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# Meniscus Repair

Long-term gains with short-term challenges?

FREDRIK BORIC-PERSSON

DEPARTMENT OF ORTHOPAEDICS | FACULTY OF MEDICINE | LUND UNIVERSITY



This book is about the menisci, the crescent shape fibrocartilage structures that are such an important part of the knee. We have progressed from open removal to arthroscopic repair when they are injured. Still, meniscus healing remains troublesome. This thesis investigates the consequences for patients following partial meniscectomy and meniscus repair in both the short- and the long-term.

The conclusions in this book will hopefully be another piece of the puzzle.



**FREDRIK BORIC-PERSSON** was born in 1978 and received his medical degree at Lund University in 2006. Before the end of his residency in orthopaedic surgery at the Department of Orthopaedics at Skåne University Hospital, the work on this doctoral thesis was commenced, under the supervision of Professor Martin Englund.

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# Meniscus Repair

Long-term gains with short-term challenges?

Fredrik Boric-Persson



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Meniscus tears are common after knee injuries. The current treatment in patients under the age of 40 is typically arthroscopic partial meniscectomy (APM) or arthroscopic meniscus repair. Meniscus tears and surgeries are associated with an accelerated progression to knee osteoarthritis (OA) and disability.

PAPER I is an observational cohort study, utilising the Skåne Healthcare Register (SHR) to identify 2,487 surgically treated patients with a diagnose of a traumatic meniscus tear between the ages of 16 and 45 years. Of these 9.2% had meniscus repair. The aim was to compare the consultation rate for knee OA observed for up to 18 years postoperatively. The absolute risk of having consulted for knee OA during that time was 10.0% after meniscus repair, 17% after APM and 2.3% in the general population.

PAPER II is an observational cohort study in which we cross-linked data from SHR, LISA and the Swedish social security agency (SSIA) during 2004–2014. The aim was to compare occurrence and duration of sick leave in persons aged 19–49 years after APM and meniscus repair. We found that after meniscus repair, individuals have more frequent and 37% longer periods of sick leave than after APM, when measured up to 2 years after surgery.

PAPER III is an observational cohort study using patient surgical records for all APM and meniscus repair surgeries in southern Skåne 2010–2015. The aim was to examine and compare reoperation rates and complications during 5–10 years of follow-up in 2098 patients and in a subgroup aged 15–40 years. We found that meniscus repair had a 4-fold increase in reoperations compared to APM, and 2.1% had medical complications.

In conclusion,

meniscus repair is associated with a lower risk of consulting for knee OA than APM during 18 years postoperatively. Meniscus repair is associated with both more prevalent and longer sick leave postoperatively than APM. The rate of reoperation is higher after meniscus repair than after APM, and more than 1/3 of all repaired menisci have a reoperation on the same meniscus within 5 years. Finally, the rate of other complications was found to be low after arthroscopic knee surgery in Skåne.

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# Meniscus Repair

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Fredrik Boric-Persson



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**MADE IN SWEDEN** 

*to my loving wife Tatjana*

*“No! Try not. Do or do not. There is no try.”*

Yoda, The Empire Strikes Back



# Table of Contents

List of Papers.....	9
Thesis at a glance .....	11
Abstract .....	13
Populärvetenskaplig sammanfattning.....	15
Index of Figures and Tables .....	17
Abbreviations .....	19
Definitions.....	21
<b>Introduction .....</b>	<b>23</b>
Preface.....	23
Anatomy .....	23
Pathology.....	30
Epidemiology .....	38
Meniscus surgery.....	41
Repairing the Meniscus.....	44
Previous research on meniscus repair and APM .....	50
<b>Aims of the thesis .....</b>	<b>53</b>
<b>Patients and methods .....</b>	<b>55</b>
Pros & cons of register-based research .....	55
Registers and data sources of this thesis .....	57
Surgical methods .....	59
General study overview.....	60
Ethics & Funding .....	70
<b>Results.....</b>	<b>71</b>
Paper I: The risk of posttraumatic OA .....	71
Paper II: Sick leave .....	73
Paper III: Reoperations and complications .....	74

<b>General Discussion .....</b>	<b>79</b>
What is <i>successful</i> meniscus surgery?.....	80
Can you really compare APM and meniscus repair? .....	81
New injuries or late consequences?.....	82
Surgical or non-surgical treatment? .....	83
Who gets surgery and why? .....	84
The cost of (not) doing surgery .....	85
Trends of sick leave after meniscus surgery .....	86
Age and time in meniscus repair .....	89
Are all meniscus tears different? .....	91
Meniscus repair healing .....	96
Measuring complications .....	97
Gender differences .....	99
Meniscus surgery and the ACL .....	101
Limitations .....	103
<b>Conclusions .....</b>	<b>105</b>
<b>Clinical implications.....</b>	<b>107</b>
<b>Future perspectives .....</b>	<b>109</b>
<b>Acknowledgements .....</b>	<b>111</b>
<b>References .....</b>	<b>113</b>
<b>Appendix .....</b>	<b>137</b>



# List of Papers

This thesis is based on the following papers:

- I        **F. Persson**, A. Turkiewicz, D. Bergkvist, P. Neuman, M. Englund; The risk of symptomatic knee osteoarthritis after arthroscopic meniscus repair vs partial meniscectomy vs the general population. *Osteoarthritis Cartilage* 2018 Feb;26(2):195-201. Epub 2017 Nov 14.
- II.      **F. Boric-Persson**, A. Turkiewicz, P. Neuman, M. Englund, Sick leave after arthroscopic meniscus repair vs. arthroscopic partial meniscectomy. *Osteoarthr Cartil Open* 2023 Jan 20;5(1):100340. eCollection 2023 Mar.
- III.     **F. Boric-Persson**, A. Turkiewicz, M. Englund, P. Neuman; Reoperations and complications after meniscal repair or partial meniscectomy with up to 10 years of follow-up. (*Manuscript submitted*)



## Thesis at a glance

Paper	I	II	III
<b>Question</b>	What is the difference in consultation rate for OA after meniscus repair vs APM compared to the rest of the population?	What is the difference in sick leave after meniscus repair vs APM compared to the rest of the population?	What is the difference in risk of reoperation and complications after meniscus repair vs APM?
<b>Study period</b>	1998–2011	2004–2015	2010–2015
<b>Design</b>	A cohort study with data from SHR and RTB in the Skåne region over a range of 5–18 years postoperatively. Follow-up until 2016.	A cohort study with linked data from SHR, SSIA, LISA and RTB registers. Followed 1 year before and 2 years after surgery.	A cohort study with medical records and OrtReg data from all APM and meniscus repair surgeries. Follow-up until 2020.
<b>Patients</b>	229 patients with MR surgery and 2258 with APM surgery and a traumatic meniscus tear. 643480 persons in the reference population. Age: 16–45 years.	All employed inhabitants in Skåne, 192 meniscus repairs and 2481 APMs, with 376345 persons in the reference population. Age: 19–49 years.	All meniscus surgeries at three hospitals between 2010–2015. 395 meniscus repairs and 1703 APM patients. Age: above 15 years.
<b>Answer</b>	Patients after meniscus repair develop more knee OA than the standard population, but less OA than those having APM surgery.	After meniscus repair surgery, more patients are on sick leave and for a longer time period than after APM.	Meniscus surgery in Skåne is safe, but meniscus repair patients have a much higher risk of needing a reoperation than patients with an APM.
<b>Clinical perspective</b>	Increased risk of OA should be considered when deciding about meniscus surgery.	An increased rate of sick leave should be known when choosing meniscus repair.	Increased risk of reoperations should be known when deciding to do a meniscus repair.

**Thesis at a glance**, OA=Osteoarthritis, APM=Arthroscopic Partial Meniscectomy



## Abstract

Meniscus tears are common after knee injuries. The current treatment in patients under the age of 40 is typically arthroscopic partial meniscectomy (APM) or arthroscopic meniscus repair. Meniscus tears and surgeries are associated with an accelerated progression to knee osteoarthritis (OA) and disability.

PAPER I is an observational cohort study, utilising the Skåne Healthcare Register (SHR) to identify 2,487 surgically treated patients with a diagnose of a traumatic meniscus tear between the ages of 16 and 45 years. Of these 9.2% had meniscus repair. The aim was to compare the consultation rate for knee OA observed for up to 18 years postoperatively. The absolute risk of having consulted for knee OA during that time was 10.0% after meniscus repair, 17% after APM and 2.3% in the general population.

PAPER II is an observational cohort study in which we cross-linked data from SHR, LISA and the Swedish social security agency (SSIA) during 2004–2014. The aim was to compare occurrence and duration of sick leave in persons aged 19–49 years after APM and meniscus repair. We found that after meniscus repair, individuals have more frequent and 37% longer periods of sick leave than after APM, when measured up to 2 years after surgery.

PAPER III is an observational cohort study using patient surgical records for all APM and meniscus repair surgeries in southern Skåne 2010–2015. The aim was to examine and compare reoperation rates and complications during 5–10 years of follow-up in 2098 patients and in a subgroup aged 15–40 years. We found that meniscus repair had a 4-fold increase in reoperations compared to APM, and 2.1% had medical complications.

In conclusion, meniscus repair is associated with a lower risk of consulting for knee OA than APM during 18 years postoperatively. Meniscus repair is associated with both more prevalent and longer sick leave postoperatively than APM. The rate of reoperation is higher after meniscus repair than after APM, and more than 1/3 of all repaired menisci have a reoperation on the same meniscus within 5 years. Finally, the rate of other complications was found to be low after arthroscopic knee surgery in Skåne.





## Populärvetenskaplig sammanfattning

Idrottsskador eller olyckor kan ibland leda till skador i knät på det som kallas meniskerna. Även åldrande och artros leder ofta till degenerativa förändringar och sprickor i meniskerna.

Meniskerna är två halvmåneformade broskskivor som sitter i knät mellan lårbenet och skenbenet, och som har flera olika funktioner när vi rör oss. Ofta kan skador på meniskerna i knät leda till smärta, svullnad och nedsatt knärlighet. När en person får denna typ av besvär är det vanligt med en operation för att minska symtom och återställa knäfunktionen.

Här finns tre olika huvudgrupper av behandlingsmetoder att välja mellan; enbart fysioterapi; operera menisken och ta bort delar som är trasiga; eller att försöka laga eller ersätta den trasiga biten vid operationen. Meniskoperationer sker nuförtiden i princip alltid genom så kallad titthålskirurgi. Dessa operationer har blivit bland de vanligaste knäoperationerna i världen och det utförs miljontals operationer årligen globalt. En menisk lagas vanligen genom att sy ihop den med någon typ av tråd. Därefter får knät inte utsättas för olämpliga påfrestningar under en tid så att menisken ska kunna läka.

Förutom att meniskskador kan vara smärtsamma och besvärliga på kort sikt, har tidigare studier visat att avsaknad av fungerande menisker leder till ökat slitage på brosket i knäleden. Ledbrosket bekläder ytorna i alla kroppens leder och gör att dessa kan röra sig lätt och smärtfritt. En gradvis förslitning och försämring av ledbrosket ingår i det vi kallar artros. Med andra ord ökar meniskskador risken för artros – en sjukdom som idag saknar en bra botande behandling.

I den första artikeln, undersökte jag risken för att utveckla artros i knät efter två typer av meniskkirurgi – en studie som byggde på ett av de största studiematerialen inom området. Även den allmänna risken för knäartros bland Skånes befolkning undersöktes. Vi fann att risken att utveckla artros halveras om menisken repareras vid operationen, jämfört med om delar av den tas bort i stället. Det visade sig också att den som opererat menisken på något sätt, löper cirka fyra gånger större risk att utveckla artros, jämfört med en person som ej genomgått en meniskoperation. Det ska påpekas att många meniskskador inte går att laga, på grund av dålig menisk kvalitet, oavsett hur erfaren kirurgen är.

Efter en operation i knät är det många som har smärtor och nedsatt funktion, vilket leder till att de inte kan återgå direkt till arbetet. I den andra artikeln tittade jag på hur sjukskrivningens längd ser ut efter reparation av menisken jämfört med att delar av menisken tagits bort. Jag jämförde också detta med hur mycket alla individer utan någon meniskdiagnos i genomsnitt är sjukskrivna. Till min hjälp hade jag en databas från Försäkringskassan med alla sjukskrivna i Skåne som erhållit ersättning. Jag kunde visa att individer som fått menisken reparerad var sjukskrivna i betydligt

större omfattning efter operationen än de personer som fått delar av menisken avlägsnad. Vidare såg jag att båda grupper var sjukskrivna mer än dubbelt så mycket som genomsnittsbefolkningen i Skåne under två år efter operationen.

Slutligen undersökte jag själva operationerna lite närmare och tittade dels på risken att patienter antingen drabbas av en komplikation efter själva knäkirurgin, dels på hur många som behövde ytterligare operationer i menisken eller i knät. Jag läste igenom alla journaler hos 2098 patienter som opererats i södra Skåne under 2010–2015 och följde hur det gick för dem till och med 2020. Min studie visade att få patienter drabbades av andra komplikationer, men att en stor del blev opererade fler än en gång. När jag jämförde patienter i åldersintervallet 15–40 år såg jag att patienter, där man försökt reparera menisken, drabbades av fyra gånger så många reoperationer.

Detta leder oss då till den kanske självklara slutsatsen: det bästa för knät är att inte skada eller operera det alls. Måste menisken trots allt opereras är det bättre på lång sikt att försöka laga menisken vid en operation, även om den typen av kirurgi ofta innebär avsevärt längre sjukskrivning och större andel sjukskrivna patienter postoperativt. Att ta bort den skadade delen av menisken, leder sannolikt till mer artros när patienten blir äldre. Slutligen har jag visat att reparation av menisken är förknippat med en högre risk för reoperationer under perioden 5–10 år efter primäroperationen jämfört med att ta bort den skadade meniskdelen. Risken att drabbas av olika medicinska komplikationer i samband med kirurgin är dock låg i både grupper.

# Index of Figures and Tables

Figure 1. Anatomy of the menisci and important adjacent ligaments. (Anneli Persson ©2025)	26
Figure 2. Schematic illustration of the meniscus vertex blood supply. (Anneli Persson ©2025)	27
Figure 3. The different layers of joint cartilage. (Anneli Persson ©2025)	29
Figure 4. New classification for the location of meniscus tears, (Beaufils modification of Cooper). (Drawing by Andrea Boric-Persson ©2025)	30
Figure 5. The different types of meniscus tears. (Anneli Persson ©2025)	31
Figure 6. X-ray image showing a knee with osteoarthritis KL grade 4, (Radiopaedia©2024)	34
Figure 7. All meniscus surgeries in Skåne region, OrtReg statistics data (includes reoperations).	40
Figure 8. All meniscus surgeries in Skåne region, OrtReg statistics data (includes reoperations).	40
Figure 9. Drawing of a modern setup for knee arthroscopic surgery. (Tatjana Boric-Persson ©2025)	42
Figure 10. Schematic drawing of, from left to right: <i>Outside-in</i> meniscus suture, <i>Inside-out</i> meniscus suture and the <i>all-inside</i> meniscus anchor sutures. (Anneli Persson ©2025)	47
Figure 11. Summarized flowchart of all 3 studies. (© Fredrik Boric-Persson)	60
Figure 12. Overview of how the included cohorts of the thesis are related to each other in size and time.	61
Figure 13. Flowchart of study I. (© Fredrik Boric-Persson)	63
Figure 14. Flowchart of study inclusion and exclusion process in paper II. (© Fredrik Boric-Persson)	64
Figure 15. Factors that might influence the outcome, Paper II. (© Fredrik Boric-Persson)	65
Figure 16. Flowchart of study inclusion and exclusion process in paper III. (© Fredrik Boric-Persson)	66
Figure 17. Possible confounders that influence the outcome, Paper III. (© Fredrik Boric-Persson)	67
Figure 18. Survival estimates for doctor-diagnosed knee OA among persons aged 16-45 years in patients after APM, meniscal repair or in the general population. 95% CI indicated by shaded areas.	72
Figure 19. Percentage of patients with only meniscus surgery (without any ACL-surgery) on sick leave per week from 1 year before to 2 years after surgery.	74
Figure 20. Same meniscus reoperation 15–40 years. The (adjusted) proportion reoperated in each group and their difference over time.	76
Figure 21. Sick leave patterns around meniscus surgery, number of patients, cohort from Paper II.	86
Figure 22. Sick leave pattern associated with meniscus surgery, percentage of patients on sick leave.	87
Figure 23. Mean number of sick leave days in the whole working population in Skåne, age 16–64 years Yellow denotes women, red denotes men and green the total. (Försäkringskassan public records).	88
Figure 24. Patterns of meniscus tear morphology in patients age 15-40 years.	92
Figure 25. Patterns of meniscus tear morphology in patients age 15–99 years.	92

Figure 26. Meniscus tear type proportions in stable and unstable knees in paper III, all ages.....	93
Figure 27. Meniscus tear type proportions in stable and unstable knees in the subgroup 15–40 years in Paper III.....	93
Figure 28. Meniscus tear distribution and size among all patients aged 15–40 years, cohort of Paper III. ....	95
Figure 29. Meniscus tear types by gender category among the patients in Paper III.....	100
Thesis at a glance, .....	11
Table 1. Kellgren-Lawrence OA radiographic grading system.....	35
Table 2. ICRS grading system for knee joint cartilage injury during arthroscopic surgery.....	35
Table 3. Meta-analysis of meniscus repair outcomes.....	52
Table 4. Meta-analysis comparing APM and meniscus repair.....	52
Table 5. Occurrence of doctor-diagnosed knee OA during follow-up.....	72
Table 6. Adjusted risk difference and risk ratio of being on sick leave after meniscus repair versus APM and ratio of mean days on sick leave for persons with sick leave.....	73
Table 7. Reoperations and complications .....	75
Table 8. Stated indications for meniscus surgery, Paper III.....	85
Table 9. (Appendix) List of Surgical NGD-codes in meniscus surgery (NOMESCO) .....	137
Table 10. (Appendix) List of ICD-10 codes for meniscus pathology .....	138
Table 11. (Appendix) List of ICD-10 codes for knee injury .....	139
Table 12. (Appendix) List of ICD-10 codes for knee OA.....	139

## Abbreviations

ACL	Anterior Cruciate Ligament
ACLR	Anterior Cruciate Ligament Reconstruction
APM	Arthroscopic Partial Meniscectomy
BMI	Body Mass Index
CI	Confidence Interval
ESSKA	European Society of Sports Traumatology, Knee Surgery and Arthroscopy
HR	Hazard Ratio
ICD10	International Classification of Diseases, version 10
ICRS	International Cartilage Regeneration & Joint preservation Society
KOOS	Knee injury and Osteoarthritis Outcome Scale
LCL	Lateral Collateral Ligament
LISA	The longitudinal database (LISA) of statistics Sweden
MCL	Medial Collateral Ligament
MR	Meniscus Repair
MRI	Magnetic Resonance Imaging
NOMESCO	Nordic Medico-Statistical Committee
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
PCL	Posterior Cruciate Ligament
PROM	Patient Reported Outcome Measure
RCT	Randomized Controlled Trial
RTB	The Population Register
SHR	Skåne Healthcare Register
SSIA	Swedish Social Insurance Agency
TKA	Total Knee Arthroplasty
VTE	Venous Thromboembolism



## Definitions

ACL reconstruction	Surgical repair of the ACL by means of replacing it with a graft, usually a muscle tendon from the same patient.
Bias by indication	Conscious or unconscious bias in a study by the way patients are selected for different treatments, thereby making the analysed sample non-random, and thus the indication might affect the outcome.
BMI	The body mass divided by body length squared. Normal range values are between 20 and 25.
Confidence interval	A confidence interval describes a range of plausible values in which the real effect lies, with a specified probability.
Confounder	A variable that influences both the exposure variable and the outcome variable.
Contralateral	On the opposite side of the body.
Ipsilateral	On the same side of the body.
Instability	Patients subjective experience of the (knee)joint giving way.
Knee laxity	Objective finding of knee joint instability during clinical examination.
Meniscus lesion	<i>“degenerative meniscus tear marked by slow progression of tissue degeneration without previous acute trauma”</i> [ESSKA].
Meniscus tear	<i>“meniscus injury associated with a sufficient knee injury and a sudden onset of knee pain”</i> [ESSKA].
Meta-analysis	The synthesis of quantitative data from multiple independent studies to address a research question. It involves calculating a combined effect size across all included studies.
Prospective cohort study	A cohort observed over a period of time, to study a predefined exposure and outcome.
Randomized Controlled Trial	A study where patients are randomly assigned to the treatments investigated, to avoid confounding. Considered the <i>gold standard</i> in medical research.
Regression analysis	A statistical method by which one assess the degree of association between two variables for one or multiple independent variables.





# Introduction

## Preface

My ambition with this thesis was to present a comprehensive picture of the results and consequences for patients following meniscus surgery. How does the choice of surgical method influence patient outcomes?

As a part-time researcher, managing the equilibrium between clinical responsibilities, family commitments, and research endeavours can occasionally prove overwhelming. There have been numerous challenges encountered during the work, including slow processes for obtaining permits and registry data, as well as the temporary suspension of my research efforts due to the COVID-19 pandemic. Over the course of my years as a PhD student, significant advancements have been made in the field, with numerous studies being published.

Along the way I have developed a deepened understanding of the valuable resource our linkable Swedish registers represent, as well as the inherent limitations of register-based research. Ideas and plans have emerged for further meniscus projects that proved to be beyond the scope of this thesis.

## Anatomy

### **The knee joint**

The knee joint is simplistically described a hinge-joint, connecting the femur and the thigh with the tibia and the lower leg. Skeletally consisting of the medial and lateral distal femur condyles, the medial and lateral proximal tibia condyles and the sesamoid patella bone.<sup>[1]</sup> The condyles are all surfaced by hyaline cartilage, forming three compartments: the medial compartment, the lateral compartment and the patello-femoral compartment. Attached to the tibia and to the joint capsule, are the medial and the lateral meniscus. Together with the tibia, the two menisci form two concave surfaces, for the convex femur condyles to articulate against. The joint is surrounded by a joint capsule and contains several ligaments that stabilize the joint while allowing motion.<sup>[2]</sup>

The knee is primarily stabilized by the anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL) counteracting antero-posterior translation.<sup>[3]</sup> These run in a X-shape, hence their names, in the centre of the knee joint connecting the femur with the tibia. The ACL is subdivided into two functional bundles, the anteromedial being more important in knee flexion and the posteromedial stabilizing more in extension.<sup>[3,4]</sup> The ACL also contributes to varus, valgus and rotational stability of the knee. Apart from the collagen fibres supplying its functional strength, the ACL also contains blood vessels and several types of nerve structures providing proprioception as well as containing cells with progenitor potential.<sup>[5,6]</sup> The menisci also contribute to counteract any antero-posterior translation.<sup>[7]</sup> On the sides of the knee joint, supplying varus–valgus stability, are the medial collateral ligament (MCL) with a longer outer portion and a shorter inner portion that also is attached to the medial meniscus. Located on the outside of the knee is the lateral collateral ligament (LCL), attaching all the way from the femur to the head of the fibula.

And finally, on the posterior side of the joint lies the popliteus tendon, the arcuate ligament and the oblique popliteal ligament, contributing with posterior stability.<sup>[1]</sup> Throughout knee motion, the sesamoid patella traverses along the femur trochlea groove, stabilized by the u-shaped surface and the medial patellofemoral ligament (MPFL).

The knee joint blood supply mainly stems from branches of the femoral artery, in particular the descending genicular artery and the popliteal artery with its branches posteriorly. The enervation is supplied by branches from both the femoral nerve, the sciatic nerve and the obturator nerve.<sup>[1,8]</sup> The knee joint-capsule is lined with a synovial membrane, filled with cells that produce the synovial fluid that fills the joint.<sup>[2]</sup> Synovial fluid is clear, pale yellow and is produced as an ultrafiltrate from blood plasma and consists mainly of water, salts, hyaluronan, lubricin, proteinases, collagenases, and prostaglandins. It lubricates the joint surfaces and provides nutrients to the avascular cartilage and the avascular portions of the menisci.<sup>[9,10]</sup> Its presence increases the ability for the cartilage to resist wear and fatigue under the cyclic compressive loading the knee joint is subjected to during locomotion.<sup>[11]</sup>

### *Joint biomechanics*

The knee joint allows complex movement and high force loading activities in humans like walking, running and jumping. The quadriceps muscle with its 4 muscle bellies, extends the knee via the quadriceps tendon. Through the patella retinaculum and the patella, it connects to the patellar tendon and then finally to the lower leg as it inserts on the tibial tuberosity.<sup>[1]</sup> The patella acts as a lever to increase the force of the knee extensor mechanism and to reduce its sliding friction.

Along with knee flexion, there is also varying degrees of tibia (lower leg) rotation performed to position the ankle and the foot into the correct position. Normal knee

range of motion (ROM) ranges from 0 to 135 (120–150) degrees with a rotation of 60 (50–80) degrees.<sup>[12]</sup> There is also the phenomenon of *rollback*, the translational shifting of the points of contact between the femur and the tibia during ROM, owing to the oval shapes of the femur condyles.<sup>[13,14]</sup>

The hamstring muscles (musculus semitendinosus, semimembranosus and biceps femoris) on the posterior side of the thigh and knee, supplies knee flexion motion. They also help with stabilizing the knee, preventing hyperextension and counteracts knee joint rotation. Then there is also the popliteus muscle, visible from inside the knee joint, assisting in the knee inward rotation during flexion.<sup>[1,2]</sup>

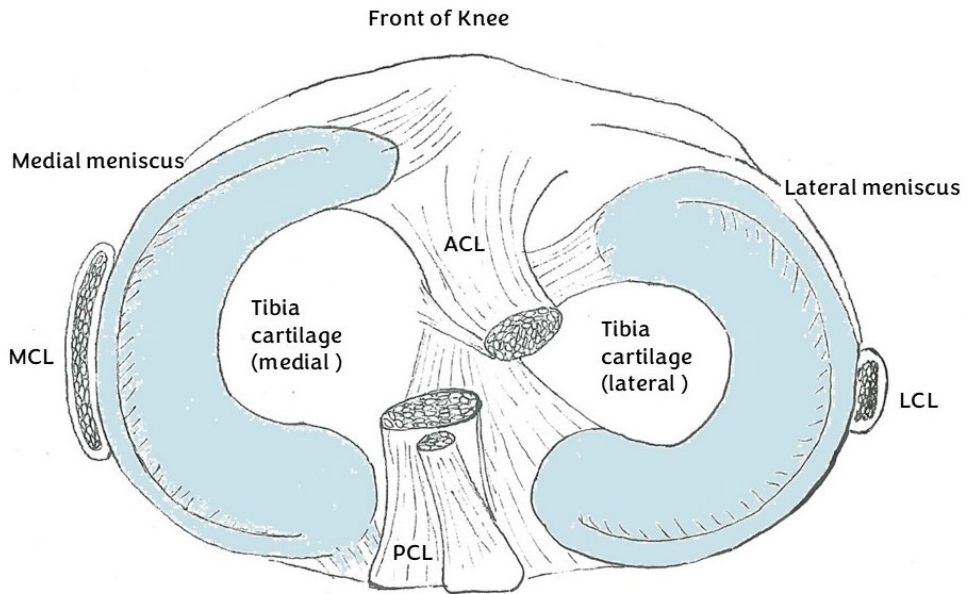
In all, the knee both enables sagittal plane extension–flexion, translation and rotation, as well as small amounts of movement in varus/valgus direction but only when in a position of knee flexion.

## **Anatomy of the meniscus**

The two menisci in a knee joint are wedge shaped semilunar cartilage structures, located between the femur and the tibia.<sup>[1]</sup> Menisci are found in all mammal knee joints but vary considerably in their anatomic shape.<sup>[15]</sup> In humans, they measure about 35 millimetres across and attaches to the joint capsule on most of their periphery.<sup>[16]</sup> The outer rim has a mean length of 110 millimetres including insertions (called “roots”) at both ends, that attaches to the tibia intercondylar fossa, near the insertions of the anterior and posterior cruciate ligaments (**figure 1**).<sup>[15]</sup>

Circumferentially the medial meniscus is connected to the capsule and the MCL, thereby providing a connection also to the femur. The lateral meniscus is more loosely connected to the capsule and subsequently more mobile. Both menisci further connect with each other anteriorly by the transverse ligament.<sup>[17]</sup> Posteriorly the lateral meniscus is attached to the femur through the ligaments of Humphrey and Wrisberg, though there is large variability in the appearance of these structures.<sup>[16,18]</sup>

The medial meniscus is slightly larger and covers nearly 60% of the medial tibia cartilage surface, while the lateral meniscus covers about 80% of the smaller lateral surface.<sup>[15,16,19]</sup>

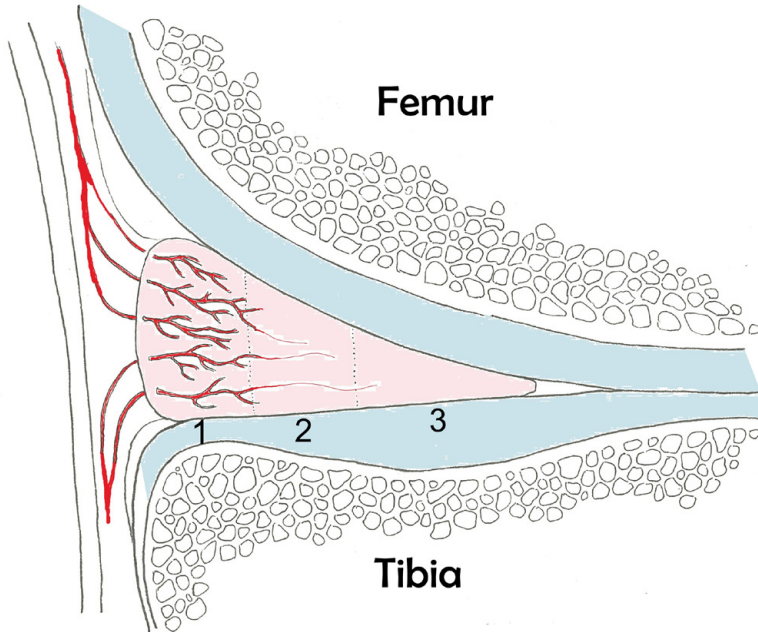


**Figure1.** Anatomy of the menisci and important adjacent ligaments. (©Anneli Persson 2025)

The nerve supply to the menisci stems from the tibial nerve and penetrates into the meniscus through its capsular insertion. Following the vascular distribution, free nerve endings are thought to provide pain sensation in the outer and middle portions of the meniscus leaves.<sup>[8,20,21]</sup> Mechanoreceptors have been found in the meniscus and are believed to provide both a sense of joint movement and one of joint position. They have been detected mainly in the outer, but also in the middle, meniscus zone.<sup>[21,22]</sup>

### *Blood supply*

The blood supply to the meniscus originates from the lateral and medial geniculate arteries and is then routed through a plexus of smaller vessels in the capsule and enters the meniscus radially from its periphery (**figure 2**). The peripheral zone (1) is well vascularized, and it was previously thought that the inner two zones were nearly avascular, leading to less potential for healing in this area. Newer studies have now in part contradicted this, indicating that there are vessels all the way to the inner zone (3), and that there is significant heterogeneity in meniscal blood supply distribution, with more vessels to the second and third zone in the posterior and anterior horn, and much less so in the vertex(central part) of the meniscus.<sup>[23]</sup> The avascular parts of the meniscus receives nutrition from the synovial fluid in the knee joint.



**Figure 2.** Schematic illustration of the meniscus vertex blood supply. (©Anneli Persson 2025)

### *Meniscus composition*

The body of a healthy meniscus contains 72% water, 22% collagen I, II, III, IV, V and VI, 0,8% glycosaminoglycans (GAGs) and small amounts of cells, proteins and other organic compounds.<sup>[16]</sup> The collagen, of which more than 90% is collagen I, is organised in a dense structure of fibres that run mainly circumferential, to resist “hoop stress”, with smaller amounts of radial and vertical fibres to resist splitting. Interposed in this web are isolated fibrocyte- and chondrocyte-like cells responsible for maintaining the structure and composition of the extracellular matrix and the healing properties of the meniscus.<sup>[24]</sup>

### *Meniscus biomechanics*

The two semi-lunar wedges of the menisci stabilize the knee joint in all directions by forming two bowls that enhances joint congruity between the rounded femur and the partially convex tibia. Especially the medial meniscus contributes to preventing antero-posterior translation in the knee, which is especially evident in the absence of an intact ACL.<sup>[7,25–27]</sup> It is more firmly attached to the tibia, and thereby more susceptible to injury, while the lateral meniscus is more mobile.

Between 40–60% of the knee joint load is transmitted to the meniscus when the knee is in extension, and the rate increases with increased flexion.<sup>[28]</sup> The load is

distributed with about 70% of it passing through the medial compartment and 30% through the lateral compartment of the knee.<sup>[29]</sup> When the meniscus is compressed, because of its wedge shape, axial loads are converted into tensile strain as the meniscus is pressed outwards. Outward displacement of the meniscus is counteracted by the important circumferential collagen fibres, resulting in what's called "hoop stress".<sup>[15,30,31]</sup>

Human bipedal locomotion induces high impact forces on the knee joint cartilage and meniscus. Compromise of meniscus form and function, such as a tear or surgical removal, reduces the area of contact between the femoral condyles and the tibia, leading to increased peak contact stress.<sup>[32,33]</sup> This dramatic increase in load per square surface area is considered to accelerate the wear and degeneration of the joint cartilage.<sup>[26,28,34,35]</sup> The ability to absorb shock is a function of the meniscus viscoelastic properties, primarily the water content and the water being pressed out of the tissue when loaded. Generally considered to have an important role in shock absorption, this is now being questioned, as the meniscus material properties to absorb shock seems not as good as previously thought.<sup>[30,36–38]</sup>

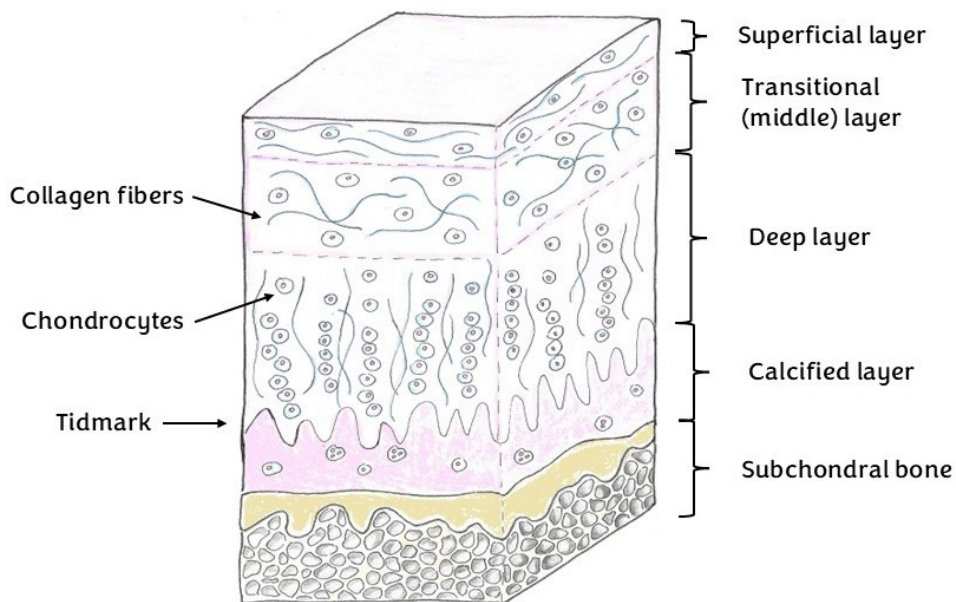
The normal meniscus changes throughout the life span of a human. During embryonic development the whole meniscus is vascularized.<sup>[16,19]</sup> During childhood the vascularization gradually diminishes. The slick and translucent meniscal surface turns opaque with age and changes toward a darker, yellow colour, with a rougher surface. It becomes less elastic and gain an increased amount of fibrous tissue components along with decreases in its collagen content.<sup>[39]</sup>

## Cartilage

Knee joint hyaline cartilage is structured in layers, contributing to its anisotropic properties. The distribution of cells and the collagen fibre distribution and direction varies with depth (**figure 3**).<sup>[40]</sup> Healthy cartilage is a tissue without vascularity or neural structures, which is rather unique in the body. The environment is hypoxic, and cells get their nutrients via diffusion from synovial fluid.

Cartilage contains primarily water, collagen (type II, VI, IX, X and XI), large hydrophilic molecules and isolated chondrocytes.<sup>[2,41]</sup> Structured with a fibrillar collagen network, mainly composed of collagen type II and proteoglycans intermingled with aggrecan providing compressive strength. Proteoglycans bind with hyaluronan, collagen and water and forms a hydrated matrix of cartilage, giving the tissue also tensile strength.<sup>[41,42]</sup>

Its function is to dampen shocks, transfer loads from the subchondral surfaces of the femur and tibia through the joint, and act as a gliding surface.<sup>[2]</sup> Studies indicate that the viscoelastic knee cartilage deforms 2–3% during everyday walking, and an additionally 2–3% with heavy loading.<sup>[43]</sup> The friction of naïve cartilage is extremely low, surpassing any humanly engineered construct.<sup>[44]</sup>



**Figure 3.** The different layers of joint cartilage. (©Anneli Persson 2025)

The functional and structural properties of cartilage are maintained by the chondrocytes, as they regulate the composition of the extracellular matrix by producing new collagens, proteoglycans and other molecules, as well as inducing proteolysis in existing structures allowing for remodelling.<sup>[42]</sup> Production in the cells respond to biochemical and biomechanical stimulus, attempting to preserve the homeostasis of the cartilage tissue.<sup>[45,46]</sup>

The articulating surfaces of the distal femur, the underside of the patella and the tibial plateau, are lined with hyaline cartilage, even on the surfaces underlying the menisci.<sup>[1]</sup> It has a thickness of only between 2–3mm on the load bearing surfaces of the femur and the tibia, while the undersurface of the patella has the thickest cartilage in the entire body, of up to 6–7mm in the central part.<sup>[40,47,48]</sup>

### *Cartilage ageing*

With knee ageing, the cartilage gradually experiences a decrease in its water content, chondrocyte numbers and both a declining amount as well as a structural degradation of proteoglycans. The result is a more brittle and less elastic tissue more susceptible to wear and injury.<sup>[41]</sup>

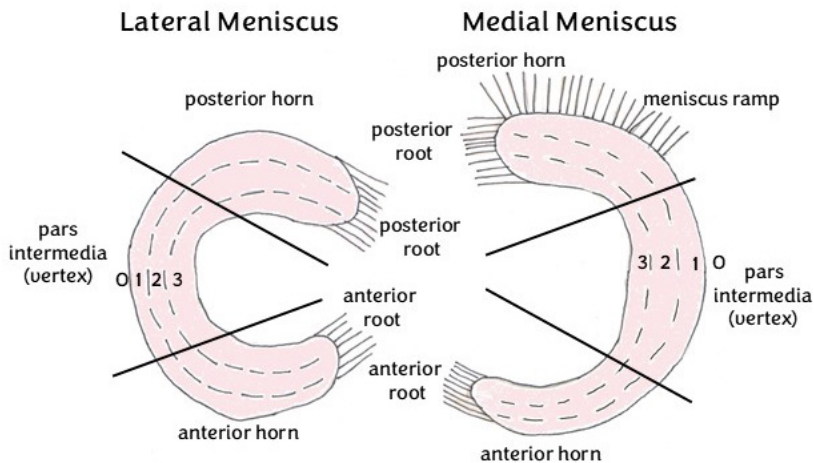


# Pathology

## Meniscal tears

There are several ways to classify a tear in the meniscus. There is the location, where it is divided into tears affecting the medial meniscus or the lateral meniscus. Further it is subdivided according to which portion of the meniscus is affected, either the posterior part, called the *posterior horn* where most tears are located, the middle portion, also referred to as the *vertex*, or the *anterior horn*.<sup>[49,50]</sup>

Further, it is classified as to whether it is engaging the outer zone close to the knee capsule (the red zone), the middle zone (the red-white zone) or the inner zone (the white zone).<sup>[51,52]</sup>

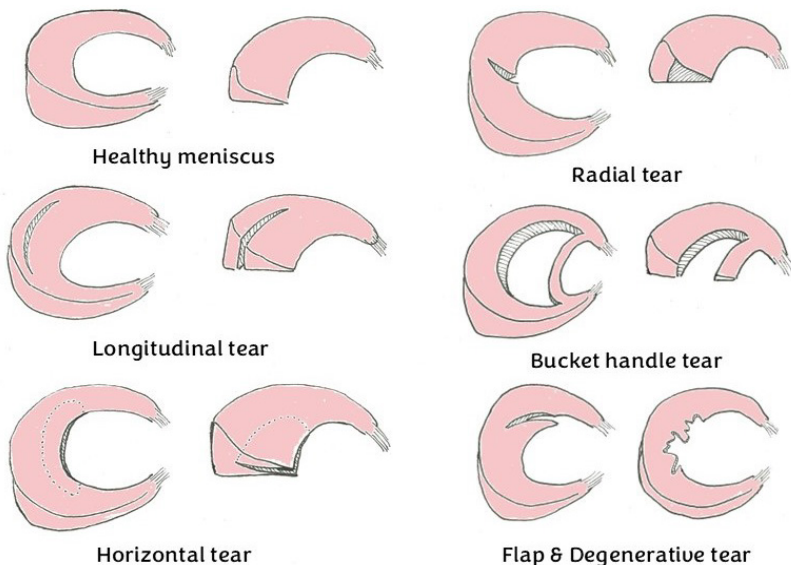


**Figure 4.** New classification for the location of meniscus tears, (Beaufils modification of Cooper).  
(©Andrea Boric-Persson 2025)

Additionally, there is the distinction between a *tear* and a *lesion* of the meniscus, where a tear is associated with a sufficient traumatic knee injury and sudden knee pain following this, while a lesion is the result of a slow progression of meniscus tissue degeneration without an acute trauma, resulting in a degenerative meniscus tear.<sup>[53]</sup> This distinction is sometimes hard to make in clinical practice.

Then, there is the *type*, or pattern/morphology, of the meniscus tear (**figure 5**). This thesis utilizes a grading into the following 7 types, which is the one present in the Swedish OrtReg database:

- Horizontal: A cleaving of the meniscus into an upper and a lower leaf. Often considered to be part of a degenerative meniscus injury, either through repetitive microtrauma or degenerative joint disease.<sup>[54]</sup>
- Degenerative: Uneven pattern, often multiple tears in a meniscus with macroscopically poor tissue quality. There is an overlap between degenerative and those classified as flap, complex and horizontal tears.
- Flap: A flap tear is a peninsula-shape tear, sometimes a residue after a bucket-handle rupture that has been torn apart. It can also be a form of degenerative tear. Some classifications use the term oblique tear as a category, which in OrtReg would be classified as a flap tear.<sup>[50]</sup>
- Complex: A meniscal tear is classified as complex, if the rupture is in several different planes, for example a combination of flap, horizontal and radial.
- Radial: A radial tear stretches from the inner portion of the meniscus and radially outwards toward the capsule in a vertical fashion. If it is long enough, it totally compromises meniscus function.
- Bucket handle: An inner portion of the meniscus is vertically separated from the outer portion but retain attachment in both ends, forming a hole, resembling the handle (the torn part) on a bucket (the remaining meniscus). The torn part can sometimes dislocate into the joint, interfering with motion.
- Longitudinal: A longitudinal tear is a vertical fissure in the meniscus, parallel to the long axis of the meniscus. Sometimes not all the way through the whole tissue.<sup>[55]</sup>



**Figure 5.** The different types of meniscus tears. (©Annali Persson 2025)

There are also other recognized tear types, listed below, that are not recognized as a part of this study. They might be present in the material, misclassified as any of the above mentioned seven categories:

- Root-avulsion: Defined as a bony root avulsion or a radial tear located within 10mm from the meniscus posterior horn or anterior horn attachments, an anterior injury being uncommon. This entity has gained more attention during the last decade. It was probably under-diagnosed during the timeframe of the studies included in this thesis. It is repaired using a totally different technique than the other meniscus tears, with drill-tunnels in the tibia and anchoring of the meniscus to the bone.<sup>[56]</sup> A tear of the meniscus root compromises all meniscus functions and is considered to seriously aggravate OA progression. Current evidence suggest they maybe should be sutured even in knees with diagnosed moderate OA.<sup>[57]</sup> No such surgeries are included in the thesis.
- Ramp-lesion: Meniscal ramp-lesions consist of a separation between the posteromedial menisco-tibial attachments of the posterior horn of the medial meniscus. It is closely associated with the ACL injury mechanism and can be difficult to spot on MRI or during arthroscopy. It may lead to a persistent meniscocapsular or meniscotibial disruption putting the medial meniscus at risk of further injuries.<sup>[58]</sup> Recent publications find a prevalence of meniscus ramp-lesions of up to 40% in knees with an ACL injury.<sup>[59,60]</sup>

### *Discoid meniscus*

A special case is the *discoid* meniscus. Its bilateral in 80–97 percent of cases, with an incidence of 3–5% (USA). It is a congenital variant, almost exclusively on the lateral side, where the meniscus is wider, sometimes circular, thus covering a larger area than normal of the tibial chondral surface. It's abnormal in fibre structure and vascularity. This increases the stress on the meniscus and makes it prone to rupture and/or knee symptoms. The advised surgical method in these cases is a so-called “saucerization”, removing the central part and leaving a rim shaped like a normal meniscus. If this rim remains unstable, or a tear propagates near the capsule, this may be stabilized with a meniscus suture. Many discoid menisci are asymptomatic.<sup>[61,62]</sup>

### *Risk factors for a meniscus tear*

Several factors have been shown to increase the risk of protracting a meniscus tear, commonly divided into *intrinsic* and *extrinsic* risk factors.

Intrinsic factors are often non-modifiable and includes sex (being more prevalent in males), age (traumatic tears being more common in younger individuals and degenerative lesions increasing with age), high BMI and knee anatomy.<sup>[63–66]</sup>

Extrinsic factors include occupational knee straining activities and high levels of physical sports participation, especially activities with knee pivoting.<sup>[65–67]</sup> A tear of

a healthy meniscus generally occurs during combined knee rotation and axial loading.<sup>[24]</sup> Ligamentous injuries, primarily ACL injuries, and knee OA both highly increase the risk of contracting a meniscus tear.<sup>[36,65,66,68]</sup>

## **Osteoarthritis**

OA is an ailment that involves all the tissues of the joint, both articular capsule, synovium, subchondral bone, nerves, meniscus and cartilage. An imbalance in knee joint loading leads to an imbalance in the normal homeostasis between regeneration and degradation of joint tissues, and an inflammatory response.<sup>[69]</sup> Degeneration of the joint leads to thinning of the joint cartilage followed by sclerosis of the underlying bone and the formation of cysts and osteophytes (**figure 6**). This includes also the degeneration of both meniscus tissue quality and macroscopic structure. Major risk factors of OA include age, obesity, joint injury, genetic predisposition, female sex, occupations with high physical loads and/or kneeling, especially studied in knee OA.<sup>[10,70–72]</sup>

Other mammals can also exhibit signs of OA, and it is frequently studied in lab rats and other animals. The prevalence of OA has been rising fast during the last century, indicating our modern way of life as a key driver of disease burden.<sup>[73]</sup> Recent anthropological studies show, that although OA is present in tribes living traditional hunter gatherer lifestyles, the prevalences in these peoples is dramatically lower than in modern societies, implicating a sedentary lifestyle as a key factor. Interestingly, marathon runners have thicker knee cartilage than healthy controls, even though they subject their joints to considerable wear.<sup>[74]</sup>



**Figure 6.** X-ray image showing a knee with osteoarthritis KL grade 4, (©Radiopaedia 2024)

### *Definitions of OA*

OA is defined by the Osteoarthritis Research Society International (OARSI) as:<sup>[69]</sup>

“Osteoarthritis is a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness.”

Radiographically it is commonly graded using the Kellgren-Lawrence (KL) grading 0–4 shown in **table 1**, which can be applied on each of the compartments in the knee.<sup>[75]</sup> This is maybe the most commonly used radiologic grading system in OA research and has been validated.<sup>[76]</sup> It relies on a weightbearing posteroanterior radiograph with the knee in 45 degrees of flexion (Rosenberg view).

**Table 1.** Kellgren-Lawrence OA radiographic grading system

Kellgren-Lawrence Grading System	
<b>Grade 0 (none)</b>	Definite absence of x-ray changes of osteoarthritis.
<b>Grade 1 (doubtful)</b>	Doubtful joint space narrowing and possible osteophytic lipping.
<b>Grade 2 (minimal)</b>	Definite osteophytes and possible joint space narrowing.
<b>Grade 3 (moderate)</b>	Moderate multiple osteophytes, definite narrowing of joint space, some sclerosis and possible deformity of bone ends.
<b>Grade 4 (severe)</b>	Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends.

Macroscopically, it is defined by grading the extent of cartilage degradation, (OARSI histology scale).

During arthroscopic surgery in Skåne and subsequent registration in OrtReg, the ICRS (International Cartilage Regeneration & Joint Preservation Society) grade for knee joint cartilage injury description is used (**table 2**).<sup>[77]</sup> This is a more comprehensive and specific description than the original Outerbridge classification used to describe the extent of cartilage damage and degeneration.<sup>[78]</sup> OrtReg combines it with a description of the size of any cartilage defects in square millimetres. In clinical research there is often the distinction made between *radiographic OA* and *symptomatic OA*.

**Table 2.** ICRS grading system for knee joint cartilage injury during arthroscopic surgery

ICRS-grade score	
<b>Grade 0 (normal)</b>	Normal cartilage.
<b>Grade 1 (nearly normal)</b>	Fibrillation and/or superficial lesions.
<b>Grade 2 (abnormal)</b>	Fissures extending down to less than 50% of cartilage depth.
<b>Grade 3 (severely abnormal)</b>	Deep fissures down to more than 50% of cartilage depth as well as down to, but not into the subchondral bone.
<b>Grade 4 (severely abnormal)</b>	Fissures down through the cartilage into the subchondral bone and/or areas of bare bone.

In clinical practice, the diagnosis is set using a combination of anamnestic symptoms and clinical examination findings while radiology is not required. It is then labelled by the ICD-10 diagnoses M17.1 – M17.9 (**appendix table 12**).<sup>[79]</sup> The typical symptoms for the diagnose of knee OA are:

- Morning stiffness or stiffness after rest that gets better with activity.
- Pain correlated to joint loading, later also at rest.
- Joint swelling, catching, stiffness and reduced range of motion.
- Reduced function, in advanced disease also feelings of knee joint instability.

Typical is a gradual onset and worsening of symptoms, with interval periods of lessening of symptoms. Clinical examination findings in the knee include reduced range of motion (especially flexion), joint swelling, width increase of the knee joint, joint line tenderness, crepitation and catching, and malalignment.

The end stage of OA is a painful and destroyed joint, where a total knee replacement (TKA) is the final step in treatment. A TKA is performed by excising the subchondral bone and cartilage surfaces of the tibia and the femur (sometimes also a part of the patella) and exchanging these for metallic implants with polyethylene inserts in-between to reduce friction. These surgeries are steadily increasing, now annually performed in Sweden there are around 17000 total knee replacements according to the Swedish Arthroplasty Register.

## Posttraumatic knee OA

Knee OA is usually divided into primary and post-traumatic (secondary) OA. The risk of developing OA increases about 3-fold after a knee trauma, with an increase to between 4–8-fold with either an ACL tear or meniscus tear. The worst outcome being in persons with a combination of both an ACL and a meniscal tear.<sup>[80,81]</sup> The structural and biomechanical changes occurring with displaced fractures, ligament injuries and meniscus tears hastens cartilage degeneration, but the initial inflammation, hemarthrosis and contusions to the cartilage and underlying bone have been increasingly recognized as factors affecting progression to posttraumatic knee OA.<sup>[82,83]</sup> Even subsequent surgery to correct the initial injury may increase the risk of developing OA, the surgical trauma contributing a new episode of hemarthrosis and joint inflammation.

Among the first to report on the connection between meniscus surgery and an increased rate of human knee OA development, was Fairbanks in 1948.<sup>[34]</sup> Numerous studies have shown that total excision of one or both menisci leads to a more rapid development of knee OA, compared with preserving as much meniscus form and function as possible.<sup>[84–87]</sup> Even partial meniscectomy has been associated with increased rates of OA.<sup>[88,89]</sup> This is thought to be mediated by the change that meniscus tissue removal imparts on cartilage loading and peak contact pressure.<sup>[90,91]</sup>

In a study by Snoeker *et al.*, comparing the rate of diagnosed OA after knee injury versus healthy controls, they found that knees with an ACL tear had a 6–8-fold increased risk of developing knee OA after trauma. Second worst was a meniscus

tear, with a 4–7-fold risk increase. It was also shown that any kind of diagnosed knee trauma more than doubled the risk of later knee OA development. It was not stated if the injured individuals had any surgery or not associated with the trauma.<sup>[80]</sup>

Minor cartilage injuries are a common finding in knee trauma with meniscus injuries. There is currently no method of restoring the cartilage back to normal, but in selected patients the method of “Pridie-drilling” or “microfracture technique” was used in Skåne during the period of this thesis, often inducing the growth of a cartilage-like structure to cover the cartilage defect.<sup>[92,93]</sup> Other possibilities for the surgical management of cartilage defects are osteochondral transplantation with an autograft or an allograft (OAT and OCA), both with promising clinical results, but they are more complex procedures and are rare or non-existent in Sweden. Less common is Autologous Chondrocyte Implantation (ACI), being a two-stage procedure and also rather expensive. The use of synthetic scaffolds is an emerging technique, where several challenges remain.<sup>[92,94]</sup>

## **Injury to the anterior cruciate ligament**

The anterior cruciate ligament (ACL) is the structure mainly responsible for sagittal knee stability, together with the PCL. Numerous studies have shown an increased risk of developing OA in the knee following ACL-deficiency, and this is sadly not alleviated by ACL-reconstruction surgery.<sup>[80,90,95–101]</sup> When observing persons with an ACL injury for between one and two decades, about 50% are found to develop radiographic OA in the injured knee.<sup>[99]</sup>

Meniscus injury is present in more than 40%, some even report in many as 80% of all knees with an acute ACL tear.<sup>[102–107]</sup> In knees with instability due to a chronic ACL tear, the prevalence of meniscus pathology increases with time and is reported in up to 100% of patients at the time of late ACLR, pertaining both to increased translational stress on the medial meniscus and to the general OA development after an ACL injury.<sup>[108,109]</sup>

Though a rupture of the ACL is considered a permanent injury, it has been known that in some cases the ACL can heal spontaneously. The semitendinosus tendon often used in ACLR surgery regenerate in 70% of cases when surgically stripped, demonstrating a regeneration potential of tendons outside the knee joint.<sup>[110]</sup> In a recent study where the KANON trial data was analysed, it was found that in 30% of participants without ACLR, an MRI done at the 2-year follow-up showed evidence of ACL healing.<sup>[111]</sup>

Recently, an RCT with a protocol for bracing the knee in 90 degrees flexion after an acute ACL-tear (ACLOAS grade 3) without other serious concomitant injuries, yielded the result of 90% of patients having evidence of healing on a 3-month MRI (continuity of the ACL).<sup>[112]</sup> This also led to an increase in functional stability, with more ACL healing on the 3-month MRI being associated with better outcome.<sup>[113]</sup>



It is under investigation what effect the natural healing of the ACL in some cases will have on the progression of posttraumatic OA. Non-operative treatment of an ACL injury seems to have similar Patient Reported Outcome Measures (PROM) as knees with an ACLR\*0, but with an increased risk of future meniscus surgery.<sup>[114]</sup>

## Epidemiology

### Knee injuries

#### *Meniscus injury*

The incidence of acute meniscus tears ranges between 0.5-0.9 per 1000 inhabitants, being about 1.5–4 times as common in men compared to women.<sup>[24,115–118]</sup> In 60–75% of cases it involves the medial meniscus.<sup>[106,118]</sup> In knees with an ACL tear, lateral meniscus injuries are more common than in stable knees, perhaps even more prevalent than medial tears.<sup>[105,108,118]</sup>

Of all traumatic knee injuries, (without a fracture) seeking medical care, an estimated around 10% have a meniscus injury, between 6–7% have an isolated meniscus tear, and others have a meniscus injury in combination with any ligament injury.<sup>[116,117]</sup> In pivoting-sport athletes, the number of meniscus injuries are reported to be doubled.<sup>[106,119]</sup> During the 21st century there has been an increase in meniscus injuries, especially in women, attributed to their increased participation in organized sports. Peak incidence of traumatic tears lies between 20–30 years of age in men and between 11–20 years of age in women.<sup>[117,120]</sup>

The prevalence of meniscus tears is approximated at between 12–14% in the whole population.<sup>[24]</sup> The incidence and prevalence of different meniscus tear types varies with age, with mostly traumatic tears below age 35 while degenerative lesions, tears without a significant knee trauma, are common in the older population.<sup>[24,115]</sup> In the elderly, 19% of women aged 50–59 years are having signs of a degenerative meniscus tear on MRI, increasing up to 56% in men of age 70–90 years. The majority of these individuals does not have knee symptoms.<sup>[121]</sup>

#### *ACL injury*

The estimated incidence of ACL tears is 68.6/100 000 person-years in the US and 70–78/100 000 in Sweden, which would translate to between 5–10 million ACL-tears per year world-wide.<sup>[96,117,122]</sup> The peak incidence lies between the ages 15–30 years, with a rapid decline of the incidence with age. The incidence has been steadily increasing during previous decades, especially in young female athletes, which have the highest risk of contracting an injury to the ACL.<sup>[123]</sup>

## Knee OA

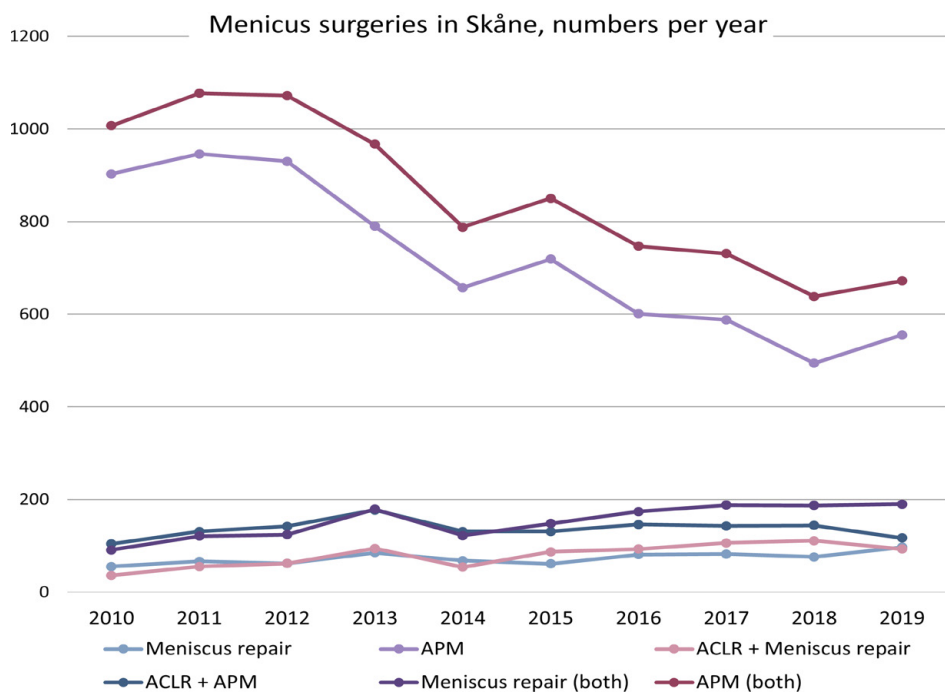
Symptomatic OA is a major cause of disability worldwide and the number of people living with OA in 2020 was estimated to 7.6% (95% CI 6.8–8.4) globally, around 600 million individuals. It has also been increasing, with approximately 132% between 1990 and 2020 and is projected to rise to 1 billion affected people around 2050, driven by increases in weight and age in the population. Knee OA contributes with the largest part of all OA, with up to 80% of the disease burden and a 4.3% prevalence worldwide.<sup>[124]</sup>

The prevalence of radiographic knee OA in southern Sweden above the age of 45 is calculated to be around 25%, rising from 17.3% between 56–64 years to 40.0% between 75–84 years, with 10.5% (ranging from 8.1% to 15.5% between age and sex groups) having symptomatic knee OA.<sup>[125]</sup> The prevalence of doctor diagnosed knee OA in southern Sweden is lower, with almost a linear increase from around 5% in persons around the age of 50 years, to about 25% around 80 years of age.<sup>[126]</sup>

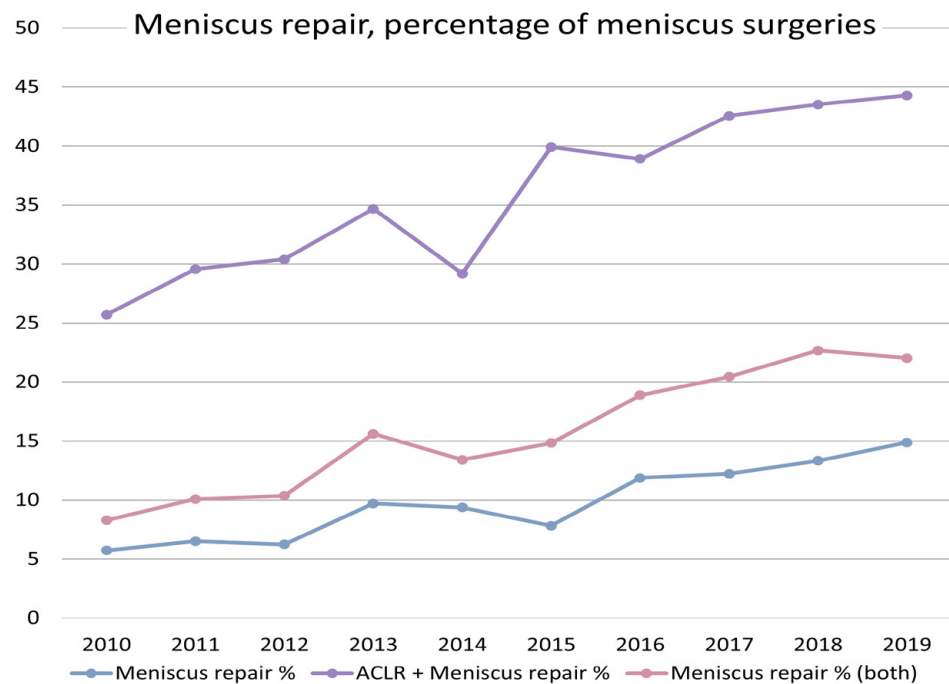
## Arthroscopic surgery

There has been a steady increase in both absolute numbers of meniscus repair surgeries in Skåne during the study period, as well as the percentage of all meniscus surgeries that includes a repair surgery, presented in **figure 7 & 8**. In the last couple of years, meniscus repair as a proportion of meniscus surgeries in Skåne has reached 40% and is still increasing[*unpublished*], while ESSKA previously had estimated that about 30% of all meniscus tears are suitable for repair.<sup>[53]</sup>

To what extent this is an effect of widened indications for repair, and what effect this will have on the rates of reoperations and future knee OA, is an interesting topic for future research. It seems unlikely that its a result of changes in the underlying meniscus tear morphology distribution, but maybe a narrowed window of surgically treated tears. From 2010 to 2015, the overall knee arthroscopy rate in Skåne decreased from 30.5 to 23.6 per 100 000 in the population aged  $\geq 40$  years.<sup>[127]</sup>



**Figure 7.** All meniscus surgeries in Skåne region, OrtReg statistics data (includes reoperations).



**Figure 8.** All meniscus surgeries in Skåne region, OrtReg statistics data (includes reoperations).

The Nordic countries have markedly different rates of meniscus surgery, despite similar publicly funded healthcare systems and equal demographics of the population.

In 2012 the Swedish incidence of meniscus surgery was 55/100 000 person-years. This meant a slow decline from the rate of 67/100 000 in the year 2001. In total more than 8000 knee arthroscopic surgeries were reported in 2012, in a population of 9.5 million people. The meniscal repair incidence was 0.7/100 000 in 2012, up from 0.4/100 000 in 2001.<sup>[128]</sup>

In Denmark there was a doubling of arthroscopic meniscal surgeries between the year 2000 and 2011, from 164/100 000 to 316/100 000 persons each year. The result was a total of 17 000 meniscus surgeries in 2011.<sup>[129]</sup>

In Finland the reports state a meniscus surgery incidence of 222/100 000 in 2012, with a corresponding rate of meniscus repairs of 2.1/100 000. A total of 15000 knee arthroscopies were reported the same year.<sup>[128]</sup>

In Norway, the rate of APM was about 250/100 000 persons in 2012, with meniscus repair numbers of 13/100 000 persons the same year. The APM rate had then declined to 80/100 000 in 2020, with meniscus repairs steadily increasing to 32/100 000.<sup>[130]</sup>

## **ACLR**

Around 2 million ACL ruptures annually occur around the world and in some countries the rate of ACLR after an ACL tear is close to 90%. Rates of ACLR varies extremely between different nations, with Swedish proportions of around 36–50% of tears being surgically treated.<sup>[96,105]</sup> In Sweden there were in 2023 more than five thousand ACL reconstructions performed (0.5/1000 inhabitants), more than a doubling in the last 20 years. During the same period the percentage of concomitantly sutured menisci has risen from 4% to 24% while the rate of APM has remained more constant, fluctuating between 26–33%.<sup>[105]</sup>

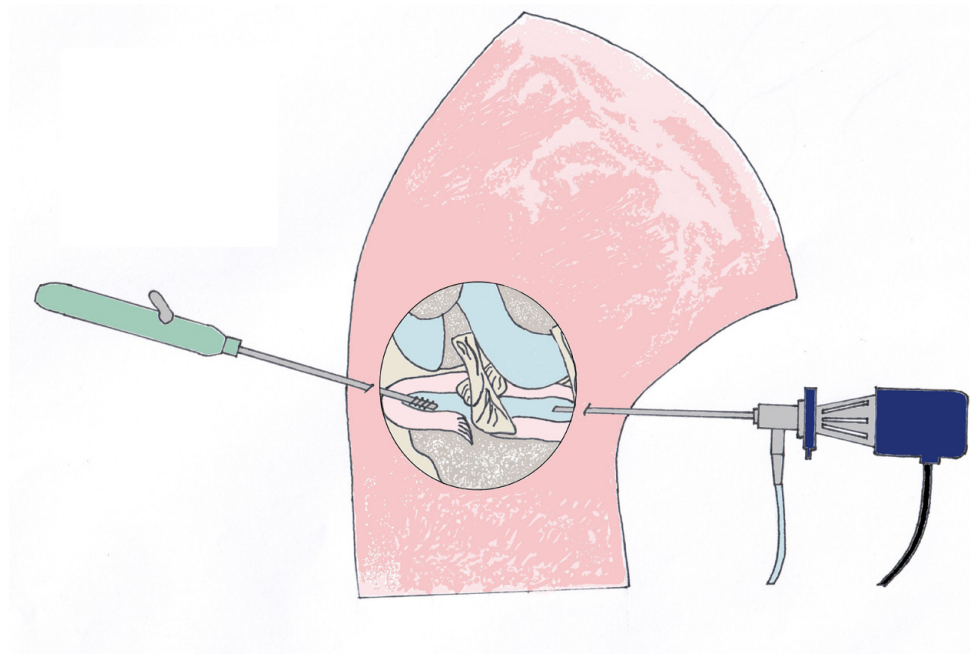
## **Meniscus surgery**

### **The history of knee arthroscopy**

The Danish physician Severin Nordentoft was first to report on arthroscopies of the knee joint in 1912 at the 41st Congress of the German Society of Surgeons in Berlin.<sup>[131]</sup> Later, the Swedish surgeon Hans Christian Jacobaeus coined the term *arthroscopy* for this procedure.

The modern design of arthroscopes originally stems from the pioneering work of Japanese surgeon Kenji Takagi, who in 1918 contrived the design. It took him until 1931 to develop a small enough arthroscope to be practical for basic surgery in the knee joint.<sup>[132]</sup> The first arthroscopic meniscus surgery was performed 1962 in Japan by Dr. Watanabe, and a few years later the technique spread to north America and Europe.

Early pioneers in Europe were the Swedish surgeons Jan Gillquist and Ejnar Eriksson, who took arthroscopic meniscus surgery to Sweden in the 1970s. Since then, it has become widely adopted globally and has increasingly replaced open surgery.<sup>[133]</sup> Arthroscopy of the knee has now risen to become the most common orthopaedic procedure in the world.<sup>[134,135]</sup>



**Figure 9.** Drawing of a modern setup for knee arthroscopic surgery. (©Tatjana Boric-Persson 2025)

## The history of meniscus surgery

In the 19<sup>th</sup> century knowledge of the anatomy and function of the meniscus was limited, and meniscal injuries were rarely treated surgically. The meniscus was often considered an unnecessary structure, and surgical interventions typically involved total meniscectomy – the removal of the entire meniscus.<sup>[136]</sup> Continuing into the early 20<sup>th</sup> century, total meniscectomy was still the surgical treatment for pain and other symptoms from the meniscus. To access the meniscus, the method was open surgery with an arthrotomy and then the excision of the meniscus with a scalpel. It

was not until much later that the researchers began to understand the biomechanical significance of the meniscus for the knee joint.

During the decades a slowly growing body of evidence pointed towards serious long-term disadvantages with total removal of the meniscus.<sup>[34]</sup> We now know that open total meniscectomy invariably results in worse knee function and dramatically increases the risk of having received a total knee replacement when measured 40 years after surgery.<sup>[137]</sup>

In the 80–90s knee surgeons in Scandinavia increasingly changed their practices towards preserving parts of the meniscus, and with that came a growing interest in implementing a new surgical method to minimize the surgical trauma and morbidity that followed from cutting open the knee joint.<sup>[115,138]</sup> During a phase mini-open surgery was tried, sometimes guided by arthroscopy, and better arthroscopic methods soon made open surgery superfluous in most cases.<sup>[139]</sup>

### **Arthroscopic Partial Meniscectomy (APM)**

The method of APM made outpatient surgery possible, sometimes performed under only local anaesthesia. This meant lower costs and that even older patients could have surgery. APM widened the indications for meniscus surgery, and the number of surgeries continued to increase until the peak around 2010.<sup>[140]</sup>

APM for treating knee pain in patients with knee OA and degenerative meniscus tears became a standard procedure. To perform an APM, two or three small stab incisions are made into the knee joint, where an arthroscope is introduced for visualization, the joint is filled with saline solution to distend it, and a sharp instrument is inserted to cut parts of the meniscus into smaller pieces that can be extracted.

Patients and surgeons were happy, and it took until 2002 when Moseley *et al.* published their study comparing APM with sham surgery, before this paradigm started to be questioned.<sup>[141]</sup> It was later followed by other studies reproducing the same results. Though APM for degenerative meniscus lesions are currently advised against, some authors still conclude that it has some benefits.<sup>[54,142]</sup>

Evidence was also starting to emerge that performing an APM in knees with traumatic meniscus tears increases the risk of developing knee OA.<sup>[143]</sup> Around the millennium, a number of studies were being published, presenting results on how the meniscus instead could successfully be sutured back into place.<sup>[144]</sup> In Sweden, Rockborn and Gillquist were among the first to publish long-term results comparing APM with meniscus repair.<sup>[145]</sup>

# Repairing the Meniscus

## The history of meniscus repair

The first documented meniscus suture was an open repair performed by the Scottish surgeon Annandale in 1883. He treated a patient with a traumatic knee injury and a meniscus tear, and after failing in the attempt to treat the knee conservatively he elected to do an open knee arthrotomy. Describing the surgery in his publication:

*“...the semilunar cartilage was completely separated from its attachments and was displaced backwards about half an inch. The anterior edge of this cartilage was seized by a pair of artery catch forceps, and it was drawn forwards into its natural position, and held there until three stitches of chromic catgut were passed through it and through the fascia and periosteum covering the margin of the tibia. The forceps were then withdrawn, the cartilage remaining securely stitched in position”.*<sup>[146]</sup>

Six months later the surgery was considered a success, as the patient stated full recovery of the knee. Annandale then went on to describe his first complete meniscectomy in 1889, in a patient where he could not repair the meniscus.<sup>[147,148]</sup>

Though this operation is considered a milestone in meniscus repair surgery, it was not until the first half of the 20th century, accompanied by a rise in sporting injuries and the development of better surgical equipment, that the practice started to develop. Pioneers such as T.P. Fagan attempted to preserve the meniscus by repairing it, rather than just surgically excising it, which was common practice at the time.

In the decade following the Second World War, there were rapid improvements in surgical technique and the understanding of the meniscus function. Fairbanks in 1948 presented a study that showed the role of the meniscus in distributing the knee load and preventing cartilage degeneration. This then led to an increase in meniscus repairs. In Sweden the first documented meniscus suture surgery was performed by Sven Johansson in 1948. In the 1960s, the introduction of the instruments and techniques for arthroscopic knee surgery had a major impact on the rate of meniscus sutures.

The first arthroscopic repair was performed in Japan by Ikeuchi in 1969. A less invasive procedure, it allowed for repairing also smaller tears on younger individuals. It also reduced morbidity and the operating time. The knee surgeon Charles Henning was the first to develop an arthroscopic meniscus repair method in the early 1980s, with an *inside-out* suture technique. He went on to also introduce the adding of rasping the meniscus tear surfaces to promote healing.

The next step was the introduction by Morgan in 1991 of the first generation of *all-inside* repair. He made use of curved suture hooks through accessory posterior portals to pass sutures across the tear. The meniscus tear was then repaired with sutures retrieved and tied arthroscopically.<sup>[149]</sup>

During the following decades it gradually evolved into an established treatment of meniscus tears, especially the ones located in the well vascularized parts of the meniscus. It continued to improve, with internal suture implants evolving to become more efficient and easier to use, with smaller incisions and fewer portals needed and less risk of any neurovascular injury. In Sweden, it was not until the 21st century that all-inside arthroscopic suturing of the meniscus started to really become a widespread surgical treatment for a meniscus tear.

## **Treatment for a meniscus tear**

Diagnosing a patient with a meniscus tear begins with clinical anamnesis focused on trauma mechanism and meniscus symptoms, followed by knee examination with meniscus test (Apley, McMurray, Thessaly, Joint Line Tenderness (JLT)).<sup>[150]</sup> Prior to today's readily available MRI examinations, diagnostic arthroscopy was used to confirm the diagnosis. In the 21st century, MRI is commonly used, while some patients still receive the diagnosis solely by clinical examination. Ultrasonography is also an option but is not as good as MRI and is rarely used in Sweden.<sup>[151]</sup>

While MRI is good at detecting meniscus tears, it is less specific in classifying the type of the tear.<sup>[152]</sup> The final classification of the tear type is performed during arthroscopy in the same seance as the surgical treatment.

Determining when surgery is indicated for a meniscus tear and what type of surgery has varied over time, depending on patient symptoms, patient age, function and comorbidities, type, zone and size of the tear. There has been a continuous trend towards suturing more and more complex meniscus tears and further towards and into the avascular zone, as well as a trend towards fewer APMs, especially in patients with degenerative meniscus tears.<sup>[127,135,153]</sup>

### *Indications and contraindications*

When deciding if a meniscus tear should be repaired, several factors are taken into account:

#### Patient factors

A BMI of more than 30 is associated with an increased ratio of degenerative menisci, but patient weight in itself has not proven to be a contraindication to repair.<sup>[53]</sup> Patient age also increases the likelihood of degenerative lesions, but in traumatic injuries chronologic age seems to not affect the suture healing-rate.<sup>[154–156]</sup>



The patient is required to be able to comply with post-operative rehabilitation and restrictions. Smoking is advised against but is not an absolute contraindication.

### Meniscus tear factors

It needs to be a tear morphology and location, that is amenable for good suture fixation. Preferably the tear should be located in the red-red or red-white zones, but that is not mandatory. There is evidence that the time from injury to surgery affects the success of a meniscus suture repair, with higher healing-rates with shorter duration. But no absolute point in time exists when its “to late”.<sup>[157–159]</sup> Concomitant ACLR is also considered to strengthen the indication for repair.

Contraindications are severe degeneration of the meniscus or the torn fragment, the inability to reduce it and the presence of KL grade 3–4 osteoarthritis in the knee.

## **Surgical techniques**

### *Open Repair*

The classic method of open repair is still used in some cases where access to the tear with arthroscopy is not possible, or when the joint has already been opened because of surgery to other structures. It is performed by a longitudinal skin incision and subsequent capsule arthrotomy without dividing any tendons or ligaments. The meniscus is then sutured with a needle and a monofilament suture, depending on tear morphology and location. Reports of re-tears ranges between 11% and 29% in patients.<sup>[63]</sup>

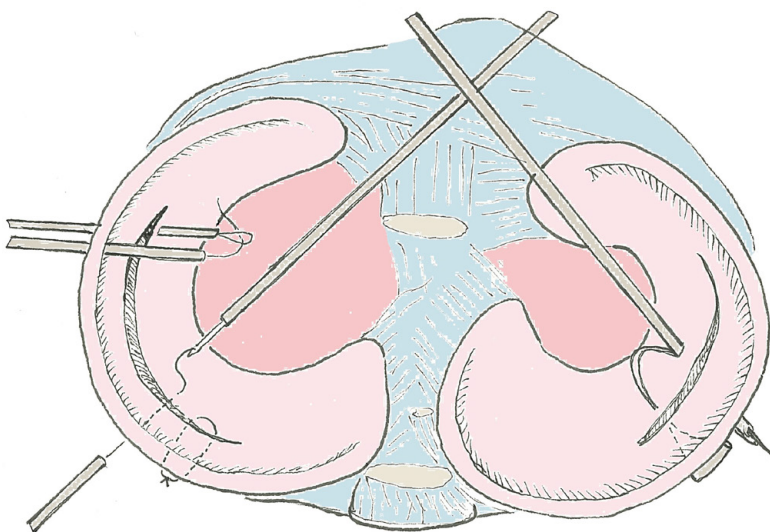
In this thesis we excluded all open meniscus surgeries.

### *Arthroscopically assisted (inside-out and outside-in)*

After introducing the arthroscopy into the joint, a second work portal is established for the intraarticular tools. Then either an accessory medial or lateral skin incision are required for suture retrieval. Nerve branches and vessels are at risk of injury, depending on location of the meniscal tear.

A vertical or horizontal mattress monofilament suture is the common stitch, encompassing the tear, the meniscus and the capsule. Inside-out sutures are passed from inside the knee, with them being knotted outside the capsule. The method is most suitable for tears in the posterior and middle thirds of the meniscus. Outside-in techniques are more suitable for the repair of anterior and middle thirds, being tied in the opposite fashion.<sup>[160]</sup>

These repairs are included in the thesis.



**Figure 10.** Schematic drawing of, from left to right: *Outside-in* meniscus suture, *Inside-out* meniscus suture and the *all-inside* meniscus anchor sutures. (©Anneli Persson 2025)

### *All-inside repair*

When repairing the meniscus with an *all-inside* technique, the whole surgery is performed via only two (but sometimes up to four) arthroscopy portals, the whole suturing process occurring inside the joint with specialized instruments and sutures.<sup>[160]</sup>

Over the years different all-inside devices have been utilized. One of the first, introduced in 1993, was the Meniscus Arrow (Bionx Implants, Blue Bell, PA) consisting of a rigid degradable polylactic acid arrow. Initially with promising short time results, a follow-up study found their success-rate having deteriorated to 71.4% at 6.6 years (recurrence of symptoms at a mean of 43 months post-repair).<sup>[161]</sup> There were also problems with implant migration and cartilage damage. Arrows were phased out during 2010 in Skåne and occur in small numbers in this thesis, where their performance was found to be even poorer.

Further development led to suture-based implants, with a sliding knot and anchors that are inserted onto the outside of the capsule, via a small puncture from the inside. Fast-Fix (Smith and Nephew Endoscopy, Andover, MA) is one example, and it is also the prevailing method occurring in this thesis.

## **Non-operative treatment and the natural history of meniscus tears**

It is unsure to what extent isolated traumatic meniscus tears in knees without degenerative changes can heal without surgery.<sup>[136]</sup> There are no studies of the healing-rate without surgery that have included second look arthroscopy. Stable meniscus tears left *in situ* during ACLR have a low rate of subsequent APM or meniscus repair.<sup>[162,163]</sup> Results for unstable tears have only been published in one small study.<sup>[164]</sup> With tears in the lateral meniscus of 10mm or less, leaving them alone without surgery is generally considered adequate treatment.<sup>[53]</sup>

Skou *et al.* performed a RCT comparing meniscus surgery and physiotherapy for meniscus tears in young adults, excluding displaced tears and locked knees.<sup>[165]</sup> The non-operative group had continuous improvement of function and symptoms during one year after trauma, with only slightly lower KOOS as compared to the surgery group. Graaf *et al.* conducted a similar study, comparing APM with physiotherapy.<sup>[166]</sup> Locked knees and repairable tears were excluded. They found that for at least during the first 24 months, in more than half of the patients, physiotherapy was equally as effective as an APM to alleviate meniscus tear symptoms and restore knee function. While neither surgical nor non-operative groups fully returned to preinjury levels, leaving a meniscus tear *in situ* in an attempt at natural healing seems a viable option for some tears.

Degenerative lesions are a result of progressive meniscus tissue degeneration, either from repetitive microtrauma or joint disease, and in many cases they are asymptomatic.<sup>[121]</sup> While degenerative lesions may not heal in a structural sense, any symptoms are best treated with physiotherapy as long as they do not severely restrict the range of motion in the knee.<sup>[167]</sup> The current view is that APM for degenerative meniscus tears in patients with manifest or developing OA, is not beneficial in treating symptoms and may instead lead to worse knee outcomes.<sup>[168–172]</sup>

## **Rehabilitation**

### *Non-operative rehabilitation*

Recommendations regarding knee physiotherapy in the Skåne region after a meniscus tear are exercises performed every day at home by the patient and supervised with regular visits to a physiotherapist. Exercises are included that enhances range of motion, blood flow and increases muscle strength and control. The program is followed for at least 12 weeks, or longer if symptoms still persist. Especially in patients above the age of 40 years, physiotherapy is the preferred choice of treatment.

### *Postoperative rehabilitation*

The postoperative rehabilitation following an APM closely resembles the physiotherapy administered after a non-surgically treat meniscus tear. Increased emphasis is directed towards the postoperative knee joint effusion. Full weightbearing is allowed and 2 crutches if needed, to normalize gait. Rehabilitation and sick leave may usually be needed for 2–4 months in patients with work requiring high knee function.

Following meniscus repair surgery, standard rehabilitation protocol includes two crutches to normalize gait, with full weight bearing. Neuromuscular rehabilitation under physiotherapist supervision is advised until normal knee function is achieved. Patients are prohibited to bear weight in knee flexion of 90 degrees or more for a period of six weeks. The need for restrictions postoperatively has been questioned.<sup>[173]</sup> Added checkups at the surgeon's office is also more prevalent than after APM. To avoid putting the repair at risk, patients are recommended to avoid sports with high knee loads for six months after surgery, and the same period of sick leave is sometimes prescribed if the patient has an occupation which includes high knee loading.

### **Measuring repair failure-rate**

Before talking about the rate of successful meniscus surgery, we must first consider what a non-successful surgery is, usually called a *failure*. There is a plethora of ways to measure this throughout different publications.<sup>[174]</sup>

MRI of the knee, with or without a contrast agent, has been used to try to determine the rate of meniscus healing after meniscus repair surgery. It remains difficult to distinguish between scar tissue in a healed meniscus and a persisting tear that has not healed, as well as correlating the image findings with symptoms and any need for a reoperation.<sup>[175,176]</sup> However, the continuous evolution of MRI technology is showing promising results.<sup>[177]</sup> New high-resolution MRI-machines and artificial intelligence (AI) interpretation might make this an even more useful tool in the future. MRI arthrography appears to be better than MRI alone but there is the added need of injecting a contrast agent.<sup>[175]</sup>

Another way of measuring the success of a meniscus repair is grading the patients knee symptoms, using PROMs like VAS, KOOS and knee function on an activity scale (Tegner, Lysholm).<sup>[157,178–181]</sup>

The need for a reoperation (usually because of knee symptoms) is maybe the most common way to measure the failure-rate after meniscus repair surgery. Mechanical symptoms with or without intolerable pain is a common symptom resulting in a reoperation, but pain and pain tolerance is very subjective and both the willingness of the patient and the surgeon to undergo a new arthroscopic surgery will affect this

outcome. With reoperation as outcome, there is the question of *what* to measure when defining the meniscus repair as a failure. Any new surgery to the same knee or any new *meniscus* surgery? New meniscus surgery to the same (lateral/medial) meniscus or new surgery in the exact same location of that meniscus? This is not always clearly stated in studies, and some register-based studies have difficulty in even distinguishing between surgery of the ipsilateral and contralateral knee.<sup>[182]</sup> Should a new ipsilateral knee trauma with a meniscus tear during follow-up also count as a failure? Of course, the observation time is an important factor in studies, with increased length of follow-up both increasing the prevalence of new knee traumas, as well as giving any asymptomatic non-healed menisci the chance to become symptomatic and/or degenerative.

Second look arthroscopy is considered the best method to measure healing after meniscus repair, and while being resource intensive, has the advantage of being able to distinguish between healing, partial healing, asymptomatic non-healing and symptomatic non-healing.<sup>[53,183,184]</sup> Still, there is only visual inspection of the meniscus surface, not revealing any internal discrepancies or degradation of meniscus function. Subsequent need for TKA surgery could also be viewed as a repair treatment failure.

## Previous research on meniscus repair and APM

### Knee OA

In a Swedish study Rockborn *et al.* reported that open meniscus repair had less signs of radiographic OA measured 13 years after surgery compared to APM.<sup>[145]</sup> The large systematic review by Paxton *et al.* in 2011 concluded that there is some evidence of arthroscopic meniscus repair being favourable in terms of OA development following surgery, but that further studies were needed.<sup>[144]</sup> A recent meta-analysis by Migliorini *et al.* was published in 2023 on knee OA following meniscus repair versus APM, where also Paper I is included.<sup>[185]</sup> The finding that meniscal repair is associated with a lower prevalence of progression to knee OA at approximately six years of follow-up compared to partial meniscectomy, was in line with the findings of this thesis. Among included studies only one other, published in 2020 by Sochacki *et al.*, had more than 139 patients in any of their included groups of patients.

## Sick leave

Sick leave after meniscus surgery is not a well-researched area. Gillquist *et al.* concluded in 1982 that half of patients took no sick leave at all after an APM and only 13% had sick leave longer than 4 weeks.<sup>[138]</sup> Rockborn *et al.* reported on sick leave in a cohort of 86 patients between 1980–81 where 20% of patients were on sick leave more than 2 weeks after surgery.<sup>[186]</sup> In a second series of 82 patients with surgery between 1995–98, they found that only about 10% had sick leave for more than 2 weeks after APM surgery, with no age correlation. Later he went on to compare open meniscus repair with APM, where it was found that patients with repair surgery had longer sick leave with a mean of 13 weeks, compared to 1.5 weeks after APM.<sup>[145]</sup>

Bergkvist *et al.* conducted a register-based study of patients aged 40–60 years with degenerative meniscus tears during 2004–2012 which had undergone APM and matched these against randomly sampled controls. Among the findings was a notable sex difference, as women with degenerative meniscus tears had more sick leave both before and after APM surgery.<sup>[187]</sup> They also studied sick leave after acute (traumatic) meniscal tears in the age group 18–59 years during the period 2004–2012, finding that 39% of the women and 27% of the men had any sick leave longer than 2 weeks associated with a meniscal tear. Analysing only the sick leave initiated at APM surgery, no gender difference remained, and only around 15% of patients had sick leave extending longer than 2 weeks.<sup>[188]</sup>

Regarding meniscus repair, many available studies measure return to sports in athletes after meniscus surgery. A meta-analysis by Lee *et al.* in 2019 concluded that most players returned to their preinjury activity level between 7 and 9 weeks after APM.<sup>[189]</sup> After isolated meniscal repair surgery, the average time to return to sports was 24.3 weeks, with only 81–89% of athletes returning to their prior activity level.

Von Essen *et al.* conducted a study of 49 patients following ACLR, where several patients also had meniscus injuries, and found the mean number of sick days associated with the surgery to be 71.7 days.<sup>[190]</sup>

## Reoperation rates

There are many studies on reoperations and repair failure after meniscus repair, but not as many comparing meniscus repair with APM. Few of them are from Sweden. Further, there is a wide heterogeneity of included menisci concerning tear types, follow-up length and definitions of repair failure. In **table 3** the larger and more recent meta-analyses regarding meniscus repair are summarized and in **table 4** the three largest comparative analyses of APM vs meniscus repair.

**Table 3.** Meta-analysis of meniscus repair outcomes

Author	Year	Follow-up (years)	Studies, N	Patients, N	Failure %	Outcome
Chand <sup>[191]</sup>	2024	2–13	10	1004	21	Reoperation
Farinelli <sup>[192]</sup>	2024	1.5–10	10	595	26	Reoperation or MRI or symptoms
Nepple <sup>[174]</sup>	2022	5–16	27	1612	22.6	Reoperation or symptoms
Petersen <sup>[193]</sup>	2022	10–20.6	12	652	5–48	Reoperation or MRI or symptoms
Schweizer <sup>[194]</sup>	2023	2–5	51	3829	14.8	Reoperation or MRI or symptoms

**Table 4.** Meta-analysis comparing APM and meniscus repair

Author	Year	Follow-up (years)	Studies, N	Patients, N	Outcome
Migliorini <sup>[185]</sup>	2023	1-13	20	31708	Knee OA
Paxton <sup>[144]</sup>	2011	1-14.6	4* (91)	(3813)	Reoperation
Xu <sup>[195]</sup>	2015	2-12	7	367	PROM

\*Only 4 studies directly comparing APM vs meniscus repair.

Scandinavian studies on reoperation- and failure-rates after meniscus repair are few, notably there is the study by Rockborn *et al.* in 2000, by Kise *et al.* in 2014 and Rönnblad *et al.* in 2020, with repair failures ranging between 22.5–26%.<sup>[145,159,196]</sup>

### Postoperative complications

Studies on the frequency of postoperative infection in arthroscopic surgery range from 0.01–1.1% and in combination with other medical complications the frequency increases to between 0.3%–2.6%, comparative studies finding up to double the risk in meniscus repair compared to APM surgery.<sup>[169,197–201]</sup> Swedish research on complications following arthroscopic meniscus surgery in Skåne reported a frequency of 1.1%.<sup>[202]</sup> With a wider definition of any adverse events defined as a complication, studies report 5–9% of postoperative complications, some studies including both concomitant ACLR and meniscus surgery.<sup>[158,186,203,204]</sup>

# Aims of the thesis

## General Aim

The overall aim of this thesis is to evaluate and compare patient outcomes associated with the surgical methods of APM and meniscus repair for the treatment of meniscus tears, in both the short term and the long term.

## Specific Aims

### *Aim of Paper I*

**Primary aim:** To compare the consultation rate for knee osteoarthritis (OA) after meniscus repair, after APM, and in the general population in the same Skåne region over a range of 5–18 years postoperatively.

### *Aim of Paper II*

**Primary aim:** To compare sick leave occurrence and duration in young and middle-aged patients undergoing APM vs meniscus repair and relate these to sick leave in the general population in southern Sweden.

### *Aim of Paper III*

**Primary aim:** To investigate the rate of all causes of knee reoperation and other medical complications after meniscus surgery with a follow-up between 5 to 10 years for all patients.

**Secondary aim:** To compare the rate of same meniscus reoperation, rate of all causes of knee reoperation and prevalence of other medical complications after APM vs meniscus repair surgery in a subgroup aged 15–40 years with a follow-up between 5 to 10 years.





# Patients and methods

## Pros & cons of register-based research

The size of the cohort that can be studied with register data far exceeds any clinical study that could be financed to answer a similar research question. There is limited drop-out or loss of follow-up in register-based research, except when people die or move out of the area that the register covers. On the other hand, only patients that seeks any attention from the healthcare or the SSIA are recorded and available for analyses regarding adverse events.

The costs for compiling prospective data independently by a researcher would be enormously higher if similar numbers of patients should be included in a study. There is also the advantage of time, both in saving work hours for gathering data, as well as giving access to long periods of patient follow-up time. Sweden, with its well-kept registers that cover the whole population, has always had a special advantage when doing this kind of research. Once a researcher has obtained all relevant approvals, registers and databases are linkable with the unique 12-digit personal number of every individual given at birth.

With register research, you are always confined to work with the data you already have, and not always the data that would be the best for answering the research question. In registers, data are usually gathered for statistical and economical purposes and the structure and included variables aren't always chosen with future research in mind. For example, in many diagnostics registers the laterality (left/right) is missing and it can be difficult to extract the date of the knee trauma and if there were any previous knee injuries in the patient history.

The quality of the Swedish National Patient Register (NPR) is very good, with only minor inconsistencies, and the quality has been improving further in recent years.<sup>[205]</sup> The accuracy of the orthopaedic injury diagnoses in the NPR has been measured for humerus fractures, with 93% of the diagnoses being correct.<sup>[206]</sup>

## Methodological considerations

When it comes to meniscus injuries in the SHR, not only is knee laterality missing, but commonly also meniscus laterality (medial vs lateral) and no registration of the meniscus tear type exists. A surgery code of APM or meniscus repair tells little of

the size of the meniscus injury or amount of meniscus tissue resected or repaired. The coding of both NGD11 and NGD21 can either mean different surgery to the lateral and the medial meniscus, or that both surgeries were performed on either one of them.

We also know little in the registers of the knee function in patients, both before and after the surgery. A healthy group to compare with is also difficult to assemble, since healthcare registers only include people that seek medical care.

In an effort to overcome some of the disadvantages of register-based research, I in Paper III undertook the monumental task of compiling our own database of meniscus surgeries, combining register data and patient records, which in the end took several years to perform. In my cross-checking of ICD and NGD codes against surgical records, only 4 out of 2319 meniscus surgeries were registered as meniscus surgery (false positive) when no surgery had been done (0.17%). How many that are false negative in OrtReg, or false positives in the SHR, with no actual meniscus surgery or injury, could not be measured. To my knowledge, there is no study comparing OrtReg data and registrations in the SHR.

When utilizing and interpreting data from insurance databases, it must be kept in mind that the rules of reimbursements and mode of data registrations changes over time. This can be hazardous when gathering long time series or comparing data from different time periods, and detailed knowledge must be attained about when changes were implemented and the specifics of what was changed.

The papers comprising this thesis handles the knee OA diagnose differently, but none of them separate between primary and secondary OA. In Paper I, OA is defined as a patient obtaining the diagnosis of knee OA when consulting a physician. The presence of radiologic confirmation of the diagnosis is unknown. In Paper II individuals with knee OA were excluded. In Paper III patients with knee OA were included and OA was treated as a confounder in the analysis.

## **Recall-bias**

Many studies rely on forms filled in by the patients, to describe previous and current knee function, as well as postoperative complications and number of reoperations. Apart from being prone to low response rates, a known problem is the tendency for the persons with bad outcomes to be more motivated to send in the forms. Also, there are certain age groups and socio-economic segments more willing to spend the extra time and effort required, as well as there are other groups and segments that are more prone to drop out or being lost in follow-up.<sup>[207]</sup> Furthermore, there are validation studies indicating a poor correlation between patient-reported health outcomes and events and the actual patient records.<sup>[208,209]</sup>

# Registers and data sources of this thesis

## Skåne Healthcare Register (SHR)

The Skåne Healthcare Register includes all patient visits to any publicly funded healthcare facility in the Skåne region, both hospital care, specialist clinics and general practitioners. The data contains information on date of consultation/admission/surgery, healthcare provider, diagnostic codes according to the ICD-10 system, and codes for surgical procedures according to the NOMESCO classification.<sup>[79,211]</sup> Neither the surgical or the diagnostic codes specify which side (right/left knee) any diagnosis or procedure refers to. The positive predictive value (PPV) of a surgical procedure code or an ICD-10 code being correct in the register overall is 85–95%, with PPV for knee trauma and knee surgery being above 90% (90–92%).<sup>[212,213]</sup> Private surgery clinics do not report to the SHR, however, they did not perform meniscus repairs during this time period, and only a small number of APMs.

## The Population Register

The population register, Swedish name *Befolkningsregistret (RTB)*, is kept and updated by the Swedish tax agency to include all legal residents in Sweden. Apart from being used for tax purposes, it is also available to other government agencies, private companies and for statistics and research purposes. It contains current address, gender, marital status, time and place of birth, time of death and information about any children and parents.

## OrtReg

The surgical database where all orthopaedic operations performed in the Skåne region public healthcare are registered is called OrtReg. The first part of the system collects all data surrounding any surgery, such as date, location, time spent in the operating room and numerous other variables. It also includes patient data, such as residential address, ASA grade, sex, age and more. It is continuously updated with information on current residential address and eventual death of the patients.

The second part contains information entered by the surgeon after each surgical procedure, with a number of mandatory fields depending on surgery type. Description of cartilage status according to ICRS grade, ACL/PCL visual status, meniscus tear type and location, knee stability evaluation, diagnostic codes according to ICD-10 and procedural codes according to NOMESCO.<sup>[77,79,211]</sup>

Most importantly, a detailed free text description about intraoperative joint findings, how the surgery was done and at the end a postoperative plan.

The system also contains a module for extracting statistical data on any type of orthopaedic surgery in the Skåne region. OrtReg is only in use by public healthcare orthopaedic clinics, there are no privately funded clinics included.

### **Swedish Social Security Agency (SSIA) database**

*Försäkringskassan*, the Swedish Social Security Agency, administers all economic social benefits in Sweden. In Sweden the system is constructed to reimburse the inhabitants that cannot work for the lost income during their period of illness. This renders a huge database on all reimbursed sick leave longer than 14 days, which is accessible to researchers. Sick leave shorter than 14 days is usually reimbursed by the employer but are in some cases (the individual being unemployed, on parental leave or studying) also included in the registry. About 76% of all people in the SSIA register belonged to the ‘employed’ group during the studied period. Self-employed persons are reimbursed according to different rules. The maximum number of reimbursed days are 364 in the majority of cases. It also includes disability payment, which we used as an exclusion criterion in Paper II.

The retrievable data includes date, length and cause (diagnosis) of each sick leave period, linked to demographic data on each individual. When analysing the data, it is important to keep track of any changes in regulations of reimbursement that has been implemented during the studied period, which may skew the statistics. Inhabitants in Sweden who cannot work, either because of illness or injury are entitled to compensation for reduced income counting from day 2 of a reported sickness period, and the degree of absence can vary between 25, 50, 75 or 100%.

### **Longitudinal Integrated database for labour market research (LISA)**

The “*Longitudinell integrationsdatabas för Sjukförsäkrings- och Arbetsmarknadsstudier*” (LISA) database includes data from a wide variety of sources and it is accessible to researchers through the government agency Statistics Sweden (SCB).<sup>[214]</sup> The data on occupation have a 95% completeness and education data is available for 98% of the population. Individuals are included from the age of 15. The data on occupation is classified according to the Swedish version of ISCO 88 (SSYK 96 (Standard för Svensk Yrkesklassificering 1996)) In my paper II we then used this to categorize the different occupations into 3 groups, “Light knee load” including mainly office work (occupational groups: 1–222, 224–244, 246–322, 324–346, 348–499), “Medium knee load”, what we considered to be light manual labour (occupational groups: 223, 323, 500–514, 516–599, 900–920, 922–930, 932–999) and finally

“High knee load” all occupations with knee demanding work, i.e. construction workers, firefighters etc. (occupational groups: 245, 347, 515, 600–899, 921, 931).

## **Melior and Orbit**

In the third paper, patient records were read in the system MELIOR (Siemens 1992©). This is the system for keeping all patient records on all the public hospitals in the Skåne Region. It also records ICD-10 diagnosis codes and includes scanned anaesthesiology documentation. It is updated regularly with information from the population register. ORBIT is the operation planning system used in Region Skåne, and from there data was collected only if it was incomplete in Melior.

## **The Skåne Region**

Skåne (*Scania*) is the southernmost region of Sweden with a population of 1.42 million inhabitants (Dec 2023) which is 13% of the total Swedish population. The population in the Skåne Region has been increasing gradually during the studied period of this thesis, from 1.13 million inhabitants in the year 2000, to 1.24 million in 2010 and finally 1.3 million in the year 2015.<sup>[210]</sup> Ten hospitals are distributed in the larger population centres, with seven of them performing arthroscopic knee surgery. Skåne covers an area of 11 000 km<sup>2</sup>. Its sociodemographic structure matches the rest of Sweden. A third of the population between 25–64 years of age has higher education.

## **Surgical methods**

A standard two portal approach was used, sometimes with added work portals if necessary. A tourniquet was used in almost all cases, and the surgery performed during general anaesthesia. During APM, any parts of the meniscus thought to cause symptoms was resected with a shaver or punch forceps through arthroscopic visualization. The aim generally being to resect as little meniscus tissue as possible.

Meniscus repair in Skåne during this time was mostly performed with all inside techniques. Up until 2011 both suture anchors and bioabsorbable arrows were used, later only suture anchors. Outside-in and inside-out techniques were used on anterior horn and vertex injuries. Prior to suture, the tear surfaces were abraded with a rasp. The addition of making small holes in the femoral notch with a Steadman peak, to introduce bone marrow into the joint, was also prevalent. This is thought to promote healing by the presence of stem cells.<sup>[55,215,216]</sup> Unfortunately this addition is often not specified in the surgical records. In a meta-analysis by Nepple *et al.* in 2022, only one study on meniscus repair consistently reported the use of this technique.<sup>[174]</sup>

# General study overview

The three studies in this thesis are based on register cohorts that have some overlap in both geographic area, time and inclusion criteria. Likely there is some patients that are included not only in two but even in all three studies. **Figure 11** depicts a summarized flowchart for all three studies, and **figure 12** attempts to visualize the temporal distribution and overlap of all the studied cohorts.

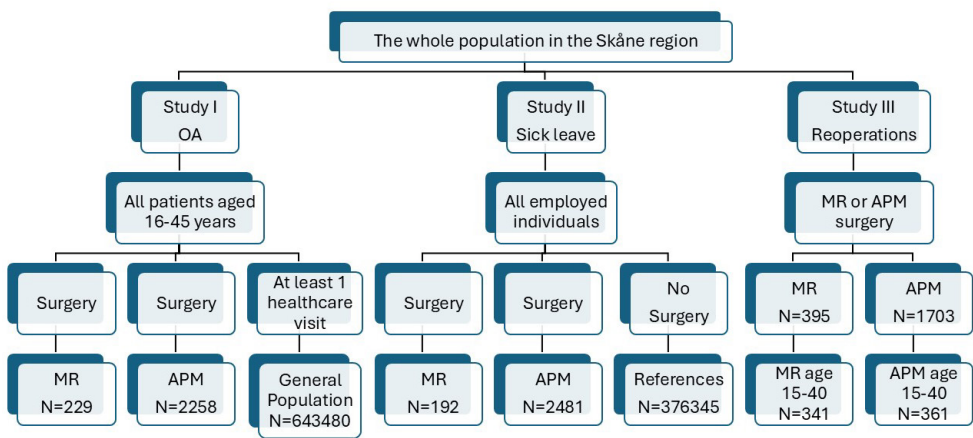


Figure 11. Summarized flowchart of all 3 studies. (© Fredrik Boric-Persson)

## Size and timeperiod of studied cohorts

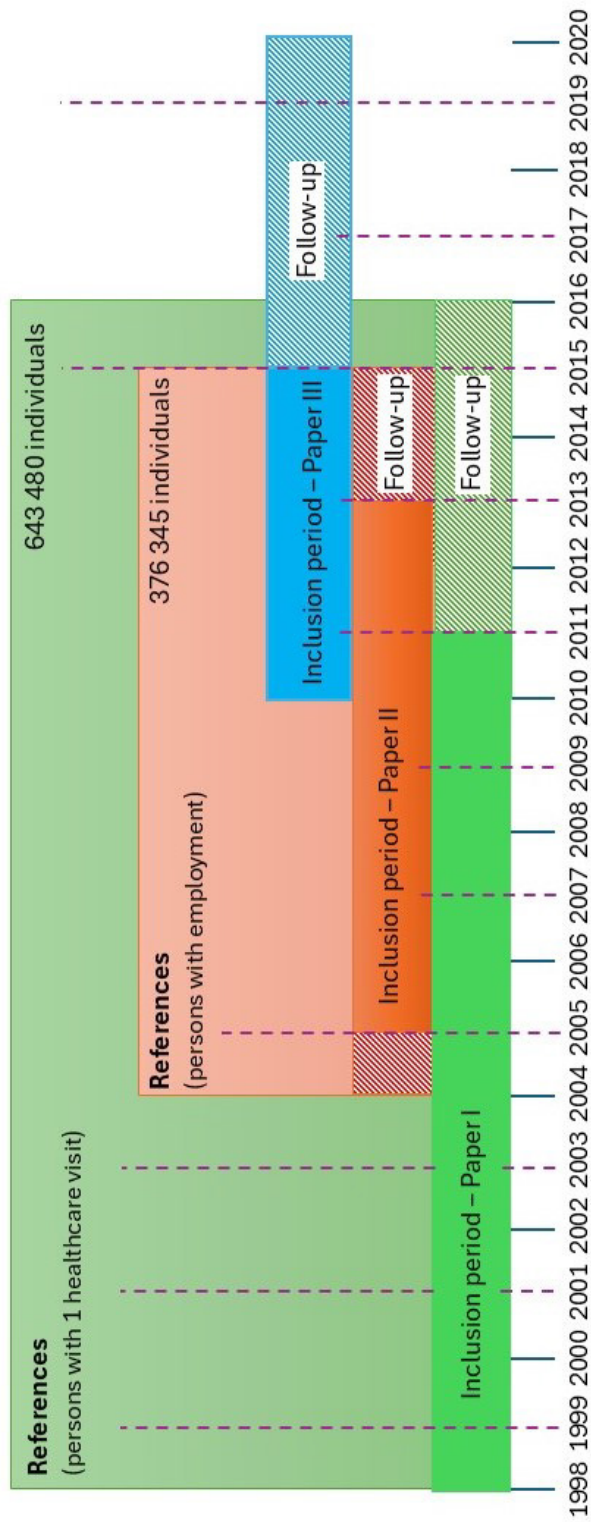


Figure 12. Overview of how the included cohorts of the thesis are related to each other in size and time.



## Design of Paper I

Using prospectively ascertained data from the SHR, we included all patients between 16 and 45 years old with a diagnostic ICD-10 code of S83.2 (Traumatic meniscus tear) and a registered surgical NOMESCO code for either APM (NGD01, NGD02, NGD10, NGD11, NGD12 and NGD19) or a code for meniscus repair (NGD20 and NGD21) or both (coding in **Appendix table 9**). When categorizing the patients where both APM and meniscus repair were performed in the same knee, we envisaged that a concomitant APM will reduce meniscus knee cartilage coverage, increase contact pressure and these knees would fit best in the APM group when studying the risk of knee OA development.

The upper end of the age interval, 45 years, was chosen to limit the number of patients with incipient knee OA at inclusion date.

Inclusion period was set to 1998–2010 to allow for a minimum of 5 years follow-up. Patients with a concomitant fracture in the knee, knee OA and undefined meniscus surgery were excluded (**figure 13**). We also excluded anyone with a reoperation within 14 days, as this could be an indication for surgical complications.

Patients having repeated knee surgery during follow-up was kept included in their original group, regardless of type of new surgery.

In order to relate the rate of knee OA after meniscus surgery to the normal population, we created a reference cohort consisting of all individuals of the same age and in the same region, that had consulted the healthcare at least once, for any reason except meniscus injury or knee OA.

### *Outcome definition*

We defined the outcome as having consulted with a public healthcare physician and receiving a diagnostic ICD-10 code of knee OA (any code M17.1 through M17.9, **Appendix table 12**). All patients were followed from inclusion until receiving a knee OA diagnosis, relocation outside the Skåne region, death or end of study period, whichever came first.

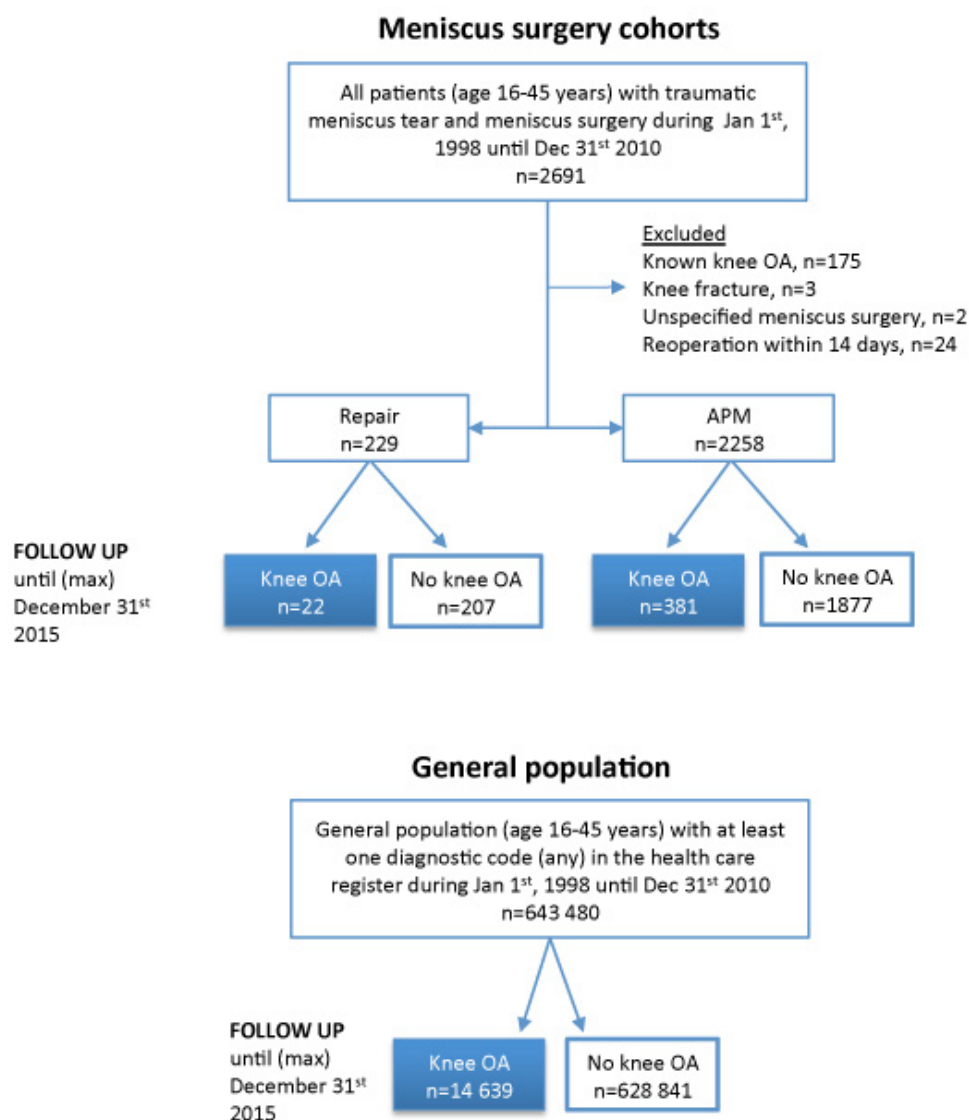
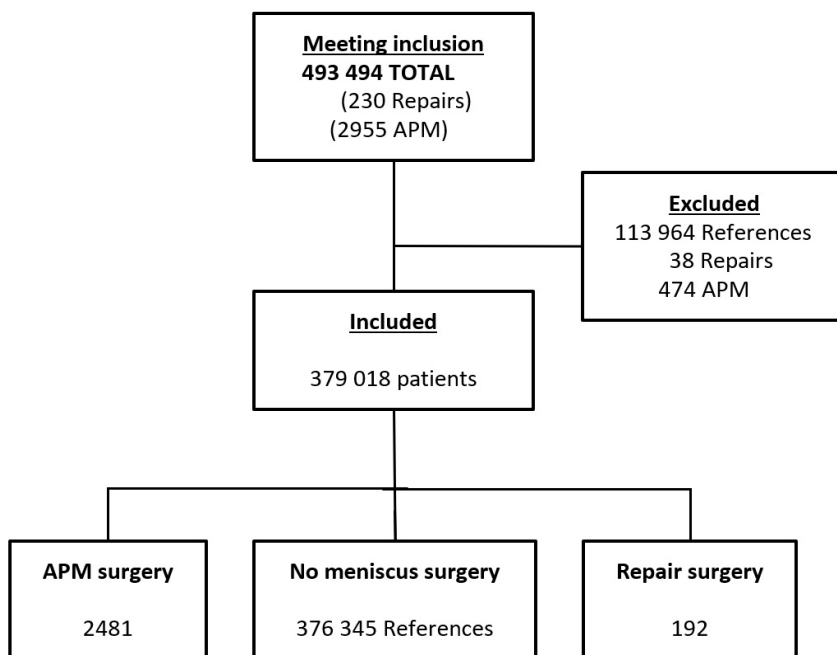


Figure 13. Flowchart of study I. (© Fredrik Boric-Persson)

## Design of Paper II

We first included all registered inhabitants in Skåne between age 19 and 49 years old with at least one healthcare visit. Of these, all patients with a surgical code in the SHR for meniscus repair was grouped into the Repair group, and all patients with a code for APM was grouped in the APM group, flowchart seen in **figure 14**. The date of first surgery was the index date. The remaining patients without any meniscus surgery was included in the control group. Here we randomly sampled one healthcare visit date as index date. Study inclusion period was January 1, 2005 until December 31, 2012.

Selection of study period was dictated by the availability of register data between 2004–2014 from SSIA and the change in reimbursement rules in 2004 which precluded earlier inclusion. Patients with both APM and meniscus repair surgery at index were considered as meniscus repairs, as the presence of any sutures would dictate the postoperative regimen.



**Figure 14.** Flowchart of study inclusion and exclusion process in paper II. (© Fredrik Boric-Persson)

We then excluded, from all groups, all patients diagnosed with any of the following during 4 years prior to inclusion date: fracture in the knee (ICD-10 code S82.1, S82.9, S72.4 and S72.9), dislocation of knee (ICD-10 code S83.1), rupture of MCL/LCL (ICD-10 code S83.4), diagnosis of knee OA (ICD-10 code M17.1–M17.9), previous meniscus surgery (NGD00–NGD99). Also excluded were all

patients without any employment, those with disability pension (at the surgery/index date) and anybody with ongoing sick leave for the whole year before surgery/index date. Further we excluded patients from the surgery group with other concomitant meniscus surgical codes at index date as well as patients with diagnosed knee OA. The latter would probably be disqualified for a meniscus repair, making the APM and meniscus repair group less comparable.

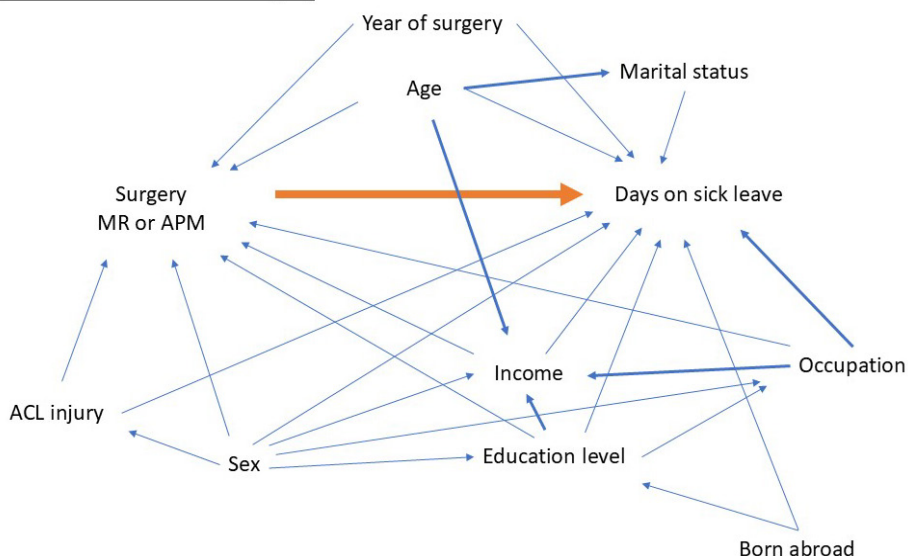
### *Outcome definition*

The primary outcome measure was a binary variable defined as having any sick leave longer than 14 days during the initial 2 years after index surgery, for any cause. The second outcome was number of net days on sick leave for any cause, during the first two years after surgery. Any day on partial sick leave was rounded up and counted as 1 full day of sick leave. Only periods longer than 14 days could be measured.

Many factors influence an individual's propensity to be on sick leave, other than type of knee injury and surgery.<sup>[217]</sup> In designing the study, a Direct Acyclic Graph (DAG) was constructed to envisage possible confounders that could be adjusted for (figure 15).

Whether a tourniquet was used or not during surgery was not considered a confounder affecting sick leave duration or length of rehabilitation.<sup>[218]</sup>

### **DAG Sick Leave and meniscus surgery**



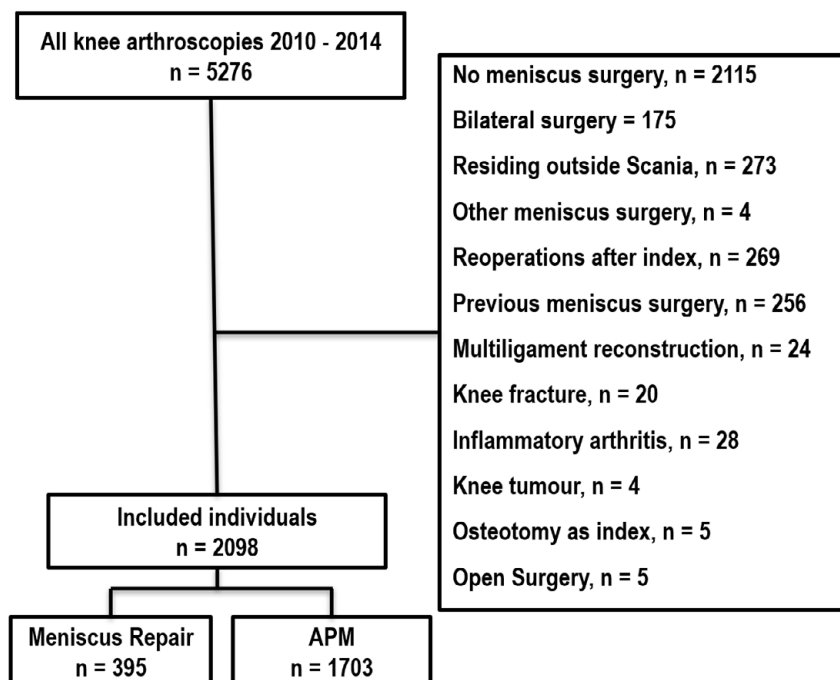
**Figure 15.** Factors that might influence the outcome, Paper II. (© Fredrik Boric-Persson)

### Design of Paper III

In the third paper we included all patients above age 14 with arthroscopic meniscus surgery registered in the OrtReg database between 2010-01-01 and 2014-12-31 at any of the three hospitals of Lund, Malmö and Trelleborg. These three hospitals have a shared orthopaedic clinic, and during the period, very few meniscus sutures were performed at other hospitals in Skåne. Patients not residing in Skåne during the whole follow-up period were excluded, as well as those with previous meniscus surgery in the index knee or with any of a number of prespecified knee conditions listed in **figure 16**. Data regarding reoperations and complications after index surgery were collected from the whole Skåne region.

All patients were followed until death or end of study 2019-12-31.

ACL injury and knee OA did not warrant exclusion but were treated as confounders in the analysis. If a patient had both APM and meniscus repair in the same knee, they were analysed in the meniscus repair group. In the case of bilateral meniscus surgery, the first knee registered was chosen only.



**Figure 16.** Flowchart of study inclusion and exclusion process in paper III. (© Fredrik Boric-Persson)

### Outcome definition

Primary outcome was defined as any reoperation in the index knee during follow-up, and secondary outcome as a reoperation in the same meniscus (medial or lateral) as treated at index. Complications were defined as any adverse event that required treatment and could be plausibly linked to the knee surgery. A period of 1 year postoperatively was chosen to include also slowly evolving conditions like arthrofibrosis and osteonecrosis.

### Secondary aim subgroup

In an attempt to compare reoperation-rates and frequency of surgical complications between APM patients and those with meniscus repair, a subgroup was constructed from patients aged 15–40 years with either bucket-handle, longitudinal or horizontal meniscus tears, as these at least in theory would all be eligible for a meniscus repair.

Before deciding on variables for the adjusted regression analysis, a DAG was constructed to envisage the relations of possible confounders, **figure 17**.

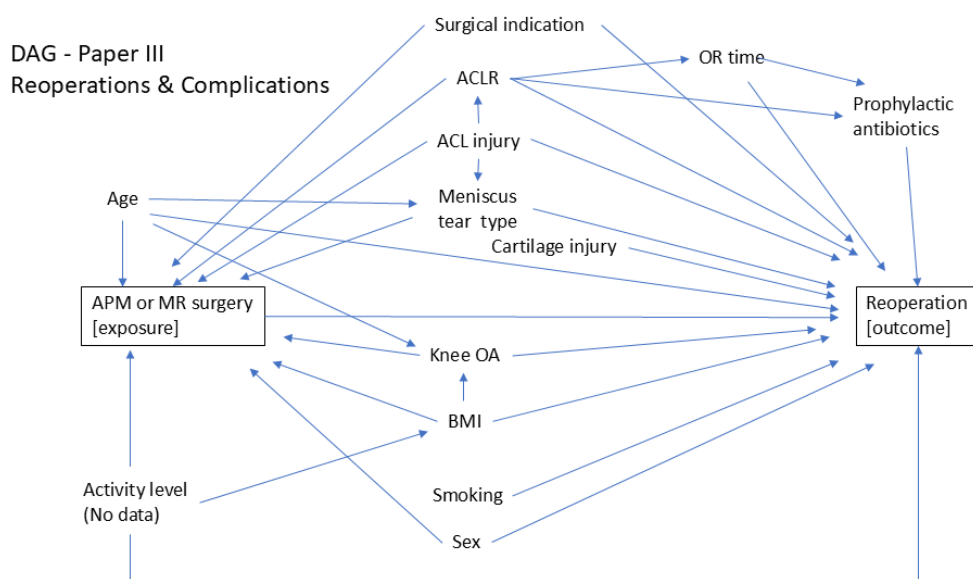


Figure 17. Possible confounders that influence the outcome, Paper III. (© Fredrik Boric-Persson)

ACL unstable knees exert an increased strain both on sutured and un-sutured menisci, and previous studies have indicated that meniscus repair in conjunction with ACLR might yield better healing-rates.<sup>[193,219]</sup> We therefore categorized all knees regarding their anteroposterior stability at index surgery into three groups:

Group 1 included stable knees at preoperative examination, either with a normal ACL or a previous ACLR. In group 2 were knees graded as unstable at preoperative examination, either with a current ACL tear or previous ACLR. The third group was comprised of knees with concomitant ACLR at index surgery.

As ACLR entails both graft harvesting, additional incisions, bone tunnel drilling and results in extended surgery time; the frequency of complications and reoperation-rates were also analysed separately for these groups.

### *Surgical data entry*

Each patient record in Melior was read, first scanning all ICD10-codes for any codes relating to knee complications, knee OA or other knee conditions that would lead to exclusion. This was all entered into a secure Excel spreadsheet.

Then all outpatient and inpatient journals for the years before and 2 years after the index surgery were read, scanning for information about the index knee and complications, previous surgery and any exclusion criteria. Here also information about smoking was collected.

Finally, the OrtReg surgical records free-text fields were read, to gather further information about the knee and the meniscus surgery, not already coded into the OrtReg database. Here the data was also doublechecked to see if the surgery described was consistent with registered surgical codes and diagnosis. Data about suture type and number of sutures was also collected.

## **Statistical analysis**

In Paper I a Cox proportional hazard regression model was used, in which we adjusted for confounders, to calculate the hazard ratio (HR) with 95% confidence intervals (CI). We then also used a method by Lin *et al.* to perform a bias analysis to evaluate the prevalence and strength of an unmeasured confounder (U, representing bias by indication) needed to explain our point estimates of the HR if there was no association between surgery type and incident knee OA.<sup>[220]</sup>

The analysis was adjusted for patient gender, as both knee OA and meniscus injuries show sex specific prevalences. We also adjusted for patient age, since prevalence of OA increases with age. Further we adjusted the model for ACL injury which is associated with knee OA development. Under the assumptions that knee OA is a slowly progressing disease, that might have been present and undiagnosed in the knee before surgery, and that a presumed traumatic meniscus tear could be the first

sign of knee OA, we also made analyses excluding all patients with early knee OA diagnosis within both 1, 2 and 3 years postoperatively.

In Paper II logistic regression and the method of standardization was utilized when computing the risk ratio and risk differences of being on sick leave. My co-worker then fitted a negative binomial model with robust standard errors to estimate the ratio of mean number of days on sick leave between groups on sick leave. Both regression models were adjusted for confounders.

The models were adjusted for possible confounders that were available, namely age, gender, income, level of education, marital status, if born in another country and finally it was adjusted for presence of ACL injury at index date, as this injury will potentially prolong any sick leave period.

For the first aim in Paper III, we calculated incidence rates of reoperations per 1000 person-years and reported 95% CI with jackknife confidence intervals derived with function `stptime` in Stata.<sup>[221,222]</sup>

For the comparison between meniscus repair and APM reoperation-rates in the second aim, we used flexible parametric survival models (with 2 degrees of freedom) and adjusted for potential confounders, with first reoperation as outcome. Both models were adjusted for possible confounders: age, gender, meniscus tear type, knee laterality, BMI, cigarette smoking, meniscus operated on (medial, lateral or both) and knee stability. Following this, we performed a separate analyses to determine if patient gender or ACLR had any influence on rates of reoperation either for all causes or specifically reoperation in the same meniscus.

My co-worker performed statistical analyses using Stata Statistical Software versions 13 and 18 (Stata-Corp. 2021. College Station, TX: StataCorp. LLC.). I used IBM SPSS version 22 and 26, (New Orchard Road, Armonk, New York, United States).



# Ethics & Funding

## **Ethical permissions**

The studies were approved by the regional ethics committee at the University of Lund and were conducted in accordance with the Declaration of Helsinki 1975, as revised in 2000. The studies were ethically approved by the following permissions: IRB\_2011-432, IRB\_2011-432 with addendum 2018-233, IRB 2016-873 and IRB 2019-02850 where two of them were written by the author and the others by my supervisors.

For the paper utilizing patient journals, an opt-out design was allowed, and information about this was published on the university web page and in the regional newspaper. Permissions for entry into OrtReg and Melior journals were obtained by the KVB-board (Kvalitetsregister, Vårddatabaser och Beredning) permission number: KVB 223-20.

All data was pseudonymized and were stored and analysed in the secure research cloud at the university of Lund, LUSEC.

## **Funding**

A large portion of the funding was a series of PhD-student grants from Södra Sjukvårdsregionen.

Other funding was, in alphabetical order:

- Governmental Funding of Clinical Research within National Health Service (ALF) and the Faculty of Medicine, Lund University, Sweden.
- Greta and Johan Kock foundation
- Swedish Research Council
- The Swedish Rheumatism Association
- Österlund Foundation

The funding sources were not involved in the design or conduction of the studies.

# Results

## Paper I: The risk of posttraumatic OA

Throughout the follow-up, median 10 years, we observed 411 cases of doctor diagnosed OA, 22 in the meniscus repair group and 381 in the APM group. The meniscus repair group comprised 9.2% of the patients and were a mean 7 years younger than the patients in the APM group. If patients had both APM and meniscus repair surgery, they were categorized as APM in the analysis.

The absolute risk of having consulted for knee OA during the study was 10.0% after meniscus repair, 17% after APM and 2.3% in the general population. Standardized to the general population, the consultation rate for knee OA was 42 per 10,000 person-years (95% CI 12, 71) in the meniscus repair group, 118 per 10 000 person-years (95% CI 101, 135) after APM, and 20 per 10 000 person-years (95% CI 19.9, 20.1) in the general population (19.6 (95% CI 19.2, 20.1) in women and 20.9 (95% CI 20.5, 21.5) in men).

When comparing meniscus repair versus APM, the crude hazard rate for consulting for knee OA after surgery was 0.61 (95% CI: 0.40, 0.94). Adjustment for age and sex yielded a HR of 0.74 (95% CI 0.48, 1.15), and further adjustment for concomitant ACL-injury left it almost unchanged at 0.74 (95% CI 0.48, 1.14).

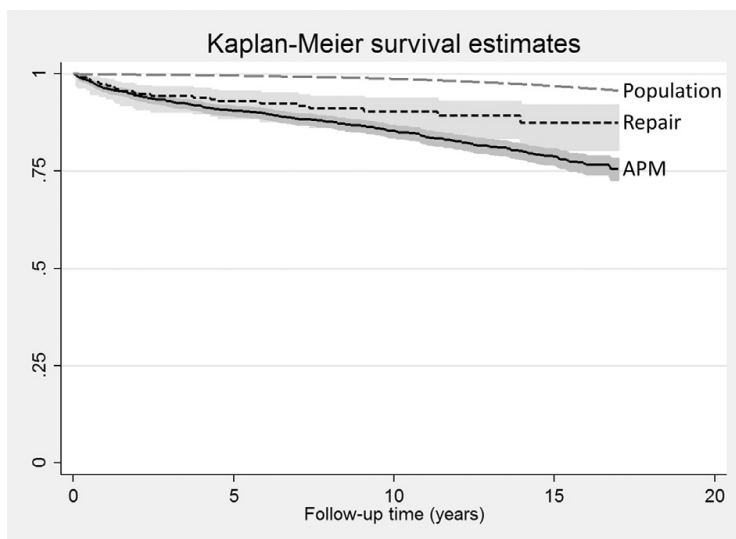
Attempting to exclude incipient OA present at time of surgery, we also examined the cohort while excluding cases with OA within 2 years post-surgery. Remaining were 10 (4.6%) knee OA cases in the meniscus repair group and 264 (12.4%) knee OA cases in the APM group. This yielded a hazard rate for knee OA (meniscus repair versus APM) of 0.51 (95% CI 0.27, 0.96). The HR adjusted for age and sex when comparing meniscus repair vs APM was 0.50 (95% CI 0.27, 0.96).

**Table 5.** Occurrence of doctor-diagnosed knee OA during follow-up

	Meniscus Repair	APM	Meniscus repair and APM	General Population
	N = 229	N = 2,258	N = 2,487	N = 643,480
Follow-up time in years, median (range)	9.4 (0–18)	11.1 (0–18)	10.3 (0–18)	11.2 (0–18)
Knee OA, n (%)	22 (10)	389 (17)	411 (17)	14,639 (2.3)
Crude consultation rate of knee OA, per 10 000 person-years (95% CI)	102 (67, 155)	165 (149, 183)	160 (145, 176)	20.0 (19.9, 20.1)
Standardized* consultation rate of knee OA, per 10 000 person-years (95% CI)	95 (46, 144)	164 (144, 183)	160 (142, 179)	20.0 (19.9, 20.1)

\* Age- and sex-standardized to the general (healthcare seeking) population aged 16–45 years.

Doing multiple sensitivity analyses did not change the results in any material way, giving HR values between 0.50 and 0.83 when adjusting the Cox regression analysis for various inclusions and exclusions among age groups, surgery date and follow-up period. In doing a bias analysis, we found that the effect of an unmeasured cofounder that would significantly alter the results, if present in at least 50 percent of patients, then needed to be 4 times more prevalent in one group and increase the risk of OA by a factor of 2. Of the meniscus repair patients 32% had an APM during the follow-up period while the proportion was 14% after APM. The second most common diagnosis at index surgery was that of an ACL injury.

**Figure 18.** Survival estimates for doctor-diagnosed knee OA among persons aged 16–45 years in patients after APM, meniscal repair or in the general population. 95% CI indicated by shaded areas.

## Paper II: Sick leave

The study included 379 018 individuals, comprising of 192 with meniscus repair, 2481 with APM and 376 345 from the general population in Skåne. The amount of sick leave was measured for 2 years after surgery and only periods longer than 14 days could be measured.

The meniscus repair group had the largest amount of sick leave with 55% having any sick leave. Mean number of days was 55 (SD 77). In the APM group 43% had any sick leave and mean number of days was 37 (SD 86) days. For reference, in the background population 17% were on any sick leave in the corresponding period.

Only measuring patients with reported sick leave, the sick leave was on average 37% (95%CI 15%, 64%) longer after meniscus repair than after APM.

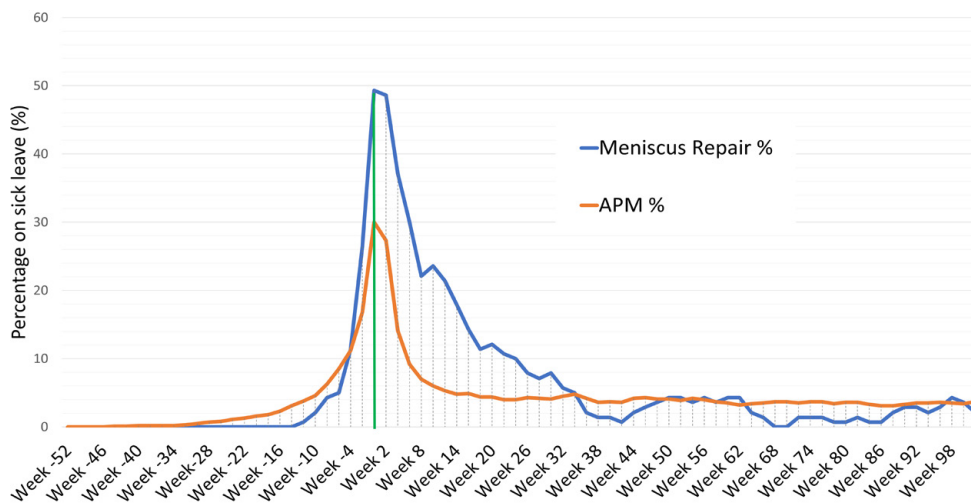
Adjusted risk ratio when comparing meniscus repair to APM was 1.8 (95% CI 1.4, 2.1) with a risk difference of 0.13 (95% CI 0.07, 0.19). The adjusted risk ratio of being on sick leave during the two years after surgery in the meniscus repair group was 3.6 (95% CI 3.3, 4.0) and had a risk difference of 0.45 (95% CI 0.38, 0.51) compared to the general population.

The similar comparison for APM versus the general population yielded a risk ratio of 2.6 (95% CI 2.5, 2.7), and risk difference 0.27 (95% CI 0.25, 0.29).

**Table 6.** Adjusted risk difference and risk ratio of being on sick leave after meniscus repair versus APM and ratio of mean days on sick leave for persons with sick leave

Model	Risk difference (95% CI)	Risk ratio (95% CI)	Ratio of mean days on sick leave (95% CI)
Adjusted for age, sex, income category, if born abroad, occupational group	0.15 (0.08, 0.22)	1.8 (1.5, 2.2)	1.37 (1.15, 1.64)
Additionally adjusted for ACL rupture diagnosis	0.12 (0.05, 0.19)	1.3 (1.1, 1.5)	1.25 (1.06, 1.49)
Additionally adjusted for concomitant ACL reconstruction	0.13 (0.05, 0.20)	1.3 (1.1, 1.5)	1.25 (1.05, 1.48)

Measuring if there was any difference in sick leave attributed to sex, the adjusted analysis indicated a small difference but with largely overlapping confidence intervals. The calculated risk difference for being on sick leave in the meniscus repair group versus the APM group was 0.15 (95% CI 0.07, 0.22) for men and 0.10 (95% CI 0.00, 0.20) for women.



**Figure 19.** Percentage of patients with only meniscus surgery (without any ACL-surgery) on sick leave per week from 1 year before to 2 years after surgery.

After meniscus repair the percentage of patients on sick leave was higher, but after 35 weeks fell to a lower degree than APM. The APM group had less sick leave and shorter duration, but after 3 months the curve levelled out and stayed at between 4% and 5% for the whole measured period.

## Paper III: Reoperations and complications

Out of 2717 patients with arthroscopic meniscus surgery in Skåne between 2010–2015, 2098 patients met inclusion criteria. The mean age was 39.0 years and women comprised 33.4%. At first surgery date (index date) 62.6% had a stable knee, 20.1% had an ACLR together with the meniscus surgery, and a bucket-handle tear was the most common tear type, present in 31.0%. All the groups had similar BMI, ASA grade and 35.9% had any signs of knee OA.

Total follow-up time was 13 624 person-years to first reoperation and 16 081 person-years in total. Incidence rate of first reoperation was 32/1000 person-years (95% CI 29, 35) and when allowing for multiple reoperations, the reoperation-rate was 34/1000 person-years (95% CI 31, 37). Measuring the rate of reoperations to the same meniscus, including any TKA, it was 19/1000 person-years (95% CI 17, 21). Postoperative complications arose after a median of 26 days (range 6, 135) from index surgery, and the proportion of postoperative complications within 1 year from index surgery was 2.1% (95% CI 1.6, 2.9) and included 29 patients in the APM and 16 in the meniscus repair group.

**Table 7.** Reoperations and complications

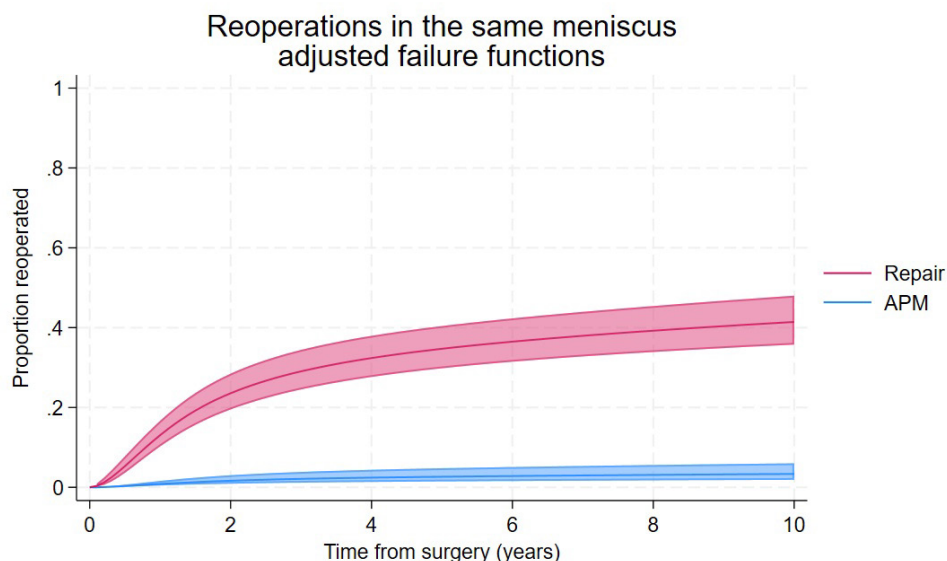
	Whole cohort of 1703 APM & 395 repairs	Subgroup 15-40 years	
		APM	Meniscus repair
<b>Patients with 1 reoperation, N(%)</b>	337 (16.1)	48 (13.3)	119 (34.9)
<b>Patients with 2 reoperations, N(%)</b>	80 (3.8)	9 (2.5)	43 (12.6)
<b>Patients with 3 reoperations, N(%)</b>	9 (0.4)	1 (0.3)	1 (0.3)
<b>Patients with 4 reoperations, N(%)</b>	4 (0.2)	0	1 (0.3)
<b>Total number of reoperations, N</b>	540	69	212
<b>Total number of reoperated patients, N(%)</b>	430 (20.5)	58 (16.1)	164 (48.1)
<b>Number of complications, N(%)</b>	47 (2.1)	8 (2.2)	15 (4.4)
<b>Number of complications in patients without concomitant ACLR), N(%)</b>	25 (1.5)	2 (0.6)	5 (.1.5)

### Subgroup age 15–40 years with bucket-handle, longitudinal and horizontal tears

For the second aim of comparing meniscus repair and APM outcomes, 702 patients with 361 APM surgeries and 341 meniscus repair surgeries was selected. Calculating the incidence rate of reoperation for all causes, it was found to be 105/1000 person-years (95% CI 90, 122) in the meniscus repair group and in the APM group it was 24/1000 person-years (95% CI 18, 31).

When comparing meniscus repair with APM, the crude HR was 3.8 (95% CI 2.8, 5.1) and when adjusting for available confounders it rose to 4.3 (95% CI 3.1, 6.0). Over time the adjusted estimated reoperation proportions stabilized at around 5 years after index surgery at 46% (95% CI 42, 52) in the meniscus repair group, and 15% (95% CI 11, 18) in the APM group. This meant a difference in reoperations at 5 years of 32% (95% CI 26, 39).

We found that 126 of the patients with meniscus repair at index had new meniscus surgery on the same sutured meniscus. Out of these, 7 lateral and 10 medial menisci had new sutures placed at the reoperation. Only 11 of the patients with APM had new surgery on the same meniscus as treated at index surgery. This yielded a rate of reoperation in the same meniscus of 68.3/1000 person-years (95% CI 56.6, 82.8) in the meniscus repair group and 4.0/1000 person-years (95% CI 2.2, 7.8) in the APM group. When comparing the meniscus repair group with the APM group, the crude HR of getting a reoperation in the same meniscus was calculated to 15 (95% CI 8, 28). When adjusting for all covariates, the HR was found to be 17 (95% CI 9, 31).



**Figure 20.** Same meniscus reoperation 15–40 years. The (adjusted) proportion reoperated in each group and their difference over time.

Looking at the adjusted marginal proportion reoperated in the same meniscus at 5 years after index surgery, it was 34.7% (95% CI 29.8, 40.4) in the meniscus repair surgery group and in the APM surgery group it was 2.6% (95% CI 1.5, 4.8). This was equivalent to a difference in proportion reoperated of 32.1% (95% CI 26.5, 37.6).

Comparing medial versus lateral reoperations for all causes, the proportion of reoperated at 5 years differed between meniscus repair and APM with 37% (95% CI 29%, 45%) on the medial side and 26% (95% CI 10%, 41%) on the lateral side. Comparison of same meniscus reoperation-rate was only possible within the meniscus repair group. It was 80/1000 person-years (95% CI 63, 101) in the medial meniscus and 57/1000 person-years (95% CI 38, 88) in the lateral meniscus. When both menisci were repaired, it was 46/1000 person-years (95% CI 28, 81). The HR of reoperation in the same meniscus was 1.53 (95% CI 0.97, 2.43) when comparing the medial meniscus to the lateral meniscus.

## Reoperation gender differences

When comparing between men and women, the unadjusted HR of reoperation was 0.65 (95% CI 0.56, 0.82) and this was virtually unchanged when adjusting for age. When adjusting for all covariates, the resulting HR of reoperation was 0.61 (95%

CI 0.47, 0.80) and the equivalent difference in proportion reoperated at 5 years was -8.5% (95% CI -13.4, -0.3.6), with men having less reoperations.

### **ACL-status and ACL-reconstructions in cohort 15–40 years old**

When including all causes for reoperation, the percentage with a reoperation among meniscus repairs with concomitant ACLR surgery was 43.3% (75 patients out of 173). For meniscus repair without ACLR at time of index, it was 53.0% (89 patients out of 168). The incidence rate of reoperation in the same meniscus after meniscus repair was 82 (95% CI 62, 109) per 1000 person-years in stable knees, 82 (95% CI 54, 123) in unstable knees and 57 (95% CI 44, 74) in knees with concomitant ACLR.

An analysis comparing APM and meniscus repair was only possible for the outcome reoperation for all causes, where we found that ACL-status at index surgery seems to modify the association of meniscal repair versus APM with reoperations on both a relative and an absolute scale. The HR of interaction was 0.31 (95% CI 0.14, 0.73) for concomitant ACLR and for unstable knees it was 0.67 (95% CI 0.28, 1.64).

The difference in proportion reoperated between meniscal repair and APM group at 5 years was 32% (95% CI 23, 41) in the stable group, 51% (95% CI 37, 65) in the unstable group and 22% (95% CI 12, 32) in the ACLR at index group.





# General Discussion

In quantitative research there is always a need to simplify and categorize examined cases. No two knees are identical, nor the individuals they are attached to, adding to that the meniscus tear location, tear size and tear type, that shows an endless variation if measured down to fine detail. Combine it with various ligament and cartilage injuries at or before the measured study event, the definition of the studied group needs to be broad to collect enough patients to measure anything with quantitative statistical methods.

There is a growing body of evidence that total meniscectomy or APM both leads to an increased risk of developing knee OA both compared to meniscus repair and to no surgical treatment.<sup>[34,84,87,185,195,223,224]</sup> But the still unanswered question is: does treating a meniscus tear with meniscus repair produce better results than physiotherapy alone, regarding knee OA development, length of sick leave and risk of future surgery? This is probably true when it comes to dislocated bucket-handle tears, root tears and complete radial tears, that abolishes the load distributing properties of the meniscus, but harder to prove in other types of more benign meniscal tears.

Are we doing to many meniscus surgeries and should we try to repair all menisci? The percentage of meniscus injuries that are deemed suitable for repair keeps rising.<sup>[130,135]</sup> Are we now still repairing too few menisci, or too many? And is it the right patient group we are operating on, both in terms of type of injury, as well as age-group?<sup>[225]</sup> Can we select certain patient subgroups where to say that a meniscus repair is not worth the risks, or should we always try in all patients?

The percentage of reoperations after meniscus repair shows highly variable results (5–48%) and studies on repairs with modern implants range closer to 20–30% with more than 5 years of follow-up.<sup>[159,174,193]</sup> I found a slightly higher rate of same meniscus reoperations in Paper III; our long follow-up could have influenced this.

Though not novel to examine the reoperation-rates after meniscus repair and APM, there is still a need to repeat such studies, since there is a disparity in the published results.<sup>[198]</sup> Indeed, there is a growing awareness of the need for repeating medical studies.<sup>[226,227]</sup>

This thesis aims to provide added insights into the postoperative consequences of meniscus repair and APM.

## What is *successful* meniscus surgery?

Is it the absence of a reoperation? Or the quick return to sports on the same level (with risk of a new knee injury)?

In the early days of open meniscus surgery, the indication for surgery was a locked knee and the definition of success was the restoration of knee range of motion and the absence of surgical-site complications.<sup>[146,148]</sup> Later the goal was alleviating pain through removal of the whole meniscus, then gradually changed to removal of only the injured parts. We are currently faced with the challenge of balancing short-term and long-term outcomes, which can occasionally conflict with one another.<sup>[228]</sup> The athlete with a promising career wanting to minimize his absence from training or individuals with manual labour and a low income, not being able to afford work absence, might favour an APM to hasten recovery despite worse outcomes in the long-term.

A shorter period of sick leave (Paper II) and reduced rates of reoperations in the medium-term (Paper III) implies that APM is more successful in the short-term while less so in the long-term, with the increased rates of knee OA concluded in Paper I.

Despite better healing-rates with modern meniscus repair techniques, neither repair nor APM restores the patients knee function and their symptoms to preinjury levels on a group level.<sup>[180,229–231]</sup>

Are all reoperations after meniscus surgery a bad thing? Some reoperations are planned secondary ACLR. A suboptimal meniscus repair that receives an APM a few years later, with perhaps a less extensive resection, might that anyway offset the risk of OA progression?<sup>[232]</sup> Is that enough to counteract the negatives of a second surgical knee inflammatory trauma, a period of postoperative recovery and any risk of complications after surgery?

Looking at APM and the same meniscus reoperation-rate in paper III, the question arises if sometimes more meniscus tissue should have been excised at the start, to decrease the risk of reoperation? But increased resection will probably lead to increased cartilage wear.<sup>[88,91]</sup> Or should it instead have received physiotherapy with a likely reduction of symptoms over time and never had any meniscus surgery in the first place?<sup>[165,166,233,234]</sup> Previously, an APM for a degenerative meniscus with symptoms in an osteoarthritic knee, was thought to alleviate symptoms and postpone TKA surgery, but several studies have found no clinical effect or worsening of outcomes.<sup>[89,168,235,236]</sup>

## Can you really compare APM and meniscus repair?

Can you really compare APM and meniscus repair using observational data? And is it possible to construct an RCT with the present paradigm of repairing the meniscus whenever possible, with a steady increase in the proportion selected for meniscus repair? In theory all surgeons adhere to the same selection criteria for APM vs meniscus repair, but the resulting treatment decision is not predictable.<sup>[237]</sup> Dadoo et al found that females as well as patients from areas with an increased neighbourhood disadvantage had increased odds of being selected for APM over meniscus repair.<sup>[238]</sup> Is there a patient preference for any surgical method? Faster return to work or to sports with APM has been shown in studies and in Paper II.<sup>[145,229,239]</sup> What kind of surgeon do you meet? Different knee surgeons opted to treat patients with meniscus lesions very differently.<sup>[237]</sup>

It is well established that both knee injury and total meniscectomy increases risk of knee OA.<sup>[80,81,137]</sup> It is harder to prove in comparative studies that APM and meniscus repair differ in the rate of posttraumatic OA, since there is inclusion bias here in the form that primary more “malign” meniscus injuries likely will get an APM. To what extent is the long-term outcome decided at time of injury, rather than by choice of surgical method – perhaps more depending on type of tear, cartilage injury and associated injuries?<sup>[240–242]</sup> This, together with the patient’s inherent knee tissue quality and neuromuscular training state, might affect both short- and long-term outcomes? Menisci of better quality, (meniscus biologic age vs meniscus chronologic age) will be the ones chosen for repair over APM and could explain at least part of the difference seen in Paper I. In the absence of significant mechanical obstruction, it would be interesting to further compare meniscus suture repair with just leaving the meniscus alone, when feasible. Studies on PROMs comparing meniscus repair and APM without a concomitant ACLR, have often failed in demonstrating better function or less pain in the group of meniscus repair patients.<sup>[180,239,243]</sup>

There is a sound theoretical framework for restoring the meniscus integrity in preventing future symptoms and knee OA, but not many studies comparing physiotherapy to meniscus repair in the long term. Here long-term follow-up of studies like the DREAM-trial will be useful. Now that the use of knee MRI has reduced the need for purely diagnostic arthroscopies, even the low complication rates we see in modern arthroscopic meniscus surgery warrants a significant improvement with surgical over non-surgical treatment. Both to justify it in complication-risks to the patient as well as the surgical resource consumption in a healthcare system with declining resources. The fact that also patients in the non-operative groups had registered serious complications during the timeframe of the studies should be noted.<sup>[165,166]</sup>

Most interesting would be to compare large numbers of specific isolated meniscus tears i.e. flap tears, minor radial tears (in the white zone) or longitudinal tears, with operative or non-operative treatment. In Paper III we saw that several knees with primary APM go on to have a second APM for symptoms of knee pain or subjective sensation of knee catching, but we have no proof that this repeated surgery relieved the symptoms either, indeed even the first surgery might have been based on an inaccurate surgical indication.<sup>[166,170,244–251]</sup>

In Paper III we registered knee OA being present at index as a confounder of the results, not specifying if this was posttraumatic OA or primary OA. In patients with previous ACL-injury or surgery, posttraumatic OA at index likely is more prevalent. It would be interesting to record the incidence of knee OA found at reoperations in the cohort and extract diagnoses of knee OA from the SHR during follow-up.

## New injuries or late consequences?

There is clinical experience that the more successful the surgery, the more strain the patient will expose the knee for again, with increased risk of new injuries, or a repair failure.<sup>[252,253]</sup>

It can be difficult in studies with a long-term follow-up to monitor for new knee injuries and distinguish if an episode is sufficient to cause a new meniscus tear or it was just making any non-healed meniscus symptomatic. The pragmatic way is to include also new injuries and any subsequent reoperations as a meniscus surgery failure.

In all three papers, an argument can be made that degenerative changes present before the meniscus injury, as well as cartilage injury sustained at the time of meniscus tear have an effect both on post-surgical OA, postoperative sick leave and reoperation-rates and suture survival. In Paper I we did a sensitivity analysis where we excluded cases with OA diagnoses in the first 1, 2 or 3 years following the surgery. In paper II we excluded patients with a previous diagnose of knee OA or other knee injuries apart from the meniscus tears and ACL injuries. In Paper III we adjusted the models for other knee injuries and knee OA as well as excluded patients with previous meniscus surgery.

## Surgical or non-surgical treatment?

### To many or not enough?

Surprisingly little is known about the *natural* healing-rate of traumatic meniscus tears in otherwise healthy knees.<sup>[136]</sup> With surgeons readily available for meniscus surgery, it is difficult to study a cohort of patients not having any treatment, and the question remain unanswered how many *asymptomatic* younger people that have minor meniscus injuries and later heal without any treatment. As for symptomatic tears, limited evidence supports non-operative treatment in some cases.<sup>[162–166]</sup>

The initial process of selecting patients for surgical treatment of a meniscus tear is limited to those individuals who seek medical attention, since only these individuals can be considered for surgery. The second filter is getting the correct diagnosis and a referral to an orthopaedic surgeon.<sup>[254]</sup>

The severity of patient symptoms will affect the willingness and decision to receive any offered meniscus surgery, not only meniscus tear morphology findings on an MRI. The patient's tolerance for pain and attitude towards surgery will affect the decision, perhaps being more important than meniscus tear size and any tear displacement. Other important questions: does the patient have adequate physiotherapy treatment and what are their demands at work or in sports?

In Paper I we demonstrated that meniscus repair had an increased rate of knee OA development compared to the general population. Snoeker *et al.* reported that meniscus injury increases the risk of OA with a HR of 4–7.5 but we don't know to what extent the included patients had surgery. An RCT comparing meniscus repair with physiotherapy with a 10–20-year follow-up could perhaps best answer the question of distinguishing between the influence of the injury and that of repair surgery on knee OA development.

In Paper III, since prior meniscus surgery was an exclusion criteria, we don't have much data on what happens if you try to repair again after a failure of the first suture repair. If a repair fails, there is sometimes the option of doing new repair surgery. Limited evidence in small studies show either comparable or worse failure-rates for revision surgery compared to primary repair.<sup>[181,255]</sup> In Paper III we saw 6 lateral menisci and 11 medial, where new sutures were placed after a failed primary repair. Out of these, 4 patients with lateral and 5 medial repairs failed, implying degraded chances of successful repair at meniscus revision surgery.

## Who gets surgery and why?

Mechanical symptoms of the knee, the patients feeling of something (the meniscus?) blocking joint motion, seems an obvious indication for surgery. Among degenerative meniscus tears, a study by Sihvonen *et al.* questioned this consensus, finding no positive value in APM surgery with mechanical symptoms compared to those without.<sup>[245,246]</sup> Is there sometimes a contradiction between treating acute meniscus symptoms, and doing what's in the best long-term interest of the knee? Is the focus more on symptoms than on pathology?<sup>[248,251]</sup> Tear type does not seem to explain so much of postoperative results regarding patient knee pain and symptoms after an APM, while patient factors such as age and BMI have been indicated in several studies to explain more of the postoperative result.<sup>[244,251,256]</sup> There is some controversy about the source of pain in certain types of meniscus tears, whether it's the tear itself or adjacent structures and inflammation.<sup>[20]</sup>

A displaced meniscus injury will get prioritized for prompt surgery if the patient is presenting with seriously impaired knee movement. In Paper III 350 patients (16,7%) had a meniscus tear that was displaced between the condyles, with only half of them registered as a locked knee preoperative. Patients with mechanical symptoms, where pain also is prevalent, is of course a diverse group, ranging from a locked knee to only minor impairment. In some patients the symptoms are attributable to cartilage defects, rather than meniscus tissue interfering with joint motion. Finally, knee pain is stated as the reason for surgery in 1/5 of younger patients and 2/5 of older patients. Looking at coexisting knee OA in patients above age 40, more than half of patients with pain or mechanical symptoms as the stated surgical indication for the meniscus surgery had at least mild knee OA in the joint. Knee OA was present among those with pain stated as the surgical indication in 54% of patients, corresponding percentage of OA in patients with a mechanical symptom indication was 66%.

In **table 8**, with data from the cohort in Paper III, the proportions of the stated reason for primary surgical intervention are different in younger and older patients.

**Table 8.** Stated indications for meniscus surgery, Paper III

Stated indication	All patients N=2098		15–40 years		Above age 40	
	N	%	N	%	N	%
<b>Instability/ACLR</b>	398	19.0	352	31.5	46	4.7
<b>Locked knee</b>	182	8.7	124	11.1	58	5.9
<b>Mechanical symptoms</b>	889	42.4	418	37.4	471	48.0
<b>Pain</b>	595	28.4	214	19.2	381	38.8
<b>Knee OA</b>	15	0.7	1	0.1	14	1.4
<b>Other</b>	19	0.9	8	0.7	11	1.1

## Surgeon's experience

Several studies have shown that surgeons with a higher volume of surgeries per year have better clinical results in the field of knee arthroscopic surgery.<sup>[182,257,258]</sup>

Measuring the success of meniscus repairs is complicated by the tendency for high-volume surgeons to suture more complex types of meniscus injuries, probably with a higher risk of non-healing, than low-volume surgeons.<sup>[238,259]</sup> While the growing number of meniscus repairs being performed in Sweden will lead to more surgical experience, widened indications for repair might also mean that a growing number of surgeons with limited experience will perform meniscus repairs.

An attempt was made during the work on Paper III to measure the influence of surgeon experience, but the confounder that the worst and most complex injuries are treated by the most experienced surgeons, precluded any results in our limited numbers of available surgeries.

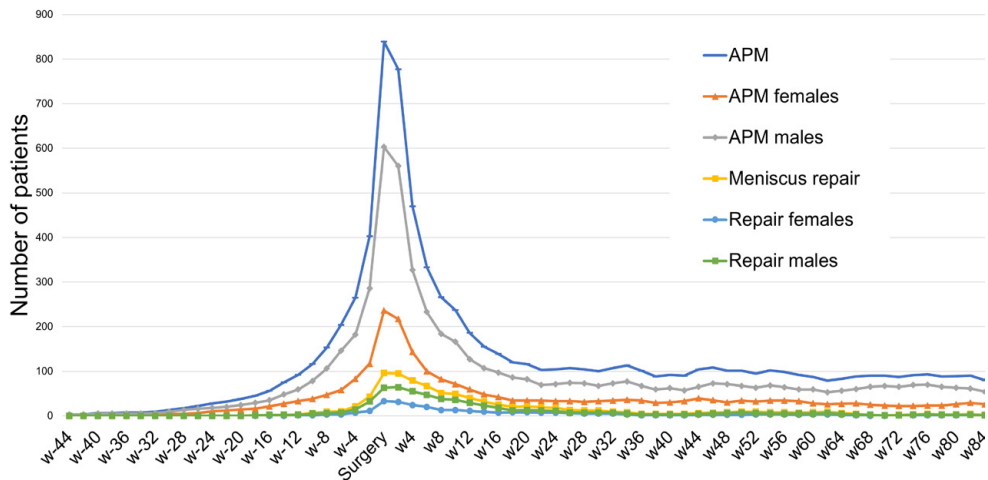
Most RCTs on meniscus repairs are initiated and handled by experienced meniscus repair surgeons.<sup>[144,174,191,260]</sup> When interpreting results, larger register-based studies including all surgeries probably have a more externally valid answer to the question of the clinical failure-rate in meniscus repair surgery.

## The cost of (not) doing surgery

Healthcare economics is an essential aspect of modern medicine due to limited resources in all healthcare systems. Usually, the cost of the meniscus suture implant or the cost of the whole surgery event is calculated, but that is only a small part of the costs.<sup>[261–265]</sup> Depending on patient reimbursement level, the cost of extended sick leave will rapidly surpass the direct surgical cost expenditures.<sup>[266]</sup> When discussing sick leave, there are substantial costs pertaining to patients being at home



while waiting for their meniscus surgery, and on a macro level, decreased revenue of the companies employing them due to work absence. Evident in **figure 21**, sick leave is increased also prior to surgery. There are also the added costs of performing reoperations and treating complications in cases of unsuccessful meniscus surgeries. Though postoperative complications are rare (Paper III) there were 543 reoperations among the 2098 studied patients, with each complication and reoperation incurring healthcare costs as well as new sick leave periods in some cases.<sup>[66]</sup>



**Figure 21.** Sick leave patterns around meniscus surgery, number of patients, cohort from Paper II.

Further expenditures can be attributed to the long-term effects of an increased incidence of knee OA after APM surgery, pertaining not only to the cost of any TKA surgery and any sick leave period associated with this event, but maybe even years of pain medications, reduced work ability and consumption of healthcare resources.<sup>[168,264]</sup> In the setting of a repairable tear, meniscus repair is nowadays considered the most cost-effective treatment.<sup>[261,267,268]</sup> With non-operative treatment of meniscus tears there is of course also a cost incurred pertaining to sick leave and physiotherapy.<sup>[269]</sup>

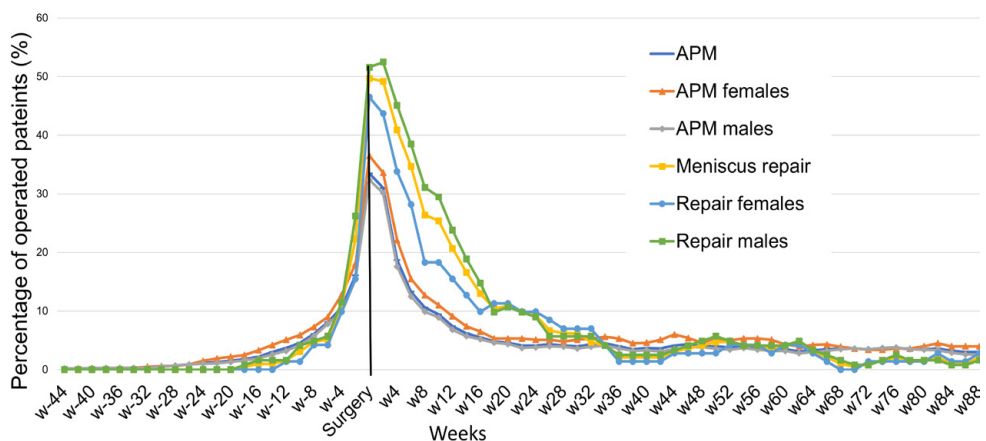
In a world of limited resources there is also the *alternative cost* – what other surgeries could the surgeon have done instead, perhaps with greater benefit to patients?

## Trends of sick leave after meniscus surgery

While the average length of sick leave following meniscus surgery shows a sharp decrease when comparing the results in Paper II against the earlier work by

Rockborn *et al.*, it can be hypothesized that further decrease might be possible, partly attributable to the presumed decrease of knee demands in many labour sectors, with increased automation taking place.<sup>[145]</sup> Altered regulations of and attitudes toward the social insurance system could also play a role in the observed changes (**figure 23**). Other factors that could have a shortening influence on the length of sick leave after meniscus repair are improved surgical technique, a reduction in postoperative restrictions and changing attitudes among prescribing surgeons.

As compared to APM, meniscus repair failure and the higher reoperation-rates after meniscus repair, have probably increased the total amount of sick leave days among patients with meniscus surgery today, since a higher proportion are now being treated with repair.<sup>[105,128,270]</sup> Seen in **figure 22**, there are several minor increases in sick leave among repairs during the 2 years following the index surgery, not seen among the APM group. My theory is that this might be explained by early reoperations, more common in this group (Paper III).



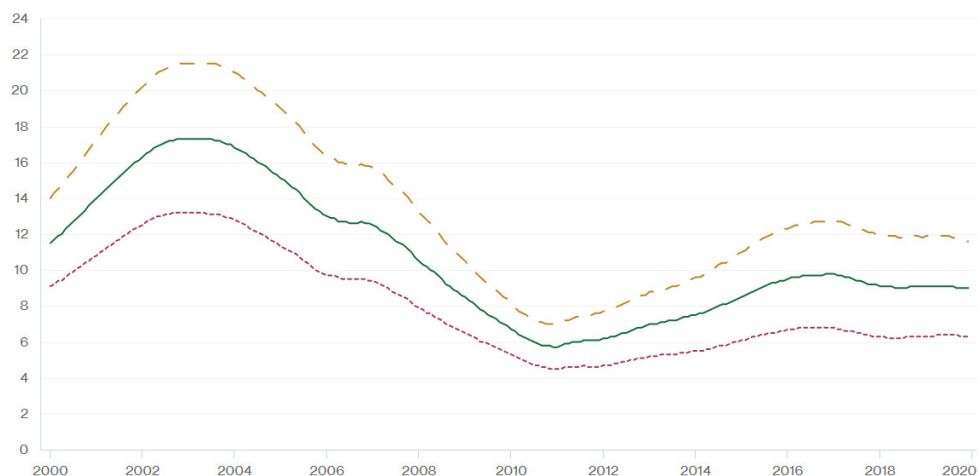
**Figure 22.** Sick leave pattern associated with meniscus surgery, percentage of patients on sick leave.

The finding in Paper II that patients after APM tend to remain on a slightly higher level of sick leave through the whole studied time frame, might indicate that this increase remains permanently. The findings in Paper I of an increased association with OA in this group might play a part in this increased level.

When discussing the difference between sick leave after meniscus repair and APM, comparisons are hard to make. There is likely a discrepancy in the amount of sick leave prescribed by the surgeons as a routine measure, as well as a longer recommended period of knee restrictions.

In Paper II, apart from our current comparison with the general population, an interesting alternative would have been to add a group of patients with meniscus injuries that had received non-operative treatment with only physiotherapy.

Many things other than surgery and the extent of the meniscus injury will affect the length of pre- and postoperative sick leave. Distance to the workplace is a factor to consider when locomotion is impaired and the attitude of healthcare personnel and of the employer likely influences the duration of sick leave taken. Patient coping ability and mental health (depressions, fear of illness/catastrophizing, social network), economic reimbursement level and job security, type of occupation, related to knee demands, as well as probably job satisfaction. When designing the next investigation into sick leave after meniscus surgery, it would therefore be interesting to include any registered ICD-10 diagnosis for “mental health”, as a proxy for lifestyle and coping ability with pain, as well as combining data on both knee specific and total level of peri-operative sick leave.



**Figure 23.** Mean number of sick leave days in the whole working population in Skåne, age 16–64 years. Yellow denotes women, red denotes men and green the total. (Försäkringskassan public records)

Another avenue of investigating sick leave could be to extract sick leave prescriptions from OrtReg on all the patients in Paper III. We would then have knee specific sick leave, since at the time of the study most sick leave was prescribed via the OrtReg system. This seems preferable to other methods used to study sick leave and work absence following surgery, a common method being to ask people about sick leave taken in relation to the meniscus surgery. Poor agreement between self-reporting and actual work absence have been found.<sup>[271]</sup>

# Age and time in meniscus repair

## Age

The age interval of included patients varies slightly in the three papers of this thesis. The lower age limit was set as not to include children with remaining growth of knee structures, or in the case of Paper II, as to only include persons with employment. Shared in all studies is the fact that primary knee OA increases with age and by middle age becomes prevalent in a significant proportion of the studied population.<sup>[125,126]</sup> Primary knee OA would be indistinguishable from post-traumatic OA in Paper I.

Meniscus repair is more commonly chosen in younger than in older patients and the likelihood for the tear to be of a degenerative nature increases with patient age. In contrast to this, when suturing traumatic tears, age alone has not proven to be a risk factor for suture repair failure.<sup>[155,156,174,199,225,257,259,272,273]</sup> The fact that older patients often have lower levels of activity, might obfuscate the interpretation of the failure- and reoperation-rates. Adolescent patients are reported to have the highest reoperation-rate, attributed to an increased prevalence of sports participation.<sup>[193]</sup>

Recent debate in Sweden has lowered the cutoff age from 40 years to 35 years when to consider a meniscus injury as likely degenerative in origin.<sup>[274]</sup> The rationale for this is to reduce the number of degenerative tears treated with an APM. In some discussions, the ICD-10 diagnosis M23.2 is used synonymously with a degenerative tear, while in clinical practice its often being used as a code for a tear that's not fresh but still is principally of a traumatic origin.

While meniscus repair is considered to reduce the risk of OA development and progression, maybe it should have a wider application even in older knees, especially as we live longer and are more active in our older years?<sup>[275]</sup> Longitudinal and bucket-handle tears should maybe be repaired in most knees, with less regard to age? What about the horizontal tear? By many considered a feature of degenerative knee changes, it has been increasingly included in meniscus repair studies, and not always with poor outcomes.<sup>[194,273,276]</sup>

We included a few horizontal repairs in Paper III, but at that time not many surgeons opted for suturing these, which I believe to be a more common practice these days. We included only horizontal tears below the age of 41 years in our comparison, but maybe horizontal meniscus tears should best be studied as a separate group, in all ages? Out of only 8 sutured horizontal tears available in the study cohort, all were below the age of 41 years, 4 had a same meniscus reoperation with 3 of those being located on the medial side. None of the knees with a horizontal tear repair had any signs of knee OA at the time of surgery.

## Timing of surgery and chronicity of the tear

Animal experiments have suggested better healing properties of the meniscus during the first 12 weeks post trauma.<sup>[277]</sup> In support of early surgery, Pujol *et al.* reported a strong correlation between meniscus tear size, time from injury to surgery and the resulting volume of meniscal resection.<sup>[232]</sup> Prolonged time from injury to surgery, for various reasons, will not only influence the diagnostic coding of S83.2 vs M23.2 but will in fact often degrade the meniscus tear fragments in the knee, imparting an appearance of a degenerative tear and creating structural challenges to a successful repair surgery. In the absence of knee OA, it is my opinion that more injuries with a bucket-handle or longitudinal tear pattern should be classified as traumatic/acute injuries, with less regard to the elapsed time from symptom debut to a doctor diagnosis.

In the *ESSKA 2019* meniscus consensus it is concluded that “acute” meniscus repair has better outcome than “late” meniscus repair. All 8 studies ranged in patient numbers between 13–90 patients, the definition of “acute” ranged between 2–12 weeks and the difference in success-rate between acute and chronic tears was only around 10 percent in half of the included studies.<sup>[53]</sup> The verdict was that chronic tears still experience good to excellent results. The age alone of a tear should in my opinion not overly influence the decision whether to perform a meniscus repair or not. In a study by Ronnblad *et al.* including some 918 patients, there was no statistically significant difference between early and late repairs, even when testing both 4- and 12-week cut-offs.<sup>[159]</sup>

The coding and classification of meniscus tears by doctors and surgeons is central to all three papers. Unfortunately, there is a low consistency in the ICD-10 coding and differentiation between acute/traumatic (S83.2) and old/degenerative (M23.2). This makes the diagnostic codes for a traumatic (ICD-code S83.2, Tear of meniscus, current) and an old/degenerative (M23.2, Derangement of meniscus due to old tear or injury) problematic to use when performing research on meniscus repair. As narrative beings, humans often retrospectively associate their meniscus symptoms with any prior minor knee trauma. This tendency further complicates distinguishing traumatic from degenerative tears based on patient history. There exists no exactly defined cut-off between the two diagnostic codes and sometimes the same injury in the same patient will get both. A number of traumatic injuries becomes coded as M23.2, it's not even unusual in traumatic injuries among young individuals, especially if the contact with a surgeon is delayed. The fact that Finland has 44% of all their meniscal tears coded as traumatic, while in Sweden only 24% get the diagnosis S83.2, indicates a disparity in coding practices more than in the tear incidence.<sup>[128]</sup>

In Paper I, the results could have been more interesting with the inclusion of patients more based on tear morphology than the limiting distinction of an ICD-10 diagnosis of acute or chronic, especially as this distinction is so variable.<sup>[128,278,279]</sup>

A further analysis of the data collected for PAPER III might be possible, using it to validate the coding and compare the diagnosis with the actual reports of trauma date, mechanism and meniscus tear type. In Paper III we opted for not imparting any weight to the diagnostic coding of included meniscus tears as “chronic” or “acute”.

An increase in waiting time between injury, to surgical consultation and decision about surgery, and from this to actual surgery date, will often prolong the sick leave with the corresponding amount of time, but might also prolong the recovery period and rehabilitation. Cinque *et al.* found better postoperative function (Tegner, Lysholm) in patients with surgery within 6 weeks of trauma compared to longer than 6 weeks.<sup>[280]</sup> Disuse and muscle wasting of the affected limb can be a contributing factor to such findings. In Paper III it is possible that any prolonged delay between diagnosis and access to surgical treatment imparts an increase in our calculated time from index surgery to any reoperation.

When interpreting the trends in number of surgeries in **figure 7**, it must be kept in mind the possible influences of new guidelines and surgical indications, changes in injury incidence, demography, and variations in surgical capacity. In Sweden, there is lately a growing number of privately practicing knee surgeons performing more and more meniscus surgeries, both primary surgeries and likely also reoperations. As previously mentioned, these surgeries are not available in our registries.

## Are all meniscus tears different?

### Tear size matters

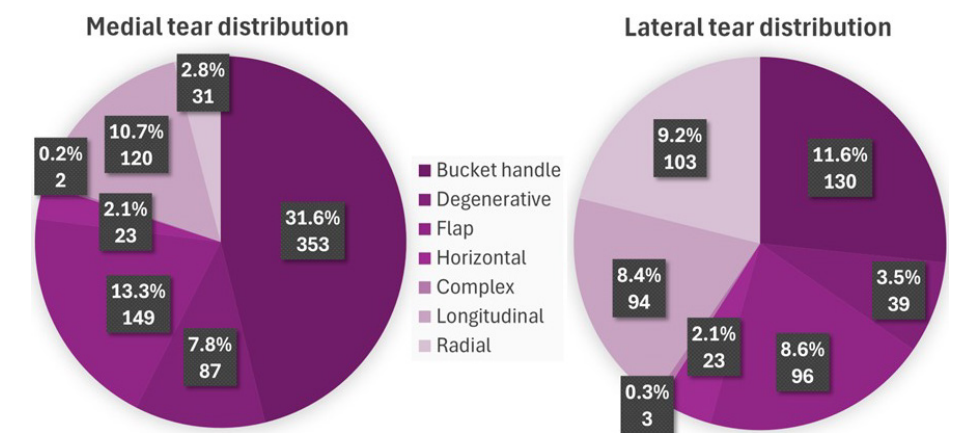
Few studies report on the sizes of the meniscus tears that are resected or repaired, and several that do have found it to not significantly influence outcome.<sup>[174,194,259]</sup> One can hypothesize that there are substantial differences in several outcomes between a tear of 10mm or one of 40mm, after meniscus repair and even more so following APM surgery, where that much more meniscus tissue is resected. It could even be more important than the tear type or the choice of surgical method.<sup>[251]</sup> While neither Saltzman *et al* nor Uzun *et al.* could detect a correlation between tear size and risk of reoperation, a recent meta-analysis by Sedgewick found tear size >20mm to be highly predictive of repair failure in patients above the age of 40 years.<sup>[203,281,282]</sup>

**Figure 28**, compiled from data in Paper III, illustrate that the tear size tends to be larger on the medial side, which could explain some of the difference between medial and lateral repair results found in studies. Several studies have tried to relate the number of sutures placed in the meniscus with the healing frequency or rate of reoperations.<sup>[192,283–285]</sup> This is difficult, because more severe injuries with presumed

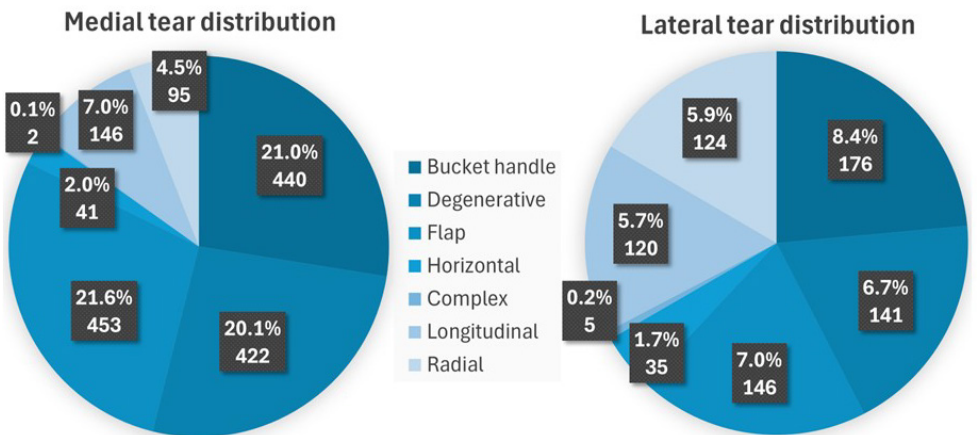
less favourable chances of healing, tend to get additional sutures during repair surgery. Exact data on tear length versus number of sutures is mostly absent. We did record the number of sutures and how many regions of the meniscus was torn in our Paper III data but have yet to do further analysis on this correlation.

### Distribution of meniscus tear types

As previous research also has shown, the type-distribution of meniscus tears in Paper III vary among patients both with age and between the medial and the lateral meniscus (**figure 24 & 25**). Degenerative tears being much less prevalent on the lateral side, where instead radial tears are more prevalent than on the medial side. Though not studied by us, there is likely a variability among surgeons in classifying tear types, especially in the distinction between a flap and a degenerative tear.<sup>[286]</sup>



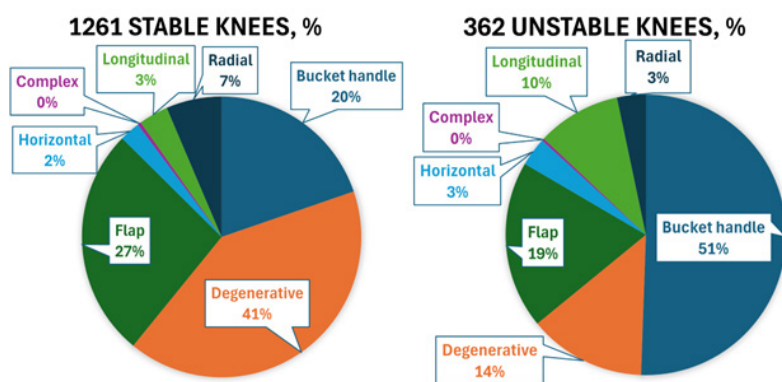
**Figure 24.** Patterns of meniscus tear morphology in patients age 15-40 years.



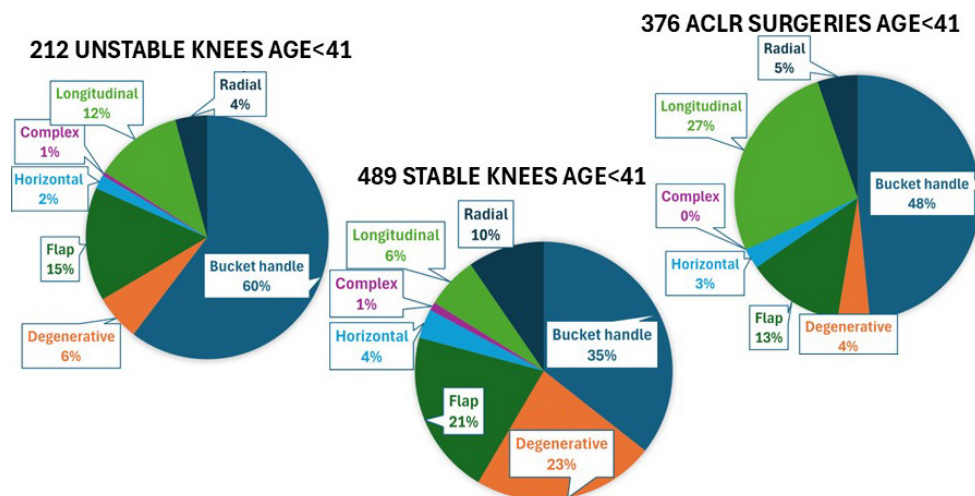
**Figure 25.** Patterns of meniscus tear morphology in patients age 15-99 years.

There is scarce data on the tear type distribution in knees grouped according to knee stability and most available data are from the tear type distribution in the setting of ACLR surgery.

The distribution of meniscus tear types seen during arthroscopic surgery is quite different, when comparing stable and unstable knees (**figure 26 & 27**). Presumably related to a different kind of trauma mechanism and a more severe trauma when also sustaining an ACL tear. Another interpretation is that there could be an underlying discrepancy in the meniscus tissue quality in these two groups, explaining the large differences between them in the number of degenerative tears and flap tears, even among patients below age 41.<sup>[278]</sup> Are perhaps meniscus injuries in knees without a ligamentous injury more of a separate entity?<sup>[287]</sup>



**Figure 26.** Meniscus tear type proportions in stable and unstable knees in paper III, all ages.



**Figure 27.** Meniscus tear type proportions in stable and unstable knees in the subgroup 15–40 years in Paper III.



A British study of 1737 knee MRIs performed between 2015–2017, excluding all patients with an ACL injury, found an incidence of 222 meniscus tears per 100 000 inhabitants and revealed a distribution of tear types similar to the one in Paper III.<sup>[254]</sup> They also studied what kind of treatment that was later administered. Interestingly, a majority of symptomatic bucket-handle tears were treated without any surgery. Of all the patients, on average only 1/5 had a knee arthroscopy, with very variable rates of surgery between different tear types.

Perhaps it's the heterogeneous types of meniscus injuries included in most studies that "dilute" results whilst investigating the effects of risk factors in meniscus surgery, when different tear types have such various repair failure-rates.<sup>[174,194,259]</sup> Since different tear types are found to have variable outcomes after both APM and meniscus repair; should we then more often study medial bucket-handle tears separately from lateral longitudinal tears or other tear types?<sup>[49,192,282,288]</sup> Does maybe age or BMI affect the healing-rate more in *stable knees* with certain types of meniscus tears? Might this specific influence even be different in women than in men? To assemble large enough cohorts with increasingly narrow patient definitions is hard, but maybe future pooled analysis of original study data from numerous smaller studies can yield a large enough dataset? There's still a need for additional research on the surgical treatment of meniscus tears.

## Medial versus lateral meniscus tears

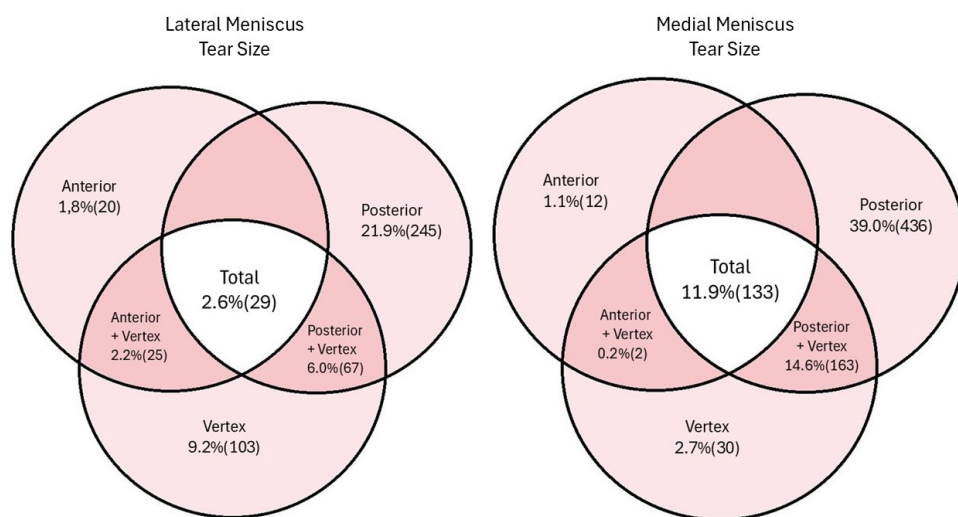
The medial and the lateral meniscus differ in size, shape, mobility and patterns of injury. Healing-rates have also been reported to differ between the two, both explained by different strain on the sutures and because the aetiology differs, with an increased association with degenerative lesions on the medial side.<sup>[289,290]</sup> Several large studies have reported lateral repairs to exhibit about half the failure-rate of medial repairs, while regrettably many studies don't discern or adjust for any variations in tear type.<sup>[144,159,174,282,290]</sup> In posteromedial tears, perhaps the tear most associated with both repair failure and with degenerative tears, repairing the meniscus still has been shown as the favoured treatment in the long-term.<sup>[291]</sup>

Possibly the rates of OA in Paper I in medial and lateral meniscus injuries would be different, in both the APM and the meniscus repair treatment group. In the SHR, SSIA or other large registers based on ICD-10 codes, there's seldom a distinction between lateral and medial injuries, though technically possible (**Appendix table 10**), while the ICD-10 knee OA diagnosis is not possible to specify by compartment. This also makes it hard distinguishing between medial and lateral injuries in the investigating of sick leave.

In my third paper, I reported surgical results favouring a lateral repair with an adjusted reoperation-rate of 80/1000 person-years (95% CI 63, 101) in the medial meniscus and a lesser incidence rate of 57/1000 person-years (95% CI 38, 88) in the

lateral meniscus among our patients between the ages of 15–40 years with either bucket-handle, longitudinal or horizontal repairs.

The **figure 28**, with the distribution of approximate tear sizes in Paper III, visualizes that medial tears seem to be larger in general, which might explain some of the increase in the failure-rate of medial repairs. When looking at bucket-handle tears as a separate entity, there was much less difference between the percentages of medial and lateral reoperations to the same meniscus after meniscus repair (44% vs 39%), (these proportions not adjusted for confounders). An attempt to compare the reoperation-rate in the same meniscus between APM and meniscus repair yielded too few reoperations in the material for a conclusion about any differences in medial versus lateral outcomes.



**Figure 28.** Meniscus tear distribution and size among all patients aged 15–40 years, cohort of Paper III.

## Discoid meniscus prevalence

We only found a small percentage of discoid menisci, about 1% in our material. This is higher than in the previous study by Albertsson and Gillquist, yet lower than most other studies, especially in surgical studies on Asian populations.<sup>[292]</sup> It could be that the condition is less common in a Scandinavian population.<sup>[62]</sup> Still, its higher than the calculated prevalence in the population of around 5/100 000, probably explained by the fact that only around 70% of all discoid menisci are thought to be symptomatic.<sup>[62]</sup> Some patients experience symptoms at an early age, while many live their entire lives without even knowing they have the condition.<sup>[136]</sup> The natural history of patients with a discoid meniscus is largely unknown. Three different types are recognised: incomplete, complete and the Wrisberg type, the latter lacking the meniscotibial ligaments thus making it highly unstable.

## Meniscus repair healing

Failure-rates of meniscus repair increases in studies with increased follow-up time. In pooled data the average rate of failure is 17–25% within 30 months and above 17–32% with longer follow-up. Bucket-handle tears seem to have a higher rate of failure than less displaced injuries.<sup>[159,174,284,290,293]</sup>

MRI investigation has shown a continuous healing process after a meniscus suture of about 6 months.<sup>[294]</sup> In determining the healing success of a meniscus injury, special consideration is warranted for partially healed tears. Though limited study material exists, research indicates that menisci with only partial healing have similar long-term results regarding function and knee OA as do completely healed menisci.<sup>[260,295]</sup> If such a patient is presenting with recurring knee symptoms, this should not routinely be attributed to partial healing, and new surgery is probably not warranted, unless new injuries have occurred.

There is evidence of improved meniscal repair healing-rates in more recent studies, despite the increasing percentage of injured menisci being sutured, probably because of evolving surgical technique and experience.<sup>[128,270,296,297]</sup> It must be mentioned that the surgical repair method and type of implant have an effect on failure-rates after meniscus repair, where all-inside repair with the most modern devices often show better results.<sup>[193,293]</sup> Improved survival-rates will necessitate larger patient sample-sizes in future studies when examining risk factors for failure.

Over time, there has been a shift from repairing only red zone tears close to the capsule to now repairing tears in all meniscus zones. The general consensus is that tears in the white-white zone has the lowest rate of healing, followed by the red-white zone.<sup>[53,280,282]</sup> A recent study from 2019 has questioned this, with non-significant differences in rates of reoperation and postoperative knee function, and the large systematic review by Yeo *et al.* could not ascertain vascular zone as a factor predictive of repair failure.<sup>[259,280]</sup>

### Other risk factors of non-healing and reoperation

In the beginning of this PhD-project, the aim was to perform also a fourth study, examining risk factors for reoperation and lack of meniscus healing after suture repair, which available time did not permit. Diving into the research literature on risk factors for a failed meniscus repair, results are sometimes contradictory, and the effect-size of individual risk factors can be difficult to untangle.

A successful repair will often result in a return to the activity that caused the tear in the first place. Patient age has been difficult to elucidate as a cause of increased repair failure, but we know that increased age generally covariates with decreased physical activity. A similar case can be made for an increased BMI, often correlating

inversely with less physical activity, decreasing the risk of any new sports-related injury to the meniscus previously repaired.

There is a long list of risk factors investigated and suggested to influence the outcome after meniscal repair. The most prevalently discussed in the literature are tear location, geometry and size of the tear, surgical timing, operative technique, surgeon experience, age, gender, ACL injury and reconstruction, rehabilitation protocol, and pre-existing joint degeneration.<sup>[259]</sup> Lately there has been increased attention also to BMI and smoking as risk factors for poor outcome, where available studies remain inconclusive. While cigarette smoking is known to be detrimental to wound healing, despite several studies smoking has not been proven to affect the outcomes in meniscus surgery or specifically the meniscus repair healing-rate, suggesting a need for further studies.<sup>[298]</sup> Results in several studies can be interpreted as that the effect of smoking is more pronounced in bucket-handle tears in younger individuals than in older or less selected cohorts.<sup>[288]</sup> Athletes, common participants in repair cohorts, can be expected to be less exposed to cigarette smoke than the general population.

In Paper III we included smoking as a confounder, as it is suspected of being a risk factor for both suture failure and surgical complications, even though there is currently not enough evidence to say that smoking is a risk factor for reoperation after meniscus surgery.<sup>[284,288,298,299]</sup>

In orthopaedic surgery, BMI is often linked to higher rates of complications after surgery and there is consensus that increased patient weight places more strain on the meniscus.<sup>[300,301]</sup> Though one study found a high BMI to increase the rate of meniscus repair failure, several other studies have failed to prove the connection.<sup>[203,259,284,302,303]</sup>

Regarding the use of different postoperative rehabilitation protocols, two meta-analyses could not determine any effect on healing-rate after meniscus repair.<sup>[174,304]</sup>

## Measuring complications

The prevalence of postoperative complications will depend on the definition of a complication and what period is being measured after surgery. Sometimes it's hard to distinguish if a complication is a result of the surgery or the knee trauma. If a complication is associated with surgery or not can be harder to determine the longer the follow-up period is extended. Several conditions, like pain, swelling, hemarthrosis and loss of skin sensation might be considered unavoidable side effects by the surgeon, while thought of as a complication by the patient and any consulted doctor in the emergency department.

Other complications, like VTE, might go unrecognized because of symptoms resembling the post-surgical state.<sup>[305]</sup> Measuring serious adverse events in diagnostic registers only captures the “tip of the iceberg”. The completeness of minor postoperative adverse events in ICD-10-based registration has been found to be modest, while a thorough review of medical records will uncover many more.<sup>[306]</sup> The registration of a more serious adverse event has a high positive predictive value (PPV).<sup>[307]</sup> In a register-based study of the complications following arthroscopy in Skåne, my colleagues found a 1.1% risk of serious complications within 30 days.<sup>[202]</sup>

Rates of complications that stem from an ACLR are higher than those following meniscus surgery alone. Surprisingly, the rate of VTE after meniscus surgery didn’t differ much from that following ACLR, 0.3% in our study and 0.4% in the study of Friberg *et al.*, while their incidence of infections of 1.1% are more than doubled in one ACLR study, also in line with the results of Paper III with more complications in the ACLR patients.<sup>[308,309]</sup> Similar to the study by Kartus *et al.*, our aim was to also capture complications not visible in the SHR register data.<sup>[310]</sup>

## **Risk factors for complications after surgery**

Before investigating what the risk factors for postoperative complications are, it must first be specified what’s considered a complication? Large register-based studies usually opt for the definition of infections and serious medical events, as these are often reliably registered, and then measures a short period post-surgery, considering adverse events in close proximity to the surgery to be associated with it. Though the treatment chosen in a case of suspected infection will also influence the registered reoperation-rate or hospital readmissions. If a knee with septic arthritis is treated with arthroscopic lavage or just needle arthrocentesis and NaCl lavage with a syringe, is largely depending on local hospital practice in Skåne, as well as access to arthroscopic surgeons and the availability of the operating room. Some surgeons will also advocate for performing an arthroscopic lavage if there are sutures or an ACL graft present, while after an APM a non-operative treatment might be more likely.

While some surgical complications might result in one or several reoperations, many complications do not. The risk factors for a complication might differ from the risk factors for reoperation, and ever further from the risk factors for OA and for non-healing. On the other hand, a postoperative joint infection might increase the likelihood of contracting all three of them.

Consensus appears to be established on the following risk factors for postoperative complications after arthroscopic meniscus surgery: smoking and co-morbidity is associated with an increased rate of readmission.<sup>[199,311]</sup> An increased but low rate of serious medical complications is seen in elderly patients following meniscectomy.<sup>[199,311]</sup>

Known to increase the number of surgical complications in other types of surgery, time in the operating room has been suggested as a risk factor also for complications in meniscus surgery. It can be a proxy for the size of surgery, multiple meniscus suture anchors or a concomitant ACL graft requiring added time to perform.

## Gender differences

### Sex and knee OA

There are substantial gender differences in both the incidence of diagnosed meniscus injuries, and the total number of meniscus surgeries, with lower incidences among women.<sup>[115,118,130,159,223,238,312]</sup> The prevalences of knee OA and TKA surgery are higher in women, while there seem to be no major gender difference in PTOA prevalence.<sup>[80,96,99,313,314]</sup>

In Paper I we only examined sex-specific knee consultation rate for OA in the general population in Skåne, finding it to be slightly higher in men (20.9 per 10 000 person-years) than in women (19.6 per 10 000 person-years).

### Do men have less sick leave?

In Paper II we found an increased propensity for women to be on sick leave after APM, in line with previous work by Bergkvist *et al.* and with the general pattern of a higher level of sick leave in the female population.<sup>[187,188,217,315]</sup> As a possible explanation, women are reported to have increased pain sensitivity and lower pain tolerance across a spectrum of painful conditions. This may be attributable to both biological, psychosocial and cultural factor.<sup>[313]</sup>

Interestingly, no clinically relevant sex difference in the propensity to be on sick leave after meniscus repair was found. This stands in contrast to reported worse clinical outcomes among women following meniscus repair as well as APM.<sup>[312]</sup>

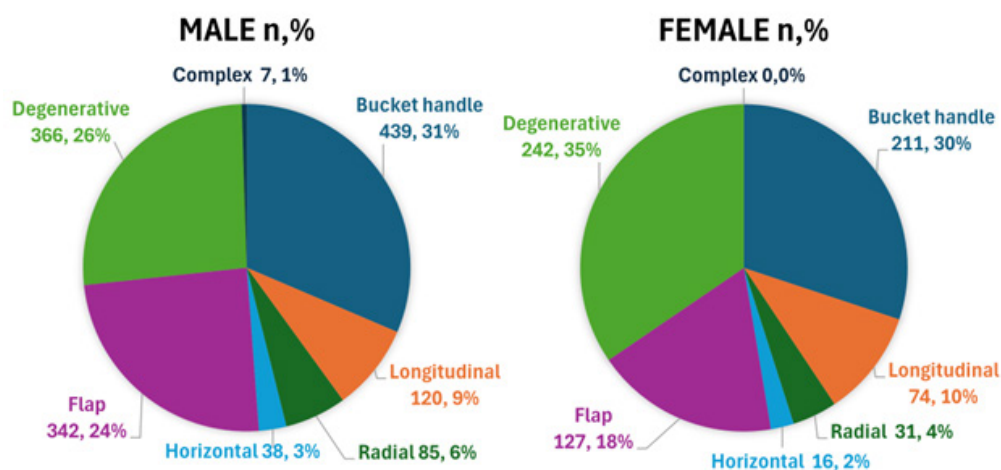
On a group level, men and women often have jobs with different knee demands. We tried to account for this by adjusted for education level and stratifying into different categories of jobs according to the estimated knee demands, but of course this is a blunt solution. Additionally, this does not take into account their different amount of unpaid household work and any gender inequality in expectations from the surrounding society.

## Sex and reoperations

The influence of patient sex on meniscus reoperation-rates has been investigated previously, where both male and female sex has been concluded as a risk factor for reoperation.<sup>[288,293]</sup> There are several studies indicating worse outcomes in women following meniscus surgery, including Paper III.<sup>[188,194,312]</sup> Longer time to recovery and worse KOOS for women after meniscus injury might influence both sick leave and the risk of reoperation.<sup>[312,316]</sup> In Paper III it was more common among women to have a reoperation because of knee pain when compared to males. In men the surgical indication of a locked knee or catching/locking was more prevalent. Additionally, having yet another reoperation due to pain symptoms was more common among women.

Instead of actual biological differences in meniscus healing, could the findings of a sex difference in some studies be a proxy for other differences like physical activity, occupation, tobacco use, body weight, initial choice of meniscus repair over APM, propensity to seek medical care and the willingness of the surgeon to do repeated surgery, influenced by an amplified expression of pain? A future study that assesses meniscus healing through second-look arthroscopy or MRI could provide valuable insights into potential differences of meniscus healing properties between the sexes.

Dan Bergkvist concluded in his thesis that in the age span 40–60 years women comprised around 29% of the cohort treated with APM, while 42% of the group treated without surgery were women. And in the study by Ahmed *et al.* it was likewise observed that women are proportionally less likely to receive surgery when presenting with a meniscus tear.<sup>[254]</sup>



**Figure 29.** Meniscus tear types by gender category among the patients in Paper III.

Are the higher rates of reoperation an effect of more severe knee injuries in the women that *do* get meniscal surgery (as indicated in the study by Alerskans *et al.*)?<sup>[180]</sup> When observing the tear type distribution in Paper III (**figure 29**), there are no apparent major differences, if one considers a flap tear as a degenerative type of tear, and the prevalence of ACLR and ACL injury were similar in both gender groups. However, knee OA was more prevalent at index surgery (40% vs 34%) among women. Reoperations attributable to knee OA, with either TKA or tibia osteotomy, were twice as common in women, though their mean age was only slightly higher (40.8 vs 38.1 years). These latter findings were all unadjusted proportions with a small number of patients for each outcome.

## Meniscus surgery and the ACL

### ACL injury and meniscus surgery

Other serious traumatic injuries in the knee, most commonly an ACL tear, tend to overshadow both the meniscus symptoms and other outcomes in meniscus research. Being a common combination of injuries in clinical practice, it is still relevant to include also ACL deficient knees and knees with an ACLR in meniscus studies.

If a recently conducted study on bracing of ACL tears proves successful and leads to a shift towards a more non-operative management of ACL tears with bracing, the next logical step would be to examine what effect this has on any concomitant meniscus injuries.<sup>[111,113]</sup> Will braced knees show an increased healing-rate among their meniscus repairs? Become less or more symptomatic? Might we even see a decreased rate of posttraumatic OA after ACL injury?<sup>[90,96,98–100]</sup> We will probably see more longitudinal meniscus tears left to non-operative treatment.<sup>[162–164]</sup>

Even though restricted motion after a meniscus repair have shown no benefit, this is not necessarily the same as saying that knee bracing will not affect the healing of an undisplaced meniscus tear, especially in the setting of an ACL tear and hemarthrosis.<sup>[173]</sup> Prophylactic bracing in risky environments have also shown promising results in reducing the number of knee injuries.<sup>[66]</sup>

During the process of reviewing surgical records for Paper III, there was a strong impression that smaller tears of the menisci were operated on, both in the APM and especially the meniscus repair group, in the presence of a concurrent ACLR, than was the case when meniscus surgery was the sole procedure. Many of these were around 10mm, occasionally reported as asymptomatic, and would probably have healed regardless of sutures being placed or not.<sup>[53]</sup> Or in the cases of asymptomatic tears treated with an APM during ACLR, remained asymptomatic. The lack of



consistent reporting on tear length and preoperative meniscus symptoms in the cohort, precluded any statistical analysis on this subject.

## **ACLR and reoperations**

In register-studies, between 2–16 percent of all ACLR patients go through a reoperation that is not related to any meniscus pathology.<sup>[310,317]</sup> Graft revision after ACLR is performed in 5.2% of patients in Sweden after an ACLR.<sup>[102]</sup> In Paper III, an example of a reoperation not related to the meniscus can be an ACLR graft rupture, either incurred at the index trauma or at an event both before or after study inclusion date.

In all three papers we take the presence of ACL injury or ACLR into consideration. ACLR affects both the extent of surgery, the stability and function of the knee and the stress on the meniscus and on the cartilage in the years following surgery. Following an ACLR that is not biomechanically perfect, there will be some residual instability and increased sheer stress on the meniscus, compared to an intact ACL.

On the other hand, better healing-rates have been reported after meniscus repair accompanied by an ACLR. A speculation is that a contributing fact could be that ACLR patients have longer rehabilitation and less return to pivoting sports activity than isolated meniscus surgeries.<sup>[182,259]</sup> Several studies, including the one by Rönblad *et al.* have reported better healing-rates among meniscus repairs in the setting of concomitant ACLR, while larger meta-analyses have found no difference.<sup>[159,174,194,282]</sup>

The PROMs and clinical outcomes are not substantially different in the short- or medium-term when comparing APM and meniscus repair in conjunction with an ACLR.<sup>[228,243,318–320]</sup> An ACLR might also affect what kind of level of function and amount of pain the patient and the surgeon are expecting and what they consider to be a “normal” postoperatively results. I.e. residual knee pain might get attributed to the ACLR and not warrant a new arthroscopy with reoperation of any small meniscal defects found present in the knee.

## **The timing of ACLR**

Many factors influence the timing of the ACLR after an ACL rupture. The common practice for most ACL injuries in Skåne is 3–4 months of physiotherapy knee rehabilitation and then an evaluation if surgery is indicated or not.<sup>[321,322]</sup> This is further influenced by patient adherence to the rehab protocol. If opting for surgery, there’s then the possibility of a prolonged waiting period, either due to queues for surgery, summer vacations, or other patient factors when trying to find a suitable surgery date. In a study by Bergerson *et al.*, results indicated that early ACLR had better patient functional outcomes than delayed surgery, but a limitation was the

lack of baseline data, meaning that it's unclear whether the different groups had comparable knee function prior to the surgery.<sup>[323]</sup>

In the case of a coexisting large meniscus tear, not only might it aggravate the symptom of knee instability, but if meniscus sutures have been placed, it enhances the need for swift knee stabilisation and the surgeon will both recommend and hasten the time to an ACLR.<sup>[27]</sup> All to protect the placed meniscus sutures and promote meniscus healing. Despite this, we saw in Paper III that many included meniscus tears with an ACL instability would get their ACLR later than 4 months following meniscus repair surgery.

## Limitations

### External validity

In register-based research, the external validity is generally high, since it includes the whole population. Very few meniscus surgeries were performed in private clinics during this period. When obtaining our reference population data for Paper I & II, only those that had visited a medical facility could be included, which could skew the results. Nonetheless, we managed to include more than half of the whole Skåne population in our reference cohorts. In Paper III all surgeries in the geographical area were included.

### Internal validity

There is confounding by indication bias at study inclusion, in that patients were not randomly assigned to the different treatments. It is likely that it was different types of meniscus tears that were repaired versus those receiving treatment with APM. During the period of Paper I & II, in Skåne it was principally only longitudinal tears in well vascularized zones of the meniscus that received a meniscus repair. It can be difficult to enrol all the patients in an RCT comparing APM vs meniscus repair. It is even harder to compare surgery versus no surgery and/or physiotherapy, as the blinding of participants to their received treatment is near impossible, and enrolment in such studies might only reach a subsection of the patients.<sup>[207]</sup>

In Paper I, neither the diagnostic ICD-10 codes or the NOMESCO surgical codes retrieved from the SHR specify which side (left/right) that is registered. Therefore, it is not known whether it is the ipsilateral or the contralateral knee that has developed OA during follow-up.

The main limitation in Paper II was that periods of sick leave shorter than 14 days are not recorded in the SSIA database while many individuals are suspected to have

at least a short period of sick leave in relation to the meniscus surgery. The amount and length of short sick leave periods could be significantly different between the two groups. Indeed, when absent from work for up to 1 week, often no formal sick leave document is required in Sweden. At the time of the study, we had no approval for retrieving OrtReg data on sick leave, but a possible way forward would be to collect both longer and shorter periods from the OrtReg sick leave data and then cross-reference this against SSIA and LISA for further variables and test the validity of OrtReg sick leave data. This would be interesting, since a majority of sick leave periods are reported to be short.<sup>[186]</sup>

The other major limitation to consider, is that we did not register the cause of sick leave, if it was related to the surgery or even to the knee, only the temporal correlation with the surgery. Thus, it is important to correlate the levels of sick leave with the background population.

In all studies, we are lacking the date of injury, we only have the date of the surgery.

We were unable to capture any OA diagnosis (Paper I) and any reoperations (Paper III) performed outside the Skåne region or at private orthopaedic clinics, but we estimated this to be few patients during the studied era. Information about meniscus tear size is missing, which could differ between groups. Even though a meniscus tear in all zones have the possibility to heal after meniscus repair, they have different healing-rates and it's a limitation that we don't have any data on which zone the tears were in.<sup>[53]</sup>

# Conclusions

- The risk of consulting for knee OA during the decades following meniscus surgery, was between 25–50% lower for meniscus repairs compared to patients with APM.
- The consultation rate for knee OA following meniscus repair was at least two times as high, compared to the general background population.
- The consultation rate for knee OA in the general population in the Skåne region was 20 per 10,000 person-years (95% CI 19.9, 20.1) among persons aged 16–45 years.
- Meniscus surgery was associated with an increase of sick leave periods longer than 14 days, where 17% of the general population had any sick leave, while 55% after meniscus repairs and only 43% after an APM.
- The mean number of days on sick leave after APM was 37 days and after meniscus repair it was 55 days, i.e. 37% higher.
- Meniscus repair was associated with a higher probability of sick leave compared to APM with an adjusted risk difference of 0.13 (95% CI 0.07, 0.19).
- One in five patients with meniscus surgery had a reoperation in the same knee, with more than half of reoperations being within 2 years of the index surgery.
- Below the age of 40 years, there was a 4-fold increase in reoperation of all causes and a 17-fold increase in reoperations in the same meniscus, after meniscal repair compared to APM.
- Males have lower reoperation-rates compared to females after meniscus surgery, with a crude HR (95% CI) of 0.65 (0.56, 0.82).
- The frequency of postoperative complications in Skåne was low after both meniscus repair and APM in all ages.



# Clinical implications

There is already a strong trend to ‘save the meniscus’ when performing arthroscopic knee surgery. The work in Paper I is highly cited and is also included in the background material for the *ESSKA 2019* guidelines for meniscus surgery and in a recent meta-analysis. It has increased the knowledge regarding the risk of knee OA after meniscus injury and surgery.

The work of Paper II will help the surgeons to better predict and to inform the patients of the need for prolonged absence from work after meniscus repair. Apart from being important economically for patients and sometimes affecting their career and employment, it will also help the SSIA when estimating what is a “normal” amount of reimbursed sick leave after surgery. It might also help in future health economic calculations, which is an important part of an increasingly expensive healthcare system.

The work of Paper III implies a high rate of reoperations after meniscus repair, and high rates of suture failure, which should be considered when informing patients and planning meniscus surgery. Low rates of other complications demonstrate that arthroscopic surgery in Skåne is a safe procedure, even without preoperative antibiotics. This practice can be safely continued. The findings in this thesis can also serve as a reference material in future research to compare meniscus repair results today and what effect the current 10-fold increase in meniscus repair prevalence might have on the rates of reoperations and knee OA.

In summary, all these findings will help the patients and surgeons to make better informed decisions when contemplating meniscus knee surgery.



# Future perspectives

Do we really need more research on meniscus repair, with the large number of publications already out there? When the expert group compiled the *ESSKA 2019 meniscus consensus: Management of traumatic meniscus tears*, they deemed that only one clinical question had grade A evidence, and further only one question had an evidence grade of B, which for me underlines the need for more research on the topic.

It is my wish to further study the association between complications, reoperations and the modifiable risk factors BMI and smoking. Despite several studies on the topic, there is still conflicting results. Though initially in low numbers, the reoperations with a TKA after meniscus surgery started to pile up in Paper III with increasing follow-up time. Now that several more years have passed, it could soon be suitable to initiate a follow-up of the current cohort regarding the risk of OA and rates of TKA 15–20 years after APM and meniscus repair, correlating not only diagnostic codes but also meniscus tear type and the location of a tear with the incidence of TKA surgery.

The exceptionally informative OrtReg-register that we have had now in Skåne for about 30 years, might soon be discontinued. It's a goldmine of register data on meniscus surgery, and my plan for the immediate future is a paper to describe the surgical trends in Skåne during this period in detail while the register is still up and running. It would nicely complement the other papers in this thesis. During my work on this thesis, the feasibility and the need of a Swedish validation-study of surgical and diagnostic codes in meniscus surgery has become apparent, since many studies are based on these and the study conclusions rely on the accuracy in the registers. Maybe comparing OrtReg and SHR data could achieve this.

Ten years has now passed since the endpoint of Paper II, allowing a new study on SSIA data to compare any changes in the sick leave after meniscus surgery. An attempt could also be made at measuring if preoperative sick leave periods have increased or decreased, and how this is related to the time waiting for surgical treatment.

Maybe the future direction lies in more RCTs comparing meniscus repair and no surgery for different morphologic types of traumatic tears, with separate arms for any concomitant ligament injury and ACL surgery? This would then have to become a multicentre study to include enough patients. With the right amount of collected data, the same cohort could be used both to investigate sick leave, knee OA, suture survival-time and the reoperation-rate.





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# Appendix

**Table 9. (Appendix) List of Surgical NGD-codes in meniscus surgery (NOMESCO)**

Swedish version of NOMESCO Classification of Surgical Procedures; KKA97*	
<b>Meniscectomy</b>	
<b>NGD00</b>	Percutaneous total excision of meniscus of knee
<b>NGD01</b>	Arthroscopic total excision of meniscus of knee
<b>NGD02</b>	Open total excision of meniscus of knee
<b>NGD09</b>	Total excision of meniscus of knee, unspecified
<b>NGD10</b>	Percutaneous partial excision of meniscus of knee
<b>NGD11</b>	Arthroscopic partial excision of meniscus of knee
<b>NGD12</b>	Open partial excision of meniscus of knee
<b>NGD19</b>	Partial excision of meniscus of knee, unspecified
<b>Meniscus repair</b>	
<b>NGD20</b>	Percutaneous reinsertion of meniscus of knee
<b>NGD21</b>	Arthroscopic reinsertion of meniscus of knee
<b>NGD22</b>	Open reinsertion of meniscus of knee
<b>NGD29</b>	Reinsertion of meniscus of knee, unspecified
<b>Other</b>	
<b>NGD90</b>	Other surgery of meniscus, percutaneous
<b>NGD91</b>	Other surgery of meniscus
<b>NGD92</b>	Other surgery of meniscus, open surgery

\*more than 1 code can be registered at surgery.

**Table 10. (Appendix)** List of ICD-10 codes for meniscus pathology

ICD-10 code	Definition
<b>M23.1</b>	Discoid meniscus (congenital)
<b>M23.1M</b>	Discoid meniscus (congenital) medial
<b>M23.1L</b>	Discoid meniscus (congenital) lateral
<b>M23.0</b>	Cystic meniscus
<b>M23.0M</b>	Cystic meniscus medial
<b>M23.0L</b>	Cystic meniscus lateral
<b>M23.3</b>	Other meniscus derangements
<b>M23.3M</b>	Other meniscus derangements medial
<b>M23.3L</b>	Other meniscus derangements lateral
<b>M23.2</b>	Derangement of meniscus due to old tear or injury
<b>M23.2M</b>	Derangement of meniscus due to old tear or injury medial
<b>M23.2L</b>	Derangement of meniscus due to old tear or injury lateral
<b>M23.9</b>	Internal derangement of knee, unspecified
<b>M67.4M</b>	Meniscus ganglion, medial
<b>M67.4L</b>	Meniscus ganglion, lateral
<b>S83.2</b>	Tear of meniscus, current
<b>S832.M</b>	Tear of meniscus, current, medial
<b>S832.L</b>	Tear of meniscus, current, lateral
<b>S832.X</b>	Tear of meniscus, current, unspecified
<b>S83.7</b>	Injury to multiple structures of knee Injury to (lateral)(medial) meniscus in combination with (collateral)(cruciate) ligaments

The following supplementary subclassification to indicate the site of involvement is provided for optional use with appropriate subcategories in M23.-.

**0 Multiple sites**

**1 Anterior cruciate ligament or Anterior horn of medial meniscus**

**2 Posterior cruciate ligament or Posterior horn of medial meniscus**

**3 Medial collateral ligament or Other and unspecified medial meniscus**

**4 Lateral collateral ligament or Anterior horn of lateral meniscus**

**5 Posterior horn of lateral meniscus**

**6 Other and unspecified lateral meniscus**

**7 Capsular ligament**

**9 Unspecified ligament or Unspecified meniscus**

**Table 11. (Appendix)** List of ICD-10 codes for knee injury

ICD-10 code	Definition
<b>S83.5</b>	Sprain and strain involving anterior/posterior cruciate ligament of knee
<b>S83.5S</b>	Sprain and strain involving posterior cruciate ligament of knee
<b>S83.5R</b>	Sprain and strain involving anterior cruciate ligament of knee
<b>S83.5X</b>	Sprain involving cruciate ligament of knee
<b>S82.0</b>	Fracture of the patella
<b>S72.4</b>	Fracture of lower end of femur
<b>S82.1</b>	Fracture of upper end of tibia
<b>M23.5</b>	Chronic instability of knee
<b>S83.7</b>	Injury to multiple structures of knee Injury to (lateral)(medial) meniscus in combination with (collateral)(cruciate) ligaments
<b>S83.2</b>	Tear of meniscus, current
<b>S83.2M</b>	Tear of meniscus, current medial
<b>S83.2L</b>	Tear of meniscus, current lateral
<b>S83.2X</b>	Tear of meniscus, current, unspecified

**Table 12. (Appendix)** List of ICD-10 codes for knee OA

ICD-10 code	Definition
<b>M17</b>	Gonarthrosis (arthrosis of knee)
<b>M17.0</b>	Primary gonarthrosis, bilateral
<b>M17.1</b>	Other primary gonarthrosis, NOS, unilateral
<b>M17.2</b>	Post-traumatic gonarthrosis, bilateral
<b>M17.3</b>	Other post-traumatic gonarthrosis, NOS, unilateral
<b>M17.4</b>	Other secondary gonarthrosis, bilateral
<b>M17.5</b>	Other secondary gonarthrosis, NOS, unilateral
<b>M17.9</b>	Gonarthrosis, unspecified

