Collectively, ontology and epistemology, in conjunction with methodology, create a comprehensive framework of interconnected practices and thought processes that delineate the nature of research.

Positivism

In empiricists footsteps, during the mid-19th century, the French philosopher Comte developed the positivism, a philosophical standpoint which infers that all knowledge regarding facts is based on the "positive" data of experience and that the realm of facts can be explained by pure logic and mathematics[212]; meaning that reality is measurable and is made only of what the researcher can observe.[213] Positivists repudiate everything that is not evident, such as metaphysics or religion. On the same line, the "Circle of Vienna" in 1920s and 1930s developed the "logical positivism", which included the notion that all sciences that were not empirically verifiable were meaningless, and that all knowledge could be reconducted to one common standard language of science. The role of the positivist researcher then becomes to observe and measure patterns to test different hypotheses, or predict reality through quantitative methods.[214]

Post-positivism

During the 1960s and 1970s it became obvious that the independence between researcher and data propagated by positivism could not be achieved. A new stream of thoughts emerged, collected under the term "post-positivism". Post-positivism argues that the researcher and his/her theories, hypothesis and previous knowledge can influence how data can be interpreted. The application of a rigorous scientific method, and the transparent reporting of all relevant information can, however, limit the bias inferred by the researcher on the results [213]. In terms of positivism, complex phenomena are reduced to measurable

data, and all objects can be reduced to small elements. The positivistic development in that period greatly influenced medical sciences. Medical sciences refer to a broad field of study that encompasses the scientific investigation and understanding of various aspects related to health, disease, and medical care. It is a multidisciplinary field that integrates knowledge from biology, chemistry, physics, and other related disciplines to explore the structure and function of the human body, mechanisms of diseases, and the development of medical interventions. The positivistic influence in medical sciences implied that the "diseased" became detached from the experiencing self. The signs of sickness were seen as local symptoms and were interpreted by a physician who was supposed to know the truth about the disease. Due to this influence, medical science, as it is today, is largely positivistic and post-positivistic.

Hermeneutics

While the quantitative branch of medical science advanced under the positivist and post-positivistic influence, claiming that the whole is the sum of the parts, a concurrent line of thoughts, claiming the whole has more behind it (a meaning) was re-discovered in hermeneutics. The word hermeneutics comes from the Greek god "Hermes" who was the God´s messenger, responsible to interpret the God´s commandments to humans. Hermeneutics is then referred to as "the art/study of interpretation".

Hermeneutics was first developed to interpret metaphors in the Bible, but then spread to anthropology, social and medical sciences as well. Hermeneutics has a long historical tradition, but flourished during the late 1800s and early 1900s with philosophers such as Heidegger and Husserl. Due to the world wars, and the consequent ban of all German culture after the second world war, hermeneutics were set aside to benefit for the positivistic philosophies. After the 1960s hermeneutics gained new importance thanks to another German philosopher, Gadamer.[215] Hermeneutics were explored as a critique towards positivism, since hermeneutic philosophers claimed there are things in the world that can barely be observed or calculated, such as feelings or experiences. Husserl defined everything that cannot be measured as "the lifeworld", which is a realm of what is self-evident or given: a world with open horizons that each person might experience as true.[216] Gadamer[215] further explores the idea of lifeworld and claimed it to be about the world as it is experienced (as it appears in different people); in other words, the world is created by our experiences. For Gadamer, to gain an understanding of a subject does not imply only to understand the meaning of the subject, but implies to gain an agreement, a unanimity for the studied subject as well.[217] There is a substantial difference between "to understand" and "to interpret": To understand a phenomenon is to grasp it in its context, while to interpret a phenomenon does not require an hypothesis behind.[217]

Within hermeneutics there is no single truth, the focus is on the experience - the intentionality. Intentionality is related to the awareness being directed outwards into the world, not inwards towards ourselves.[215] The process of creating knowledge (research) becomes then a never-ending process that

changes all the time, with no distinct beginning and no distinct end. In hermeneutics, the researcher can influence data and results of the analysis, since according to Gadamer[215], a researcher can never completely free himself/herself from his/her prejudices. It is then important for researchers to have an open attitude and approach when doing research from a hermeneutic perspective. Moreover, it is important for researchers who conduct qualitative research to bracket own prejudices during the process.[217]

Inductive vs deductive approach

In theory of science, inductive and deductive are two different approaches to new knowledge search.[218] The inductive approach is free from an existing theory: it starts with empirical observations, and then possibly a theory is formulated from the observations. On the other hand, deductive approach starts with a theory, and then collects and analyses data with the existing theory as a starting point.[218]

Qualitative vs quantitative research

Within medical sciences and medical professions, there is/has been a debate in terms of the usefulness of results from qualitative, as opposed to quantitative research.[219] A good example to understand how and why both scientific approaches are needed is reported in Thorsten Turén´s book "theory of science for beginners"[220], and is the example of bees and ants: *"it is easy to explain why bees and ants leave their hives and hills to build new colonies: they have become too many in relation to the opportunity of supplies, that is, they leave to get better living conditions somewhere else. In the same way, the great migration from Western Europe to the USA during the 1800s can be explained. However, we cannot understand ants and bees. We cannot understand how they experience their situation. On the other hand, we can understand how humans react. When we study or discuss migration, we understand people not only in an intellectual way. We understand them because we are humans and we can put ourselves in somebody else´s shoes and grasp their feelings and thoughts".*[220] Qualitative and quantitative research should not be seen as opposed to each other, but rather as complements. Importantly, in contrast to quantitative studies, which are often hypothesis-testing, qualitative studies are hypothesis-generating. Qualitative studies can be precursors of quantitative studies, or a complement to explore further areas of a subject, where quantitative paradigms cannot be applied.[217]

Evidence Based Medicine

David L. Sackett has been regarded as the "father" of Evidence Based Medicine (EBM).[221] According to Sackett,[221] EBM is the *"conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients"*. The aim of EBM is to use the scientific method to organize and employ best available data in the management of healthcare decisions. This means acting on the base of three pillars, integrating (i) the best available research with (ii) the clinical expertise, and (iii) the patient´s values and preferences (Figure 14). Importantly, according to Sackett,[221] by clinical expertise is meant "*the proficiency and judgment that individuals acquire through clinical experience and clinical practice*".

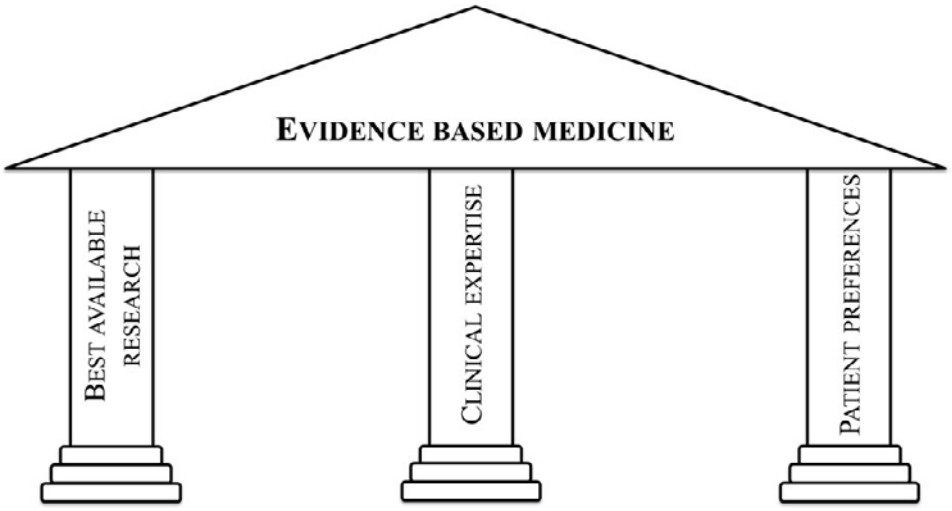


Figure 14: Evidence Based Medicine. Created by Eric Hamrin Senorski.

Since EBM aims to organize and employ best available data in healthcare, one important aspect to consider is the hierarchy of evidence. The principle of the evidence hierarchy suggests that as the level of evidence increases, so does the study results' generalizability, reproducibility, and relevance.[222] The level of evidence is given by the study design and consequently the expected risk of bias in the study. There are several different versions of the hierarchy of evidence. In this thesis, the Oxford Centre for Evidence Based Medicine version is used.[223] In the Oxford version, the hierarchy of evidence has 5 levels, in descending order, where studies at level 1 are supposed to be of the highest quality, while studies at level 5 of the lowest quality (Figure 15)

Level 1:	systematic reviews or randomized controlled trials
Level 2:	prospective cohort studies
Level 3:	retrospective cohort studies and case control studies
Level 4:	case series
Level 5:	mechanism based reasoning and expert opinions

Figure 15: Hierarchy of evidence model suggested by the Oxford Centre for Evidence Based Medicine.

Systematic reviews or randomized control trials.

A systematic review is a comprehensive and structured synthesis of the available evidence on a particular research question or topic. This process entails a methodical and clear strategy for identifying, choosing, and rigorously evaluating pertinent studies, followed by the analysis and summarization of their conclusions.[224] The aim of a systematic review is to provide a robust and unbiased summary of the current state of knowledge on a specific subject. Key characteristics of a systematic review include a systematic search, extraction of relevant data from included studies, synthesis of results, and assessment of risk of bias in included studies.[225] A further important addition in key characteristics of a systematic review is grading the certainty of evidence from the synthesis of the results.[226 227]

In this thesis, Study II is a systematic review. The review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[228] The PRISMA guidelines aim to ensure transparent, accurate, and comprehensive reporting of systematic reviews by delineating the minimum elements that should be included in such reviews.[229]

A RCT is a type of study that is commonly used in medical and clinical research to evaluate the efficacy of interventions or treatments. It is considered the gold standard for assessing the causal relationship between a treatment and its effects on a specific outcome.[230] Key features of a RCT comprise randomization, which means that participants are randomly assigned to either the treatment group (receiving the intervention) or the control group (not receiving the intervention or receiving a placebo). Randomization helps to ensure that the two groups are comparable at baseline, minimizing the influence of confounding variables. Other key features include blinding (single, double, or triple), and concealment of the randomization process. Randomized controlled trials provide strong evidence for assessing causality and establishing the efficacy of interventions.[231 232] No study in the present thesis was a RCT.

Prospective cohort studies

A prospective cohort study is an observational research that tracks a group of people who possess a shared trait over time, such as for example an ACL injury, to examine the association between certain exposures e.g. treatment with ACL reconstruction and subsequent outcomes. Key features of a prospective cohort study include selection of participants, who share a common exposure (ACL reconstruction), follow-up over time, assessment of outcome and data analysis. Participants are commonly categorized into exposed and unexposed groups based on different characteristics. This study design is particularly valuable to investigate the natural course of diseases, to identify risk factors, and to assess the impact of interventions.[233 234] Unlike retrospective cohort studies that analyze past data, prospective cohort studies, which gather data in real time, are deemed more robust in determining causality. Compared with RCTs, prospective cohort studies do

not control for possible confounders, and have therefore a limited generalizability.[233 234]

Retrospective cohort studies and case control studies

A retrospective cohort study is a type of observational study that analyzes historical data to investigate the relationship between exposure to certain risk factors or interventions and the occurrence of outcomes over time.[233 235] Unlike a prospective cohort study, which follows participants from the present into the future, a retrospective cohort study identifies participants based on their past exposure status and then examines their outcomes from that point onward. Key features for retrospective cohort studies include selection of participants, who share a common exposure (ACL reconstruction), outcome assessment over time, where data on outcomes are collected through existing records, such as medical records, administrative databases, or other sources, and finally data analysis. Retrospective cohort studies are useful when conducting a prospective study from the present would be impractical, too costly, or time-consuming.[233 235] They are commonly used in epidemiological and public health research, especially when investigating the long-term effects of exposures. One limitation of retrospective cohort studies is the need to rely on existing data, which might be incomplete or subject to bias.

A case-control study is a type of observational study designed to investigate the association between a specific outcome or disease (the "case") and potential risk factors or exposures.[236] This method entails contrasting individuals who exhibit the desired outcome (cases) with those who lack the outcome (controls) to uncover factors potentially linked to the disease's incidence. Key features of a case-control study include selection of cases and control, performed with matching of certain characteristics, the retrospective nature of the study, the exposure assessment, and the analysis of association. Case-control studies are particularly suitable for exploring potential risk factors for an outcome of interest.[236]

Registry studies

Registries are organized systems that collect information about individuals, events, or conditions, usually for a specific purpose such as monitoring disease trends, assessing treatment outcomes, or tracking the safety and effectiveness of interventions.[237] Registry studies involve the systematic collection and analysis of data from existing registries. Key points of registry studies include the data source (the register) and the observational and longitudinal nature of the data collection. The observational and longitudinal nature of data collection allow researchers to observe trends, changes, and outcomes over an extended period, without intervening. Registry studies are not directly included in the Oxford Centre for Evidence Based Medicine version.[223] However, registry studies are cohort studies in nature, where data is commonly collected prospectively but analyzed retrospectively. One major strength of registry studies can be the large patient population which can be representative of the real-world population,

thereby increasing the external validity of the results. Registry studies play a crucial role in providing real-world evidence and insights into various fields of medicine and public health by leveraging existing data sources to answer specific research questions. In this thesis, Study III, IV and V were performed with data extracted from a rehabilitation specific registry, Project ACL (Projekt Korsband; described in detail under "Project ACL" heading). Study III was designed as a matched cohort study, where patients who suffer a second ACL injury were matched by age sex and pre-injury activity levels with counterparts who did not suffer a second ACL injury. The matched groups were prospectively followed and outcomes between groups were compared. Study IV was a cohort study where data prospectively collected from Project ACL was used to create different test batteries. We explored whether passing the test batteries or not had an association with a second ACL injury. In Study V, prospectively collected data from Project ACL was used to calculate the cut-off scores on PROs that could best differentiate between patients who will suffer a second ACL injury from patients who will not.

Case series

A case series is a type of scientific study that involves the detailed analysis and presentation of a group or series of similar cases, typically patients with a particular medical condition or those who have undergone a specific treatment.[238] Unlike experimental studies, case series lack a control group for comparison and are often considered observational in nature. The primary focus of a case series is to describe the characteristics, outcomes, and trends observed in the group of cases. While case series contribute with valuable information about clinical observations and may be the first step in exploring a new phenomenon or condition, they have limitations. The absence of a control group makes it challenging to draw conclusions about causation or the efficacy of interventions.

Mechanism based reasoning and expert opinions

At the base of the hierarchy is expert opinion, which is considered the weakest form of evidence. Expert Opinion refers to the subjective judgment, insights, and recommendations of individuals or groups considered experts in a particular field. While expert opinions can provide valuable insights and guidance, they are inherently subjective and lack the systematic and empirical foundation present in higher levels of the evidence hierarchy.

Qualitative studies

A further study type not included in the Oxford Centre for Evidence Based Medicine hierarchy of evidence version[223] is qualitative studies. Qualitative studies are a research methodology that focuses on collection of rich and contextual information to understand individuals' perspectives, experiences, beliefs, and behaviors. Unlike quantitative studies that use numerical data, qualitative studies emphasize the exploration of meanings, motivations, and social phenomena. Qualitative data can be collected through several different methods such as

observation, surveys, or interviews. One common way of collecting qualitative data is through individual or focus-group interviews.[239] Key aspects of qualitative interview studies include research objectives, data collection, sampling, data analysis and trustworthiness. The research objectives of qualitative interview studies are often to explore and gain a deeper understanding of human phenomena. Researchers aim to uncover the subjective experiences, perceptions, and meanings that individuals attribute to their lives or situations. Data is often gathered via interviews with open-ended questions, which prompt participants to express their thoughts, emotions, and experiences. The interviews are typically semi-structured, allowing for flexibility and the emergence of unexpected insights. The sampling in qualitative studies is usually called "purposeful sampling", which infers to select participants who can provide rich and relevant information related to the research question. Qualitative data analysis involves systematically examining and interpreting the interview transcripts or recordings. Common methods include thematic analysis, content analysis, and grounded theory. Trustworthiness ensures the credibility, transferability, dependability, and confirmability of findings and it is very important in qualitative research.

Overall, qualitative interview studies offer a valuable approach for researchers seeking to explore and understand the complexities of human experiences and social phenomena in a holistic and contextually rich manner. Qualitative interview studies provide rich and nuanced insights, but typically involve smaller sample sizes and are not designed to generate generalizable findings. The emphasis is on depth rather than width. In this thesis, Study I and VI were qualitative interview studies. In Study I sport physiotherapists were interviewed in focus groups, to allow for group interactions, discussions, and dynamics among participants. Focus groups as a data collection method can generate a range of perspectives and ideas, and the group setting can stimulate participants to express opinions they might not share in a one-on-one interview. In Study VI young active females treated with ACL reconstruction, who wanted to RTS, suffered a second ACL injury, and were treated with ACL revision were interviewed in individual interviews. In individual interviews participants may feel more comfortable to share personal or sensitive information. Individual interviews provide a confidential environment, fostering openness and honesty in responses. In both Study I and VI, collected data was analyzed with qualitative content analysis according to the description of Graneheim and Lundman.[240 241] Within qualitative research, a hierarchy of evidence has been proposed,[242] as follows:

1) Generalizable studies, in which the sampling approach is guided by theoretical frameworks and literature and is further expanded through analysis to encompass a wide range of experiences. The analytic procedures are thorough and transparently outlined. Additionally, the findings are contextualized within the broader literature to evaluate their applicability to different settings.

2) Conceptual studies, in which sample selection is directed by theoretical concepts, which are derived from a thorough analysis of existing literature. Conceptual studies might focus on a singular group about which little is known, or it could involve several key subgroups. Through conceptual analysis, the diversity of participants' perspectives is acknowledged and examined.

3) Descriptive studies, in which the sample is chosen to highlight practical issues instead of theoretical ones. Data report is enriched by a variety of quotes that exemplify results.

4) Single case studies, which provides extensive data on the views or experiences of one person.

In this thesis, Study I and VI were designed to be descriptive studies.

Psychometric properties of outcome measures

In health care studies, a widely used method to assess outcomes are questionnaires, commonly referred to as PROs. A PRO is defined as "a measurement of any aspect of a patient's health status that comes directly from the patient, i.e., without the interpretation of the patient's responses by a physician or anyone else".[243] In clinical trials employing PROs, it is very important to ensure a meaningful interpretation of the results. Meaningful interpretation of results infers to have a clearly defined variable (such as age, temperature, distance), a recognized unit of measurement (e.g., months, °C, kilometres), and an understanding of the contextual factors influencing the outcome. The significance and interpretation of numerical data extend beyond the study itself, relying on practical relevance, that is, numerical data has practical meaning only within a context.

Without a practical meaning, statistics and other calculations lose their significance. An example can be the famous "New Cuyama" sign, where population, feets above sea level and when the city was established are summed (Figure 16).

Figure 16: New Cuyama sign where numerical data are added without practical meaning.

When PROs are used to measure something in a clinical study, challenges arise. Since study design and statistical analysis cannot compensate for deficient measurements, the quality of conclusions from studies depends on the quality of the measurements used. A significant challenge regarding the quality of the measurement tool used (in this case PROs) centres on two key aspects: first, what we actually measure (the PRO's validity), and second, the accuracy of this measurement, which is determined by the PRO's reliability. Validity and reliability are commonly referred to as

"psychometric properties" of a PRO. One common example to visualize validity and reliability is the one with archery targets, shown in Figure 17, where high validity and high reliability implies that the PRO used hits the bull´s eye with consistency.

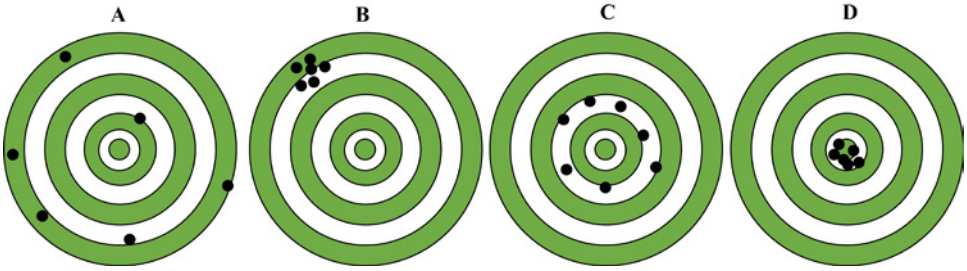


Figure 17: Visual representation of validity and reliability. A = low validity and low reliability. B = low validity and high reliability. C= acceptable validity but low reliability. D = high validity, high reliability.

Validity can be further divided into several types of validity: content validity, construct validity and criterion validity, which constitutes external validity, as opposed to internal validity. On the other hand, reliability can be further divided into internal and external reliability. Internal reliability comprises internal consistency, that is, the extent to which all parts of the PRO contribute equally to what is being measured. External reliability refers to the extent to which a measure varies from one use to another and comprises test re-test reliability, inter-rater reliability, and intra-rater reliability (Table 2).

In the realm of psychometric properties, a hierarchy exists (Figure 18). At the pinnacle of the hierarchy stands content validity, regarded as the most crucial measurement property. This is because the items within PROs not only must be pertinent but also comprehensive and intelligible in relation to the construct under scrutiny and the target population.[244] Content validity is not a binary, yes/no characteristic; rather, it necessitates a subjective judgment by reviewers. The assessment of content validity should encompass insights into the PRO's developmental process, the quality of the results, and any study or trial addressing content validity for the specific PRO. Moreover, a subjective rating, such as the content validity index,[245] should be considered in evaluating the PRO's content. Moving down the hierarchy, the next tier focuses on internal properties, occasionally denoted as "unidimensionality," which encompasses internal validity and internal consistency. The internal structure of PROs refers to the interrelationships among the various items, determining whether item scores can be combined into a scale or, in some cases, a subscale. Ensuring proper internal properties hinges on the quality of individual items that constitute the instrument. Construct validity is the subsequent psychometric property on the hierarchy. A significant facet of construct validity is structural validity, which refers to whether

the PRO's items accurately represent the underlying structure or dimensions they are designed to measure. Techniques such as factor analysis are frequently used to assess structural validity, explaining the extent to which items cluster together to form coherent factors or dimensions. This process affirms the PRO's possession of structural validity. While other psychometric properties such as criterion validity and various types of reliability are essential, they are considered of equal importance. Notably, despite the apparent hierarchy, the validation process for a PRO does not need to be a one-time trial. Instead, it should be seen as an iterative, ongoing process of evidence accumulation, employing tests from both Classical Test Theory (CTT) and Modern Test Theory (MTT) to build a robust body of evidence for the PRO's validity and reliability.

Table 2: Summary of psychometric properties and definitions.

Property		Definition
Validity		
External	Content validity	ensures that the items effectively represent what the measure intends to assess, guaranteeing comprehensive coverage of the targeted construct.
	Construct validity	ensures the items accurately measure the intended theoretical concept, distinguishing it from content validity that emphasizes the extent of content coverage.
	Criterion Validity	assesses how well a questionnaire or measurement tool correlates with a criterion or an external standard that is already established. Can further be divided in concurrent or predictive validity
Internal	Internal validity	assess the extent to which the observed results or scores obtained from the questionnaire reflect true relationships between the variables being measured, without interference from extraneous factors or confounding variables.
Reliability		
External	Inter-rater reliability	the consistency and agreement among different raters or observers when using a PRO across multiple occasions or instances.
	Intra-rater reliability	the consistency and stability of ratings or measurements made by the same rater or observer when using a PRO across multiple occasions or instances.
	Test-retest reliability	the consistency and stability of ratings or measurements made by the same rater or observer when using a PRO or assessment tool across multiple occasions or instances.
Internal	Split-half method	the consistency and stability of ratings within the PRO measured.
	Internal consistency	assesses the extent to which items within a PRO or test are consistent in measuring the same underlying construct or attribute. It evaluates the coherence and homogeneity of the items, indicating how well they relate to each other within the PRO.

PRO = patient reported outcome measure

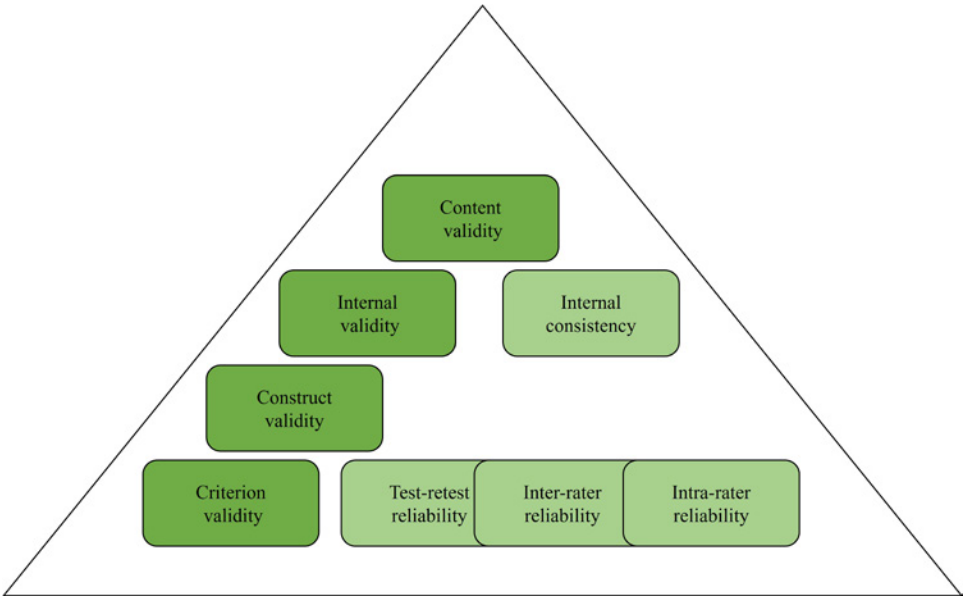


Figure 18: Hierarchy of psychometric properties of PROs.

Methods used in this thesis

Quantitative methods

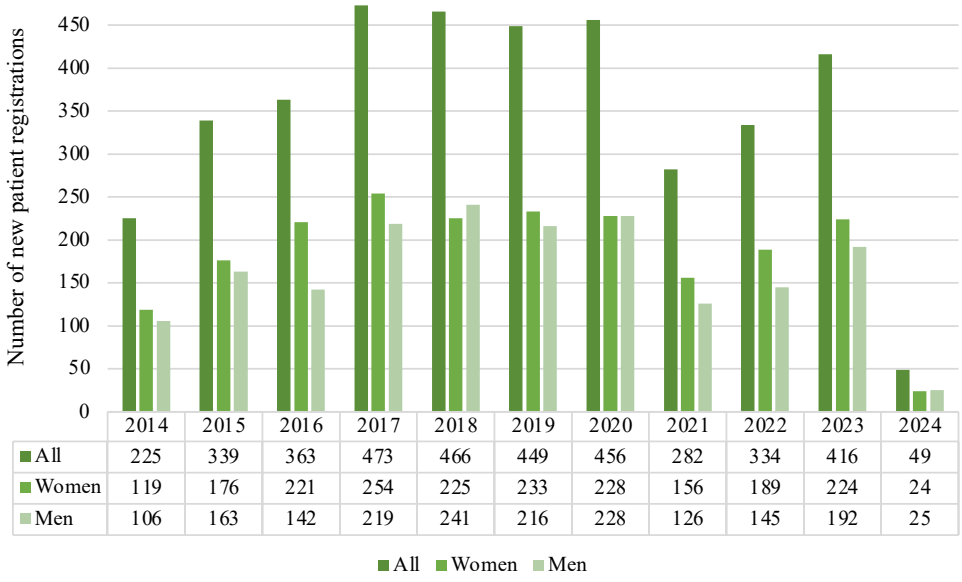
PROJECT ACL (QUANTITATIVE DATA COLLECTION)

Project ACL started in 2014 in Gothenburg (Sweden). The project started as a co-operation between surgeons, physical therapy clinics, and the University of Gothenburg. At the time in which Project ACL was developed, large registry studies were few, or lacking. Therefore, the creators launched Project ACL with the aim of enhancing care for all patients who have sustained an ACL injury, irrespective of the treatment method. Thus, a prospective registry which aims to improve care for patients who suffer an ACL injury by providing patients and responsible healthcare workers with continuous evaluation was started. In the first 10 years of Project ACL, 3,852 (women = 2,049; 53%) unique patients were registered (as per February 14th, 2024) (Figure 19). As per February 14th, 2024, answers to 15,924 PROs and results for 12,791 muscle function tests have been recorded.

Patients are informed about Project ACL by their responsible health care provider, that is, physiotherapists or orthopedic surgeon. Participation in the project is voluntary, informed consent is collected, and all patient-related data is treated confidentially. Upon registration in Project ACL, patients connect their profile to the profiles of the respective health care workers, such as physiotherapist and orthopedic surgeon.

Patients registered in Project ACL are invited to perform standardized muscle function tests and respond to PROs according to a pre-defined follow-up timeline. Upon enrolling in Project ACL, the point of injury or surgery establishes the baseline. Subsequently, patients undergo evaluations at 10 weeks, 4, 8, 12, 18, 24 months, 5 years, and thereafter at five-year intervals (Figure 20). When scheduled for ACL reconstruction, patients are invited to perform pre-operative tests, which should be performed up to a week before surgery.

After performing muscle function tests and responding to PROs, every patient and the responsible health care workers are provided with a report, where data from the last three follow-up tests are plotted with both absolute values and percentage of symmetry (Figure 21). There is an opportunity to choose which three follow-up results to plot on the report, as well. The rationale is to provide patients and health care workers with objective measures of how the rehabilitation is progressing and if there are any areas of rehabilitation that need further emphasis.



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
All	225	339	363	473	466	449	456	282	334	416	49
Women	119	176	221	254	225	233	228	156	189	224	24
Men	106	163	142	219	241	216	228	126	145	192	25

Figure 19: Patient registrations in Project ACL for each year from 2014 to February 14th, 2024.

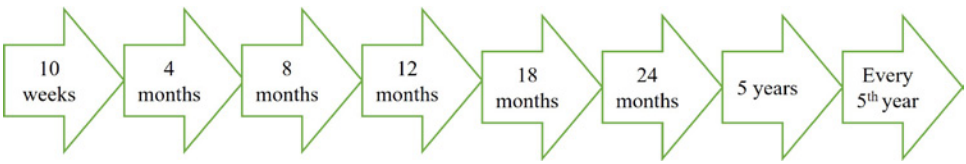


Figure 20: Follow-up timeline in project ACL.

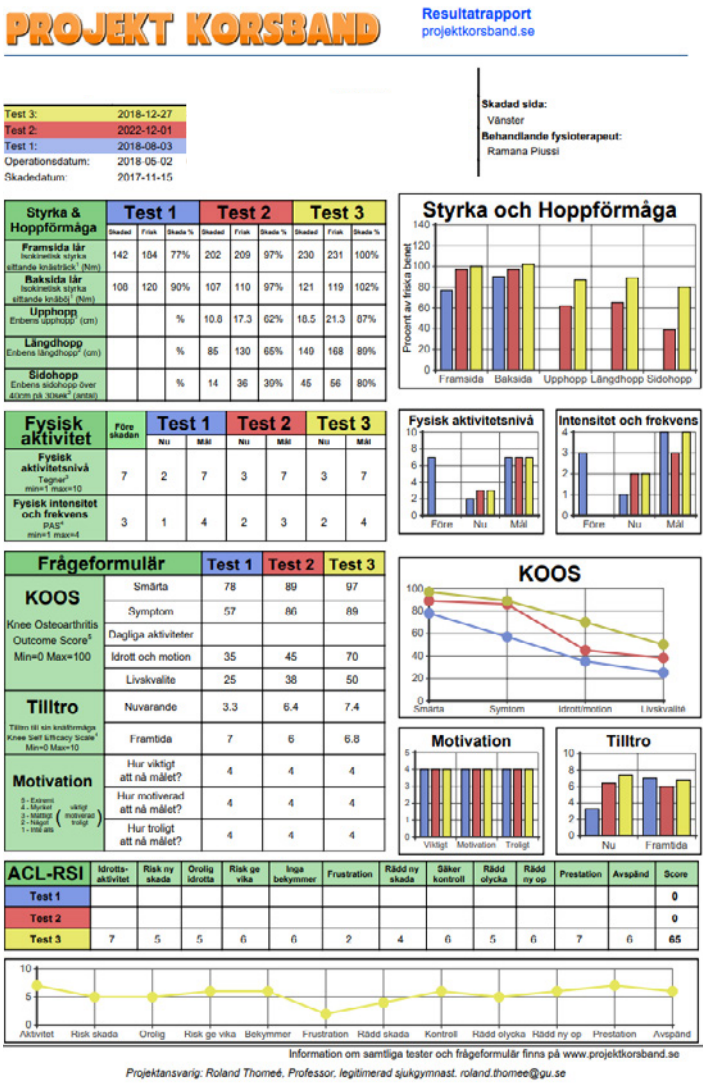


Figure 21: Example of report from project ACL. The results of the NordBord are not shown when more than one follow-up is plotted on the report due to technical difficulties.

Table 3: Muscle function test in Project ACL.

Test	Isokinetic quadriceps and hamstring strength	Vertical Hop	Hop for distance	Side hop	Eccentric hamstring strength
Maximal repetitions	3 per movement	3	3	1	3 x 3
Rest between repetitions	40 seconds	Up to patient	Up to patient	3 minutes	2 minutes
Measure unity	Newton meters	Centimeters	Centimeters	Number	Newton

Muscle function tests in Project ACL

Muscle function tests included in Project ACL (Table 3), and performed in the following order, are:

- Isokinetic strength for quadriceps and hamstrings
- Vertical hop
- Hop for distance
- 30 seconds side hop
- Eccentric hamstring peak strength

To be allowed to perform muscle function tests, patients are required to have tested the actual movements in their rehabilitation, and to have approval from their responsible physiotherapist to perform the tests. All muscle function tests are performed by patients, recorded unilaterally, and supervised by physiotherapists (or physiotherapists candidate students), trained by Project ACL. All test supervisors have regular meetings every year where responsible staff from Project ACL go through the test procedure to standardize tests performance as much as possible. Before the test session is started, patients are required to warm up according to a standardized warm-up procedure (Figure 22). Patients' warm-up for 10 minutes on a stationary bike at a self-chosen intensity. During warm-up, test supervisors are required to ask patients standardized questions about patients' knee-specific and general health. Test supervisors need to screen for any possible knee-related symptoms which might put patients at risk of injury while performing the tests. All answers to the screening questions are recorded in Project ACL database. After the warm-up on the stationary bike, patients move on to the Biodex dynamometer Biodex System 4 (Biodex Medical System, Shirley, New York, USA), where sub-maximal trial repetitions are performed before strength test. Hop tests start at the 4 months follow-up at the earliest. To perform the tests, patients need to be judged ready by the test supervisor and by the responsible physiotherapist.

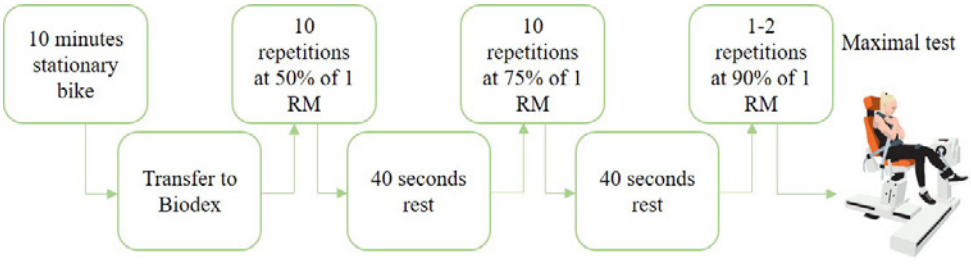


Figure 22: Warm-up procedure in Project ACL.

Isokinetic strength for quadriceps and hamstrings

Patients sit with 85 degrees of hip flexion and are secured with two straps over the torso, one over the hips and waist and one securing the thigh which is tested. The test is performed unilaterally, and the injured leg is tested first (Figure 23).

Figure 23: Strength test on the Biodex.

If patients have suffered ACL injuries on both limbs, the limb with the latest injury is tested first. Patients undertake a quadriceps test moving from 90 degrees of knee flexion to complete knee extension, which is promptly followed by a hamstring test that involves flexing the knee from full extension to 90 degrees of flexion. The dynamometer is set to an angular speed of 90 degrees per second. The decision to set the rotation speed at 90 degrees per second was made by the developers of the register, who aimed for a slower pace to evaluate maximal strength. Nevertheless, at both 30 and 60 degrees per second, significant internal forces are exerted on the knee, which could potentially cause discomfort for patients and hinder their ability to undergo tests at the 10-week mark. Patients are allowed to hold arms across the chest and grasp the straps. After illustrated warm-up, patients are required to perform three maximum effort trials, with approximatively 40 second rest in between each trial. During the maximum effort trials, the test supervisor is allowed to verbally encourage the patient. Every attempt is documented in the test protocol, but only the highest peak effort for knee extension and flexion, measured in Newton meters (Nm), is logged into the Project ACL database for further analysis. The isokinetic concentric test is considered reliable for test-retest measurements of peak torque and work during a single repetition in individuals without injuries, achieving an intraclass correlation coefficient (ICC) ranging from 0.95 to 0.97, varying by the speed evaluated. However, 90 degrees per second was not assessed.[246] [247] Further, the Biodex validity for strength measurement was tested for position, torque, and velocity. The position was assessed by comparing it to a hand-held inclinometer, while torque was examined by applying a lever arm perpendicular to the gravitational force. In this configuration, the Biodex System 3 quantified six different torques (Nm) using calibrated weights. The moment generated by the weighted lever arm was computed and served as the standard measure. Velocity assessment involved placing a calibrated weight at the end of a lever arm attached

to the dynamometer. The dynamometer was manually accelerated to various test velocities. The lever arm velocity for each tested velocity was then calculated, serving as the benchmark for velocity measurement. The results of position and torque comparisons revealed a nearly perfect agreement between measures and their respective criteria. This level of agreement also held true for the range of velocities tested, reaching up to 300 degrees per second. [247] After isokinetic strength testing patients move on to the hop tests.

Hop tests

All hop tests are performed with patients holding hands behind their back to isolate lower limb function and reduce potential variations in the performance of different subjects. Firstly, patients test the vertical hop (Figure 24).

Patients stand on one leg and are instructed to hop as high as possible while stretching the hop leg, that is, patients are not allowed to bend knee and hip while jumping. A contact grid (Muscle lab, Ergotest Technology, Oslo, Norway) measures the flight time and converts it into centimeters (cm). Patients are allowed to take two-three submaximal trials to familiarize with the test before three maximal trials. All jump heights are recorded in the protocol, and only the highest jump for each limb is recorded in the database and used for analysis. After the vertical hop, patients move to the hop for distance (Figure 25).

Patients are instructed to stand on the leg to be tested and to jump as long as possible beside a meter taped on the floor. Patients are required to have a stable landing, that is, not to release hands or

Figure 24: Vertical hop.

Figure 25: Hop for distance.

move the foot at landing. Patients are allowed to take three submaximal trials to familiarize with the test before the maximal trials are performed. Patients are allowed to hop several times to get three hops with a stable landing. The distance in cm between toes at take-off and heel at landing is recorded. The decision to measure from toes to heel was made to mirror standard athletic measurements and accommodate variations in foot size. All jump lengths are recorded in the protocol, and only the longest jump for each limb is recorded in the database and used for analysis.

The last hop test is the side hop test (Figure 26). Patients stand beside two lines on the floor, 40 cm aside. For 30 seconds, patients are asked to jump as many times as possible sideways between the two lines. Patients are allowed one maximal trial per leg and 3 minutes rest between each trial. Prior to the maximal trials, patients are allowed to test some hops. Patients are required not to touch lines with the jumping foot, and if this occurs the current hop is discarded from the total number of valid hops. The total amount of hops is recorded and then the number of failed hops is subtracted. The total number of hops without touching the lines is recorded in the database for analysis.

The three hop tests used in Project ACL are performed as described by Gustavsson et al.,[248] selected for their superior capacity to differentiate hop performance both in individuals who have experienced an ACL injury and those who have undergone ACL reconstruction. The hop tests exhibited a high degree of sensitivity, effectively detecting anomalies in individuals with an ACL injury (with a sensitivity of 87%) and in those who had received ACL reconstruction (with a sensitivity of 91%), provided that at least one of the three tests indicated an abnormal LSI value. An LSI was considered abnormal if the difference between the sides was greater than 10%. Moreover, these tests were accurate in distinguishing healthy individuals as normal when all three tests resulted in a normal LSI value (less than 10% difference between sides). Tests also accurately identified abnormalities in patients with an ACL injury (84% accuracy) and patients who had ACL reconstruction (88% accuracy) when at least one test showed an abnormal LSI.

Eccentric hamstring strength

The test of eccentric hamstring strength is a part of Project ACL but not included in the present thesis and will therefore be briefly described. The test of eccentric muscle strength in project ACL started in February 2018 and is performed with the NordBord hamstring testing system (version 1.0, Vald™ Performance, Australia; Figure 27)). The NordBord utilizes the Nordic hamstring exercise as its foundation. It has been noted to exhibit satisfactory reliability in test-retest scenarios when assessing differences in force between limbs, particularly regarding peak force observed during bilateral tests (ICC = 0.85).[249]

Patient Reported Outcome Measures

Within one week from the date of muscle function test patients are invited to answer to PROs online. Patients' answers are automatically registered in Project ACL´s database.

In Project ACL, patients are invited to answer to the following PROs:

- The KOOS
- The knee self-efficacy scale (K-SES)
- The ACL-RSI (from 8 months onwards)
- The Tegner Activity Scale
- The Physical Activity Scale (PAS) (not used in this thesis)
- The European Quality 5 Dimensions 3 levels (EQ5D-3L) (not used in this thesis).

The KOOS stands out as one of the most frequently utilized questionnaires for the evaluation of subjective knee function in patients treated with ACL reconstruction.[55] Its primary objective is to gauge subjective knee function, consisting of 42 items divided into 5 distinct subcategories.[250] These KOOS subcategories encompass:

1) Pain (comprising 9 items),
2) Symptoms (comprising 7 items),
3) Activities of daily living (ADL, comprising 17 items),
4) Function in sports and recreation (comprising 5 items), and
5) Quality of life (comprising 4 items).

Figure 26: Side hop.

Figure 27: NordBord testing.

Each question within the KOOS questionnaire is graded on a 5-point Likert scale, ranging from 0 to 4. Subsequently, a normalized score for each sub-scale is computed, ranging from 0 to 100, where 0 signifies the most severe symptoms and 100 signifies the absence of symptoms. Notably, the KOOS was initially designed to appraise individuals suffering from knee osteoarthritis, and no patients with ACL injury were involved in the development of the scale.[250] In terms of the questionnaire's validity and reliability, the content validity of the KOOS is somewhat limited.[251] Moreover, only the KOOS subscale related to function and recreation exhibits acceptable construct validity when tested against specific hypotheses,[252] while only the subscales Sports and Quality of life respect criteria for unidimensionality.[253] Additionally, it is important to acknowledge that the KOOS demonstrates suboptimal psychometric properties, especially in terms of its content and structural validity.[55 254] In comparison to other PROs, the KOOS subcategories display the lowest responsiveness.[255] The KOOS was reported to possess test-retest reliability with an ICC within the range of 0.75 to 0.97.[256 257] An investigation into the validity of using the KOOS for patients recovering from an ACL injury has been undertaken.[257] However, caution is advised in the interpretation of the results due to language barriers and limited statistical options. The assessment of construct validity relied on correlating the KOOS with the Persian version of the SF-36, which, at the time of the study, had not undergone reliability testing.[257] Moreover, it is noteworthy that the ADL sub-scale demonstrated the highest reliability (Cronbach's alpha 0.96). Interestingly, the ADL sub-scale has been considered not clinically relevant for patients recovering from an ACL injury, thus, the "KOOS4" was introduced, consolidating the scores of the remaining four sub-scales into a single composite score, effectively excluding the ADL sub-scale from consideration.[52]

The K-SES[137] is designed to assess self-efficacy related to the knee, specifically gauging confidence in performing physical tasks among individuals with an ACL injury. In Project ACL, the 18-item version of the scale ($K\text{-}SES_{18}$) is utilized.[258] The $K\text{-}SES_{18}$ comprises two subscales: present (consisting of 14 items) and future (consisting of 4 items). Each item is rated on a scale of 0 to 10, where 10 indicates the highest level of confidence in performing a specific physical task. The scores for all items within each subscale are summed and then divided by the total number of items to calculate the mean value for each subscale. The K-SES has been reported to have good test-retest reliability (ICC =0.92 for both subscales), and acceptable construct validity to assess knee self-efficacy in patients who suffer an ACL injury, explored with factor analysis with eigenvalues.[259] However, content validity for the short 18 items version has not been explored, for which structural validity, internal consistency and construct validity were explored.[258] Construct and structural validity were explored by hypothesis testing, and factor analysis by correlation with other scales (KOOS, Physical Activity Scale and ACL-RSI).[258] Internal consistency was assessed with Chronbach´s alpha for each subscale. Results show high alpha for the future subscale (0.81-0.91), and very high

alpha (0.93-0.96) for the present subscale, with risk for item redundancy, two factors with eigenvalues ≥ 1, and good construct validity (as all seven predefined hypothesis were confirmed).[258]

The ACL-RSI was developed in 2008 and aims to assess emotions, confidence and risk appraisal towards RTS.[260] The ACL-RSI comprises 12 items, with each item graded on a scale from 1 to 10. A score of 10 indicates the most favorable psychological response to RTS, characterized by high confidence and positive emotion, along with low risk appraisal. The total score is derived by summing up the scores of all items (with a maximum possible score of 120) and subsequently converting it to a 10-100 scale.[260] When the scale was developed, psychometric properties were assessed with Cronbach's alpha, inter-item correlations, item-total correlations, principal component analysis, and divergent validity using a sample of 220 athletes who had undergone an ACL reconstruction 8-22 months earlier.[260] The scale was found to have a Cronbach's alpha of 0.96. Inter-item correlations had a mean of 0.69 (min-max, 0.49-0.83).[260] Principal components analysis was interpreted as showing the presence of one underlying factor with an eigenvalue of 8.14 that accounted for 67.8% of the total variance. The ACL-RSI has always been reported as a single total score, typically considered to reflect "readiness to RTS". However, it should be noted that readiness to RTS was not defined in the original paper in 2008.[260] Moreover, summing the scale in one score is not confirmed in the Spanish translation, where Sala-Barat et al.[261] found two underlying factors explaining 62.5% of variance. Divergent validity analysis showed significant differences between patients who returned to sport and patients who did not.[262] A systematic review from 2018 found strong evidence for internal consistency, reliability and structural validity of the ACL-RSI, whereas evidence for test-retest reliability, cross-cultural validity, hypothesis testing validity and content validity was moderate or limited.[55] The Swedish version used in Project ACL provided corresponding psychometric results compared with the original version.[263]

The Tegner Activity Scale was developed to assess the degree to which a physical activity is knee-demanding.[264] The scale ranges from 0 to 10, with 0 being the least knee demanding activity (work absence due to sick leave) and 10 the highest knee demanding activity (professional football). Up to level 5 on the scale, working activities are present. From level 6, only sporting activities are present. In Project ACL, a modified version is used. In the modified version, level 0 (work absence due to sick leave) has been removed. The test-retest reliability for the Tegner was reported to be 0.82 (ICC). Floor and ceilings effects were reported to be acceptable (less than 30%), which authors interpreted as a measure of good content validity. Answers on the Tegner correlated with the physical components of the SF-12 scale, indicating good criterion validity. The Tegner was reported to have good construct validity tested with pre-set hypothesis. Importantly, all above mentioned psychometric properties were tested on patients treated with ACL reconstruction.[265]

QUANTITATIVE ANALYSIS

In statistics, specificity and sensitivity are important measures used to evaluate the performance of clinical tests, diagnostic tools, or predictive models. Specificity and sensitivity provide insights into the accuracy and reliability of a test in correctly identifying the presence or absence of a condition. Sensitivity can be named true positive rate as well and is the proportion of true positives among all individuals who have the condition. Sensitivity measures the ability of a test to correctly identify individuals with the condition. Mathematically, sensitivity is true positives / (true positives + false negatives). A high sensitivity indicates that the test has a low rate of false negatives, meaning the test effectively captures most individuals with the condition.

Specificity, known as the true negative rate, is the proportion of true negatives among all individuals who do not have the condition. Specificity measures the ability of a test to correctly identify individuals without the condition. Mathematically, specificity is true negatives / (true negatives + false positives). A high specificity indicates that the test has a low rate of false positives, meaning it accurately excludes individuals without the condition (Figure 28).

Further important concepts to highlight in statistics include null hypothesis, p-values, effect sizes and confidence intervals. The theory behind the p-value and hypothesis testing were developed during the early 1920s.[266] The null hypothesis theory offers a structured approach for evaluating scientific hypotheses. It posits that there is no discernible effect or distinction

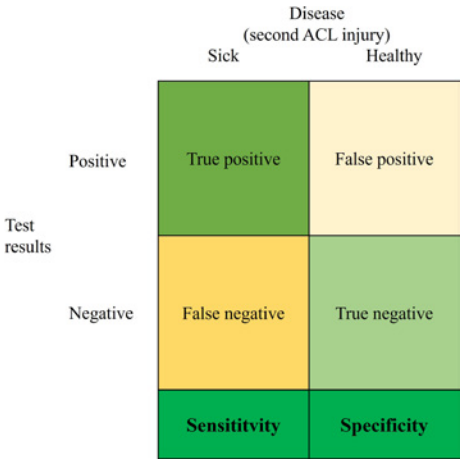


Figure 28: Graphical representation of specificity and sensitivity.

between the groups being studied (the null hypothesis). Subsequently, the likelihood of detecting any potential differences between these groups, assuming the null hypothesis holds true, is computed. This method enables scientists to render more objective and measurable determinations regarding whether the observed data presents sufficient evidence to reject the null hypothesis and embrace an alternative hypothesis, which proposes the existence of some form of effect or difference. The theory behind null hypothesis is closely tied with the development of the p-value.[266] The p-value, or probability value, measures the strength of evidence against the null hypothesis. A p-value tells the researcher the likelihood of observing the exact same difference observed between groups, or a more extreme value, if the null hypothesis was true. A low p-value (typically < 0.05) suggests that the observed data are unlikely under the null hypothesis. Thus, researchers reject the null hypothesis. Nev-

ertheless, a p-value does not quantify the magnitude of an effect or the significance of a finding. Instead, the effect size serves as a quantitative metric that illustrates the extent of a difference or correlation between variables, often used to understand the practical significance of research findings. The effect size informs researchers about the magnitude of the eventual difference highlighted by the p-value and helps in understanding the real-world importance of a statistical result. Researchers might need to provide confidence intervals alongside p-values. A confidence interval gives a range of values within which the true parameter (e.g. a difference between groups) is expected to lie, with a certain degree of confidence (commonly 95%). It provides more information than a p-value because it offers a range of plausible values for the parameter being estimated, not just a test of whether a difference exists.

In terms of statistics there are two common type of errors: type I and type II. Type I error (known as false positive) occurs when the null hypothesis is incorrectly rejected when it is true. For example, concluding that a treatment is effective when it is not. The probability of committing a type I error is denoted by significance level (typically 95%). A Type II error, also referred to as a false negative, occurs when the null hypothesis is retained despite being false. For instance, failing to detect an effect (like the effectiveness of a treatment) when there is one. Type II errors are closely tied with the concept of statistical power. Statistical power is the test´s ability to correctly reject a null hypothesis that is indeed false.[267] The statistical power is influenced by the researcher's chosen level of significance, the sample size, and the effect size, which indicates the degree to which the groups diverge.[268] Power is strongly associated with sample size. Small sample sizes imply a higher risk of type II error, unless effect sizes are large.[268] Mathematically, power is calculated as 1 minus the probability of making a Type II error. If the probability of a Type II error is 0.20 (or 20%), then the power of the test (1-0.20) would be 0.80 (or 80%). This means there's an 80% chance that the test will correctly identify an effect if there really is one. High power (closer to 1) is desirable because it means the test has a high likelihood of detecting an effect that exists, reducing the risk of a Type II error. If a test has low power, it might not be sensitive enough to detect true differences or effects, which could lead researchers to incorrectly conclude that their hypothesis has no support.[268]

In Study III, IV and V qualitative statistical analysis methods were used. In all statistical analysis the significance level was set at 95%. One important aspect to mention when the significance level is set at 95% is that over, e.g. 100 comparisons, 5 will turn statistically significant, despite not being significant, due to type 1 error.[268]

In Study III, statistical analyses were conducted using Statistical Product and Service Solutions (IBM Corp. Released 2017; IBM SPSS Statistics for Windows, Version 25.0; Armonk, NY: IBM Corp.). Demographic data were presented as mean values with standard deviations (SD) or medians with min-max. Group comparisons were executed using a t-test for mean values, a median test (k samples) for ordinal variables such as

the Tegner Activity Scale, and a chi-square test for percentage comparisons. Significantly different results from these tests were reported with delta (Δ) and confidence intervals (CI). Delta refers to the measure of difference or change in the parameter of interest between groups.

In Study IV, statistical analyses were conducted using the Statistical Analysis System (SAS) software version 9.4 (Copyright © 2013, SAS Institute Inc., Cary, NC, USA). Demographic data for the entire cohort and stratified by sex were presented as mean values with standard deviations (SD) or medians with min-max. For the specific objectives of Study IV, multiple test batteries were created. The assessment of whether patient passed or failed each test battery was treated as an independent variable during analysis. Subsequently, a multivariable Cox proportional hazard model analysis was carried out, with the occurrence of a second ACL injury (yes/no) acting as the dependent variable. Cox Proportional Hazard Models are statistical techniques used to analyse the time until an event of interest occurs. The fundamental assumption of the Cox model is that the hazard (the risk of experiencing the event at any given time) for any two individuals is proportional over time. In other words, the ratio of the hazards for any two individuals is constant. The model incorporates covariates (independent variables) to assess their impact on the hazard function, which describes how the hazard changes over time. The hazard function is not assumed to follow a specific distribution, making Cox models non-parametric. The output of the Cox model is the hazard ratio (HR). The HR represents the ratio of the hazard rates between two groups (e.g., treatment vs. control) or for different levels of a covariate. In the context of Cox proportional hazard models, a hazard ratio exceeding 1 indicates a positive association with the dependent variable (in this case, a second ACL injury), while a hazard ratio below 1 suggests a negative association.[269 270] In Study IV, additional sub-analyses were conducted to distinguish between ipsilateral and contralateral occurrences of the second ACL injury. Results from the Cox proportional hazard model were presented in terms of HR, along with 95% CI and corresponding p-values. To explore variables associated with the risk of experiencing a second ACL injury, demographic factors were examined in relation to the outcome (occurrence of a second ACL injury: yes/no) using Fisher's exact test. Subsequently, the model analysis was adjusted to account for variables that exhibited a significant association with a second ACL injury.

In Study V, statistical analyses were conducted using Statistical Analysis System (SAS) software, version 9 (SAS Institute Inc., Cary, North Carolina, USA). Demographic data were presented as mean values with SD or medians with min-max. For the study's objective, answers to PROs were analysed, and receiver operating characteristic (ROC) curves were generated. The ROC curve serves as a visual aid to depict how effectively a marker, such as responses to PROs, discriminates between two groups: individuals who suffered a second ACL injury and those who did not. A result is deemed "positive" if the PRO value surpasses a predefined threshold;

otherwise, it is considered "negative".[271] The accuracy of each threshold is measured by the probability of true positives (sensitivity) and true negatives (1-specificity) (Figure 29). The accuracy of all assessed thresholds (that is, different sensitivity and 1-specificity values) are plotted on a graphical curve and can be summarized by two ROC curve measures: the area under the curve (AUC) and Youden index. Interestingly, the ROC curve has a fascinating historical development, and its origins can be traced back to World War II. The ROC curve was initially developed for military applications, that is, for radar signal detection during the 1940s. The United States military faced the challenge of distinguishing between signals from incoming enemy aircraft (Japanese "kamikaze") and signals from other sources, such as birds or noise. Engineers and statisticians were tasked with developing a method that could help operators make decisions about whether a blip on the radar indicated a real threat. The concept of the ROC curve emerged as a solution to this problem. The curve was used to illustrate the trade-off between sensitivity (the ability to detect true positives, i.e., enemy aircraft) and specificity (the ability to avoid false positives, i.e., misidentifying harmless objects).

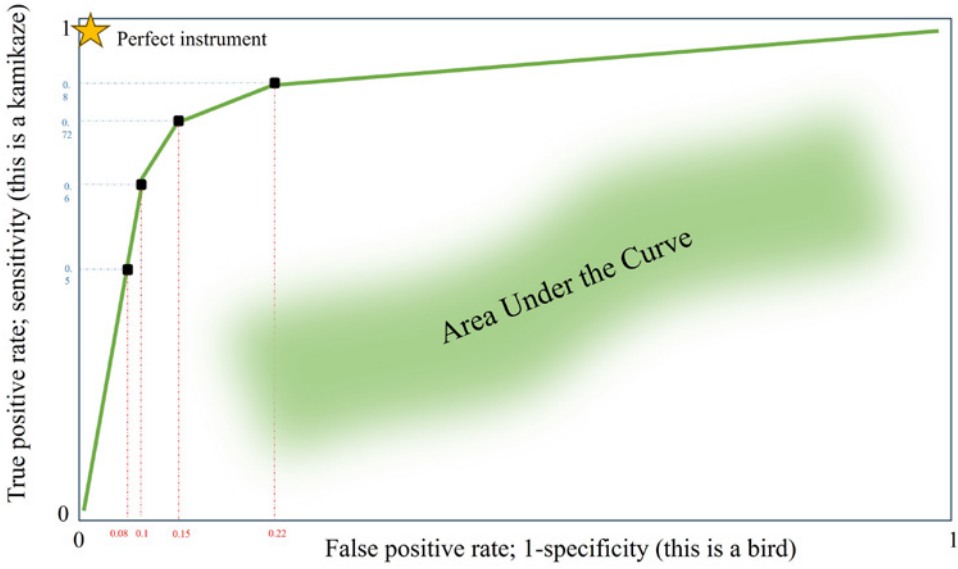


Figure 29: Visual representation of a receiver operating characteristic (ROC) curve.

The top left corner of the ROC curve means perfect sensitivity and specificity. Therefore, the closer the curve will be to the top left corner, the bigger will be the area under it. Consequently, the area under the curve (AUC) reflects a classifier's ability to distinguish outcomes, that is, accuracy. Greater AUC values indicate superior performance,

following this general guideline: 0.5 implies no discrimination, akin to a coin flip; 0.5-0.7 suggests poor discrimination, marginally better than chance; 0.7-0.8 signifies acceptable discrimination; 0.8-0.9 denotes excellent discrimination; and >0.9 signifies outstanding discrimination.[272] Therefore, when interpreting the AUC, values falling between 0.7 and 0.8 are typically regarded as reflecting acceptable accuracy.[273] Another summary measure of the ROC curve is the Youden index. The Youden index considers both sensitivity and specificity, providing a single value that reflects the effectiveness of a diagnostic marker or test. Mathematically, the Youden index is expressed as the sum of sensitivity (true positive rate) and specificity (true negative rate), minus 1. The Youden Index, ranges from 0 to 1, and evaluates the effectiveness of a diagnostic marker and aids in selecting an optimal threshold.[271] A Youden Index of 0 implies a useless test, while a value of 1 suggests a perfect test with no false positives or false negatives.[274] In practical application, the Youden Index serves as a tool for pinpointing the most effective threshold or cut-off point for a continuous diagnostic marker. By evaluating the Youden Index across various threshold values, it becomes possible to identify the threshold that optimizes the overall performance of the test.

Qualitative methods

QUALITATIVE DATA COLLECTION

In tandem with the quantitative data collection methods presented in the preceding sections, this thesis embraced the depth and nuance offered by qualitative methodologies, to provide a complementary lens to enrich results. Two distinct qualitative studies were included in the thesis (I and VI) employing interview as the method of data collection. The first qualitative study (I) explored the experiences of sports physiotherapists through focus group interviews, fostering a collective exploration of diverse viewpoints. In Study VI, a deeper layer of understanding for experiences of two ACL injuries was pursued through individual interviews, in order to afford a more intimate exploration of patients experiences and perspectives. By seamlessly integrating both quantitative and qualitative methodologies, this research seeks to present a comprehensive and nuanced portrayal of the complex phenomena, ensuring a well-rounded analysis that transcends the limitations of a singular methodological approach. This integrative approach not only contributes to the holistic perspective in the results but also aligns with the multifaceted nature of the research questions at hand.

In Study I, semi-structured focus groups interviews were conducted. An interview guide was created by several of the authors through discussion and screening of the literature and was not pilot tested. The focus groups took place physically at different sport rehabilitation clinics in the Gothenburg area. Focus groups interviews were recorded, transcribed verbatim, and the transcripts were then used for analysis. In Study VI, individual semi-structured interviews were performed. An interview was created by several authors, through discussion and screening of the literature, and was not pilot tested. Data collection occurred from September to November

2020 in Gothenburg. Due to the COVID-19 pandemic, some interviews deviated from the traditional physical setting; nine were conducted within a conference room at a sports rehabilitation clinic, while six were executed digitally using the Zoom™ web-based application. For both studies, recorded interviews and transcripts were saved on the responsible researcher´s laptop, in a folder protected by a security key. All interviews were anonymized during the transcription process and all data was treated confidentially.

TRUSTWORTHINESS

One crucial aspect to assess when addressing quality in qualitative research is trustworthiness.[240 275] According to Elo et al[275] trustworthiness is a process that needs to be included in the whole qualitative research process, from preparation, through organisation to reporting. Several criteria and strategies are commonly employed to enhance trustworthiness in qualitative research, including credibility, dependability, conformability, transferability, and authenticity. Credibility refers to the confidence in the truth of the findings. Establishing credibility involves the demonstration that the research accurately represents the experiences and perspectives of the participants. Techniques such as prolonged engagement, member checking (where participants review and confirm the accuracy of findings), and triangulation contribute to credibility. Although, member checking has received some critique since it has been reported not to alter the accuracy of transcripts, but rather to create complications due to the text alterations made by patients.[276] To ensure credibility, data triangulation during analysis was performed between authors involved in the analysis in both Study I and VI.

Dependability relates to the stability and consistency of the research findings over time and across different researchers. An accurate documentation of the research process, and to provide clear and detailed methodological choices contribute to dependability. Important for dependability is to not change the analytical process once it started. For instance, amendments to the e.g. interview guide should be made a priori, and not after the study started. In both Study I and VI the interview guide was not changed after the study started.

Confirmability focuses on the objectivity and neutrality of the research findings. Researchers should strive to minimize personal bias and subjectivity throughout the research process. Reflexivity, where researchers disclose who they are, acknowledge and reflect on their own biases and assumptions, contributes to confirmability. To transparently report the decision-making process can also enhance confirmability. In both Study I and VI the involved author´s background and bias was briefly summarized to enhance confirmability.

Transferability assesses the extent to which the findings can be applied or transferred to other contexts or settings. Providing rich and detailed descriptions of the research context, participants, and procedures enhances transferability. Researchers should also consider the similarities and differences between their study and other

contexts. Importantly, transferability does not necessarily need to be an aim for a qualitative study. In Study VI we provided detailed description of the study participants, as well as answer to PROs to give the opportunity to judge transferability in readers/researchers who would want to do so. In Study I the same detailed description was not applied due to confidentiality.

Authenticity refers to how well the data and process of analysis address the research question. Authenticity is a matter of discussion, as it is influenced by the researchers' individual beliefs. For instance, in Study VI, the subject under investigation, namely the rupture of an ACL and the ensuing rehabilitation, constitutes a distinctive and profoundly subjective experience shaped by memories, sensations, feelings, impressions, and interpersonal interactions. Hence, we believe that semi-structured individual interviews followed by qualitative content analysis provide a suitable method to address our research question. However, it is acknowledged that diverse perspectives exist, and other researchers may hold different opinions, perhaps favouring approaches such as narrative analysis.[240 275]

Another central aspect within qualitative research is data saturation. Data saturation is achieved when collecting additional data no longer reveals new information or insights. This indicates that the researcher has thoroughly explored the topic, contributing to the trustworthiness of the study. Saturation is particularly relevant in qualitative studies with a limited sample size. In Study VI saturation was assessed during data analysis. In Study I, we aimed to include at least 12 individuals as this was reported to be enough to reach data saturation in interview studies.[277] To further enhance the quality of qualitative studies, research can use different checklists to report information. As an example, in this thesis, both Study I and VI used the Consolidated criteria for Reporting Qualitative research (COREQ).[278]

QUALITATIVE ANALYSIS

In Study I, II and VI qualitative methods of analysis were used. Study I and VI are based on data generated by interviews: focus groups (Study I) and individual interviews (Study VI).

The ontological and epistemological standpoint of a researcher is important in qualitative research because it shapes the foundational assumptions and perspectives guiding the entire research process. The ontological standpoint influences how a researcher perceive the nature of reality and what researchers believe exists, while the epistemological standpoint guides the researcher's beliefs about how knowledge is generated. The researcher's ontological and epistemological standpoint directs the selection of research methods. For example, a constructionist may prefer qualitative methods that capture subjective experiences, while a positivist might lean towards quantitative methods emphasizing objectivity and generalizability.

The research team holds the perspective that an ACL injury is a subjective experience influenced by individual perceptions, emotions, and contextual factors. Additionally, the experience of sports phys-

iotherapists in addressing psychological outcomes in patients who have suffered an ACL injury can be included under the same subjective umbrella. Thus, we started from a constructivist ontological standpoint, recognising that reality is socially and personally constructed. Consequently, our standpoint is that interviews serve as a valuable method to capture the nuanced and personal dimensions of the ACL injury experience, as well as the clinical experience of working with psychological factors. Qualitative interviews allow participants to articulate their unique perspectives, emotions, and responses. Additionally, our epistemological stance aligns with interpretivism, emphasizing the importance of understanding the meaning individuals attribute to their experiences. In terms of analysis, qualitative content analysis was chosen as it aligns with the constructivist approach, and qualitative content analysis´s roots align with the predominant positivistic philosophy in sport medicine.[279] From an historical perspective, qualitative content analysis has evolved from the quantitative approach rooted in logical positivism, as well as hermeneutics (interpretation of text). The initial endeavours in the conduction of qualitative content analysis involved the straightforward counting of words, focusing on assessing the frequency of specific words within a given text.[280] The duality of qualitative content analysis, that is, historical roots both in positivism and hermeneutics has led to several critiques to the method.[281] Qualitative content analysis has been reported to lack a theoretical foundation and to be unfit to express the meaning of something due to its positivistic roots since qualitative content analysis is a reduction of qualitative data to identify core consistencies and meanings.[281 282] The absence of a theoretical framework can be considered both as problematic but as an opportunity as well. The opportunity arises since an atheoretical qualitative content analysis is both flexible and versatile. Analysis performed with qualitative content analysis can either go very deep, close to the meaning of what is being studied, or stay on the surface of what has been said. The depth of the analysis depends on the purpose of the study. There is a difference between "to explore the experiences of patients who suffer an ACL injury" and "to illuminate the meaning of suffering an ACL injury". This method allows to identify and explore patterns, themes, and meanings within the subjective accounts of ACL injury experiences and working with psychological impairments.

In terms of qualitative analysis, and specifically qualitative content analysis in our example, it is important to disclose about preconceptions. Preconceptions in qualitative content analysis refer to existing beliefs, assumptions, or biases that researchers bring into the research process. Preconceptions, also known as pre-understandings, stem from the researcher's background, experiences, and knowledge. Preconceptions can also influence how researchers interpret and make sense of the data. Preconceptions act as a lens through which researchers view and analyse the content, thus researchers may unconsciously emphasize or downplay certain aspects based on their pre-existing beliefs.[283] While some researchers argue that preconceptions can be totally set aside,[284] others argue that

preconceptions are inherent to the research process.[240 241 285] Edmond Husserl minted the term "bracketing"[216], which refers to the capacity of the researcher to put his/her own preconceptions within brackets when performing the analysis. We assume that preconceptions are inherent to the research process, [240 241 285] and can not be entirely set aside. Rather, researchers should engage in reflexivity: a process of self-awareness, to critically examine and disclose preconceptions. This self-awareness helps to minimize the potential biases that might affect the analysis. To acknowledge and reflect on preconceptions is essential to maintain transparency and rigor in qualitative research.

The analysis of data generated by interviews in Study I and VI was performed with qualitative content analysis according to the description of Granheim and Lundman.[240 241] In both the interview studies, interviews were recorded and transcribed. Transcripts were not sent to participants for corrections or comments. The data were analysed according to the following steps:

- Initially, all authors involved in the analysis process extensively read the transcripts to gain a comprehensive understanding of the collected data.

- Following this, meaning units were identified, extracted, and succinctly summarized. These condensed meaning units were subsequently abstracted in a Microsoft Excel™ spreadsheet. A meaning unit refers to a cluster of words or statements interconnected by a shared central meaning. In Graneheim and Lundman´s [240 241] conceptualization, a meaning unit encompasses words, sentences, or paragraphs that cohesively address interconnected aspects through both the content and the context.

- Condensed meaning units were then coded. A code is the label of a meaning unit. To assign a code to a condensed meaning unit provides the opportunity to explore the data from a different perspective. The code can be associated with discrete objects, events, and various phenomena, emphasizing the importance of understanding the meaning unit in relation to the given context.

- In the fourth step codes were grouped for similarities and differences in sub-categories. During the process of grouping codes in sub-categories transcripts were read again several times. Subsequently, sub-categories were cross-validated against the transcripts to verify that no data were overlooked or inadvertently incorporated. The process of grouping codes into subcategories was performed by continuous discussion between authors involved in the analysis until consensus was reached. Up to this stage, authors made a strong effort to minimize interpretation and keep close to the text.

- The fifth step is considered as the core feature of qualitative content analysis.[240] Here, sub-categories were grouped for similarities and differences into main-categories (sometimes referred to as categories). A category represents a grouping of content that shares common characteristics. Due to the intercon-

nected nature of human experiences, creating strictly exclusive categories in texts dealing with such experiences is often a challenge. The primary purpose of a category is to answer the question 'What?' and can be identified as a recurring thread throughout the codes. Essentially, a category pertains to a descriptive level of content, serving as an expression of the text's manifest content. Typically, a category encompasses several sub-categories. Despite categories reflecting the manifest content, at this stage a minimal interpretation of the content of text was allowed. The interpretation was allowed mainly to create a category name that would reflect the core of the included codes for better interpretation by the readers. For example, sport physiotherapists experienced to struggle to find knowledge about psychological factors, and this was summarized in a category called "calling for a guiding light".

- The sixth step involves the collection of several main categories into a theme. This step is optional, not always necessary, and not always performed. A theme embodies a fundamental layer of meaning interwoven within condensed meaning units, codes, or categories at an interpretive level. It serves as a tangible expression of the deeper, underlying content within the text. Fundamentally, themes help researchers organize and interpret data by highlighting essential aspects and connections within the information collected. Themes go beyond surface-level details to uncover the latent content or underlying meanings present in the text. At this stage, interpretation is allowed. In Study I and VI, no theme was generated by the data.

Systematic review

DATA COLLECTION

Study II in this thesis was a systematic review. In a systematic review, the first step in data collection is a comprehensive literature search, which was performed for Study II in the databases PubMed, Cochrane Library, PsycINFO, Allied and Complementary Medicine Database (AMED), and Physiotherapy Evidence Database (PEDro). When conducting the literature search, a blend of Medical Subject Heading (MeSH) terms associated with ACL, depression, anxiety, and their synonyms was employed. The results of the search were then sifted through, with eligible studies subsequently evaluated in full text for potential inclusion. In Study II, this process was performed in the Rayyan QCRI[286] web application for systematic reviews. From the included studies, data was then extracted. In Study II, data was extracted to a Microsoft Excel spreadsheet (version 16; Microsoft Corporation, Redmond, Washington, USA) and consisted of author, journal, purpose, publishing year, statistical analysis, sample size, time of follow-up, study population, outcomes, results, and conclusion.

DATA ANALYSIS

Due to substantial heterogeneity in the outcome assessment methods used in the included studies, no meta-analysis was possible. Instead the data synthesis method employed was the qualitative

based Emerging Synthesis Approach[287 288]: a systematic methodology proposed for synthesizing diverse literature within a given topic, encompassing various data types and study designs. This approach facilitated the organization of results through a combination of narrative expression, summarization, and tabulation. The presentation of results was structured with the use of subheadings.[287 288] Due to discrepancies in the collected data regarding outcome measurements, a method was employed to standardize the results. This involved calculating a percentage, achieved by dividing the mean score obtained from a particular outcome (PROs) in a study by the highest possible score for that specific outcome measurement. This standardized approach was chosen to unify the results concerning the levels of depression and anxiety severity across studies. The outcomes in terms of the severity of anxiety and depression were then depicted as percentages (ranging from 0% to 100%) of the PRO utilized to evaluate the targeted outcome.

RISK OF BIAS AND CERTAINTY OF EVIDENCE

The risk of bias assessment of studies included in a systematic review is fundamental to ensure the trustworthiness, reliability, and applicability of the synthesized evidence. Risk of bias assessment helps to evaluate the internal validity of individual studies as well as to establish transparency of evidence synthesis results and findings. Studies with a high risk of bias are more likely to produce results that may not accurately represent the true relationship between variables.[289 290] Several tools have been reported in the literature to assess risk of bias in studies included in a systematic review, such as the the Risk of Bias Assessment tool for Non-randomized Studies (RoBANS).[291] It has been reported that systematic reviewers might interchange the terms "quality assessment" and "risk of bias assessment," though these terms hold distinct meanings.[229] The term "quality" is often vaguely defined but is commonly employed to express the effectiveness of how the research was carried out and reported. On the other hand, "bias" specifically refers to systematic deviations from the truth, which can arise from deficiencies in research design, conduct, analysis, and/or reporting.[229] In Study II, the term "quality" was interchanged with "risk of bias". The studies included in Study II were assessed using the Methodological Index for Non-Randomized Studies (MINORS).[292] The MINORS is a tool used to judge the quality of a study. For non-comparative studies, 8 items are assessed, and for comparative studies, there are 4 additional items, resulting in 12 items to assess. Each item is rated on a scale of 0 to 2 points, where 0 indicates the item was not reported, 1 signifies the item was reported inadequately, and 2 denotes adequate reporting. Consequently, non-comparative studies have a maximum score of 16 points, and comparative studies have a maximum of 24 points. Interpretation of scores is as follows: non-comparative studies scoring 0-4 points are considered very low quality, 5-8 points are rated as low quality, 9-12 points as fair quality, and 13-16 points as high quality. For comparative studies, scores of 0-6 points are considered very low quality, 7-12 points as low quality, 13-18 points as fair quality, and 19-24 points as high quality.[292] A corresponding tool to judge the quality of a study for a qualitative

study is the Mixed Methods Appraisal Tool (MMAT),[293 294] and was used in Study II. The MMAT provides specific criteria for appraising different components of research, such as the study's design, data collection, data analysis, and the integration of qualitative and quantitative methods. The MMAT comprises a maximum of 25 screening questions which are rated "yes", "no" or "cannot tell".[293 294]

To grade the certainty of evidence in a systematic review enhances the usefulness, credibility, and applicability of the synthesized information, supporting evidence-based decision-making across various fields. Further, to grade the certainty of evidence adds transparency to the systematic review process and provides a clear indication of the level of confidence that can be placed in the synthesized evidence, allowing users to assess the robustness of the conclusions. Certainty of evidence reflects the confidence one can have in the findings. With graded certainty, reviewers can prioritize interventions or recommendations based on the strength of the evidence. High-certainty evidence is more likely to have a substantial impact on decision-making compared with low-certainty evidence.[226] The most widely used tool to grade the certainty of evidence is the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group methodology.[295] According to the GRADE, the starting certainty for an included study is 'high' for randomised controlled trials, and 'low' for study designs other than case series (or any other study without control), which starts at 'very low'.[229] Subsequently, the certainty of evidence can be downgraded one or two levels for each of the five domains of the GRADE approach: study limitations, inconsistency, indirectness, imprecision of the estimates and the risk of publication bias accordingly:

- the assessment of study limitations, refers to the assessment of risk of bias. Risk of bias can arise from several different factors, which further differ between RCTs or observational studies. In RCTs, risk of bias can be due to lack of allocation concealment, lack of blinding, incomplete accounting of patients and event, selective outcome reporting, recruitment bias or stopping the trial early for benefit. In observational studies risk of bias might arise in case of flawed measurement of exposure and/or outcome, failure to control confounding factors or incomplete follow-up. Evidence can be downgraded if >75% of studies have high or unclear risk of bias;[296]

- for inconsistency, the highest level of certainty in a body of evidence is achieved when multiple studies demonstrate consistent effects. Due to inconsistency, evidence can be downgraded if large heterogeneity is found, based on the similarity of point estimates, statistical heterogeneity and I^2 >50%;[297]

- for imprecision, the assessment of imprecision centres around the 95% confidence interval surrounding the best estimate of the absolute effect. Certainty is diminished if the clinical decision would likely differ based on whether the true effect falls at the upper or lower end of the confidence interval. Authors

may opt to downgrade for imprecision in cases where the effect estimate is derived from only one or two small studies or if there were a limited number of events. Commonly, evidence can be downgraded if the sample size of at least 2,000 patients is not met, or the CIs of the effect in the included studies is too wide, i.e. includes no effect.[298]

- for indirectness, evidence can be downgraded if the studied patients differ from those to whom the recommendation applies. Indirectness can also arise when the interventions studied deviate from the real-world perspectives. Moreover, indirectness occurs when the studied outcome serves as a surrogate for a different outcome.[299]

- for publication bias, approaches based on examination of the pattern of data are available to detect possible publication bias. Publication bias infers that studies which do not show positive significant results are on many occasions not published. Publication bias is more prevalent in observational data and when most published studies receive funding from industry. For publication bias, evidence can be downgraded due to for instance asymmetry in funnel plots (where enough studies are available). Egger's test is a widely employed method for evaluating the potential presence of publication bias in a meta-analysis. Egger's test utilizes funnel plot asymmetry by conducting a linear regression of intervention effect estimates on their standard errors, with weighting based on their inverse variance.[300]

Finally, the certainty of evidence for the studied outcome is defined as high, moderate, low or very low.[295] In very rare occasions, certainty of evidence can be upgraded.[295] High certainty of evidence suggests that additional research is improbable to alter the confidence level in the estimated effect. Moderate certainty implies that further investigation is likely to significantly influence confidence in the estimated effect. Low certainty indicates that additional research is highly probable to have a notable impact on confidence in the estimated effect. Very low certainty signifies substantial uncertainty surrounding the estimate.

Grading the certainty of evidence was performed in Study II, albeit poorly described in the manuscript.

Individual studies

Study I

STUDY DESIGN

Qualitative study

METHODS

Data for Study I was collected via semi-structured interviews held in focus groups with sport physiotherapists. To ensure transparency with research, the COREQ[301] checklist was used to report methodological information. An interview guide was created through discussion between the involved authors. The interview was not pilot tested. The interviews were conducted at four distinct sports rehabilitation clinics in Gothenburg between May and

October 2019. Clinics were chosen for their clear emphasis on sport injuries rehabilitation within the study's geographical area. After selection, clinics were contacted by phone, and participants were selected by their supervisors, considering factors like age, sex, experience, and availability. Fourteen participants, including 7 men and 7 women, were recruited, and all contacted clinics agreed to participate (Table 4). The target was to have at least 12 participants, as this has been recommended to ensure data saturation.[277] Prior to their participation, all sports physiotherapists were provided with comprehensive details about the study's objectives and procedures, both orally and in writing. They were clearly informed that their involvement was entirely voluntary and that they had the freedom to withdraw from the study at any point without needing to provide a reason. The confidentiality of the statements made by the sports physiotherapists was strictly maintained, and no patient data was collected or recorded. According to Swedish law, health care providers sharing of professional experiences is not subject to ethical approval.

Table 4. Demographics of sport physiotherapists included in Study I.

Sport physiotherapists (n = 14)	
Male sex (n)	7
Age, mean (SD)	34 (8)
Age, median (range)	32 (26-49)
Years of experience, mean (SD),	9 (7)
Years of experience, median (range)	5.5 (2-22)

n: number; SD: Standard Deviation

The interviews lasted between 39-66 minutes.

OUTCOME

The outcome of interest in Study I was sport physiotherapists own experiences of addressing psychological impairments in patients after an ACL reconstruction.

ANALYSIS

Analysis was performed with qualitative content analysis according to the description of Granheim and Lundman.[240 241]

Study II

STUDY DESIGN

Systematic review

METHODS

Study II was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42020181678), and reported according to the PRISMA guidelines.[228] An electronic search was performed by a librarian with expertise in medical

electronic searches, at the Sahlgrenska University Hospital Library, on 25 May 2020. Subsequently, two authors independently conducted the screening of abstracts for inclusion and exclusion criteria. The agreement between the two authors was assessed using Cohen's kappa coefficient, revealing a moderate level of agreement ($k = 0.57$).[302] The eligibility criteria encompassed various study designs, including RCTs, longitudinal studies, cohort studies, case-control studies, cross-sectional studies, and qualitative studies. Additionally, the selected studies needed to be written in English, published in peer-reviewed journals, and involve patients with an injured and/or reconstructed ACL within the age range of 16 to 65 years. A total of 16 reports were included in Study II (Figure 30). As Study II was a systematic review, no ethical approval was necessary.

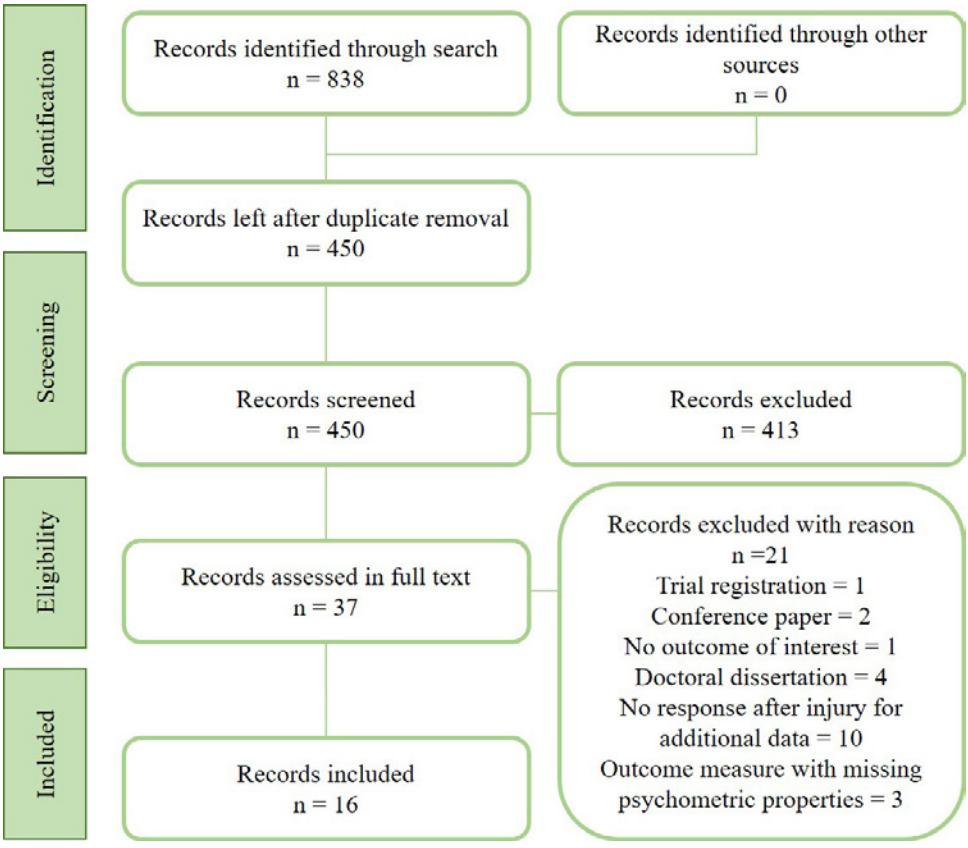


Figure 30: PRISMA flowchart of inclusion process. n = number

OUTCOME

The outcome of interest was the presence and severity of self-reported symptoms of depression or anxiety reported in psychometric tested PROs. Additional outcomes were considered based on the type of outcome measurement utilized, the timing of administration (from baseline injury/reconstruction), and the possible impact on treatment outcomes. Quality of included studies was assessed with the MINORS, and certainty of evidence was judged by two authors using GRADE.

ANALYSIS

Data synthesis was performed using an Emerging Synthesis Approach.[287] The results were summarized in narrative expression and in tables, according to the proposed method.[287] Results were summarized under two main headings: symptoms of depression and symptoms of anxiety, each comprising the following sub-headings: severity, prevalence and time. To provide a visual overview of the prevalence and intensity of self-reported symptoms of depression and anxiety, a percentage was derived by dividing the mean score obtained from the utilized outcome measurement in each study by the maximum achievable score for that measurement. Findings regarding the severity of anxiety and depression were then depicted as percentages (ranging from 0 to 100%) of PRO utilized to evaluate the outcome of interest.

Study III

STUDY DESIGN

Matched registry cohort study

METHODS

Study III was written following the RECORD checklist, extended from the STROBE statement.[303] Demographic data, results from muscle function tests and answers to the K-SES and the ACL-RSI for Study III were extracted from Project ACL´s database in November 2019. Patients aged 16-40 years at the time of ACL reconstruction, who registered one or two ACL injuries in Project ACL were eligible for inclusion. Patients who suffered a contralateral second ACL injury, who suffered a second ACL injury later than 24 months after index reconstruction and who participated in pre-injury physical activity below Tegner 6 were excluded. After inclusion, all patients who suffered a second ipsilateral ACL injury within 24 months of index ACL reconstruction were matched 1:3 in terms of age (±1 year), patient sex, and preinjury Tegner activity scale (± 1 unit, but not below level 6) with patients not suffering a second ACL injury within 24 months of index ACL reconstruction (Figure 31; Table 5).

Outcome of interests were compared in a cross-sectional manner between patients who suffered a second ipsilateral ACL injury and patients who did not according to Project ACL´s follow-ups (10 weeks, 4, 8, and 12 months) during the first year after ACL reconstruction. Importantly, outcomes for the group of patients who suffered a second ACL injury were taken from the follow-ups before patients suffered a second ACL injury. Due to the inherent nature of the study, cohort sizes varied, and the number of participating patients differed at each follow-up assessment. However, a consistent 1:3 ratio was maintained

between patients who suffered second ACL injury and patients in the matched group. Data from the matched group were restricted to patients specifically matched against individuals in the second ACL injury group who participated in each follow-up. Any patients in the second ACL injury group who did not participate in a particular follow-up, either due to missing data or experiencing a second ACL injury, had their data excluded. To mitigate potential sources of bias, demographic comparisons were conducted between cohorts and between patients present and patients missing at each follow-up. Ethical approval was granted by the Swedish Ethical Review Authority (registration number 2020-02501).

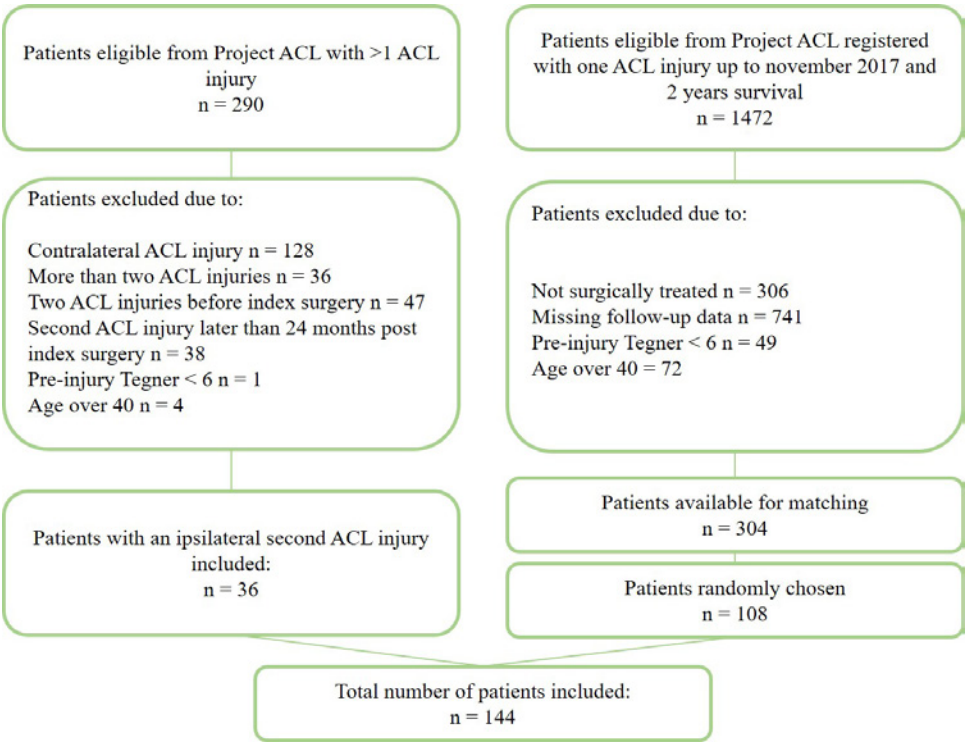


Figure 31: Flowchart for inclusion and exclusion for Study III. n = number

Table 5. Demographics of patients included in Study III. Mean±SD or count and proportion (n; %).

	Ipsilateral second ACL injury (n = 36)	ACL reconstruction (n = 108)
Sex (men) n, (%)	17 (47%)	51 (47%)
Age at reconstruction (years)	22.9 ± 4.5	23.0 ±4.5
Weight (kg)	71 ± 14	71 ±13
Height (cm)	173.0 ± 9.7	173.9 ±9.7
BMI (kg/m^2)	23.5 ± 3	23.2 ±3
Pre-injury Tegner level, median (range)	9 (7-10)	9 (6-10)
10, n, (%)	13 (36%)	22 (20%)
9, n, (%)	9 (25%)	38 (35%)
8, n, (%)	9 (25%)	29 (27%)
7, n, (%)	5 (14%)	14 (13%)
6, n, (%)	0 (0%)	5 (4.6%)
Graft choice		
Patella, n, (%)	6 (17%)	14 (13%)
Hamstring, n, (%)	26 (72%)	94 (87%)
Other, n, (%)	2 (6%)	0 (0%)
Missing	2 (6%)	0 (0%)

ACL = anterior cruciate ligament; BMI = body mass index; cm = centimeters; kg = kilograms; m^2 = square meters; n = number; Tegner = Tegner Activity Scale; SD = standard deviation.

OUTCOME

Outcomes of interest included the results of tests of muscle function, reported both as the limb symmetry index (LSI) and as absolute results relative to body weight and answers to the K-SES and the ACL-RSI.

ANALYSIS

Demographic data were summarized using mean values accompanied by SD or medians with min-max. Group comparisons were conducted utilizing various statistical methods: mean value comparisons were assessed using t-tests, while for ordinal variables such as the Tegner Activity Scale, a median test (k samples) was employed. Percentages were compared using chi-square tests. All the tests that were statistically significant were reported with delta (differences; Δ) and CI.

Study IV

STUDY DESIGN

Registry study

METHODS

Study IV was written following the RECORD checklist, extended from the STROBE statement.[303] Demographic data, results from muscle function tests and answers to the KOOS, subscale Quality of life (QoL) and the ACL-RSI were extracted from Project ACL´s database for Study IV in April 2021. Patients registered in Project ACL, 16-50 years at time of reconstruction with a Tegner pre-injury activity level of ≥ 6 were eligible for inclusion. In this specific study, returning to Tegner ≥ 6 was defined as RTS. If patients did not RTS or did not participate in all muscle function tests and answered to PROs within 6 months from the follow-up in which they reported to RTS, patients were excluded (Figure 32).

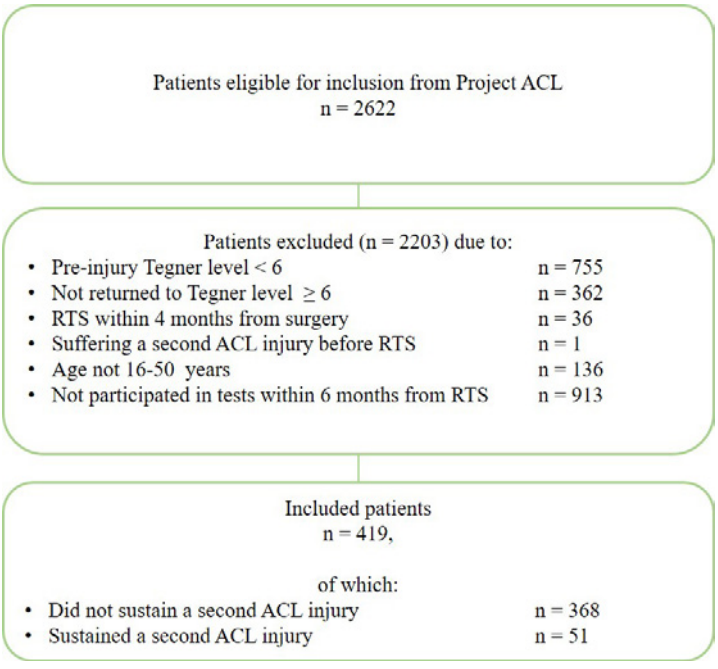


Figure 32: Flowchart of inclusion process in Study IV. n = number

Upon inclusion (Table 7), data from the follow-up closest in time in which patients reported to RTS was used for further analysis. Patients were tracked for a period of 2 years from RTS following ACL reconstruction, with follow-up concluding either at the end of the 2-year period or upon occurrence of a second ACL injury, whichever event came first. To address the study's objective, results from muscle function tests and responses to PROs were merged into four distinct test batteries (Table 6). Ethical approval was granted by the Swedish Ethical Review Authority (registration number 2020-02501).

Table 6: Test batteries created for Study IV.

Test battery	Strength tests included	Hop tests included	PROs included
Test battery 1		Vertical hop Hop for distance	
Test battery 2		Vertical hop Hop for distance	KOOS QoL ACL-RSI
Test battery 3	Knee extension Knee flexion	Vertical hop Hop for distance Side hop	
Test battery 4	Knee extension Knee flexion	Vertical hop Hop for distance Side hop	KOOS QoL ACL-RSI

ACL-RSI = Anterior Cruciate Ligament Return to Sport after Injury scale; KOOS QoL = Knee injury and Osteoarthritis Outcome Score, Quality of Life subscale.

For each of the different tests comprised in one test battery, a cut-off was chosen to determine whether patients passed or not the single test. To interpret the outcomes of the muscle function tests, a threshold of ≥ 90% LSI was selected to determine whether a patient successfully passed a test.[108 304 305]

When patients successfully completed all tests within a particular battery, they were categorized as having passed that battery. Test battery 1 focused on the vertical hop and hop for distance, chosen for their frequent usage post-ACL reconstruction.[306] As for the ACL-RSI, a cut-off score of 76.6 points was applied, as studies have identified this threshold as optimal in differentiating patients prone to a second ACL injury from those who are not.[205] Similarly, the KOOS QoL utilized a score of 62.5 points, which has been associated with a sense of "feeling well" following primary ACL reconstruction.[307]

Lastly, the components of test battery 3 were selected based on current consensus criteria.[308] Answers to psychological PROs were added to both test battery 1 and test battery 3. Thus, test battery 2 and 4, comprising both answers to PROs and results of muscle function tests were created.

OUTCOME

The outcome of interest was the possible association between passing a test battery and to suffer a second ACL injury, expressed as a hazard ratio. The hazard ratio was defined as a measure of how often a particular event happens in one group compared with how often it happens in another group, over time. A further outcome of interest was the passing rates of the different test batteries, between patients who suffered a second ACL injury and patients who did not.

ANALYSIS

The study employed a dichotomous variable (yes/no) to determine whether patients passed a test battery. This served as an independent variable for subsequent analysis. A multivariable Cox proportional hazard model was then applied, with the occurrence of a second ACL injury (yes/no) as the dependent variable. Subsequent sub-analyses were performed based on whether the subsequent ACL injury occurred on the ipsilateral or contralateral side. The results of the Cox proportional hazard model, including HR, 95% CI, and p-values, were presented. To explore variables linked to the risk of a second ACL injury, demographic factors were evaluated using Fisher's exact test in relation to the outcome of interest—specifically, the occurrence of a second ACL injury (yes/no). Following this, adjustments were made to the model analysis to incorporate variables that displayed a significant association with the risk of a second ACL injury.

Study V

STUDY DESIGN

Registry study

METHODS

The Standards for Reporting Diagnostic Accuracy (STARD) statement was used as a checklist to report Study V.[309] Demographic data, results from muscle function tests and answers to the KOOS, subscale QoL as well as Sport and recreation (Sport), the ACL-RSI and the K-SES were extracted from Project ACL´s database for Study V in November 2021. Patients consecutively registered in Project ACL, who had undergone ACL reconstruction with or without experiencing a subsequent second ACL injury within two years from the time of RTS were eligible for inclusion. Exclusion criteria were age at reconstruction below 16 or over 50 years, non-participation in knee-strenuous sports before index ACL injury (Tegner Activity Scale < 6), occurrence of a second ACL injury before surgical reconstruction, or failure to participate in any follow-up in Project ACLs (Figure 33). Ethical approval has been granted by the Swedish Ethical Review Authority (registration number 2020-02501).

Table 7: Demographics of patients included in Study IV. Mean (SD) or count and proportion (n; %).

	All patients; n=419	Women; n=205	Men; n=214
Age at reconstruction (years)	23.9 (7.5)	22.8 (7.5)	25.0 (7.3)
Weight (kg)	72.4 (12.3)	63.8 (8.4)	80.6 (9.7)
Height (cm)	175.0 (9.8)	167.5 (6.7)	182.2 (6.2)
BMI (kg/m^2)	23.5 (2.5)	22.7 (2.2)	24.3 (2.5)
Tegner pre-injury (level) n (%)			
10	76 (18.1%)	35 (17.1%)	41 (19.2%)
9	141 (33.7%)	61 (29.8%)	80 (37.4%)
8	114 (27.2%)	73 (35.6%)	41 (19.2%)
7	64 (15.3%)	25 (12.2%)	39 (18.2%)
6	24 (5.7%)	11 (5.4%)	13 (6.1%)
Graft choice			
Hamstring, n (%)	331 (85.1%)	164 (86.2%)	167 (83.9%)
Patellar, n (%)	53 (13.7%)	24 (12.7%)	29 (14.6%)
Other, n (%)	5 (1.3%)	2 (1.1%)	3 (1.5%)
Missing (graft) n (%)	30	15	15
Second ACL injury within 2 years of RTS			
Yes n (%)	51 (12.2%)	28 (13.7%)	23 (10.7%)
Ipsilateral ACL injury n (%)	31 (61.0%)	16 (7.8%)	15 (7.0%)
Contralateral ACL injury n (%)	20 (39.2%)	12 (5.9%)	8 (3.7%)
Time to RTS (months)	11.0 (4.2)	11.8 (4.4)	10.2 (3.8)
Returned to pre-injury Tegner			
Yes n (%)	147 (35.1%)	72 (35.1%)	75 (35.0%)

ACL = anterior cruciate ligament; BMI = body mass index; cm = centimeters; kg = kilograms; n = number; m^2 = square meters; RTS = return to sport, defined as Tegner ≥ 6; SD = standard deviation.

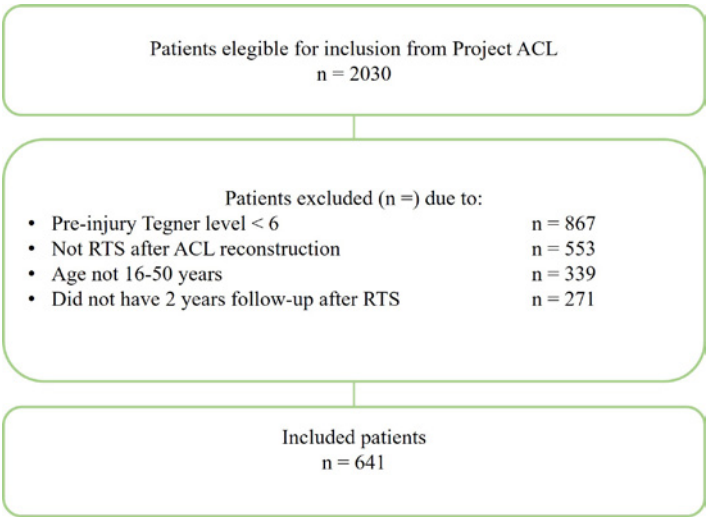


Figure 33: Flowchart of inclusion process in Study V. n = number

In this study, a return to Tegner score of ≥ 6 was considered indicative of RTS. The follow-up period extended to two years post-RTS. For the patients included in the study (Table 8), the results of PROs and strength tests from the follow-up closest to the RTS event were designated as the "index test."

OUTCOME

In Study V, the primary focus was on identifying optimal cut-offs with maximum sensitivity and 1-specificity to differentiate between patients who experienced a second ACL injury and those who did not, for each PRO included. Additionally, a secondary objective was to assess the recovery of symmetrical quadriceps strength as a potential protective factor. Consequently, sensitivity analyses were conducted to compare patients who had achieved ≥90% recovery of quadriceps strength in the injured limb relative to the uninjured limb, against those who had not.

ANALYSIS

The ROC curve was calculated for each PRO, based on patient´s answers at the follow-up closest to RTS. Results were presented with two summary measures for the ROC: the AUC and Youden index. Mean values with SD or medians with minimum and maximum are presented for the demographic data.

Table 8: Demographics of patients included in Study V. Mean (SD) or count and proportion (n; %).

	All patients; n=641	Women; n=286	Men; n=355
Age at reconstruction, years	24.8 (7.6)	23.5 (7.6)	25.8 (7.4)
Weight, kg	73.5 (12.7)	64.2 (8.9)	80.9 (10.2)
Height, cm	175.7 (9.3)	168.2 (6.5)	181.7 (6.4)
BMI (kg/m^2)	23.7 (2.8)	22.7 (2.7)	24.5 (2.6)
Tegner pre-injury level, n (%)			
10	118 (18.4%)	47 (16.4%)	71 (20.0%)
9	213 (33.2%)	84 (29.4%)	129 (36.3%)
8	158 (24.6%)	89 (31.1%)	69 (19.4%)
7	108 (16.8%)	42 (14.7%)	66 (18.6%)
6	44 (6.9%)	24 (8.4%)	20 (5.6%)
Time to RTS, months	11.8 (15.1)	13.6 (16.4)	10.3 (13.8)
Returned to pre-injury Tegner			
Yes, n (%)	442 (69.0%)	194 (67.8%)	248 (69.9%)
Time to return to pre-injury Tegner, months from index reconstruction			
4	108 (24.4%)	29 (15.0%)	79 (31.8%)
5-8	75 (17%)	30 (15.5%)	45 (18.1%)
9-12	128 (29%)	67 (34.5%)	61 (24.6%)
12-24	70 (15.8%)	35 (18.0%)	35 (14.1%)
>24	61 (13.8%)	33 (17.0%)	28 (11.3%)
Graft choice			
Hamstring, n (%)	465 (72.5%)	205 (71.7%)	260 (73.2%)
Patellar, n (%)	77 (12.0%)	34 (11.9%)	43 (12.1%)
Other, n (%)	6 (0.9%)	4 (1.4%)	2 (0.6%)
Unknown n (%)	93 (14.5%)	43 (15.0%)	50 (14.1%)
Second ACL injury within 24 months from RTS			
Yes n (%)	64 (10.0%)	33 (11.5%)	31 (8.7%)
Ipsilateral second ACL injury n (%)	43 (67.2%)	21 (63.6%)	22 (71.0%)
Contralateral second ACL Injury n (%)	21 (32.8%)	12 (36.4%)	9 (29.0%)

ACL = Anterior Cruciate Ligament; BMI = Body Mass Index; cm = centimeters; kg = kilograms; n = number; m^2 = square meters; RTS= Return to Sport; Tegner = Tegner Activity Scale; SD = standard deviation.

Study VI

STUDY DESIGN

Qualitative study

METHODS

Data for Study VI was collected via individual semi-structured interviews with young active female patients who had been treated with ACL reconstruction, aimed to RTS and suffered an ipsilateral second ACL injury. To ensure transparency with research, the COREQ[301] checklist was used to report methodological information. An interview guide was created through discussion between the involved authors. The interview was not pilot tested. Patients were recruited through verbal advertisements by sports physiotherapists at various rehabilitation clinics in Western Sweden. Subsequently, patients who were interested in participating were contacted via telephone to verify eligibility. Inclusion criteria encompassed female individuals, aged between 16 and 25 years, with a pre-injury Tegner Activity Scale level of at least 6, treated with ACL reconstruction, who aimed to RTS after reconstruction and suffered an ipsilateral second ACL injury. Patients were provided with information about the study and were asked about their interest to participate. Upon receiving a positive response, interviews were scheduled. No patient declined participation, resulting in a final cohort of 15 patients, all treated with revision after the ipsilateral second ACL injury. (Table 9 and 10).

The decision to include 15 patients was made based on the consideration that it would be feasible to achieve data saturation, a determination made during the analysis process. Data was collected in Gothenburg from September to November 2020. Due to the COVID-19 pandemic, not all interviews were conducted in person. Nine interviews were held in a conference room at a sports rehabilitation clinic, while six interviews were conducted digitally using Zoom™ web-based application (Zoom Video Communications, Inc. in San José, California, USA). Interviews lasted between 21 and 47 minutes. At time of interview patients responded to four different PROs: the Short Form (36) Health Survey (SF-36); [310 311] the Hospital Anxiety and Depression Scale (HADS);[310 311] the Montgomery Åsberg Depression Rating Scale (MADRS),[312] and the Athletic Identity Measurement Scale (AIMS).[313] Importantly, answers to PROs were intended as demographics (Table 11). Consequently, answers to PROs were not taken into consideration during the data analysis process. Ethical approval has been granted by the Swedish Ethical Review Authority (registration number 2020-02834).

OUTCOME

The outcomes of interest in Study VI were young female patient´s own experiences of going through one ACL injury, reconstruction, the rehabilitation period, and suffering an ipsilateral second ACL injury.

ANALYSIS

Analysis was performed with qualitative content analysis according to the description of Granheim and Lundman.[240 241] The analysis process, was performed with a deductive approach based on the "*integrated model of psychological response to injury*

and rehabilitation".[128] Given the objective was to investigate the experiences of young females on a journey which culminates to a second ipsilateral ACL injury, the findings were organized chronologically, encapsulating the progression from the initial ACL injury, through rehabilitation, to the subsequent ACL injury, and through rehabilitation once more. Consequently, results were depicted along two lines, aligning with the four domains in the model,[128] to visually represent findings. Sub- and main categories were categorized within the respective domains of the model, with further stratification into positive or negative responses.

Table 9: Demographics of patients included in Study VI.

Patients (n = 15)	Mean (range)
Age	19.1 (16-23)
Time between ACL reconstruction to ipsilateral second ACL injury (months)	13.4 (4-26)
Weight, kg	63.3 (58-79)
Height, cm	169 (162-184)
BMI, (kg/m^2)	22 (19.1-23-7)

cm = centimeters; kg = kilograms; n = number; m^2 = square meters; BMI = Body Mass Index

Table 10: Months from index ACL reconstruction to return to training with restrictions, return to unrestricted sport, and ACL re-rupture for each patient included in Study VI.

Patient	Time in months from index ACL reconstruction to:			
	Return to training with restrictions	Return to unrestricted sport	ACL re-rupture	Time of interview
15	9	11	11	29
14	10	11	15	27
13	12	24	26	70
12	5	11	11	47
11	10	12	17	68
10	11	12	12	59
9	10	12	12	59
8	5	10	12	54
7	6	10	16	54
6	9	12	12	47
5	4	n/a	15	45
4	9	10	10	31
3	n/a	n/a	4	23
2	5	15	23	42
1	9	10	10	29

n/a = not applicable (patient not reaching stated goal); ACL: Anterior Cruciate Ligament; revision: second ACL reconstruction performed after re-rupture

Table 11: Answers to patient reported outcomes for patients included in Study VI; presented for description.

SF-36								
	Physical functioning	Role physical	Role emotions	Energy/ vitality	Emotional well being	Social functioning	Pain	General health
Mean (range)	87.3 (75-100)	76.7 (0-100)	84.5 (33-100)	68.0 (40-80)	79.7 (60-96)	89.2 (63-100)	81.5 (58-100)	85.7 (70-95)
AIMS								
Median (range)				34 (16-48)				
MADRS								
Median (range)				5 (0-14)				
HADS								
	Depression				Anxiety			
Median (range)	1 (0-4)				6 (1-9)			

AIMS: Athletic Identity Measurement Scale, highest score 50 (strongest athletic identity).

HADS: Hospital Anxiety and Depression Scale, highest score 21 (most severe symptoms) for each subscale

MADRS: Montgomery Åsberg Depression Rating Scale, highest score 54 (most severe symptoms)

SF-36: Short Form Health Survey, highest score 100 (no symptoms) for each subscale: physical functioning; physical role limitations; emotional role limitations; energy/vitality; mental health; social functioning; bodily pain, and general health perceptions.

Results

"...le mie mani come vedi non tremano più, e ho nell' anima, in fondo all' anima, cieli immensi, e immenso amore..."

Study I

Inquiry:
Sport physiotherapists own experiences of addressing psychological factors during rehabilitation after an ACL reconstruction

The experiences of sports physiotherapists of addressing psychological factors in the rehabilitation in patients after an ACL injury were summarized in four main categories:

1) Calling for a guiding light;
2) Meeting the burden of psychological impairments;
3) Trying to balance physical and psychological aspects;
4) Goal setting: a helpful challenge

CALLING FOR A GUIDING LIGHT

The sport physiotherapists expressed a gap in knowledge with regard to the identification and management of psychological impairments in rehabilitation after ACL reconstruction. There was uncertainty among sport physiotherapists about the extent of their responsibility in the face of psychological challenges, where some sport physiotherapists questioned their confidence in such matters. Sport physiotherapists emphasized that their knowledge of how to address psychological impairments in rehabilitation after an ACL injury primarily evolves through clinical experience, an intuitive sense developed while working with patients, and learning from past errors. Collaborative discussions with colleagues and professionals were integral to the learning process. The sport physiotherapists also mentioned to mentor physical therapy students, to pursue advanced education, to participate in rehabilitation-specific courses, and to engage with social media as additional avenues which contribute to their understanding of psychological challenges. Throughout all four interviews, interactions with colleagues emerged as the primary source to gain a deeper insight into psychological challenges. Interestingly, certain sport physiotherapists believed they actively contributed to improve psychological well-being and recovery, even if the exact mechanisms remained unclear to them.

Quote: *"... you have some kind of theoretical reference, and, as [physiotherapist A] says, there are great differences between patients, so there's a little bit of trial and error with each patient, but, of course, that is based on the theoretical knowledge you have of healing and recovery and muscles and so on."*[314]

MEETING THE BURDEN OF PSYCHOLOGICAL IMPAIRMENTS

Sport physiotherapists emphasized that psychological impairments pose a more significant challenge than physical ones during ACL injury rehabilitation. Sport physiotherapists considered the management of psychological impairments particularly difficult, with the central focus on patients' fear of pain. The sport physiotherapists outlined various challenges associated with psychological impairments, such as diminished motivation and heightened stress levels among patients. In cases where injuries led to team training absences an additional hurdle for sport physiotherapists

was found: to help patients who report feeling socially isolated. Patients who report pain, fear of movements, or fear of pain were identified by sport physiotherapists as particularly challenging to treat, especially when patients have limited time for rehabilitation commitment. Sport physiotherapists highlighted the use of conversations and to be present for patients as primary interventions to help patients overcome psychological impairments. In addition, sport physiotherapists implemented strategies such as support to patients and joint training sessions for individuals with similar injuries. Based on the long rehabilitation time, sport physiotherapists expressed a sense to become an integral part of patients' lives, which could foster an environment where patients felt comfortable in discussing psychological impairments. While sport physiotherapists believe the courage to inquire about psychological challenges is important, they admit hesitation in initiating such conversations.

Quote: "*The mental part is really hard (for patients) […] most of those patients who get injured might have friends or relatives who injure themselves and might know what it means. But it is mentally difficult for them to get injured. Even the long absence from the activity. One year can feel like an eternity when you (patient) are … We are talking about people who are 15, 16, 17 years old. So it is very hard. I think the mental aspect is worse than the physical aspect."*[314]

TRYING TO BALANCE PHYSICAL AND PSYCHOLOGICAL ASPECTS

Patient education was mentioned as a crucial element of rehabilitation, with emphasis on the need for patients to comprehend the non-linear nature and time commitment of ACL injury recovery. Key to this educational approach was to adapt the rehabilitation program to align with each patient's current physical and psychological status. Sport physiotherapists highlighted the importance of regular structured evaluations, incorporating standardized tests, alongside informal assessments such as non-tool-based conversations. Direct feedback during each visit was deemed essential to this process. Despite that the sport physiotherapists felt confidence to provide feedback on physical test outcomes, there was a reported hesitancy in addressing psychological well-being. Specifically, sport physiotherapists acknowledged their reluctance to delve into psychological aspects during evaluations, which generates a gap in the assessment of these crucial components of the rehabilitation process.

Quote: *"[…] I think I do that much more than I do a 'clear' evaluation, when they (patients) score on different scores on a computer, except for project ACL, that is. It is more of an oral evaluation, alongside what they (patients) do at the gym. More than filling in different questionnaires. But you can be better. But it is easier this way. More time effective."*[314]

GOAL SETTING: A HELPFUL CHALLENGE

According to sport physiotherapists, the attainment of patients' goals signifies successful rehabilitation. Sport physiotherapists stated that the commitment to attain each patient's primary goal, irrespective of its nature, plays a crucial role to foster motivation and discipline towards rehabilitation. Sport physiotherapists emphasized that goals are dynamic and may undergo

changes throughout the rehabilitation journey. If a patient's goal shifts during rehabilitation, their motivation toward that goal may also change. To establish and to achieve interim goals in the rehabilitation process was reported to enhance patient motivation. Sport physiotherapists asserted that breaking down rehabilitation into manageable subgoals, and to achieve the subgoals facilitates the process and provides patients with the necessary encouragement to persevere.

Quote: "Y*es, we (physiotherapists) have it like this… return to training without contact and we have a couple of boxes to tick… or criteria that we want patients to meet before. And you even get… You can give the paper to the patients and ask them to tick the boxes. Then I think like… they light up. They go like 'I have achieved all of those!'*".[314]

Study II

Inquiry:
The prevalence and severity of negative psychological response following an ACL injury

A total of 450 unique records were retrieved from the electronic search. Of those, 37 records were assessed in full text, and 11 records were excluded: 3 records did not use validated outcome measures, 4 records were doctoral dissertations, 2 records were conference papers, 1 record was a trial registration, and 1 record did not report the outcome of interest. From the remaining 26 records of 26 studies, we contacted the corresponding authors of 15 studies by email and received responses from the corresponding authors of 5 studies, of which 2 were based on the same cohort. Data from 16 studies were therefore extracted (Table 12), comprising 683 patients (411 males, 60%). Two of the included studies were qualitative studies, and 14 were quantitative studies.

QUALITY APPRAISAL

In the assessment of the quality of evidence using the MINORS tool, non-comparative studies scored between 5 and 11 out of a maximum of 16 points, with a median score of 9 points, indicating fair quality. Comparative studies, on the other hand, ranged from 10 to 18 out of a maximum of 24 points, with a median score of 16 points. Almost all comparative studies, except one, achieved scores between 13 and 18, indicating fair quality. The two qualitative studies were assessed with MMAT, and showed good quality.

GRADING EVIDENCE

Originally, in Study II, grading of the evidence according to GRADE was performed on each single study (Table 13). Although, GRADE can be performed on outcome level. On outcome level, the certainty of evidence for the prevalence and severity of self-reported symptoms of both depression and anxiety was "very low". Evidence started at level "low" and was then downgraded one point due to risk of bias (based on item 5 on the MINORS "unbiased evaluation of endpoints"), one point due to inconsistency, based on a qualitative judgement of included studies heterogeneity, and one point due to imprecision, as the sample size of 2000 individuals was not met. No downgrading was performed due to publication bias or indirectness.

SYMPTOMS OF ANXIETY

Ten included studies assessed symptoms of anxiety, although none reported the prevalence. Three studies assessed symptoms of anxiety using the State and Trait Anxiety inventory (STAI), 2 using the Hospital Anxiety and Depression Scale (HADS), 1 using the Brief Symptom Inventory (BSI), 1 the Profile of Mood States (POMS) and 1 the European Quality Five Dimension (EQ5D). In addition, 2 qualitative studies were included. The severity of self-reported symptoms of anxiety is presented in figure 34.

Table 12: Summary of the included studies, number of patients and follow-ups.

Study	Patients included (n)	Baseline	Last follow-up
Anxiety			
Celebi et al.[315]	38	ACLR	6 weeks after ACLR
Filbay et al.[316]	162	5-20 years after ACLR	N/A
Brewer et al.[146]	61	ACL injury	N/A
Lepley et al.[317]	20		6 months after ACLR
Oztekin et al.[318]	30	ACL injury	3 weeks after ACLR
Hemsley et al.[319]	22	6 weeks after ACLR	N/A
Tripp et al.[320]	20	ACLR	N/A
Brewer et al.[321]	91	ACL injury	24 months after ACLR
Depression			
Oztekin et al.[318]	30	ACL injury	3 weeks after ACLR
Filbay et al.[316]	162	ACLR	5-20 years after ACLR
Tripp et al.[320]	20	ACLR	N/A
Celebi et al.[315]	38	ACLR	6 weeks after ACLR
Garcia et al.[67]	64	Pre-ACLR	One year after ACLR
Feyzioglu et al.[322]	30	ACLR	6 weeks after ACLR
Mainwaring et al.[323]	7	ACL injury	30 days
Baranoff et al.[324]	44	ACLR	6 months after ACLR
Langford et al.[325]	87	ACLR	6 months after ACLR
Brewer et al.[146]	91	ACL injury	24 months after ACLR
Brewer et al.[326]	61	ACL injury	N/A

n: number; N/A: not applicable (due to the lack of reported data, or the use of an outcome measurement for which cut-offs were not found in the literature); ACLR: Anterior Cruciate Ligament Reconstruction.

Table 13: Rating the quality of evidence using GRADE in each included study in Study II.

Study	Initial GRADE	Final GRADE
Mainwaring et al.[323]	Low	Very low †
Baranoff et al.[324]	Low	Low
Langford et al.[325]	Low	Low
Oztekin et al.[318]	Low	Very low ‡
Filbay et al.[316]	Low	Low
Tripp et al.[320]	Low	Low
Celebi et al.[315]	Low	Low
Brewer et al.[146]	Low	Low
Brewer et al.[326]	Low	Low
Garcia et al.[67]	Low	Low
Feyzioglu et al.[322]	Low	Low
Hemsley et al.[319]	Low	Low
Lepley et al.[317]	Low	Low
Brewer et al.[321]	Low	Low

GRADE: Grading of Recommendations Assessment Development and Evaluation; †: downgraded due to the risk of bias, imprecision and indirectness; ‡ downgraded due to the risk of bias

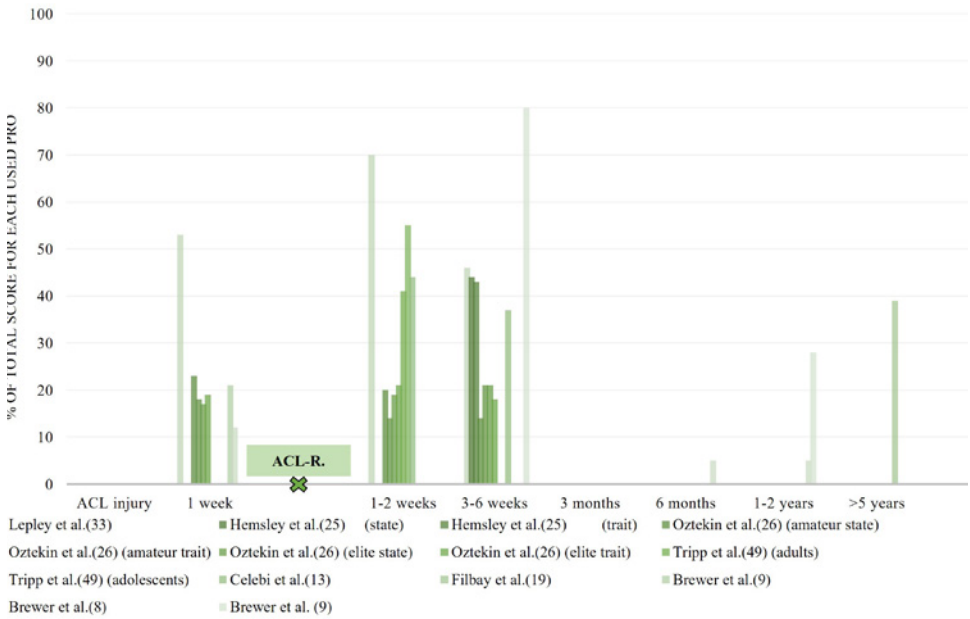


Figure 34: Severity of self-reported symptoms of anxiety. Severity grade calculated as a percentage of the total score in the outcome measure used in each study. State anxiety: anxiety level about an event; trait anxiety: anxiety level as a personal characteristic.

There were no reported differences in anxiety levels between adults (>18 years old) and adolescents (16-18 years old), patients who recovered knee range of motion fast or slow after reconstruction or professional and recreational athletes.[319 320 322] However, in qualitative studies, professional rugby players exhibited anxiety feelings before RTS.[327] A specific case study focusing on one rugby player revealed perceived anxiety symptoms immediately following ACL reconstruction.[328]

Self-reported symptoms levels did not overreach the threshold for diagnosis of anxiety at any point. Self-reported symptoms of anxiety appear to peak in the first weeks after ACL reconstruction, although this is the time in which symptoms are assessed the most. In a long-term follow-up, one study reported that 73% of patients exhibited no anxiety, 19% showed possible anxiety, and 2% were likely to have anxiety 5-20 years after ACL reconstruction.[316]

SYMPTOMS OF DEPRESSION

Twelve included studies assessed self-reported symptoms of depression. Three studies used the Beck Depression Inventory (BDI), 2 studies used the HADS, 2 studies used the POMS, and one study each used the Quick Inventory of Depressive Symptomatology (QUIDS), the Depression Anxiety and Stress Scale (DASS-21) and the BSI, respectively. Additionally, one qualitative study reported depression as a theme. The severity of self-reported symptoms of depression is presented in figure 35. The prevalence of depression, diagnosticated by reaching a determined cut-off in the PRO used, was reported to range between 42% (1 year follow-up)[67] to 1% (5-20 years follow-up).[316] Seven studies on depression symptoms showed a general decrease over time.[67 315 321-325] Two studies hinted at variations in symptom severity between ACL reconstruction and six months later. No significant differences in symptoms of depression were noted between adults and adolescents post-reconstruction, except for one rugby player showing symptoms two weeks after ACL injury.[315 320 324 328] Regarding rehabilitation adherence, three studies found a connection between negative mood, stress, and lower adherence, even though depression values didn't exceed scale values for the diagnosis of depression.[146 321 326]

Professional athletes exhibited a greater severity of depression symptoms both pre and post ACL reconstruction and before and after accelerated rehabilitation compared to recreational athletes. Furthermore, athletes with an ACL injury reported higher levels of depression symptoms compared to athletes with a concussion or healthy controls.[315 318 322]

Study III

Inquiry:
The association between psychological factors and second ACL injury risk

At baseline, 36 patients were included in the ipsilateral second ACL injury group and were matched against 108 patients, who did not suffer a second ACL injury within 24 months of index reconstruction. No statistical differences in demographic variables between cohorts were present at baseline or at any follow-up (Table 14).

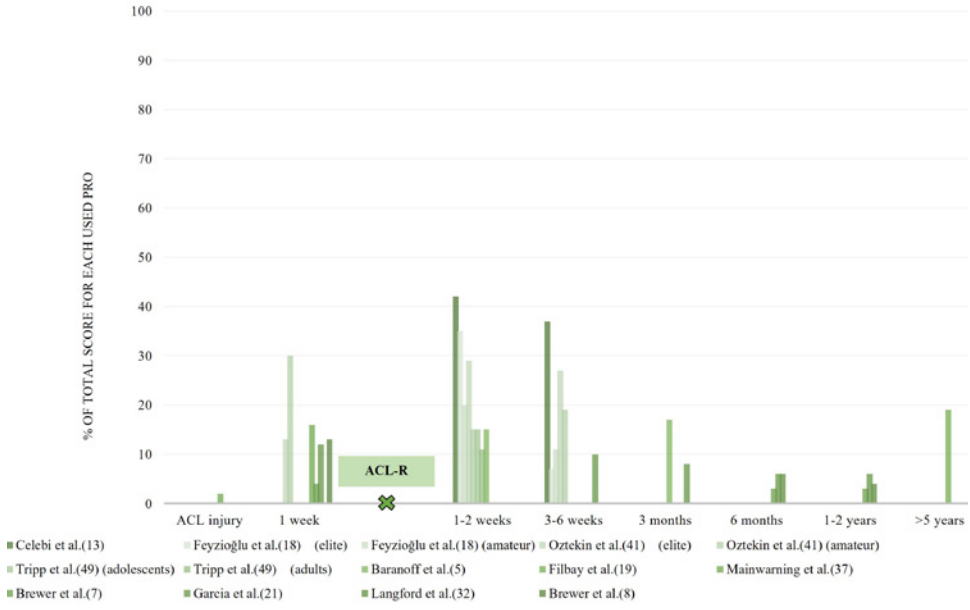


Figure 35: Severity of self-reported symptoms of depression. Severity grade calculated as a percentage of the total score in the outcome measure used in each study.

Table 14: Between-groups statistical differences in demographics of patients included in Study III.

Variable	P value baseline	P value 10 weeks	P value 4 months	P value 8 months	P value 12 months
Age at reconstruction	0.999 *	0.999 *	0.999 *	0.999 *	0.999 *
Weight	0.949 *	0.980 *	0.943 *	0.921 *	0.968 *
Height	0.927 *	0.750 *	0.926 *	0.829 *	0.388 *
BMI	0.636 *	0.614 *	0.620 *	0.583 *	0.371 *
Pre-injury Tegner level	0.613 ‡	0.398 ‡	0.845 ‡	0.429 ‡	0.422 ‡
Graft choice	0.411 †	0.116 †	0.142 †	0.099 †	0.778 †

† chi-square test; * independent sample t test; ‡ median test (k samples).

The mean time between index reconstruction and ipsilateral second ACL injury was 12.2 ± 4.5 months. Of the 36 patients included in the ipsilateral second ACL injury group, 21 (58%) suffered the second injury within the first 12 months, and 15 (42%) between 12 and 24 months after index reconstruction (Figure 36).

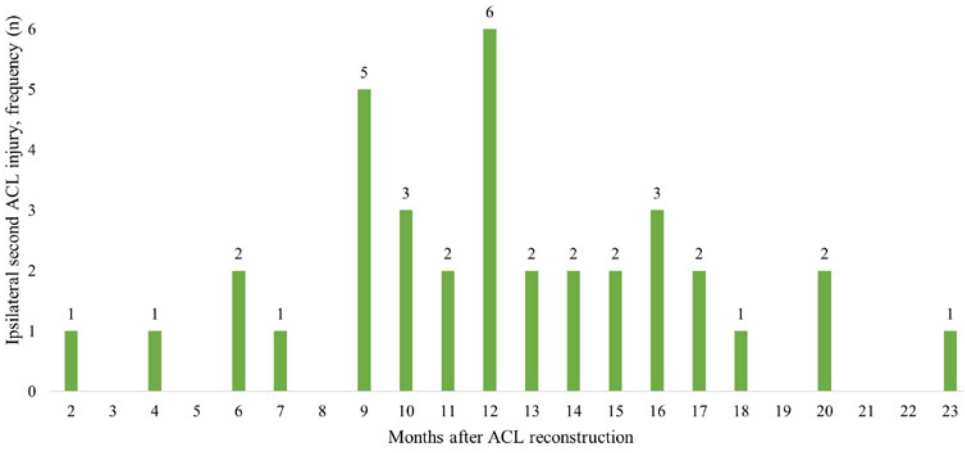


Figure 36: Number of patients (y axis) who sustained an ipsilateral second ACL injury for each of the first 24 months after index ACL reconstruction. n = number.

In Table 15 the number of patients participating in each follow-up per group is shown.

The absolute strength was normalized to bodyweight for the non-injured limb's hamstring. Patients who would suffer an ipsilateral second ACL injury showed higher hamstring strength compared with matched counterparts at the 10-week's follow-up (1.5 vs. 1.3 Nm/kg, ΔCI = 0.1-0.4, p = 0.029).

No other significant differences between the groups were observed during all subsequent follow-ups. The LSI remained consistent across all follow-ups. Additionally, there was no disparity in the percentage of patients achieving an LSI ≥90% in all five muscle function tests at any follow-up between groups. Moreover, there were no discernible differences in the percentage of patients returning to their pre-injury activity level at any follow-up.

Table 15: Number of patients participating in each follow-up, stratified by group.

	Muscle function tests		Answer to PROs	
	Ipsilateral second ACL injury (n)	No second ACL injury (n)	Ipsilateral second ACL injury (n)	No second ACL injury (n)
10 weeks	24	72	25	70
4 months	27	78	30	81
8 months	26	78	27*	64*
12 months	17	51	16*	32*

PRO = patient reported outcomes; n = number. * = the ACL-RSI was responded by 22/27 patients at 8 months and 15/16 at 12 months; ACL-RSI = anterior cruciate ligament return to sport after injury scale.

Table 16: Limb Symmetry Index (LSI) for quadriceps and hamstrings, stratified by group.

Follow up	Quadriceps		Hamstring		Percentage of patients reaching 90% LSI on all five muscle function test. (ipsilateral second ACL injury / no second ACL injury)
	Ipsilateral second ACL injury	No second ACL injury	Ipsilateral second ACL injury	No second ACL injury	
10 weeks	73.5±12.3	76.7±12.4	85.1±19.5	81.6±19.8	4% / 12%
4 months	83.9±11.6	87.6±13.0	92±14.9	92.2±15.0	4% / 2%
8 months	94.3±10.7	97.1±12.6	96.8±8.7	97.6±11.8	46% /34%
12 months	97.5±8.9	99.9±22.3	99.3±10.6	102.3±23.2	41% /25%

Mean values ± Standard Deviations are presented for LSI; ACL, Anterior Cruciate Ligament; LSI, Limb Symmetry Index.

There were no differences in the percentage of patients reaching pre-injury level of Tegner at any follow-up. Although, at the 12 months follow-up, patients who would go on and suffer an ipsilateral second ACL injury reported a higher level of Tegner (median: 9 vs 6, p = 0.018) (Figure 37 A and B).

Patients who would go on and suffer an ipsilateral second ACL injury rated higher present knee-related self-efficacy at both 8 months (8.6 vs 8.0 [95% ΔCI = 0.1-1.2], p = 0.021) and 12 months (9.4 vs 8.1, [95% ΔCI = 0.3-2.2] p = 0.012) after index reconstruction, as well as higher future knee-related self-efficacy at 12 months. (8.2 vs 7.0, [95% ΔCI = 0.01-2.4], p = 0.049) (Figure 38).

Patients who would go on and suffer an ipsilateral second ACL injury reported higher values of confidence, emotions and risk appraisal at both 8 months (81.2 vs 67.9, (95% ΔCI = 2.7-23.8) p = 0.014) and at 12 months (95.2 vs 67.1, (95% ΔCI = 14.3-41.8) p ≤ 0.001) (Figure 39)

Study IV

Inquiry:
The association between adding psychological questionnaires to RTS test batteries and the risk for second ACL injury

A total of 419 patients were included in Study IV. Of those patients, 51 (12.2%) suffered a second ACL injury within the first 2 years after RTS (defined as return to Tegner level 6 or higher), of which 31 (61%) were ipsilateral and 20 (39%) were contralateral. (Figure 40 And 41)

No differences in passing the test batteries were found between patients who would suffer a second ACL injury and patients who did not (Figure 42). Moreover, no differences were found when patients were stratified whether the second injury was ipsilateral or contralateral.

Patient's sex and time to RTS expressed in months were significantly associated to suf-

fering a second ACL injury, both regardless of second ACL injury side and for ipsilateral second ACL injury, but not for contralateral. They were considered as confounders in the Cox hazard model. Passing any of the test batteries was not associated with the risk of suffering a second ACL injury (Table 17)

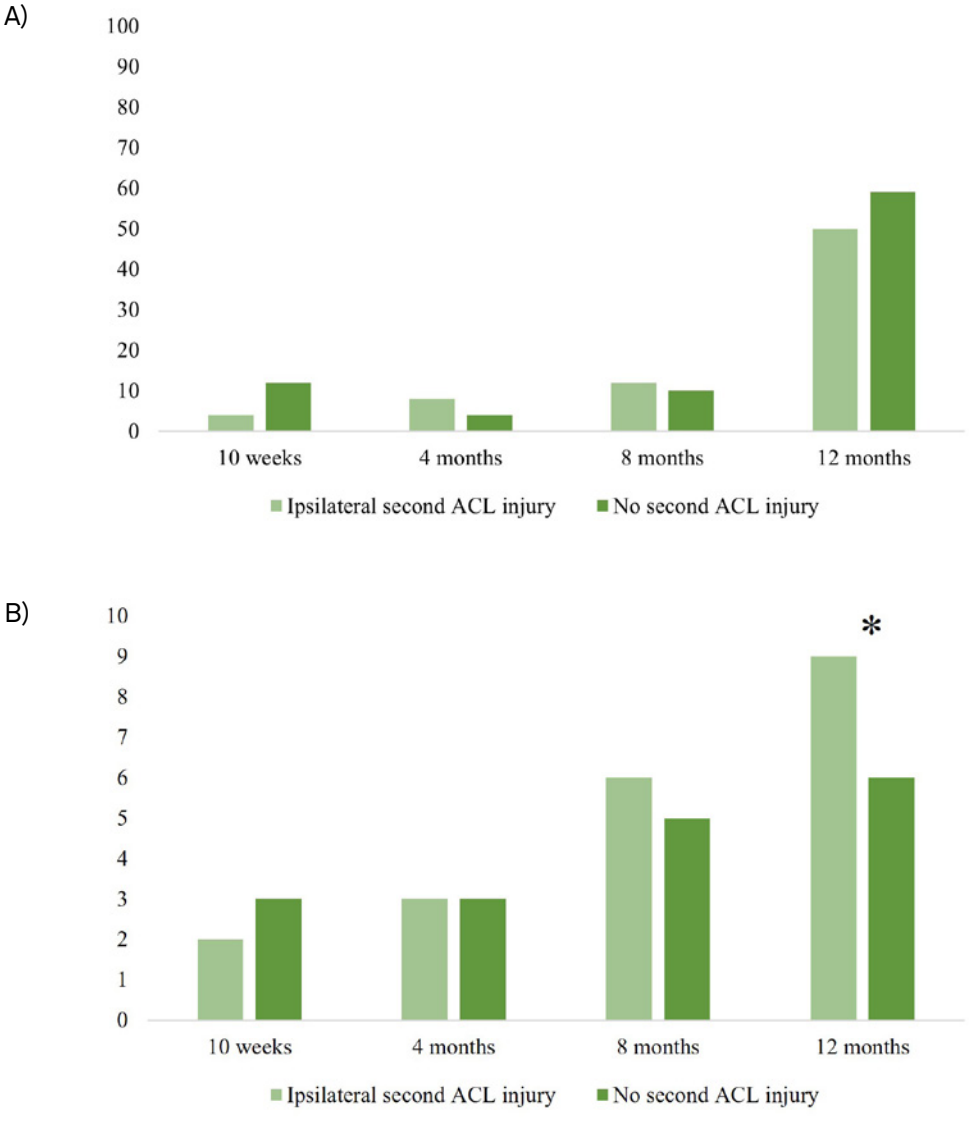


Figure 37: Panel A: percentage of patients who returned to pre-injury Tegner level; panel B: median present Tegner level. * = statistical significant difference.

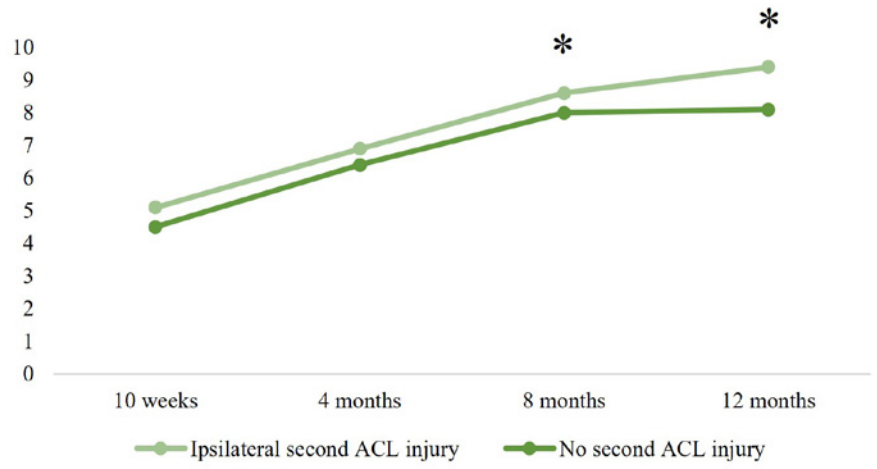


Figure 38: Mean K-SES present between groups. K-SES = knee self-efficacy scale; * = statistical significant difference.

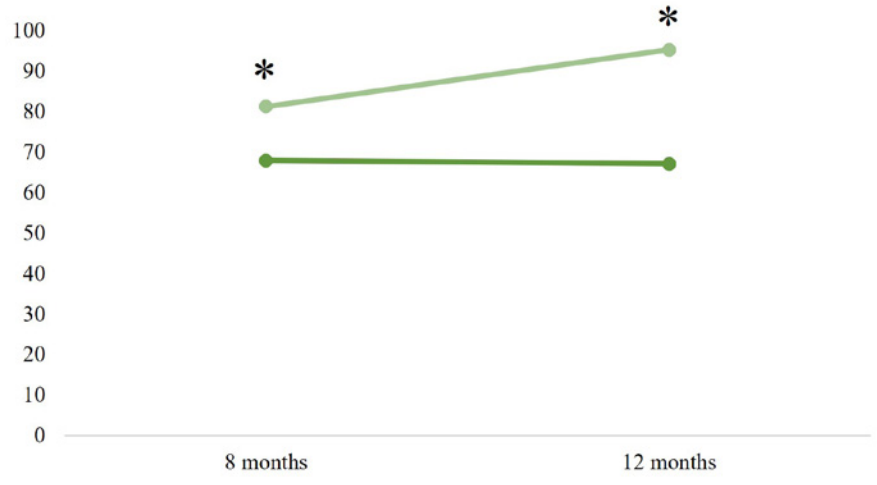


Figure 39: Mean ACL-RSI between groups. ACL-RSI = anterior cruciate ligament return to sport after injury scale; * = statistical significant difference.

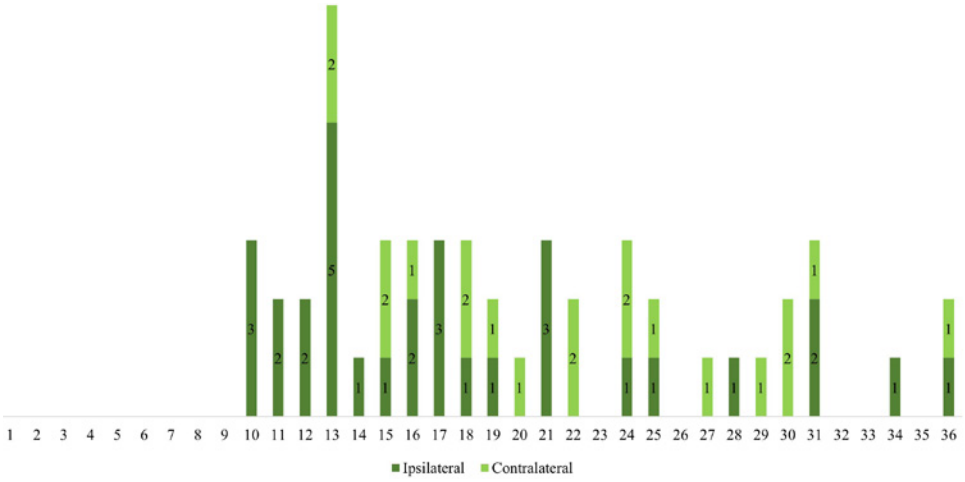


Figure 40: Monthly incidence of second ACL injury starting from index ACL reconstruction as baseline. ACL = anterior cruciate ligament;

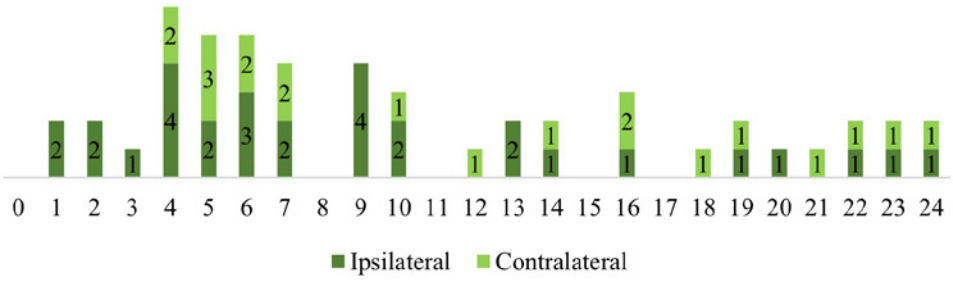


Figure 41: Monthly incidence of second ACL injury starting from return to sport as baseline. ACL = anterior cruciate ligament;

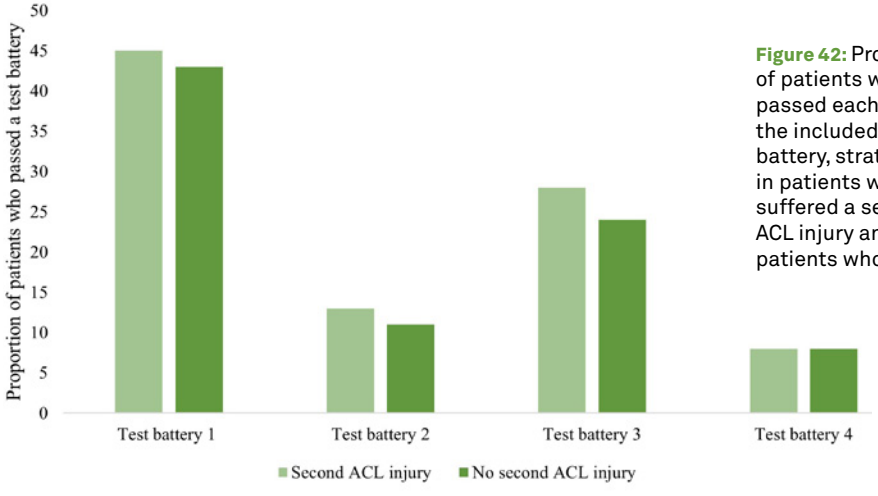


Figure 42: Proportion of patients who passed each of the included test battery, stratified in patients who suffered a second ACL injury and patients who did not.

Table 17: Univariable and adjusted for time to return to sport (months) and patient sex Cox hazard ratios associated with a second ACL injury.

Outcome	Event rate (fail/pass)	HR of a second ACL injury	P value	Adjusted HR of a second ACL injury	P value
Test battery 1	28 of 236 / 23 of 183	0.93 (0.54 - 1.61)	0.79	0.82 (0.47 - 1.44)	0.50
Test battery 2	33 of 258 / 5 of 34	0.83 (0.33 - 2.14)	0.71	0.76 (0.29 - 1.94)	0.56
Test battery 3	35 of 297 / 14 of 96	0.78 (0.42 - 1.45)	0.43	0.71 (0.38 - 1.32)	0.27
Test battery 4	34 of 252 / 3 of 22	0.97 (0.30 - 3.17)	0.96	0.94 (0.29 - 3.10)	0.93
Ipsilateral; adjusted for patient sex and time to return to sport (months)					
Test battery 1	18 of 236 / 13 of 183	1.06 (0.52 - 2.16)	0.88	0.90 (0.44 - 1.84)	0.77
Test battery 2	21 of 258 / 4 of 34	0.67 (0.23 - 1.94)	0.46	0.57 (0.20 - 1.67)	0.31
Test battery 3	20 of 297 / 10 of 96	0.63 (0.29 - 1.34)	0.23	0.54 (0.25 - 1.15)	0.11
Test battery 4	22 of 252 / 3 of 22	0.63 (0.19 - 2.11)	0.46	0.53 (0.16 - 1.77)	0.30
Contralateral; not adjusted					
Test battery 1	10 of 236 / 10 of 183	0.76 (0.32 - 1.83)	0.55	//	//
Test battery 2	12 of 258 / 1 of 34	1.51 (0.20 - 11.60)	0.69	//	//
Test battery 3	15 of 297 / 4 of 96	1.16 (0.39 - 3.50)	0.79	//	//
Test battery 4	12 of 252 / 0 of 22	3725267 (0.00 -)	0.99	//	//

ACL = anterior cruciate ligament; HR = hazard ratio; analysis regardless of second ACL injury side and ispsilateral side adjusted for time to return to sport (Tegner ≥ 6; months) and patient sex; ACL = anterior cruciate ligament.

Study V

Inquiry:
The best cut-off values on questionnaires used to evaluate patients who suffer an ACL reconstruction that can differentiate patients who suffer a second ACL injury from patients who do not

A total of 641 patients were included in Study V, of which 64 (10%) suffered a second ACL injury within 24 months from RTS. In total, 43 (67.2%) second ACL injury were ipsilateral and 21 (32.8%) contralateral.

Forty-five second ACL injury happened within the first 12 months after RTS, and 18 happened between 13-24 months after RTS (Figure 43.)

Answers to PROs were collected from the follow-up closest in time to RTS (defined as return to Tegner level 6 or higher). For each PRO, the optimal score (cut-off) with the best possible properties, that could differentiate between patients who would go on and suffer a second ACL injury and patients who did not, were calculated (Table 18).

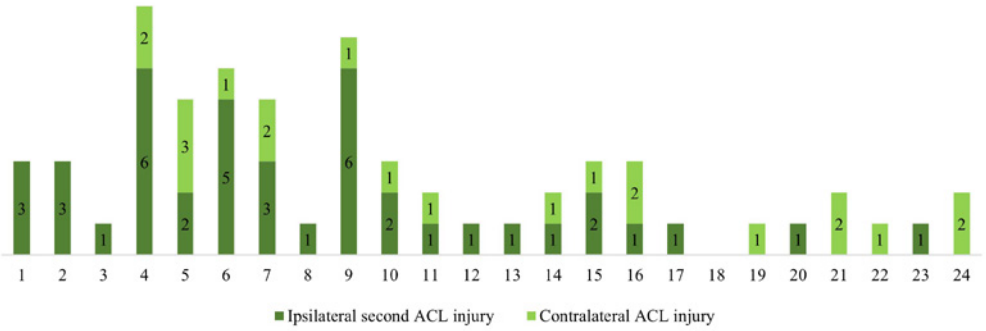


Figure 43: Monthly incidence of second ACL injury from return to sport as baseline. ACL = anterior cruciate ligament;

Table 18: Cut-off for the included PROs.

	Patients	Cut-off	Youden Index	Model AUC	Sensitivity	1 - Specificity
K-SES$_{18}$ present	630	9.4	0.09	0.520	0.34	0.26
K-SES$_{18}$ future	630	7.0	0.08	0.511	0.78	0.70
KOOS QoL	627	56.0	0.12	0.531	0.59	0.47
KOOS Sports	627	96.0	0.12	0.557	0.19	0.07
ACL-RSI	382	71.7	0.13	0.553	0.50	0.37

PROs = Patient Reported Outcomes; ACL-RSI = Anterior Cruciate Ligament Return to Sport after Injury Scale; KOOS = Knee injury and Osteoarthritis Outcome Score; QoL = subscale Quality of Life; K-SES = Knee Self-Efficacy Scale; AUC = Area Under the Curve

The cut-offs displayed AUC and Youden index values below acceptable levels. The best Youden index was 0.13, and the best AUC 0.557. Table 19 presents the proportion of patients who suffered a second ACL injury scoring above or below calculated cut-offs.

A sensitivity analysis to account for the recovery of symmetrical quadriceps strength as a protective factor was performed. Cut-offs were calculated for patients who recovered ≥90% of their quadriceps strength in the injured limb compared to the uninjured limb, and patients who did not, respectively (Table 20).

After stratification based on whether patients achieved symmetrical quadriceps strength (LSI ≥90%) or not, the new calculated cut-offs did not show acceptable AUC or Youden index values (Table 20): the best Youden index was 0.24, and the best AUC was 0.613. Thus, regardless of quadriceps strength symmetry recovery, optimal cut-offs do not properly differentiate between patients who would go on and suffer a second ACL injury and patients who did not.

Table 19: Number of patients who suffered a second ACL injury scoring above or below calculated cut-offs.

PROs	Cut off	Patients who suffered a second ACL injury, % (n)	95% CI	
K-SES present	≥9.4	23% (12)	12.5%	36.8%
	<9.4	9% (52)	6.8%	11.7%
K-SES future	≥7	23% (12)	12.5%	36.8%
	<7	9% (52)	6.8%	11.7%
KOOS QoL	≥56	10% (40)	7.2%	13.2%
	<56	11% (24)	7.0%	15.6%
KOOS Sports	≥96	23% (12)	12.5%	36.8%
	<96	9% (52)	6.8%	11.7%
ACL RSI	≥71.7	14% (19)	8.4%	20.5%
	<71.7	9% (21)	5.4%	12.9%

PROs = Patient Reported Outcomes; ACL = Anterior Cruciate Ligament; CI = Confidence Interval; ACL-RSI = Anterior Cruciate Ligament Return to Sport after Injury Scale; KOOS = Knee injury and Osteoarthritis Outcome Score; QoL = subscale Quality of Life; K-SES = Knee Self-Efficacy Scale

Table 20: Sensitivity analysis with new cut-offs for patients who had recovered symmetrical muscle strength (LSI ≥90%) and patients who did not. Youden index, 1-specificity, sensitivity, model AUC and proportion (n) of patients who score equal or above (≥) or below (<) cut-off and suffer a second ACL injury.

Patients with LSI of ≥90% (n=308)								
	n	Cut-off	Youden Index	1 - Specificity	Sensitivity	Model AUC	≥cut-off; % (n) 95% CI	<cut-off; % (n) 95% CI
K-SES$_{18}$ present	308	9.4	0.17	0.34	0.51	0.569	29.4% (10) 15.1%-47.5%	9.9% (27) 6.6%-14.1%
K-SES$_{18}$ future	308	8.3	0.05	0.62	0.68	0.495	29.4% (10) 15.1%-47.5%	9.9% (27) 6.6%-14.1%
KOOS QoL	307	56.0	0.24	0.35	0.59	0.580	11.6% (27) 7.8%-16.5%	13.3% (10) 6.6%-23.2%
KOOS Sports	307	96.0	0.18	0.09	0.27	0.600	29.4% (10) 15.1%-47.5%	9.9% (27) 6.6%-14.1%
ACL-RSI	220	71.7	0.22	0.35	0.57	0.591	18.7% (15) 10.9%-29.0%	9.3% (13) 5.0%-15.4%
Patients with LSI of <90% (n=181)								
K-SES$_{18}$ present	180	6.1	0.21	0.74	0.95	0.537	8.9% (19) 5.5%-13.6%	7.4% (8) 3.3%-14.1%
K-SES$_{18}$ future	180	8.0	0.22	0.57	0.79	0.523	8.9% (19) 5.5%-13.6%	7.4% (8) 3.3%-14.1%
KOOS QoL	179	38.0	0.13	0.81	0.94	0.537	9.1% (24) 5.9%-13.3%	5.3% (3) 1.1%-14.6%
KOOS Sports	179	55.0	0.24	0.61	0.84	0.613	8.9% (19) 5.5%-13.6%	7.4% (8) 3.3%-14.1%
ACL-RSI	87	46.7	0.23 0.77		1.00	0.561	7.2% (9) 3.3%-13.2%	8.1% (3) 1.7%-21.9%

n = number; LSI = Limb Symmetry Index; ACL-RSI = Anterior Cruciate Ligament Return to Sport after Injury Scale; KOOS = Knee injury and Osteoarthritis Outcome Score; QoL = subscale Quality of Life; K-SES = Knee Self-Efficacy Scale; AUC = Area Under the Curve; CI = confidence interval

Study VI

Inquiry:
Experiences of patients who suffer two ACL injuries and are treated with two ACL reconstructions

The experiences of young female patients of going through one ACL injury, reconstruction, the rehabilitation period, and suffering an ipsilateral second ACL injury were analysed deductively and presented on two timelines with further stratification into positive or negative responses for each of the respective domains of the model used in the analysis.[128] The first timeline encompasses the experiences between the first and the second ACL injury. The second timeline encompasses the experiences between the second ACL injury and the day of interview.

Table 21: Main and sub-categories stratified as positive or negative in the timeline between ACL injury to second ipsilateral ACL injury.

POSITIVE RESPONSES		**Finding hope for the journey** *- A light in the tunnel* *- See progress, feel good*	**Accepting my ACL injury** *- What I could have done* *- Standing on a steady ground*	**I succeeded** *- Returned to sport* *- Rehab journey was smooth*
Model domain[128]	**Cognition**	**Affect**	**Behaviour**	**Outcome**
NEGATIVE RESPONSES	**What matters now?** *- Injury made sport lose its meaning* *- Missing a piece* *- Loss of identity* *- I am alone*	**Who am I?** *- I could not stand watching the others play* *- Disappointment with health care system* *- I could not find hope*	**Where will this end?** *- Fighting myself*	**What is going to happen?** *- My knee was not ready* *- Setbacks* *- Not listening to my body* *- Performance stress*

In the period between the first and second ACL injury (Table 21), patients faced losses in sport meaning and self-identity, which led to a sense of loneliness and existential questioning. Emotional struggles were compounded by unmet healthcare expectations, yet a desire to RTS provided a glimmer of hope. The importance to accept the injury and the varied outcomes in rehabilitation, from setbacks to success, shaped the overall experience.

COGNITION:
Patients grappled with profound losses, both in the meaning of their sport and a sense of self. The injury disrupted their sport participation, leading to an identity crisis, heightened by feelings of loneliness. Emotional struggles culminated in the main category of "what matters now?" No positive experiences were identified post-initial ACL injury.

Quote: "*it is so sick that something (the sport) … can mean so much. It is like a second home. It really is. When you grow up with the sport and the happiness that the sport gives you and…. To disappear from it… It has been extremely hard".*[114]

AFFECT:

The cognitive losses manifested as desperation and depressive responses and made it difficult for patients to envision a brighter future. The inability to participate in team training resulted in despair, and delays in diagnosis contributed to dissatisfaction with the healthcare system. Despite the mentioned challenges, a strong desire to return to sport provided a glimmer of hope. Rehabilitation brought satisfaction through observable progress, which was experienced as a beacon of hope in the journey.

Quote: "*The period following the first moments after surgery was better, since you come into the routine, you go to rehabilitation and train. Then you start seeing small improvements… and… those improvements trigger you to keep on going and fighting. And then, when some time has passed, you get to start with tougher exercises, and then running… and it keeps on triggering you… to fight even more…"*[114]

BEHAVIOR:

Patients felt clear physical issues and experienced lack of appropriate support. This struggle, labeled "where will this end?" stemmed from unmet expectations for help. Conversely, receiving support from social circles and teammates provided a stable foundation. Looking back, patients acknowledged the importance to accept the ACL injury to find the energy for rehabilitation efforts.

Quote: "*I had amazing support from my physiotherapists… We were close. We talked a lot and I had all the chances to ask all the questions that were running around in my head… and we had mental support from the club as well…so even if you are alone in that situation, meaning that you alone have to do the work, and you have the injury… but still…"*[114]

OUTCOME:

The RTS phase after the first ACL reconstruction brought challenges. Patients felt unprepared, faced setbacks in physical and psychological domains and questioned the future with performance stress. Yet, some patients experienced a smoother rehabilitation, which led to a sense of completeness and success, encapsulated in the main category "I succeeded."

Quote: "*at that time (upon return to sport) … everything went so well. Rehabilitation… and I was… everything fell in the right place when I was back (returned to sport). It felt great. I was so positive. No doubt it would just work. I just thought… now it goes straight forward."*[114]

Unfortunately, all included patients suffered a second ipsilateral ACL injury.

In the aftermath of an ipsilateral second ACL injury (Table 22), patients dealt with profound emotional challenges, from loneliness to fears of re-injury. However, driven by a resilient fighting spirit and supported by teammates and loving ones, patients persevered through rehabilitation. Despite the second ACL injury being a

negative happening, the experience led to personal growth, increased self-awareness, and a transformed perspective, culminating in a newfound sense of self and purpose.

Table 22: Main and sub-categories stratified as positive or negative in the timeline between second ipsilateral ACL injury and the day of interview.

POSITIVE RESPONSES	**Fighting spirit** - Personality, determination - Was it worth it - Unchanged dreams - Knowledge	**A helping hand** - Reach goals is satisfying - Part of the team	**Working hard** - Share thoughts - Face your fears - Acceptance - Variation in rehabilitation - Sharing injury experiences	**I am a new me** - I have grown as a person - I am much stronger now - My body is different - I am smarter - I am more patient
Model domain[128]	**Cognition**	**Affect**	**Behaviour**	**Outcome**
NEGATIVE RESPONSES	**I am destroyed** - Helplessness - I will not make it - Cannot accept this - Life on pause - I am alone	**Loneliness** - Impossibility to participate - Afraid to move - Afraid of re-injury - Depression - My best years on crutches	**Painful changes** - Going nowhere - Renounce social life - Eating disorder - Lower goals - I was a worse player	**I could have made it to the pro´s**

COGNITION:

After an ipsilateral second ACL injury, patients faced deep emotional struggles, feeling a profound sense of loneliness and a sense that their lives were 'on hold.' Despite the difficulty, the previous experience of ACL injury and rehabilitation helped patients recognize the challenges ahead. Driven by a strong fighting spirit, patients decided to persevere through rehabilitation, demonstrating resilience and determination.

Quote: "*it was so hard (getting through the rehabilitation journey) but… I always had the feeling that I am the one who decides if I am going to play or not. There is only one way, and that is forward. It is tough since you know what you have ahead of you (rehabilitation), but you know it is worth it when you get there*".[114]

AFFECT:

Depressive symptoms and fears of re-injury affected patients post ipsilateral second ACL injury, which hindered participation in sports and daily activities. The struggle was termed as "loneliness". However, positive experiences, like team support and to achieve rehabilitation goals, provided a helping hand and motivation to continue the fight.

Quote: "*when you reached a goal (physical goal set with rehabilitation), you got so happy and felt successful. And even if sometimes it was hard (the rehabilitation journey), I always had support of people around me and I would like to say that it is easier when you feel supported…. And when you reach your goals… it is pure joy and everything becomes possible".*[114]

BEHAVIOUR:

Rehabilitation posed painful challenges, such as not progressing in rehabilitation, which impacted patients' self-perception and social lives. However, to connect with other people in similar situations, and supportive physiotherapy, played a crucial role the process of alleviation of loneliness. To face fears and to accept the situation led to positive progression, which shaped the main category of "working hard".

Quote: "*I love the sport, and this is what I want to do… and… now I am in this situation, but I did it once already. Why wouldn´t I be able to do it again? I decided to give it everything I had. But… I was too isolated in my own bubble in order to make the effort… 'I…] my fear (of another ACL injury) is not an obstacle. It is there, but it is something to overcome rather than something that stops me".*[114]

OUTCOME:

Despite some patients did not return to their pre-injury sport level, patients gained inner strength, determination, and awareness post- ipsilateral second ACL injury. The experience fostered personal growth, increased patience, and a new perspective on life. To give up sport led to the discovery of new interests and friendships, and resulted in a transformed self, epitomized by "I am a new me".

Quote: "*I think it has changed me a lot. I do not think I would want to be without (the ACL injury process). Or, I mean… Maybe I would want to be without (the ACL injury process) since I could play (the sport). But I have a different mental strength now. I can help people in a different way. I have become more supportive and I understand other people differently. And then, manage to pull yourself through two big things (ACL injuries) will… I am young now but … in the future… I have learned how to handle things and think positive. It is extremely hard (the ACL injury process) but it has shaped me as a human being and made me to somebody who does not give up."*[114]

Discussion

"...e quando pensi, che sia finita, é proprio allora che comincia la salita..."

The overall objective of this thesis was to investigate and better understand the psychological outcomes of patients after ACL reconstruction, and possible associations with a subsequent second ACL injury. The collective findings from the included studies illuminate the multifaceted nature of ACL rehabilitation and not only emphasize the physical recovery, but also the profound psychological ramifications of ACL injuries and subsequent rehabilitation processes. The collection of evidence in Study II, the qualitative insights from Study I and VI, with the quantitative insights of Study III and the lack of association between tests and second ACL injury in Study IV and V underscore the pivotal role of psychological well-being in the ACL rehabilitation journey. The results of this thesis suggest that there is a critical gap in current practices regarding the assessment and management of psychological impairments.

The present thesis aimed to explore psychological factors during rehabilitation after ACL reconstruction from an EBM perspective, where the three pillars of EBM are integrated: clinical expertise, patient's preferences and best available evidence. Importantly, the purpose of this thesis was to further study psychological outcomes during rehabilitation after ACL reconstruction in light of a holistic approach which assumes patients are more than just a biomechanical knee where some connective tissue has suffered a damage. This does neither mean that rehabilitation specialists such as physiotherapists can be psychologists, nor that psychologists are not needed. However, clinicians and rehabilitation specialists, representing the "clinical expertise pillar of EBM" are thus called to adopt a more holistic approach to ACL rehabilitation, one that encompasses both the physical and mental health of their patients. The call for a more holistic approach to ACL rehabilitation automatically leads to the question of what constitutes the clinical expertise pillar, that is, what do sport physiotherapists know and think about psychological factors in this specific patient category.

Clinical expertise pillar

To address the clinical expertise pillar of EBM, in Study I we inquired *"what do physiotherapists know about psychological factors during rehabilitation after an ACL reconstruction?"*, in a qualitative focus group interview study with sport physiotherapists. Our findings reveal that sport physiotherapists primarily rely on a blend of clinical experience, intuition, and peer discussions to navigate the psychological dimensions of rehabilitation and acknowledge a significant gap in formal training and knowledge. The results suggest that sport physiotherapists search for enhanced understanding and guidelines to address psychological impairments, but do not know how. Furthermore, sport physiotherapists believe the intricate challenges posed by psychological factors surpass those of physical injuries, but do not know how to synchronize physical with psychological rehabilitation. Sport physiotherapists acknowledge the strategic role of goal setting in fostering patient motivation and progress. Sport physiotherapists expressed a dual sentiment of competence

and uncertainty, feeling skilled to handle physical aspects yet often ill-equipped and lacking confidence when addressing psychological impairments. One of the key challenges highlighted in this thesis was the physiotherapists' difficulty to address the signs of psychological distress. Unlike physical injuries, which can have clear, observable symptoms,[329] psychological impairments can be subtle and vary greatly among individuals.[330] [331] The lack of specific knowledge, and eventual training in psychological support techniques leaves many physiotherapists uncertain about the best approach to take. In the uncertainty, physiotherapists go with their gut feelings. This uncertainty can lead to variations in the support provided to patients, potentially affecting the consistency and effectiveness of psychological support provided within rehabilitation programs. Another study has reported that physiotherapists feel insufficiently trained to address psychological impairments during ACL injury rehabilitation.[332] Thus, an improvement of the physiotherapy education at the bachelor's degree provided at universities might be warranted.

Since clinician´s expertise is one of the pillars of EBM, an effort should be made to implement more teaching and knowledge of psychology and the psychological consequences of an injury for bachelor's physiotherapy students, as well as to provide specific courses at advanced level. Without the necessary skills and confidence, physiotherapists may inadvertently overlook or inadequately address psychological impairments, potentially delaying recovery or exacerbating the patient's distress. The need for enhanced training in psychological support is evident, pointing towards the integration of psychological principles and intervention strategies into the core curriculum of sports physiotherapy education and ongoing professional development programs. Enhanced training should not only focus on recognizing psychological impairments but also on effective communication strategies,[86] the development of therapeutic alliances, and interventions to support mental health and resilience.[333] Such training would equip physiotherapists with a more holistic set of skills, enabling them to support the patient's psychological well-being alongside physical recovery.

To guarantee that universities can provide courses on psychological factors and that professional development programs can effectively include skill learning, it is crucial that the core element of EBM—which is the knowledge produced through research—is both available and transparent. This requirement leads to the next section of the discussion: the best evidence pillar.

Best evidence pillar

To contribute to the best evidence pillar of EBM, Study II, III, IV and V were performed. In Study II, a systematic review, we inquired *"what is the prevalence and severity of negative psychological response following an ACL injury?"* and employed a comprehensive search strategy and stringent selection criteria to examine the psychological outcomes, especially depression and anxiety, in patients who

have undergone ACL reconstruction. The review identified a notable prevalence and severity of self-reported symptoms of depression and anxiety in the studied population. However, the prevalence and severity of these symptoms varied, influenced by factors such as the time elapsed since surgery and the specific measures used to assess the psychological outcomes. This variation could both reflect the individualized nature of psychological responses following ACL reconstruction, and the unstructured knowledge of the field. Depression symptom have both been widely reported after orthopedic traumas,[334] and reported to be of lesser magnitude in non-professional and recreational athletes compared with professional athletes,[318 322] who appear to have a slower psychosocial recovery and greater mood changes.[335] The notable prevalence of depression and anxiety symptoms post-ACL reconstruction, coupled with the very low quality of evidence in Study II, underscores an urgent need for the integration of psychological support within rehabilitation protocols. The psychological response during rehabilitation after ACL reconstruction is of great magnitude. Nevertheless, how psychological factors are related to a second ACL injury risk is less clear.

In Study III, we inquired "*how are psychological factors related to a second ACL injury risk?*", and assessed psychological factors in relation to the suffering of a second ACL injury. In Study III results point out that patients who will suffer a second ACL injury score higher on both the ACL-RSI and the K-SES compared to counterparts who "survive" 24 months from reconstruction without suffering an ipsilateral second ACL injury. There were no differences between patients who will suffer a second ACL injury and patients who will not in terms of physical variables, such as strength or symmetry. Results in Study III were different compared with results from McPherson et al.,[205] who reported that patients who will suffer a second ACL injury showed lower ACL-RSI scores compared with counterparts. However, in the study from McPherson et al.,[205] answers to the ACL-RSI were recorded 12 months after reconstruction, and patients were followed up to 36 months to monitor second ACL injury occurrence. Arguably, a lot can happen for a patient´s emotions, confidence, and risk appraisal to RTS in 36 months. In the present thesis this limitation was addressed by performing a cross-sectional analysis during the first 12 months after reconstruction, which is the time frame in which rehabilitation efforts are supposed to peak.[336]

Effective rehabilitation protocols aim to achieve optimal recovery by improvement of knee strength and proprioception, and by preparation of patients for a safe return to their previous level of activity or sport. Moreover, rehabilitation plays an important role in the prevention of secondary injuries (even though evidence is inconclusive)[337], which are a significant risk due to the altered biomechanics and potential compensatory movements after ACL injury.[185 338] Thus, it is recommended[339] to test patients with RTS test batteries at late-stage rehabilitation. Since Study III showed a difference in PROs answers between patients who will suffer a second ACL injury and patients who will not, we

aimed to investigate further by integrating answer to PROs to RTS test batteries. In 2019 a systematic review was published, where all evidence pertinent to RTS testing in patients treated with ACL reconstruction was collected.[119] Seventeen studies were included, but only seven included PROs in the RTS test batteries, of which two included the ACL-RSI, two the IKDC subjective and four included two self-reports (KOS-ADLS and a global rating scale).[119] The systematic review[119] concluded that passing any test battery had a minimal risk reduction rate (0.80) for second ACL injury, which made authors question the validity of RTS testing, when used to assess the risk for second ACL injury.[119] The methodology (and consequently the findings) of the review were questioned,[340] which contributes to the uncertainty of whether RTS testing is protective of second ACL injury. However, the lack of association between RTS testing and second ACL injury risk was confirmed by another systematic review from the same year.[341]

In an attempt to find a clinical test which would lower the risk for second ACL injury, we added answer to PROs to RTS test batteries in Study IV, where we inquired "*can the adding of psychological questionnaires to RTS test batteries lower the risk for second ACL injury?*". In Study IV, the association between passing RTS test batteries, with or without PROs, and the occurrence of a second ACL injury could not be established. One potential explanation for the test batteries' inability to capture the risk of a second ACL injury might lie in the thresholds used to define test success or failure. For instance, the cut-off of 90% LSI has been proposed as a definition of successful outcome,[108] but not validated as a preventive measure for a second ACL injury. Cut-offs for the ACL-RSI were taken from the study of McPherson et al.,[205] (with the limitation of answers recorded at 12 months and follow-up up to 48 months after ACL reconstruction), and for the KOOS QoL from the study of Muller et al,[307] which quantified the cut-off for the state of "feeling well". Since the cut-offs could be a reason for the RTS test batteries not capturing a second ACL injury risk, in Study V we inquired "*which cut-off values on the questionnaires used to evaluate patients who suffer an ACL reconstruction can differentiate patients who suffer a second ACL injury from those who do not?*", and we aimed to calculate the best cut-offs for the ACL-RSI, K-SES, KOOS Sports and QoL.

Study V could show that the best cut-offs in the ACL-RSI, K-SES, KOOS Sports and QoL to discriminate between patients who suffer a second ACL injury from patients who do not were rarely better than the flip of a coin. The study of McPherson et al.,[205] reported a cut-off of 76.6 points on the ACL-RSI in patients younger than 20 years to differentiate between patients who will suffer a second ACL injury and patients who will not. The cut-off was reported with 90% sensitivity, which infers that that 90% of the patients who will go on to suffer a second ACL injury are correctly identified by the test as being at risk, that is, the true positives. However, the reported cut-off has a low specificity: 47%, which contributed to the summary measures, the AUC and the Youden index being below acceptable levels (0.66 and 0.37 respectively).[205] One possible problem

with the application of cut-offs could be of conceptual character: the use of cut-offs in the evaluation of patient outcomes, particularly in the context of ACL rehabilitation, raises important conceptual concerns regarding the dichotomization of patient experiences and outcomes. This issue is especially pertinent for the psychological impacts of injury, where the spectrum of experiences can range from mild distress to severe depression.

Dichotomizing patients based on arbitrary cut-off scores—such as to judge a patient with a score of 89 to have "passed" a test, while a patient who scores 88 has "failed", overlooks the continuous nature of psychological experiences. Psychological states, particularly following a traumatic event like an ACL injury, exist on a continuum that cannot be easily segmented into binary categories without the loss of valuable information. Two patients on either side of a cut-off may have more in common than different, yet the binary classification could result in markedly different recommendations for their continued rehabilitation or return-to-play timelines. Still, both in the study of McPherson et al.,[205] and in Study V in this thesis, PROs could not be used to properly differentiate between patients who will suffer a second ACL injury from patients who will not, even if a difference was found in Study III. The discrepancies between the findings of Study III and those of Study IV and V highlight the challenges inherent in using psychological PROs to predict second ACL injuries. The content of the PROs may be more closely aligned with the outcomes measured in Study III than with the broader or more diverse outcomes considered in Study IV and V. If the PROs are more sensitive to specific psychological states or recovery phases, their predictive utility might vary across studies. Second ACL injuries are influenced by a complex interplay of physical, psychological, and possibly biomechanical factors.[185 342 343] The PROs used may capture only a subset of the relevant psychological dimensions, and their predictive capacity might be diluted when considered alongside or within broader test batteries that include diverse measures. How effective a PROs can predict a second ACL injuries might be contingent upon contextual factors such as the timing of assessment, rehabilitation progress, and individual patient characteristics. Variations in how and when PROs were administered across studies could influence their predictive value, which is most likely one of the reasons for the discrepancy between Study III, IV and V.

Finally, it is essential to recognize that the PROs are primarily designed to assess psychological states such as knee self-efficacy and return-to-sport after injury confidence emotions and risk appraisal, rather than directly predicting injury risk. Psychometric properties indicate how well PROs measure these constructs, but to translate PROs into predictors of second ACL injuries introduces additional complexity.

In the KOOS[250] and the ACL-RSI,[260] no patient was involved in the development of the items included in the scale. In the development of the K-SES, authors state "[…] *more items were generated from discussions between the health professionals and patients"*.[259] However, no details are

provided on how many patients, how the discussions were held, and which items or changes those discussions generated. This is a clear limitation for the content validity of the scales[245] (the most important psychometric property), which might have led to widely used PROs which do not assess factors of importance for patients (or do it in an improper way, such as summing all items in one single score). This highlights the next question: how do we study and measure psychological factors when it comes to sports injury rehabilitation?

As seen in the Scandinavian knee registries,[344] in the three RCTs comparing ACL reconstruction and rehabilitation,[45 52 345] and in clinical practice guidelines,[121] PROs are the common way to assess and study outcomes (specifically psychological outcomes) in patients after ACL injury or reconstruction. In 2018, Gagnier et al.[55] identified 24 different PROs used in patients who suffer an ACL injury, whereas the IKDC and the KOOS were the most commonly used. In Study II, self-reported symptoms of depression and anxiety were assessed with a variety of different PROs, which presents both challenges and implications for research, clinical practice, and patient care. The diversity in assessment tools introduces complexity in the interpretation and comparison of findings across studies. The use of different questionnaires to assess depression and anxiety symptoms as well as psychological factors, poses a challenge to standardize findings across studies. Each tool has its own scoring system, sensitivity, specificity, and interpretation guidelines, which complicate efforts to compare results directly or to aggregate data for meta-analyses. Each assessment tool may capture slightly different aspects of depression, anxiety or other psychological factors, potentially leading to questionnaire-specific biases. Some tools might be more sensitive to certain symptoms or better suited for certain populations, which influences the prevalence and severity rates reported in study II. In addition, the heterogeneity in assessment methods complicates the synthesis of evidence, as seen in Study II. Diverse measurement tools contribute to variability in findings, affecting the quality of evidence and the confidence in conclusions drawn. There is an obvious need for harmonization in the instruments used to assess psychological symptoms in ACL rehabilitation research. To adopt a common set of assessment tools could facilitate more meaningful comparisons between studies, enhance the validity of future meta-analyses, and ultimately lead to more robust conclusions, which could lead to proper and robust university education, and altogether, to better patient care.

A further extremely important implication with the use of PROs, is that researchers, clinicians, and health care workers (a piece in the puzzle of implementing research findings in the educational system for physiotherapists and other health care providers) rely on the appropriateness of PROs to do what PROs should do. That is, if a very high quality RCT shows that treatment A is no better than treatment B, clinicians and researchers are supposed to trust findings. Too seldom, clinicians and researchers ask the question "A is no better than B, measured with what?" and more

importantly, "how does the instrument used to measure the difference really works?".[251]

In this thesis we used the KOOS,[250] the ACL-RSI,[260] and the K-SES.[137] The KOOS was originally developed to assess symptoms and function in patients with knee osteoarthritis, but has been extensively used in the field of ACL research.[55] The KOOS has been reported to have insufficient psychometric properties in patients who suffer an ACL injury,[346] thus, the ADL subscale has been removed from trials which employ the KOOS on ACL injured patients.[52] One attempt to validate the KOOS in athletes who suffer an ACL injury has been made.[257] Reported results have shown good reliability and acceptable construct validity. However, reliability could be inflated due to item redundancy,[347] and construct validity (which is lower than content validity and internal validity in the hierarchy of psychometric properties) was assessed by correlation with the SF-36, which is not a scale specific to athletes who suffer knee injury.[257] When assessed with the RASCH measurement analysis, only the KOOS subscales of QoL and Sports met presumptions for unidimensionality,[253] which is why these subscales were used in the studies included in the present thesis. The ACL-RSI showed strong positive evidence for internal consistency and structural validity, moderate positive evidence for test-retest reliability, cross-cultural validity, and hypothesis testing validity.[55] However, in the hierarchy of evidence, the highest levels are occupied by internal and content validity. Limited positive evidence for construct validity was found in the Swedish translation when assessed with hypothesis testing and correlation with other questionnaires.[263] However, such methods of assessment contain limitations, that is, tests within CTT are largely based on a correlation matrix, typically Pearson product-moment correlations, which assume quantitative normally distributed data, not ordered categorical or dichotomous item-level rating scale data.[348 349] The analysis of the ACL-RSI with a more stringent psychometric testing method, such as the RASCH,[350] has not been published, yet. The K-SES$_{18}$ has been reported with acceptable reliability and construct validity, as well as structural validity.[258] However, precisely as for the ACL-RSI, hypothesis testing and correlation with other questionnaires were used, and a RASCH analysis is not yet published. Taken together, the psychometric properties of the PROs used in this study need refinement. The assessment of content validity should be the first step to take, to know what we measure, and that we are not only assessing random numbers.

However, PROs should not be intended as the sole factors contributing to the development of the "best evidence" pillar of EBM. Results from muscle function tests play an important role as well. In this thesis, results from isokinetic muscle function tests were used in Study III, IV and V. In Study III no differences were observed between patients who will suffer a second ACL injury and patients who will not in any of the muscle function tests included. In Study IV, to pass or not to pass (defined as to achieve an LSI ≥90%) a muscle function test did not alter the risk of a second ACL injury. In Study V, when symmetrical

quadriceps muscle function was taken into consideration, cut-offs on PROs could not differentiate between patients who would suffer a second ACL injury from patients who would not. One obvious limitation with the use of such measures is the accessibility and cost: isokinetic testing equipment is expensive and not always readily available in all clinical settings. While isokinetic tests provide valuable data on muscle function, tests are conducted in a controlled environment that may not fully replicate the dynamic and unpredictable nature of sports and daily activities. This can limit the application of test results to real-world performance. Nevertheless, tests of muscle function are recommended in clinical practice guidelines[121] and by expert groups.[120]

Results from tests of muscle function offer valuable insights into the recovery process and allow for precise assessment of the rehabilitation progress. Objective assessment is important to set baseline measures, monitor recovery, and to make informed decisions about RTS or physical activities, and what to focus on during rehabilitation.[351] Strength testing is commonly reported as LSI, and can identify side-to-side differences in muscle strength, which are important in ACL rehabilitation, since asymmetries have been linked to worse outcomes such as decreased function, lower RTS rates and higher risk for knee osteoarthritis.[352-355] To address imbalances is essential to ensure a balanced recovery and better outcomes. However, LSI has been reported to possibly overestimate capacity, since symmetrical strength can be achieved by bilateral weakness.[106 356]

Isokinetic tests are a valuable component of ACL rehabilitation, and offer precise, objective measures of muscle function that can significantly inform and enhance rehabilitation protocols. However, the relationship between strength tests and second ACL injury is unclear due to inconsistent findings in the literature.[357] In Study III in this thesis no difference were found in LSI and absolute strength between patients who will suffer a second ACL injury and patients who will not. In Study IV, no association between tests of muscle function in test battery 1 and 3, and occurrence of second ACL injury was found (LSI ≥90% was used to define whether a patient passed a test or not). Whether muscle strength is a risk factor for second ACL injury likely depends on the type and timing of strength testing. Despite the inconclusive association between strength tests and the occurrence of a second ACL injury, an important aspect to consider within the domain of strength testing is patient motivation. As reported by patients in Study VI, to test patients and provide them with tangible, objective data on their progress can be highly motivating, which opens the discussion on patient´s experiences and preferences, the third pillar of EBM.

Patient´s preference pillar

To integrate the final pillar in EBM: patient´s preferences and experiences, Study VI was performed, where we inquired "*what are the experiences of patients who suffer two ACL injuries and are treated with two ACL reconstructions*." Fifteen young females who navigated the path of suffering two ACL

injuries within a mean time of 13.4 months between primary reconstruction and second ACL injury were recruited.

Our findings reveal a remarkable resilience among the included females. At the time of the interview, despite the physical setbacks, participants did not report significant symptoms of depression or anxiety. Instead, they demonstrated a commendable level of general health and maintained a moderate athletic identity. The qualitative analysis unraveled the emotional and cognitive complexity of the young females´ experiences, categorized into phases of loss, struggle, adaptation, and ultimately transformation into a stronger self.

The initial injury catalyzed a profound sense of loss, challenged their athletic identity and induced feelings of loneliness and despair. However, the journey from second ipsilateral ACL injury to the present day painted a picture of determination, support, hard work, and personal growth. Participants narrated a shift from devastation to a fighting spirit, aided by the support of peers, family, and healthcare professionals, which propelled them towards recovery and personal development. Importantly, young active females in Study VI and other patients who participated in interview studies about ACL reconstruction rehabilitation, reported that to achieve pre-set goals during rehabilitation inject patients with joy and motivation.[358] [359] To see improvements in muscle strength and function can reinforce adherence to rehabilitation protocols and encourage continued effort towards recovery, which is an important question for patients who suffer two ACL injuries. Another study published in 2021 aimed to capture the experiences of women who suffer a second ACL injury.[64] The results were summarized in one theme: "a lifelong adaptive coping process".[64] Similar to the results in Study VI, patients reported a shift in life interests, where personal sport goals were replaced by personal life goals instead. In Study VI, despite the challenges, the rehabilitation journey was also marked by transformation into a stronger person and by growth. This process of personal maturation captures the resilience and strength that patients develop as they navigate their recovery. It highlights the journey of self-discovery, where patients learn about their physical and emotional resilience, and emerge with a stronger sense of self and a deeper appreciation for their body's capabilities. This transformation into a stronger person experienced by young active females, can lead to a broadened perspective on life, sport, and personal priorities.

Interestingly, young active females interviewed in Study VI reported they did not feel ready to RTS despite physical tests and health care providers stated they were ready. Furthermore, young active females in Study VI reported to be "fighting myself" and "not listening to my body" when they felt they had to RTS because tests and health care providers were positive towards it, despite not feeling ready.

EBM

From an EBM perspective, integrating knowledge from all three pillars of

evidence, the finding that PROs could not be used to properly differentiate between patients who would suffer a second ACL injury from patients who would not calls into question the current paradigms of rehabilitation and RTS assessment, highlighting a potential gap in our understanding of what is important to measure. This gap should be seen considering the finding that young active females, before suffering a second ACL injury felt not ready to RTS even though test results were deemed as "good". Thus, the question of whether we as clinicians measure what is important for patients arises, and further, whether the findings imply that even patients who meet the established criteria for physical and psychological landmarks may still be at risk of re-injury, suggesting that other, unmeasured factors may play a critical role in determining the actual risk of a second ACL injury.

To incorporate qualitative assessments or patient interviews could complement quantitative PROs, and provide a richer, more holistic and EBM view of the patient's psychological state. In research, a more thorough knowledge and comprehensive understanding of the nature of PROs, what and how PROs measure is essential for their effective application in both research and clinical settings. To understand the specific dimensions and constructs that these PROs assess, and to ensure their psychometric robustness, will enable clinicians and researchers to appreciate, trust and use these tools with confidence. Once we achieve a deeper understanding and validation of these PROs through methodologies like the RASCH analysis, we can pave the way for their widespread adoption in educational curricula. This, in turn, will equip future healthcare professionals with the knowledge and tools necessary to integrate PROs seamlessly into their practice, which will substantially strengthen the "clinical experience" pillar of EBM. Moreover, a refined understanding of PROs could enhance the clinical and treatment decision-making processes. Taken together, the journey to enhance the psychometric properties of PROs like the KOOS, ACL-RSI, and K-SES is not merely an academic exercise but a critical step towards transforming how we approach, understand, and optimize the rehabilitation of ACL injuries. By ensuring these tools are valid, reliable, and well understood, we can trust them to guide our teaching, inform clinical decisions, and most importantly, improve the care and recovery of patients. This commitment to rigor and understanding in the assessment of PROs underscores our dedication to evidence-based, patient-centered care in the field of sports injury rehabilitation where every treatment decision is informed by robust data and genuine patient feedback, that is, two of the three pillars in EBM. Such future would shape the third pillar as well: experiences of health care providers; contributing to the best possible EBM.

Methodological considerations

In this thesis, a comprehensive methodological approach was adopted to explore the multifaceted nature of ACL injury rehabilitation, encompassing both the

psychological and physical dimensions of recovery. The diversity of methods—from qualitative content analysis and systematic review with qualitative synthesis to registry studies employing various statistical analyses—provides a rich and multidimensional perspective on the subject. However, this methodological plurality also introduces complexities in terms of data integration, interpretation, and the possibility of drawing overarching conclusions.

Qualitative content analysis, used in Study I and VI, offers deep insights into the lived experiences of sports physiotherapists and young female patients, respectively. The strength of qualitative content analysis lies in its ability to generate rich, detailed narratives that illuminate the subjective aspects of rehabilitation, which are often overlooked in quantitative research. However, the interpretive nature of this analysis means that findings are inherently bound to the researchers' perspectives, potentially introducing bias. While offering depth, the qualitative approach limits generalizability, making it challenging to apply findings broadly across different populations or settings. One way to increase quality of qualitative research is to apply to trustworthiness,[240 275] and to transparently report methodological information. In both Study I and VI data triangulation during analysis was performed between authors involved in the analysis in order to ensure credibility, the interview guide was not changed after the study started to add on dependability, and the involved author´s background was briefly summarized to enhance confirmability. Methodological choices were reported according to the COREQ.[278] One important limitation for eventual transferability in Study VI is the inclusion of females only. However, this is a strength as well since females are at higher risk of second ACL injury.[360] There are reported differences between males and females both in answer to PROs and results of muscle function.[361 362] Whether findings of Study VI can be transferred into a male population is debatable. The systematic review with qualitative synthesis in Study II provides a depth in the literature examination. However, the risk of bias, inconsistency and imprecision in the included study leads to difficulties in appreciating the results, and the grading of evidence to be very low.

The use of registry data allows for the analysis of real-world outcomes across a wide patient population, which enhances the external validity and applicability of findings. Statistical analyses in these studies provide objective, quantifiable insights into factors influencing rehabilitation success and risk of re-injury. However, registry studies are limited by the quality and completeness of the recorded data. In Project ACL the completeness of data is highest within the first 12 months and then decreases as the time passes (Table 23).

Table 23: Completeness of data in Project ACL.

Follow-up (after ACL reconstruction)	Percentage of registered patients participating in a test
Pre-operative	50%
10 weeks	62%
4 months	65%
8 months	61%
12 months	50%
18 months	32%
24 months	24%
36 months	22%
48 months	15%
60 months	13%
10 years	22%

ACL = anterior cruciate ligament

Registry studies which are supposed to reflect the real world due to the limited control on included individuals, are also subject to confounding variables that may not be fully accounted for in the analysis, potentially skewing results. Furthermore, the observational nature of registry studies limits the ability to infer causality from associations found.

Thanks to the integration of diverse methodological approaches, this thesis navigates the tension between depth and breadth, subjective insight and objective analysis. Each method brings its own strengths and limitations to the investigation of ACL rehabilitation, from the rich, detailed understanding of patient experiences provided by qualitative research to the broad, generalizable insights offered by registry studies.

Study related limitations

Study I

In qualitative studies, limitations discussion should be accompanied with trustworthiness discussion. Trustworthiness is divided into three core concepts: credibility, dependability and transferability. To establish credibility, researchers and participants should be thoroughly described. The respondents in Study I could only be described at the group level to ensure confidentiality. The researchers involved were briefly described according to the COREQ. Dependability refers to the certainty with which the analytical process has been carried out and the stability of the data over time. To enhance dependability, the interview guide was created before the study started and not amended afterwards. Transferability is the potential for extrapolating the results to other groups or

situations. The potential to transfer results was not planned for, but rather to describe sport physiotherapists own experiences of addressing psychological impairments in patients after ACL reconstruction in western Sweden. Further limitations for Study I include the subjectivity of qualitative content analysis, and the potential for confirmation bias in the selection of sport physiotherapists. The method used to recruit sport physiotherapists for interviews could be subject to confirmation bias, where sport physiotherapists with particular interests or experiences in psychological aspects of ACL rehabilitation were more interested in participating, potentially skewing the findings towards sport physiotherapists more concerned with or aware of these issues. Lastly, we chose to include at least 12 sport physiotherapists to be able to answer the study aim. The choice was based on a published paper, which recommends at least 12 participants to achieve data saturation.[277] However, no standard amount of participants in a qualitative study to ensure the capture of the study aim (in some contexts defined as saturation) exists, and data collection should continue until no further sub-categories emerge from the analysis.

Study II

One limitation in Study II is the low number of studies and participants included, together with diverse methods employed to evaluate symptoms of depression and anxiety. Six and five different outcome measures, respectively, were used to assess symptoms of depression or anxiety. The outcome measures used vary in whether they assess symptoms or align with Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for depression or Generalized Anxiety Disorder (GAD). The absence of uniform definitions across these scales introduces uncertainties in interpreting the severity of conditions, complicating comparisons across different measures of for example "moderate" depression or anxiety. A further limitation is the overweight of male patients included in the review (60%) which further limits generalizability of the results. The qualitative research included was solely based on male participants, which undermines the potential for sex-specific insights, especially given the small number of participants (n=6) involved in these qualitative studies. A limitation in the study is that the GRADE was not performed entirely according to the description. When GRADE was performed on outcome level the evidence was graded as very low. The study populations were notably heterogeneous, spanning various ages, levels of athletic participation, and sport types. This diversity presents challenges in amalgamating results cohesively. Finally, risk of bias of the included studies was not assessed.

Study III

One limitation in Study III relates to its cross-sectional nature, reflecting different cohorts at each follow-up. This limitation was taken into account by only including patients in the matched group that matched with the patients included in the second ACL injury group who participated at a given follow-up. We did not include contralateral ACL injury, and did not perform a sample size calculation, thus several comparisons might be underpowered. There is a risk of type 1 error, that is, erroneously rejecting the null hypothesis, due to the several

statistical analyses performed, and a risk for type II error due to small sample size. To mitigate the risk for type II error, we reported Cohen´s d as a measure of effect size. Moreover, Study III does not detail or account for the rehabilitation protocols followed by patients or the criteria used to clear patients for RTS. These factors can significantly influence outcomes and the risk of second ACL injury. Study III´s design limits its ability to establish causation between psychological variables, increased sports participation level, and the risk of second ACL injury. Further, we did not account for external factors such as sports type, intensity of participation, and competitive level. Those external factors could influence both psychological variables and the risk of second ACL injury.

Study IV

As mentioned for Study III, Study IV does not detail or account for the rehabilitation protocols followed by patients or the criteria used to clear patients for RTS. Concomitant injuries such as cartilage or meniscal injuries were not considered. Study IV consists of several analyses which carry the limitation of the risk of type 1 error. We accounted for possible type 1 error risk by providing CIs for all hazard ratios. A further limitation was that the RTS data were taken from the follow-up (according to Project ACL´s timeline) in which patients stated to have returned to Tegner 6 or higher. If a patient achieved Tegner level 6 at 9 and a half months after ACL reconstruction, results from the 8 months follow-up would be used for analysis. However, a lot can happen for a patient´s strength and psychological status in one and a half month. Moreover, the use of Tegner to define RTS is a limitation as this does not account for the time and intensity of exposure to sports. The use of LSI can be a limitation as well, due to the possibility that LSI overestimates limb function, if achieved due to bilateral weakness.[106] Finally, treating RTS as a dichotomous variable, without a sport-specific definition is a limitation. Return to training in professional football or amateur boxing poses different requirements on a patient´s knee. Finally, evaluating psychological status through a cross-sectional approach presents a notable limitation. Psychological factors, including confidence and emotional state, can fluctuate significantly within a single day. For example, a patient might feel more self-efficent about the knee's stability and ability to handle stress after a training session, as opposed to feeling uncertain or anxious prior to the session (or the other way around). This variability underscores the complexity of psychological assessments, highlighting that a snapshot in time may not fully capture the dynamic nature of a patient's psychological status and confidence in the knee's recovery. To obtain a more accurate representation of psychological status, it may be beneficial to conduct assessments at multiple points throughout the rehabilitation process, especially before and after key activities or milestones.

Study V

One potential limitation in Study V is the inherent complexity of the factors contributing to a second ACL injury. Given that the risk can be influenced by both high and low scores on PROs,[185] it might be incorrect

to rely on a single threshold to signal an increased risk of a second injury. Specifically, overly high or low levels of knee-related self-confidence could predispose individuals to a greater likelihood of reinjury. Therefore, if PROs are to be effective in forecasting a second ACL injury, future research might benefit from employing dual threshold values. For instance, in the case of the K-SES, one threshold could indicate excessively high self-efficacy, while another could denote critically low self-efficacy. Further limitations include those mentioned for Study III and IV, where Tegner is used as a proxy for RTS not accounting for intensity and duration, and data are collected in the follow-up closest to RTS. Additionally, the cross-sectional approach for psychological variables evaluation is a limitation. Finally, one limitation is the influence of age on the sensitivity of the ACL-RSI, particularly since it has shown greater sensitivity to changes in younger individuals (≤ 20 years) who experience a second ACL injury. Given that the average age in the study group was 24.8 years, the applicability and accuracy of the established cut-offs across different age groups remain uncertain, suggesting a potential need for age-specific thresholds to predict the risk of subsequent ACL injuries more accurately.

Study VI

Limitations in qualitative studies are tied to the definition of trustworthiness. To ensure credibility, participants were thoroughly described, with the addition of psychological PROs at time of interview. To ensure dependability, no amendments were made to the interview guide after beginning data collection. Transferability is rarely the goal with descriptive qualitative studies and was not the goal with this study. In addition to the method related limitations, another limitation was that participants in this study were included from a region that benefits from a specialized ACL injury registry (Project ACL), which offers the advantage of ongoing progress evaluations throughout rehabilitation. Thus, individuals with a heightened commitment to their rehabilitation journey, given their involvement in Project ACL and routine assessments of muscle function and PROs, might have been prone to be selected, inferring some degree of confirmation bias. Another limitation of this study is the geographic concentration; the participants' experiences might be affected by the local culture, potentially limiting the broader applicability of the findings. Moreover, the study specifically targeted young, active women, a demographic notably susceptible to second ACL injury, introducing a selection bias. Additionally, the potential for recall bias should be acknowledged, as there was a significant delay between the initial ACL injury and the interviews, possibly affecting the accuracy of reported experiences.

Ethical consideration

Considering the different methodology of Study I-VI, it is essential to explore both internal and external ethical considerations that arise from research in the realm of ACL reconstruction rehabilitation. These considerations ensure that the research upholds the highest standards of integrity while protecting and respecting the rights and well-being of participants.

INTERNAL ETHICS:

For Study I and VI, which used qualitative content analysis, there is an inherent risk of researcher bias which might influence the interpretation of data. Internal ethics demand rigorous reflexivity from researchers, where researchers must continually examine and disclose their biases, preconceptions, and how their background influences the research process. Implementing checks such as triangulation and transparently report background information can mitigate bias, ensuring a more objective and credible analysis. Across all studies, especially the systematic review in Study II and the registry Study in III, IV, and V, to maintain methodological rigor is crucial. This involves transparently reporting search strategies, inclusion criteria, and statistical analyses to allow for reproducibility and critical evaluation by the research community. Adhering to established protocols and ethical guidelines ensures the integrity of the research process. Handling sensitive patient data, particularly in registry and in qualitative studies, demands strict adherence to data protection laws and ethical guidelines. Researchers are ethically obliged to ensure that all patient information is anonymized and securely stored, protecting participants' privacy and confidentiality.

EXTERNAL ETHICS

In all studies which involved patient data or participation, obtaining informed consent is paramount. This ensures that participants are fully aware of the study's nature, its potential risks and benefits, and their rights, including the right to withdraw at any time without penalty. For studies involving physical testing, such as muscle function tests in Study III, IV, and V, it is crucial to clearly communicate and supervise the procedures, any associated risks, and how these risks will be managed. External ethics emphasize the principle of "do no harm." In the context of ACL rehabilitation research, this principle is particularly relevant for physical tests that could pose a risk of injury or psychological assessments that might evoke distress. Researchers must ensure that all protocols are designed to minimize potential harm, employing strategies such as to ensure that physical tests are conducted by trained professionals and to provide psychological support if distressing emotions are elicited during the study. The research should aim to benefit participants or, at the very least, not harm them. This involves carefully considering the balance between the knowledge gained from the research and the potential risks to participants. For example, when performing muscle function tests, the potential insights into rehabilitation efficacy must outweigh any risk of injury. Moreover, researchers should be prepared to act if the research reveals that participants are at risk, such as providing referrals for further support.

Conclusion

This thesis critically examined the psychological outcomes of patients treated with ACL reconstruction and explored the intricate association between psychological outcomes and a second ACL injury. Key findings indicate that sport physiotherapists, despite their clinical acumen, often feel underprepared to address psychological

impairments due to a lack of formal training and resources. The lack of preparation to face psychological impairments is mirrored in the wide diversity of outcomes used to assess psychological factors in patients who suffer an ACL injury. The results in this thesis highlight that conventional muscle function tests and PROs, when used dichotomously, possess limitations in accurately identifying patients at risk for second ACL injury. Finally, upon suffering a second ACL injury, patients' narratives of resilience, determination, and personal growth contributed with valuable perspectives to an evidence based picture of the subject studied. The lack of clear associations between test battery outcomes and second injury rates, alongside the significant psychological challenges faced by patients, underscores the need for a more holistic, patient-centered approach to rehabilitation.

Future perspectives

Future research should focus on developing integrated evaluation frameworks that capture the full spectrum of recovery, from physical readiness to psychological resilience, to improve rehabilitation outcomes and reduce the risk of second injuries. It is important to address the identified gaps in ACL rehabilitation by fostering an interdisciplinary approach that bridges physiotherapy with psychological support. Future research should prioritize the development and validation of integrated rehabilitation protocols that are responsive to the psychological states and needs of patients, facilitating a comprehensive recovery journey. There is a need for the creation and implementation of advanced training modules in sports physiotherapy education that encompass psychological assessment and intervention strategies. Moreover, the exploration of novel patient-reported outcome measures that accurately reflect the psychological dimensions influencing the risk of second ACL injuries will be crucial. These measures should aim for sensitivity to the nuanced psychological changes over the rehabilitation period and be incorporated into routine clinical practice to guide individualized patient care. Additionally, future studies should consider the patient's voice in the development and assessment of psychological interventions, ensuring that the care provided resonates with their personal experiences and recovery goals. By advancing our understanding and specific methodologies in addressing the psychological components of rehabilitation after ACL reconstruction, we can enhance the quality of care, improve patient outcomes, and ultimately and hopefully, it will become possible to reduce the incidence of second ACL injuries, charting a path towards a more resilient and holistic recovery process for individuals affected by ACL injuries. The journey toward optimizing ACL rehabilitation is ongoing, and the studies presented in this thesis represent important steps forward in understanding and addressing the multifaceted challenges involved. Moreover, personalized rehabilitation plans that address both the physical injuries and the psychological scars left by such injuries can pave the way for more effective recovery, ultimately improving patients' quality of life after ACL injury and ACL reconstruction.

Acknowledgments

Ramana Piussi, first and foremost, thank you for being such a stubborn, disciplined, and courageous mountain goat (person). Thank you for always holding on, no matter how difficult stuff gets.

The staff at the research and development unit for Gothenburg and Southern Bohuslän: special thanks to Ulrika Engström, Carin Greenwood, and Inger Hansson for their invaluable support to emerging researchers. Your encouragement, readiness to answer our myriad questions, and generous spirit have been pivotal. Your contribution truly makes a difference.

Eric Hamrin Senorski, well, where to start? My mentor, supervisor, friend, colleague, partner-in-crime, ally, boss, guide, teammate… I could probably go on. None of this would have ever been possible without you. Thank you for always pushing me to improve; thank you for being present every day and at any time; thank you for your time, dedication, and generosity in sharing your development; thank you for being such a pinecone at times, you know what I mean. Thank you for being you, I am truly happy I got to know you. Felicitá!

Kristian Samuelsson, my mentor, colleague, supervisor and friend. I believe your weakness for sicilian oranges bought me my way into research. Thank you for your support, for sharing your knowledge and for always being there to help, in- and outside of work. Last, thank you for taking 8 months to read my article, and then calling me up on the phone and telling me "hey Ramana, this looks great, but it is wrong. You have to do it again". I am still laughing about that!

Jon Karlsson, my supervisor and mentor. Jon, your expertise and stature in orthopedic surgery are unparalleled. You are a legend! Yet, you have the remarkable ability to make a novice feel acknowledged. Always just a call or email away, your support has been a cornerstone of my journey. Working with you is an honor I deeply cherish.

Andreas Ivarsson, my supervisor and mentor. Thank you Andreas for all the help during these years. Your priceless knowledge and your guidance, enriched with profound insights, has been like a splash of color in a monochrome scene. I greatly appreciated your support, and I am looking forward to more cooperation with you.

Rebecca Simons(s?)on, my dear friend, teammate, and doubtlessly favorite colleague. I really enjoy all we do together: work, study, research, train, as well as cooking and enjoying food. Thank you for always being supportive, for all the work you have put in our projects, but mostly, thank you for putting up with me and Eric.

Johan Högberg, my dear friend, teammate and colleague. Thank you Johan for all the effort you put in our projects; thank you for coming into the picture and spell Roland´s surname wrong, so he noticed there was somebody worse than me. I have a lot of fun with you, and I am looking forward to more cooperations. But let us not forget we managed to publish in BOSEM that you do not show up at the morning training session.

Jakob Lindskog, my dear friend, teammate, and colleague. It is a lot of fun to work with you. You always have a joke ready, no

matter the situation. Your contribution of knowledge, enthusiasm, and levity is greatly appreciated. How to forget when you dragged along the sport medicine banner to a conference and stood on a railway platform selling to students that "we know sport injuries".

Axel Sundberg, my dear friend, teammate, and colleague. Your departure from the clinic was a poignant moment for me, reflecting your significance as a mentor and the calm you bring to challenging situations, like hiding behind the conference room door when an angry patient was looking for you. I am truly happy you decided to join the research group, and I am looking forward to cooperate with you in the future.

Jens Augustsson, my dear friend, teammate, and colleague. Jens, stop following me. First you took my place in Alingsås, then you followed me in Gothenburg as well. Nevertheless, I am really happy you got involved in the research group. Your endless organizing talent and your presence provide extra gear. Despite not being able to effectively read a map or geographically lead a group, "intellijens" is still one of the best names I have come across.

The research team, both the rehabilitation research team, and the Sahlgrenska Sports Medicine Centre. Special mention to Jasmine, Moa, and Ella for their energy and potential; your participation is inspiring. It is a lot of fun working with you, even though Jasmine can be a bit of an egoist at times, and it is hard to understand Moa sometimes. I hope you will pursue a research career to work with you. In the Sahlgrenska Sports Medicine Centre, a great thank you to all the people who provide energy, ideas, support, motivation, and fun.

Janina Kaarre, you are like a nuclear battery which spreads energy to everything and everybody around you, but no matter what happens, I will always do more burpees than you. Especially as long as you do not do a proper push-up. It is a lot of fun working with you.

Balint Zsisdai, you know what I am going to say: I wish I had a fifth of your writing talent. You turn manuscripts into masterpieces. To read one of your manuscripts is like to eat a proper carbonara. It just feels right. I learn a lot working with you.

Alexandra Horvath, your guidance through the thesis maze, based on your firsthand experience, was invaluable. But, you went to Sicily by yourself, and it got a shitshow. You went to Rome with the least geographically talented guy in the research team, and it got a shitshow. Please consider me next time you travel to Italy.

Alberto Grassi, your assistance in our studies and constant availability have been invaluable. Your legendary status is well-earned, and I eagerly anticipate our future collaborations.

Stefano Zaffagnini, a great thank you to you, professor Zaffagnini for being part of the journey throughout this project. Thank you for being a part of this team, offering your support, and very valuable insights. I look forward to working together again in the future.

Francesco Della Villa, I am sorry but the JOSPT review is not yet published... Jokes aside, many thanks Francesco for introducing us to the Isokinetic world, and for being such a source of inspiration and energy. I hope and look forward to further cooperate in the future.

Ferid Krupić, thank you for your willingness and openness in teaching me about qualitative research. Your help on this journey has been much appreciated.

Mikael Sansone, thank you for the valuable help, insights and availability in our studies. The way you switch from academic Swedish to street Napolitan is priceless. Too bad Danilo moved from Buono!

Urban Johnson, thank you for the valuable insights, the help, and the availability during our cooperation.

Eleonor Svantesson, another writing genius. Thank you Eleonor for your help in our cooperations.

Thorkell Snaebjörnsson, or should I say Baldur? Thank you for all the help and avalilabilty you have provided in our cooperations.

Baldur Thorolfsson, or should I say Thorkell? Thank you for all the help and avalilabilty you have provided in our cooperations.

David Sundemo, thank you for all the assistance and availability you've offered throughout our collaborations.

Tora Beghdal, thank you for all your valuable help in the completion of Study II.

Bengt Bengtsson and the Statistiska konsultgruppen, your expertise in data analysis and interpretation has been crucial to our collaboration. Your guidance is greatly appreciated.

Roland Thomeé, my former boss. Roland, thank you for having paved the way for all of us to walk on. Your work, dedication and achievements have made our current endeavors possible, and for that, I am profoundly thankful.

Test supervisor´s in Project ACL. To all past, present, and future supervisors, your contributions to knowledge building and patient care are invaluable. Thank you for your dedication and commitment.

JOSPT´s famous reviewer 1, the best reviewer one could wish. When you send to JOSPT a systematic review consisting of 10 pages, and reviewer 1 sends you back 13 pages of comments you can be sure of two things: 1) you have not done a proper job; 2) you got JOSPT reviewer 1. Jokes aside, I have never learned so much in one go as when reviewer 1 commented on our paper, for which reviewer 1 deserves a mention. Thank you, dear reviewer 1, we actually greatly appreciated your help and dedication, and the very professional way in which you conducted your work.

Almir Fazlić, I do not know where I should start. Maybe the beginning is a good idea. When I was alone like a dog, you offered your unwavering support. I rarely felt as

home as when I came to your parent´s place the first time, where nobody spoke a word of a language I knew. Still, it is what you do, not what you say that matters. In the last 15 years you have been the rock to stand on when stuff gets tough. You always manage to shake my prejudices and you made (and make) me grow as a person every day. No matter what happens I know you will always be there to help. You are amazingly generous, and I have to thank you for who I am today. I will regret my whole life not being there at your father´s funeral. How not to conclude mentioning all the Fifa nights. Even though I have a painting hanging on the wall which says that statistically you might have won more matches than me, I know I am the better player anyway, and statistics do not tell the whole picture.

Kulturköket, among the best friends a person could ever wish for: Vincent, Oskar, Simon, Kristoffer, thank you for all the fun we have had together through all these years. I truly wish never to stop hiking and seeking new adventures with you guys. Not to mention the training sessions, dart sessions, the bike rides to the summer cabins, board games, food cooking… I could go on.

Vincent, how not to mention when I asked you "nice phone, how much does it cost?" and you "1000 kr". "where did you buy it?" "In Elgiganten". I go there the day after and the phone costs 1500 kr. The day after in school I tell you "Vincent you were lucky the phone costed 1500 kr in Elgiganten". "Yes". "But you say it costed 1000 kr." "Yes, it costed 1000 kr online but I bought it for 1500 in Elgiganten…"

Oskar, having you trapped in a tunnel balancing on a plank on the water and throwing pinecones at you was really fun.

Simon, winning the eggs at the lottery, being a bad winner, and then losing them to broke on the staircase 10 seconds after, is the definition of karma.

Kristoffer, I tried for a whole year to wash the chair you rubbed your family jewels on. I ended up selling the chair.

Carl Senorski, should I say we met by accident? Or how should we define when I accidentally kicked you in the face when you were about to head a ball? Jokes aside, Thank you, Carl, for your invaluable support on our projects and for the countless enjoyable moments we've shared over the years at the clinic. I eagerly anticipate continuing this blend of productive work and delightful (for us at least) experiences with you.

Dimitri Zornik, we were four years old. You looked at me running forth and back in a corridor for months. One day I stopped and finally we got to know each other. One of the better choices I made in life. I would not be the same person if it was not for you, and the grasso di rattotalpa for the argano in the caverna del sole. You know what I am talking about.

Calogero Polizzi, we have known each other since we were three years old. Except for those three years in middle school, I have put up with you my whole life. And even if you made me feel very ashamed that time on a Swedish playground in which you were extensively describing the physical details of

your female colleagues, and an Italian mom approached us saying “hi guys” in Italian, just to make you shut up, I really like you. You are my tradition when I change house.

Matteo Quaglia, five years of high school together definitely shape one´s life. I am actually surprised you decided to pay for the flight ticket to come to the disseration, and I am very happy you did that.

Emanuele Vaglio, the good old “mu”. The agreement stipulated that for any misdeed I committed in Coccau, I would attribute it to you when explaining to my parents, and conversely, for any wrongdoing you committed in Camporosso, you would place the blame on me with your parents. This arrangement led your father to harbor ill feelings towards me for many years, almost as long as it took us to enlighten you about the incident involving Vucinic and you know who.

Nawar Hermez, we met by chance, and even if I did not really like you in the beginning, I must say you surprised me, and keep on doing so, every time we meet. I think you are a particularly wise person; we share a lot of points of views about life and I really enjoy spending time with you.

My family-in-law: My wife´s parents, Hans & Agnete, brother with family, Jonas, Sara, Aksel and Ebbe, and sister with family, Ulrika, Patrik, Stina, Kerstin and Bo. Thank you, guys, for receiving me into your family and for all the support provided in these years.

My beloved aunts, Anita and Tina. Zie (Sie), I am profoundly grateful for your unwavering support and for all the contributions you've made to my life. The cherished memories of our summer holidays together are still vivid in me.

My parents, Cinzia and Maurizio. Mom and Dad, I owe you both my deepest gratitude. Thank you for everything you've done for me—before my birth, throughout my childhood, and anow that I am supposed to be an adult. Your unwavering, unconditional support has been my constant. You both are truly inspirational, and the growth and resilience you've shown throughout your lives deeply motivate me. Mom, your perseverance is both admirable and inspiring. Dad, I do not know anybody else with balls big enough to put his life on the line 5 years before retirement. I hope I got some of those attributes from you.

Finally, my family: my wife, Mia and my children, Leonard and Frank. Mia, we met on the other side of the world, and look where we are today. It was just meant to be. We have been going through ups and downs, and no matter what, you have always been by my side. It is a great pleasure to share my life with you, and I will always be grateful for the family we have created together. Our circle. I love you.

Leonard and Frank, it took me some time to become a dad, but now it is so much fun. I love the games we play, the time we spend together, and teaching you about life. Thank you, my dear kids, for becoming such a wonderful people, and for pushing me every day to become a better person. It is truly a pleasure to be your father. I love you guys.

References

1. Meyer JJ, Obmann MM, Gießler M, et al. Interprofessional approach for teaching functional knee joint anatomy. *Ann Anat* 2017;210:155-59. doi: 10.1016/j.aanat.2016.10.011 [published Online First: 20161125].

2. Martelli S, Pinskerova V. The shapes of the tibial and femoral articular surfaces in relation to tibiofemoral movement. *J Bone Joint Surg Br* 2002;84(4):607-13. doi: 10.1302/0301-620x.84b4.12149.

3. Fox AJ, Wanivenhaus F, Rodeo SA. The basic science of the patella: structure, composition, and function. *J Knee Surg* 2012;25(2):127-41. doi: 10.1055/s-0032-1313741.

4. Fox AJ, Wanivenhaus F, Burge AJ, et al. The human meniscus: a review of anatomy, function, injury, and advances in treatment. *Clin Anat* 2015;28(2):269-87. doi: 10.1002/ca.22456 [published Online First: 20140814].

5. Arnoczky SP, Warren RF. Microvasculature of the human meniscus. *Am J Sports Med* 1982;10(2):90-5. doi: 10.1177/036354658201000205.

6. Aagaard H, Verdonk R. Function of the normal meniscus and consequences of meniscal resection. *Scand J Med Sci Sports* 1999;9(3):134-40. doi: 10.1111/j.1600-0838.1999.tb00443.x.

7. Buckwalter JA, Mankin HJ. Articular cartilage: tissue design and chondrocyte-matrix interactions. *Instr Course Lect* 1998;47:477-86.

8. Chen S, Fu P, Wu H, Pei M. Meniscus, articular cartilage and nucleus pulposus: a comparative review of cartilage-like tissues in anatomy, development and function. *Cell Tissue Res* 2017;370(1):53-70. doi: 10.1007/s00441-017-2613-0 [published Online First: 20170417].

9. Efskind L. Studies on the anatomy of the knee joint capsule. *Acta Pathol Microbiol Scand* 1947;24(1):59-75. doi: 10.1111/j.1699-0463.1947.tb00576.x.

10. Athwal KK, Willinger L, Shinohara S, et al. The bone attachments of the medial collateral and posterior oblique ligaments are defined anatomically and radiographically. *Knee Surg Sports Traumatol Arthrosc* 2020;28(12):3709-19. doi: 10.1007/s00167-020-06139-6 [published Online First: 20200731].

11. Andrews K, Lu A, McKean L, Ebraheim N. Review: Medial collateral ligament injuries. *J Orthop* 2017;14(4):550-54. doi: 10.1016/j.jor.2017.07.017 [published Online First: 2017/09/08].

12. LaPrade RF, Engebretsen AH, Ly TV, et al. The anatomy of the medial part of the knee. *J Bone Joint Surg Am* 2007;89(9):2000-10. doi: 10.2106/jbjs.F.01176 [published Online First: 2007/09/05].

13. Haimes JL, Wroble RR, Grood ES, Noyes FR. Role of the medial structures in the intact and anterior cruciate ligament-deficient knee. Limits of motion in the human knee. *Am J Sports Med* 1994;22(3):402-9. doi: 10.1177/036354659402200317.

14. D'Ambrosi R, Corona K, Guerra G, et al. Posterior oblique ligament of the knee: state of the art. *EFORT Open Rev* 2021;6(5):364-71. doi: 10.1302/2058-5241.6.200127 [published Online First: 2021/06/22].

15. Logan CA, O'Brien LT, LaPrade RF. Post operative rehabilitation of grade III medial collateral ligament injuries: evidence based rehabilitation and return to play. *Int J Sports Phys Ther* 2016;11(7):1177-90. [published Online First: 2016/12/22].

16. Espregueira M, da Silva MV. Anatomy of the lateral collateral ligament: a cadaver and histological study. *Knee Surg Sports Traumatol Arthrosc* 2006;14(3):221-8. doi: 10.1007/s00167-005-0681-2 [published Online First: 20051012].

17. Hefti F, Müller W, Jakob RP, Stäubli HU. Evaluation of knee ligament injuries with the IKDC form. *Knee Surg Sports Traumatol Arthrosc* 1993;1(3-4):226-34. doi: 10.1007/bf01560215.

18. Naraghi A, White LM. MR imaging of cruciate ligaments. *Magn Reson Imaging Clin N Am* 2014;22(4):557-80. doi: 10.1016/j.mric.2014.07.003 [published Online First: 20140824].

19. Lee SH, Petersilge CA, Trudell DJ, et al. Extrasynovial spaces of the cruciate ligaments: anatomy, MR imaging, and diagnostic implications. *AJR Am J Roentgenol* 1996;166(6):1433-7. doi: 10.2214/ajr.166.6.8633458.

20. Voos JE, Mauro CS, Wente T, et al. Posterior cruciate ligament: anatomy, biomechanics, and outcomes. *Am J Sports Med* 2012;40(1):222-31. doi: 10.1177/0363546511416316 [published Online First: 20110729].

21. Siegel L, Vandenakker-Albanese C, Siegel D. Anterior cruciate ligament injuries: anatomy, physiology, biomechanics, and management. *Clin J Sport Med* 2012;22(4):349-55. doi: 10.1097/JSM.0b013e3182580cd0.

22. Tantisricharoenkul G, Linde-Rosen M, Araujo P, et al. Anterior cruciate ligament: an anatomical exploration in humans and in a selection of animal species. *Knee Surg Sports Traumatol Arthrosc* 2014;22(5):961-71. doi: 10.1007/s00167-013-2463-6 [published Online First: 20130308].

23. Chhabra A, Starman JS, Ferretti M, et al. Anatomic, radiographic, biomechanical, and kinematic evaluation of the anterior cruciate ligament and its two functional bundles. *J Bone Joint Surg Am* 2006;88 Suppl 4:2-10. doi: 10.2106/jbjs.F.00616.

24. Boden BP, Dean GS, Feagin JA, Jr., Garrett WE, Jr. Mechanisms of anterior cruciate ligament injury. *Orthopedics* 2000;23(6):573-8. doi: 10.3928/0147-7447-20000601-15.

25. Quatman CE, Quatman-Yates CC, Hewett TE. A 'plane' explanation of anterior cruciate ligament injury mechanisms: a systematic review. *Sports Med* 2010;40(9):729-46. doi: 10.2165/11534950-000000000-00000.

26. Villa FD, Buckthorpe M, Grassi A, et al. Systematic video analysis of ACL injuries in professional male football (soccer): injury mechanisms, situational patterns and biomechanics study on 134 consecutive cases. *Br J Sports Med* 2020;54(23):1423-32. doi: 10.1136/bjsports-2019-101247.

27. Boden BP, Torg JS, Knowles SB, Hewett TE. Video analysis of anterior cruciate ligament injury: abnormalities in hip and ankle kinematics. *Am J Sports Med* 2009;37(2):252-9. doi: 10.1177/0363546508328107.

28. Frobell RB, Lohmander LS, Roos HP. Acute rotational trauma to the knee: poor agreement between clinical assessment and magnetic resonance imaging findings. *Scand J Med Sci Sports* 2007;17(2):109-14. doi: 10.1111/j.1600-0838.2006.00559.x [published Online First: 2007/03/31].

29. Montalvo AM, Schneider DK, Webster KE, et al. Anterior Cruciate Ligament Injury Risk in Sport: A Systematic Review and Meta-Analysis of Injury Incidence by Sex and Sport Classification. *J Athl Train* 2019;54(5):472-82. doi: 10.4085/1062-6050-407-16 [published Online First: 20190422].

30. Chia L, De Oliveira Silva D, Whalan M, et al. Non-contact Anterior Cruciate Ligament Injury Epidemiology in Team-Ball Sports: A Systematic Review with Meta-analysis by Sex, Age, Sport, Participation Level, and Exposure Type. *Sports Med* 2022;52(10):2447-67. doi: 10.1007/s40279-022-01697-w [published Online First: 20220527].

31. Griffin LY, Albohm MJ, Arendt EA, et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. *Am J Sports Med* 2006;34(9):1512-32. doi: 10.1177/0363546506286866 [published Online First: 2006/08/15].

32. Hewett TE, Myer GD, Ford KR, et al. Mechanisms, prediction, and prevention of ACL injuries: Cut risk with three sharpened and validated tools. *J Orthop Res* 2016;34(11):1843-55. doi: 10.1002/jor.23414 [published Online First: 2016/09/10].

33. Rozzi SL, Lephart SM, Gear WS, Fu FH. Knee joint laxity and neuromuscular characteristics of male and female soccer and basketball players. *Am J Sports Med* 1999;27(3):312-9. doi: 10.1177/03635465990270030801 [published Online First: 1999/06/03].

34. Griffin LY, Agel J, Albohm MJ, et al. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J Am Acad Orthop Surg* 2000;8(3):141-50. doi: 10.5435/00124635-200005000-00001 [published Online First: 2000/06/30].

35. Myklebust G, Maehlum S, Engebretsen L, et al. Registration of cruciate ligament injuries in Norwegian top level team handball. A prospective study covering two seasons. *Scand J Med Sci Sports* 1997;7(5):289-92. doi: 10.1111/j.1600-0838.1997.tb00155.x [published Online First: 1997/10/27].

36. Gokeler A, Benjaminse A, Della Villa F, et al. Anterior cruciate ligament injury mechanisms through a neurocognition lens: implications for injury screening. *BMJ Open Sport Exerc Med* 2021;7(2):e001091. doi: 10.1136/bmjsem-2021-001091 [published Online First: 2021/06/01].

37. Sutton KM, Bullock JM. Anterior cruciate ligament rupture: differences between males and females. *J Am Acad Orthop Surg* 2013;21(1):41-50. doi: 10.5435/jaaos-21-01-41 [published Online First: 2013/01/03].

38. Sundemo D, Hamrin Senorski E, Karlsson L, et al. Generalised joint hypermobility increases ACL injury risk and is associated with inferior outcome after ACL reconstruction: a systematic review. *BMJ Open Sport Exerc Med* 2019;5(1):e000620. doi: 10.1136/bmjsem-2019-000620 [published Online First: 2019/12/05].

39. Hewett TE, Zazulak BT, Myer GD. Effects of the Menstrual Cycle on Anterior Cruciate Ligament Injury Risk:A Systematic Review. *Am J Sports Med* 2007;35(4):659-68. doi: 10.1177/0363546506295699.

40. Herzberg SD, Motu'apuaka ML, Lambert W, et al. The Effect of Menstrual Cycle and Contraceptives on ACL Injuries and Laxity: A Systematic Review and Meta-analysis. *Orthop J Sports Med* 2017;5(7):2325967117718781. doi: 10.1177/2325967117718781 [published Online First: 2017/08/11].

41. The female ACL: Why is it more prone to injury? *J Orthop* 2016;13(2):A1-4. doi: 10.1016/s0972-978x(16)00023-4 [published Online First: 2016/04/08].

42. Diermeier T, Rothrauff BB, Engebretsen L, et al. Treatment after anterior cruciate ligament injury: Panther Symposium ACL Treatment Consensus Group. *Knee Surg Sports Traumatol Arthrosc* 2020;28(8):2390-402. doi: 10.1007/s00167-020-06012-6 [published Online First: 2020/05/11].

43. Chalmers PN, Mall NA, Moric M, et al. Does ACL reconstruction alter natural history?: A systematic literature review of long-term outcomes. *J Bone Joint Surg Am* 2014;96(4):292-300. doi: 10.2106/jbjs.L.01713 [published Online First: 2014/02/21].

44. Snoeker BA, Roemer FW, Turkiewicz A, et al. Does early anterior cruciate ligament reconstruction prevent development of meniscal damage? Results from a secondary analysis of a randomised controlled trial. *Br J Sports Med* 2020;54(10):612-17. doi: 10.1136/bjsports-2019-101125 [published Online First: 2019/10/28].

45. Beard DJ, Davies L, Cook JA, et al. Rehabilitation versus surgical reconstruction for non-acute anterior cruciate ligament injury (ACL SNNAP): a pragmatic randomised controlled trial. *Lancet* 2022;400(10352):605-15. doi: 10.1016/s0140-6736(22)01424-6.

46. Kim SJ, Choi CH, Kim SH, et al. Bone-patellar tendon-bone autograft could be recommended as a superior graft to hamstring autograft for ACL reconstruction in patients with generalized joint laxity: 2- and 5-year follow-up study. *Knee Surg Sports Traumatol Arthrosc* 2018;26(9):2568-79. doi: 10.1007/s00167-018-4881-y [published Online First: 2018/03/05].

47. Arnold MP, Calcei JG, Vogel N, et al. ACL Study Group survey reveals the evolution of anterior cruciate ligament reconstruction graft choice over the past three decades. *Knee Surg Sports Traumatol Arthrosc* 2021;29(11):3871-76. doi: 10.1007/s00167-021-06443-9 [published Online First: 2021/01/25].

48. Mouarbes D, Menetrey J, Marot V, et al. Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis of Outcomes for Quadriceps Tendon Autograft Versus Bone-Patellar Tendon-Bone and Hamstring-Tendon Autografts. *Am J Sports Med* 2019;47(14):3531-40. doi: 10.1177/0363546518825340 [published Online First: 2019/02/23].

49. Musahl V, Diermeier T, de Sa D, Karlsson J. "ACL surgery: when to do it?". *Knee Surg Sports Traumatol Arthrosc* 2020;28(7):2023-26. doi: 10.1007/s00167-020-06117-y.

50. Eitzen I, Holm I, Risberg MA. Preoperative quadriceps strength is a significant predictor of knee function two years after anterior cruciate ligament reconstruction. *Br J Sports Med* 2009;43(5):371-6. doi: 10.1136/bjsm.2008.057059 [published Online First: 2009/02/20].

51. Kitaguchi T, Tanaka Y, Takeshita S, et al. Preoperative quadriceps strength as a predictor of return to sports after anterior cruciate ligament reconstruction in competitive athletes. *Phys Ther Sport* 2020;45:7-13. doi: https://doi.org/10.1016/j.ptsp.2020.06.001.

52. Frobell RB, Roos EM, Roos HP, et al. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med* 2010;363(4):331-42. doi: 10.1056/NEJMoa0907797.

53. Reijman M, Eggerding V, van Es E, et al. Early surgical reconstruction versus rehabilitation with elective delayed reconstruction for patients with anterior cruciate ligament rupture: COMPARE randomised controlled trial. *Bmj* 2021;372:n375. doi: 10.1136/bmj.n375 [published Online First: 2021/03/11].

54. Frobell RB, Roos HP, Roos EM, et al. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *Bmj* 2013;346:f232. doi: 10.1136/bmj.f232 [published Online First: 20130124].

55. Gagnier JJ, Shen Y, Huang H. Psychometric Properties of Patient-Reported Outcome Measures for Use in Patients with Anterior Cruciate Ligament Injuries: A Systematic Review. *JBJS Rev* 2018;6(4):e5. doi: 10.2106/jbjs.Rvw.17.00114 [published Online First: 2018/04/11].

56. Hansen CF, Jensen J, Odgaard A, et al. Four of five frequently used orthopedic PROMs possess inadequate content validity: a COSMIN evaluation of the mHHS, HAGOS, IKDC-SKF, KOOS and KNEES-ACL. *Knee Surg Sports Traumatol Arthrosc* 2021 doi: 10.1007/s00167-021-06761-y [published Online First: 2021/10/08].

57. Filbay SR, Dowsett M, Chaker Jomaa M, et al. Healing of acute anterior cruciate ligament rupture on MRI and outcomes following non-surgical management with the Cross Bracing Protocol. *Br J Sports Med* 2023 doi: 10.1136/bjsports-2023-106931 [published Online First: 2023/06/15].

58. Paterno MV. Non-operative Care of the Patient with an ACL-Deficient Knee. *Curr Rev Musculoskelet Med* 2017;10(3):322-27. doi: 10.1007/s12178-017-9431-6 [published Online First: 2017/08/02].

59. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. *Am J Sports Med* 1982;10(6):329-35. doi: 10.1177/036354658201000601 [published Online First: 1982/11/01].

60. Beischer S, Gustavsson L, Senorski EH, et al. Young Athletes Who Return to Sport Before 9 Months After Anterior Cruciate Ligament Reconstruction Have a Rate of New Injury 7 Times That of Those Who Delay Return. *J Orthop Sports Phys Ther* 2020;50(2):83-90. doi: 10.2519/jospt.2020.9071.

61. Nagelli CV, Hewett TE. Should Return to Sport be Delayed Until 2 Years After Anterior Cruciate Ligament Reconstruction? Biological and Functional Considerations. *Sports Med* 2017;47(2):221-32. doi: 10.1007/s40279-016-0584-z [published Online First: 2016/07/13].

62. Piussi R, Krupic F, Sundemo D, et al. 'I was young, I wanted to return to sport, and re-ruptured my ACL' - young active female patients' voices on the experience of sustaining an ACL re-rupture, a qualitative study. *BMC Musculoskelet Disord* 2022;23(1):760. doi: 10.1186/s12891-022-05708-9 [published Online First: 2022/08/09].

63. Piussi R, Magnusson C, Andersson S, et al. Some, but not all, patients experience full symptom resolution and a positive rehabilitation process after ACL reconstruction: an interview study. *Knee Surg Sports Traumatol Arthrosc* 2023;31(7):2927-35. doi: 10.1007/s00167-022-07271-1 [published Online First: 20221209].

64. Heijne A, Silbernagel KG, Lundberg M. "I don't opt out of things because I think I will get a sore knee, but I don't expose myself to stupid risks either": patients' experiences of a second ACL injury-an interview study. *Knee Surg Sports Traumatol Arthrosc* 2022;30(7):2244-50. doi: 10.1007/s00167-021-06762-x [published Online First: 2021/10/19].

65. Heijne A, Axelsson K, Werner S, Biguet G. Rehabilitation and recovery after anterior cruciate ligament reconstruction: patients' experiences. *Scand J Med Sci Sports* 2008;18(3):325-35. doi: 10.1111/j.1600-0838.2007.00700.x [published Online First: 20071207].

66. Mayr HO, Hochrein A, Hein W, et al. Rehabilitation results following anterior cruciate ligament reconstruction using a hard brace compared to a fluid-filled soft brace. *Knee* 2010;17(2):119-26. doi: 10.1016/j.knee.2009.07.002 [published Online First: 2009/08/18].

67. Garcia GH, Wu HH, Park MJ, et al. Depression Symptomatology and Anterior Cruciate Ligament Injury: Incidence and Effect on Functional Outcome--A Prospective Cohort Study. *Am J Sports Med* 2016;44(3):572-9. doi: 10.1177/0363546515612466 [published Online First: 2015/12/03].

68. Jewiss D, Ostman C, Smart N. Open versus Closed Kinetic Chain Exercises following an Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-Analysis. *J Sports Med (Hindawi Publ Corp)* 2017;2017:4721548. doi: 10.1155/2017/4721548 [published Online First: 2017/09/16].

69. Wright RW, Preston E, Fleming BC, et al. A systematic review of anterior cruciate ligament reconstruction rehabilitation: part II: open versus closed kinetic chain exercises, neuromuscular electrical stimulation, accelerated rehabilitation, and miscellaneous topics. *J Knee Surg* 2008;21(3):225-34. doi: 10.1055/s-0030-1247823 [published Online First: 2008/08/09].

70. Heijne A, Werner S. Early versus late start of open kinetic chain quadriceps exercises after ACL reconstruction with patellar tendon or hamstring grafts: a prospective randomized outcome study. *Knee Surg Sports Traumatol Arthrosc* 2007;15(4):402-14. doi: 10.1007/s00167-006-0246-z [published Online First: 2007/01/16].

71. Perriman A, Leahy E, Semciw AI. The Effect of Open- Versus Closed-Kinetic-Chain Exercises on Anterior Tibial Laxity, Strength, and Function Following Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *J Orthop Sports Phys Ther* 2018;48(7):552-66. doi: 10.2519/jospt.2018.7656 [published Online First: 20180423].

72. Forelli F, Barbar W, Kersante G, et al. Evaluation of Muscle Strength and Graft Laxity With Early Open Kinetic Chain Exercise After ACL Reconstruction: A Cohort Study. *Orthop J Sports Med* 2023;11(6):23259671231177594. doi: 10.1177/23259671231177594 [published Online First: 20230627].

73. Patel AD, Bullock GS, Wrigley J, et al. Does sex affect second ACL injury risk? A systematic review with meta-analysis. *Br J Sports Med* 2021;55(15):873-82. doi: 10.1136/bjsports-2020-103408 [published Online First: 20210517].

74. Sturgill LP, Snyder-Mackler L, Manal TJ, Axe MJ. Interrater reliability of a clinical scale to assess knee joint effusion. *J Orthop Sports Phys Ther* 2009;39(12):845-9. doi: 10.2519/jospt.2009.3143.

75. Pietrosimone B, Lepley AS, Kuenze C, et al. Arthrogenic Muscle Inhibition Following Anterior Cruciate Ligament Injury. *J Sport Rehabil* 2022;31(6):694-706. doi: 10.1123/jsr.2021-0128 [published Online First: 20220214].

76. Buckthorpe M, Pirotti E, Villa FD. Benefits and use of aquatic therapy during rehabilitation after ACL reconstruction - a clinical commentary. *Int J Sports Phys Ther* 2019;14(6):978-93. [published Online First: 2019/12/06].

77. Kim K-M, Croy T, Hertel J, Saliba S. Effects of Neuromuscular Electrical Stimulation After Anterior Cruciate Ligament Reconstruction on Quadriceps Strength, Function, and Patient-Oriented Outcomes: A Systematic Review. *J Orthop Sports Phys Ther* 2010;40(7):383-91. doi: 10.2519/jospt.2010.3184.

78. Lake DA. Neuromuscular electrical stimulation. An overview and its application in the treatment of sports injuries. *Sports Med* 1992;13(5):320-36. doi: 10.2165/00007256-199213050-00003.

79. Jack RA, 2nd, Lambert BS, Hedt CA, et al. Blood Flow Restriction Therapy Preserves Lower Extremity Bone and Muscle Mass After ACL Reconstruction. *Sports Health* 2023;15(3):361-71. doi: 10.1177/19417381221101006 [published Online First: 20220627].

80. Pearson SJ, Hussain SR. A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. *Sports Med* 2015;45(2):187-200. doi: 10.1007/s40279-014-0264-9.

81. Hughes L, Rosenblatt B, Haddad F, et al. Comparing the Effectiveness of Blood Flow Restriction and Traditional Heavy Load Resistance Training in the Post-Surgery Rehabilitation of Anterior Cruciate Ligament Reconstruction Patients: A UK National Health Service Randomised Controlled Trial. *Sports Med* 2019;49(11):1787-805. doi: 10.1007/s40279-019-01137-2.

82. Charles D, White R, Reyes C, Palmer D. A systematic review of the effects of blood flow restriction training on quadriceps muscle atrophy and circumference post ACL recosntruction. *Int J Sports Phys Ther* 2020;15(6):882-91. doi: 10.26603/ijspt20200882.

83. Lambert B, Hedt CA, Jack RA, et al. Blood flow restriction therapy preserves whole limb bone and muscle following ACL reconstruction. *Orthop J Sports Med* 2019;7 doi: 10.1177/2325967119S00196.

84. de Queiros VS, Dantas M, Neto GR, et al. Application and side effects of blood flow restriction technique: A cross-sectional questionnaire survey of professionals. *Medicine (Baltimore)* 2021;100(18):e25794. doi: 10.1097/md.0000000000025794.

85. Harput G, Ulusoy B, Yildiz TI, et al. Cross-education improves quadriceps strength recovery after ACL reconstruction: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc*;27(1):68-75. doi: 10.1007/s00167-018-5040-1.

86. Piussi R, Ivarsson A, Johnson U, Senorski EH. Psychological Factors in Sports Injury Rehabilitation: How Can a Sports Rehabilitation Practitioner Facilitate Communication? *J Orthop Sports Phys Ther Open* 2024;2(1):1-3. doi: 10.2519/josptopen.2023.0007.

87. Andersen MB, Ivarsson A. A methodology of loving kindness: how interpersonal neurobiology, compassion and transference can inform researcher–participant encounters and storytelling. *Qual Res Sport Exerc Health* 2016;8(1):1-20. doi: 10.1080/2159676X.2015.1056827.

88. Brewer BVR, J; Petitpas, A. Patient-Practitioner Interaction in Sport Injury Rehabilitation. In: Ivarsson A, Johnson U, eds. Psychological Bases of Sport Injuries. Morgantown: FIT Publishing 2022.

89. Stone MH, Hornsby WG, Suarez DG, et al. Training Specificity for Athletes: Emphasis on Strength-Power Training: A Narrative Review. *J Funct Morphol Kinesiol* 2022;7(4) doi: 10.3390/jfmk7040102 [published Online First: 2022/11/23].

90. Lorenz D, Morrison S. Current concepts in periodization of strength and conditioning for the sports physical therapist. *Int J Sports Phys Ther* 2015;10(6):734-47. [published Online First: 2015/12/01].

91. Sugimoto D, Jackson SS, Howell DR, et al. Association between training volume and lower extremity overuse injuries in young female athletes: implications for early sports specialization. *Phys Sportsmed* 2019;47(2):199-204. doi: 10.1080/00913847.2018.1546107 [published Online First: 20181119].

92. Jones CM, Griffiths PC, Mellalieu SD. Training Load and Fatigue Marker Associations with Injury and Illness: A Systematic Review of Longitudinal Studies. *Sports Med* 2017;47(5):943-74. doi: 10.1007/s40279-016-0619-5.

93. Buckthorpe M. Optimising the Late-Stage Rehabilitation and Return-to-Sport Training and Testing Process After ACL Reconstruction. *Sports Med* 2019;49(7):1043-58. doi: 10.1007/s40279-019-01102-z.

94. Slater LV, Hart JM, Kelly AR, Kuenze CM. Progressive Changes in Walking Kinematics and Kinetics After Anterior Cruciate Ligament Injury and Reconstruction: A Review and Meta-Analysis. *J Athl Train* 2017;52(9):847-60. doi: 10.4085/1062-6050-52.6.06.

95. Johnston PT, McClelland JA, Webster KE. Lower Limb Biomechanics During Single-Leg Landings Following Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-Analysis. *Sports Med* 2018;48(9):2103-26. doi: 10.1007/s40279-018-0942-0.

96. Kotsifaki R, Sideris V, King E, et al. Performance and symmetry measures during vertical jump testing at return to sport after ACL reconstruction. *Br J Sports Med* 2023;57(20):1304-10. doi: 10.1136/bjsports-2022-106588 [published Online First: 20230601].

97. Kotsifaki A, Van Rossom S, Whiteley R, et al. Single leg vertical jump performance identifies knee function deficits at return to sport after ACL reconstruction in male athletes. *Br J Sports Med* 2022;56(9):490-98. doi: 10.1136/bjsports-2021-104692 [published Online First: 20220208].

98. Buckthorpe M. Recommendations for Movement Re-training After ACL Reconstruction. *Sports Med* 2021;51(8):1601-18. doi: 10.1007/s40279-021-01454-5.

99. Gokeler A, Benjaminse A, Hewett TE, et al. Feedback techniques to target functional deficits following anterior cruciate ligament reconstruction: implications for motor control and reduction of second injury risk. *Sports Med* 2013;43(11):1065-74. doi: 10.1007/s40279-013-0095-0.

100. Wulf G, Höß M, Prinz W. Instructions for motor learning: differential effects of internal versus external focus of attention. *J Mot Behav* 1998;30(2):169-79. doi: 10.1080/00222899809601334.

101. Rambaud AJM, Ardern CL, Thoreux P, et al. Criteria for return to running after anterior cruciate ligament reconstruction: a scoping review. *Br J Sports Med* 2018;52(22):1437-44. doi: 10.1136/bjsports-2017-098602.

102. Foster C, Florhaug JA, Franklin J, et al. A new approach to monitoring exercise training. *J Strength Cond Res* 2001;15(1):109-15. DOI: 10.1519/00124278-200102000-00019.

103. Petersen J, Sørensen H, Nielsen R. Cumulative loads increase at the knee joint with slow-speed running compared to faster running: a biomechanical study. *J Orthop Sports Phys Ther* 2015;45(4):316-22. doi: 10.2519/jospt.2015.5469 [published Online First: 20150101].

104. Buckthorpe M, Della Villa F. Optimising the 'Mid-Stage' Training and Testing Process After ACL Reconstruction. *Sports Med* 2020;50(4):657-78. doi: 10.1007/s40279-019-01222-6.

105. Grindem H, Snyder-Mackler L, Moksnes H, et al. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the Delaware-Oslo ACL cohort study. *Br J Sports Med* 2016;50(13):804-8. doi: 10.1136/bjsports-2016-096031 [published Online First: 20160509].

106. Piussi R, Broman D, Musslinder E, et al. Recovery of preoperative absolute knee extension and flexion strength after ACL reconstruction. *BMC Sports Sci Med Rehabil* 2020;12(1):77. doi: 10.1186/s13102-020-00222-8 [published Online First: 20201210].

107. Undheim MB, Cosgrave C, King E, et al. Isokinetic muscle strength and readiness to return to sport following anterior cruciate ligament reconstruction: is there an association? A systematic review and a protocol recommendation. *Br J Sports Med* 2015;49(20):1305-10. doi: 10.1136/bjsports-2014-093962 [published Online First: 2015/06/25].

108. Lynch AD, Logerstedt DS, Grindem H, et al. Consensus criteria for defining 'successful outcome' after ACL injury and reconstruction: a Delaware-Oslo ACL cohort investigation. *Br J Sports Med* 2015;49(5):335-42. doi: 10.1136/bjsports-2013-092299 [published Online First: 20130723].

109. Thomeé R, Neeter C, Gustavsson A, et al. Variability in leg muscle power and hop performance after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2012;20(6):1143-51. doi: 10.1007/s00167-012-1912-y [published Online First: 2012/02/09].

110. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb Symmetry Indexes Can Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop Sports Phys Ther* 2017;47(5):334-38. doi: 10.2519/jospt.2017.7285 [published Online First: 2017/03/31].

111. Haddad M, Stylianides G, Djaoui L, et al. Session-RPE Method for Training Load Monitoring: Validity, Ecological Usefulness, and Influencing Factors. *Front Neurosci* 2017;11:612. doi: 10.3389/fnins.2017.00612 [published Online First: 20171102].

112. Swinton PA, Lloyd R, Agouris I, Stewart A. Contemporary Training Practices in Elite British Powerlifters: Survey Results From an International Competition. *J of Strength Cond Res*2009;23(2):380-84. doi: 10.1519/JSC.0b013e31819424bd.

113. Buckthorpe M, Della Villa F. Recommendations for Plyometric Training after ACL Reconstruction - A Clinical Commentary. *Int J Sports Phys Ther* 2021;16(3):879-95. doi: 10.26603/001c.23549 [published Online First: 20210601].

114. Piussi R, Krupic F, Sundemo D, et al. 'I was young, I wanted to return to sport, and re-ruptured my ACL' – young active female patients' voices on the experience of sustaining an ACL re-rupture, a qualitative study. *BMC Musculoskeletal Disorders* 2022;23(1):760. doi: 10.1186/s12891-022-05708-9.

115. Dos'Santos T, Thomas C, Comfort P, Jones PA. The Effect of Angle and Velocity on Change of Direction Biomechanics: An Angle-Velocity Trade-Off. *Sports Med* 2018;48(10):2235-53. doi: 10.1007/s40279-018-0968-3.

116. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 2016;50(14):853-64. doi: 10.1136/bjsports-2016-096278 [published Online First: 20160525].

117. Ekstrand J, Lundqvist D, Davison M, et al. Communication quality between the medical team and the head coach/manager is associated with injury burden and player availability in elite football clubs. *Br J Sports Med* 2019;53(5):304-08. doi: 10.1136/bjsports-2018-099411.

118. Burland JP, Toonstra J, Werner JL, et al. Decision to Return to Sport After Anterior Cruciate Ligament Reconstruction, Part I: A Qualitative Investigation of Psychosocial Factors. *J Athl Train* 2018;53(5):452-63. doi: 10.4085/1062-6050-313-16 [published Online First: 20180305].

119. Webster KE, Hewett TE. What is the Evidence for and Validity of Return-to-Sport Testing after Anterior Cruciate Ligament Reconstruction Surgery? A Systematic Review and Meta-Analysis. *Sports Med* 2019;49(6):917-29. doi: 10.1007/s40279-019-01093-x.

120. Svantesson E, Hamrin Senorski E, Webster KE, et al. Clinical outcomes after anterior cruciate ligament injury: panther symposium ACL injury clinical outcomes consensus group. *Knee Surg Sports Traumatol Arthrosc* 2020;28(8):2415-34. doi: 10.1007/s00167-020-06061-x [published Online First: 20200806].

121. Andrade R, Pereira R, van Cingel R, et al. How should clinicians rehabilitate patients after ACL reconstruction? A systematic review of clinical practice guidelines (CPGs) with a focus on quality appraisal (AGREE II). *Br J Sports Med* 2020;54(9):512-19. doi: 10.1136/bjsports-2018-100310 [published Online First: 20190607].

122. Burgi CR, Peters S, Ardern CL, et al. Which criteria are used to clear patients to return to sport after primary ACL reconstruction? A scoping review. *Br J Sports Med* 2019;53(18):1154-61. doi: 10.1136/bjsports-2018-099982 [published Online First: 20190202].

123. Grassi A, Smiley SP, Roberti di Sarsina T, et al. Mechanisms and situations of anterior cruciate ligament injuries in professional male soccer players: a YouTube-based video analysis. *Eur J Orthop Surg Traumatol* 2017;27(7):967-81. doi: 10.1007/s00590-017-1905-0 [published Online First: 20170125].

124. Gokeler A, Dingenen B, Hewett TE. Rehabilitation and Return to Sport Testing After Anterior Cruciate Ligament Reconstruction: Where Are We in 2022? *Arthrosc Sports Med Rehabil* 2022;4(1):e77-e82. doi: 10.1016/j.asmr.2021.10.025 [published Online First: 20220128].

125. Nimphius S, Callaghan SJ, Spiteri T, Lockie RG. Change of Direction Deficit: A More Isolated Measure of Change of Direction Performance Than Total 505 Time. *J Strength Cond Res* 2016;30(11):3024-32. doi: 10.1519/jsc.0000000000001421.

126. Marques JB, Paul DJ, Graham-Smith P, Read PJ. Change of Direction Assessment Following Anterior Cruciate Ligament Reconstruction: A Review of Current Practice and Considerations to Enhance Practical Application. *Sports Med* 2020;50(1):55-72. doi: 10.1007/s40279-019-01189-4.

127. Brewer B, Andersen MB, Van Raalte J. Psychological aspects of sport injury rehabilitation: Toward a biopsychosocial approach. In: Mostofsky DI, Zaichkowsky LD, eds. Medical and Psychological Aspects of Sport and Exercise. Morgantown: Fitness Information Technology 2002.

128. Wiese-Bjornstal DM. Psychology and socioculture affect injury risk, response, and recovery in high-intensity athletes: a consensus statement. *Scand J Med Sci Sports* 2010;20 Suppl 2:103-11. doi: 10.1111/j.1600-0838.2010.01195.x [published Online First: 2010/09/25].

129. Hagger MS, Chatzisarantis NLD, Griffin M, Thatcher J. Injury Representations, Coping, Emotions, and Functional Outcomes in Athletes With Sports-Related Injuries: A Test of Self-Regulation Theory1. *J App Soc Psychol* 2005;35(11):2345-74. doi: https://doi.org/10.1111/j.1559-1816.2005.tb02106.x.

130. Roy-Davis K, Wadey R, Evans L. A grounded theory of sport injury-related growth. *Sport Exerc Perform Psychol* 2017;6(1):35-52. doi: 10.1037/spy0000080.

131. Wiese-bjornstal DM, Smith AM, Shaffer SM, Morrey MA. An integrated model of response to sport injury: Psychological and sociological dynamics. *J Appl Sport Psychol* 1998;10(1):46-69. doi: 10.1080/10413209808406377.

132. Morrey MA, Stuart MJ, Smith AM, Wiese-Bjornstal DM. A Longitudinal Examination of Athletes' Emotional and Cognitive Responses to Anterior Cruciate Ligament Injury. *Clin J Sport Med* 1999;9(2):63-69. doi: 10.1097/00042752-199904000-00004.

133. Walker N, Thatcher J, Lavallee D. Psychological responses to injury in competitive sport: a critical review. *J R Soc Promot Health* 2007;127(4):174-80. doi: 10.1177/1466424007079494.

134. Kvist J, Ek A, Sporrstedt K, Good L. Fear of re-injury: a hindrance for returning to sports after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2005;13(5):393-7. doi: 10.1007/s00167-004-0591-8 [published Online First: 20050210].

135. Ray R, Wiese-Bjornstal DM. Counseling in Sports Medicine: Human Kinetics 1999.

136. DiSanti J, Lisee C, Erickson K, et al. Perceptions of Rehabilitation and Return to Sport Among High School Athletes With Anterior Cruciate Ligament Reconstruction: A Qualitative Research Study. *J Orthop Sports Phys Ther* 2018;48(12):951-59. doi: 10.2519/jospt.2018.8277 [published Online First: 20180622].

137. Thomeé P, Währborg P, Börjesson M, et al. Self-efficacy, symptoms and physical activity in patients with an anterior cruciate ligament injury: a prospective study. *Scand J Med Sci Sports* 2007;17(3):238-45. doi: 10.1111/j.1600-0838.2006.00557.x [published Online First: 2006/06/16].

138. te Wierike SCM, van der Sluis A, van den Akker-Scheek I, et al. Psychosocial factors influencing the recovery of athletes with anterior cruciate ligament injury: A systematic review. *Scand J Med Sci Sports* 2013;23(5):527-40. doi: https://doi.org/10.1111/sms.12010.

139. Langford J, Webster KE, Feller JA. A prospective longitudinal study to assess psychological changes following anterior cruciate ligament reconstruction surgery. *Br J Sports Med* 2009;43(5):377-81. doi: 10.1136/bjsm.2007.044818.

140. Ardern CL. Anterior cruciate ligament reconstruction—not exactly a one-way ticket back to the preinjury level: a review of contextual factors affecting return to sport after surgery. *Sports health* 2015;7(3):224-30. doi: 10.1177/1941738115578131.

141. Ohji S, Aizawa J, Hirohata K, et al. Athletic identity and sport commitment in athletes after anterior cruciate ligament reconstruction who have returned to sports at their pre-injury level of competition. *BMC Sports Sci Med Rehabil* 2021;13(1):37. doi: 10.1186/s13102-021-00264-6.

142. Edison BR, Christino MA, Rizzone KH. Athletic Identity in Youth Athletes: A Systematic Review of the Literature. *Int J Environ Res Public Health* 2021;18(14) doi: 10.3390/ijerph18147331 [published Online First: 20210708].

143. Brewer BW, Cornelius AE. Self-Protective Changes in Athletic Identity Following Anterior Cruciate Ligament Reconstruction. *Psychol Sport Exerc* 2010;11(1):1-5. doi: 10.1016/j.psychsport.2009.09.005.

144. McGinley J, Stapleton E, Gale E, et al. Differences in athletic identity, sport participation, and psychosocial factors following anterior cruciate ligament rehabilitation in youth athletes. *Front Psychol* 2023;14:1303887. doi: 10.3389/fpsyg.2023.1303887 [published Online First: 20240108].

145. Simpson EH, Balsam PD. The Behavioral Neuroscience of Motivation: An Overview of Concepts, Measures, and Translational Applications. *Curr Top Behav Neurosci* 2016;27:1-12. doi: 10.1007/7854_2015_402.

146. Brewer BW, Cornelius AE, Van Raalte JL, et al. Age-Related Differences in Predictors of Adherence to Rehabilitation After Anterior Cruciate Ligament Reconstruction. *J Athl Train* 2003;38(2):158-62. https://doi.org/10.1037/a0031297.

147. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol* 2000;55(1):68. doi: 10.1037//0003-066x.55.1.68.

148. Ryan RM, Deci EL. Intrinsic and extrinsic motivation from a self-determination theory perspective: Definitions, theory, practices, and future directions. *Contemp Educ Psychol* 2020;61:101860. doi: https://doi.org/10.1016/j.cedpsych.2020.101860.

149. Bandura A. Self-efficacy: Toward a unifying theory of behavioral change. *Psychol Rev* 1977;84(2):191-215. doi: 10.1037/0033-295X.84.2.191.

150. Piussi R, Beischer S, Thomeé R, Hamrin Senorski E. Superior knee self-efficacy and quality of life throughout the first year in patients who recover symmetrical muscle function after ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2020;28(2):555-67. doi: 10.1007/s00167-019-05703-z [published Online First: 20190925].

151. Cordova JR, Sinatra GM, Jones SH, et al. Confidence in prior knowledge, self-efficacy, interest and prior knowledge: Influences on conceptual change. *Contemp Educ Psychol* 2014;39(2):164-74. doi: https://doi.org/10.1016/j.cedpsych.2014.03.006.

152. Rotter JB. Generalized expectancies for internal versus external control of reinforcement. *Psychol Monogr* 1966;80(1):1-28. doi: 10.1037/h0092976.

153. Christino MA, Fantry AJ, Vopat BG. Psychological aspects of recovery following anterior cruciate ligament reconstruction. *J Am Acad Orthop Surg* 2015;23(8):501-09. doi: 10.5435/JAAOS-D-14-00173.

154. Nyland J, Mauser N, Caborn D. Sports involvement following ACL reconstruction is related to lower extremity neuromuscular adaptations, subjective knee function and health locus of control. *Knee Surg Sports Traumatol Arthrosc* 2013;21:2019-28. doi: 10.1007/s00167-013-2366-6.

155. Brewer BW, Cornelius AE, Van Raalte JL, et al. Attributions for recovery and adherence to rehabilitation following anterior cruciate ligament reconstruction: A prospective analysis. *Health Psychol* 2000;15(2):283-91. doi: 10.1080/08870440008400307.

156. Ivarsson A, Johnson U. Psychological Bases of Sport Injuries: FIT Publishing 2022.

157. Folkman S, Moskowitz JT. Coping: pitfalls and promise. *Annu Rev Psychol* 2004;55:745-74. doi: 10.1146/annurev.psych.55.090902.141456.

158. Coronado RA, Bird ML, Van Hoy EE, et al. Do psychosocial interventions improve rehabilitation outcomes after anterior cruciate ligament reconstruction? A systematic review. *Clin Rehabil* 2018;32(3):287-98. doi: 10.1177/0269215517728562 [published Online First: 20170824].

159. Levack WM, Weatherall M, Hay-Smith JC, et al. Goal setting and strategies to enhance goal pursuit in adult rehabilitation: summary of a Cochrane systematic review and meta-analysis. *Eur J Phys Rehabil Med* 2016;52(3):400-16. doi: 10.1002/14651858.CD009727.pub2. [published Online First: 20160115].

160. Chronister J, Chou CC, Frain M, Cardoso EdS. The relationship between social support and rehabilitation related outcomes: a meta-analysis. *J Rehabil* 2008;74:16. https://www.proquest.

com/scholarly-journals/relationship-between-social-support/docview/236401050/se-2.

161. APA Dictionary of Psychology. Washington, DC, US: American Psychological Association 2007.

162. Arvinen-Barrow M, Clement D. The Psychology of Sport Injury and Rehabilitation: Taylor & Francis 2024.

163. Lu FJ, Hsu Y. Injured athletes' rehabilitation beliefs and subjective well-being: the contribution of hope and social support. *J Athl Train* 2013;48(1):92-8. doi: 10.4085/1062-6050-48.1.03.

164. Johnston LH, Carroll D. Coping, Social Support, and injury: Changes Over Time and the Effects of Level of Sports involvement. *J Sport Rehabil* 2000;9(4):290-303. doi: 10.1123/jsr.9.4.290.

165. Morrow EL, Duff MC, Mayberry LS. Mediators, Moderators, and Covariates: Matching Analysis Approach for Improved Precision in Cognitive-Communication Rehabilitation Research. *J Speech Lang Hear Res* 2022;65(11):4159-71. doi: 10.1044/2022_jslhr-21-00551 [published Online First: 20221028].

166. Gaudreau P, Blondin J-P. Different athletes cope differently during a sport competition: a cluster analysis of coping. *Pers Individ Dif* 2004;36(8):1865-77. doi: https://doi.org/10.1016/j.paid.2003.08.017.

167. Leger KA, Charles ST, Turiano NA, Almeida DM. Personality and stressor-related affect. *J Pers Soc Psychol* 2016;111(6):917-28. doi: 10.1037/pspp0000083 [published Online First: 20160121].

168. Childs E, White TL, de Wit H. Personality traits modulate emotional and physiological responses to stress. *Behav Pharmacol* 2014;25(5-6):493-502. doi: 10.1097/fbp.0000000000000064.

169. Nawasreh Z, Adams G, Pryzbylkowski O, Logerstedt D. Influence of patient demographics and graft types on second ACL injury rates in ipsilateral versus contralateral knees: a systematic review and meta-analysis. *Int J Sports Phys Ther* 2018;13(4):561-74. https://doi.org/10.26603/ijspt20180561 [published Online First: 2018/08/25].

170. Wright RW, Magnussen RA, Dunn WR, Spindler KP. Ipsilateral graft and contralateral ACL rupture at five years or more following ACL reconstruction: a systematic review. *J Bone Joint Surg Am* 2011;93(12):1159. doi: 10.2106/JBJS.J.00898.

171. Bourke HE, Salmon LJ, Waller A, et al. Survival of the anterior cruciate ligament graft and the contralateral ACL at a minimum of 15 years. *Am J Sports Med* 2012;40(9):1985-92. doi: 10.1177/0363546512454414 [published Online First: 2012/08/08].

172. Wiggins AJ, Grandhi RK, Schneider DK, et al. Risk of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med* 2016;44(7):1861-76. doi: 10.1177/0363546515621554 [published Online First: 2016/01/17].

173. Webster KE, Feller JA, Klemm HJ. Second ACL Injury Rates in Younger Athletes Who Were Advised to Delay Return to Sport Until 12 Months After ACL Reconstruction. *Orthop J Sports Med* 2021;9(2):2325967120985636. doi: 10.1177/2325967120985636 [published Online First: 2021/03/16].

174. Paterno MV, Thomas S, VanEtten KT, Schmitt LC. Confidence, ability to meet return to sport criteria, and second ACL injury risk associations after ACL-reconstruction. *J Orthop Res* 2022;40(1):182-90. doi: 10.1002/jor.25071 [published Online First: 2021/05/01].

175. van Melick N, Pronk Y, Nijhuis-van der Sanden M, et al. Meeting movement quantity or quality return to sport criteria is associated with reduced second ACL injury rate. *J Orthop Res* 2022;40(1):117-28. doi: 10.1002/jor.25017 [published Online First: 2021/03/03].

176. Fältström A, Hägglund M, Kvist J, Mendonça LD. Risk Factors for Sustaining a Second ACL Injury after Primary ACL Reconstruction in Female Football Players: A Study Investigating the Effects of Follow-Up Time and the Statistical Approach. *Sports Med Open* 2023;9(1):29. doi: 10.1186/s40798-023-00571-x [published Online First: 2023/05/12].

177. Almeida GPL, Albano TR, Rodrigues CAS, et al. _Combining return to sport, psychological readiness, body mass, hamstring strength symmetry, and hamstring/quadriceps ratio increases the risk of a second anterior cruciate ligament injury. *Knee Surg Sports Traumatol Arthrosc* 2023;31(11):5087-95. doi: 10.1007/s00167-023-07559-w [published Online First: 2023/09/20].

178. Zhao D, Pan J-k, Lin F-z, et al. Risk Factors for Revision or Rerupture After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med* 2023;51(11):3053-75. doi: 10.1177/03635465221119787.

179. Zsidai B, Piussi R, Thomeé R, et al. Generalised joint hypermobility leads to increased odds of sustaining a second ACL injury within 12 months of return to sport after ACL reconstruction. *Br J Sports Med* 2023;57(15):972-78. doi: 10.1136/bjsports-2022-106183 [published Online First: 20230516].

180. Marigi EM, Hale RF, Bernard CD, et al. Are 6-Month Functional and Isokinetic Testing Measures Risk Factors for Second Anterior Cruciate Ligament Injuries at Long-T Follow-Up? *J Knee Surg* 2023;36(10):1060-68. doi: 10.1055/s-0042-1748824 [published Online First: 20220610].

181. Simonson R, Piussi R, Högberg J, et al. Effect of Quadriceps and Hamstring Strength Relative to Body Weight on Risk of a Second ACL Injury: A Cohort Study of 835 Patients Who Returned to Sport After ACL Reconstruction. *Orthop J Sports Med* 2023;11(4):23259671231157386. doi: 10.1177/23259671231157386 [published Online First: 2023/05/08].

182. Maletis GB, Inacio MC, Funahashi TT. Risk factors associated with revision and contralateral anterior cruciate ligament reconstructions in the Kaiser Permanente ACLR registry. *Am J Sports Med* 2015;43(3):641-7. doi: 10.1177/0363546514561745.

183. Kaeding CC, Pedroza AD, Reinke EK, et al. Risk Factors and Predictors of Subsequent ACL Injury in Either Knee After ACL Reconstruction: Prospective Analysis of 2488 Primary ACL Reconstructions From the MOON Cohort. *Am J Sports Med* 2015;43(7):1583-90. doi: 10.1177/0363546515578836 [published Online First: 2015/04/23].

184. Schilaty ND, Nagelli C, Bates NA, et al. Incidence of Second Anterior Cruciate Ligament Tears and Identification of Associated Risk Factors From 2001 to 2010 Using a Geographic Database. *Orthop J Sports Med* 2017;5(8):2325967117724196. doi: 10.1177/2325967117724196 [published Online First: 2017/08/26].

185. Fältström A, Kvist J, Bittencourt NFN, et al. Clinical Risk Profile for a Second Anterior Cruciate Ligament Injury in Female Soccer Players After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2021;49(6):1421-30. doi: 10.1177/0363546521999109 [published Online First: 20210415].

186. Cronström A, Tengman E, Häger CK. Risk Factors for Contra-Lateral Secondary Anterior Cruciate Ligament Injury: A Systematic Review with Meta-Analysis. *Sports Med* 2021;51(7):1419-38. doi: 10.1007/s40279-020-01424-3 [published Online First: 20210130].

187. Tan SH, Lau BP, Khin LW, Lingaraj K. The Importance of Patient Sex in the Outcomes of Anterior Cruciate Ligament Reconstructions: A Systematic Review and Meta-analysis. *Am J Sports Med* 2016;44(1):242-54. doi: 10.1177/0363546515573008 [published Online First: 20150323].

188. Svantesson E, Senorski EH, Baldari A, et al. Factors associated with additional anterior cruciate ligament reconstruction and register comparison: a systematic review on the Scandinavian knee ligament registers. *Br J Sports Med* 2019;53(7):418-25. doi: 10.1136/bjsports-2017-098192.

189. Persson A, Fjeldsgaard K, Gjertsen JE, et al. Increased risk of revision with hamstring tendon grafts compared with patellar tendon grafts after anterior cruciate ligament reconstruction: a study of 12,643 patients from the Norwegian Cruciate Ligament Registry, 2004-2012. *Am J Sports Med* 2014;42(2):285-91. doi: 10.1177/0363546513511419 [published Online First: 20131209].

190. Gifstad T, Foss OA, Engebretsen L, et al. Lower risk of revision with patellar tendon autografts compared with hamstring autografts: a registry study based on 45,998 primary ACL reconstructions in Scandinavia. *Am J Sports Med* 2014;42(10):2319-28. doi: 10.1177/0363546514548164 [published Online First: 20140908].

191. Rahardja R, Zhu M, Love H, et al. Effect of Graft Choice on Revision and Contralateral Anterior Cruciate Ligament Reconstruction: Results From the New Zealand ACL Registry. *Am J Sports Med* 2020;48(1):63-69. doi: 10.1177/0363546519885148 [published Online First: 20191115].

192. Andernord D, Björnsson H, Petzold M, et al. Surgical Predictors of Early Revision Surgery After Anterior Cruciate Ligament Reconstruction: Results From the Swedish National Knee Ligament Register on 13,102 Patients. *Am J Sports Med* 2014;42(7):1574-82. doi: 10.1177/0363546514531396 [published Online First: 20140428].

193. Snaebjörnsson T, Svantesson E, Sundemo D, et al. Young age and high BMI are predictors of early revision surgery after primary anterior cruciate ligament reconstruction: a cohort study from the Swedish and Norwegian knee ligament registries based on 30,747 patients. *Knee Surg Sports Traumatol Arthrosc* 2019;27(11):3583-91. doi: 10.1007/s00167-019-05487-2 [published Online First: 20190316].

194. DiSilvestro KJ, Jauregui JJ, Glazier E, et al. Outcomes of Anterior Cruciate Ligament Reconstruction in Obese and Overweight Patients: A Systematic Review. *Clin J Sport Med* 2019;29(4):257-61. doi: 10.1097/jsm.0000000000000521.

195. Cristiani R, Forssblad M, Edman G, et al. Age, time from injury to surgery and quadriceps strength affect the risk of revision surgery after primary ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2021;29(12):4154-62. doi: 10.1007/s00167-021-06517-8 [published Online First: 20210304].

196. Blucher NC, Feller JA, Devitt BM, et al. Is There an Association in Young Patients Between Quadriceps or Hamstring Strength After ACL Reconstruction and Graft Rupture? *Orthop J Sports Med* 2022;10(6):23259671221101003. doi: 10.1177/23259671221101003 [published Online First: 20220603].

197. King E, Richter C, Daniels KAJ, et al. Can Biomechanical Testing After Anterior Cruciate Ligament Reconstruction Identify Athletes at Risk for Subsequent ACL Injury to the Contralateral Uninjured Limb? *Am J Sports Med* 2021;49(3):609-19. doi: 10.1177/0363546520985283 [published Online First: 20210209].

198. King E, Richter C, Daniels KAJ, et al. Biomechanical but Not Strength or Performance Measures Differentiate Male Athletes Who Experience ACL Reinjury on Return to Level 1 Sports. *Am J Sports Med* 2021;49(4):918-27. doi: 10.1177/0363546520988018 [published Online First: 20210222].

199. Della Villa F, Buckthorpe M, Grassi A, et al. Systematic video analysis of ACL injuries in professional male football (soccer): injury mechanisms, situational patterns and biomechanics study on 134 consecutive cases. *Br J Sports Med* 2020;54(23):1423-32. doi: 10.1136/bjsports-2019-101247 [published Online First: 20200619].

200. Donelon TA, Dos'Santos T, Pitchers G, et al. Biomechanical Determinants of Knee Joint Loads Associated with Increased Anterior Cruciate Ligament Loading During Cutting: A Systematic Review and Technical Framework. *Sports Med Open* 2020;6(1):53. doi: 10.1186/s40798-020-00276-5 [published Online First: 20201102].

201. Harper DJ, McBurnie AJ, Santos TD, et al. Biomechanical and Neuromuscular Performance Requirements of Horizontal Deceleration: A Review with Implications for Random Intermittent Multi-Directional Sports. *Sports Med* 2022;52(10):2321-54. doi: 10.1007/s40279-022-01693-0 [published Online First: 20220529].

202. Maestroni L, Read P, Turner A, et al. Strength, rate of force development, power and reactive strength in adult male athletic populations post anterior cruciate ligament reconstruction - A systematic review and meta-analysis. *Phys Ther Sport* 2021;47:91-104. doi: 10.1016/j.ptsp.2020.11.024 [published Online First: 20201110].

203. Aagaard P. Spinal and supraspinal control of motor function during maximal eccentric muscle contraction: Effects of resistance training. *J Sport Health Sci* 2018;7(3):282-93. doi: 10.1016/j.jshs.2018.06.003 [published Online First: 20180621].

204. Ivarsson A, Johnson U, Andersen MB, et al. Psychosocial Factors and Sport Injuries: Meta-analyses for Prediction and Prevention. *Sports Med* 2017;47(2):353-65. doi: 10.1007/s40279-016-0578-x.

205. McPherson AL, Feller JA, Hewett TE, Webster KE. Psychological Readiness to Return to Sport Is Associated With Second Anterior Cruciate Ligament Injuries. *Am J Sports Med* 2019;47(4):857-62. doi: 10.1177/0363546518825258 [published Online First: 20190212].

206. Zarzycki R, Cummer K, Arhos E, et al. Female Athletes With Better Psychological Readiness Are at Higher Risk for Second ACL Injury After Primary ACL Reconstruction. *Sports Health* 2023:19417381231155120. doi: 10.1177/19417381231155120 [published Online First: 20230319].

207. Sutherland K, Clatworthy M, Chang K, et al. Risk Factors for Revision Anterior Cruciate Ligament Reconstruction and Frequency With Which Patients Change Surgeons. *Orthop J Sports Med* 2019;7(11):2325967119880487. doi: 10.1177/2325967119880487 [published Online First: 20191121].

208. Cronström A, Tengman E, Häger CK. Return to Sports: A Risky Business? A Systematic Review with Meta-Analysis of Risk Factors for Graft Rupture Following ACL Reconstruction. *Sports Med* 2023;53(1):91-110. doi: 10.1007/s40279-022-01747-3 [published Online First: 20220824].

209. Bates NA, Schilaty ND, Ueno R, Hewett TE. Timing of Strain Response of the ACL and MCL Relative to Impulse Delivery During Simulated Landings Leading up to ACL Failure. *J Appl Biomech* 2020;36(3):148-55. doi: 10.1123/jab.2019-0308 [published Online First: 20200422].

210. Newman L. Descartes' Epistemology. In: Zalta EN, ed. The Stanford Encyclopedia of Philosophy (Winter 2017 Edition). Stanford: Metaphysics Research Lab, Stanford University, 2017.

211. Markie PaF, M. Rationalism vs. Empiricism. In: Nodelman ENZaU, ed. The Stanford Encyclopedia of Philosophy. Stanford: Metaphysics Research Lab, Stanford University, 2023.

212. Fuller S. Positivism, History of. In: Smelser NJ, Baltes PB, eds. International Encyclopedia of the Social & Behavioral Sciences. Oxford: Pergamon 2001:11821-27.

213. Shannon-Baker P. Philosophical underpinnings of mixed methods research in education. In: Tierney RJ, Rizvi F, Ercikan K, eds. International Encyclopedia of Education (Fourth Edition). Oxford: Elsevier 2023:380-89.

214. Tashakkori A, Johnson RB, Teddlie C. Foundations of Mixed Methods Research: Integrating Quantitative and Qualitative Approaches in the Social and Behavioral Sciences: SAGE Publications 2020.

215. Gadamer HG. Truth and Method: Bloomsbury Publishing 2013.

216. Dorfman E. History of the Lifeworld. *Philosophy Today* 2009;53(3):294-303. https://doi.org/10.5840/philtoday200953317.

217. Nilstun T, Lundqvist A, Löfmark R. Vetenskapsteori i medicin och klinik: Studentlitteratur 2007.

218. Azungah T. Qualitative research: deductive and inductive approaches to data analysis. *Qualitative research journal* 2018;18(4):383-400. https://doi.org/10.1108/qrj-d-18-00035.

219. Shuval K, Harker K, Roudsari B, et al. Is qualitative research second class science? A quantitative longitudinal examination of qualitative research in medical journals. *PloS one* 2011;6(2):e16937.

220. Thurén T. Vetenskapsteori för nybörjare: Liber 1996.

221. Sackett DL. Evidence-based medicine. *Semin Perinatol* 1997;21(1):3-5. doi: https://doi.org/10.1016/S0146-0005(97)80013-4.

222. Evans D. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. *J Clin Nurs* 2003;12(1):77-84. doi: 10.1046/j.1365-2702.2003.00662.x.

223. Jeremy Howick IC, Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, and Hazel Thornton. The 2011 Oxford CEBM Levels of Evidence (Introductory Document). 2011.

224. Uman LS. Systematic reviews and meta-analyses. *J Can Acad Child Adolesc Psychiatry* 2011;20(1):57-9. doi: 10.1002/9781444311723.ch8.

225. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71.

226. Guyatt GH, Oxman AD, Kunz R, et al. What is "quality of evidence" and why is it important to clinicians? *BMJ* 2008;336(7651):995-98. doi: 10.1136/bmj.39490.551019.BE.

227. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336(7650):924-26. doi: 10.1136/bmj.39489.470347.AD.

228. Stewart LA, Clarke M, Rovers M, et al. Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement. *Jama* 2015;313(16):1657-65. doi: 10.1001/jama.2015.3656 [published Online First: 2015/04/29].

229. Ardern CL, Büttner F, Andrade R, et al. Implementing the 27 PRISMA 2020 Statement items for systematic reviews in the sport and exercise medicine, musculoskeletal rehabilitation and sports science fields: the PERSiST (implementing Prisma in Exercise, Rehabilitation, Sport medicine and SporTs science) guidance. *Br J Sports Med* 2022;56(4):175-95. doi: 10.1136/bjsports-2021-103987 [published Online First: 20211008].

230. Anglemyer A, Horvath HT, Bero L. Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials. *Cochrane Database Syst Rev* 2014;2014(4):Mr000034. doi: 10.1002/14651858.MR000034.pub2 [published Online First: 20140429].

231. Sessler DI, Imrey PB. Clinical Research Methodology 3: Randomized Controlled Trials. *Anesth Analg* 2015;121(4):1052-64. doi: 10.1213/ane.0000000000000862.

232. Fuller J. Rationality and the generalization of randomized controlled trial evidence. *J Eval Clin Pract* 2013;19(4):644-7. doi: 10.1111/jep.12021 [published Online First: 20130131].

233. Setia MS. Methodology Series Module 1: Cohort Studies. *Indian J Dermatol* 2016;61(1):21-5. doi: 10.4103/0019-5154.174011.

234. Sessler DI, Imrey PB. Clinical Research Methodology 1: Study Designs and Methodologic Sources of Error. *Anesth Analg* 2015;121(4):1034-42. doi: 10.1213/ane.0000000000000815.

235. Capili B, Anastasi JK. Cohort Studies. *Am J Nurs* 2021;121(12):45-48. doi: 10.1097/01.Naj.0000803196.49507.08.

236. Tenny S, Kerndt CC, Hoffman MR. Case Control Studies. StatPearls. Treasure Island (FL): StatPearls Publishing, Copyright © 2024, StatPearls Publishing LLC. 2024.

237. Lancet T. National disease registries for advancing health care: Elsevier, 2011:2050.

238. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med* 2018;23(2):60-63. doi: 10.1136/bmjebm-2017-110853 [published Online First: 20180202].

239. Jamshed S. Qualitative research method-interviewing and observation. *J Basic Clin Pharm* 2014;5(4):87-8. doi: 10.4103/0976-0105.141942.

240. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today* 2004;24(2):105-12. doi: 10.1016/j.nedt.2003.10.001.

241. Graneheim UH, Lindgren BM, Lundman B. Methodological challenges in qualitative content analysis: A discussion paper. *Nurse Educ Today* 2017;56:29-34. doi: 10.1016/j.nedt.2017.06.002 [published Online First: 2017/06/27].

242. Daly J, Willis K, Small R, et al. A hierarchy of evidence for assessing qualitative health research. *J Clin Epidemiol* 2007;60(1):43-9. doi: 10.1016/j.jclinepi.2006.03.014 [published Online First: 20060928].

243. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes* 2006;4:79. doi: 10.1186/1477-7525-4-79 [published Online First: 20061011].

244. Prinsen CAC, Mokkink LB, Bouter LM, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. *Qual Life Res* 2018;27(5):1147-57. doi: 10.1007/s11136-018-1798-3.

245. Polit DF, Beck CT. The content validity index: are you sure you know what's being reported? Critique and recommendations. *Res Nurs Health* 2006;29(5):489-97. doi: 10.1002/nur.20147.

246. Feiring DC, Ellenbecker TS, Derscheid GL. Test-retest reliability of the biodex isokinetic dynamometer. *J Orthop Sports Phys Ther* 1990;11(7):298-300. doi: 10.2519/jospt.1990.11.7.298 [published Online First: 1990/01/01].

247. Drouin JM, Valovich-mcLeod TC, Shultz SJ, et al. Reliability and validity of the Biodex system 3 pro isokinetic dynamometer velocity, torque and position measurements. *Eur J Appl Physiol* 2004;91(1):22-9. doi: 10.1007/s00421-003-0933-0 [published Online First: 2003/09/26].

248. Gustavsson A, Neeter C, Thomeé P, et al. A test battery for evaluating hop performance in patients with an ACL injury and patients who have undergone ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2006;14(8):778-88. doi: 10.1007/s00167-006-0045-6 [published Online First: 2006/03/10].

249. Opar DA, Piatkowski T, Williams MD, Shield AJ. A novel device using the Nordic hamstring exercise to assess eccentric knee flexor strength: a reliability and retrospective injury study. *J Orthop Sports Phys Ther* 2013;43(9):636-40. doi: 10.2519/jospt.2013.4837 [published Online First: 2013/07/28].

250. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64. doi: 10.1186/1477-7525-1-64 [published Online First: 2003/11/14].

251. Krogsgaard MR, Hansen CF. Patient-reported outcome measures: it is time for authors, reviewers, journal editors and health care strategists to take sufficient responsibility. *Knee Surg Sports Traumatol Arthrosc* 2022;30(11):3589-93. doi: 10.1007/s00167-022-07138-5 [published Online First: 20220901].

252. van Meer BL, Meuffels DE, Vissers MM, et al. Knee injury and Osteoarthritis Outcome Score or International Knee Documentation Committee Subjective Knee Form: which questionnaire is most useful to monitor patients with an anterior cruciate ligament rupture in the short term? *Arthroscopy* 2013;29(4):701-15. doi: 10.1016/j.arthro.2012.12.015 [published Online First: 2013/02/14].

253. Comins J, Brodersen J, Krogsgaard M, Beyer N. Rasch analysis of the Knee injury and Osteoarthritis Outcome Score (KOOS): a statistical re-evaluation. *Scand J Med Sci Sports* 2008;18(3):336-45. doi: 10.1111/j.1600-0838.2007.00724.x [published Online First: 20071119].

254. Marmura H, Tremblay PF, Getgood AMJ, Bryant DM. The Knee Injury and Osteoarthritis Outcome Score Does Not Have Adequate Structural Validity for Use With Young, Active Patients With ACL Tears. *Clin Orthop Relat Res* 2022;480(7):1342-50. doi: 10.1097/corr.0000000000002158 [published Online First: 2022/03/04].

255. Comins JD, Siersma VD, Lind M, et al. KNEES-ACL has superior responsiveness compared to the most commonly used patient-reported outcome measures for anterior cruciate ligament injury. *Knee Surg Sports Traumatol Arthrosc* 2018;26(8):2438-46. doi: 10.1007/s00167-018-4961-z [published Online First: 2018/05/01].

256. Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement. *Health Qual Life Outcomes* 2003;1:17. doi: 10.1186/1477-7525-1-17 [published Online First: 2003/06/13].

257. Salavati M, Akhbari B, Mohammadi F, et al. Knee injury and Osteoarthritis Outcome Score (KOOS); reliability and validity in competitive athletes after anterior cruciate ligament reconstruction. *Osteoarthritis Cartilage* 2011;19(4):406-10. doi: 10.1016/j.joca.2011.01.010 [published Online First: 20110119].

258. Beischer S, Hamrin Senorski E, Thomeé P, Thomeé R. Validation of an 18-item version of the Swedish Knee Self-Efficacy Scale for patients after ACL injury and ACL reconstruction. *J Exp Orthop* 2021;8(1):96. doi: 10.1186/s40634-021-00414-2 [published Online First: 20211025].

259. Thomeé P, Währborg P, Börjesson M, et al. A new instrument for measuring self-efficacy in patients with an anterior cruciate ligament injury. *Scand J Med Sci Sports* 2006;16(3):181-7. doi: 10.1111/j.1600-0838.2005.00472.x.

260. Webster KE, Feller JA, Lambros C. Development and preliminary validation of a scale to measure the psychological impact of returning to sport following anterior cruciate ligament reconstruction surgery. *Phys Ther Sport* 2008;9(1):9-15. doi: 10.1016/j.ptsp.2007.09.003 [published Online First: 20071105].

261. Sala-Barat E, Álvarez-Díaz P, Alentorn-Geli E, et al. Translation, cross-cultural adaptation, validation, and measurement properties of the Spanish version of the anterior cruciate ligament-return to sport after injury (ACL-RSI-Sp) scale. *Knee Surg Sports Traumatol Arthrosc* 2020;28(3):833-39. doi: 10.1007/s00167-019-05517-z [published Online First: 2019/05/16]

262. Webster KE, Feller JA. Development and Validation of a Short Version of the Anterior Cruciate Ligament Return to Sport After Injury (ACL-RSI) Scale. *Orthop J Sports Med* 2018;6(4):2325967118763763. doi: 10.1177/2325967118763763 [published Online First: 20180404]

263. Kvist J, Österberg A, Gauffin H, et al. Translation and measurement properties of the Swedish version of ACL-Return to Sports after Injury questionnaire. *Scand J Med Sci Sports* 2013;23(5):568-75. doi: 10.1111/j.1600-0838.2011.01438.x [published Online First: 2012/01/20]

264. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res* 1985(198):43-9. https://doi.org/10.1097/00003086-198509000-00007

265. Briggs KK, Lysholm J, Tegner Y, et al. The reliability, validity, and responsiveness of the Lysholm score and Tegner activity scale for anterior cruciate ligament injuries of the knee: 25 years later. *Am J Sports Med* 2009;37(5):890-7. doi: 10.1177/0363546508330143 [published Online First: 20090304]

266. Biau DJ, Jolles BM, Porcher R. P value and the theory of hypothesis testing: an explanation for new researchers. *Clin Orthop Relat Res* 2010;468(3):885-92. doi: 10.1007/s11999-009-1164-4

267. Bezeau S, Graves R. Statistical power and effect sizes of clinical neuropsychology research. *J Clin Exp Neuropsychol* 2001;23(3):399-406. doi: 10.1076/jcen.23.3.399.1181

268. Shreffler J, Huecker MR. Type I and Type II Errors and Statistical Power. StatPearls. Treasure Island (FL): StatPearls Publishing, Copyright © 2024, StatPearls Publishing LLC. 2024.

269. Bewick V, Cheek L, Ball J. Statistics review 12: survival analysis. *Crit Care* 2004;8(5):389-94. doi: 10.1186/cc2955 [published Online First: 20040906]

270. Bradburn MJ, Clark TG, Love SB, Altman DG. Survival analysis part II: multivariate data analysis--an introduction to concepts and methods. *Br J Cancer* 2003;89(3):431-6. doi: 10.1038/sj.bjc.6601119 [published Online First: 2003/07/31]

271. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its Associated Cutoff Point. *Biom J* 2005;47(4):458-72. doi: https://doi.org/10.1002/bimj.200410135

272. Hosmer DW Jr, Lemeshow S. Applied Logistic Regression. 2nd ed. John Wiley & Sons; 2004.

273. Mandrekar JN. Receiver Operating Characteristic Curve in Diagnostic Test Assessment. *J Thorac Oncol* 2010;5(9):1315-16. doi: https://doi.org/10.1097/JTO.0b013e3181ec173d.

274. Youden WJ. Index for rating diagnostic tests. *Cancer* 1950;3(1):32-35. doi: https://doi.org/10.1002/1097-0142(1950)3:1<32.

275. Elo S, Kääriäinen M, Kanste O, et al. Qualitative Content Analysis: A Focus on Trustworthiness. *SAGE Open* 2014;4(1):2158244014522633. doi: 10.1177/2158244014522633.

276. Hagens V, Dobrow MJ, Chafe R. Interviewee Transcript Review: assessing the impact on qualitative research. *BMC Med Res Methodol* 2009;9:47. doi: 10.1186/1471-2288-9-47 [published Online First: 20090706].

277. Guest G, Bunce A, Johnson L. How Many Interviews Are Enough? *Field Methods* 2016;18(1):59-82. doi: 10.1177/1525822x05279903.

278. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care* 2007;19(6):349-57. doi: 10.1093/intqhc/mzm042.

279. Mayring P. Qualitative Content Analysis: Theoretical Background and Procedures. In: Bikner-Ahsbahs A, Knipping C, Presmeg N, eds. Approaches to Qualitative Research in Mathematics Education: Examples of Methodology and Methods. Dordrecht: Springer Netherlands 2015:365-80.

280. Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs* 2008;62(1):107-15. doi: 10.1111/j.1365-2648.2007.04569.x.

281. Dahlberg H, Dahlberg K. The question of meaning—a momentous issue for qualitative research. *Int J Qual Stud Health Well-being* 2019;14(1):1598723. doi: 10.1080/17482631.2019.1598723.

282. Cho JY, Lee E-H. Reducing confusion about grounded theory and qualitative content analysis: Similarities and differences. *Qual Rep* 2014;19(32).

283. Galdas P. Revisiting Bias in Qualitative Research:Reflections on Its Relationship With Funding and Impact. *Int J Qual Methods* 2017;16(1):1609406917748992. doi: 10.1177/1609406917748992.

284. Krippendorff K. Content Analysis: An Introduction to Its Methodology. Fourth Edition ed. Thousand Oaks, California, 2019.

285. Gadamer HG. Truth and Method: Seabury Press 1975.

286. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Systematic reviews* 2016;5(1):210. doi: 10.1186/s13643-016-0384-4 [published Online First: 2016/12/07].

287. Schick-Makaroff K, MacDonald M, Plummer M, et al. What Synthesis Methodology Should I Use? A Review and Analysis of Approaches to Research Synthesis. *AIMS public health* 2016;3(1):172-215. doi: 10.3934/publichealth.2016.1.172 [published Online First: 2016/03/30].

288. Oliver S, Harden A, Rees R, et al. An Emerging Framework for Including Different Types of Evidence in Systematic Reviews for Public Policy. *Evaluation* 2005;11(4):428-46. doi: 10.1177/1356389005059383.

289. Drucker AM, Fleming P, Chan AW. Research Techniques Made Simple: Assessing Risk of Bias in Systematic Reviews. *J Invest Dermatol* 2016;136(11):e109-e14. doi: 10.1016/j.jid.2016.08.021.

290. Büttner F, Winters M, Delahunt E, et al. Identifying the 'incredible'! Part 1: assessing the risk of bias in outcomes included in systematic reviews. *Br J Sports Med* 2020;54(13):798-800. doi: 10.1136/bjsports-2019-100806.

291. Kim SY, Park JE, Lee YJ, et al. Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. *J Clin Epidemiol* 2013;66(4):408-14. doi: 10.1016/j.jclinepi.2012.09.016 [published Online First: 20130118].

292. Slim K, Nini E, Forestier D, et al. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003;73(9):712-6. doi: 10.1046/j.1445-2197.2003.02748.x [published Online First: 2003/09/06].

293. Hong QN, Gonzalez-Reyes A, Pluye P. Improving the usefulness of a tool for appraising the quality of qualitative, quantitative and mixed methods studies, the Mixed Methods Appraisal Tool (MMAT). *J Eval Clin Pract* 2018;24(3):459-67. doi: 10.1111/jep.12884 [published Online First: 20180221].

294. Hong QN, Pluye P. A Conceptual Framework for Critical Appraisal in Systematic Mixed Studies Reviews. *J Mix Methods Res* 2019;13(4):446-60. doi: 10.1177/1558689818770058.

295. Schünemann H BJ, Guyatt G, Oxman A. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. In: Schünemann H BJ, Guyatt G, Oxman A, ed.: The GRADE Working Group, 2013.

296. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). *J Clin Epidemiol* 2011;64(4):407-15. doi: 10.1016/j.jclinepi.2010.07.017 [published Online First: 2011/01/21].

297. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 7. Rating the quality of evidence--inconsistency. *J Clin Epidemiol* 2011;64(12):1294-302. doi: 10.1016/j.jclinepi.2011.03.017 [published Online First: 2011/08/02].

298. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. *J Clin Epidemiol* 2011;64(12):1283-93. doi: 10.1016/j.jclinepi.2011.01.012 [published Online First: 2011/08/16].

299. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 8. Rating the quality of evidence--indirectness. *J Clin Epidemiol* 2011;64(12):1303-10. doi: 10.1016/j.jclinepi.2011.04.014 [published Online First: 2011/08/02].

300. Guyatt GH, Oxman AD, Montori V, et al. GRADE guidelines: 5. Rating the quality of evidence--publication bias. *J Clin Epidemiol* 2011;64(12):1277-82. doi: 10.1016/j.jclinepi.2011.01.011 [published Online First: 2011/08/02].

301. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care* 2007;19(6):349-57. doi: 10.1093/intqhc/mzm042 [published Online First: 2007/09/18].

302. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. *Biometrics* 1977;33(1):159-74. doi: 10.2307/2529310.

303. Benchimol EI, Smeeth L, Guttmann A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med* 2015;12(10):e1001885.doi: 10.1371/journal.pmed.1001885.

304. Meredith SJ, Rauer T, Chmielewski TL, et al. Return to sport after anterior cruciate ligament injury: Panther Symposium ACL Injury Return to Sport Consensus Group. *Knee Surg Sports Traumatol Arthrosc* 2020;28(8):2403-14. doi: 10.1007/s00167-020-06009-1 [published Online First: 2020/04/30].

305. Thomeé R, Kaplan Y, Kvist J, et al. Muscle strength and hop performance criteria prior to return to sports after ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2011;19(11):1798-805. doi: 10.1007/s00167-011-1669-8 [published Online First: 2011/09/21].

306. Abrams GD, Harris JD, Gupta AK, et al. Functional Performance Testing After Anterior Cruciate Ligament Reconstruction: A Systematic Review. *Orthop J Sports Med* 2014;2(1):2325967113518305. doi: 10.1177/2325967113518305 [published Online First: 2014/01/01].

307. Muller B, Yabroudi MA, Lynch A, et al. Defining Thresholds for the Patient Acceptable Symptom State for the IKDC Subjective Knee Form and KOOS for Patients Who Underwent ACL Reconstruction. *Am J Sports Med* 2016;44(11):2820-26. doi: 10.1177/0363546516652888 [published Online First: 2016/07/31].

308. Meredith SJ, Rauer T, Chmielewski TL, et al. Return to sport after anterior cruciate ligament injury: Panther Symposium ACL Injury Return to Sport Consensus Group. *Knee Surg Sports Traumatol Arthrosc* 2020 doi: 10.1007/s00167-020-06009-1.

309. Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *Bmj* 2015;351:h5527. doi: 10.1136/bmj.h5527 [published Online First: 2015/10/30].

310. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83. doi: 10.1097/00005650-199206000-00002 [published Online First: 1992/06/11].

311. Ware JEJ. SF-36 Health Survey Update. *Spine* 2000;25(24):3130-39.

312. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. *Br J Psych* 1979;134:382-9. doi: 10.1192/bjp.134.4.382 [published Online First: 1979/04/01].

313. Brewer BW, Van Raalte JL, Linder DE. Athletic identity: Hercules' muscles or Achilles heel? *Int J Sport Psychol* 1993;24(2):237-54. doi: 10.1037/t15488-000.

314. Piussi R, Krupic F, Senorski C, et al. Psychological impairments after ACL injury - Do we know what we are addressing? Experiences from sports physical therapists. *Scand J Med Sci Sports* 2021;31(7):1508-17. doi: 10.1111/sms.13959 [published Online First: 20210406].

315. Çelebi MM, Başkak B, Saka T, et al. Psychiatric and functional evaluation of professional athletes following anterior cruciate ligament reconstruction. *Acta Orthop Traumatol Turc* 2015;49(5):492-6. doi: 10.3944/aott.2015.14.0380 [published Online First: 2015/10/01].

316. Filbay SR, Ackerman IN, Russell TG, Crossley KM. Return to sport matters-longer-term quality of life after ACL reconstruction in people with knee difficulties. *Scand J Med Sci Sports* 2017;27(5):514-24. doi: 10.1111/sms.12698 [published Online First: 2016/05/12].

317. Lepley AS, Pietrosimone B, Cormier ML. Quadriceps Function, Knee Pain, and Self-Reported Outcomes in Patients With Anterior Cruciate Ligament Reconstruction. *J Athl Train* 2018;53(4):337-46. doi: 10.4085/1062-6050-245-16 [published Online First: 2018/04/19].

318. Oztekin HH, Boya H, Ozcan O, et al. Pain and affective distress before and after ACL surgery: A comparison of amateur and professional male soccer players in the early postoperative period. *The Knee* 2008;15(5):368-72. doi: 10.1016/j.knee.2008.05.007.

319. Hemsley K, Sitler M, Moyer R, Oatis C. Neuromuscular and psychological influences on range of motion recovery in anterior cruciate ligament reconstruction patients. *J Electromyogr Kinesiol* 2010;20(4):684-92. doi: 10.1016/j.jelekin.2009.11.006 [published Online First: 2009/12/26].

320. Tripp DA, Stanish WD, Reardon G, et al. Comparing Postoperative Pain Experiences of the Adolescent and Adult Athlete After Anterior Cruciate Ligament Surgery. *J Athl Train* 2003;38(2):154-57. [published Online First: 2003/08/26].

321. Brewer BW, Cornelius AE, Van Raalte JL, et al. Predictors of adherence to home rehabilitation exercises following anterior cruciate ligament reconstruction. *Rehabil Psychol* 2013;58(1):64-72. doi: 10.1037/a0031297 [published Online First: 2013/02/27].

322. Feyzioğlu Ö, Öztürk Ö, Sirmen B, Muğrabi S. Does an Accelerated Program Give Equivalent Results in Both Elite Athletes and Nonathletes? *J Sport Rehabil* 2019;29(5):1. doi: 10.1123/jsr.2018-0346.

323. Mainwaring LM, Hutchison M, Bisschop SM, et al. Emotional response to sport concussion compared to ACL injury. *Brain Inj* 2010;24(4):589-97. doi: 10.3109/02699051003610508.

324. Baranoff J, Hanrahan S, Connor J. The roles of acceptance and catastrophizing in rehabilitation following anterior cruciate ligament reconstruction. *J Sci Med Sport* 2015;18(3):250-54. doi: 10.1016/j.jsams.2014.04.002.

325. Langford JL, Webster KE, Feller JA. A prospective longitudinal study to assess psychological changes following anterior cruciate ligament reconstruction surgery. *Br J Sports Med* 2009;43(5):377-81. doi: 10.1136/bjsm.2007.044818 [published Online First: 2008/11/21].

326. Brewer BW, Raalte JLV, Cornelius AE, et al. Psychological Factors, Rehabilitation Adherence, and Rehabilitation Outcome After Anterior Cruciate Ligament Reconstruction. *Rehabil Psychol* 2000;45(1):20-37. doi: 10.1037/0090-5550.45.1.20.

327. Carson F, Polman R. Experiences of professional rugby union players returning to competition following anterior cruciate ligament reconstruction. *Phys Ther Sport* 2012;13(1):35-40. doi: 10.1016/j.ptsp.2010.10.007.

328. Carson F, Polman RCJ. ACL injury rehabilitation: A psychological case study of a professional rugby union player. *J Clin Sport Psychol* 2008;2(1):71-90. doi: 10.1123/jcsp.2.1.71.

329. Evans J, Mabrouk A, Nielson JL. Anterior Cruciate Ligament Knee Injury. StatPearls. Treasure Island (FL): StatPearls Publishing, Copyright © 2024, StatPearls Publishing LLC. 2024.

330. Clement D, Arvinen-Barrow M, Fetty T. Psychosocial responses during different phases of sport-injury rehabilitation: a qualitative study. *J Athl Train* 2015;50(1):95-104. doi: 10.4085/1062-6050-49.3.52 [published Online First: 20141016].

331. Walker N, Heaney C. Psychological responses to injury: A review and critique of existing models. In: Arvinen-Barrow M, Walker N, eds. The psychology of sport injury and rehabilitation. New York, NY: Routledge/Taylor & Francis Group 2013:23-39, 210 Pages.

332. Kaye JA, Spence D, Alexanders J. Using a biopsychosocial approach within acl rehabilitation: an exploration of student physiotherapists` perceptions and experiences. *Physiother Theory Pract* 2022;38(11):1718-30. doi: 10.1080/09593985.2021.1882019 [published Online First: 20210208].

333. Vella SA, Swann C, Batterham M, et al. An Intervention for Mental Health Literacy and Resilience in Organized Sports. *Med Sci Sports Exerc* 2021;53(1):139-49. doi: 10.1249/mss.0000000000002433.

334. Crichlow JR, Andres LP, Morrison MS, et al. Depression in Orthopaedic Trauma Patients: Prevalence and Severity. *J Bone Jt Surg* 2006;88(9):1927-33. doi: 10.2106/JBJS.D.02604.

335. Morrey MA, Stuart MJ, Smith AM, Wiese-Bjornstal DM. A longitudinal examination of athletes' emotional and cognitive responses to anterior cruciate ligament injury. *Clin J Sport Med* 1999;9(2):63-9. doi: 10.1097/00042752-199904000-00004 [published Online First: 1999/08/12].

336. Lai CCH, Ardern CL, Feller JA, Webster KE. Eighty-three per cent of elite athletes return to preinjury sport after anterior cruciate ligament reconstruction: a systematic review with meta-analysis of return to sport rates, graft rupture rates and performance outcomes. *Br J Sports Med* 2018;52(2):128-38. doi: 10.1136/bjsports-2016-096836.

337. Wong CT, Mok KM, Yung SP. Secondary Anterior Cruciate Ligament Injury Prevention Training in Athletes: What Is the Missing Link? *Int J Environ Res Public Health* 2023;20(6) doi: 10.3390/ijerph20064821 [published Online First: 20230309].

338. Villa FD, Hägglund M, Villa SD, et al. High rate of second ACL injury following ACL reconstruction in male professional footballers: an updated longitudinal analysis from 118 players in the UEFA Elite Club Injury Study. *Br J Sports Med* 2021;55(23):1350-57. doi: 10.1136/bjsports-2020-103555.

339. Svantesson E, Hamrin Senorski E, Webster KE, et al. Clinical Outcomes After Anterior Cruciate Ligament Injury: Panther Symposium ACL Injury Clinical Outcomes Consensus Group. *Orthop J Sports Med* 2020;8(7):2325967120934751. doi: 10.1177/2325967120934751.

340. Capin JJ, Snyder-Mackler L, Risberg MA, Grindem H. Keep calm and carry on testing: a substantive reanalysis and critique of 'what is the evidence for and validity of return-to-sport testing after anterior cruciate ligament reconstruction surgery? A systematic review and meta-analysis'. *Br J Sports Med* 2019;53(23):1444-46. doi: 10.1136/bjsports-2019-100906 [published Online First: 2019/07/11].

341. Losciale JM, Zdeb RM, Ledbetter L, et al. The Association Between Passing Return-to-Sport Criteria and Second Anterior Cruciate Ligament Injury Risk: A Systematic Review With Meta-analysis. *J Orthop Sports Phys Ther* 2019;49(2):43-54. doi: 10.2519/jospt.2019.8190.

342. Paterno MV, Huang B, Thomas S, et al. Clinical Factors That Predict a Second ACL Injury After ACL Reconstruction and Return to Sport: Preliminary Development of a Clinical Decision Algorithm. *Orthop J Sports Med* 2017;5(12):2325967117745279. doi: 10.1177/2325967117745279.

343. Cronström A, Tengman E, Häger CK. Risk Factors for Contra-Lateral Secondary Anterior Cruciate Ligament Injury: A Systematic Review with Meta-Analysis. *Sports Med* 2021;51(7):1419-38. doi: 10.1007/s40279-020-01424-3.

344. Svantesson E, Hamrin Senorski E, Baldari A, et al. Factors associated with additional anterior cruciate ligament reconstruction and register comparison: a systematic review on the Scandinavian knee ligament registers. *Br J Sports Med* 2019;53(7):418-25. doi: 10.1136/bjsports-2017-098192 [published Online First: 20180717].

345. Reijman M, Eggerding V, Es Ev, et al. Early surgical reconstruction versus rehabilitation with elective delayed reconstruction for patients with anterior cruciate ligament rupture: COMPARE randomised controlled trial. *BMJ* 2021;372:n375. doi: 10.1136/bmj.n375.

346. Collins NJ, Prinsen CAC, Christensen R, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS): systematic review and meta-analysis of measurement properties. *Osteoarthr Cartilage* 2016;24(8):1317-29. doi: https://doi.org/10.1016/j.joca.2016.03.010.

347. Marais I, Andrich D. Formalizing dimension and response violations of local independence in the unidimensional Rasch model. *J Appl Meas* 2008;9(3):200-15. PMID: 18753691.

348. Hobart J, Cano S. Improving the evaluation of therapeutic interventions in multiple sclerosis: the role of new psychometric methods. *Health Technol Assess* 2009;13(12):iii, ix-x, 1-177. doi: 10.3310/hta13120.

349. Stemler SE, Naples A. Rasch measurement v. item response theory: Knowing when to cross the line. *Pract Assess Res Eval* 2021;26:11. doi: 10.7275/v2gd-4441.

350. Hobart JC, Cano SJ, Zajicek JP, Thompson AJ. Rating scales as outcome measures for clinical trials in neurology: problems, solutions, and recommendations. *Lancet Neurol* 2007;6(12):1094-105. doi: 10.1016/s1474-4422(07)70290-9.

351. Simonsson R, Piussi R, Högberg J, et al. Rehabilitation and Return to Sport After Anterior Cruciate Ligament Reconstruction. *Clin Sports Med* 2023; doi: 10.1016/j.csm.2023.07.004.

352. Tourville TW, Jarrell KM, Naud S, et al. Relationship between isokinetic strength and tibiofemoral joint space width changes after anterior cruciate ligament reconstruction. *Am J Sports Med* 2014;42(2):302-11. doi: 10.1177/0363546513510672 [published Online First: 20131125].

353. Schmitt LC, Paterno MV, Hewett TE. The impact of quadriceps femoris strength asymmetry on functional performance at return to sport following anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 2012;42(9):750-9. doi: 10.2519/jospt.2012.4194 [published Online First: 20120719].

354. Di Stasi SL, Logerstedt D, Gardinier ES, Snyder-Mackler L. Gait patterns differ between ACL-reconstructed athletes who pass return-to-sport criteria and those who fail. *Am J Sports Med* 2013;41(6):1310-8. doi: 10.1177/0363546513482718 [published Online First: 20130405].

355. Zwolski C, Schmitt LC, Quatman-Yates C, et al. The influence of quadriceps strength asymmetry on patient-reported function at time of return to sport after anterior cruciate ligament reconstruction. *Am J Sports Med* 2015;43(9):2242-9. doi: 10.1177/0363546515591258 [published Online First: 20150716].

356. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb Symmetry Indexes Can Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop Sports Phys Ther* 2017;47(5):334-38. doi: 10.2519/jospt.2017.7285.

357. Straub RK, Powers CM. Is muscular strength a predictor for primary or secondary ACL injury? A scoping review of prospective studies. *Phys Ther Sport* 2023;61:91-101. doi: https://doi.org/10.1016/j.ptsp.2023.03.004.

358. Simonsson R, Magnusson C, Piussi R, et al. To achieve the unachievable—Patients' experiences of opting for delayed anterior cruciate ligament reconstruction after trying rehabilitation alone as primary treatment: A qualitative study. *Scand J Med Sci Sports* 2024;34(2):e14569. doi: https://doi.org/10.1111/sms.14569.

359. Walker A, Hing W, Gough S, Lorimer A. 'Such a massive part of rehab is between the ears'; barriers to and facilitators of anterior cruciate ligament reconstruction rehabilitation: a qualitative focus group analysis. *BMC Sports Sci Med Rehabil* 2022;14(1):106. doi: 10.1186/s13102-022-00499-x.

360. Allen MM, Pareek A, Krych AJ, et al. Are Female Soccer Players at an Increased Risk of Second Anterior Cruciate Ligament Injury Compared With Their Athletic Peers? *Am J Sports Med* 2016;44(10):2492-98. doi: 10.1177/0363546516648439 [published Online First: 20160603].

361. Ageberg E, Forssblad M, Herbertsson P, Roos EM. Sex differences in patient-reported outcomes after anterior cruciate ligament reconstruction: data from the Swedish knee ligament register. *Am J Sports Med* 2010;38(7):1334-42. doi: 10.1177/0363546510361218 [published Online First: 20100421].

362. Branche K, Bradsell HL, Lencioni A, Frank RM. Sex-Based Differences in Adult ACL Reconstruction Outcomes. *Curr Rev Musculoskelet Med* 2022;15(6):645-50. doi: 10.1007/s12178-022-09801-3 [published Online First: 20221015].