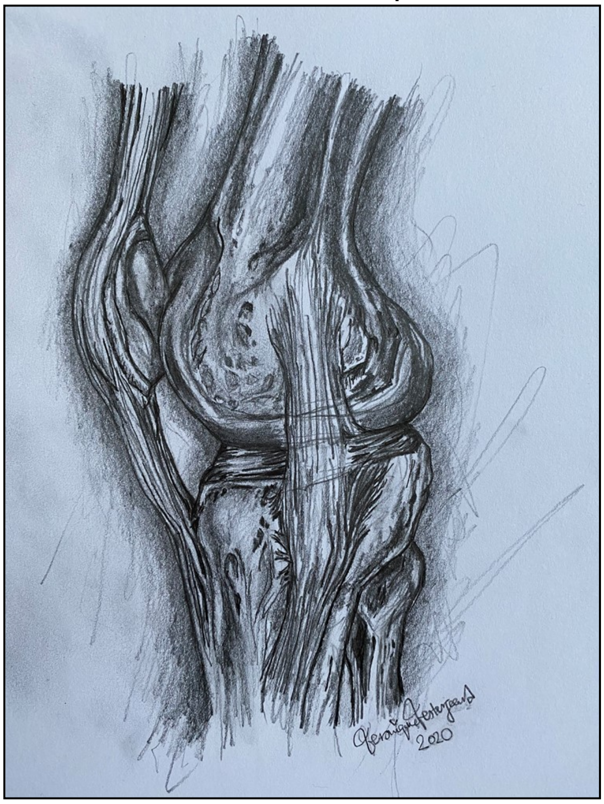
UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

PhD Thesis

Veronique Vestergaard

Distal Femoral, Patellar, and Proximal Tibial Fractures

Incidences, Patient-Reported Outcomes, and Risk of Total Knee Arthroplasty



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Selected Proceedings from the 2019 European Knee Society Meeting
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Abbreviations

ACL	Anterior Cruciate Ligament
CCI	Charlson Comorbidity Index
CPR	Civil Personal Register
CRS	Civil Registration System
DNPR	Danish National Patient Registry
EQ5D-5L	EuroQol 5-Dimensions Questionnaire-5L
EQ5D-5L VAS	EuroQol 5-Dimensions Questionnaire-5L Visual Analogue Scale
FJS-12	Forgotten Joint Score-12
HR	Hazard Ratio
ICD-10	World Health Organization 10th revision of International Classification of Diseases and Health Related Problems
IQR	Interquartile Range
IR	Incidence Rate
IRR	Incidence Rate Ratio
KOOS	Knee Injury and Osteoarthritis Outcome Score
NOMESCO	Nordic Medico-Statistical Committee Classification of Surgical Procedures
OA	Osteoarthritis
OKS	Oxford Knee Score
OR	Odds Ratio
ORIF	Open Reduction Internal Fixation
PPV	Positive Predictive Value
PROM	Patient-Reported Outcome Measure
PTOA	Posttraumatic Osteoarthritis
PYRS	Person-Years at Risk
QOL	Quality of Life
THA	Total Hip Arthroplasty
TKA	Total Knee Arthroplasty
95% CI	95% Confidence Interval

English Summary

Background
Knee fractures are comprised of distal femoral fractures, patellar fractures, and proximal tibial fractures and may result in complications for the individual patient in the form of knee pain, reduced knee function, reduced quality of life (QOL), reduced work performance, posttraumatic osteoarthritis (PTOA), and risk of total knee arthroplasty (TKA). Current literature is sparse on the 1) incidences of knee fractures, 2) patient-reported outcomes of knee fractures, and 3) risk of TKA following knee fracture. This PhD thesis was divided into three studies to address the three abovementioned points.

Study I: Incidences
Without knowledge of the treatment burden of knee fractures, the proper allocation of hospital resources in the healthcare system will remain unknown. To calculate the treatment burden of knee fractures, knowledge of incidence rates (IRs) and epidemiology of knee fractures is essential. Current studies estimate an annual knee fracture IR of 9 per 10^5 per year in the United States. The epidemiology of knee fractures is sparsely described, involving only certain types of knee fractures, and small sample studies.

Study II: Patient-Reported Outcomes
Knee fractures reduce knee mobility and function and negatively influence QOL, as is reported by patient-reported outcome measures (PROMs). PROM studies on knee fracture patients and their prognoses are sparse, only studying certain knee fracture types, certain knee fracture treatments, and using small samples, and have reported varying outcomes in knee fracture patients. To our knowledge, studies on the risk factors of poor PROM scores after knee fracture are non-existing. By describing the prognoses of knee fracture patients by reporting PROM scores (using knee-specific and generic PROMs) of knee fracture patients at different follow-up periods, and investigating the risk factors of poor PROM scores in knee fracture patients, the current quality of care of knee fracture patients can be described, leading to the implementation of future directives to improve quality of care initiatives.

Study III: Risk of Total Knee Arthroplasty
Current increases in the number of TKAs performed worldwide cannot solely be explained by growing populations, increased longevity, and the rise in obesity rates. Knee injuries including knee fractures also lead to TKA rates increasing as some patients may develop PTOA and undergo subsequent TKA as a result from knee fracture. Furthermore, TKA procedures for PTOA are often less successful than TKA procedures for knee osteoarthritis (OA). All the while, knowledge of risk estimates of TKA following knee fracture and other risk factors for TKA in knee fracture patients is largely unknown.

By investigating these parameters, the treatment burden of knee fractures would be established, and health care professionals would be better able to counsel patients on their expected prognoses including their future risk of TKA.

Aims

Study I: Specific Aims

1) What are the 20-year trends in IRs of knee fractures?
2) What are the patient-, fracture-, and treatment-related characteristics of knee fracture patients in Denmark during 1998-2017?

Study II: Specific Aims

1) Report on knee-specific and generic median PROM scores of knee fracture patients at 0 to >5 years after knee fracture.
2) Identify risk factors for poor outcome defined by low median PROM scores.

Study III: Specific Aims

1) What is the short-term risk of TKA after knee fracture?
2) What is the long-term risk of TKA after knee fracture?
3) What are the risk factors for TKA in patients with knee fractures?

Methods

Two national Danish registries were used: the Civil Personal Register (CRS) and the Danish National Patient Registry (DNPR). Every resident in Denmark is given the Danish version of a social security number, a Civil Personal Register (CPR) number, which is registered in the CRS together with a resident's date of birth, sex, residency status, emigration status, and vital status, all of which are updated daily. Data can be linked between the CRS, the DNPR, and other registries using the CPR number. Data in the DNPR includes all admissions to public hospitals and emergency departments, some admissions to private hospitals, admission date, CPR number, age, sex, World Health Organization 10th revision of International Classification of Diseases and Health Related Problems (ICD-10) diagnosis codes, and the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) surgery codes. Patients registered with ICD-10 diagnosis codes for knee fractures (distal femur fracture (DS724), patella fracture (DS820), and proximal tibia fracture (DS821)) with/without NOMESCO surgery codes for knee fracture in Denmark were included in all three studies of the PhD thesis. Data was prospectively collected from the CRS and DNPR. Patient comorbidity level was calculated using the modified Charlson Comorbidity Index (CCI).

Study I: Methods

In this nationwide Danish cohort study, all patients registered with ICD-10 knee fracture diagnosis codes, with/without NOMESCO knee fracture surgery codes from January 1st, 1998 to December 31st, 2017 were included.

The epidemiology of knee fractures was described using patient- (age, sex, CCI level), fracture-, and treatment-related characteristics of the knee fracture population collected from the DNPR. Annual overall IRs of knee fractures, and IRs according to age category, sex, knee fracture type, and surgical/non-surgical treatment of knee fracture were defined as number of knee fractures divided by number of inhabitants within each year presented as per 10^5 inhabitants with 95% confidence intervals (95% CIs). Characteristics of the knee fracture population were described using proportions and median with interquartile range (IQR).

Study II: Methods
In this national Danish population-based cross-sectional study, all patients over age 15 years registered with ICD-10 knee fracture diagnosis codes, with/without NOMESCO knee fracture surgery codes from January 1st, 2011 to December 31st, 2017 were included. The questionnaire containing a link to four PROMs was delivered via a national digital CPR number-linked e-mail system. Four PROMs: two knee-specific (Oxford Knee Score (OKS) and Forgotten Joint Score-12 (FJS-12)) and two generic (EuroQol 5-Dimensions Questionnaire-5L (EQ5D-5L) Index and EQ5D-5L Visual Analogue Scale (VAS)) were used to describe the outcomes and prognoses of the knee fracture population sample. OKS is a 0-48 scale with higher values indicating less knee pain and higher knee function. FJS-12 is a 0-100 scale with higher values indicating better ability to forget about the knee joint and therefore having no knee joint problems in daily life. The EQ5D-5L Index is a -0.21 to 1.00 index with higher index values indicating better general health using five health dimensions. The EQ5D-5L VAS is a 0-100 scale health thermometer, with higher values indicating better general health. A PROM score of below the median PROM score was defined as poor outcome score. Increasing age, sex, CCI level, knee fracture type, and treatment type were potential risk factors for poor PROM score. Proportions and median with IQR described responders and non-responders. Odds ratios (ORs) with 95% CIs of risk factors for poor PROM score were estimated for all four PROMs and within all four follow-up periods using binary logistic regression models.

Study III: Methods
In this nationwide Danish 20-year matched-case comparison cohort study, every patient over age 15 years registered with ICD-10 knee fracture diagnosis codes, with/without NOMESCO knee fracture surgery codes from January 1st 1998 to April 30th 2018 was matched by sex and age (same birth year) to five people without registered knee fractures (population controls) from the general population in Denmark. Both knee fracture patients and population controls were followed from the date of knee fracture registration to date of TKA, amputation, knee fusion, emigration, death, or end of follow-up on April 30th 2018. Amputation, knee fusion, emigration, and death were modelled as competing events for TKA. Frequency, percentage, and median with IQR described the study population.

Hazard Ratios (HRs) with 95% CIs and p values using Cox proportional hazard models were used to estimate short-term and long-term risk for TKA in knee fracture patients vs population controls and risk factors for TKA in knee fracture patients.

Results

Study I: Results

During 1998-2017, the IR for knee fractures increased by 12% to 70 per 10^5 inhabitants and the IR for surgically treated knee fractures increased by 35% to 23 per 10^5 inhabitants. Females aged >51 years had the highest knee fracture IR. Proximal tibia fracture had an IR of 32 per 10^5 inhabitants, the highest of the knee fracture types. A total of 60,823 patients (median age 55 years; 57% female) were registered with 74,106 knee fractures during the 20-year study period. A total of 74% of knee fracture patients had a CCI of 0 while 18% had a CCI of ≥2. Knee fracture distribution was 51% proximal tibia fracture, 31% patella fracture, and 18% distal femur fracture. At knee fracture registration date, one fifth of patients were also registered with concomitant near-knee fractures (femur/tibia/fibula shaft/hip/ankle fracture), 13% were registered with concomitant fractures (pelvic/spine/thorax/upper extremity fracture), 5% were registered with osteoporosis, and 4% were registered with primary knee OA. Surgically treated knee fractures comprised over one third of registered knee fractures, of which 86% were registered as open reduction internal fixations (ORIFs), 9% were registered as external fixations, and 5% were registered as knee arthroplasties. Proximal tibia plating was the most frequent type of surgery (n= 4,868; 60% female). Females aged >51 years and patients with registered comorbidities were associated with sustaining knee fracture, proximal tibia fracture, proximal tibia fracture surgery, and knee arthroplasty for PTOA following knee fracture.

Study II: Results

There were 7,133 (53%) responders (median age 60 years; 63% female). At short-term follow-up (0-1 years after knee fracture), median PROM scores were 31 (OKS), 27 (FJS-12), 0.50 (EQ5D-5L Index), and 74 (EQ5D-5L VAS). Within each PROM, median PROM scores were similar at 3-5 years and >5 years of follow-up after knee fracture. At long-term follow-up (>5 years after knee fracture), median PROM scores were 40 (OKS), 54 (FJS-12), 0.76 (EQ5D-5L Index), and 80 (EQ5D-5L VAS). Knee fracture patients reported relatively high OKS, EQ5D-5L Index, and EQ5D-5L VAS scores, corresponding to relatively low knee pain, high knee function, and high general health/QOL. Knee fracture patients reported low FJS-12 scores, corresponding to inability to forget about the knee joint in everyday activities. Different risk factors for poor PROM score were present in different PROMs and follow-up periods. In all follow-up periods, age >40 years had high odds for poor OKS and FJS-12 scores. Comorbidity burden, distal femur fracture, treatment of knee fracture with external fixation, and treatment of knee fracture with knee arthroplasty had high odds of poor PROM scores at long-term follow-up after knee fracture, in all four PROMs.

Study III: Results
Knee fracture patients had a 3.7 times higher risk (HR 3.74; 95% CI 3.44-4.07; $p<0.01$) of undergoing TKA in the first 3 years following knee fracture, compared to population controls. Knee fracture patients had a sustained increased risk of 1.6 times (HR 1.59; 95% CI 1.46-1.71; $p<0.01$) that of population controls of undergoing TKA after the first 3 years following knee fracture, suggesting that the risk for TKA in knee fracture patients is lifelong. In the 20-year period, 4% knee fracture patients had TKA surgery while 1% of population controls had TKA surgery. Other risk factors adding to the risk for TKA in knee fracture patients were primary knee OA vs no primary knee OA (HR 9.57), surgical treatment with external fixation of knee fracture vs ORIF and reduction only of knee fracture (HR 1.92), proximal tibia fracture vs patella fracture (HR 1.75), and distal femur fracture vs patella fracture (HR 1.68). Surgical treatment of knee fracture vs non-surgical treatment of knee fracture was a risk factor for TKA in knee fracture patients: HR was 2.05 in the first 5 years following knee fracture and HR was 1.19 at 5 years and onward following knee fracture.

Conclusions
Patient-related factors such as female sex, increasing age, and comorbidity including primary knee OA, fracture-related factors such as proximal tibia fracture and distal femur fracture, and treatment-related factors such as surgical treatment of knee fracture, external fixation, and knee arthroplasty are associated with incidences, outcomes, and risk of TKA in knee fracture patients. Future studies should further investigate patient-related factors such as other comorbidities and trauma severity, fracture-related factors such as subclassifications of knee fractures, and treatment-related factors such as subclassifications of surgery types, to further describe the complex knee fracture population and its incidences, outcomes, and risk of TKA, as well as expected prognoses, to help the health care system plan the optimal management of knee fracture patients accordingly. The need for a re-evaluation of current hospital resources directed at the knee fracture population is therefore warranted.

Danish Summary

Baggrund
Knæfrakturer består af distal femurfrakturer, patellafrakturer og proksimal tibiafrakturer og kan give komplikationer for den enkelte patient i form af smerter i knæet, nedsat funktion i knæet, nedsat livskvalitet (QOL), nedsat arbejdsevne, posttraumatisk osteoartrose (PTOA) og risiko for total knæalloplastik (TKA). Den nuværende litteratur er sparsom angående 1) incidenser af knæfrakturer, 2) patient-rapporterede spørgeskemaer af knæfrakturer og 3) risiko for TKA efter knæfraktur. Denne PhD afhandling blev delt op i tre studier for at adressere de tre ovenstående punkter.

Studie I: Incidenser
Uden viden om behandlingsbyrden af knæfrakturer vil viden om den rette fordeling af hospitalets ressourcer i sundhedsvæsenet forblive ukendt. For at beregne behandlingsbyrden af knæfrakturer er kendskab til incidensrater (IRs) og epidemiologien af knæfrakturer afgørende. Aktuelle studier estimerer en årlig IR af knæfraktur på 9 pr. 10^5 pr. år i Amerikas Forenede Stater. Epidemiologien af knæfrakturer er sparsomt beskrevet og involverer kun visse typer af knæfrakturer og studier med få antal patienter.

Studie II: Patient-Rapporterede Spørgeskemaer
Knæfrakturer mindsker mobiliteten og funktionen i knæet og påvirker QOL negativt, som rapporteres af patient-rapporterede spørgeskemaer (PROMs). PROM-studier omhandlende knæfrakturpatienter og deres prognoser er sparsomme, disse undersøger kun visse knæfrakturtyper, visse knæfrakturbehandlinger og er studier med få antal patienter og har rapporteret forskellige outcomes hos knæfrakturpatienter. Så vidt vi ved, er studier af risikofaktorer for dårlige PROM-scores efter knæfraktur ikke-eksisterende. Ved at beskrive prognoser for knæfrakturpatienter ved at rapportere PROM-scores (ved hjælp af knæspecifikke og generiske PROMs) for knæfrakturpatienter i forskellige opfølgningsperioder og undersøge risikofaktorerne for dårlig PROM-score hos knæfrakturpatienter, kan den aktuelle plejekvalitet af knæfrakturpatienter beskrives, hvilket fører til implementering af fremtidige direktiver for at forbedre initiativer vedrørende plejekvaliteten.

Studie III: Risiko for Total Knæalloplastik
De aktuelle stigninger i antallet af TKAs der udføres verden over, kan ikke alene forklares udefra voksende populationstal, øget levetid og stigning i antallet af overvægtige. Knæskader inklusive knæfrakturer fører også til øgede TKA-rater, da nogle patienter kan udvikle PTOA og gennemgå efterfølgende TKA som følge af knæfraktur. Derudover er TKA-procedurer for PTOA ofte mindre vellykkede end TKA-procedurer for knæ osteoartrose (OA).

I mellemtiden er viden om risikoestimater af TKA efter knæfraktur og andre risikofaktorer for TKA hos knæfrakturpatienter stort set ukendt. Ved at undersøge disse parametre ville behandlingsbyrden for knæfrakturer blive fastlagt, og sundhedspersonale ville være bedre i stand til at rådgive deres patienter om deres forventede prognoser inklusive deres fremtidige risiko for TKA.

Formål

Studie I: Specifikke Formål

1) Hvilke er de 20-årige trender i IRs af knæfrakturer?
2) Hvilke patient-, fraktur- og behandlingsrelaterede egenskaber har knæfrakturpatienter i Danmark i perioden 1998-2017?

Studie II: Specifikke Formål

1) Rapportere medianer af knæspecifikke og generiske PROM scores for knæfrakturpatienter fra 0 til >5 år efter knæfraktur.
2) Identificere risikofaktorer for dårlig outcome defineret ved lave medianer af PROM-scores.

Studie III: Specifikke Formål

1) Hvad er den kortvarige risiko for TKA efter knæfraktur?
2) Hvad er den langvarige risiko for TKA efter knæfraktur?
3) Hvad er risikofaktorerne for TKA hos patienter med knæfrakturer?

Metoder

To nationale danske registre blev brugt: Det Centrale Personregister (CRS) og Landspatientregisteret (DNPR). Hver beboer i Danmark får en dansk version af et social security number, Det Centrale Personregister (CPR) nummer, der registreres i CRS sammen med beboerens fødselsdato, køn, opholdsstedsstatus, emigrationsstatus og vital status, hvilket opdateres dagligt. Data kan linkes mellem CRS, DNPR og andre registre ved hjælp af CPR-nummeret. Data i DNPR inkluderer alle indlæggelser på offentlige hospitaler og akutafdelinger, nogle indlæggelser på private hospitaler, indlæggelsesdato, CPR-nummer, alder, køn, World Health Organization 10th revision of International Classification of Diseases and Health Related Problems (ICD-10) diagnosekoder og den danske version af Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) kirurgikoder. Patienter, der er registreret med ICD-10-diagnosekoder for knæfraktur (distal femurfraktur (DS724), patellafraktur (DS820) og proksimal tibiafraktur (DS821)) med/uden NOMESCO-kirurgikoder for knæfraktur i Danmark blev inkluderet i alle PhD-afhandlingens tre studier. Data blev prospektivt indsamlet fra CRS og DNPR. Patientkomorbiditetsniveau blev beregnet ved anvendelse af det modificerede Charlson Comorbidity Index (CCI).

Studie I: Metoder
I dette landsdækkende danske kohortestudie blev alle patienter, der var registreret med ICD-10-knæfrakturdiagnosekoder, med/uden NOMESCO-knæfrakturkirurgikoder fra 1. januar 1998 til 31. december 2017 inkluderet. Epidemiologien af knæfrakturer blev beskrevet ved hjælp af patient- (alder, køn, CCI-niveau), fraktur- og behandlingsrelaterede karakteristika for knæfrakturpopulationen, indsamlet fra DNPR. Årlige samlede IRs for knæfrakturer og IRs efter alderskategori, køn, knæfrakturtype, og kirurgisk/ikke-kirurgisk behandling af knæfraktur defineredes som antallet af knæfrakturer divideret med antal indbyggere inden for hvert år præsenteret som per 10^5 indbyggere med 95% konfidensintervaller (95% CIs). Knæfrakturpopulationens karakteristika blev beskrevet ved hjælp af proportioner og median med interkvartil afstand (IQR).

Studie II: Metoder
I dette nationale danske befolkningsbaserede tværsnitsstudie blev alle patienter over 15 år, der var registreret med ICD-10-knæfrakturdiagnosekoder, med/uden NOMESCO-knæfrakturkirurgikoder fra 1. januar 2011 til 31. december 2017 inkluderet. Spørgeskemaet, der indeholdt et link til fire PROMs, leveredes via et nationalt digitalt CPR-nummer-linket e-mail system. Fire PROMs: to knæspecifikke (Oxford Knee Score (OKS) og Forgotten Joint Score-12 (FJS-12)) og to generiske (EuroQol 5-Dimensions Questionnaire-5L (EQ5D-5L) Index og EQ5D-5L Visual Analogue Scale (VAS)) blev anvendt til at beskrive outcomes og prognoser for knæfrakturpopulationsudsnittet. OKS er en skala fra 0-48 med højere værdier, der indikerer færre knæsmerter og højere knæfunktion. FJS-12 er en skala fra 0-100 med højere værdier, der indikerer bedre evne til at glemme knæleddet og dermed ingen knæledsproblemer i dagligdagen. EQ5D-5L Index er et -0,21 til 1,00 indeks med højere indeksværdier, der indikerer bedre generelt helbred ved hjælp af fem sundhedsdimensioner. EQ5D-5L VAS er et 0-100 sundhedstermometer med højere værdier, der indikerer bedre generelt helbred. En PROM-score under median PROM-score defineredes som dårlig PROM-score. Stigende alder, køn, CCI-niveau, knæfrakturtype og behandlingstype var potentielle risikofaktorer for dårlig PROM outcome score. Respondenter og ikke-respondenter blev beskrevet ved proportioner og median med IQR. Odds ratioer (ORs) med 95% CIs af risikofaktorer for dårlig PROM-score blev estimeret for alle fire PROMs og inden for alle fire opfølgningsperioder ved hjælp af binære logistiske regressionsmodeller.

Studie III: Metoder
I dette landsdækkende danske 20-årige matchet-case comparison kohorte-studie blev hver patient over 15 år, der var registreret med ICD-10-knæfrakturdiagnosekoder, med/uden NOMESCO-knæfrakturkirurgikoder fra 1. januar 1998 til 30. april 2018 matchet efter køn og alder (samme fødselsår) til fem personer uden registrerede knæfrakturer (befolkningskontroller) fra den generelle befolkning i Danmark.

Både knæfrakturpatienter og populationskontroller blev fulgt fra datoen for registrering af knæfraktur til dato for TKA, amputation, knæfusion, emigration, død eller til slutningen af opfølgningen den 30. april 2018. Amputation, knæfusion, emigration og død blev modelleret som konkurrerende events for TKA. Studiepopulationen blev beskrevet ved hjælp af frekvenser, procenter og median med IQR. Ved hjælp af Cox proportional hazardmodeller blev hazard ratioer (HRs) med 95% CIs og p-værdier brugt til at estimere kortvarig og langvarig risiko for TKA hos knæfrakturpatienter vs populationskontroller og risikofaktorer for TKA hos knæfrakturpatienter.

Resultater

Studie I: Resultater

I løbet af 1998-2017 steg IR for knæfrakturer med 12% til 70 pr. 10^5 indbyggere, og IR for kirurgisk behandlede knæfrakturer steg med 35% til 23 pr. 10^5 indbyggere. Kvinder i alderen >51 år havde den højeste knæfraktur IR. Proksimal tibiafraktur havde en IR på 32 pr. 10^5 indbyggere, den højeste af knæfrakturtyperne. I alt 60.823 patienter (median alder 55 år; 57% kvinder) blev registreret med 74.106 knæfrakturer i løbet af den 20-årige studieperiode. I alt havde 74% af knæfrakturpatienterne en CCI på 0, mens 18% havde en CCI på ≥2. Knæfrakturfordelingen var 51% proksimal tibiafraktur, 31% patellafraktur og 18% distalfemur fraktur. Ved datoen for registrering af knæfraktur blev en femtedel af patienterne ligeledes registreret med ledsagende knænære frakturer (femur/tibia/fibulaskaft/hofte/ankelfraktur), 13% blev registreret med ledsagende frakturer (bækken/ rygsøjle/thorax/øvre ekstremitetsfraktur), 5% blev registreret med osteoporose, og 4% blev registreret med primær knæ OA. Kirurgisk behandlede knæfrakturer omfattede over en tredjedel af de registrerede knæfrakturer, hvoraf 86% blev registreret som åben reduktion intern fiksationer (ORIFs), 9% blev registreret som eksterne fiksationer og 5% blev registreret som knæalloplastikker. Proksimal tibiaskinne var den hyppigste operationstype (n = 4.868; 60% kvinder). Kvinder >51 år og patienter med registrerede komorbiditeter var associerede med pådragelse af knæfraktur, proksimal tibiafraktur, proksimal tibiafrakturkirurgi og knæalloplastik for PTOA efter knæfraktur.

Studie II: Resultater

Der var 7.133 (53%) respondenter (median alder 60 år; 63% kvinder). Ved kortvarig opfølgning (0-1 år efter knæfraktur) var median PROM-scores 31 (OKS), 27 (FJS-12), 0,50 (EQ5D-5L Index) og 74 (EQ5D-5L VAS). Indenfor hvert PROM fandtes lignende median PROM-scores ved 3-5 år og >5 års opfølgning efter knæfraktur. Ved langvarig opfølgning (>5 år efter knæfraktur) var median PROM-scores 40 (OKS), 54 (FJS-12), 0,76 (EQ5D-5L Index) og 80 (EQ5D-5L VAS). Knæfrakturpatienter rapporterede relativt høje OKS, EQ5D-5L Index og EQ5D-5L VAS scores, svarende til relativt lave knæsmerter, høj knæfunktion og højt generelt helbred/QOL. Knæfrakturpatienter rapporterede lave FJS-12 scores, svarende til manglende evne til at glemme knæleddet i hverdagen. Forskellige risikofaktorer for dårlig PROM-score var til stede i forskellige PROMs og opfølgningsperioder.

Alder >40 år havde høje odds for dårlige OKS og FJS-12 scores i alle opfølgningsperioder. Komorbiditetsbyrde, distal femurfraktur, behandling af knæfraktur med ekstern fiksation og behandling af knæfraktur med knæalloplastik havde høje odds for dårlig PROM-score ved langvarig opfølgning efter knæfraktur i alle fire PROMs.

Studie III: Resultater
Knæfrakturpatienter havde en 3,7 gange højere risiko (HR 3,74; 95% CI 3,44-4,07; p <0,01) for at gennemgå TKA i de første 3 år efter knæfraktur sammenlignet med populationskontroller. Knæfrakturpatienter havde en vedvarende øget risiko på 1,6 gange (HR 1,59; 95% CI 1,46-1,71; p <0,01) det af befolkningskontroller for at gennemgå TKA efter de første 3 år efter knæfraktur, hvilket antyder, at risikoen for TKA hos knæfrakturpatienter er livslang. Under den 20-årige periode fik 4% af knæfrakturpatienterne TKA-kirurgi, mens 1% af befolkningskontrollerne fik TKA-kirurgi. Andre risikofaktorer, der føjede til risikoen for TKA hos knæfrakturpatienter, var primær knæ OA vs ingen primær knæ OA (HR 9,57), kirurgisk behandling med ekstern fiksation af knæfraktur vs ORIF og kun reduktion af knæfraktur (HR 1,92), proksimal tibiafraktur vs patellafraktur (HR 1,75) og distal femurfraktur vs patellafraktur (HR 1,68). Kirurgisk behandling af knæfraktur vs ikke-kirurgisk behandling af knæfraktur var en risikofaktor for TKA hos knæfrakturpatienter: HR var 2,05 i de første 5 år efter knæfraktur og HR var 1,19 efter 5 år og fremover efter knæfraktur.

Konklusioner
Patientrelaterede faktorer såsom kvindeligt køn, stigende alder og komorbiditet inklusive primær knæ OA, frakturrelaterede faktorer såsom proksimal tibiafraktur og distal femurfraktur og behandlingsrelaterede faktorer såsom kirurgisk behandling af knæfraktur, ekstern fiksation og knæalloplastik er forbundet med incidenser, outcomes og risiko for TKA hos knæfrakturpatienter. Fremtidige studier bør yderligere undersøge patientrelaterede faktorer såsom andre komorbiditeter og traume-sværhedsgrad, frakturrelaterede faktorer såsom underklassifikationer af knæfrakturer og behandlingsrelaterede faktorer såsom underklassifikationer af operationstyper, for yderligere at beskrive den komplekse knæfrakturpopulation og dens incidenser, outcomes og risiko for TKA, såvel som forventede prognoser, for at hjælpe sundhedsvæsenet med at planlægge den optimale håndtering af knæfrakturpatienter hensigtsmæssigt. Behovet for en reevaluering af nuværende hospitalsressourcer rettet mod knæfrakturpopulationen er derfor berettiget.

Introduction

Knee fractures consist of fractures in the distal femur, patella, and proximal tibia. After a knee fracture event, patients can suffer from a variety of complications including decreased knee function [1][2][3][4], decreased quality of life (QOL) [3][5][4], decreased work output [5][4], posttraumatic osteoarthritis (PTOA) [6][3][7][8][9][10][11], and in some cases undergo total knee arthroplasty (TKA) surgery [6][8][10][11].

There is a paucity in literature regarding 1) incidences of knee fractures, 2) patient-reported outcomes of knee fractures, and 3) risk of TKA following knee fracture. To study the three abovementioned points, three studies made up the PhD thesis:

Study I: Incidences

Knowing the incidence rates (IRs) and epidemiology of knee fractures will help establish the treatment burden of knee fractures and subsequently aid health care systems in delivering appropriate hospital resources to the management of patients with knee fractures.

Study II: Patient-Reported Outcomes

By reporting patient-reported outcome measures (PROMs) (both knee-specific and generic PROM scores) and risk factors for poor PROM scores, the outcomes and prognoses of knee fracture patients can be appropriately described and in turn guide future health care investments and regulations to ensure high quality of care for all knee fracture patients, regardless of their patient-, fracture-, and treatment-related risk factors.

Study III: Risk of Total Knee Arthroplasty

By providing risk estimates and describing risk factors for TKA, health care systems will better be able to estimate the treatment burden of knee fractures and in the future, clinicians will more accurately be able to inform patients of their prognosis after knee fracture based on patient-, fracture-, and treatment-specific factors.

Incidences

It has been estimated that the IR of knee fractures is 9 in 10^5 per year in the United States [12]. Current research has not described knee fractures extensively, using only small sample sizes [13][14], and only focusing on lower extremity fractures, tibial fractures [15], tibial plateau fractures [16], or patellar fractures [17]. To our knowledge, population-based studies describing IR trends over time of knee fractures, and IRs according to sex, age, knee fracture type, and treatment type, as well as patient-, fracture-, and treatment-related characteristics of knee fracture patients are lacking.

Patient-Reported Outcomes

Few studies have investigated the outcomes after knee fracture using PROMs as well as the risk factors associated with poor PROM scores in knee fracture patients. Knowledge of this would provide valuable information on the different prognoses of knee fracture patients as well as insight into the current quality of care of knee fracture patients. Literature on the outcomes of knee fracture patients remains sparse and diffusely described. PROMs such as the Knee Injury and Osteoarthritis Outcome Score (KOOS) and Functional Status Score have shown decreased functional outcomes as well as reduced QOL in knee fracture patients [4][5]. A study using Sanders Score reported good to excellent functional outcome in anatomic lateral locking plate-treated open distal femoral fracture patients [18]. In a study using Short Form-36 Health Survey and KOOS, surgically treated patella fracture patients experienced continuing long-term symptoms, pain, and diminished function [3]. A study using KOOS showed decreased long-term function of open reduction internal fixation (ORIF) treated tibial plateau fracture patients [4]. In another study of surgically treated tibial plateau fracture patients, a mean long-term Forgotten Joint Score-12 (FJS-12) score of 70 was reported [19]. As evidenced above, current knowledge of the outcomes after knee fracture involve limited patient samples of certain knee fracture types and only involve some treatment types of knee fractures [18][3][4].

In Study II, four PROM questionnaires, two knee-specific: Oxford Knee Score (OKS) [20][21] and FJS-12 [22][23][24][25], and two generic: EuroQol 5-Dimensions Questionnaire-5L (EQ5D-5L) Index [26][27][28], and EQ5D-5L Visual Analogue Scale (VAS) [26][27][28] were used to describe the outcomes of the study population. OKS describes a patient's knee pain and function on a 0-48 scale with higher values indicating better knee function and less pain, and has been used in knee osteoarthritis (OA) patients [21] as well as both knee OA and PTOA patients undergoing TKA [20]. FJS-12 describes a patient's ability to forget about their knee joint in their daily life on a 0-100 scale with higher values indicating better ability to forget about the knee joint and thus indicating a life without knee problems [22][23][24]. The FJS-12 is mainly used in TKA patients [22][23][29][30], but also in PTOA patients after ORIF-treated tibial plateau fracture [24], and in anterior cruciate ligament (ACL) reconstruction patients [31][32]. Studies have shown that FJS-12 has the ability to discern between good and excellent outcome [22], presents with lower ceiling effects compared to KOOS [32], WOMAC [32][22], and OKS [23], and has a high responsiveness in terms of more accurately describing outcomes after TKA than generic or clinician-reported questionnaires [30]. The EQ5D-5L Index is an index of five health dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) ranging from -0.21 to 1.00 with higher index values indicating better general health and QOL [26][27][28]. The EQ5D-5L VAS is a general health scale of 0-100 with value 100 indicating perfect general health and QOL [26][27].

Risk of Total Knee Arthroplasty

Increases in populations, longevity, and obesity rates can only partly explain the increasing rates of TKA surgeries, as knee injuries also contribute to the increases [33][34]. As previously stated, knee fractures represent an approximate IR of 9 per 10^5 per year in the United States [12]. Furthermore, primary TKA for primary knee OA is often more successful than secondary TKA for PTOA after knee fracture regarding outcomes in function [35][11], rates of complications [36][11], reoperations [36][9], and rates of survival [35]. Current literature has only sparingly researched risk estimates of [37][38] TKA in knee fracture patients compared to people without knee fractures and identified risk factors for [38] TKA in knee fracture patients.

Aims

The overall aims of this PhD thesis were to:

Study I: General Aims

Follow a Danish knee fracture population cohort over a 20-year period to calculate IRs and describe patient-, fracture-, and treatment-related characteristics of knee fracture patients.

Study II: General Aims

Describe the prognoses and quality of care of knee fracture patients by using knee-specific and generic PROMs in a national population-based cross-sectional study with 1-, 3-, and 5-year follow-up to describe short-term and long-term PROM scores of knee fracture patients, as well as risk factors of poor PROM outcome scores.

Study III: General Aims

Estimate the short-term and long-term risk of TKA after knee fracture by matching a Danish knee fracture population cohort to people from the Danish general population without knee fractures over a 20-year period, as well as identifying risk factors for TKA in knee fracture patients.

The specific aims for this PhD thesis were:

Study I: Specific Aims

1) What are the 20-year trends in IRs of knee fractures?
2) What are the patient-, fracture-, and treatment-related characteristics of knee fracture patients in Denmark during 1998-2017?

Study II: Specific Aims

1) Report on knee-specific and generic median PROM scores of knee fracture patients at 0 to >5 years after knee fracture.
2) Identify risk factors for poor outcome defined by low median PROM scores.

Study III: Specific Aims

1) What is the short-term risk of TKA after knee fracture?
2) What is the long-term risk of TKA after knee fracture?
3) What are the risk factors for TKA in patients with knee fractures?

Data Sources

All residents of approximately 5.7 million people [39] legally residing in Denmark are assigned a Civil Personal Register (CPR) number [40] which is used in the Danish national database Civil Registration System (CRS) [40] to register and daily update a resident's birth date, sex, residency, emigration status, and vital status. The CPR number is used in the Danish National Patient Registry (DNPR) [41] and other registries to link data. The DNPR is a national database containing information on all public admissions and visits to emergency departments, and some private hospital admissions, date of admission, CPR number, age, sex, World Health Organization 10th revision of International Classification of Diseases and Health Related Problems (ICD-10) [42] diagnosis codes, and the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) [43] surgery codes (See Supplementary Material). As the current NOMESCO surgery code system was implemented in 1995, all years prior to 1996 were not analysed in order to reduce surgery code bias in Study I and Study III. Years 1996-1997 were also taken out from the analysis to reduce prevalent knee fractures and the already existing follow-ups of knee fracture patients in Study I and Study III. Of note is that all hospitals must report to the DNPR for reimbursement [41], although, private hospitals do not treat knee fracture patients in Denmark and rarely perform TKAs.

Materials and Methods

Patient data including CPR number, age, sex, comorbidities from ICD-10 diagnosis codes, residency status, emigration status, and vital status, and fracture- and treatment data including ICD-10 diagnosis codes for distal femur fracture (DS724), patella fracture (DS820), and proximal tibia fracture (DS821) with/without NOMESCO surgery codes for knee fracture, were prospectively collected from the CRS and DNPR in all three studies of the PhD project. Comorbidities included in the modified Charlson Comorbidity Index (CCI) [44][45] which were registered on or prior to the registered date of knee fracture were included in all three studies. The Danish Data Protection Agency approved all three studies (record number REG-085-2017). As all three studies were registry studies, no institutional review board approval was needed. All three studies were reported according to the Strengthening the Reporting of Observational studies in Epidemiology guidelines [46] and statistical analyses were performed using the statistical software R 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Study I: Materials and Methods

Patients registered with ICD-10 [42] diagnosis codes for distal femoral (DS724), patellar (DS820), and proximal tibial fractures (DS821), with/without NOMESCO [43] surgery codes for knee fractures in the DNPR from January 1st, 1998 to December 31st, 2017 were included in this nationwide cohort study of prospectively collected data from the CRS and DNPR (See Supplementary Material Study I). New knee fracture, surgically treated knee fracture, and non-surgically treated knee fracture is defined in Figure 1. Patient- (age, sex, comorbidity-level according to the modified CCI [44][45]), fracture- (distal femur, patella, and proximal tibia), and treatment-related (surgically treated: ORIF, external fixation, and knee arthroplasty, and non-surgically treated knee fractures) characteristics of knee fracture patients in Denmark during the 20-year period during 1998-2017, were registered in the DNPR and presented in the study.

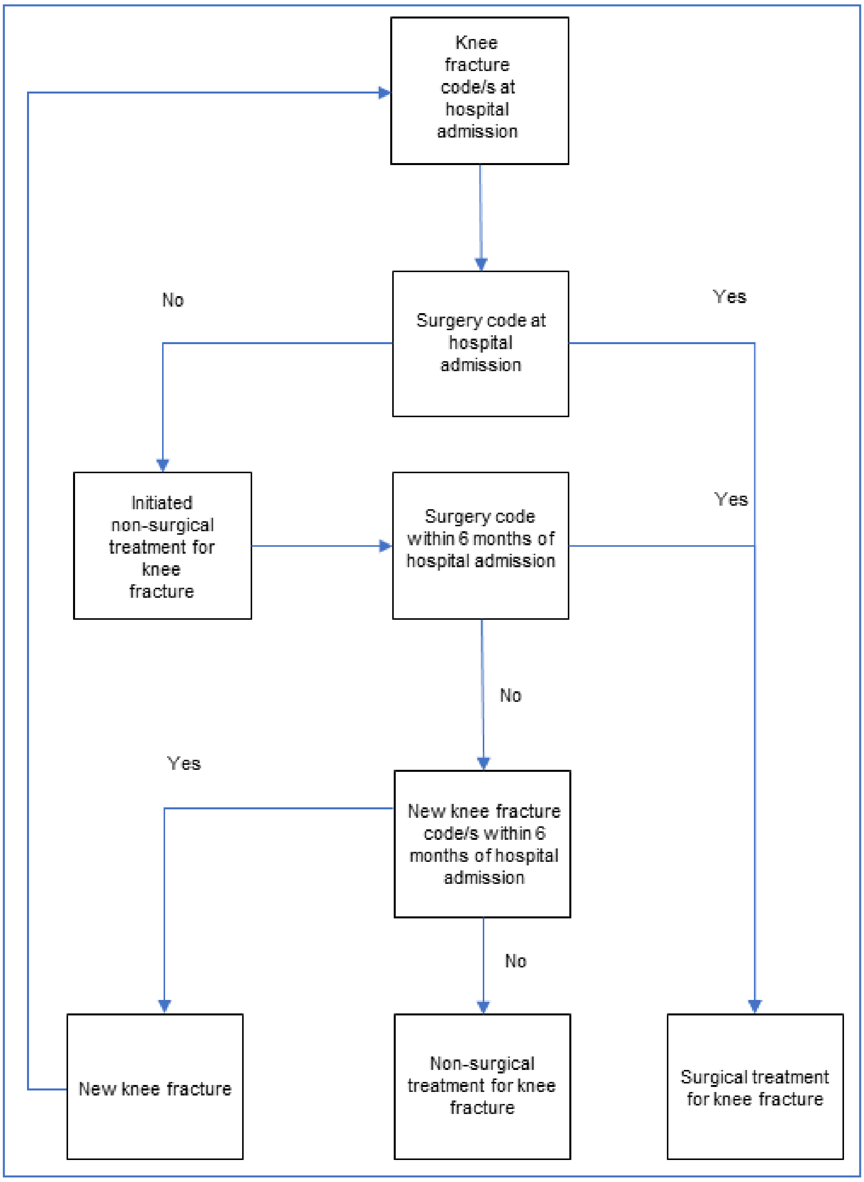

Figure 1. Definition of new knee fracture, surgically treated knee fracture and non-surgically treated knee fracture.

Study I: Statistical Analysis

The study population was described using proportions, median, and interquartile range (IQR). Overall yearly IRs were calculated as the number of knee fractures per calendar year divided by the total number of inhabitants at risk in Denmark in the same year and presented as IR per 10^5 inhabitants. IRs within age category, sex, knee fracture types, surgical treatments of knee fractures, and non-surgical treatments of knee fractures were also calculated using the same IR definition. All IRs were presented per year with 95% confidence intervals (95% CIs). Incidence rate ratios (IRRs) showed the relative IR change in the years 1999-2017 with year 1998 as reference and were estimated from Poisson regression models.

Study II: Materials and Methods

This national population-based cross-sectional study included all patients over the age of 15 years registered with prospectively collected data from the CRS and DNPR for ICD-10 [42] diagnosis codes for distal femur fracture (DS724), patella fracture (DS820), and proximal tibia fracture (DS821), with/without NOMESCO [43] surgery codes for knee fractures from January 1st, 2011 to December 31st, 2017 (See Supplementary Material Study II). Patient inclusion criteria included: the patient had to be registered as alive, had to be registered with a non-confidential name, had to be registered with a non-confidential Danish address, and not be registered as incapacitated. Data was pulled on August 3rd, 2018 and the questionnaire including all four PROMs was sent out using a national e-mail system (E-boks) linked to CPR number on October 26th, 2018 to all patients whom fulfilled the inclusion criteria (Figure 2).

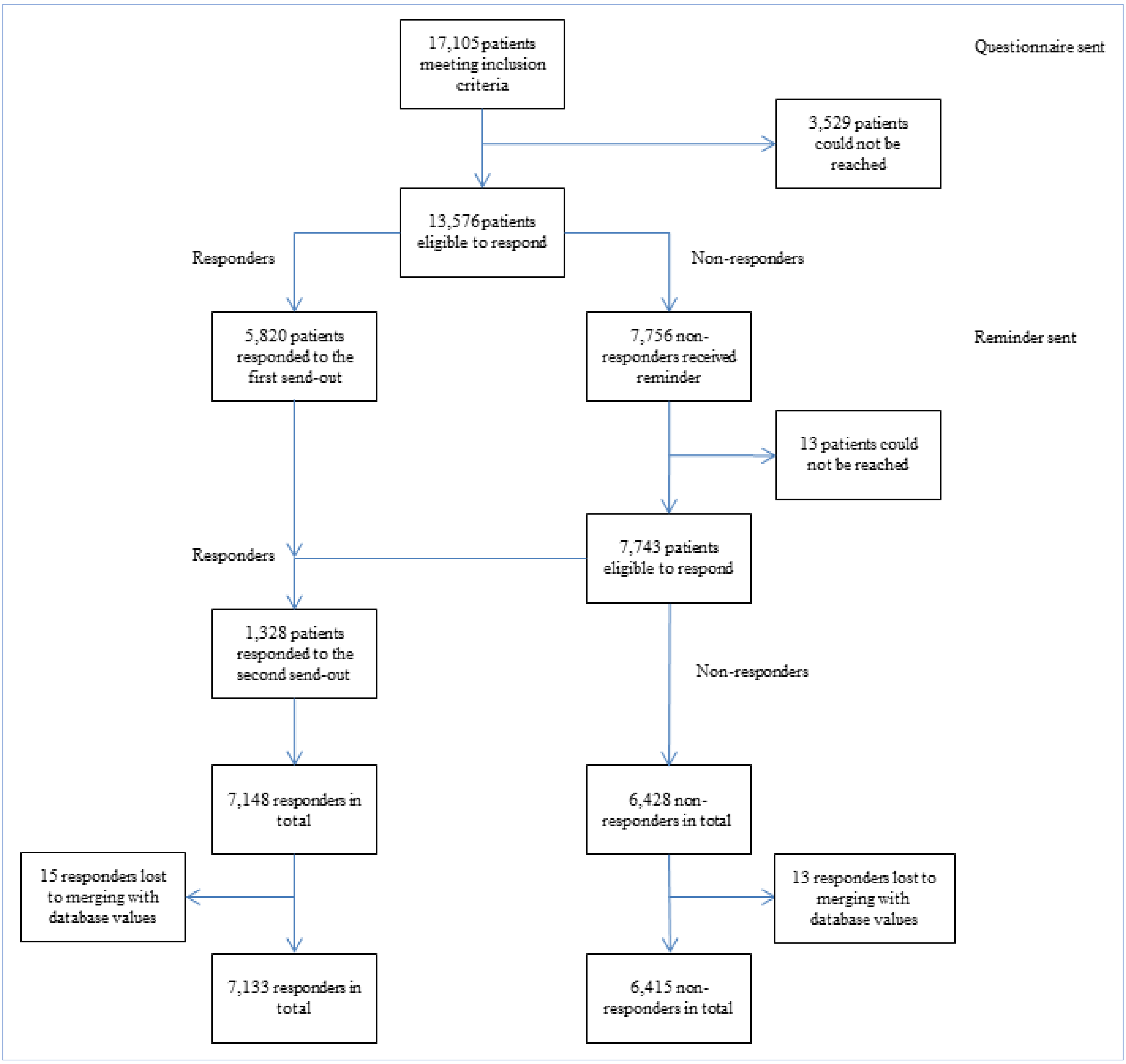

Figure 2. Flowchart of responders and non-responders.

The e-mail contained a study description with a statement stating that participation was optional and an electronic link to the questionnaire which included all four PROMs. Some patients lacked an E-boks subscription or could not be found in the E-boks system (n=3,529), therefore the total number of patients available for response were 13,576. On January 2nd, 2019, a reminder was sent electronically via E-boks to all non-responders.

Because PROM scores were unevenly distributed and because PROM cut-off values for knee fracture patients are not known in literature, median PROM scores were therefore reported. A PROM score of lower than the median PROM score was defined as poor outcome and a PROM score of higher than the median PROM score was defined as good outcome. To ensure enough patients in each follow-up group as well as periods of clinical relevance, follow-up periods were divided into 0-1, 1-3, 3-5, and >5 years following knee fracture. Potential risk factors for poor median PROM score were age (reference group age <40 years vs age 40-60 years, and age >60 years), sex (reference group male vs female), CCI level (reference group CCI 0 vs CCI 1, CCI 2, and CCI ≥3), knee fracture type (reference group patella fracture vs proximal tibia facture and distal femur fracture), and treatment type (reference group ORIF and reduction only vs non-surgical treatment, external fixation, and knee arthroplasty). The modified version of CCI [44][45] categorized comorbidity levels of responders and non-responders by registering comorbidities included in the CCI before or at the time of registered knee fracture.

Study II: Statistical Analysis

Responders and non-responders were described using proportions, median, and IQR. PROM scores were presented as median with IQR. Potential risk factors for poor PROM score (PROM score lower than the median PROM score) were estimated as odds ratios (ORs) with 95% CIs from binary logistic regression models. ORs with 95% CIs of all potential risk factors were presented for all combinations of PROMs and follow-up periods in the specific models. All potential risk factors were included as variables, therefore model reduction was not performed, and therefore ORs were adjusted for all potential risk factors. Of note is that a multiple fracture level was included in the knee fracture type in all models, but was not described in the study's results due to challenges regarding comparing all possible multiple knee fracture combinations to each other as well as to single knee fractures. Logistic regression was also used to compare individual knee fracture type within each treatment type and individual treatment type within each knee fracture type. Hosmer-Lemeshow goodness of fit test was used to assess the fit of the binary logistic regression models.

Study III: Materials and Methods

Each patient aged 15 years and above with ICD-10 [42] diagnosis codes registered in the DNPR for distal femoral (DS724), patellar (DS820), and proximal tibial (DS821) fracture with/without NOMESCO [43] knee fracture surgery codes from January 1st 1998 to April 30th 2018 was matched by sex and age (same birth year) to five people without knee fracture from the general population in a Danish nationwide 20-year matched-case comparison cohort study of prospectively collected data from the CRS and the DNPR (See Supplementary Material Study III).

Knee fracture patients and patients without knee fractures (population controls) were followed from knee fracture registration date to date of TKA, amputation, knee fusion, emigration, death, or end of follow-up on April 30th 2018. The modified CCI was used to describe comorbidity level [44][45]. In 19% of population controls the CCI could not be calculated because patients were either not registered with diseases used in the calculation of CCI or they did not have hospital admissions. The CCI was thus set at 0 for this proportion of the population controls. In this study primary knee OA was defined as pre-existing knee OA registered on or prior to the time of knee fracture registration (See Supplemental Material Study III). Surgical treatment consisted of external fixation, ORIF, and reduction, defined as index procedures. In this study, there was no access to medical records, therefore the true number of conversions from external fixation to ORIF were unknown, as such every external fixation registration was allocated to the external fixation group.

Study III: Statistical Analysis

The study population was described using median and IQR or frequency and percentage. Wilcoxon's rank sum test was used to calculate the p value for age in knee fracture patients and population controls because data could not be assumed to be normally distributed when observing QQ-plots. Pearson's chi-square test was used to calculate the p value for sex and CCI in knee fracture patients and population controls. Short-term and long-term risk of TKA in knee fracture patients vs population controls and risk factors for TKA in knee fracture patients were calculated as hazard ratios (HR) with 95% CIs and p values from Cox proportional hazard models. Competing events for TKA were amputation, knee fusion, emigration, and death and risk time was censored when these events occurred. The Cox proportional hazards model was divided into two models to answer the first and second research questions. The first model was for the first 3 years after knee fracture, where all non-events were censored at 3 years. The second model was for after the 3 years and onward, where knee fracture patients and population controls were only included if they did not have any events during the first 3 years and if they had a follow-up of over 3 years. The reason for dividing the model into two models was because when comparing knee fracture patients to population controls, the HR was not constant during all 20 years of follow-up, i.e. the proportional hazard assumption was not fulfilled when observing the Schoenfeld residuals for the 20-year period, but was however constant in each of the two models. The proportional hazard assumption could be fulfilled for the entire 20-year period for most of the risk factors in research question three, therefore risk factors for TKA in knee fracture patients were presented as HRs for the 20-year period. When comparing surgically treated knee fracture patients with non-surgically treated patients in research question three however, the proportional hazards assumption could only be fulfilled when the model was divided into two models: one for the first 5 years after knee fracture and the second for after the 5 years and onward. HRs of risk factors for the first 5 years and from 5 years and onward were therefore presented for surgically treated vs non-surgically treated knee fracture patients.

Results

Study I: Results

1) What are the 20-Year Trends in IRs of Knee Fractures?

Overall Incidence Rates

The average IR for knee fractures during the 20-year study period was 63 (95% CI 62-63) per 10^5 inhabitants. The IR of knee fracture was 64 (95% CI 61-66) per 10^5 inhabitants in 1998 and increased to 70 (95% CI 67-72) per 10^5 inhabitants in 2017, equivalent to a 12% increase (Figure 3). The corresponding IRR in 2017 was 1.1 (95% CI 1.0-1.2) compared to year 1998 (Table 1).

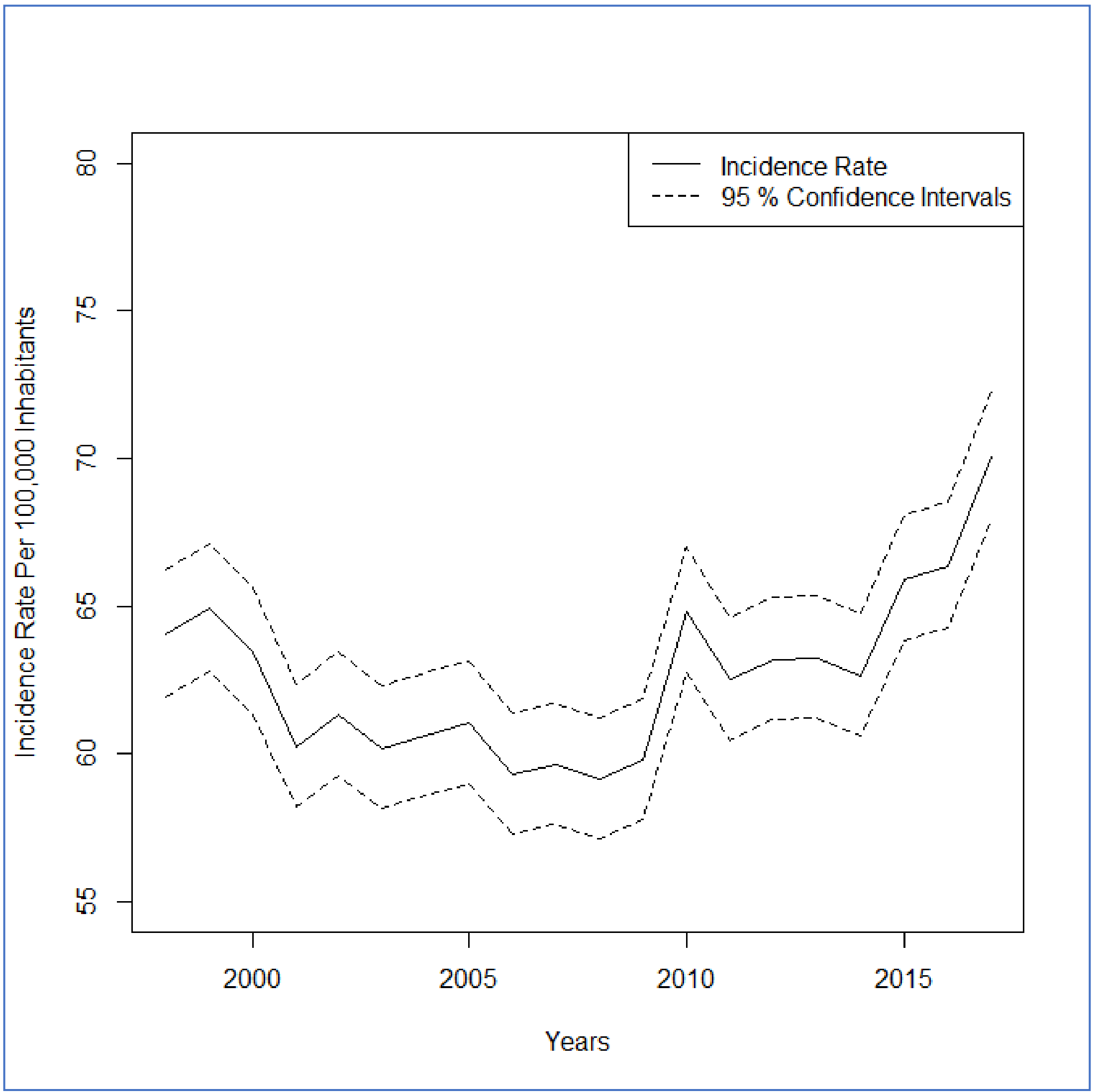

Figure 3. Incidence rate of knee fractures per 10^5 inhabitants during 1998-2017 with 95% confidence intervals.

Table 1. Annual Incidence Rates with 95% Confidence Intervals and Incidence Rate Ratios for the Study Population Registered in the DNPR during 1998-2017.

Year	IR (95% CI)	IRR (95% CI)
1998	64.0 (61.9-66.2)	Reference
1999	64.9 (62.8-67.1)	1.01 (0.97-1.06)
2000	63.5 (61.4-65.6)	0.99 (0.94-1.04)
2001	60.3 (58.2-62.4)	0.94 (0.90-0.99)
2002	61.3 (59.3-63.5)	0.96 (0.91-1.00)
2003	60.2 (58.2-62.3)	0.94 (0.90-0.99)
2004	60.6 (58.6-62.8)	0.95 (0.90-0.99)
2005	61.0 (59.0-63.2)	0.95 (0.91-1.00)
2006	59.3 (57.3-61.4)	0.93 (0.88-0.97)
2007	59.6 (57.6-61.7)	0.93 (0.89-0.98)
2008	59.2 (57.1-61.2)	0.92 (0.88-0.97)
2009	59.8 (57.8-61.9)	0.93 (0.89-0.98)
2010	64.8 (62.8-67.0)	1.01 (0.97-1.06)
2011	62.5 (60.5-64.6)	0.97 (0.93-1.02)
2012	63.2 (61.1-65.3)	0.99 (0.94-1.03)
2013	63.3 (61.2-65.4)	0.99 (0.94-1.04)
2014	62.6 (60.6-64.8)	0.98 (0.93-1.03)
2015	65.9 (63.8-68.1)	1.03 (0.98-1.08)
2016	66.4 (64.3-68.5)	1.04 (0.99-1.09)
2017	70.0 (67.9-72.2)	1.09 (1.04-1.15)

DNPR = Danish National Patient Registry. IR = incidence rate per 10^5 inhabitants. 95% CI = 95% confidence interval. IRR = incidence rate ratio with year 1998 as reference.

Incidence Rates by Sex and Age

In females with knee fractures, IR increased from 70 (95% CI 67-73) to 83 (95% CI 80-86) from 1998 to 2017 (Figure 4). In males the corresponding IRs were 58 (95% CI 55-61) in 1998 and 57 (95% CI 54-60) in 2017 (Figure 4). Corresponding IRRs were 1.2 (95% CI 1.1-1.3) for females in 2017 and 1.0 (95% CI 0.9-1.1) for males in 2017, when compared to year 1998. In females over age 71 years especially, the absolute highest knee fracture IRs were seen: IR 240 (95% CI 223-258) in 1998 and IR 223 (95% CI 209-239) in 2017. During 1998-2017, increases in IRs were seen in females between ages 51-70 years (IR 95 (95% CI 87-103) in 1998 and IR 124 (95% CI 116-132) in 2017), children aged 0-5 years, (in females IR was 23 (95% CI 17-30) in 1998 and 78 (95% CI 66-93) in 2017, while in males IR was 24 (95% CI 19-32) in 1998 and 71 (95% CI 60-84) in 2017), and in both sexes aged 6-18 years (in females IR was 31 (95% CI 26-37) in 1998 and 38 (95% CI 33-44) in 2017, and in males IR was 57 (95% CI 50-65) in 1998 and 70 (95% CI 63-79) in 2017.

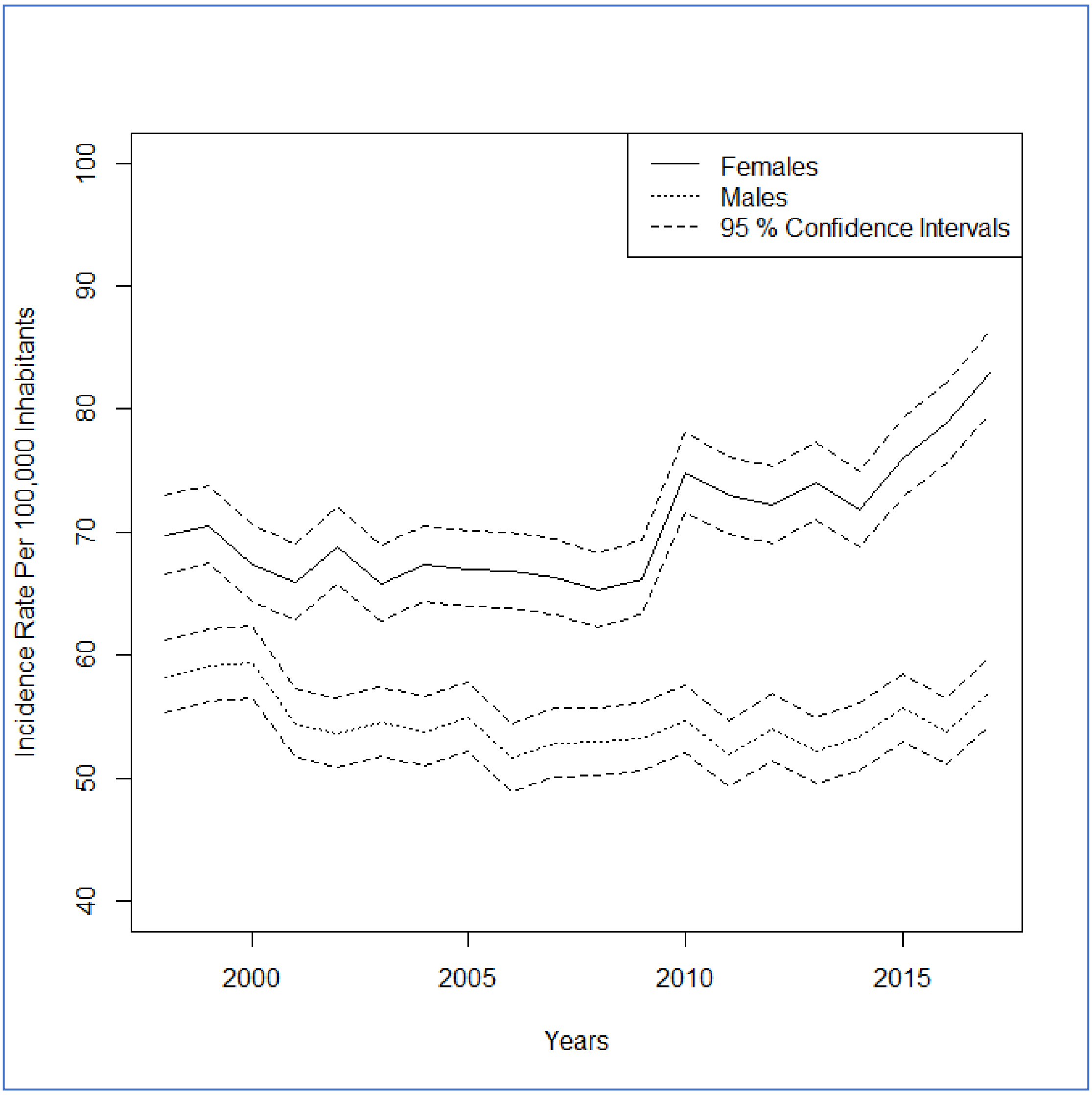

Figure 4. Incidence rates of knee fractures per 10^5 inhabitants during 1998-2017 by sex.

Incidence Rates by Knee Fracture Type

The highest knee fracture type IR was found in proximal tibia fracture (average IR: 32 per 10^5 inhabitants). The average IR for each knee fracture type during the 20-year period was 32 (95% CI 31-32) for proximal tibia fracture, 21 (95% CI 21-21) for patella fracture, and 12 (95% CI 12-12) for distal femur fracture. During the 20-year study period, the IRs of distal femur fracture and patella fracture were relatively unchanged while the IR of proximal tibia fracture increased after year 2010 (Figure 5).

Incidence Rates by Treatment Type

For surgically treated knee fractures during the 20-year period, the average IR was 21 (95% CI 21-21). Surgically treated knee fracture IR was 17 (95% CI 16-18) per 10^5 inhabitants in 1998 and increased to 23 (95% CI 22-24) per 10^5 inhabitants in 2017, equivalent to a 35% increase (Figure 6). In year 2017, the corresponding surgically treated knee fracture IRR was 1.4 (95% CI 1.2-1.5) compared to reference year 1998. For non-surgically treated knee fractures during the 20-year period, the average IR was 42 (95% CI 41-42). Non-surgically treated knee fracture IR was 47 (95% CI 45-49) per 10^5 inhabitants in 1998 and also 47 (95% CI 45-49) per 10^5 inhabitants in 2017 (Figure 6). In year 2017, the corresponding non-surgically treated knee fracture IRR was 1.0 (95% CI 1.0-1.1) compared to reference year 1998.

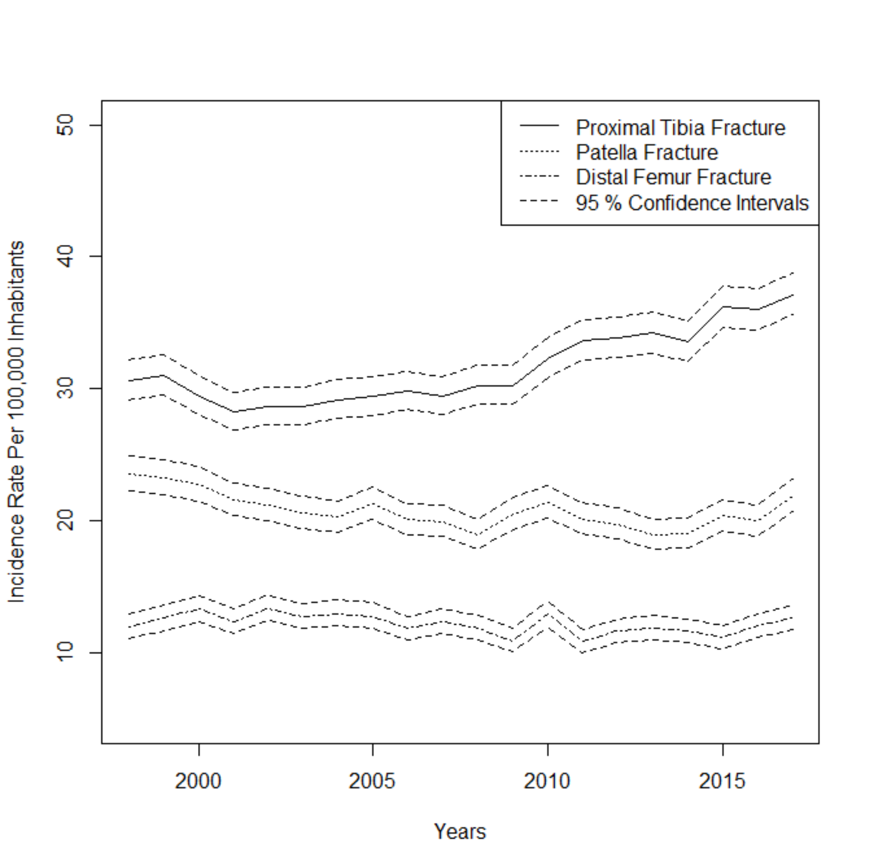

Figure 5. Incidence rates of knee fractures per 10^5 inhabitants during 1998-2017 by knee fracture type.

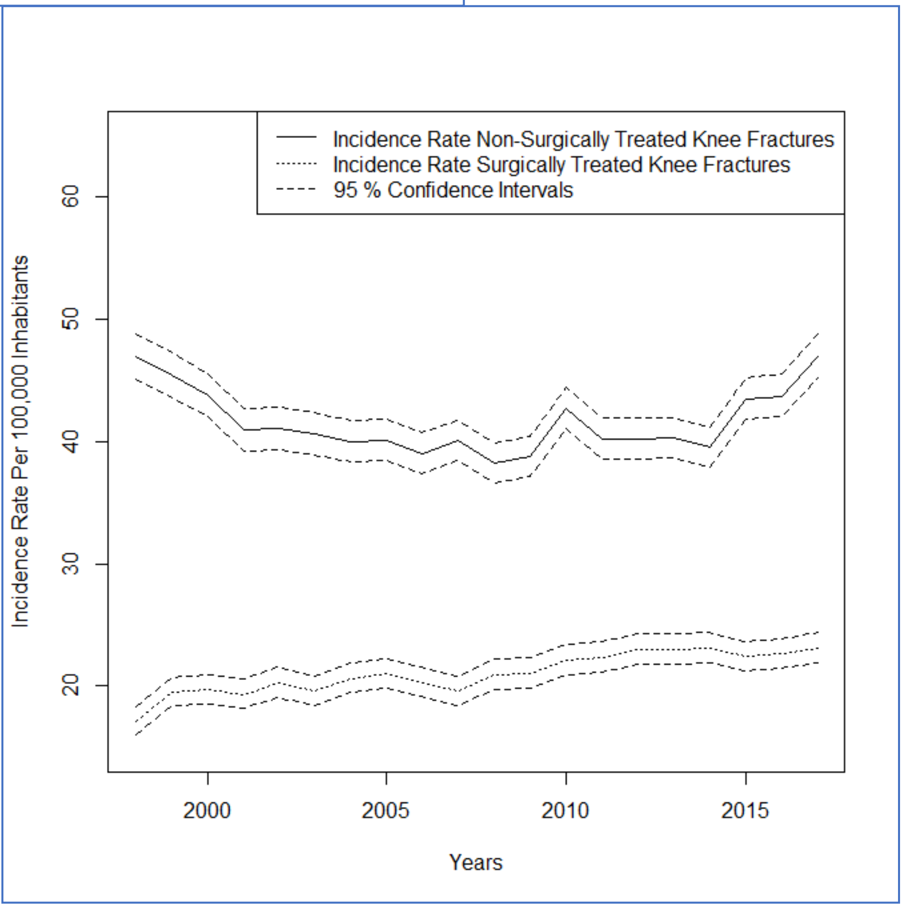

Figure 6. Incidence rates of surgically treated knee fractures and non-surgically treated knee fractures per 10^5 inhabitants during 1998-2017.

2) What are the Patient-, Fracture-, and Treatment-Related Characteristics of Knee Fracture Patients in Denmark during 1998-2017?

60,823 patients (median age 55; 57% female) had 74,106 knee fractures during the 20-year period (Table 2). Median age for females was 64 years (IQR 46-78) while median age for males was 42 years (IQR 19-59). The highest distributions of knee fracture patients were seen in children aged 0-5 years, males aged 5-50 years, and females aged >50 years (Figure 7). Most patients were not registered with comorbidities (74% had CCI 0). 8% had CCI 1, while 18% had CCI ≥2. At the time of registered knee fracture, one fifth of patients had concomitant near-knee fracture registrations in the femur/tibia/fibula shaft/hip/ankle, with tibia shaft fracture (5%) and femur shaft fracture (4%) being most common, and 13% were registered with concomitant fractures in the pelvis/spine/thorax/upper extremities (See Supplemental Material Study I). Other registrations at the time of registered knee fracture were lesions inside the knee in 10%, while 5% were registered with osteoporosis, and 4% with primary knee OA (See Supplemental Material Study I). Knee fracture distribution was proximal tibia (51%), patella (31%), and distal femur (18%). In Table 3, the distribution of knee fracture types and treatment types of the study population during the 20-year study period is shown.

11% of knee fracture patients were registered with >1 knee fracture, and 90% were registered with only 1 knee fracture. There were 68,419 knee fracture treatments in total during the 20-year period, with some treatments involving multiple knee fractures. Of the surgically treated patients, 11% were surgically treated more than once, the remaining 89% had only 1 knee fracture surgery. Of all 68,419 treatments, 34% were surgically treated and 66% of treatments were non-surgically treated. In non-surgically treated patients, 4% had >1 non-surgical treatment and 96% had 1 non-surgical treatment. A total of 6% of knee fracture treated patients were treated both surgically and non-surgically for knee fracture.

20,350 patients were surgically treated for 24,215 knee fractures during the 20-year period. There were 22,996 knee fracture surgeries in total during 1998-2017. The median age of surgically treated patients was 59 years (IQR 42-72) with median age for females being 66 years (IQR 54-77). Of surgical treatments, 86% were registered with ORIFs, 9% with external fixations, and 5% with knee arthroplasties. Proximal tibia plating was the most frequent type of surgery (n= 4,868; 60% female). The six most frequent surgical procedures are listed with frequencies, age, and sex distribution in Table 4.

Table 2. Demographic Data on the Study Population Registered in the DNPR during 1998-2017.

Year	1998	1999-2004	2005-2010	2011-2016	2017
Study Population No. of Patients 60,823					
Patient Demographics Total No.	3262	17623	17557	18870	3511
Age Median (IQR)	54 (33-73)	55 (33-74)	55 (30-72)	56 (27-71)	57 (27-72)
Sex No.					
Females	1800	9804	9875	11012	2073
(%)	55%	56%	56%	58%	59%
CCI No.					
Index Zero, CCI=0	2710	13729	12784	13303	2491
(%)	83%	78%	73%	71%	71%
Index Low, CCI=1	169	1186	1482	1788	355
(%)	5%	7%	8%	10%	10%
Index Medium, CCI=2	229	1601	1757	2056	368
(%)	7%	9%	10%	11%	11%
Index High, CCI≥3	154	1107	1534	1723	297
(%)	5%	6%	9%	9%	9%
Other Diagnoses No.					
Concomitant Near-Knee Fractures	666	3970	3763	3293	448
(%)	20%	23%	21%	18%	13%
Concomitant Fractures	390	2314	2355	2259	269
(%)	12%	13%	13%	12%	8%
Lesions Inside the Knee	303	1767	1826	2034	315
(%)	9%	10%	10%	11%	9%
Primary Knee OA	116	789	786	708	63
(%)	4%	5%	5%	4%	2%
Osteoporosis	76	571	879	1128	102
(%)	2%	3%	5%	6%	3%
Knee Fracture Type No.					
Proximal Tibia	1613	9342	9643	11622	2126
(%)	46%	46%	48%	53%	52%
Patella	1242	6913	6653	6627	1254
(%)	36%	34%	33%	30%	31%
Distal Femur	632	4136	3961	3884	724
(%)	18%	20%	20%	18%	18%
Total No.	3487	20391	20257	22133	4104
Total No. of Inhabitants at Risk in the Specific Calendar Period	5,220,478.5				5,722,369.5

DNPR = Danish National Patient Registry. No. = Number. IQR = interquartile range. CCI = Charlson Comorbidity Index.

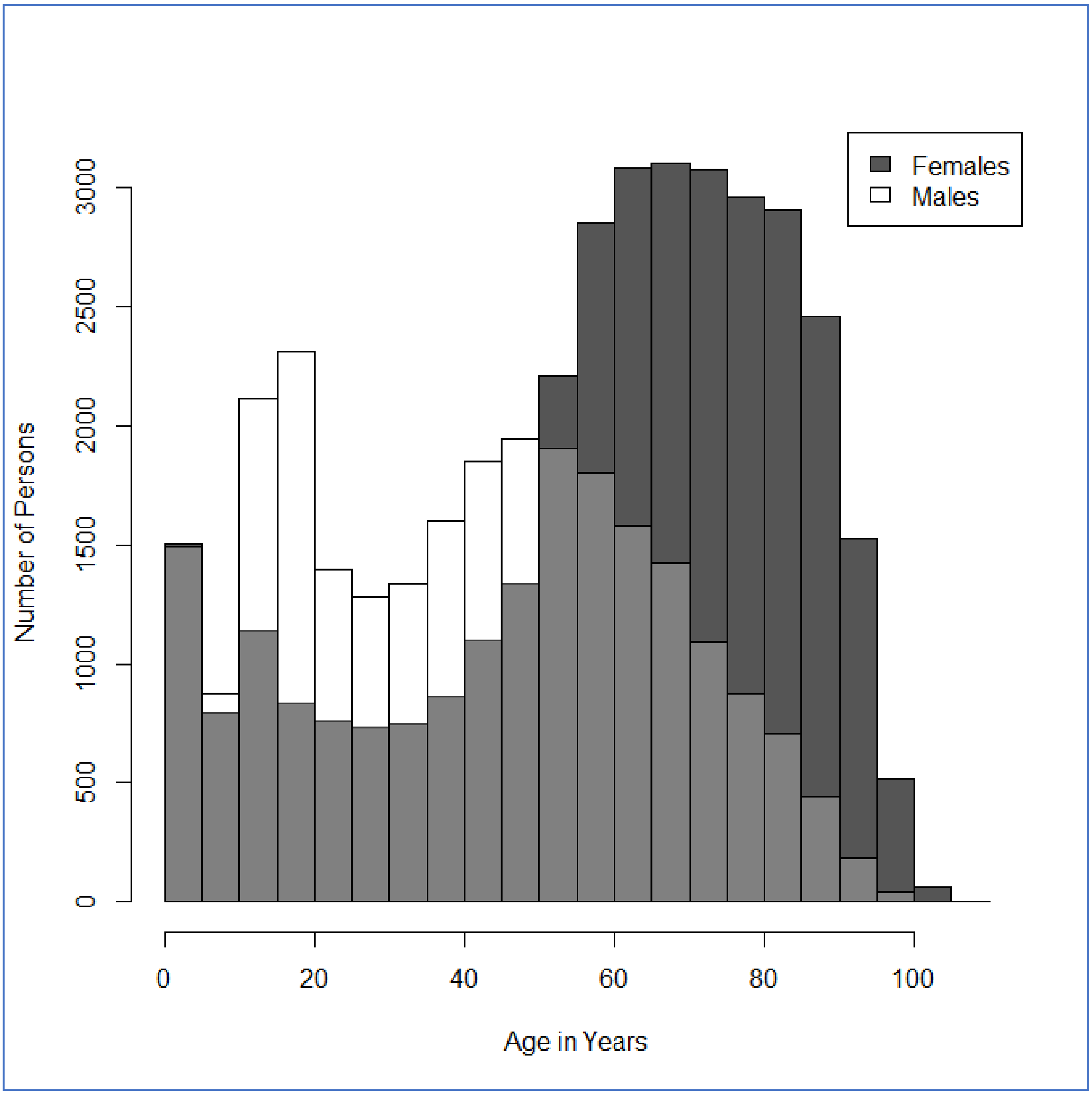

Figure 7. Sex and age distribution of the study population registered in the DNPR during 1998-2017.

Table 3. Distribution of Knee Fracture Type in the Study Population Including Surgically and Non-Surgically Treated Knee Fractures in the DNPR during 1998-2017.

Knee Fracture Type Distribution	Study Population	Surgically Treated Knee Fractures	Non-Surgically Treated Knee Fractures
Proximal Tibia No. (%)	38,080 (51%)	12,175 (50%)	22,411 (48%)
Patella No. (%)	22,689 (31%)	5,977 (24%)	16,712 (36%)
Distal Femur No. (%)	13,337 (18%)	6,063 (25%)	7,274 (16%)
Total No. of Knee Fractures	74,106	24,215	46,397

DNPR = Danish National Patient Registry. No. = Number.

Table 4. Frequency, Age, and Sex Distribution of Most Frequent Knee Fracture Surgery Types Registered in the DNPR during 1998-2017.

Knee Fracture Surgery Type	Frequency	Median Age (IQR)	Female Sex (%)
Proximal Tibia Plate and Screws	4,868	57 (45-67)	60%
Patella Wiring	4,592	61 (44-72)	58%
Proximal Tibia Screw Fixation	3,635	50 (32-63)	50%
Distal Femur Plate and Screws	2,517	74 (61-85)	73%
Distal Femur Intramedullary Nail	1,350	75 (59-85)	74%
Primary Cemented Knee Arthroplasty	855	68 (59-76)	74%

DNPR = Danish National Patient Registry. IQR = interquartile range.

Study II: Results

The response rate was 53%, the number of responders were 7,133, median age of responders was 60 years, and 63% were female (Table 5). The number of non-responders were 6,415 (47%) (Table 5). Responders were approximately 11 years older than non-responders, there were more female responders, and fewer responders were treated non-surgically (Table 5). Both groups were comparable in terms of CCI level, distributions of follow-up periods, knee fracture type, and type of treatment (Table 5). The minimum follow-up period following knee fracture was 0.8 years. The maximum follow-up period following knee fracture was 15.1 years, and 32 patients had more than 8 years of follow-up time.

Table 5. Characteristics of Knee Fracture Patients Divided into Responders and Non-Responders

Patient Demographics	Responders	Non-Responders
No. (%)	7133 (52.6 %)	6415 (47.4 %)
Age Median (IQR)	60.1 (45.2-69.7)	49.6 (27.3-66.4)
Female Sex No. (%)	4460 (62.5 %)	3071 (47.9 %)
CCI No. (%)		
Index Zero, CCI=0	5628 (78.9 %)	4950 (77.2 %)
Index Low, CCI=1	630 (8.8 %)	590 (9.2 %)
Index Medium, CCI=2	576 (8.1 %)	566 (8.8 %)
Index High, CCI ≥3	299 (4.2 %)	309 (4.8 %)
Follow-Up Period No. (%)		
0-1 Years	246 (3.4 %)	174 (2.7 %)
1-3 Years	2412 (33.8 %)	1962 (30.6 %)
3-5 Years	2070 (29.0 %)	1771 (27.6 %)
>5 Years	2405 (33.7 %)	2508 (39.1 %)
Knee Fracture Type No. (%)		
Distal Femur	571 (8.2 %)	707 (11.3 %)
Patella	2424 (34.8 %)	2243 (35.8 %)
Proximal Tibia	3965 (57.0 %)	3308 (52.9 %)
Multiple Knee Fractures	173 (2.4 %)	157 (2.4 %)
Treatment Type No. (%)		
Non-Surgical Treatment	4274 (59.9 %)	4683 (73.0 %)
ORIF and Reduction Only	2621 (36.7 %)	1549 (24.1 %)
External Fixation	152 (2.1 %)	107 (1.7 %)
Knee Arthroplasty	86 (1.2 %)	76 (1.2 %)

No. = Number. IQR = interquartile range. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

1) Report on Knee-Specific and Generic Median PROM Scores of Knee Fracture Patients at 0 to >5 Years after Knee Fracture

During the entire study period of between 0 years to >5 years, median PROM scores were: 38 (OKS), 46 (FJS-12), 0.72 (EQ5D-5L Index), and 80 (EQ5D-5L VAS) (Table 6). Median OKS score was 31 (IQR 23-41), median FJS-12 score was 27 (IQR 10-58), median EQ5D-5L Index score was 0.50 (IQR -0.07 - 0.79), and median EQ5D-5L VAS score was 74 (IQR 51-85), at 0-1 years following knee fracture (Table 6). Median PROM scores within each PROM were similar at 3-5 years and >5 years of follow-up. Median OKS score was 40 (IQR 32-45), median FJS-12 score was 54 (IQR 25-85), median EQ5D-5L Index was 0.76 (IQR 0.32-0.82), and median EQ5D-5L VAS score was 80 (IQR 61-90), at >5 years following knee fracture (Table 6). Median PROM scores as well as IQR values for all four PROMs failed to reach maximum values during the entire study period.

Table 6. Median Patient-Reported Outcome Measure (PROM) Scores with Interquartile Range (IQR)

PROM (Possible Minimum - Maximum Value)	Median PROM Scores (IQR) by Years after Knee Fracture				Median PROM Scores (IQR) for Total Study Population
	0-1 years	1-3 years	3-5 years	>5 years	0 - >5 years
Number of Patients in Each Follow-Up Group	246 patients	2412 patients	2070 patients	2405 patients	7133 patients
OKS (0-48)	31 (23-41)	37 (27-44)	39 (30-45)	40 (32-45)	38 (29-45)
FJS-12 (0-100)	27 (10-58)	40 (16-75)	49 (20-85)	54 (25-85)	46 (19-81)
EQ5D-5L Index (-0.21-1.00)	0.50 (-0.07-0.79)	0.68 (0.20-0.82)	0.72 (0.27-0.84)	0.76 (0.32-0.82)	0.72 (0.26-0.82)
EQ5D-5L VAS (0-100)	74 (51-85)	77 (56-90)	80 (60-90)	80 (61-90)	80 (60-90)

2) Identify Risk Factors for Poor Outcome Defined by Low Median PROM Scores

OKS

Using patients <40 years of age as a reference group, patients between the ages of 40-60 years had higher odds of poor OKS score (OKS score lower than the median) at 0-1 years following knee fracture (OR 2.9; 95% CI 1.1-7.7) (Table 7). Sex did not have different odds of poor OKS score at 0-1 years following knee fracture (OR 1.0; 95% CI 0.5-1.9 for female vs male sex) and CCI level did not have increased odds of poor OKS score at 0-1 years following knee fracture (Table 7). Patients with distal femur fracture vs patella fracture, and patients with proximal tibia fracture vs patella fracture reported ORs with wide 95% CIs, and thus uncertainty of the estimates (Table 7). Non-surgically treated knee fracture patients reported lower odds of poor OKS score at 0-1 years following knee fracture, compared to ORIF and reduction only treated knee fracture patients (Table 7). At longer follow-up (3-5 years and >5 years following knee fracture) different risk factors presented themselves compared to short-term 0 to 1-year follow-up following knee fracture. At 3-5 years and >5 years following knee fracture, female patients had higher odds of poor OKS score (Table 7). At 3-5 years and >5 years following knee fracture, increasing comorbidity (i.e. OR 3.1; 95% CI 1.8-5.2 for patients with CCI ≥3 compared to patients with CCI 0 at >5 years following knee fracture) presented with higher odds of poor OKS score (Table 7). Patients with distal femur fractures and patients with proximal tibia fractures had higher odds of poor OKS scores at >5 years following knee fracture, compared to patients with patella fractures (Table 7, Figure 8). Non-surgically treated knee fracture patients reported lower odds of poor OKS score at all four follow-up periods (Table 7, Figure 9). Compared to patients treated with ORIF and reduction only, patients treated with external fixation (OR 2.6; 95% CI 1.4-4.8 for external fixation knee fracture patients at >5 years following knee fracture) and patients treated with knee arthroplasty (OR 8.0; 95% CI 1.9-34.1 for knee arthroplasty knee fracture patients at 3-5 years following knee fracture) presented higher odds of poor OKS score at longer follow-up following knee fracture (Table 7, Figure 9).

Table 7. Risk Factors for Poor Outcome Measured with Oxford Knee Score

Patient Demographics	Oxford Knee Score Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	2.9 (1.1-7.7)	1.7 (1.3-2.2)	1.7 (1.3-2.3)	1.4 (1.1-1.8)
Age >60 Years Versus Age <40 Years	2.0 (0.7-5.2)	1.3 (1.0-1.6)	1.3 (1.0-1.6)	1.2 (1.0-1.6)
Female Versus Male Sex	1.0 (0.5-1.9)	1.1 (0.9-1.3)	1.4 (1.1-1.7)	1.3 (1.1-1.6)
CCI=1 Versus 0	1.5 (0.6-3.8)	1.4 (1.1-2.0)	1.5 (1.1-2.0)	1.9 (1.4-2.6)
CCI=2 Versus 0	1.2 (0.4-3.5)	1.3 (1.0-1.8)	1.5 (1.0-2.0)	1.1 (0.8-1.5)
CCI≥3 Versus 0	1.0 (0.3-3.3)	1.8 (1.2-2.6)	1.2 (0.7-2.0)	3.1 (1.8-5.2)
Distal Femur Versus Patella Fracture*	3.1 (0.8-12.3)	2.8 (2.0-3.9)	2.1 (1.4-3.1)	2.4 (1.7-3.4)
Proximal Tibia Versus Patella Fracture*	1.9 (1.0-3.6)	1.1 (0.9-1.4)	1.0 (0.8-1.2)	1.3 (1.1-1.5)
Non-Surgical Treatment Versus ORIF and Reduction Only	0.2 (0.1-0.4)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.7 (0.6-0.8)
External Fixation Versus ORIF and Reduction Only	0.4 (0.1-2.6)	1.3 (0.6-2.5)	1.4 (0.8-2.6)	2.6 (1.4-4.8)
Knee Arthroplasty Versus ORIF and Reduction Only	0.1 (0.0-2.1)	0.7 (0.3-1.6)	8.0 (1.9-34.1)	2.5 (1.0-6.1)

Poor outcome = Oxford Knee Score in each group below median Oxford Knee Score value of 38 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

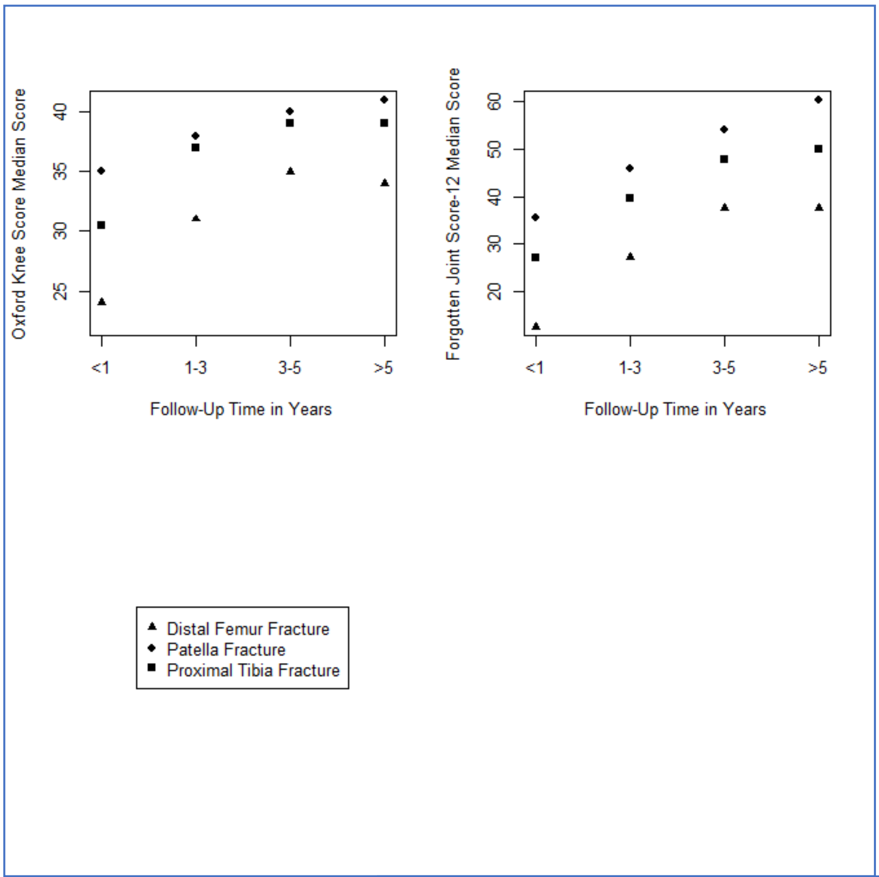

Figure 8. Median Oxford Knee Score and Forgotten Joint Score-12 according to knee fracture type.

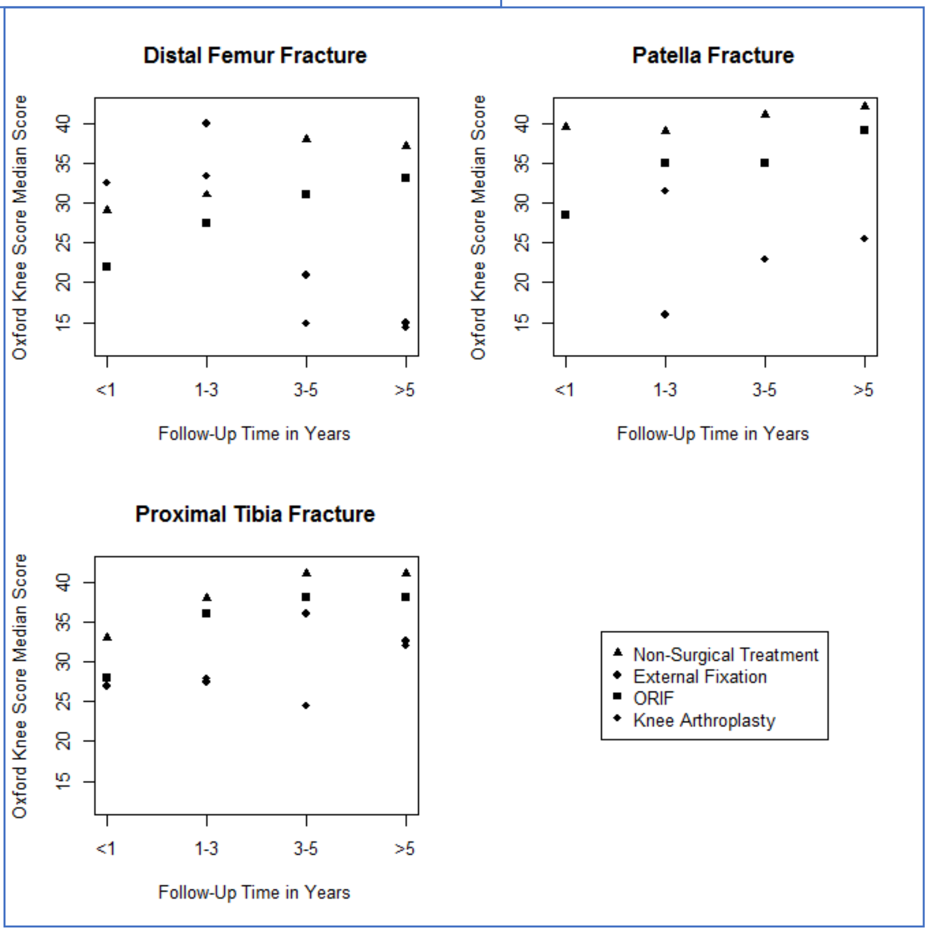

Figure 9. Median Oxford Knee Score according to knee fracture type and treatment type.

FJS-12

Compared to patients aged <40 years, patients aged 40-60 years had moderately higher odds for poor FJS-12 score at 0-1 years after knee fracture, and the odds of poor FJS-12 outcome were higher at longer follow-up (Table 8). After 1 year of follow-up, females had higher odds of poor FJS-12 score (Table 8). Comorbidity burden was a risk factor for poor FJS-12 score at longer follow-up: OR was 1.5; 95% CI 1.1-2.0 for patients with CCI 1 at >5 years after knee fracture, and odds for patients with CCI ≥3 were moderately high with an OR of 1.7; 95% CI 1.0-2.7 at >5 years after knee fracture (Table 8). Regarding knee fracture types, distal femur fracture was a risk factor for poor FJS-12 score at 1-3 years following knee fracture (OR 2.1; 95% CI 1.5-2.9), and at >5 years following knee fracture (OR 1.9; 95% CI 1.4-2.7) (Table 8, Figure 8). Proximal tibia fracture was a risk factor for poor FJS-12 score at short-term follow-up (OR 2.1; 95% CI 1.1-3.9 at 0-1 years after knee fracture) and at long-term follow-up (OR 1.3; 95% CI 1.1-1.5 at >5 years after knee fracture) (Table 8, Figure 8). During all four follow-up periods, non-surgically treated knee fracture patients reported lower odds of poor FJS-12 score while external fixation knee fracture patients and knee arthroplasty knee fracture patients reported higher odds of poor FJS-12 score at longer follow-up after knee fracture (Table 8, Figure 10).

Table 8. Risk Factors for Poor Outcome Measured by Forgotten Joint Score-12

Patient Demographics	Forgotten Joint Score-12 Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	2.9 (1.0-8.2)	1.9 (1.5-2.5)	2.0 (1.6-2.6)	1.7 (1.3-2.2)
Age >60 Years Versus Age <40 Years	1.9 (0.7-5.4)	1.2 (1.0-1.6)	1.3 (1.0-1.7)	1.2 (1.0-1.5)
Female Versus Male Sex	1.4 (0.7-2.7)	1.3 (1.1-1.5)	1.5 (1.2-1.8)	1.4 (1.2-1.7)
CCI=1 Versus 0	1.4 (0.5-3.5)	1.2 (0.9-1.6)	1.3 (1.0-1.8)	1.5 (1.1-2.0)
CCI=2 Versus 0	0.6 (0.2-1.8)	1.2 (0.9-1.7)	1.3 (0.9-1.8)	1.1 (0.8-1.6)
CCI≥3 Versus 0	0.5 (0.1-1.8)	1.4 (0.9-2.0)	1.2 (0.7-2.0)	1.7 (1.0-2.7)
Distal Femur Versus Patella Fracture*	1.8 (0.5-6.6)	2.1 (1.5-2.9)	1.5 (1.0-2.2)	1.9 (1.4-2.7)
Proximal Tibia Versus Patella Fracture*	2.1 (1.1-3.9)	1.1 (0.9-1.4)	0.9 (0.8-1.1)	1.3 (1.1-1.5)
Non-Surgical Treatment Versus ORIF and Reduction	0.1 (0.1-0.3)	0.6 (0.5-0.7)	0.5 (0.4-0.6)	0.6 (0.5-0.8)
External Fixation Versus ORIF and Reduction	-	1.5 (0.7-3.1)	1.4 (0.7-2.5)	1.9 (1.1-3.4)
Knee Arthroplasty Versus ORIF and Reduction	-	1.1 (0.5-2.7)	7.8 (1.8-33.5)	4.3 (1.6-11.4)

Poor outcome = Forgotten Joint Score-12 score in each group below median Forgotten Joint Score-12 value of 46 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included. - Number of observations not enough for calculating OR estimates. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

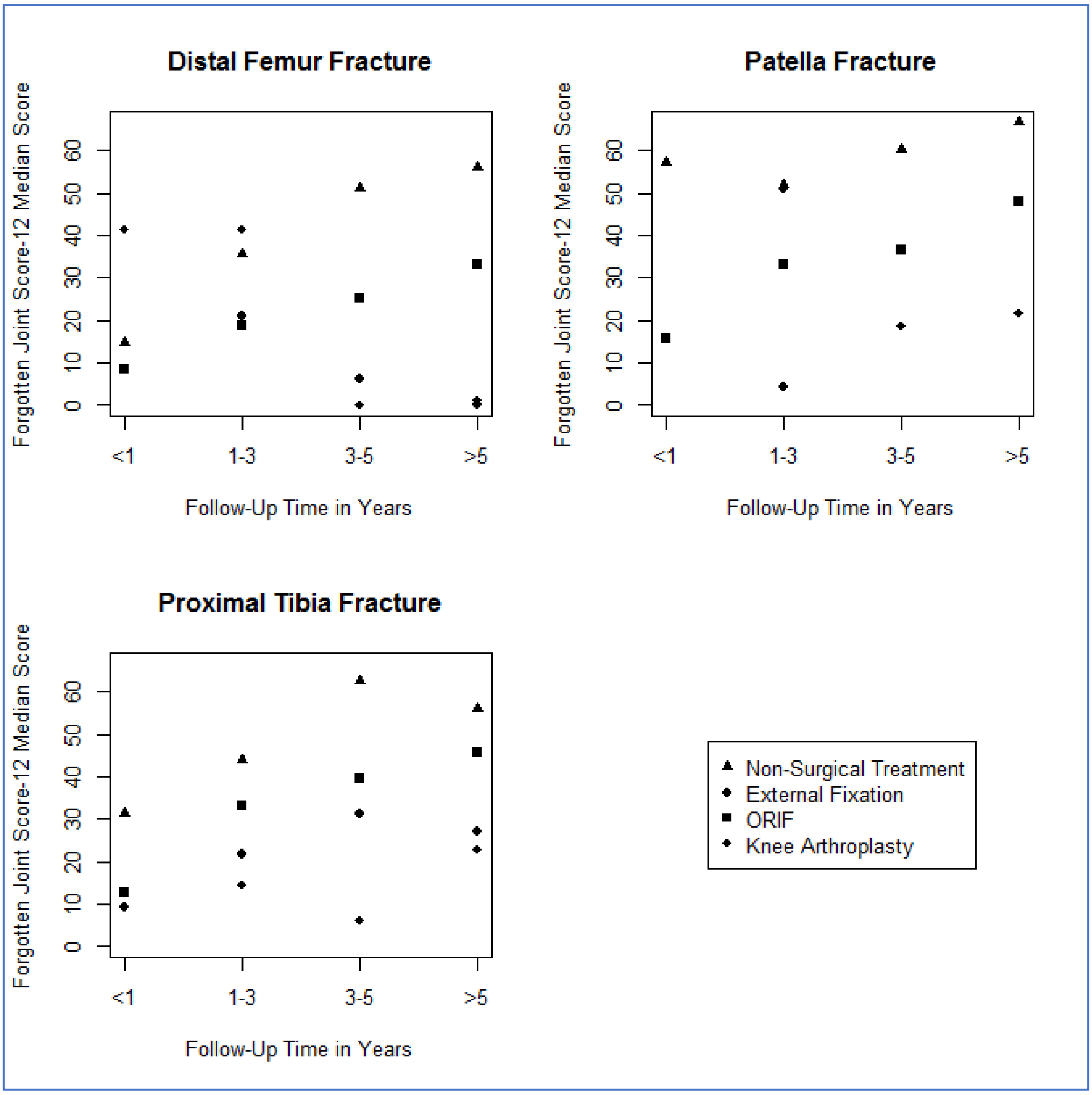

Figure 10. Median Forgotten Joint Score-12 according to knee fracture type and treatment type.

EQ5D-5L Index

Increasing age (patients aged 40-60 years vs patients aged <40 years) showed higher odds for poor EQ5D-5L Index score at short-term follow-up (OR 1.6; 95% CI 1.3-2.1 at 1-3 years after knee fracture) and provided unclear estimates of ORs with longer follow-up (Table 9). Just as with increasing age, female sex also provided unclear estimates of ORs for poor EQ5D-5L Index score (Table 9). At longer follow-up after knee fracture, higher comorbidity level was a risk factor for poor EQ5D-5L Index score (Table 9). Distal femur fracture and proximal tibia fracture were risk factors for poor EQ5D-5L Index score at longer follow-up after knee fracture (Table 9, Figure 11). In all four follow-up periods, non-surgically treated knee fracture patients reported lower odds of poor EQ5D-5L Index score, while knee fracture patients treated with external fixation and knee fracture patients treated with knee arthroplasty showed higher odds of poor EQ5D-5L Index score at longer follow-up (Table 9, Figure 12).

Table 9. Risk Factors for Poor Outcome Measured by EQ5D-5L Index

Patient Demographics	EQ5D-5L Index Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	1.0 (0.4-2.7)	1.6 (1.3-2.1)	1.3 (1.0-1.7)	1.2 (1.0-1.5)
Age >60 Years Versus Age <40 Years	0.6 (0.2-1.7)	1.0 (0.8-1.2)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Female Versus Male Sex	1.2 (0.6-2.2)	1.1 (0.9-1.3)	1.2 (1.0-1.4)	1.1 (0.9-1.3)
CCI=1 Versus 0	1.7 (0.7-4.1)	1.3 (0.9-1.7)	1.5 (1.1-2.1)	2.0 (1.5-2.7)
CCI=2 Versus 0	0.8 (0.3-2.2)	1.5 (1.1-2.0)	1.6 (1.2-2.3)	1.1 (0.8-1.6)
CCI≥3 Versus 0	2.1 (0.6-7.5)	1.5 (1.0-2.2)	1.9 (1.2-3.2)	2.7 (1.6-4.4)
Distal Femur Versus Patella Fracture*	3.2 (0.8-12.2)	2.8 (2.0-3.9)	2.1 (1.5-3.1)	2.4 (1.7-3.4)
Proximal Tibia Versus Patella Fracture*	1.4 (0.8-2.6)	1.1 (0.9-1.4)	1.1 (0.9-1.3)	1.3 (1.1-1.6)
Non-Surgical Treatment Versus ORIF and Reduction	0.3 (0.1-0.5)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.7 (0.6-0.9)
External Fixation Versus ORIF and Reduction	0.5 (0.1-2.8)	1.8 (0.8-3.9)	1.2 (0.7-2.3)	2.7 (1.5-5.1)
Knee Arthroplasty Versus ORIF and Reduction	-	0.9 (0.4-2.0)	8.1 (1.9-34.7)	2.6 (1.1-6.2)

Poor outcome = EQ5D-5L Index score in each group below median EQ5D-5L Index value of 0.7 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included.
- Number of observations not enough for calculating OR estimates. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

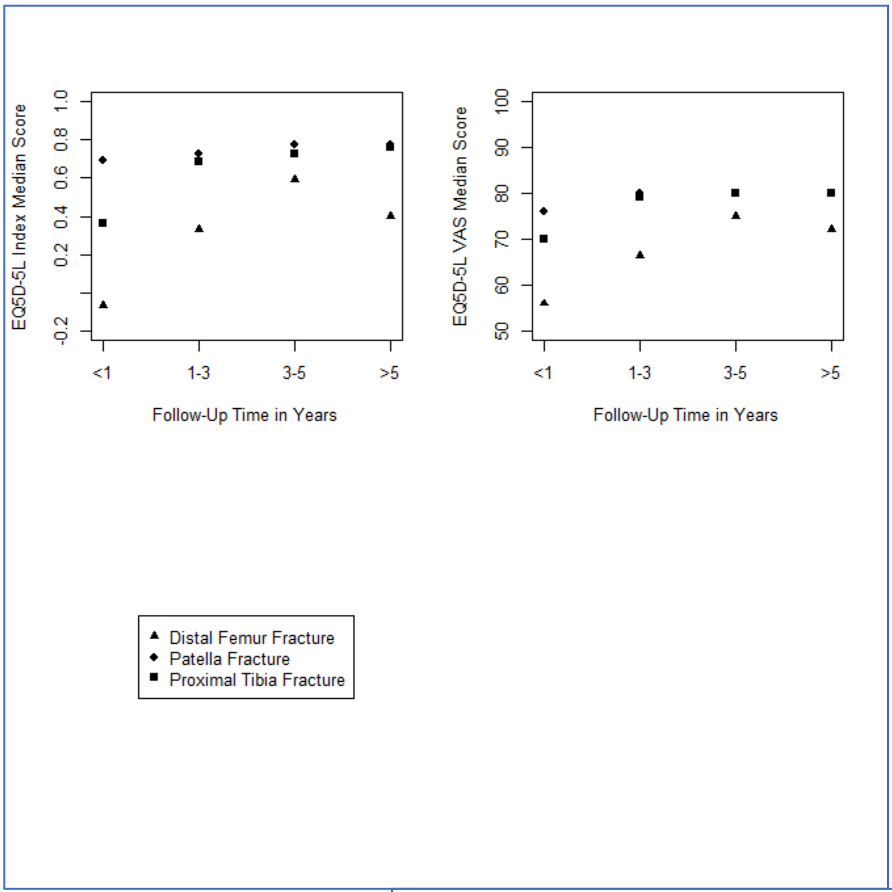

Figure 11. Median EQ5D-5L Index and EQ5D-5L VAS score according to knee fracture type.

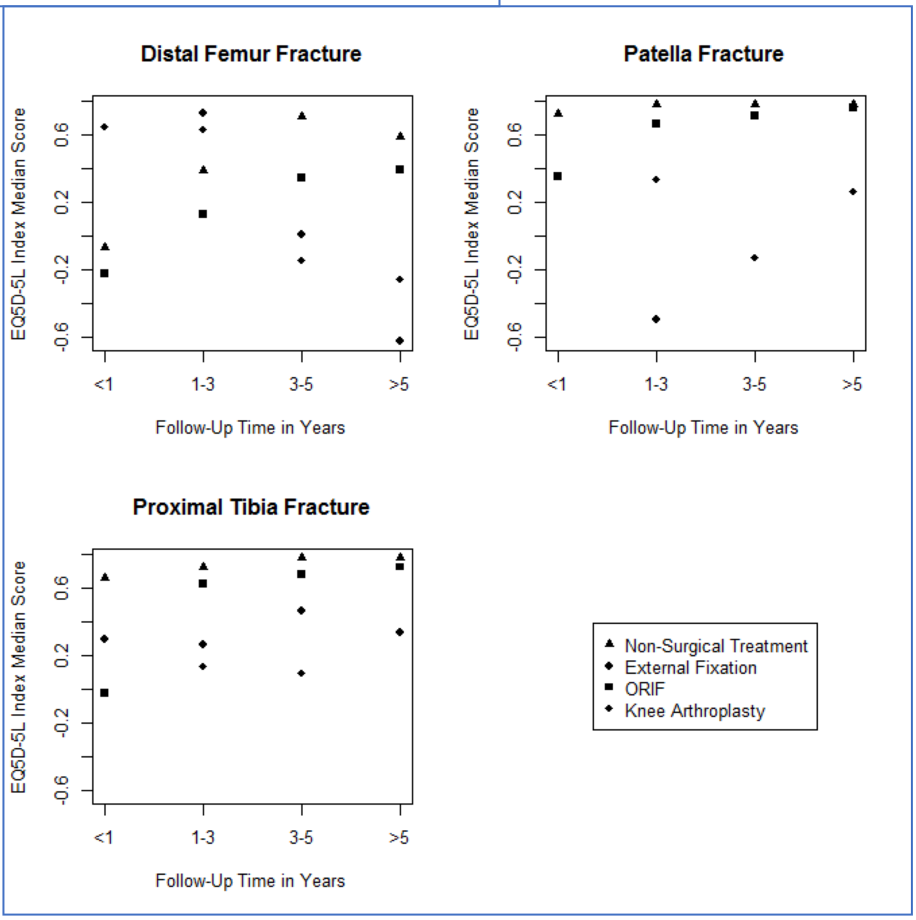

Figure 12. Median EQ5D-5L Index score according to knee fracture type and treatment type.

EQ5D-5L VAS

Increasing age and female sex were not clear risk factors for poor EQ5D-5L VAS score: patients aged 40-60 years had higher odds of poor EQ5D-5L VAS score at 1-3 years and 3-5 years of follow-up, but not at shorter (0-1 year) or longer (>5 years) follow-up, and female sex was only a risk factor for poor EQ5D-5L VAS at 3-5 years after knee fracture (Table 10). Comorbidity burden had higher odds of poor EQ5D-5L VAS score at longer follow-up after knee fracture (Table 10). At longer follow-up after knee fracture, distal femur fracture patients had higher odds of poor EQ5D-5L VAS score, compared to patella fracture patients (Table 10, Figure 11). Non-surgically treated knee fracture patients had lower odds for poor EQ5D-5L VAS score during all four follow-up periods after knee fracture, while external fixation knee fracture patients and knee arthroplasty knee fracture patients had higher odds of poor EQ5D-5L VAS score at longer follow-up periods after knee fracture (Table 10, Figure 13).

Table 10. Risk Factors for Poor Outcome Measured by EQ5D-5L VAS

Patient Demographics	EQ5D-5L VAS Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	0.5 (0.2-1.4)	1.5 (1.2-1.9)	1.5 (1.2-1.9)	1.2 (1.0-1.5)
Age >60 Years Versus Age <40 Years	0.5 (0.2-1.4)	1.2 (0.9-1.5)	1.2 (1.0-1.6)	1.1 (0.9-1.4)
Female Versus Male Sex	1.5 (0.8-2.8)	1.0 (0.8-1.2)	1.3 (1.1-1.6)	1.1 (0.9-1.3)
CCI=1 Versus 0	1.6 (0.6-3.8)	1.7 (1.3-2.3)	1.6 (1.2-2.2)	1.8 (1.3-2.5)
CCI=2 Versus 0	1.0 (0.4-3.0)	1.6 (1.2-2.2)	1.6 (1.1-2.3)	1.3 (0.9-1.8)
CCI≥3 Versus 0	1.4 (0.4-5.0)	2.7 (1.8-4.2)	2.1 (1.2-3.6)	3.4 (1.9-6.1)
Distal Femur Versus Patella Fracture*	1.6 (0.5-5.4)	1.8 (1.3-2.5)	1.5 (1.1-2.3)	1.7 (1.2-2.5)
Proximal Tibia Versus Patella Fracture*	1.0 (0.5-1.8)	1.0 (0.9-1.2)	0.9 (0.7-1.1)	1.1 (0.9-1.3)
Non-Surgical Treatment Versus ORIF and Reduction	0.5 (0.3-0.9)	0.8 (0.7-0.9)	0.7 (0.6-0.8)	0.9 (0.7-1.0)
External Fixation Versus ORIF and Reduction	2.1 (0.2-19.4)	1.5 (0.7-3.1)	1.0 (0.5-1.7)	3.4 (1.7-6.7)
Knee Arthroplasty Versus ORIF and Reduction	-	1.6 (0.6-4.0)	1.8 (0.7-4.6)	5.7 (1.7-19.1)

Poor outcome = EQ5D-5L VAS score in each group below median EQ5D-5L VAS value of 80 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included.
- Number of observations not enough for calculating OR estimates. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

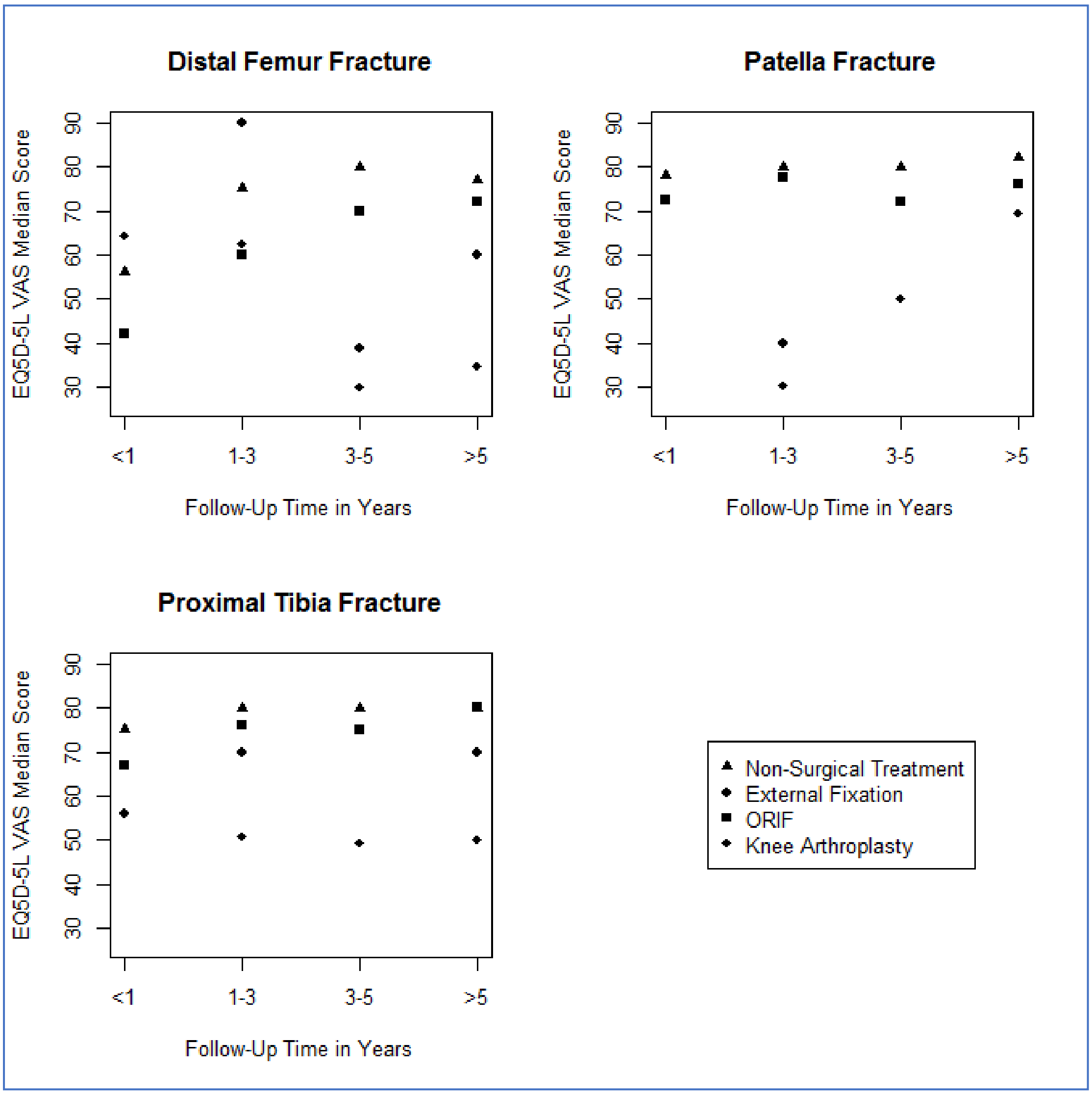

Figure 13. Median EQ5D-5L VAS score according to knee fracture type and treatment type.

Knee Fracture Type and Treatment Type Subanalysis

Compared to patella fracture treated with ORIF and reduction only, distal femur fracture treated with ORIF and reduction only showed higher ORs (all ORs between 1.7-3.1), for poor scores in all four PROMs at 1-3 years after knee fracture, for OKS and EQ5D-5L Index at 3-5 years after knee fracture, and for OKS, FJS-12, and EQ5D-5L Index at >5 years after knee fracture. Compared to non-surgically treated patella fracture, non-surgically treated distal femur fracture showed higher ORs (all ORs between 1.6-2.8), for poor OKS and EQ5D-5L Index scores at 1-3, 3-5, and >5 years after knee fracture, and for poor FJS-12 and EQ5D-5L VAS scores at 1-3, and >5 years after knee fracture. Compared to ORIF and reduction only of patella fracture, non-surgically treated patella fracture showed lower ORs (all ORs between 0.4-0.7) for poor scores in all four PROMs at 3-5, and >5 years after knee fracture. Compared to ORIF and reduction only of proximal tibia fracture, non-surgically treated proximal tibia fracture showed lower ORs (all ORs between 0.5-0.7) for poor OKS, FJS-12, and EQ5D-5L Index scores at 1-3, 3-5, and >5 years after knee fracture, and for poor EQ5D-5L VAS score at 3-5 years after knee fracture. Compared to ORIF and reduction only of proximal tibia fracture, external fixation of proximal tibia fracture showed higher ORs (1.9-3.3) for poor scores in all four PROMs at >5 years after knee fracture.

Study III: Results

A total of 48,791 knee fracture patients (median age 58 years [IQR 41-73]; 58% female) and 263,593 population controls (median age 59 [IQR 42-74]) were followed in the study (Table 11). Both cohorts had a mean observation period to TKA of 7 years. As patients with multiple knee fractures only comprised 3% of all knee fracture patients, they were not included in the analysis because of interpretation issues between different multiple knee fractures and patients with single knee fractures.

1) What is the Short-Term Risk of TKA after Knee Fracture?

Compared to population controls, the short-term risk for TKA in knee fracture patients was 3.7 times higher (HR 3.74 [95% CI 3.44-4.07]; p<0.01; HR adjusted for increasing age per year, sex, and CCI) in the first 3 years following knee fracture (Figure 14 and Table 12) [47]. In the first 3 years following knee fracture, 2% (967 out of 48,791 people) of knee fracture patients and 0.5% (1280 out of 263,593 people) of population controls had TKA surgery [47].

Table 11. Demographic Data of Patients with Knee Fractures and Population Controls

Variable	Patients with Knee Fractures	Population Controls	p value
Number of Patients	48,791	263,593	
Age (Years)			< 0.01[a]
Median (Interquartile Range)	58 (41-73)	59 (42-74)	
Sex			< 0.01[b]
Female (%)	28,221 (58)	154,733 (59)	
Male (%)	20,570 (42)	108,860 (41)	
Charlson Comorbidity Index (%)			< 0.01[b]
0	36,297 (74)	210,506 (80)	
1	3920 (8)	15,544 (6)	
2	4915 (10)	23,196 (9)	
≥ 3	3659 (8)	14,347 (5)	

[a]The p value calculated using Wilcoxon's rank sum test. [b]The p value calculated using Pearson's chi-square test.

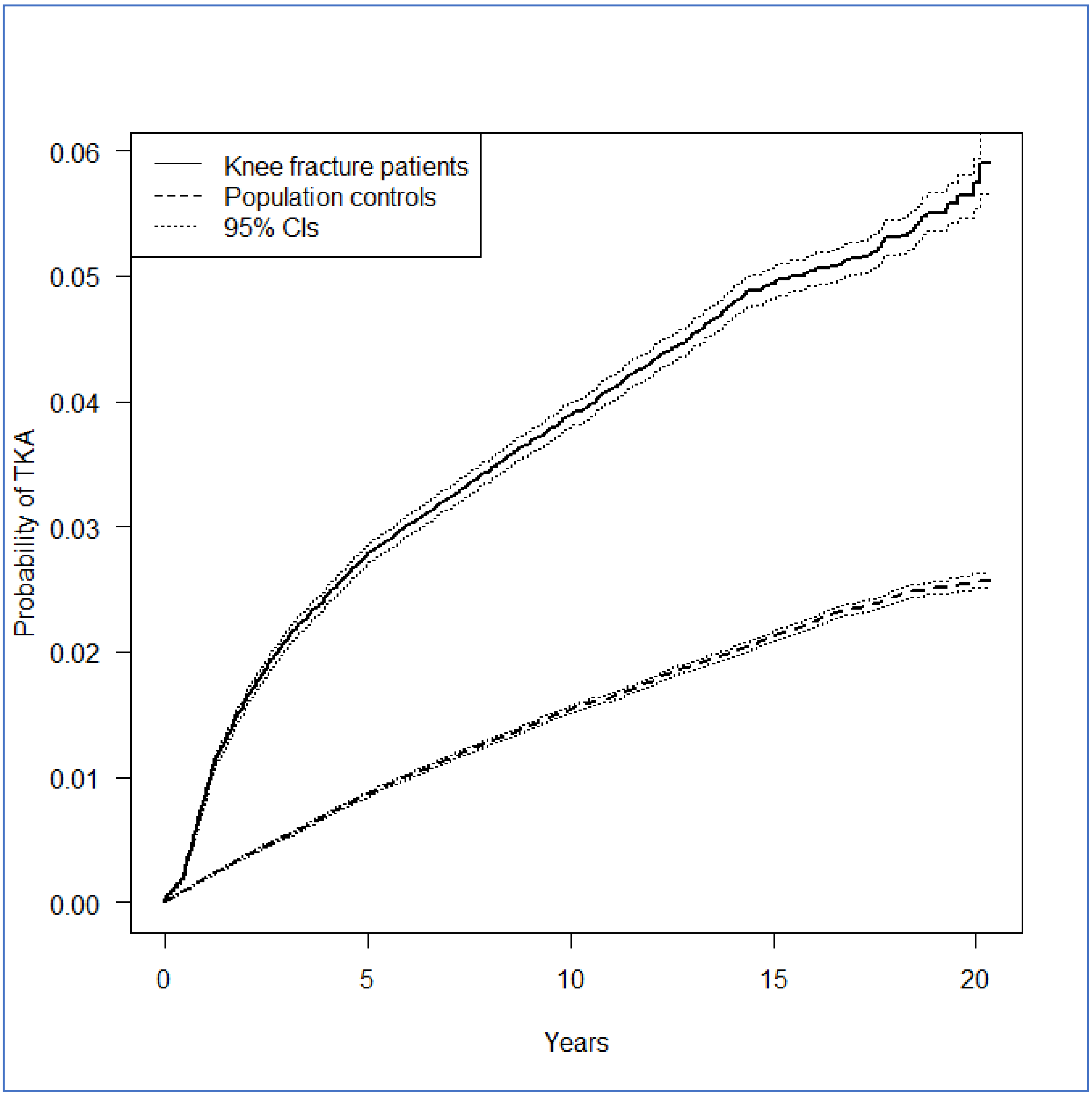

Figure 14. Cumulative incidence of probability of TKA in knee fracture patients and patients without knee fractures (population controls) during the 20-year period with 95% CIs.

Table 12. Cox Proportional Hazards Model with Short-Term and Long-Term Hazard Ratios for TKA in Patients with Knee Fractures versus Population Controls

Variable	0-3 Years from Inclusion			More than 3 Years from Inclusion		
	Hazard Ratio (95% CI)	p value	Number of Events/ Number at Risk (%)	Hazard Ratio (95% CI)	p value	Number of Events/ Number at Risk (%)
Population Controls	1		1280/263,593 (0.5)	1		2395/180,418 (1)
Patients with Knee Fractures vs Population Controls[a]	3.74 (3.44 to 4.07)	< 0.01	967/48,791 (2)	1.59 (1.46 to 1.71)	< 0.01	849/36,272 (2)

[a]Adjusted for increasing age per year, sex, and Charlson Comorbidity Index.

2) What is the Long-Term Risk of TKA after Knee Fracture?

Compared to population controls, the long-term risk for TKA in knee fracture patients was 1.6 times higher (HR 1.59 [95% CI 1.46-1.71]; p<0.01; HR adjusted for increasing age per year, sex, and CCI) after the first 3 years following knee fracture (Figure 14 and Table 12) [47]. After the first 3 years following knee fracture, 2% (849 out of 36,272 people) of knee fracture patients and 1% (2395 out of 180,418 people) of population controls underwent TKA [47]. In the entire 20-year period, 4% (1816 out of 48,791) of knee fracture patients and 1% (3675 out of 263,593) of population controls had TKA surgery [47].

3) What are the Risk Factors for TKA in Patients with Knee Fractures?

Risk factors other than knee fracture, adding to the risk for TKA in knee fracture patients, were primary knee OA, surgically treated knee fracture, external fixation, proximal tibia fracture, and distal femur fracture (Table 13, Table 14). Knee fracture patients with primary knee OA vs knee fracture patients with no primary knee OA had a HR of 9.57 (95% CI 5.39-16.98; p<0.01; HR adjusted for surgically treated vs non-surgically treated knee fracture, increasing age per year, and CCI) during the 20-year period (Table 13) [47]. When comparing knee fracture patients with primary knee OA to knee fracture patients with no primary knee OA in the 20-year study period, 26% (494 out of 1899) of knee fracture patients with primary knee OA had TKA surgery while 3% (1322 out of 46,892) of knee fracture patients with no primary knee OA had TKA surgery (Table 13) [47]. Treatment with external fixation vs ORIF and reduction only had a HR of 1.92 (95% CI 1.01-3.66; p=0.05; HR adjusted for increasing age per year, CCI, sex, primary knee OA vs no primary knee OA, and single fracture (distal femur fracture vs patella fracture and proximal tibia fracture vs patella fracture)) during the 20-year period (Table 13) [47]. 9% (141 out of 1518) knee fracture patients treated with external fixation had TKA surgery while 35% (1675 out of 47,273) of knee fracture patients treated with ORIF and reduction only had TKA surgery during the 20-year period (Table 13) [47]. Proximal tibial fracture vs patellar fracture had a HR of 1.75 (95% CI 1.30-2.36; p<0.01; HR adjusted for surgically treated vs non-surgically treated knee fracture, increasing age per year, and CCI) during the 20-year period (Table 13) [47]. When comparing proximal tibia fracture patients and patella fracture patients during the 20-year study period, 4% (1013 out of 22,988) of proximal tibia fracture patients had TKA surgery while 3% (455 out of 17,205) of patella fracture patients had TKA surgery (Table 13) [47]. Distal femoral fracture vs patellar fracture had a HR of 1.68 (95% CI 1.08-2.64; p=0.02; HR adjusted for surgically treated vs non-surgically treated knee fracture, increasing age per year, and CCI) during the 20-year period (Table 13) [47]. 4% (268 out of 7135) of distal femur fracture patients had TKA surgery during the 20-year study period (Table 13) [47]. Female vs male sex had a HR of 1.21 (95% CI 0.92-1.60; p=0.17) for TKA during the 20-year period (Table 13) [47]. 4% (1181 out of 28,221) of females had TKA surgery while 3% (635 out of 20,570) of males had TKA surgery during the 20-year period (Table 13) [47]. Increasing age per year had a HR of 1.02 (95% CI 1.02-1.02; p<0.01) for TKA in knee fracture patients during the 20-year period (Table 13) [47].

Surgical treatment for knee fracture vs non-surgical treatment for knee fracture was also a risk factor for TKA in the first 5 years following knee fracture (HR 2.05 [95% CI 1.83-2.30]; p<0.01; HR adjusted for primary knee OA vs no primary knee OA, increasing age per year, sex, and CCI), and after the first 5 years following knee fracture (HR 1.19 [95% CI 1.01-1.41]; p=0.04; HR adjusted for primary knee OA vs no primary knee OA, increasing age per year, sex, and CCI) (Table 14) [47]. 4% (728 out of 17,636) of surgically treated knee fracture patients had TKA surgery while 2% (508 out of 31,155) of non-surgically treated knee fracture patients had TKA surgery in the first 5 years following knee fracture (Table 14) [47]. 3% (258 out of 10,321) of surgically treated knee fracture patients had TKA surgery while 2% (322 out of 17,583) of non-surgically treated knee fracture patients had TKA surgery after the first 5 years following knee fracture (Table 14) [47].

Table 13. Cox Proportional Hazards Model with Hazard Ratios for Risk Factors for TKA in Patients with Knee Fractures during the 20-Year Study Period

Variable	Hazard Ratio (95% CI)	p value	Number of Events/Number at Risk (%)
Increasing Age per Year[a]	1.02 (1.02-1.02)	< 0.01	
CCI 0	1		1,322/36,297 (3.6)
CCI 1 versus 0[a]	1.09 (0.93-1.29)	0.28	181/3,920 (4.6)
CCI 2 versus 0[a]	0.78 (0.65-0.93)	0.01	155/4,915 (3.2)
CCI ≥ 3 versus 0[a]	0.92 (0.76-1.10)	0.34	158/3,659 (4.3)
Male Sex	1		635/20,570 (3.1)
Female Sex versus Male Sex[b]	1.21 (0.92-1.60)	0.17	1,181/28,221 (4.2)
No Primary Knee OA	1		1,322/46,892 (2.8)
Primary Knee OA versus no Primary Knee OA[b]	9.57 (5.39-16.98)	< 0.01	494/1,899 (26.0)
Patella Fracture	1		455/17,205 (2.6)
Proximal Tibia Fracture versus Patella Fracture[b]	1.75 (1.30-2.36)	< 0.01	1,013/22,988 (4.4)
Distal Femur Fracture versus Patella Fracture[b]	1.68 (1.08-2.64)	0.02	268/7,135 (3.8)
Proximal Tibia Fracture versus Distal Femur Fracture[b]	1.04 (0.68-1.60)	0.85	
ORIF and Reduction Only	1		1,675/47,273 (3.5)
External Fixation versus ORIF and Reduction Only[c]	1.92 (1.01-3.66)	0.05	141/1,518 (9.3)

[a]Change per age in years, adjusted for surgically treated versus non-surgically treated knee fracture, sex, primary knee OA versus no primary knee OA, and single fracture. [b]Adjusted for surgically treated versus non-surgically treated knee fracture, increasing age per year, and CCI. [c]Model is based on surgically treated knee fractures, adjusted for increasing age per year, CCI, sex, primary knee OA versus no primary knee OA, and single fracture. CCI = Charlson Comorbidity Index. Primary knee OA = primary knee osteoarthritis. ORIF = open reduction internal fixation. Single fracture = distal femur fracture versus patella fracture and proximal tibia fracture versus patella fracture.

Table 14. Cox Proportional Hazards Model with Hazard ratios for TKA in Surgically Treated versus Non-Surgically Treated Knee Fractures

Variable	0-5 Years from Inclusion			More than 5 Years from Inclusion		
	Hazard Ratio (95% CI)	p value	Number of TKAs/Number at Risk	Hazard Ratio (95% CI)	p value	Number of TKAs/Number at Risk
Non-Surgically Treated Knee Fracture	1		508/31,155 (1.6%)	1		322/17,583 (1.8%)
Surgically Treated versus Non-Surgically Treated Knee Fracture[a]	2.05 (1.83-2.30)	< 0.01	728/17,636 (4.1%)	1.19 (1.01-1.41)	0.04	258/10,321 (2.5%)

[a]Adjusted for primary knee OA versus no primary knee OA, increasing age per year, sex, and CCI. Primary knee OA = primary knee osteoarthritis.

Discussion

Study I: Summary

During the 20-year study period, the IRs of knee fractures increased by 12% to 70 per 10^5 inhabitants, and surgically treated knee fractures increased especially (by 35%) [48]. Proximal tibia fracture had the highest IR (32 per 10^5 inhabitants) of all knee fracture types [48]. Females aged >51 years and patients with comorbidity burden were more likely to sustain knee fracture, proximal tibia fracture, proximal tibia fracture surgery, and treatment with knee arthroplasty for PTOA [48].

Study I: Study Limitations

Study limitations in Study I concerned information bias in registry studies regarding missing or incomplete registrations of variables and diagnosis codes and misclassifications of diagnosis codes. The bias was most likely diminished by several factors: when registering knee fracture patients, two coding systems were available (ICD-10 knee fracture diagnosis codes and NOMESCO knee fracture surgery codes), DNPR registrations are constantly improving, public hospitals have to register to the DNPR for reimbursement, and orthopaedic diagnoses have been found to have the highest positive predictive value (PPV) (91%) of all diagnosis types [41]. Laterality of knee fracture is infrequently registered in the DNPR which would likely result in IRs being over/underestimated. ABC extensions of ICD-10 diagnosis codes, i.e. knee fracture subtype classifications, as well as trauma severity are also infrequently registered in the DNPR [41]. Therefore, IRs and characteristics of the knee fracture population including for instance high-energy intra-articular, comminuted tibial plateau fractures, low-energy extra-articular distal femur fractures, simple patella fractures, and other trauma-levels and fracture subtypes could therefore not be further investigated. Because conversion surgery codes do not exist in the NOMESCO surgery code system and because the study was a registry study where medical records could not be accessed, the true number of conversion surgeries of for instance external fixations being converted to ORIFs, and the true number of secondary TKAs due to knee fracture were not known. Another limitation is that IRs in year 1998 or later could still be overestimated because of a residual backlog of already prevalent knee fracture patients being followed up in the hospitals. On the other hand, this possible error should diminish over time during the 20-year period which should provide a relatively accurate calculation of average knee fracture IR during the period. Overestimations of IRs should further be diminished because of the 6-month wash-out period (Figure 1), and as only 11% of patients were registered with more than 1 knee fracture, the 6-month wash-out period was likely of adequate length. This study is a 20-year nationwide cohort study from a population of relatively homogenous composition which should increase the external validity of the study results, at least in the Scandinavian countries where health care systems are similar.

1) What Are the 20-Year Trends in IRs of Knee Fractures?

Overall Incidence Rates

In our study, the incidence rates of knee fractures increased 12% during the 20-year study period. In an American study of emergency department visits from a sample of the population, a knee fracture IR of 9 per 10^5 per year was calculated [12] which because of different study design and study populations makes comparison difficult to the knee fracture IR of approximately 63 per 10^5 inhabitants during the 20-year study period in our nationwide study (Figure 3).

Incidence Rates by Sex, Age, Knee Fracture Type, and Treatment Type

In our study, the IRs of females aged >51 years with knee fracture increased, proximal tibial fracture had the highest IR of all knee fracture types, and the IRs of surgically treated knee fracture patients increased by 35% during the 20-year study period [48]. In a Danish national 1-year study [49] of lower extremity fractures which did not differentiate between proximal tibia fractures and distal femur fractures, IRs of lower extremity fractures increased in males aged <50 years, females aged >50 years, and in both males and females aged >75 years. In our 20-year study on the other hand, knee fracture IRs in females aged >51-70 years, and in both females and males aged 0-18 years increased.

Our results are relatively comparable to a British single-center study [50] of knee fractures in patients aged >65 years which presented IRs between 8 and 37 per 10^5 person-years at risk (PYRS) which can be compared to our IRs of between 12 and 32 per 10^5 inhabitants. Similarities between the studies include high IRs in older patients, especially female patients, and high IR of proximal tibia fractures.

A Swedish tibia fracture study [15] described a higher ratio of females sustaining fractures (58%) and females having higher mean age (54) when sustaining tibia fracture, which is demographically comparable to our results regarding older females being more likely to sustain proximal tibia fractures. The Swedish study [15] estimated an IR of 27 per 10^5 PYRS for proximal tibia fracture, which is similar to the results in our study (IR 32 per 10^5 inhabitants for proximal tibia fracture). Both studies showed increases in proximal tibia fracture IR and increases in IRs in females with increasing age in relation to males, as well as flattened curves for IRs of knee fractures in males.

The results in our study showed high proximal tibia fracture IRs, and high IRs in females aged >51 years which can be compared to a Danish study [16] of tibial plateau fractures showing increases in IRs of tibial plateau fractures in males aged <50 years and in females aged >50 years suggesting that intra-articular proximal tibia fractures should be a focus point of future treatment initiatives because of the increasing treatment burden of these fractures.

A Danish study by Driessen et al. [49] of patella fractures estimated an annual IR of 33 per 10^5 PYRS. Another Danish study by Larsen et al. [17] of patella fractures estimated IRs of between 11 and 17 per 10^5 PYRS with the highest IRs being found in females aged 60-80 years. Despite the studies having different populations and study length periods, the results from our study also present high patella fracture IRs (21 per 10^5 inhabitants), and females aged >51 years and >71 years having the highest knee fracture IRs.

The 35% increase in surgically treated knee fracture IRs over the 20-year study period could be explained by higher quality of registrations to the DNPR, a cultural change in society where orthopaedic surgery is more demanded than previously, as well as a lower threshold for knee fracture surgery where patients with more comorbidities also receive knee fracture surgery. As 89% of patients were only registered with 1 knee fracture surgery, double registrations of knee fractures would likely not inflate surgically treated knee fracture IRs.

2) What are the Patient-, Fracture-, and Treatment-Related Characteristics of Knee Fracture Patients in Denmark during 1998-2017?

Patient-, Fracture-, and Treatment-Related Characteristics of Knee Fracture Patients

During the 20-year period, 18% of patients were registered with CCI ≥2, 20% were registered with concomitant near-knee fractures, 13% with concomitant fractures, 10% with lesions inside the knee, 5% with osteoporosis, and 4% with primary knee OA at the time of knee fracture registration [48]. In our study, females aged >51 years and patients with comorbidity were associated with sustaining knee fracture, proximal tibia fracture, requiring proximal tibia fracture surgery, and knee arthroplasty for PTOA [48]. Several studies have presented that knee fractures [13][50][16][17][15][49][51] are prevalent in females and older patients and that TKA procedures [52] are prevalent in females and older patients, which accords with our results.

Study II: Summary

Median PROM scores at short-term follow-up (0-1 years) after knee fracture were: 31 (OKS), 27 (FJS-12), 0.50 (EQ5D-5L Index), and 74 (EQ5D-5L VAS). At 3-5 years and >5 years of follow-up, median PROM scores were similar for each PROM. Median PROM scores at long-term follow-up (>5 years) after knee fracture were 40 (OKS), 54 (FJS-12), 0.76 (EQ5D-5L Index), and 80 (EQ5D-5L VAS). During the study period, knee fracture patients presented with relatively high PROM scores describing knee function (OKS score) and relatively high general health and quality of life (EQ5D-5L Index and EQ5D-5L VAS score) albeit their ability to disregard their knee joint in everyday life was diminished (FJS-12 score). PROM scores did not reach maximum values during the study period. Because the study is a cross-sectional study, temporal sequences between different risk factors and different outcomes could not described, thus causality could also not be explored. Different risk factors for poor PROM score presented themselves depending on the PROM studied and the follow-up period after knee fracture studied.

At both short-term and long-term follow-up, higher age (age >40 years) had higher odds of poor OKS and FJS-12 scores. At longer follow-up, female knee fracture patients presented slightly higher odds of poor OKS and FJS-12 scores. Comorbidity burden, distal femoral fracture, treatment with external fixation, and treatment with knee arthroplasty were risk factors for poor PROM score in all four PROMs at long-term follow-up. At longer follow-up after knee fracture, distal femur fracture treated with ORIF and reduction only showed higher ORs for poor PROM scores in all four PROMs compared to patella fracture treated with ORIF and reduction only, and non-surgically treated distal femur fracture showed higher ORs for poor PROM scores in all four PROMs compared to non-surgically treated patella fracture. At longer follow-up after knee fracture, non-surgically treated patella fracture showed lower ORs for poor PROM scores in all four PROMs compared to ORIF and reduction only treated patella fracture, and non-surgically treated proximal tibia fracture showed lower ORs for poor PROM scores in all four PROMs compared to ORIF and reduction only treated proximal tibia fracture. At >5 years after knee fracture, proximal tibia fracture treated with external fixation showed higher ORs for poor PROM scores in all four PROMs compared to ORIF and reduction only treated proximal tibia fracture.

Study II: Study Limitations

Study limitations of Study II included the fact that because the study was a registry study, medical records could not be accessed, meaning that conversion surgeries could not be properly described (i.e. conversion of external fixation of knee fracture to ORIF of knee fracture). The NOMESCO surgery code system also does not have conversion surgery codes. In the DNPR, registrations regarding laterality were not sufficient, which could result in the contralateral knee being fractured or receiving surgical/non-surgical treatment, affecting the presented PROM scores and ORs. Furthermore, registrations regarding trauma severity of knee fracture and subclassifications of knee fracture were also insufficient, resulting in no available descriptions of potential risk factors regarding trauma-level and knee fracture subtypes. Only 2% of responders acquired multiple knee fractures, and as such were excluded from the analysis, because of difficulty in interpreting data appropriately when comparing people with different types of multiple knee fractures to each other as well as to those with single fractures, likely leading to uncertain estimates (Table 5). Furthermore, 47% of patients registered with knee fracture during 2011-2017 did not respond to the questionnaire (Table 5), and these patients had a higher proportion of younger patients and male patients which are less represented in the responder group. Thus, younger patients and male patients could potentially report differing PROM scores and ORs than the ones presented in our study. Nevertheless, we sought to diminish the bias from age and sex regarding the presented ORs by taking age and sex into account when fitting the binary logistic regression models. Selection bias is probably present in the study, as it is unknown if patients with more positive knee fracture treatment experiences decided to answer the questionnaire because they were so satisfied with the outcome, or if in fact patients with more unsatisfactory experiences from knee fracture treatment decided to reply in order to share their negative outcomes with research.

There was also a higher distribution of non-surgically treated non-responders, perhaps because some non-responders believed that they did not have to respond to the questionnaire because they were treated non-surgically, also possibly affecting the median PROM scores and ORs presented in this study. In terms of other variables, responders and non-responders were similar in composition, these variables therefore most likely did not bias the results. Potential confounders in this study are certain comorbidities (i.e. osteopenia, osteoporosis, OA, muscle disease, and other progressive disease) which are not included in the CCI and can thus potentially affect the presented PROM scores as PROM scores describe a patient's knee pain, knee mobility, knee QOL, and a patient's general health status and QOL. In this study, follow-up periods of between 0 and >5 years were included, but there were no pre-treatment PROMs available for analysis, as such assumptions about the development of PROM scores could not be made. Another limitation lies in PROMs themselves, as they are patient-reported, and studies have shown that knee function at times needs to be objectively measured to ensure a proper representation of real knee joint function [53][54][55]. On the other hand, the strength of PROMs lies in the fact that they take the patient's perspective into account, which is especially important when evaluating subjective outcome measures [26][20][28][21][22][23][19][56].

Another important limitation is the binary nature of poor/good PROM outcomes. In this study, PROM scores under the median represented poor outcome, because PROM scores in this study were skewed and because cut-off scores for poor/good PROM outcomes in knee fracture patients are unknown in literature. If PROM scores under/over the median actually represent poor/good clinical outcomes in knee fracture patients is therefore also unknown, and should be investigated further in future studies.

Questions from the PROMs involving both knee-specific questions and general health questions are subject to interpretation by the individual in terms of if they have chronic diseases or not, as well as by groups of individuals from different countries and cultures [57][28]. When regarding surgically treated knee fracture patients, response shift bias might be present because surgery success/failure might affect surgically treated knee fracture patients' responses to the questionnaire [58]. The strengths of this study are in its design as an electronic questionnaire sent via a digital e-mail system linked to patient CPR number, thus reaching a large population sample efficiently without risking loss of responses in the postal delivery system as well as avoiding misreading paper responses when converting them to electronic data. Literature has reported that patients also prefer electronic questionnaires instead of manually filling out and sending paper questionnaires [25]. The DNPR is a high-quality, national database where studies have shown that orthopaedic diagnoses registered in the DNPR have the highest PPV of all diagnoses [41]. This national, cross-sectional study included a representative population sample from Denmark which has a comparably homogenous population, and included all different knee fracture types including the distal femur, patella, and proximal tibia, treated surgically or non-surgically with both short-term and long-term follow-up (0 to >5 years of follow-up with a maximum of 15.1 years of follow-up) of patient responses to both knee-specific and generic PROMs in order to ensure a proper description of the outcomes of the knee fracture population in terms of knee pain, knee function, forgetfulness of the knee joint in everyday life, and patient general health and quality of life.

1) Report on Knee-Specific and Generic Median PROM Scores of Knee Fracture Patients at 0 to >5 Years after Knee Fracture

At short-term follow-up (0-1 years after knee fracture), median PROM scores were 31 (OKS), 27 (FJS-12), 0.50 (EQ5D-5L Index), and 74 (EQ5D-5L VAS). At both 3-5 years and >5 years after knee fracture, median PROM scores were similar according to each PROM. At long-term follow-up (>5 years after knee fracture), median PROM scores were 40 (OKS), 54 (FJS-12), 0.76 (EQ5D-5L Index), and 80 (EQ5D-5L VAS). The knee fracture patients in our study presented with relatively high OKS, EQ5D-5L Index, and EQ5D-5L VAS scores, thus expressing high knee function, low knee pain, and high general health and QOL. On the other hand, they reported low FJS-12 scores indicating that their knee joint was impacting their everyday life in such a way that they could not disregard it. The discrepancy between the relatively high OKS, EQ5D-5L Index, and EQ5D-5L VAS scores and low FJS-12 scores could be explained in that FJS-12 measures an individual's ability to disregard their knee joint in everyday life, as one does not think about one's joint if it is healthy and works seamlessly, while OKS measures knee pain and knee function, and EQ5D-5L Index, and EQ5D-5L VAS measure an individual's general health and QOL. Another interesting result is that distal femur fracture patients had poor PROM scores in all four PROMs in our study (Figure 8, Figure 11). The results are nevertheless relatively uncertain because only 8% of responders were patients with distal femur fractures (Table 5).

A study of patients with surgically treated tibial plateau fractures with median 13-year follow-up presented a mean FJS-12 score of 70 [19]. Our median FJS-12 score at >5 years of follow-up after knee fracture was lower (50) for patients with proximal tibia fractures (Figure 8). A study of patients undergoing ACL-reconstruction showed mean FJS-12 scores of 72 at minimum 1 year of follow-up and mean FJS-12 score of 70 at minimum 10 years of follow-up [31]. A study of patients treated with TKA for tricompartmental OA and patients with hip OA treated with total hip arthroplasty (THA) reported pre-operative and 1-year post-operative FJS-12 scores of 24 and 70 for TKA patients and 22 and 80 for THA patients [29]. In our study, median FJS-12 scores were between 27 to 54, and the average median FJS-12 score was 46 (Table 6). Literature is lacking in terms of properly describing FJS-12 scores and other PROM scores of knee fracture patients. When comparing the FJS-12 scores of knee fracture patients to those of tibial plateau fracture patients, ACL-reconstruction patients, TKA patients, and THA patients, FJS-12 scores were lower for knee fracture patients, suggesting that more studies are needed to describe the development of PROM scores in knee fracture patients, but also a need for improving the quality of knee fracture management in general.

2) Identify Risk Factors for Poor Outcome Defined by Low Median PROM Scores

Risk factors for poor median PROM score differed according to PROM and follow-up period. Increasing age (>40 years) had higher OR for poor OKS and FJS-12 score at both short-term follow-up and long-term follow-up after knee fracture.

Patients with more comorbidities, patients with distal femur fracture, patients treated with external fixation for knee fracture, and patients treated with knee arthroplasty for knee fracture had higher odds for poor median PROM score for all four PROMs at longer follow-up after knee fracture. At longer follow-up, female patients had slightly higher odds of having poor OKS and FJS-12 scores. A study of TKA patients revealed that female patients and younger patients reported lower FJS-12 scores [59]. Other TKA studies also argue that because older patients are more likely influenced by their comorbidity burden because of increasing age than any potential knee joint problems, and are less physically active and as such demand less of their knee joint, they consequently have higher FJS-12 scores than younger patients [59][22][29]. Our study also presented slightly higher odds for female patients reporting poor knee-specific PROM scores (OKS and FJS-12 scores) at least at long-term follow-up, but in contrast, our study showed higher odds for older patients (aged >40 years) of reporting poor knee-specific PROM scores (OKS and FJS-12 scores) at both short-term and long-term follow-up. The conflicting results could be explained by the fact that knee fracture patients as a patient population are different than TKA patients, and as such present with other outcome challenges and demands than those of TKA patients.

When comparing ORIF and reduction only treated distal femur fracture to ORIF and reduction only treated patella fracture, and when comparing non-surgical treatment of distal femur fracture to non-surgical treatment of patella fracture, patients with distal femur fractures reported higher odds of poor PROM score in all four PROMs at long-term follow-up following knee fracture. When comparing non-surgically treated patella fracture to ORIF and reduction only treated patella facture, and when comparing non-surgically treated proximal tibia fracture to ORIF and reduction only treated proximal tibia fracture, non-surgically treated patients reported lower odds of poor PROM scores in all four PROMs at long-term follow-up following knee fracture. When comparing externally fixated proximal tibia fracture to ORIF and reduction only treated proximal tibia fracture, patients treated with external fixation reported higher odds for poor PROM scores in all four PROMs at >5 years following knee fracture. Patients with distal femur fracture reported higher odds of poor PROM score in all four PROMs at longer follow-up after knee fracture. Additionally, ORIF and reduction only treated distal femur fractures, and non-surgically treated distal femur fractures presented higher ORs for poor PROM scores in all four PROMs at long-term follow-up following knee fracture, which mirrors current literature in the fact that distal femur fractures are known to have complex fracture patterns and in turn are more surgically challenging [60].

In our study, non-surgically treated knee fractures reported lower ORs for poor PROM scores in all four PROMs throughout all four follow-up periods. Furthermore, non-surgical treatment of patella fractures and non-surgical treatment of proximal tibia fractures showed lower ORs for poor PROM scores in all four PROMs at longer follow-up periods after knee fracture, when compared to patella fractures and proximal tibia fractures treated with ORIF and reduction only.

When contemplating the proper treatment type for different knee fractures, both patient-related factors such as increasing age, comorbidity (especially comorbidities affecting risk of sustaining fracture and/or affecting bone healing after fracture such as osteopenia, osteoporosis, OA, muscle disease, and other progressive disease), as well as patient compliance, and fracture-related factors such as fracture communition or complexity, are taken into consideration [9][10][11]. Current literature withholds that patients with bone loss and more complex knee fractures are more prone to undergo TKA while patients with multiple comorbidities and low compliance might be more prone to only be treated with external fixation for knee fracture compared to less comorbid and more compliant patients [9][10][11]. Perhaps that is why patients treated with external fixation for knee fracture (i.e. highly comorbid patients and especially patients with the above listed comorbidities not included in the CCI as well as less compliant patients) and patients treated with knee arthroplasty for knee fracture (i.e. older patients with poor bone stock and highly complex knee fractures) therefore report higher odds of poor PROM scores as has been presented in our study. This might also potentially explain the lower odds of poor PROM scores reported in non-surgically treated knee fracture patients - patients which most likely had simple knee fractures that only required non-surgical treatment and thus had higher odds of reporting high PROM scores. On the other hand, only a small proportion of responders were treated with external fixation (2%) and knee arthroplasty (1%) for knee fracture, therefore these results are uncertain (Table 5). Nevertheless, the higher odds for poor PROM scores in all four PROMs reported at >5 years of follow-up by patients treated with external fixation of proximal tibia fracture vs patients treated with ORIF and reduction only of proximal tibia fracture suggest that external fixation should be viewed as a risk factor for poor PROM outcomes in knee fracture patients, and at the very least in proximal tibia fracture patients. When analysing our results involving knee arthroplasty patients, literature involving patients undergoing TKA for OA and PTOA has presented diverging results. One study reported similar PROM scores and revision rates in PTOA patients as in OA patients [61]. One study reported higher complication rates in PTOA patients but similar survivalship as in OA patients if early complications were evaded [62]. Another study reported similar improvement in PROM scores arguing that this is because PTOA patients have lower pre-operative PROM scores to begin with than OA patients, albeit they end up with lower post-operative PROM scores compared to OA patients [63]. Yet another study reported improvement in functional outcomes but high complication rates in PTOA patients [9], while other studies have reported lower functional outcome, lower QOL, and lower survival rate in PTOA patients compared to OA patients [35], functional improvement but higher failure rate [64], and significant functional improvement but higher complication rates in PTOA patients [65][66]. Some studies have offered a possible explanation for PTOA patients reporting lower outcomes: PTOA patients usually start out with lower pre-operative PROM scores and as such end up reporting lower post-operative PROM scores compared to OA patients [63][35]. Current research as well as the results in our study (i.e. patients treated with knee arthroplasty for knee fracture reporting high odds for poor PROM scores for all four PROMs at long-term follow-up) highlight the complexity of the knee fracture treated with knee arthroplasty patient group.

Study III: Summary

In the first 3 years after knee fracture, knee fracture patients had a 3.7 times higher risk of TKA compared to people without knee fractures from the general population [47]. After the first 3 years following knee fracture, the risk remained 1.6 times greater, suggesting lifelong risk for TKA [47]. During the 20-year study, 4% of knee fracture patients underwent TKA and 1% of population controls underwent TKA [47]. We found the risk factors for TKA in knee fracture patients to be primary knee OA (HR 9.6), surgical treatment of knee fracture (HR 2.1 in the first 5 years after knee fracture and HR 1.2 after the first 5 years following knee fracture), treatment with external fixation (HR 1.9), proximal tibia fracture (HR 1.8), and distal femur fracture (HR 1.7), which all independently increased the risk of TKA [47].

Study III: Study Limitations

Study limitations were of data completeness in the form of diagnosis codes and surgery codes being insufficiently or incorrectly registered. The NOMESCO surgery code system does not have conversion codes for surgically treated knee fractures being converted to TKA, nor any surgery codes for when external fixation is converted to ORIF, and because of the study design, medical records could not be accessed to calculate the number of conversion surgeries. On the other hand, the DNPR has high data quality with orthopaedic diagnoses having the highest PPV [41]. The number of patients with multiple knee fractures were only 3%, and because comparison of one combination of multiple knee fractures to all other types of combinations of multiple knee fractures, and yet again comparing those to single fractures would be complex, patients with multiple knee fractures were not analysed. It is unknown if procedures were performed on the contralateral knee because knee fracture laterality was insufficiently registered in the DNPR, as such knee fracture surgery, TKA, amputation, and knee fusion could potentially have been performed on the contralateral knee, resulting in over/underestimations of the risk of TKA. ABC extensions (fracture subclassifications) of ICD-10 knee fracture diagnosis codes and trauma type were also insufficiently registered in the DNPR, as such one could not for instance, differentiate between a high-energy, comminuted, intra-articular proximal tibia fracture and a low-energy, simple, extra-articular patella fracture in this study, therefore, the presented risk estimates can possibly be confounded. Nevertheless, the presented study describes the level of short-term as well as long-term risk of TKA a patient has when they fracture their knee, what part of the knee that presents the highest risk, and what comorbidities and surgical treatments further add to the risk of TKA and by how much. Another limitation is the 20-year follow-up period, which although it should sufficiently describe the risk of TKA for older patients, might not be long enough to fully describe the TKA risk for younger patients. On the other hand, the HR for the first 3 years following knee fracture was higher than the HR after the first 3 years, which might indicate that the HR beyond 20 years should be relatively similar to the long-term HR presented in this study, including younger patients. The results presented in this study should be generable to Scandinavian countries as the study covered a relatively homogenous population-sized sample in a Danish nationwide study for a period of 20 years.

As access to TKA is different in other parts of the world because of differing health care systems, and this could not be accounted for in this study, international generalizability can only be assumed.

1) What is the Short-Term Risk of TKA after Knee Fracture?

We found an increased risk of TKA for knee fracture patients compared to population controls in the first 3 years following knee fracture in our study. A Danish single-region study by Larsen et al. [37] of patellar fracture patients and a matched cohort estimated a HR of 3.02 for patella fracture patients in the first 5 years following patella fracture, which is relatively similar to the HR of 3.74 in the first 3 years following knee fracture in our study, although differences in the knee fracture types studied, population samples, and study design should be taken into consideration when comparing results.

2) What is the Long-Term Risk of TKA after Knee Fracture?

Our study found that the risk of TKA after 3 years and in the long-term remained high which suggests that the risk of complications such as secondary TKA for PTOA, pain, and reduced function after knee fracture persists throughout life. In the previously mentioned study by Larsen et al. [37] a HR of 1.56 was estimated at 5 to 10 years after patella fracture for patella fracture patients which is relatively comparable to the HR of 1.59 at over 3 years and onward in knee fracture patients in our study, although the same differences, i.e. different knee fracture types, geographical differences, and study design differences between the studies apply. In a study of ORIF-treated tibial plateau fractures by Wasserstein et al. [38] and a matched cohort without ORIF-treated tibial plateau fractures, a HR of 5.29 (adjusted for comorbidity) for TKA was calculated for patients with ORIF-treated tibial plateau fractures during a 14-year period. In our study, a HR of 1.59 (adjusted for increasing age per year, sex, and CCI) for TKA was calculated for knee fracture patients. In the study by Wasserstein et al. [38], 7% of ORIF-treated tibial plateau fracture patients and 2% of matched cohorts had TKA surgery after 10 years, while 4% of knee fracture patients and 1% of population controls had TKA surgery during the 20-year study period in our study. Again, a true comparison between the studies is difficult because of different fracture and treatment types studied, and differences in matching criteria, population samples, data sources, study design, and length of study period.

3) What are the Risk Factors for TKA in Patients with Knee Fractures?

We found several risk factors adding to the risk of TKA in knee facture patients. The study by Wasserstein et al. [38] found a HR of TKA for females with ORIF-treated tibial plateau fracture of 1.25; $p=0.029$, during the 14-year period, while our study presented a HR for TKA in females with knee fractures in the 20-year period of 1.21; $p=0.17$ (Table 13). Increasing age per year produced a HR of 1.03; $p<0.01$ in the study by Wasserstein et al. [38], while our results were similar (HR 1.02; $p<0.01$). In the study by Wasserstein et al. [38], treatment with prior external fixation of ORIF-treated tibial plateau fractures had a HR of 1.56; $p<0.20$, which is comparable to our results of treatment with external fixation vs ORIF and reduction only (HR 1.92; $p=0.05$).

However, we only studied index procedures of external fixation, ORIF, and reduction whereas the ORIF-treated tibial plateau study studied conversion surgery from external fixation to ORIF.

Current international research has also described females and older patients being more prevalent in terms of number of TKA procedures [52], as well as females and older patients being more prevalent in terms of number of knee fractures [13][50][16][17][15]. Our results of HR 1.21; p=0.17 for female knee fracture patients' risk of TKA and HR 1.02; p<0.01 for increasing age per year in our study do not contradict current literature, although the estimate for female knee fracture patients' risk was not significant and the HR estimate of 1.02 in increasing age was very small. Treating primary knee OA with TKA is an established procedure, therefore our results regarding knee fracture patients with pre-existing/primary knee OA having a high HR (9.57) for TKA agree with this, although it is interesting exactly how much risk there is (almost ten times higher risk) in having pre-existing knee OA as a knee fracture patient, of subsequently undergoing TKA. As surgically treated knee fractures per definition are more complex than non-surgically treated fractures, and therefore require surgery, it is again not surprising that the HRs for surgically treated knee fracture patients vs non-surgically treated knee fracture patients were higher both in the first 5 years following knee fracture and from 5 years and onward (HR 2.05 and HR 1.19). Furthermore, proximal tibia fractures had the highest HR of all knee fracture types for risk of TKA (1.75). The abovementioned risk factors presented illustrate the need for further research investigating patient-, fracture-, and treatment-related factors in order to optimize both initial and long-term knee fracture management of patients following knee fracture to minimize the risk of subsequently undergoing TKA. Perhaps focus should be put on patients with pre-existing knee OA, proximal tibia fracture patients, and distal femur fracture patients when regarding knee fracture types, and patients with complex knee fractures undergoing surgical treatment for knee fracture, including treatment with external fixation, as HRs for TKA were especially high for these patient groups. Nevertheless, future research should delve into exploring more patient-, fracture-, and treatment-related factors to reduce upcoming treatment burden and complications after knee fracture such as TKA.

Discussion of Study I, Study II, and Study III

As described above, current literature has been sparse on the incidences, patient-reported outcomes, and risk of TKA in knee fracture patients. All three studies of the PhD thesis share common trends and these are described below.

The IRs of knee fractures, and especially of surgically treated knee fractures increased during the 20-year study period, indicating that this should be taken into consideration when planning future health care plans and subsequent resource allocations (Study I). Furthermore, proximal tibia fractures had the highest IRs of all knee fractures, and females >51 years of age and patients with comorbidities were associated with sustaining knee fractures, especially proximal tibial fractures, and undergoing proximal tibia fracture surgery, and knee arthroplasty for PTOA (Study I) [48].

Knee fracture patients with primary knee OA had almost ten times higher risk (HR 9.57) of TKA compared to knee fracture patients without primary knee OA (Study III). Study I illustrated that the knee fracture population is a diverse population group, consisting of both younger and older patients, with a majority being females over the age of 51 years, as well as patients with no comorbidities according to the CCI but also a substantial proportion of patients with comorbidities represented by CCI ≥2, as well as other comorbidities not included in the CCI such as primary knee OA and osteoporosis. Comorbidity burden was also a risk factor in Study II for poor long-term PROM scores involving both knee-specific and general health outcomes in all four PROMs, further illustrating the fact that patients with comorbidities should be cared for not only at initial fracture treatment but also in the long-term. Given that patient comorbidity was found to be linked to adverse outcomes in Study I, Study II, and to some extent in Study III (regarding primary knee OA), patients with comorbidities should be a target group for knee fracture care improvement in future treatment directives.

Of note is that although trauma severity was incompletely registered in the DNPR [41], an indirect way of understanding trauma severity in the knee fracture population lies in the 20% of knee fracture patients simultaneously being registered with concomitant near-knee fractures, 13% with concomitant fractures, 10% with lesions inside the knee, 5% with osteoporosis, and 4% with primary knee OA (Study I). This indicates that a substantial proportion of knee fracture patients are either involved in high-energy trauma or have comorbidities that influence their risk of sustaining multiple fractures and injuries in low-energy trauma.

As stated in Study I, proximal tibia fracture IRs were the highest of all knee fracture types, and the incidence rate of surgical treatment of knee fractures increased during the 20-year period. In Study III, proximal tibia fracture and surgical treatment for knee fracture were independent risk factors for TKA in knee fracture patients. As IRs of proximal tibia fractures are the highest of all knee fracture types and surgically treated knee fracture IRs are increasing, and the risk of TKA seems to be high in proximal tibia fracture patients and surgically treated patients, it is likely that the IRs of posttraumatic TKA procedures will continue to increase in Denmark and Scandinavia, and most likely on a global scale as well. This should be accounted for in future health care initiatives. Patients with proximal tibia fractures might be a specific target group for further research into helping improve treatment guidelines to avoid future TKA surgery, as this patient group seems more likely to experience adverse events such as TKA (Study III). Furthermore, proximal tibia fractures treated with external fixation had higher ORs for poor PROM scores in all four PROMs at >5 years of follow-up compared to proximal tibia fractures treated with ORIF and reduction only (Study II). Also in Study II, treatment with external fixation and treatment with knee arthroplasty had high odds for poor long-term PROM scores in all four PROMs. Treatment with external fixation and surgical treatment of knee fracture were risk factors for TKA in Study III. The results from Study II and Study III suggest that surgical treatment of knee fractures including treatment with external fixation not only raises the risk for TKA, but it also contributes to poorer long-term outcomes.

Patients with distal femur fractures had a higher risk for TKA in Study III, and patients with distal femoral fractures had higher odds of poorer long-term PROM outcomes in all four PROMs in Study II, indicating that treatment with TKA following knee fracture is linked to poor outcomes, both in terms of functional outcomes [35][11] and in terms of complications [36][11], re-operations [36][9], and survival rates [35], as is supported by literature. These results suggest that not only proximal tibia fracture patients as stated previously, but also distal femur fracture patients seem to be a fragile group. Distal femur fracture patients have a risk of subsequent TKA (Study III), distal femur fractures are often complex fractures requiring technically challenging surgery [60], and Study II also showed that distal femur fracture patients, treatment of distal femur fracture patients with ORIF and reduction only, and non-surgical treatment of distal femur fracture patients, had higher odds for poor PROM outcome scores in all four PROMs at long-term follow-up after knee fracture.

In Study II, knee fracture patients reported high function, low pain, and high general health/QOL, while their ability to forget about the knee joint in everyday life was low. These findings paired with the fact that risk factors for poor PROM scores were different depending on the PROM and the follow-up period studied, suggests that there is still a long way to go in terms of ensuring high quality of care for all knee fracture patients, regardless of their accompanying patient-, fracture-, and treatment-related factors. In all four PROMs, PROM scores were low at 0-1 year following knee fracture, suggesting that optimization of initial fracture treatment and rigorous rehabilitation initiatives should be implemented early on in the knee fracture treatment process and consistent rehabilitation seems essential especially in the first year after knee fracture, while there is time for functional improvement. In Study III, the highest risk for TKA was seen in the first 3 years following knee fracture, suggesting that proper management of knee fractures is crucial in avoiding complications which can be devastating to the individual patient, in terms of lower functional outcomes, pain, knee-related and health-related quality of life (Study II), and high risk of TKA (Study III).

In Study III, the long-term risk of TKA in knee fracture patients remained 1.6 times greater after 3 years and onward, this result paired with the fact that treatment with knee arthroplasty was a risk factor for poor PROM scores at long-term follow-up in all four PROMs in Study II, further suggests that knee fracture patients have a long-term risk of TKA and that when treated with any knee arthroplasty or TKA, they seem to report poorer long-term outcomes, signifying that knee fracture patients treated with knee arthroplasty is another patient group specifically vulnerable to adverse outcomes.

The variables of increasing age and sex were less clear in terms of PROM outcomes (Study II) and risk for TKA (Study III). Age >40 years had higher odds of poor knee function, high knee pain, and poor ability to forget about the knee joint in daily life (poor OKS and FJS-12 scores) at both short-term and long-term follow-up, while at longer follow-up, female patients had slightly higher odds of having poor OKS and FJS-12 scores (Study II). Increasing age and sex did not have higher odds for poor EQ5D-5L Index and EQ5D-5L VAS scores, neither at short-term nor at long-term follow-up (Study II).

In the previously discussed TKA study [59], female patients and younger patients reported lower scores in a knee-specific PROM (FJS-12). Also as previously discussed, TKA studies have provided the argument that an increasing comorbidity burden due to the increasing age of older patients is more likely an influencing factor than their knee joint issues, as well as decreasing physical activity of older patients resulting in less demand on their knee joint leading to higher knee-specific PROM scores in older patients compared to younger patients [59][22][29]. Our study presented slightly higher odds of female knee fracture patients reporting poor knee-specific PROM scores at long-term follow-up, but in contrast, our study showed higher odds for older knee fracture patients (aged >40 years) of reporting poor knee-specific PROM scores at short-term and long-term follow-up. In Study III, the association between increasing age per year and risk of TKA in knee fracture patients was less clear (HR 1.02), which is supported by a TKA study of patients with previous tibial plateau fractures [38], and female sex had a HR of 1.21; p=0.17 for risk of TKA in female knee fracture patients in our study, again producing unclear estimates (Study III), although the previously mentioned tibial plateau fracture study found a more significant estimate (HR 1.25; p=0.029) [38]. Again, an explanation for the differing results between our study and TKA studies [59][22][29], is probably that knee fracture patients present with other challenges and demands than patients treated with TKA for OA. The abovementioned points in our study suggest that increasing age and female sex have higher odds for poor outcomes in knee-related PROMs, but are not associated with risk for TKA following knee fracture.

Conclusions

Study I: Conclusions

During the 20-year study period, the IRs of knee fractures increased to 70 per 10^5 inhabitants, corresponding to a 12% increase, surgically treated knee fracture IRs increased by 35% to 23 per 10^5 inhabitants, and the highest knee fracture IR in patients was found in females aged >51 years, while the highest knee fracture type IR was found in the proximal tibia [48]. Females aged >51 years and patients with comorbidities were associated with sustaining knee fractures, especially proximal tibia fractures, proximal tibia fracture surgery, and posttraumatic knee arthroplasty [48]. Further research is needed when preparing to allocate hospital resources appropriately to knee fracture patients because of the described treatment burden, increasing IRs, and the diverse patient group constellations.

Study II: Conclusions

Median PROM scores at short-term follow-up (0-1 years) after knee fracture were: 31 (OKS), 27 (FJS-12), 0.50 (EQ5D-5L Index), and 74 (EQ5D-5L VAS). Median PROM scores at long-term follow-up (>5 years) after knee fracture were 40 (OKS), 54 (FJS-12), 0.76 (EQ5D-5L Index), and 80 (EQ5D-5L VAS). In each PROM, median PROM score was similar at 3-5 years and at >5 years of follow-up following knee fracture. It was not possible to investigate causality in this study and temporality between risk factors and outcomes, because of the study design, as the study was cross-sectional.

Knee fracture patients reported relatively high knee function, low knee pain, and high general health and QOL (OKS, EQ5D-5L Index, and EQ5D-5L VAS) although their ability to forget about the knee joint in everyday life was diminished (FJS-12). Risk factors for poor PROM score varied depending on the PROM and follow-up period studied. Patient age >40 years had higher ORs of poor OKS and FJS-12 scores at short-term and long-term follow-up, while comorbidity, distal femoral fracture, treatment with external fixation, and treatment with knee arthroplasty had higher odds of poor PROM scores in all four PROMs at long-term follow-up. Patients treated with ORIF and reduction only for distal femur fracture, and patients treated non-surgically for distal femur fracture reported higher ORs for poor PROM scores in all four PROMs at long-term follow-up when compared to ORIF and reduction only treated and non-surgically treated patella fracture patients. Non-surgically treated patella fracture patients and non-surgically treated proximal tibia fracture patients reported lower odds for poor PROM scores in all four PROMs at long-term follow-up compared to ORIF and reduction only treated patella fracture and proximal tibia fracture patients. Proximal tibia fracture patients treated with external fixation reported higher ORs for poor PROM scores in all four PROMs at >5 years of follow-up compared to proximal tibia fracture patients treated with ORIF and reduction only. Future studies should continue to investigate the presented risk factors and how they impact a patient's prognosis so that patients can be informed of their expected outcomes after knee fracture. This study indicates that the quality of care of knee fracture patients is unequal and dependent on patient-, fracture-, and treatment-specific risk factors. Emphasis should be made on quality-improvement directives to neutralize these patient-, fracture-, and treatment-specific differences in knee fracture patients to ensure excellent outcomes and prognoses for all knee fracture patients in the future.

Study III: Conclusions

In the first 3 years following knee fracture, knee fracture patients had a 3.7 times higher risk of TKA compared to people without knee fractures [47]. After the first 3 years following knee fracture, the risk for knee fracture patients remained 1.6 times higher compared to people without knee fractures, suggesting that the risk for TKA in knee fracture patients is lifelong [47]. The risk for TKA after knee fracture was further added to if the following risk factors for TKA in knee fracture patients were present: primary knee OA (HR 9.6), surgical treatment for knee fracture (HR 1.2-2.1), treatment with external fixation (HR 1.9), proximal tibial fracture (HR 1.8), and distal femoral fracture (HR 1.7) [47]. By providing short-term and long-term risk estimates for TKA, we now know just how high the risk for TKA is in knee fracture patients, especially in the short-term, emphasizing the importance of first-rate initial knee fracture management, but also the importance of maintaining high-ranking rehabilitation programmes to avoid secondary TKA in the long-term. As the treatment burden of knee fractures is described in this study, future resource allocations can now be planned accordingly. Future studies will be able to further investigate the risk factors for TKA in knee fracture patients, providing a basis for clinicians to inform patients on if they have any other patient-, fracture-, and treatment-related risk factors for TKA which are additive to their already established risk for TKA.

Perspectives and Future Research

The results from this PhD thesis have described 1) incidence rates of knee fractures, incidence rates of knee fractures according to age category, sex, knee fracture type, and treatment type, as well as patient-, fracture-, and treatment-related characteristics of knee fracture patients, 2) short-term and long-term patient-reported outcomes of knee fracture patients as well as patient-, fracture-, and treatment-related risk factors for poor patient-reported outcomes, and 3) short-term and long-term risk for TKA as well as patient-, fracture-, and treatment-related risk factors for TKA in knee fracture patients. The results from this study can be used in clinical practice to highlight future incidence trends of knee fracture patients and aid in the planning of proper hospital resource allocations to focus on certain patient groups being more likely to sustain knee fracture, inform knee fracture patients of their expected short-term and long-term patient-reported outcomes after knee fracture including knee pain, knee function, and general health and quality of life, their potential risk factors for poor knee-related and general health-related outcome after knee fracture, and their short-term and long-term risk of TKA compared to the general population, as well as any additive patient-, fracture-, and treatment-related risk factors for TKA.

Our results illustrate that the knee fracture population is a multifaceted patient group. IRs of knee fractures and surgically treated knee fractures are increasing, and the IR of proximal tibia fracture is the highest of all knee fracture types [48]. Females aged >51 years and patients with comorbidities are associated with knee fractures, proximal tibia fractures, proximal tibia fracture surgery, and posttraumatic knee arthroplasty [48]. Knee fracture patients often sustain concomitant near-knee fractures, other concomitant fractures, and lesions inside the knee, and some patients have pre-existing comorbidities such as osteoporosis and primary knee OA. These data suggest either high-energy trauma or presence of comorbidities influencing the risk of concomitant fractures and injuries during low-energy trauma, which most likely results in complicated rehabilitation programmes and poorer prognoses for many a knee fracture patient.

Knee fracture patients report relatively high PROM scores regarding knee function and general health but fail to do so regarding their ability to abstract from their fractured knee joint. Patients aged >40 years have higher odds of reporting poor knee-specific PROM scores at both short-term and long-term follow-up. Knee fracture patients with comorbidities, distal femur fracture patients, knee fracture patients treated with external fixation, and knee fracture patients treated with knee arthroplasty have higher odds of reporting poor knee-specific and generic PROM scores at long-term follow-up.

Knee fracture patients have a substantially higher short-term risk for TKA compared to people from the general population without knee fractures, and the risk is maintained throughout life [47]. Knee fracture patients with primary knee OA, surgically treated knee fracture patients, knee fracture patients treated with external fixation, proximal tibia fracture patients, and distal femur fracture patients have an additive risk for TKA [47].

This PhD thesis suggests that incidences, outcomes, and risk of TKA for knee fracture patients are especially associated with the following patient-related factors: female sex, increasing age, and comorbidity including primary knee OA, the following fracture-related factors: proximal tibia fracture and distal femur fracture, and the following treatment-related factors: surgically treated knee fracture, external fixation of knee fracture, and knee arthroplasty after knee fracture. Future studies should focus on not only further researching patient-related factors such as different comorbidities and trauma levels, and treatment-related factors such as different surgery types, for instance ORIF-subclassifications and knee arthroplasty types, but also divide knee fractures into subclassifications of distal femur fractures, patella fractures, proximal tibia fractures, and multiple knee fractures, in order to further describe incidences, outcomes, and risk of TKA using these differentiated risk factors, to inform patients of their prognoses, prepare the health care system accordingly, and optimize the management of knee fracture patients.

The results from this PhD thesis illustrate that the knee fracture population is a complex and heterogenous population group and should be treated as such when regarding both optimal initial fracture management as well as in different stages of follow-up after knee fracture. Appropriate measures should be taken to avoid long-term complications affecting the knee-related as well as health-related quality of life of knee fracture patients. This PhD thesis stresses the need to re-evaluate future resource allocations to ensure proper treatment of knee fracture patients, as incidences of knee fractures are on the rise, the knee fracture patient population is relatively large and diverse, their incidences, outcomes, and risk of TKA vary depending on patient-, fracture-, and treatment-related factors, and as their risks of TKA are now established, these should be accounted for in the health care system plan.

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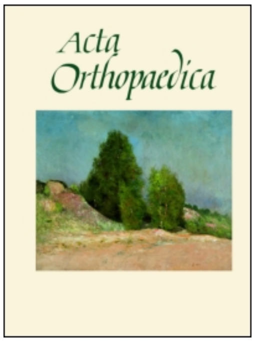
Appendix

Study I Incidences

Study II Patient-Reported Outcomes

Study III Risk of Total Knee Arthroplasty

Supplementary Material



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20-year trends of distal femoral, patellar, and proximal tibial fractures: a Danish nationwide cohort study of 60,823 patients

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20-year trends of distal femoral, patellar, and proximal tibial fractures: a Danish nationwide cohort study of 60,823 patients

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Background and purpose — Knee fracture treatment burden remains unknown, impeding proper use of hospital resources. We examined 20-year trends in incidence rates (IRs) and patient-, fracture-, and treatment-related characteristics of knee fracture patients.

Patients and methods — This nationwide cohort study of prospectively collected data including patients with distal femoral, patellar, and proximal tibial fractures from the Danish National Patient Registry during 1998–2017, assesses IRs of knee fractures (per 10^5 inhabitants) as well as patient-, fracture-, and treatment-related characteristics of knee fracture patients.

Results — During 1998–2017, 60,823 patients (median age 55; 57% female) sustained 74,106 knee fractures. 74% of the study population had a Charlson Comorbidity Index (CCI) of 0 and 18% a CCI of ≥ 2. 51% were proximal tibial fractures, 31% patellar fractures, and 18% distal femoral fractures. At the time of knee fracture, 20% patients had concomitant near-knee fractures (femur/tibia/fibula shaft/hip/ankle), 13% concomitant fractures (pelvic/spine/thorax/upper extremities), 5% osteoporosis, and 4% primary knee osteoarthritis. Over 1/3 knee fractures were surgically treated and of these 86% were open-reduction internal fixations, 9% external fixations, and 5% knee arthroplasties. The most common surgery type was proximal tibia plating (n = 4,868; 60% female). Knee fracture IR increased 12% to 70, females aged > 51 had the highest knee fracture IR, proximal tibial fracture had the highest knee fracture type IR (32) and surgically treated knee fracture IR increased 35% to 23.

Interpretation — Knee fracture IRs, especially of surgically treated knee fractures, are increasing and proximal tibial fracture has the highest knee fracture type IR. Females aged > 51 and patients with comorbidity are associated with knee fracture, proximal tibial fracture, proximal tibial fracture surgery, and posttraumatic knee arthroplasty.

Knee fractures include fractures in the distal femur, patella, and proximal tibia, with a reported incidence rate (IR) of approximately $9/10^5$ per year in the United States (Lambers et al. 2012). Knee fractures vary in type and complexity and often result in lower function, work performance, and health-related quality of life (Van Dreumel et al. 2015, Sluys et al. 2016). Previous studies are limited to small sample sizes, lower extremity fractures, tibial plateau fractures, patellar fractures, or proximal tibia fractures (Court-Brown and Caesar 2006, Scholes et al. 2014, Elsoe et al. 2015, Larsen et al. 2016, Wennergren et al. 2018). To our knowledge, there are no population-based studies describing IRs of knee fractures over time, either overall or according to sex, age, knee fracture type, and treatment type. Estimation of treatment burden of knee fractures for subsequent allocation of hospital resources requires knowledge of epidemiology and IRs. We conducted a national cohort study to examine 20-year trends in incidence rates (IRs) and patient-, fracture-, and treatment-related characteristics of knee fracture patients in Denmark during 1998–2017.

Patients and methods

Study design and data sources

The study was designed as a nationwide cohort study of prospectively collected data from the Danish Civil Registration System (CRS) and Danish National Patient Registry (DNPR) (Schmidt et al. 2014, 2015). The CRS contains complete information on Danish Civil Personal Register (CPR) number, residency, and emigration and is updated daily with vital status. The DNPR contains information on hospital admissions, emergency department visits, admission date, CPR number, age, sex, WHO ICD-10 classification, and the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Proce-

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dures (NOMESCO) (WHO 2019, NOMESCO 2019). The current NOMESCO classification was implemented in 1995; we therefore excluded the years before 1996 to reduce surgery code bias, and years 1996–1997 to exclude a potential backlog of already prevalent knee fracture cases with hospital follow-up. Data on the population were divided by sex and age for each calendar year of 1998–2017 (Statistics Denmark 2019).

Study population

The study population consisted of patients registered in the DNPR from January 1, 1998 to December 31, 2017 with hospital contacts for ICD-10 codes DS724, DS820, and DS821 (knee fracture patients) with/without subsequent knee surgery NOMESCO code(s) (Appendix 1, see Supplementary data). Figure 1 provides a definition of new knee fracture, surgically treated knee fracture, and non-surgically treated knee fracture. Surgically treated knee fractures were divided into 3 surgery types: open reduction internal fixation (ORIF), external fixation, and knee arthroplasty. The updated version of the Charlson Comorbidity Index (CCI) was used to evaluate comorbidity (Bjorgul et al. 2010, Quan et al. 2011).

Statistics

The study was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines (von Elm et al. 2014). Proportions, median, and interquartile range (IQR) were used to describe the study population. We estimated annual overall IRs of knee fractures with 95% confidence intervals (CIs) as the number of knee fractures per calendar year divided by the total number of individuals at risk in Denmark in that same year. All IRs were calculated/10^5 inhabitants. Annual IRs were calculated according to sex, age group, knee fracture type, and surgery type. Poisson regression was used to estimate incidence rate ratios (IRRs) with 1998 as year of reference. IRR expressed the relative change in IRs of knee fractures in 1999–2017 compared with year 1998 as reference IRR. All analyses were performed using the statistical software R 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics, registration, funding, and potential conflicts of interest

The study was approved by Danish Data Protection Agency, record number REG-085-2017. The study was funded by P. Carl Petersen Foundation, Danish Rheumatism Association, Research Unit Naestved, Slagelse and Ringsted Hospitals, Production, Research and Innovation Naestved, Slagelse and Ringsted Hospitals, Data and Development Support Region Zealand, Naestved, Slagelse and Ringsted Hospitals' Research Fund, and Clinical Orthopaedic Research Hvidovre, Hvidovre Hospital. Funding sources were not involved in study design, collection, analysis, interpretation, and completion. The authors declare no conflicts of interest regarding this study.

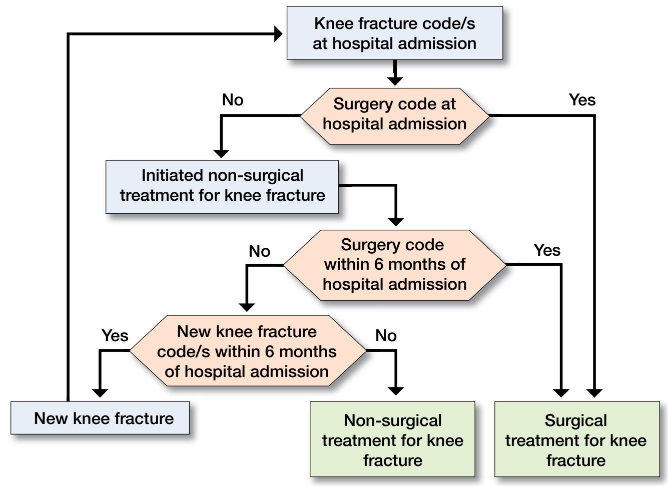

Figure 1. Definition of new knee fracture, surgically treated knee fracture and non-surgically treated knee fracture.

Results

Overall incidence rates

Average IR (per 10^5 inhabitants) for sustaining knee fracture during 1998–2017 was 63 (CI 62–63). IR for knee fracture was 64 (CI 61–66) in 1998, remaining stable in the following years and increasing from year 2010 up to 70 (CI 67–72) in 2017, corresponding to a 12% increase (Figure 2). The corresponding IRR was 1.1 (CI 1.0–1.2) in 2017 compared with 1998 (Table 1, see Supplementary data).

Incidence rates by sex and age

IR of knee fractures in females increased from 70 (CI 67–73) in 1998 to 83 (CI 80–86) in 2017. IR in males decreased slightly from 58 (CI 55–61) in 1998 to 57 (CI 54–60) in 2017 (Figure 3). The corresponding IRR was 1.2 (CI 1.1–1.3) for females and 1.0 (CI 0.9–1.1) for males in 2017 compared with 1998.

During 1998–2017, IR for knee fractures was highest among females aged > 71 (IR decreased from 240 (CI 223–258) in 1998 to 223 (CI 209–239) in 2017). During 1998–2017, IR increased in females aged 51–70 years (IR increased from 95 [CI 87–103] to 124 [CI 116–132]), children aged 0–5 years (IR in females aged 0–5 years increased from 23 [CI 17–30] to 78 [CI 66–93] and IR in males aged 0–5 years increased from 24 [CI 19–32] to 71 [CI 60–84] and females and males aged 6–18 (IR in females increased from 31 [CI 26–37] to 38 [CI 33–44] and IRs in males increased from 57 [CI 50–65] to 70 [CI 63–79]).

Incidence rates by knee fracture type

During 1998–2017, average IR for proximal tibia fracture was 32 (CI 31–32), average IR for patella fracture was 21 (CI 21–21) and average IR for distal femur fracture was 12 (CI 12–12). IR for proximal tibia fracture increased over time,

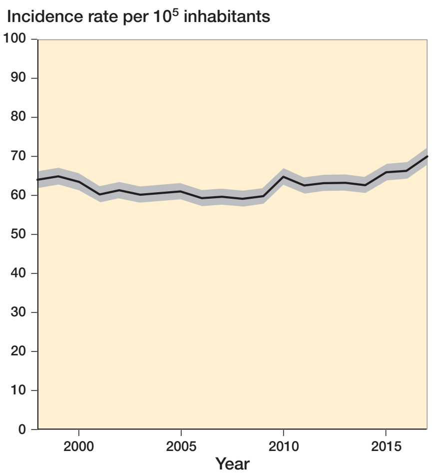

Figure 2. Incidence rate of knee fractures per 10^5 inhabitants during 1998–2017 with 95% confidence intervals.

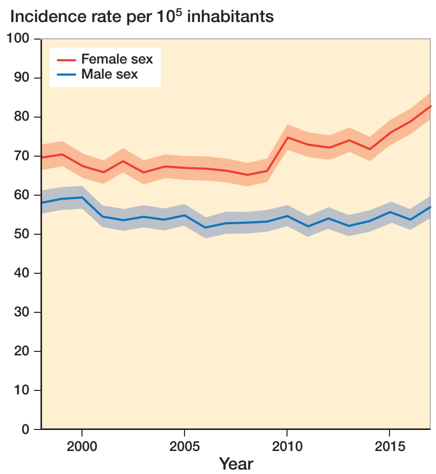

Figure 3. Incidence rates of knee fractures per 10^5 inhabitants during 1998–2017 by sex.

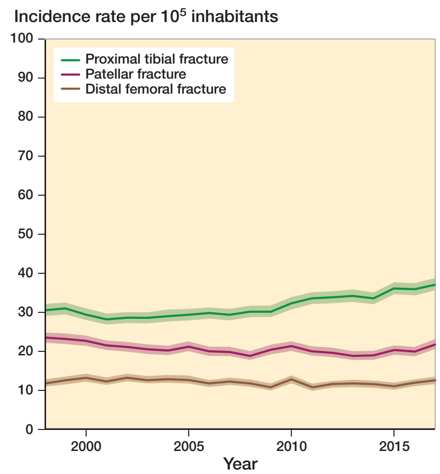

Figure 4. Incidence rates of knee fractures per 10^5 inhabitants during 1998–2017 by knee fracture type.

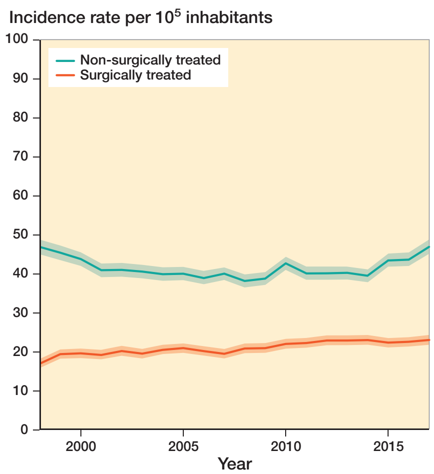

Figure 5. Incidence rates of surgically and non-surgically treated knee fractures per 10^5 inhabitants during 1998–2017.

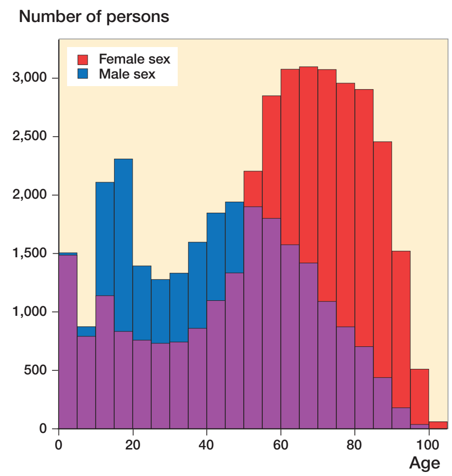

Figure 6. Sex and age distribution of the study population registered in the Danish National Patient Registry during 1998–2017.

especially after 2010, whereas IRs for patella fracture and distal femur fracture remained stable (Figure 4).

Incidence rates by treatment type

Average IR for surgically treated knee fractures was 21 (CI 21–21). IR for surgically treated knee fractures was 17 (CI 16–18) in 1998 increasing to 23 (CI 22–24) in 2017, corresponding to a 35% increase (Figure 5). The corresponding IRR for surgically treated knee fracture was 1.4 (CI 1.2–1.5) in 2017 when comparing 2017 with reference year 1998.

Average IR for non-surgically treated knee fractures was 42 (CI 41–42). IR for non-surgically treated knee fractures was 47 (CI 45–49) in 1998 and 47 (CI 45–49) in 2017, remaining stable during the 20-year period (Figure 5). The corresponding IRR for non-surgically treated knee fracture was 1.0 (CI 1.0–1.1) in 2017 when comparing 2017 with reference year 1998.

Patient-, fracture-, and treatment-related characteristics

During 1998–2017, 60,823 patients sustained 74,106 knee fractures (Table 2, see Supplementary data). Median study population age was 55 (IQR 30–72), being 64 years (IQR 46–78) in females and 42 years (IQR 19–59) in males. 57% of knee fracture patients were female. Children aged 0–5, males aged 5–50, and females aged > 50 had highest risk of knee fracture (Figure 6). 74% of the study population had CCI 0, 8% CCI 1, and 18% CCI ≥ 2. At the time of knee fracture, 20% of knee fracture patients were registered with concomitant near-knee fractures (femur/tibia/fibula shaft/hip/ankle), of which tibia shaft fracture (5%) and femur shaft fracture (4%) were most frequent, while 13% of knee fracture patients were registered with concomitant fractures (pelvic/spine/thorax/upper extremities) (Appendix, see Supplementary data). At the time of knee fracture, 10% of patients were registered with lesions inside the knee, 5% with osteoporosis,

Table 3. Distribution of knee fracture type in the study population including surgically and non-surgically treated knee fractures in the DNPR during 1998–2017. Values are frequency (%)

Knee fracture type	Study population n = 74,106	Surgically treated n = 24,215	Non-surgically treated n = 46,397
Proximal tibia	38,080 (51)	12,175 (50)	22,411 (48)
Patella	22,689 (31)	5,977 (24)	16,712 (36)
Distal femur	13,337 (18)	6,063 (25)	7,274 (16)

Table 4. Frequency, age and sex distribution of most frequent knee fracture surgery types registered in the DNPR during 1998–2017

Knee fracture surgery type	n	Median age (IQR)	Female sex (%)
Proximal tibia plate and screws	4,868	57 (45–67)	60
Patella wiring	4,592	61 (44–72)	58
Proximal tibia screw fixation	3,635	50 (32–63)	50
Distal femur plate and screws	2,517	74 (61–85)	73
Distal femur intramedullary nail	1,350	75 (59–85)	74
Primary cemented knee arthroplasty	855	68 (59–76)	74

DNPR = Danish National Patient Registry. IQR = interquartile range.

and 4% with primary knee osteoarthritis (OA) (Appendix, see Supplementary data).

The most common knee fracture type was proximal tibia fracture (51%), followed by patella fracture (31%) and distal femur fracture (18%). Table 3 shows distribution of knee fracture type in the study population including surgically and non-surgically treated knee fractures in the DNPR during 1998–2017. 90% of patients had 1 knee fracture registered and 11% patients had > 1 knee fracture registered. The total number of knee fracture treatments was 68,419 (some treatments covered multiple knee fractures). Of these 68,419 treatments, 34% were surgical treatments and 66% non-surgical treatments. 6% of knee fracture patients received both surgical and non-surgical treatments. 89% patients had 1 knee fracture surgery and 11% had > 1 knee fracture surgery. In non-surgically treated patients, the corresponding numbers were 96% with 1 non-surgical knee fracture treatment and 4% with > 1 non-surgical treatment.

22,996 surgeries were performed on 24,215 knee fractures in 20,350 patients during 1998–2017. In surgically treated patients, median population age was 59 years (IQR 42–72) and median age for females was 66 (IQR 54–77). Of surgically treated knee fractures, 86% surgeries were ORIFs, 9% external fixations, and 5% knee arthroplasties. Table 4 presents frequency, age, and sex distribution of the most frequent knee fracture surgery types registered in the DNPR during 1998–2017.

Discussion

Study limitations

Information bias, i.e., misclassifications of diagnosis codes and missing/incomplete data in variable and diagnosis registrations by discharging physicians, is present in registry studies. Fortunately, both ICD-10 and NOMESCO classifications are used to identify knee fracture patients, registering to DNPR is improving, reporting to DNPR is mandatory and is used for reimbursement by public and private hospitals (although knee fracture patients are not treated in the Danish private sector), and DNPR data quality is high with orthopedic diagnoses having the highest positive predictive value: 91% (Schmidt et al. 2015). Another study limitation is incomplete laterality registration in DNPR, likely producing overestimated IRs, but random variation cannot be excluded. The same applies for ABC extensions of ICD-10 codes: only a small percentage of the study population was registered with ABC extensions, thus distributions of knee fracture subtypes could not be described (Schmidt et al. 2015). IRs calculated at the beginning of the study period might be inflated because it is unknown if they are incidences or a backlog of prevalent knee fractures with hospital follow-up. Nevertheless, the possible error in average IR for the period decreases over the long 20-year study period. The overestimations are also reduced by the 6-month wash-out period (Figure 1). The 6-month wash-out period is likely not too short because only 11% patients had > 1 knee fracture registered. The study was a 20-year, nationwide cohort study of knee fracture patients from a relatively homogenous population, providing results of high external validity.

Overall incidence rates

The knee fracture IR was approximately $9/10^5$ per year in the United States (Lambers et al. 2012). The IR was ~$60/10^5$ inhabitants in our study (Figure 2). However, the American study included only data from emergency department visits in a population sample.

Incidence rates by sex, age, knee fracture type, and treatment type

In our study, increasing knee fracture IRs were seen in females aged > 51 and > 71 and both sexes aged 0–18. A national Danish study of fracture incidences reported increases in IRs of lower extremity fractures in males aged < 50, females aged > 50, and both sexes aged > 75 (Driessen et al. 2016). This was a 1-year study and did not discriminate between proximal tibia and distal femur fractures; it can therefore only partly be extrapolated to our results.

A British single-center study calculated IRs/10^5 person-years at risk (PYRS) for distal femoral, patellar, and proximal tibial fractures in patients aged > 65 (Court-Brown et al. 2014). Their IRs ranged between 8 and 37 compared with our IRs of $12–32/10^5$ inhabitants. As in our study, older patient groups had high knee fracture IRs, especially older females, and proximal tibia had a high knee fracture type IR.

Our demographic data accord with a Swedish tibial fracture study in which proximal tibia fracture patients were more likely to be females (58%) with higher mean age (54) (Wennergren et al. 2018). The average IR for proximal tibia fracture was $27/10^5$ PYRS, which is comparable to our results: $32/10^5$ inhabitants. Our results mirror the results of the Swedish study regarding increase in proximal tibia fracture IR, higher IRs of females with increasing age compared with males, and more flatlined IR knee fracture curves in males.

A Danish tibial plateau fracture study demonstrated that intra-articular proximal tibia fractures present a treatment burden, showing increased tibial plateau fracture IRs in males aged < 50 and females aged > 50 (Elsoe et al. 2015), which echoes our results of higher IRs in proximal tibia fractures and higher knee fracture IRs in females aged > 51.

Driessen et al. (2016) calculated an annual patella fracture IR in Denmark: $33/10^5$ PYRS. Larsen et al. (2016) studied patella fractures where IRs varied between 11 and $17/10^5$ PYRS and females aged 60–80 had the highest patella fracture IR. Our results show a similar trend in high patella fracture IR (21) and that the highest knee fracture IRs are seen in females aged > 51 and > 71. Remaining discrepancies in results can be explained by different study period lengths and in geographical differences.

Improvement in registrations to the DNPR, increased societal demand for invasive orthopedic treatments, i.e., surgical treatments of knee fractures and broader inclusion of comorbidly challenged patients with a lower threshold for knee fracture surgery, might explain the 35% increase in surgically treated knee fracture IR. Most patients (89%) had only 1 knee fracture surgery, making double registrations an unlikely contributor to IR increase.

Patient-, fracture-, and treatment-related characteristics of knee fracture patients

At the time of knee fracture, 18% patients had CCI ≥ 2, 1/5 concomitant near-knee fractures, 13% concomitant fractures, 5% osteoporosis, and 4% primary knee OA. Females aged > 51 and patients with comorbidity are associated with sustaining knee fracture, especially proximal tibial fracture, surgical treatment for knee fracture, proximal tibial fracture surgery, and posttraumatic TKA (Table 4), making our results similar to trends described in current literature with knee fractures and TKA procedures being most frequent in older females (Court-Brown and Caesar 2006, Court-Brown et al. 2014, Kremers et al. 2014, Elsoe et al. 2015, Larsen et al. 2016, Driessen et al. 2016, Krause et al. 2016, Wennergren et al. 2018).

Conclusion

In this 20-year nationwide cohort study, we observed that overall IR of knee fracture increased 12% to $70/10^5$ inhabitants while IR of surgically treated knee fracture increased 35% to $23/10^5$ inhabitants. Our findings reflect the complexity of the knee fracture population with future challenges concerning treatment burden, increasing incidences, and patient risk groups and provide the basis for proper hospital resource allocations including computing future risk-adjustment and payment models.

Supplementary data

Appendix and Tables 1–2 are available as supplementary data in the online version of this article, http://dx.doi.org/10.1080/17453674.2019.1698148.

VV planned the study, wrote the protocol, obtained permission from the Danish Data Protection Agency, secured data from CRS and DNPR, performed statistical analysis, and drafted and revised the article. ABP planned the study, revised the protocol, and revised the article. PTT planned the study and revised the article. AT planned the study, revised the protocol, and revised the article. HMS planned the study, revised the protocol, and revised the article.

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Supplementary data

Appendix

ICD-10 diagnosis codes

Concomitant near-knee fractures: DS720 (femoral neck fracture), DS721 (pertrochanteric femoral fracture), DS722 (subtrochanteric femoral fracture), DS723 (femoral shaft fracture), DS727 (multiple femoral fractures), DS728 (other femoral fracture), DS729 (femoral fracture, other, not otherwise specified), DS822 (tibial shaft fracture), DS823 (distal tibia fracture), DS824 (fibula shaft fracture), DS825 (medial malleolar fracture), DS826 (lateral malleolar fracture), DS827 (multiple fractures of the knee and lower knee), DS828 (fracture of other part of lower leg) and DS829 (fracture of lower leg, other, not otherwise specified).

Concomitant fractures: DS122 (fracture of cervical spine), DS127 (multiple fractures of cervical spine), DS22 (fracture of costae, sternum or thoracic spine), DS32 (fracture of lumbar spine or pelvis), DS42 (shoulder and/or upper arm fracture), DS52 (elbow and/or lower arm fracture), DS62 (wrist and/or hand fracture), DT021 (fractures in thorax, lumbar spine and pelvis), DT027 (fractures in thorax, lumbar spine, pelvis, upper and lower extremities) and DT08 (fracture of spine, not otherwise specified).

Lesions inside the knee: DS83 (luxation and distortion of joint and ligaments in knee).

Primary knee osteoarthritis (OA): DM170 (primary bilateral knee OA), DM171 (primary unilateral knee OA) and DM179 (knee OA other, not otherwise specified).

Osteoporosis: DM81 (osteoporosis without pathological fracture).

Proximal tibial fracture: DS821.

Patellar fracture: DS820.

Distal femoral fracture: DS724.

Femoral shaft fracture: DS723.

Tibial shaft fracture: DS822.

NOMESCO surgery codes

External fixation codes: KNFJ25 (external fixation of fracture in distal femur), KNGJ20 (external fixation of fracture in patella), KNGJ21 (external fixation of fracture in proximal tibia) and KNGJ29 (external fixation of fracture in knee, not otherwise specified).

Knee arthroplasty codes: KNGB (primary prosthesis in the knee), KNGC (secondary prosthesis in the knee) and KNGG (joint resections, arthroplasties and arthrodeses in knee joint).

Open reduction internal fixation (ORIF), external fixation and reduction codes:

Distal femur:

KNFJ0 closed reduction of femur fracture
KNFJ05 closed reduction of fracture in distal femur
KNFJ1 open reduction of femur fracture
KNFJ15 open reduction of fracture in distal femur
KNFJ2 external fixation of femur fracture
KNFJ25 external fixation of fracture in distal femur
KNFJ3 internal fixation with bio implants of femur fracture
KNFJ35 internal fixation with bio implants of fracture in distal femur
KNFJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of femur fracture
KNFJ45 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in distal femur
KNFJ5 internal fixation with intramedullary nail of femur fracture
KNFJ55 internal fixation with intramedullary nail of fracture in distal femur
KNFJ6 internal fixation with plate and screws of femur fracture
KNFJ65 internal fixation with plate and screws of fracture in distal femur
KNFJ7 internal fixation with screws only of femur fracture
KNFJ75 internal fixation with screws only of fracture in distal femur
KNFJ8 internal fixation with other or combined method of fracture in femur
KNFJ85 internal fixation with other or combined method of fracture in distal femur
KNFJ9 other surgical fracture treatment in femur
KNFJ95 other surgical fracture treatment in distal femur
KNGF2 fixation of articular surface fragment in knee joint

Patella/proximal tibia:

KNGJ fracture treatment in knee and lower leg
KNGJ0 closed reduction of fracture in knee
KNGJ00 closed reduction of fracture in patella
KNGJ01 closed reduction of fracture in proximal tibia
KNGJ09 closed reduction of fracture in knee, not otherwise specified
KNGJ1 open reduction of fracture in knee
KNGJ10 open reduction of fracture in patella
KNGJ11 open reduction of fracture in proximal tibia
KNGJ19 open reduction of fracture in knee, not otherwise specified

KNGJ2 external fixation of fracture in knee
KNGJ20 external fixation of fracture in patella
KNGJ21 external fixation of fracture in proximal tibia
KNGJ29 external fixation of fracture in knee, not otherwise specified
KNGJ3 internal fixation with bio implants of fracture in knee
KNGJ30 internal fixation with bio implants of fracture in patella
KNGJ31 internal fixation with bio implants of fracture in proximal tibia
KNGJ39 internal fixation with bio implants of fracture in knee, not otherwise specified
KNGJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee
KNGJ40 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in patella
KNGJ41 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in proximal tibia
KNGJ49 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee, not otherwise specified
KNGJ5 internal fixation with intramedullary nail of fracture in knee
KNGJ51 internal fixation with intramedullary nail of fracture in proximal tibia
KNGJ59 internal fixation with intramedullary nail of fracture in knee, not otherwise specified
KNGJ6 internal fixation with plate and screws of fracture in knee
KNGJ60 internal fixation with plate and screws of fracture in patella
KNGJ61 internal fixation with plate and screws of fracture in proximal tibia
KNGJ69 internal fixation with plate and screws of fracture in knee, not otherwise specified
KNGJ7 internal fixation with screws only of fracture in knee
KNGJ70 internal fixation with screws only of fracture in patella
KNGJ71 internal fixation with screws only of fracture in proximal tibia
KNGJ79 internal fixation with screws only of fracture in knee, not otherwise specified
KNGJ8 internal fixation with other or combined method of fracture in knee
KNGJ80 internal fixation with other or combined method of fracture in patella
KNGJ81 internal fixation with other or combined method of fracture in proximal tibia
KNGJ89 internal fixation with other or combined method of fracture in knee, not otherwise specified
KNGJ9 other surgical fracture treatment in knee
KNGJ90 other surgical fracture treatment in patella
KNGJ91 other surgical fracture treatment in proximal tibia
KNGJ99 other surgical fracture treatment in knee, not otherwise specified

Table 1. Annual incidence rates per 10^5 inhabitants with 95% confidence intervals (IR (CI)) and incidence rate ratios (IRR (CI)) for the study population registered in the DNPR during 1998–2017

Year	IR (CI)	IRR (CI)
1998	64.0 (61.9–66.2)	reference
1999	64.9 (62.8–67.1)	1.01 (0.97–1.06)
2000	63.5 (61.4–65.6)	0.99 (0.94–1.04)
2001	60.3 (58.2–62.4)	0.94 (0.90–0.99)
2002	61.3 (59.3–63.5)	0.96 (0.91–1.00)
2003	60.2 (58.2–62.3)	0.94 (0.90–0.99)
2004	60.6 (58.6–62.8)	0.95 (0.90–0.99)
2005	61.0 (59.0–63.2)	0.95 (0.91–1.00)
2006	59.3 (57.3–61.4)	0.93 (0.88–0.97)
2007	59.6 (57.6–61.7)	0.93 (0.89–0.98)
2008	59.2 (57.1–61.2)	0.92 (0.88–0.97)
2009	59.8 (57.8–61.9)	0.93 (0.89–0.98)
2010	64.8 (62.8–67.0)	1.01 (0.97–1.06)
2011	62.5 (60.5–64.6)	0.97 (0.93–1.02)
2012	63.2 (61.1–65.3)	0.99 (0.94–1.03)
2013	63.3 (61.2–65.4)	0.99 (0.94–1.04)
2014	62.6 (60.6–64.8)	0.98 (0.93–1.03)
2015	65.9 (63.8–68.1)	1.03 (0.98–1.08)
2016	66.4 (64.3–68.5)	1.04 (0.99–1.09)
2017	70.0 (67.9–72.2)	1.09 (1.04–1.15)

DNPR = Danish National Patient Registry.

Table 2. Demographic data on the study population (N = 60,823) registered in the DNPR during 1998–2017. Values are frequency (%) unless otherwise specified

Patient demographics	Year 1998	1999–2004	2005–2010	2011–2016	2017
Patients, total no.	3,262	17,623	17,557	18,870	3,511
Age, median (IQR)	54 (33–73)	55 (33–74)	55 (30–72)	56 (27–71)	57 (27–72)
Female sex	1,800 (55)	9,804 (56)	9,875 (56)	11,012 (58)	2,073 (59)
Charlson co-morbidity index					
Zero (CCI = 0)	2,710 (83)	13,729 (78)	12,784 (73)	13,303 (71)	2,491 (71)
Low (CCI = 1)	169 (5)	1,186 (7)	1,482 (8)	1,788 (10)	355 (10)
Medium (CCI = 2)	229 (7)	1,601 (9)	1,757 (10)	2,056 (11)	368 (11)
High (CCI ≥ 3)	154 (5)	1,107 (6)	1,534 (9)	1,723 (9)	297 (9)
Other diagnoses					
Concomitant near-knee fractures	666 (20)	3,970 (23)	3,763 (21)	3,293 (18)	448 (13)
Concomitant fractures	390 (12)	2,314 (13)	2,355 (13)	2,259 (12)	269 (8)
Lesions inside the knee	303 (9)	1,767 (10)	1,826 (10)	2,034 (11)	315 (9)
Primary knee OA	116 (4)	789 (5)	786 (5)	708 (4)	63 (2)
Osteoporosis	76 (2)	571 (3)	879 (5)	1,128 (6)	102 (3)
Knee fractures, total no.	3,487	20,391	20,257	22,133	4,104
Knee fracture type					
Proximal tibia	1,613 (46)	9,342 (46)	9,643 (48)	11,622 (53)	2,126 (52)
Patella	1,242 (36)	6,913 (34)	6,653 (33)	6,627 (30)	1,254 (31)
Distal femur	632 (18)	4,136 (20)	3,961 (20)	3,884 (18)	724 (18)
Inhabitants at risk [a]	5,220,478				5,722,369

DNPR = Danish National Patient Registry. IQR = interquartile range.
[a] Total number of inhabitants at risk in the specific calendar period.

Patient-Reported Outcomes of 7,133 Distal Femoral, Patellar, and Proximal Tibial Fracture Patients: A National Cross-Sectional Study with 1-, 3-, and 5-Year Follow-Up

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Keywords: Distal femoral fracture; patellar fracture; proximal tibial fracture; Oxford Knee Score; Forgotten Joint Score-12; EQ5D-5L

Abstract

Background
Few studies have described patient-reported outcomes (PROMs) in knee fracture patients. We reported knee-specific and generic median PROM scores after knee fracture and identified risk factors for poor outcome defined by low median PROM scores.

Methods
In a Danish cross-sectional study of 7,133 distal femoral, patellar, and proximal tibial fracture patients during 2011-2017, OKS, FJS-12, EQ5D-5L Index, and EQ5D-5L Visual Analogue Scale (VAS), were collected electronically (response rate 53%; median age 60; 63% female). Poor outcome was defined as score lower than median PROM score. Poor outcome risk factors were estimated as odds ratios from binary logistic regression models.

Results
At 0-1 years after knee fracture, median PROM scores were 31 (OKS), 27 (FJS-12), 0.50 (EQ5D-5L Index), and 74 (EQ5D-5L VAS). At >5 years after knee fracture, median OKS score was 40, median FJS-12 score was 54, median EQ5D-5L Index was 0.76, and median EQ5D-5L VAS score was 80. Age >40 years had higher odds for poor OKS and FJS-12 scores at short- and long-term follow-up after knee fracture. Comorbidity burden, distal femoral fracture, and treatment with external fixation and knee arthroplasty were risk factors for poor outcome at long-term follow-up, for all four PROMs. Treatment with ORIF and reduction only of distal femur fracture vs ORIF and reduction only of patella fracture, and non-surgical treatment of distal femur fracture vs non-surgical treatment of patella fracture, had higher odds for poor PROM scores in all four PROMs at longer follow-up. Non-surgical treatment of patella fracture vs ORIF and reduction only of patella fracture, and non-surgical treatment of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture, had lower odds for poor PROM scores in all four PROMs at longer follow-up. External fixation of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture, had higher odds for poor PROM scores in all four PROMs at >5 years of follow-up.

Conclusions
Although knee fracture patients have relatively high knee function and quality of life, their ability to forget about the knee joint after knee fracture is compromised. We identified several important risk factors for poor outcome measured by PROMs at different follow-up periods following knee fracture, which will help direct future quality-improvement initiatives.

1.1
Introduction

Knee fractures include distal femoral, patellar and proximal tibial fractures. Knee fractures present with complications such as reduced function and decreased quality of life (QOL) measured by patient-reported outcome measures (PROMs) such as the Knee Injury and Osteoarthritis Outcome Score (KOOS) and Functional Status Questionnaire [1][2]. The incidence rate of knee fractures is reported to be about 9 per 100,000 per year in the United States [3], but studies on knee fracture prognosis are lacking. In a study of open distal femoral fractures treated with anatomic lateral locking plates, good to excellent functional outcome, measured by Sanders Score was reported [4]. In a study of surgically treated patella fractures, patients had persisting symptoms, pain and decreased function at long-term follow-up, measured by the Short Form-36 Health Survey and KOOS [5]. In a study of tibial plateau fractures treated with open reduction internal fixation (ORIF), lower function reported by lower KOOS scores was observed at long-term follow-up [1]. In a study of surgically treated tibial plateau fractures, mean Forgotten Joint Score-12 (FJS-12) was 70 at long-term follow-up [6]. Knowledge of the outcomes after knee fracture is limited to distal femoral, tibial plateau and patellar fractures, certain treatment procedures, and small sample studies [4][1][5]. To our knowledge, no studies have examined the broad range of risk factors for poor outcome after knee fracture. Studying risk factors is an important step toward understanding the key drivers of poor outcome and in directing future quality-improvement initiatives. The overall aim of this population-based cross-sectional study was to describe the quality of patient care in knee fracture patients using short-term and long-term PROM outcome scores. The specific aims were 1) to report on knee-specific and generic median PROM scores of knee fracture patients at 0 to >5 years following knee fracture and 2) to identify risk factors for poor outcome defined by low median PROM scores.

2.1
Material and Methods
2.1.1
Settings

The study was approved by the Danish Data Protection Agency, record number REG-085-2017, and reported according to The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines [7]. No institutional review board approval was needed as the study is a registry study.

2.1.2
Data Sources

The study was designed as a national cross-sectional study using Danish Civil Registration System (CRS) and Danish National Patient Registry (DNPR) [8][9]. The Danish Civil Personal Register (CPR) number is given to each individual at birth or immigration, enabling data-linking between different registries [8]. CRS contains information on birth date, sex, residency, and emigration and is updated daily with vital status. DNPR contains information on all public hospital admissions and emergency department visits [9]. Reporting to DNPR is mandatory and is used for public and private hospital reimbursement [9]. In Denmark, private

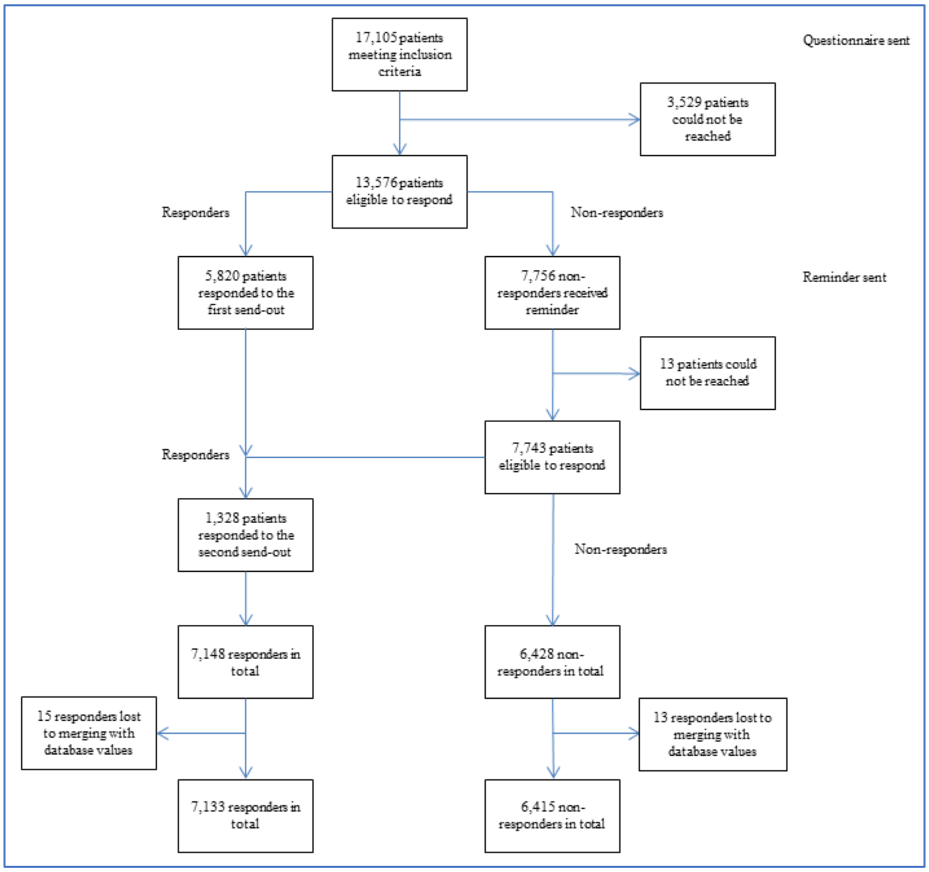


Figure 1. Flowchart of responders and non-responders.

hospitals do not treat patients with knee fracture. DNPR contains information on admission date, CPR number, age, sex, World Health Organization 10th revision of International Classification of Diseases and Health Related Problems (ICD-10) classification, and the Danish version of Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) [10][11].

2.1.3 Study Population and Data Collection

Patients aged 15 years and above were registered in DNPR from January 1st, 2011 to December 31st, 2017, with hospital contacts for distal femur, patella, and proximal tibia fracture ICD-10 codes, with/without subsequent NOMESCO knee surgery codes (See Supplementary Material Appendix 1). Patients had to be registered as alive with a Danish address, not have a name/address made confidential, and not be incapacitated on the date of data pull August 3rd, 2018. The questionnaire was sent out October 26th, 2018 to all patients matching the inclusion criteria via a national e-mail system (E-boks) linked to CPR number (Figure 1).

The e-mail contained a description of the study, statement that participation was voluntary, and link to the online questionnaire including all four PROMs. 3,529 patients were missing because the user could not be found in E-boks/lacking E-boks subscription, yielding 13,576 patients. A reminder was sent out to non-responders on January 2nd, 2019.

2.1.4
Patient-Reported Outcome Measures

The outcomes and prognoses of the study population were described using two knee-specific questionnaires: Oxford Knee Score (OKS), and Forgotten Joint Score-12 Knee (FJS-12), and two generic questionnaires: EuroQol 5-Dimensions Questionnaire-5L (EQ5D-5L) Index, and EQ5D-5L Visual Analogue Scale (VAS) [12][13][14][15][16][17][18][6]. OKS is a 0 to 48 scale with higher values representing higher knee function and less knee pain, and is used in knee osteoarthritis (OA) patients as well as patients treated with total knee arthroplasty (TKA) for OA and posttraumatic OA (PTOA) [13][16]. FJS-12 describes the ability to forget about the knee joint in activities of daily living, which is indicative of greater ability to forget about the joint, i.e. good outcome, ranges from 0 to 100 with higher scores indicating better outcome, and is primarily used for measuring outcomes in TKA patients, although, it has been validated in determining outcomes in patients with PTOA after tibial plateau fracture treated with ORIF and after ACL- reconstruction [17][18][19][20][6][21][22]. FJS-12 has the ability to distinguish between good and excellent outcome, has lower ceiling effects than KOOS, Western Ontario and McMaster Universities osteoarthritis index, and OKS, and high responsiveness, i.e. FJS-12 can describe TKA outcomes more precisely compared to generic or physician-reported PROMs [17][22][18][20]. EQ5D-5L Index validly measures a patient's general health state using five health dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, which are calculated into an index ranging from -0.21 to 1.00, with higher values indicating higher QOL [12][14][15]. EQ5D-5L VAS is a health thermometer ranging from 0 to 100 with higher values indicating higher patient health [12][14]. Because cut-off values for good outcome in OKS, FJS-12, EQ5D-5L Index, and EQ5D-5L VAS scores for knee fracture patients are not established in literature, and because PROM scores were not normally distributed, PROM outcome score was dichotomized as either lower than median PROM score (poor outcome) or higher than median PROM outcome score (good outcome). Follow-up periods were divided into 0-1, 1-3, 3-5, and >5 years after knee fracture based on two criteria: 1) to describe clinically relevant periods after knee fracture for improvement in outcome, and 2) to have a sufficient number of patients in each follow-up group to be able to draw precise estimates.

2.1.5
Risk Factors

The following variables were included as potential risk factors based on clinical relevance and sparsely documented previous literature on the subject: age (<40 years (reference group), 40-60 years, and >60 years), sex (male sex as reference group), knee fracture type (patella fracture (reference group), distal femur fracture, and proximal tibia fracture), and treatment type (ORIF and reduction only (reference group), non-surgical treatment, external fixation, and knee arthroplasty). The updated version of Charlson Comorbidity Index (CCI) was used to evaluate comorbidity in responders and non-responders using CCI comorbidities registered on or prior to the date of knee fracture registration [23][24]. Patients were categorized into four comorbidity levels: CCI 0 (reference group), 1, 2, and ≥3.

2.1.6 Statistics

Proportions, median, and interquartile range (IQR) were used to describe responders and non-responders, while median and IQR were used to present PROM scores. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using binary logistic regression models to examine risk factors for poor PROM outcome. Risk factors were examined for each PROM and all follow-up periods, with separate models fitted for each combination of these. Each individual model included all risk factors as independent co-variables. No model reduction was evaluated as all included variables were of interest. Because of this, ORs were mutually adjusted for all risk factors. However, fracture type included a multiple fracture level in the models, but estimates for this level were not reported in the results as interpretations of combinations of multiple knee fractures versus single knee fractures would be difficult and provide estimates with high uncertainty. The fit of the logistic regression models was assessed by Hosmer-Lemeshow goodness of fit test. Additionally, subanalysis of each knee fracture type within specific treatments and vice versa: each treatment type within specific knee fracture types, were also modelled as the logistic regression described above. All analyses were performed using the statistical software R 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1 Study Population

There were 7,133 (53%) responders and 6,415 (47%) non-responders available for analysis. Responders (median age 60 years; 63% female) were 11 years older, had a higher proportion of females, and had to a lesser degree received non-surgical treatment compared to non-responders (Table 1). Responders and non-responders were similar with respect to distribution of CCI, follow-up period, knee fracture type, and treatment type. Minimum and maximum follow-up time after knee fracture was 0.8 and 15.1 years (only 32 patients had >8 years follow-up).

3.2 Knee-Specific and Generic Median PROM Scores of Knee Fracture Patients

Median PROM scores for the study population, irrespective of follow-up period after knee fracture, were 38 (OKS), 46 (FJS-12), 0.72 (EQ5D-5L Index), and 80 (EQ5D-5L VAS) (Table 2). Median PROM scores were higher at longer follow-up periods for all four PROMs, and for each PROM, median PROM scores were similar between 3-5 years and >5 years after knee fracture. At no point in time did the PROM scores reach maximum values, not even when observing the IQR values. At 0-1 years after knee fracture, median PROM scores were 31 (IQR: 23-41) for OKS, 27 (IQR: 10-58) for FJS-12, 0.50 (IQR: -0.07-0.79) for EQ5D-5L Index, and 74 (IQR: 51-85) for EQ5D-5L VAS (Table 2). At 3-5 years after knee fracture, median OKS score was 39 (IQR: 30-45), median FJS-12 score was 49 (IQR: 20-85), median score for EQ5D-5L Index was 0.72 (IQR: 0.27-0.84), and median EQ5D-5L VAS score was 80 (IQR: 60-90).

Table 1. Characteristics of Knee Fracture Patients Divided into Responders and Non-Responders

Patient Demographics	Responders	Non-Responders
Number (%)	7133 (52.6 %)	6415 (47.4 %)
Age Median (IQR)	60.1 (45.2-69.7)	49.6 (27.3-66.4)
Female Sex No. (%)	4460 (62.5 %)	3071 (47.9 %)
CCI No. (%)		
Index Zero, CCI=0	5628 (78.9 %)	4950 (77.2 %)
Index Low, CCI=1	630 (8.8 %)	590 (9.2 %)
Index Medium, CCI=2	576 (8.1 %)	566 (8.8 %)
Index High, CCI ≥3	299 (4.2 %)	309 (4.8 %)
Follow-Up Period No. (%)		
0-1 Years	246 (3.4 %)	174 (2.7 %)
1-3 Years	2412 (33.8 %)	1962 (30.6 %)
3-5 Years	2070 (29.0 %)	1771 (27.6 %)
>5 Years	2405 (33.7 %)	2508 (39.1 %)
Knee Fracture Type No. (%)		
Distal Femur	571 (8.2 %)	707 (11.3 %)
Patella	2424 (34.8 %)	2243 (35.8 %)
Proximal Tibia	3965 (57.0 %)	3308 (52.9 %)
Multiple Knee Fractures	173 (2.4 %)	157 (2.4 %)
Treatment Type No. (%)		
Non-Surgical Treatment	4274 (59.9 %)	4683 (73.0 %)
ORIF and Reduction Only	2621 (36.7 %)	1549 (24.1 %)
External Fixation	152 (2.1 %)	107 (1.7 %)
Knee Arthroplasty	86 (1.2 %)	76 (1.2 %)

Table 2. Median Patient-Reported Outcome Measure (PROM) Scores with Interquartile Range (IQR)

PROM (Possible Minimum - Maximum Value)	Median PROM Scores (IQR) by Years after Knee Fracture				Median PROM Scores (IQR) for Total Study Population
	0-1 years	1-3 years	3-5 years	>5 years	0 - >5 years
Number of Patients in Each Follow-Up Group	246 patients	2412 patients	2070 patients	2405 patients	7133 patients
OKS (0-48)	31 (23-41)	37 (27-44)	39 (30-45)	40 (32-45)	38 (29-45)
FJS-12 (0-100)	27 (10-58)	40 (16-75)	49 (20-85)	54 (25-85)	46 (19-81)
EQ5D-5L Index (-0.21-1.00)	0.50 (-0.07 - 0.79)	0.68 (0.20-0.82)	0.72 (0.27-0.84)	0.76 (0.32-0.82)	0.72 (0.26-0.82)
EQ5D-5L VAS (0-100)	74 (51-85)	77 (56-90)	80 (60-90)	80 (61-90)	80 (60-90)

IQR = interquartile range. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

3.3 Risk Factors for Poor Outcome Defined by Low Median PROM Scores

3.3.1 OKS

At 0-1 year of follow-up, patients aged 40-60 years had higher odds of having poor OKS scores (OR 2.9; CI: 1.1-7.7), while patients aged >60 years also had high odds but wider CIs (OR 2.0; CI: 0.7-5.2), compared to younger patients (<40 years of age) (Table 3). Female patients had similar odds of reporting poor OKS scores as male patients during 0-1 year of follow-up (OR 1.0; CI: 0.5-1.9) (Table 3). Comorbidity did not have increased odds of reporting poor OKS at 0-1 year of follow-up (Table 3). At 0-1 years of follow-up, OR estimates of poor OKS score for patients with distal femoral and proximal tibial fractures were reported with high uncertainty, i.e. wide CIs (Table 3).

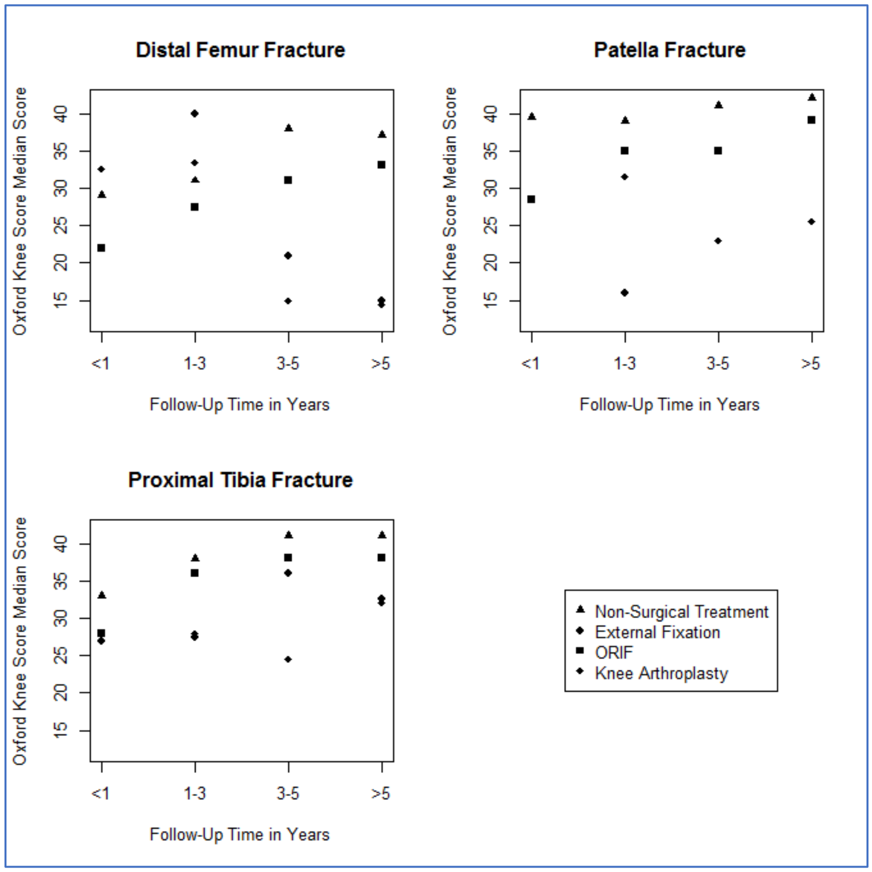
Table 3. Risk Factors for Poor Outcome Measured with Oxford Knee Score

Patient Demographics	Oxford Knee Score Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	2.9 (1.1-7.7)	1.7 (1.3-2.2)	1.7 (1.3-2.3)	1.4 (1.1-1.8)
Age >60 Years Versus Age <40 Years	2.0 (0.7-5.2)	1.3 (1.0-1.6)	1.3 (1.0-1.6)	1.2 (1.0-1.6)
Female Versus Male Sex	1.0 (0.5-1.9)	1.1 (0.9-1.3)	1.4 (1.1-1.7)	1.3 (1.1-1.6)
CCI=1 Versus 0	1.5 (0.6-3.8)	1.4 (1.1-2.0)	1.5 (1.1-2.0)	1.9 (1.4-2.6)
CCI=2 Versus 0	1.2 (0.4-3.5)	1.3 (1.0-1.8)	1.5 (1.0-2.0)	1.1 (0.8-1.5)
CCI≥3 Versus 0	1.0 (0.3-3.3)	1.8 (1.2-2.6)	1.2 (0.7-2.0)	3.1 (1.8-5.2)
Distal Femur Versus Patella Fracture*	3.1 (0.8-12.3)	2.8 (2.0-3.9)	2.1 (1.4-3.1)	2.4 (1.7-3.4)
Proximal Tibia Versus Patella Fracture*	1.9 (1.0-3.6)	1.1 (0.9-1.4)	1.0 (0.8-1.2)	1.3 (1.1-1.5)
Non-Surgical Treatment Versus ORIF and Reduction Only	0.2 (0.1-0.4)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.7 (0.6-0.8)
External Fixation Versus ORIF and Reduction Only	0.4 (0.1-2.6)	1.3 (0.6-2.5)	1.4 (0.8-2.6)	2.6 (1.4-4.8)
Knee Arthroplasty Versus ORIF and Reduction Only	0.1 (0.0-2.1)	0.7 (0.3-1.6)	8.0 (1.9-34.1)	2.5 (1.0-6.1)

Poor outcome = Oxford Knee Score in each group below median Oxford Knee Score value of 38 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

Non-surgical treatment versus ORIF and reduction only for knee fracture had lower odds of poor OKS score at 0-1 years of follow-up (Table 3, Figure 2). When looking at patients with 3-5 years of follow-up and at >5 years of follow-up, we found that patients ages 40-60 years had higher odds of reporting poor OKS scores, compared to patients ages <40 years (Table 3). However, we found that different risk factors played a role in relation to poor OKS score at 3-5 years and >5 years compared with patients with 0-1 year of follow-up (Table 3). At 3-5, and >5 years of follow-up, female patients were at increased odds of reporting poor OKS score compared with male patients, and patients with comorbidity burden were also at increased odds of reporting poor OKS scores compared with patients with CCI 0 (OR 3.1; CI: 1.8-5.2 at >5 years of follow-up for patients with CCI ≥3) (Table 3). At >5 years of follow-up, patients with distal femoral or proximal tibial fracture were at increased odds of poor OKS scores compared to patients with patella fracture (Table 3, Figure 3). Non-surgically treated patients consistently had lower odds of reporting poor OKS scores during all follow-up periods (Table 3, Figure 2). Patients treated with external fixation or knee arthroplasty had higher odds of reporting poor OKS at longer follow-up compared to patients treated with ORIF and reduction only (OR 2.6; CI: 1.4-4.8 for patients treated with external fixation at >5 years of follow-up and OR 8.0; CI: 1.9-34.1 for patients treated with knee arthroplasty at 3-5 years of follow-up) (Table 3, Figure 2).

Figure 2. Median Oxford Knee Score according to knee fracture type and treatment type.



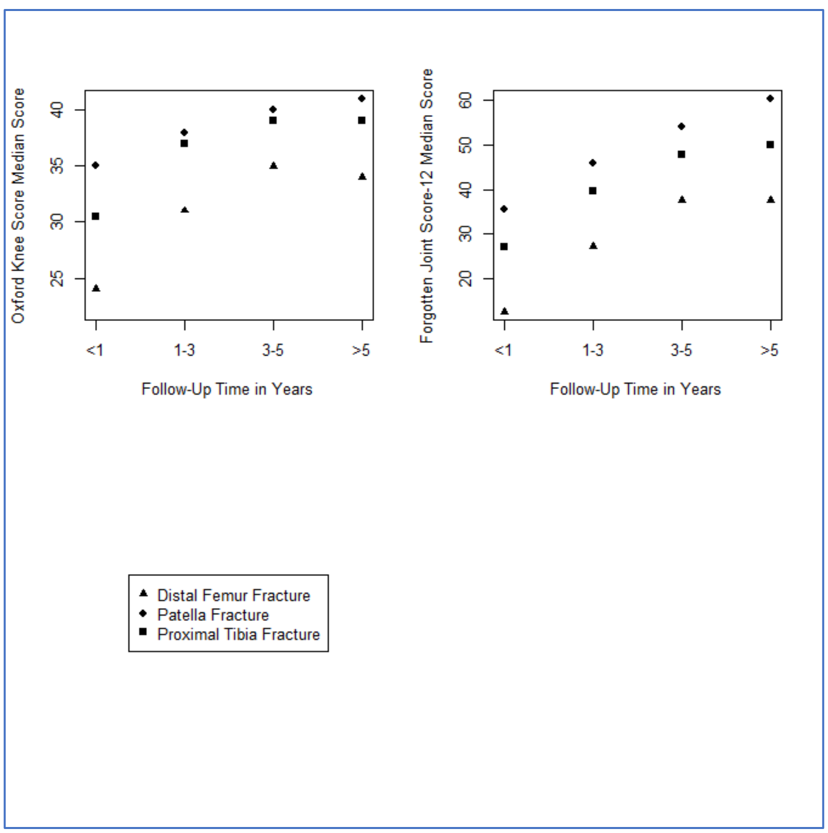


Figure 3. Median Oxford Knee Score and Forgotten Joint Score-12 according to knee fracture type.

3.3.2 FJS-12

At 0-1 year after knee fracture, patients ages 40-60 years had relatively high odds of having poor FJS-12 scores, and estimates were more certain at longer follow-up where patients ages 40-60 years were at increased odds of reporting poor FJS-12 scores compared with patients ages <40 years (Table 4). Female sex had increased odds of poor FJS-12 score at follow-up periods over 1 year after knee fracture (Table 4). The results for comorbidity as a risk factor were less clear at short-term follow-up, but comorbidity was a risk factor for poor FJS-12 score at longer follow-up, i.e. at >5 years of follow-up for patients with CCI 1 (OR 1.5; CI:1.1-2.0), and relatively high odds were seen for poor FJS-12 score for patients with CCI ≥3 at >5 years of follow-up (OR 1.7; CI: 1.0-2.7) (Table 4). Patients with distal femoral fractures had higher odds of poor FJS-12 score at 1-3 years (OR 2.1; CI:1.5-2.9), and >5 years (OR 1.9; CI: 1.4-2.7) of follow-up, while patients with proximal tibial fractures had high odds of poor FJS-12 scores at 0-1 years (OR 2.1; CI: 1.1-3.9), and >5 years (OR 1.3; CI: 1.1-1.5) of follow-up (Table 4, Figure 3).

Table 4. Risk Factors for Poor Outcome Measured by Forgotten Joint Score-12

Patient Demographics	Forgotten Joint Score-12 Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	2.9 (1.0-8.2)	1.9 (1.5-2.5)	2.0 (1.6-2.6)	1.7 (1.3-2.2)
Age >60 Years Versus Age <40 Years	1.9 (0.7-5.4)	1.2 (1.0-1.6)	1.3 (1.0-1.7)	1.2 (1.0-1.5)
Female Versus Male Sex	1.4 (0.7-2.7)	1.3 (1.1-1.5)	1.5 (1.2-1.8)	1.4 (1.2-1.7)
CCI=1 Versus 0	1.4 (0.5-3.5)	1.2 (0.9-1.6)	1.3 (1.0-1.8)	1.5 (1.1-2.0)
CCI=2 Versus 0	0.6 (0.2-1.8)	1.2 (0.9-1.7)	1.3 (0.9-1.8)	1.1 (0.8-1.6)
CCI≥3 Versus 0	0.5 (0.1-1.8)	1.4 (0.9-2.0)	1.2 (0.7-2.0)	1.7 (1.0-2.7)
Distal Femur Versus Patella Fracture*	1.8 (0.5-6.6)	2.1 (1.5-2.9)	1.5 (1.0-2.2)	1.9 (1.4-2.7)
Proximal Tibia Versus Patella Fracture*	2.1 (1.1-3.9)	1.1 (0.9-1.4)	0.9 (0.8-1.1)	1.3 (1.1-1.5)
Non-Surgical Treatment Versus ORIF and Reduction	0.1 (0.1-0.3)	0.6 (0.5-0.7)	0.5 (0.4-0.6)	0.6 (0.5-0.8)
External Fixation Versus ORIF and Reduction	-	1.5 (0.7-3.1)	1.4 (0.7-2.5)	1.9 (1.1-3.4)
Knee Arthroplasty Versus ORIF and Reduction	-	1.1 (0.5-2.7)	7.8 (1.8-33.5)	4.3 (1.6-11.4)

Poor outcome = Forgotten Joint Score-12 score in each group below median Forgotten Joint Score-12 value of 46 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included. - Number of observations not enough for calculating OR estimates. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

Non-surgically treated patients had lower odds of reporting poor FJS-12 scores during all follow-up periods (Table 4, Figure 4). Treatment with external fixation or knee arthroplasty had high odds of reporting poor FJS-12 score at longer follow-up periods (Table 4, Figure 4).

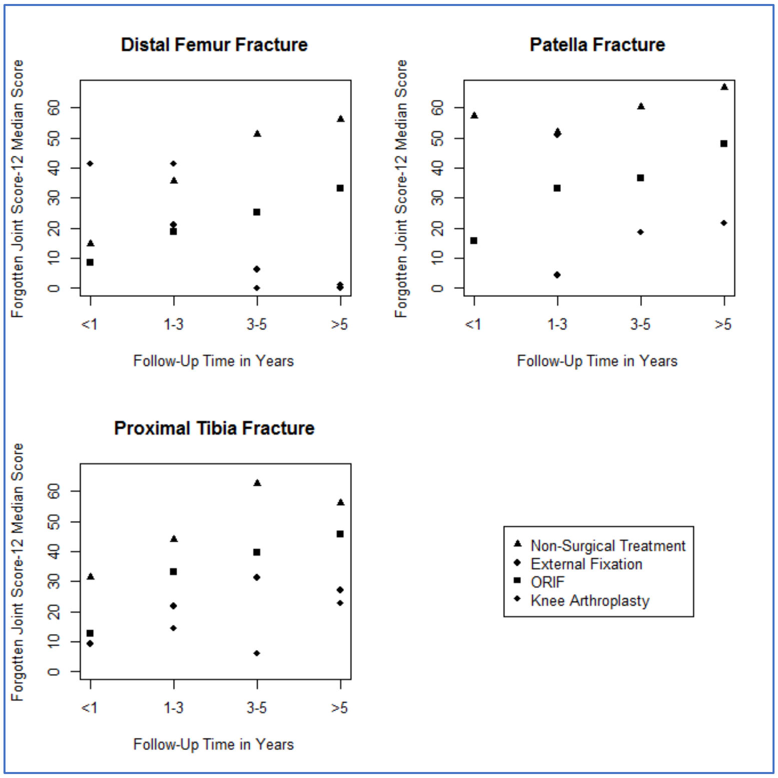


Figure 4. Median Forgotten Joint Score-12 according to knee fracture type and treatment type.

3.3.3 EQ5D-5L Index

Patients aged 40-60 years had increased odds of reporting poor EQ5D-5L Index score at 1-3 years of follow-up (OR 1.6; CI:1.3-2.1) and produced less certain estimates at longer follow-up periods while female sex did not have high odds for poor EQ5D-5L Index score, making trends less clear on age and sex being risk factors in poor EQ5D-5L Index outcome (Table 5). Comorbidity burden had higher odds for poor EQ5D-5L Index score at longer follow-up (Table 5).

Table 5. Risk Factors for Poor Outcome Measured by EQ5D-5L Index

Patient Demographics	EQ5D-5L Index Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	1.0 (0.4-2.7)	1.6 (1.3-2.1)	1.3 (1.0-1.7)	1.2 (1.0-1.5)
Age >60 Years Versus Age <40 Years	0.6 (0.2-1.7)	1.0 (0.8-1.2)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Female Versus Male Sex	1.2 (0.6-2.2)	1.1 (0.9-1.3)	1.2 (1.0-1.4)	1.1 (0.9-1.3)
CCI=1 Versus 0	1.7 (0.7-4.1)	1.3 (0.9-1.7)	1.5 (1.1-2.1)	2.0 (1.5-2.7)
CCI=2 Versus 0	0.8 (0.3-2.2)	1.5 (1.1-2.0)	1.6 (1.2-2.3)	1.1 (0.8-1.6)
CCI≥3 Versus 0	2.1 (0.6-7.5)	1.5 (1.0-2.2)	1.9 (1.2-3.2)	2.7 (1.6-4.4)
Distal Femur Versus Patella Fracture*	3.2 (0.8-12.2)	2.8 (2.0-3.9)	2.1 (1.5-3.1)	2.4 (1.7-3.4)
Proximal Tibia Versus Patella Fracture*	1.4 (0.8-2.6)	1.1 (0.9-1.4)	1.1 (0.9-1.3)	1.3 (1.1-1.6)
Non-Surgical Treatment Versus ORIF and Reduction	0.3 (0.1-0.5)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.7 (0.6-0.9)
External Fixation Versus ORIF and Reduction	0.5 (0.1-2.8)	1.8 (0.8-3.9)	1.2 (0.7-2.3)	2.7 (1.5-5.1)
Knee Arthroplasty Versus ORIF and Reduction	-	0.9 (0.4-2.0)	8.1 (1.9-34.7)	2.6 (1.1-6.2)

Poor outcome = EQ5D-5L Index score in each group below median EQ5D-5L Index value of 0.7 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included. - Number of observations not enough for calculating OR estimates. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

Patients with either distal femoral or proximal tibia fracture had increased odds of poor EQ5D-5L Index scores compared with patients with patella fracture at longer follow-up periods (Table 5, Figure 5). Non-surgically treated patients had lower ORs for poor EQ5D-5L Index score irrespective of follow-up period after knee fracture (Table 5, Figure 6). Treatment with external fixation or knee arthroplasty versus ORIF and reduction only had high ORs for poor EQ5D-5L Index score at longer follow-up periods following knee fracture (Table 5, Figure 6).

3.3.4
EQ5D-5L VAS

Patients aged 40-60 years had high ORs for poor EQ5D-5L VAS scores at 1-3, and 3-5 years after knee fracture but not at 0-1 year of follow-up and not at longer follow-up (>5 years), while female sex had high ORs for poor outcome in EQ5D-5L VAS at 3-5 years following knee fracture, making trends less clear on age and sex being risk factors in poor EQ5D-5L VAS outcome (Table 6).

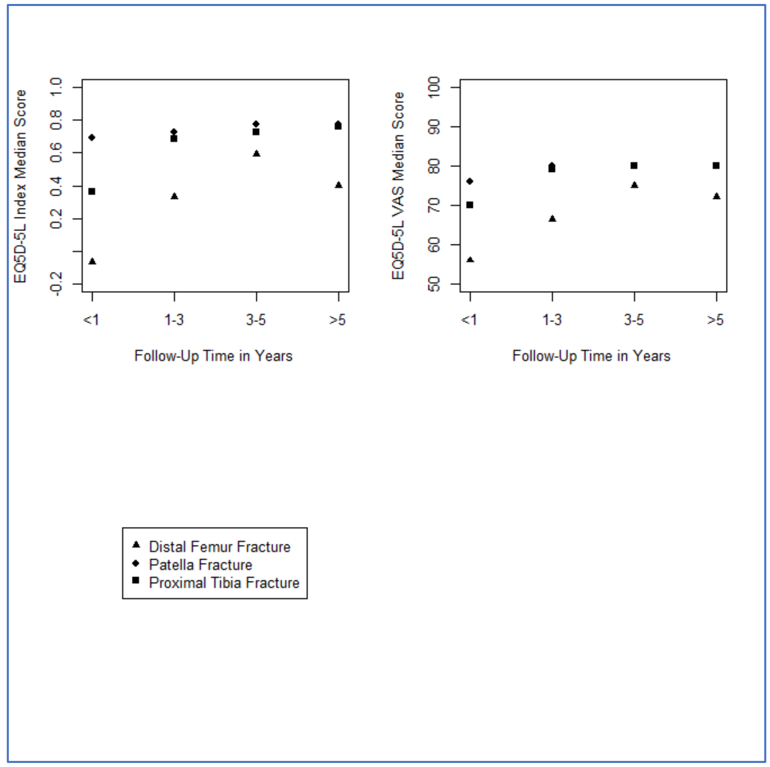


Figure 5. Median EQ5D-5L Index and EQ5D-5L VAS score according to knee fracture type.

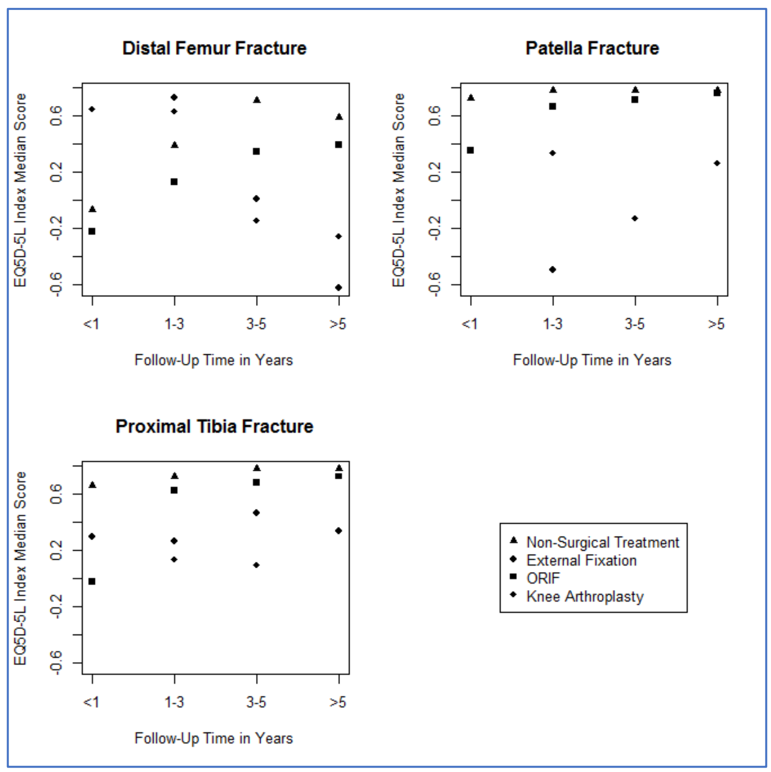


Figure 6. Median EQ5D-5L Index score according to knee fracture type and treatment type.

Table 6. Risk Factors for Poor Outcome Measured by EQ5D-5L VAS

Patient Demographics	EQ5D-5L VAS Odds Ratios with (95 % Confidence Intervals) Years after Knee Fracture			
	0-1 years	1-3 years	3-5 years	>5 years
Number of Patients in Each Follow-Up Group	246	2412	2070	2405
Ages 40-60 Years Versus Age<40 Years	0.5 (0.2-1.4)	1.5 (1.2-1.9)	1.5 (1.2-1.9)	1.2 (1.0-1.5)
Age >60 Years Versus Age <40 Years	0.5 (0.2-1.4)	1.2 (0.9-1.5)	1.2 (1.0-1.6)	1.1 (0.9-1.4)
Female Versus Male Sex	1.5 (0.8-2.8)	1.0 (0.8-1.2)	1.3 (1.1-1.6)	1.1 (0.9-1.3)
CCI=1 Versus 0	1.6 (0.6-3.8)	1.7 (1.3-2.3)	1.6 (1.2-2.2)	1.8 (1.3-2.5)
CCI=2 Versus 0	1.0 (0.4-3.0)	1.6 (1.2-2.2)	1.6 (1.1-2.3)	1.3 (0.9-1.8)
CCI≥3 Versus 0	1.4 (0.4-5.0)	2.7 (1.8-4.2)	2.1 (1.2-3.6)	3.4 (1.9-6.1)
Distal Femur Versus Patella Fracture*	1.6 (0.5-5.4)	1.8 (1.3-2.5)	1.5 (1.1-2.3)	1.7 (1.2-2.5)
Proximal Tibia Versus Patella Fracture*	1.0 (0.5-1.8)	1.0 (0.9-1.2)	0.9 (0.7-1.1)	1.1 (0.9-1.3)
Non-Surgical Treatment Versus ORIF and Reduction	0.5 (0.3-0.9)	0.8 (0.7-0.9)	0.7 (0.6-0.8)	0.9 (0.7-1.0)
External Fixation Versus ORIF and Reduction	2.1 (0.2-19.4)	1.5 (0.7-3.1)	1.0 (0.5-1.7)	3.4 (1.7-6.7)
Knee Arthroplasty Versus ORIF and Reduction	-	1.6 (0.6-4.0)	1.8 (0.7-4.6)	5.7 (1.7-19.1)

Poor outcome = EQ5D-5L VAS score in each group below median EQ5D-5L VAS value of 80 for the entire study population. *ORs based on single knee fractures only, multiple knee fractures not included. - Number of observations not enough for calculating OR estimates. CCI = Charlson Comorbidity Index. ORIF = open reduction internal fixation.

Patients with more comorbidities had higher OR of poor EQ5D-5L VAS score at longer follow-up, but not during the 0-1 year of follow-up (Table 6). Patients with distal femoral fractures had high odds of poor EQ5D-5L VAS outcome during longer follow-up periods (Table 6, Figure 5). During all follow-up periods, non-surgically treated patients vs those treated with ORIF and reduction only had low ORs for poor EQ5D-5L VAS outcome (Table 6, Figure 7). Treatment with external fixation or knee arthroplasty had a high OR at longer follow-up for poor EQ5D-5L VAS outcome (Table 6, Figure 7).

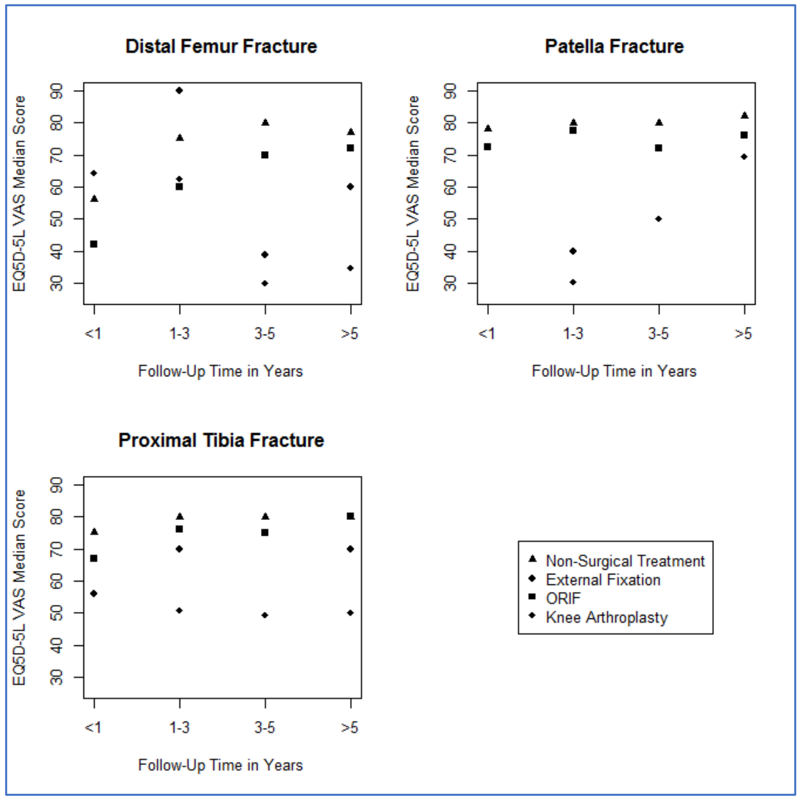


Figure 7. Median EQ5D-5L VAS score according to knee fracture type and treatment type.

3.3.5 Knee Fracture Type and Treatment Type Subanalysis

Treatment with ORIF and reduction only of distal femur fracture vs ORIF and reduction only of patella fracture had higher odds for poor PROM scores at 1-3 years (all PROMs), 3-5 years (OKS and EQ5D-5L Index), and >5 years (OKS, FJS-12, and EQ5D-5L Index), all ORs were between 1.7-

3.1. Non-surgical treatment of distal femur fracture vs non-surgical treatment of patella fracture had higher odds for poor PROM scores at 1-3, 3-5, and >5 years (OKS and EQ5D-5L Index) and at 1-3, and >5 years (FJS-12 and EQ5D-5L VAS), ORs were between 1.6-2.8. Non-surgical treatment of patella fracture vs ORIF and reduction only of patella fracture had lower odds for poor PROM scores at 3-5 and >5 years of follow-up for all four PROMs, ORs were between 0.4-0.7. Non-surgical treatment of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture had lower odds for poor PROM scores at 1-3, 3-5, and >5 years (OKS, FJS-12, and EQ5D-5L Index), and at 3-5 years (EQ5D-5L VAS), all ORs were between 0.5-0.7. External fixation of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture had higher odds for poor PROM scores in all four PROMs at >5 years of follow-up, with ORs between 1.9-3.3.

4. Discussion

4.1 Summary

The general trends in our study point to PROM scores being similar at 3-5 years and >5 years of follow-up within each PROM. We identified several risk factors of poor PROM scores, depending on the PROM and follow-up studied, of which some were risk factors at short-term follow-up, while others were risk factors at long-term follow-up. Patients aged >40 years had high ORs for poor OKS and FJS-12 scores at both short-term and long-term follow up, although this was not seen for EQ5D-5L Index or EQ5D-5L VAS scores irrespective of follow-up. Female sex had slightly higher odds for poor OKS and FJS-12 scores at longer follow-up, but this was not seen for EQ5D-5L Index or EQ5D-5L VAS scores. Comorbidity burden, distal femoral fracture, treatment with external fixation, and treatment with knee arthroplasty were risk factors for poor outcome during long-term follow-up, but not during short-term follow-up after knee fracture, for all four PROMs. Treatment with ORIF and reduction only of distal femur fracture vs ORIF and reduction only of patella fracture, and non-surgical treatment of distal femur fracture vs non-surgical treatment of patella fracture had higher odds for poor PROM scores in all four PROMs at longer follow-up. Non-surgical treatment of patella fracture vs ORIF and reduction only of patella fracture, and non-surgical treatment of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture had lower odds for poor PROM scores in all four PROMs at longer follow-up. External fixation of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture had higher odds for poor PROM scores in all four PROMs at >5 years of follow-up.

4.2 Study Limitations

In this study, there was no access to medical records, therefore the correct sequence of events was unknown (i.e. if external fixation was subsequently converted to ORIF), and data on fracture severity/knee fracture subclassifications of each knee fracture type, and laterality, were insufficiently registered in DNPR, thus affecting the presented results in terms of OR estimates for external fixations and ORIF and reduction only, not presenting ORs according to knee fracture subtype, and also possibly leading to bias of presented median PROM scores and ORs because the laterality of knee fracture was unknown. Another study limitation was the 47% non-responder rate, and non-responders were younger and had a lower proportion of females, consequently younger patients and males might not present with the PROMs/ORs observed. To reduce potential bias for the ORs, age and sex variables were included in the binary logistic regression models. The study might have experienced selection bias in terms of whom decided to respond to the questionnaire. Perhaps more responders whom were satisfied with their treatment decided to respond because they wanted to share their positive experiences, or perhaps more patients with unsatisfactory outcomes after their knee fracture treatment were prone to respond because they felt obligated to give their feedback back to research. There were more non-responders receiving non-surgical treatment for knee fracture, perhaps some non-responders whom were treated non-surgically thought that they did not have to participate because they believed non-surgical treatment did not qualify a response. Remaining covariates were similar between responders and non-responders, likely limiting potential non-responder bias. CCI does not include comorbidities such as osteopenia, osteoporosis, OA, muscle disease, and other progressive disease, which can impact knee function, pain, and general health/QOL, making these potential confounders in our study. Responders with multiple knee fractures only comprised 2% (Table 1), and because of difficulty in comparing multiple knee fracture patients to patients with other types of multiple knee fractures and comparing all possible multiple knee fracture patient groups to patients with single knee fractures, patients with multiple knee fractures were omitted from the study. The development of PROM scores over time could not be sufficiently evaluated because of lack of pre-treatment PROMs. PROMs only measure outcomes from a patient perspective which might not always represent the actual function of the knee joint [25][26][27]. However, the strength of PROMs, including their importance in measuring outcomes from a patient perspective, i.e. when evaluating subjective measures of outcome, should not be undervalued [12][13][15][16][17][18][6][28]. People of different nationalities, cultures, and with/without chronic disease, might interpret knee variable questions and general health states differently, which might bias the presented results [29][15]. The study might have experienced response shift bias, when surgically treated patients' responses are affected by the success or failure of the surgery [30]. Because cut-off PROM values for knee fracture patients are not established in literature, and because PROM scores were not normally distributed, binary outcome median PROM scores were used to represent poor/good outcome. However, we do not know if a PROM score under the median is in fact clinically representative of a poor outcome seen from the patient's point of view, therefore the actual poor/good PROM outcome scores presented in this study have yet to be verified in future knee fracture studies.

Nevertheless, this study has several strengths. By sending the questionnaire electronically, a large patient group was quickly reached countrywide, eliminating data loss in the postal system and avoiding misreading responses in the transfer of written responses to electronic databases. Studies have also shown that patients prefer electronic questionnaires over paper ones [31]. We used DNPR which is known for high data quality and with the highest positive predictive value being found in Orthopaedic diagnoses [9]. The study is a national, cross-sectional study with a large patient sample from a relatively homogenous population with patients in different stages of follow-up after knee fracture (0-1, 1-3, 3-5, and >5 years, with a maximum of 15.1 years of follow-up)) using validated knee-specific and generic PROMs, providing a description of the outcomes on knee function, knee pain, ability to forget about the knee joint, and general health/QOL in surgically treated and non-surgically treated distal femoral, patellar and proximal tibial fracture patients.

4.3 Knee-Specific and Generic Median PROM Scores of Knee Fracture Patients

Knee fracture patients have relatively high knee function and low pain (OKS) and high general health/QOL (EQ5D-5L Index and EQ5D-5L VAS), while their ability to forget about the knee joint after knee fracture is compromised (FJS-12). The difference between the relatively high median OKS, EQ5D-5L Index, and EQ5D-5L VAS, and low median FJS-12 scores could be explained by the fact that FJS-12 measures a different aspect of knee function – the ability to forget about one's knee joint in daily life, which appears to be compromised in knee fracture patients. Patients with distal femoral fractures had lower outcome scores in all four PROMs (Figures 3 and 5). However, they comprised 8% of responders and will therefore have a larger uncertainty for their PROM score estimates compared to the other knee fracture types (Table 1).

In a study of surgically treated tibial plateau fracture patients, mean FJS-12 score was 70 with median 13-year follow-up [6]. In an ACL-reconstruction study, mean FJS-12 score was 72 (minimum 1-year follow-up) and 70 (minimum 10-year follow-up) [21]. In a study of pre- and 1-year post-operative FJS-12 scores of tricompartmental knee OA patients treated with TKA and hip OA patients treated with total hip arthroplasty (THA), pre-operative and 1-year post-operative FJS-12 scores were 24 and 70 (TKA patients) and 22 and 80 (THA patients) [19]. In our study, median FJS-12 score was 50 for proximal tibia fracture after 5 years (Figure 3), median FJS-12 score was 46 in knee fracture patients for the entire study period, and median scores were between 27-54 at 0 to >5 years follow-up (Table 2). As evidenced above, there is a lack in literature describing patient-reported outcomes of knee fracture patients. Furthermore, when comparing FJS-12 scores of knee fracture patients to tibial plateau fracture patients, ACL-reconstruction surgery patients, and knee and hip OA patients, knee fracture patients report lower FJS-12 scores. This in turn demonstrates a need for improving current treatment directives to advance knee fracture patient care.

4.4 Risk Factors for Poor Outcome Defined by Low Median PROM Scores

Patients aged >40 years had higher odds of poor outcome in OKS and FJS-12 scores at both short- and long-term follow-up, while comorbidity, distal femoral fracture, treatment with external fixation, and treatment with knee arthroplasty had higher ORs for poor outcome score in all four

PROMs at long-term follow-up. In a TKA study, younger age and female sex were associated with lower FJS-12 scores [32]. This study as well as other studies, argue that older patients score higher because they likely have lower activity levels, lower performance demand for the knee joint, and other comorbidities that might affect their outcome more than their knee-joint issues [17][32][19]. In our study, female sex and increasing age (patients aged >40 years) had high ORs for poor PROM outcomes. A potential explanation for the differing results between the studies could be that knee fracture patients present with other demands than TKA patients.

Treatment with ORIF and reduction only of distal femur fracture vs ORIF and reduction only of patella fracture, and non-surgical treatment of distal femur fracture vs non-surgical treatment of patella fracture had higher odds for poor PROM scores in all four PROMs at longer follow-up. Non-surgical treatment of patella fracture vs ORIF and reduction only of patella fracture, and non-surgical treatment of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture had lower odds for poor PROM scores in all four PROMs at longer follow-up. External fixation of proximal tibia fracture vs ORIF and reduction only of proximal tibia fracture had higher odds for poor PROM scores in all four PROMs at >5 years of follow-up. Distal femur fracture was a risk factor for poor PROM outcome at long-term follow-up in our study. Even distal femur fracture treated with ORIF and reduction only, and non-surgically treated distal femur fracture also had higher odds for poor PROM scores in all four PROMs at long-term follow-up, which is in accordance with current literature regarding the known challenges and complexities of distal femoral fractures [33].

Non-surgical treatment of knee fracture had lower odds for poor PROM scores in all follow-up periods in our study. When comparing non-surgically treated patella fractures and proximal tibia fractures to ORIF and reduction only treated patella fractures and proximal tibia fractures, the odds for poor PROM scores were also lower at long-term follow-up. Choice of treatment type is governed by knee fracture complexity and comminution, surgeon preference, and patient-related factors i.e. compliance, osteopenia, osteoporosis, OA, muscle disease, and other progressive disease [34][35][36]. Patients with complex knee fractures and comorbidities not included in the CCI, might have a harder time scoring above the PROM median score, potentially explaining the high ORs for poor outcome after external fixation and knee arthroplasty, compared to non-surgical treatment for likely, less complex fractures. However, since only 1% and 2% of responders received knee arthroplasty and external fixation, our results should be interpreted with caution (Table 1). Nevertheless, our results regarding external fixation of proximal tibia fracture having higher odds for poor PROM scores at >5 years of follow-up when compared to ORIF and reduction only of proximal tibia fracture, also support the notion of external fixation being a risk factor for poor PROM scores. Literature comparing functional outcomes and QOL of patients treated with TKA for PTOA with patients treated with TKA for OA has reported mixed results: PTOA patients have been shown to both have poorer outcomes than OA patients, as well as similar outcomes to OA patients [37][38][39][40][41][42][34][43]. Some studies argue that because PTOA patients have lower pre-operative PROM scores to begin with, they consequently report lower post-operative scores than OA patients

[41][43]. Knee fracture patients treated with TKA is a complex patient group as evidenced by current literature and the exceptionally high ORs for poor outcome in knee arthroplasty knee fracture patients presented in our study.

5. Conclusions

Knee fracture patients have relatively high knee function, low pain and high general health/QOL (OKS, EQ5D-5L Index, and EQ5D-5L VAS), while their ability to forget about the knee joint after knee fracture remains compromised (FJS-12). Due to the cross-sectional nature of this study, causality cannot be inferred because a temporal sequence between risk factors and outcomes cannot be established. We have nevertheless identified several important risk factors for poor PROM scores, which are dependent on the PROM as well as on the follow-up period studied. These findings may help guide future clinical work in order to improve the quality of knee fracture management and diminish the differences in quality of care to ensure high quality of care for all patient groups regardless of their associated patient-, fracture-, and treatment-related factors. This study has important implications for future studies in which health care providers will be able to inform patients on varying aspects of expected outcome after knee fracture, including the presented risk factors which modulate their outcome.

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Supplementary Material

Appendix 1

ICD-10 diagnosis codes and NOMESCO surgery codes

ICD-10 diagnosis codes

Proximal tibia fracture: DS821.

Patella fracture: DS820.

Distal femur fracture: DS724.

NOMESCO surgery codes

External fixation codes: KNFJ25 (external fixation of fracture in distal femur), KNGJ20 (external fixation of fracture in patella), KNGJ21 (external fixation of fracture in proximal tibia) and KNGJ29 (external fixation of fracture in knee, not otherwise specified).

Knee arthroplasty codes: KNGB (primary prosthesis in the knee) and KNGC (secondary prosthesis in the knee).

Open reduction internal fixation (ORIF) and reduction codes:

Distal femur:

KNFJ0 closed reduction of femur fracture

KNFJ05 closed reduction of fracture in distal femur

KNFJ1 open reduction of femur fracture

KNFJ15 open reduction of fracture in distal femur

KNFJ3 internal fixation with bio implants of femur fracture

KNFJ35 internal fixation with bio implants of fracture in distal femur

KNFJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of femur fracture

KNFJ45 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in distal femur

KNFJ5 internal fixation with intramedullary nail of femur fracture

KNFJ55 internal fixation with intramedullary nail of fracture in distal femur

KNFJ6 internal fixation with plate and screws of femur fracture

KNFJ65 internal fixation with plate and screws of fracture in distal femur

KNFJ7 internal fixation with screws only of femur fracture

KNFJ75 internal fixation with screws only of fracture in distal femur

KNFJ8 internal fixation with other or combined method of fracture in femur

KNFJ85 internal fixation with other or combined method of fracture in distal femur

KNFJ9 other surgical fracture treatment in femur

KNFJ95 other surgical fracture treatment in distal femur

KNGF2 fixation of articular surface fragment in knee joint

Patella/proximal tibia:

KNGJ fracture treatment in knee and lower leg

KNGJ0 closed reduction of fracture in knee

KNGJ00 closed reduction of fracture in patella

KNGJ01 closed reduction of fracture in proximal tibia

KNGJ09 closed reduction of fracture in knee, not otherwise specified

KNGJ1 open reduction of fracture in knee

KNGJ10 open reduction of fracture in patella

KNGJ11 open reduction of fracture in proximal tibia

KNGJ19 open reduction of fracture in knee, not otherwise specified

KNGJ3 internal fixation with bio implants of fracture in knee

KNGJ30 internal fixation with bio implants of fracture in patella

KNGJ31 internal fixation with bio implants of fracture in proximal tibia

KNGJ39 internal fixation with bio implants of fracture in knee, not otherwise specified

KNGJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee

KNGJ40 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in patella

KNGJ41 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in proximal tibia

KNGJ49 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee, not otherwise specified

KNGJ5 internal fixation with intramedullary nail of fracture in knee

KNGJ51 internal fixation with intramedullary nail of fracture in proximal tibia

KNGJ59 internal fixation with intramedullary nail of fracture in knee, not otherwise specified

KNGJ6 internal fixation with plate and screws of fracture in knee

KNGJ60 internal fixation with plate and screws of fracture in patella

KNGJ61 internal fixation with plate and screws of fracture in proximal tibia

KNGJ69 internal fixation with plate and screws of fracture in knee, not otherwise specified

KNGJ7 internal fixation with screws only of fracture in knee

KNGJ70 internal fixation with screws only of fracture in patella

KNGJ71 internal fixation with screws only of fracture in proximal tibia

KNGJ79 internal fixation with screws only of fracture in knee, not otherwise specified

KNGJ8 internal fixation with other or combined method of fracture in knee

KNGJ80 internal fixation with other or combined method of fracture in patella

KNGJ81 internal fixation with other or combined method of fracture in proximal tibia

KNGJ89 internal fixation with other or combined method of fracture in knee, not otherwise specified

KNGJ9 other surgical fracture treatment in knee

KNGJ90 other surgical fracture treatment in patella

KNGJ91 other surgical fracture treatment in proximal tibia

KNGJ99 other surgical fracture treatment in knee, not otherwise specified

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Knee Fracture Increases TKA Risk After Initial Fracture Treatment and Throughout Life

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Abstract

Background Knee fractures may lead to post-traumatic knee osteoarthritis and subsequent TKA in some patients. However, absolute risk estimates and risk factors for TKA in patients with knee fractures compared with those of the general population remain largely unknown. Such knowledge would help establish the treatment burden and direct patient counseling after a knee fracture is sustained.

Questions/purposes (1) What is the short-term risk of TKA after knee fracture? (2) What is the long-term risk of TKA after knee fracture? (3) What are the risk factors for TKA in patients with knee fractures?

Methods A nationwide 20-year, matched-case comparison cohort study of prospectively collected data from the Danish National Patient Registry included all patients at

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least 15 years old with International Classification of Diseases, 10th revision codes DS724, DS820, or DS821 (knee fractures) on the date their knee fracture was registered. Each patient with a knee fracture was matched (by sex and age) to five people without knee fractures from the general Danish population on the date the knee fracture patient's knee fracture was registered (population controls). Patients with knee fractures and people in the population control group were followed from the date the knee fracture patient's knee fracture was registered to the date of TKA, amputation, knee fusion, emigration, death, or end of follow-up in April 2018. TKA risks for patients with knee fractures versus those for population controls and TKA risk factors in patients with knee fractures were estimated using hazard ratios (HRs) with 95% CIs. A total of 48,791 patients with knee fractures (median age 58 years [interquartile range 41-73]; 58% were female) were matched to 263,593 people in the population control group.

Results The HR for TKA in patients with knee fractures compared with population controls was 3.74 (95% CI 3.44 to 4.07; $p < 0.01$) in the first 3 years after knee fracture. Among knee fracture patients, the risk of undergoing TKA was 2% (967 of 48,791) compared with 0.5% (1280 of 263,593) of people in the population control group. After the first 3 years, the HR was 1.59 (95% CI 1.46 to 1.71) and the number of patients with knee fractures with TKA events divided by the number at risk was 2% (849 of 36,272), compared with 1% (2395 of 180,418) of population controls. During the 20-year study period, 4% of patients with knee fractures underwent TKA compared with 1% of population controls. Risk factors for TKA in patients with knee fractures were: primary knee osteoarthritis (OA) versus no primary knee OA (HR 9.57 [95% CI 5.39 to 16.98]), surgical treatment with external fixation versus open reduction and internal fixation and reduction only (HR 1.92 [95 % CI 1.01 to 3.66]), proximal tibia fracture versus patellar fracture (HR 1.75 [95 % CI 1.30 to 2.36]), and distal femur fracture versus patellar fracture (HR 1.68 [95 % CI 1.08 to 2.64]). Surgical treatment of knee fractures was also a risk factor for TKA. The HRs for TKA in patients with knee fractures who were surgically treated versus those who were treated non-surgically were 2.05 (95% CI 1.83 to 2.30) in the first 5 years after knee fracture and 1.19 (95% CI 1.01 to 1.41) after 5 years.

Conclusions Patients with knee fractures have a 3.7 times greater risk of TKA in the first 3 years after knee fracture, and the risk remains 1.6 times greater after 3 years and throughout their lifetimes. Primary knee OA, surgical treatment of knee fractures, external fixation, proximal tibia fractures, and distal femur fractures are TKA risk factors. These risk estimates and risk factors highlight the treatment burden of knee fractures, building a foundation for future studies to further counsel patients on their risk of undergoing TKA based on patient-, fracture-, and treatment-specific factors.

Level of Evidence Level III, prognostic study.

Introduction

Knee injuries play a part in the rising rates of TKA procedures, which cannot be explained by increases in population size, longevity, and obesity rates alone [14]. Fractures of the distal femur, proximal tibia, and patella represent a substantial proportion of these injuries (incidence rate in the United States: 9 per 100,000 per year) [10], and often result in lower functional outcomes [1, 3, 13, 27], lower work performance [23, 27], lower health-related quality of life [13, 23, 27], and post-traumatic knee osteoarthritis (OA) [7, 13, 16, 17, 20, 24, 26] with subsequent TKA in some patients [7, 17, 24, 26]. To date, secondary TKA for post-traumatic OA after knee fracture has had less successful results compared with primary TKA for primary knee OA in terms of functional outcomes [15, 26], complication rates [8, 26], reoperations [8, 20], and survival rates [15].

Actual risk estimates of [12, 29] and risk factors for [29] TKA in patients with knee fractures compared with those of the general population remain largely unknown. Such knowledge would help establish the treatment burden and direct patient counseling after a patient sustains a knee fracture.

Therefore, in this study, we asked: (1) What is the short-term risk of TKA after knee fracture? (2) What is the long-term risk of TKA after knee fracture? (3) What are the risk factors for TKA in patients with knee fractures?

Patients and Methods

Study Design and Setting

The study was designed as a nationwide, matched-case comparison cohort study of prospectively collected data from the following population-based data sources: the Danish Civil Registration System [21] and the Danish National Patient Registry [22], which covers the entire population of Denmark of approximately 5.7 million residents [25]. The study was approved by the Danish Data Protection Agency, record number REG-085-2017. No institutional review board approval was needed because the study is a registry study of prospectively collected data. The study was conducted according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines [28].

Participants

We used the World Health Organization's 10th revision of International Classification of Diseases (ICD-10) [31] to identify the study population in the Danish National Patient Registry. The study population consisted of all patients at least 15 years old registered in the Danish National Patient Registry from January 1, 1998 to April 30, 2018, with hospital encounters with ICD-10 codes DS724, DS820, or DS821 (knee fractures), with or without subsequent knee surgery codes (see Supplemental Digital Content 1, http://links.lww.com/CORR/A286). Only 3% of knee fracture patients were registered with multiple knee fractures, making the comparison with patients with only one knee fracture and the interpretation of different multiple fractures imprecise; consequently, they were removed from the analysis. Each patient with a knee fracture was matched according to sex and age (same birth year) with five people from the general Danish population without a knee fracture on the date the knee fracture patient's injury was registered (population controls). Patients with knee fractures and participants in the population control group were followed from the date the patient's knee fracture was registered to the date of TKA, amputation, knee fusion, emigration, death, or end of follow-up on April 30, 2018. A total of 48,791 patients with knee fractures (median age 58 years [interquartile range 41-73]; 58% were female) were matched to 263,593 population controls (median age 59 [42-74]; 59% were female) (Table 1). For participants in both groups, the mean observation period to TKA was 7 years.

Description of Experiment, Treatment, or Surgery

Because a unique Danish Civil Personal Register number is assigned to individuals at birth or at immigration, an unambiguous individual-level link between clinical and administrative databases is possible [21]. The Danish Civil Registration System contains complete information on date of birth, sex, residency, and immigration and is updated daily with an individual's vital status. Every person legally residing in Denmark is registered in the database. The Danish National Patient Registry contains information on all public hospital admissions and emergency department visits. Reporting to the Danish National Patient Registry is mandatory and is used for reimbursement by public and private hospitals [22]. However, private hospitals do not treat patients with knee fractures, and private-paid TKA is rare. The Danish National Patient Registry contains information on date of admission, Civil Personal Register number, age, sex, ICD-10 classification [31], and the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO classification) [18].

Table 1. Demographic data of patients with knee fractures and population controls

Variable	Patients with knee fractures	Population controls	p value
Number of patients	48,791	263,593	
Age (years)			< 0.01[a]
Median (interquartile range)	58 (41-73)	59 (42-74)	
Sex			< 0.01[b]
Female (%)	28,221 (58)	154,733 (59)	
Male (%)	20,570 (42)	108,860 (41)	
Charlson comorbidity index (%)			< 0.01[b]
0	36,297 (74)	210,506 (80)	
1	3920 (8)	15,544 (6)	
2	4915 (10)	23,196 (9)	
≥ 3	3659 (8)	14,347 (5)	

[a]The p value calculated using Wilcoxon's rank sum test.
[b]The p value calculated using Pearson's chi-square test.

Variables, Outcome Measures, Data Sources, and Bias

The current NOMESCO classification [18] was implemented in 1996; therefore, we excluded all years before 1996 to reduce surgery code bias. We also excluded years 1996 and 1997 to exclude a potential backlog of already prevalent knee fractures in patients with hospital follow-up. We used the updated version of the Charlson comorbidity index [2, 19] to evaluate comorbidities in patients with knee fractures and population controls. The Charlson comorbidity index could not be calculated in 19% of population controls because they lacked hospital admissions or were not registered with diagnoses used to calculate the Charlson comorbidity index. For these patients, the value was thus set at 0. Primary knee OA was defined as pre-existing knee OA registered at the time of knee fracture (see Supplemental Digital Content 1, http://links.lww.com/CORR/A286). Surgical treatment was divided into external fixation, open reduction internal fixation (ORIF), and reduction. External fixation, ORIF, and reduction procedures were defined by the index procedure, and because we did not have access to medical records, the true proportion of conversions from external fixation to ORIF was unknown. Consequently, to avoid inaccurate assumptions, patients registered with external fixation were allocated to the external fixation group.

Statistical Analysis, Study Size

Descriptive measures are presented as the median and interquartile range or as frequencies and percentages.

Based on QQ-plots, the data did not follow a normal distribution, thus we calculated the p value for age in patients with knee fractures and population controls using the Wilcoxon's rank sum test. We calculated the p value for sex and Charlson comorbidity index in patients with knee fractures and population controls using Pearson's chi-square test. To answer the first and second research questions, we analyzed the short-term and long-term risk of TKA for patients with knee fractures versus that of population controls with Cox proportional hazard models. Amputation, knee fusion, emigration, and death were considered competing events for TKA, and risk times were therefore censored at these events. Based on an evaluation of the Schoenfeld residuals, the proportional hazard assumption was not satisfied for comparing patients with knee fractures to population controls for the 20-year follow-up; when considering the relationship between knee fracture patients and population controls, the hazard ratio (HR), did not appear to be constant across all 20 years. Because the Cox proportional hazards model assumes this constant HR, this model did not fit our data. The model was therefore split into two separate models, the first fitted to the first 3 years of follow-up, with all non-event observations censured at 3 years; and the second model following observations from 3 years onward. Patients with knee fractures and patients in the population control group were only included in the second model if they did not have any event within the first 3 years, and if they had a follow-up interval of 3 years or longer. Evaluation of the Schoenfeld residuals suggested the proportional hazard could be assumed in these models, that is, a constant HR could be assumed within each model. Estimates from the models are presented as HRs with 95% CIs and p values. Adjusted HRs for patients with knee fractures versus patients in the population control are presented and interpreted for both models. To answer the third research question, when evaluating risk factors for TKA in patients with knee fractures, we could assume proportionality for the entire follow-up period; therefore, risk factors were estimated from a model for the entire 20-year study period. To further answer the third research question, we analyzed the risk factor of TKA in individuals with surgically treated knee fractures versus non-surgically treated fractures with a similar Cox proportional hazards model. A similar issue with the proportionality assumption was present in the model comparing patients with knee fractures to population controls; thus, we used two separate models: the first in the first 5 years after knee fracture and the second from 5 years onward. All analyses were performed in in the statistical software R 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria). A p value < 0.05 was considered statistically significant.

Results

What Is the Short-term Risk of TKA After Knee Fracture?

Patients who sustained knee fractures were 3.7 times more likely to undergo TKA within 3 years than patients in the comparable control group (Fig. 1). After adjusting for increasing age per year, sex, and Charlson comorbidity index, the HR for TKA in individuals with knee fractures versus patients in the population control group was 3.74 (95% CI 3.44 to 4.07; p < 0.01) in the first 3 years after knee fracture (Table 2). Within the first 3 years after knee fracture, 2% of patients (967 of 48,791) with knee fractures underwent TKA compared with 0.5% of patients (1280 of 263,593) in the control population.

What Is the Long-term Risk of TKA After Knee Fracture?

Patients with knee fractures were 1.6 times more likely to undergo TKA at 3 years or more after their injury than the comparable patients in the control population (Fig. 1). After adjusting for increasing age per year, sex, and Charlson comorbidity index, the HR for TKA in individuals with knee fractures versus population controls was 1.59 (95% CI 1.46 to 1.71; p < 0.01) after the first 3 years after knee fracture (Table 2). After the first 3 years after knee fracture, 2% (849 of 36,272) of patients with knee fractures underwent TKA compared with 1% of patients (2395 of 180,418) in the control population (Table 2). During the 20-year period, 4% (1816 of 48,791) of patients with knee fractures underwent TKA compared with 1% (3675 of 263,593) among patients in the population control group.

What Are the Risk Factors of TKA in Patients with Knee Fractures?

When examining independent risk factors, we found that primary knee OA, surgical treatment of knee fracture, external fixation, proximal tibia fracture, and distal femur fracture were all risk factors for treatment with TKA in patients with knee fractures during the 20-year period (Table 3). After adjusting for surgically treated versus non-surgically treated knee fractures, increasing age per year, and Charlson comorbidity index, the HR for TKA in individuals with primary knee OA and knee fracture versus patients with no primary knee OA and knee fracture was 9.57 (95% CI 5.39 to 16.98; p < 0.01) during the 20-year period (Table 3). During the 20-year period, 26% (494 of 1899) of patients with knee fractures and primary knee OA

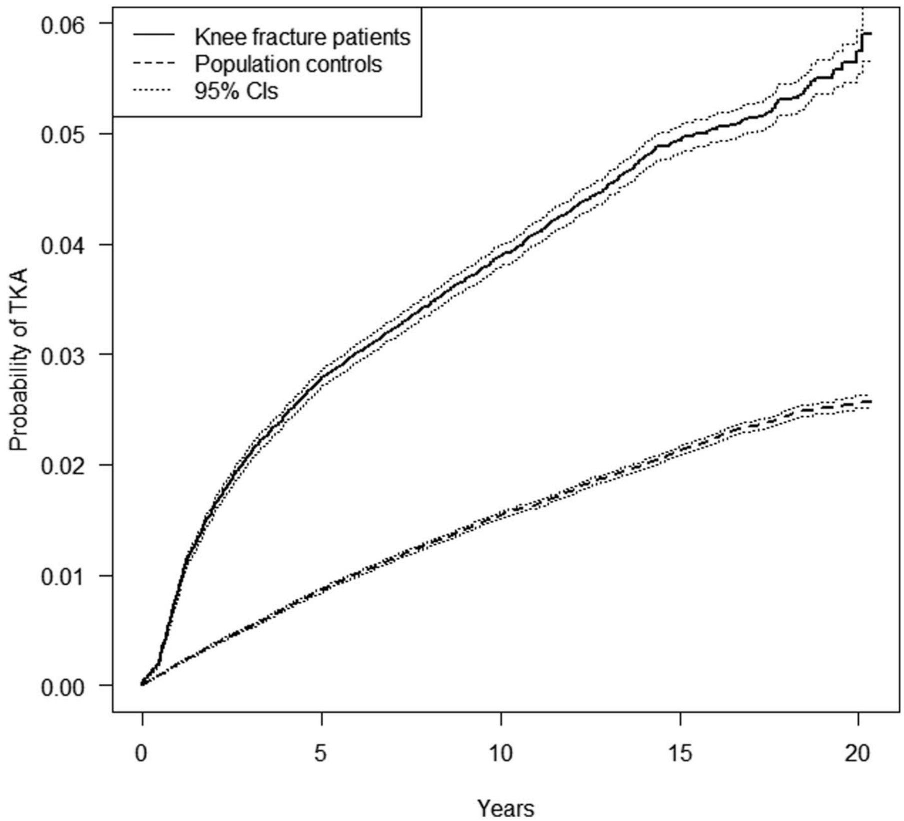

Fig. 1 This graph shows the cumulative incidence of TKA probability in patients with knee fractures and patients in the population control group during the 20-year study period with 95% CIs.

underwent TKA compared with 3% (1322 of 46,892) of patients with knee fractures and no primary knee OA (Table 3). After adjusting for surgically treated versus non-surgically treated knee fractures, increasing age per year, and Charlson comorbidity index, the HR for TKA in individuals with proximal tibia fractures versus patella fractures was 1.75 (95% CI 1.30 to 2.36; $p < 0.01$) during the 20-year period (Table 3). During the 20-year period, 4% (1013 of 22,988) of patients with proximal tibia fractures underwent TKA compared with 3% (455 of 17,205) of patients with patella fractures (Table 3). After adjusting for surgically treated versus non-surgically treated knee fractures, increasing age per year, and Charlson comorbidity index, the HR for TKA in individuals with distal femur fracture versus patella fracture was 1.68 (95% CI 1.08 to 2.64; $p = 0.02$) during the 20-year period (Table 3). During the 20-year period, 4% (268 of 7135) of patients with distal femur fracture underwent TKA (Table 3). The HR of TKA and female versus male sex was 1.21 (95% CI 0.92 to 1.60; $p = 0.17$) during the 20-year period (Table 3). During the 20-year period, 4% (1181 of 28,221) of female patients with knee fractures underwent TKA, and 3% (635

Table 2. Cox proportional hazards model with short-term and long-term hazard ratios for TKA in patients with knee fractures versus population controls

	0-3 years from inclusion			More than 3 years from inclusion		
Variable	Hazard ratio (95% CI)	p value	Number of events/number at risk (%)	Hazard ratio (95% CI)	p value	Number of events/number at risk (%)
Population controls	1		1280/263,593 (0.5)	1		2395/180,418 (1)
Patients with knee fractures vs population controls[a]	3.74 (3.44 to 4.07)	< 0.01	967/48,791 (2)	1.59 (1.46 to 1.71)	< 0.01	849/36,272 (2)

[a]Adjusted for increasing age per year, sex, and Charlson comorbidity index.

Table 3. Cox proportional hazards model with hazard ratios for risk factors for TKA in patients with knee fractures during the 20-year study period

Variable	Hazard ratio (95% CI)	p value	Number of events/number at risk (%)
Increasing age per year[a]	1.02 (1.02 to 1.02)	< 0.01	
CCI 0	1		1322/36,297 (4)
CCI 1 versus 0[a]	1.09 (0.93 to 1.29)	0.28	181/3920 (5)
CCI 2 versus 0[a]	0.78 (0.65 to 0.93)	0.01	155/4915 (3)
CCI ≥ 3 versus 0[a]	0.92 (0.76 to 1.10)	0.34	158/3659 (4)
Male sex	1		635/20,570 (3)
Female sex versus male sex[b]	1.21 (0.92 to 1.60)	0.17	1181/28,221 (4)
No primary knee OA	1		1322/46,892 (3)
Primary knee OA versus no primary knee OA[b]	9.57 (5.39 to 16.98)	< 0.01	494/1899 (26)
Patella fracture	1		455/17,205 (3)
Proximal tibia fracture versus patella fracture[b]	1.75 (1.30 to 2.36)	< 0.01	1013/22,988 (4)
Distal femur fracture versus patella fracture[b]	1.68 (1.08 to 2.64)	0.02	268/7135 (4)
Proximal tibia fracture versus distal femur fracture[b]	1.04 (0.68 to 1.60)	0.85	
ORIF and reduction only	1		1675/47,273 (35)
External fixation versus ORIF and reduction only[c]	1.92 (1.01 to 3.66)	0.05	141/1518 (9)

[a]Change per age in years, adjusted for surgically treated versus non-surgically treated knee fracture, sex, primary knee OA versus no primary knee OA, and single fracture.
[b]Adjusted for surgically treated versus non-surgically treated knee fracture, increasing age per year, and CCI.
[c]Model is based on surgically treated knee fractures, adjusted for increasing age per year, CCI, sex, primary knee OA versus no primary knee OA, and single fracture; CCI = Charlson comorbidity index. Primary knee OA = primary knee osteoarthritis. ORIF = open reduction internal fixation. Single fracture = distal femur fracture versus patella fracture and proximal tibia fracture versus patella fracture.

of 20,570) of male patients with knee fractures underwent TKA (Table 3). The HR of TKA with increasing age per year in patients with knee fractures was 1.02 (95% CI 1.02 to 1.02; $p < 0.01$) during the 20-year period (Table 3). After adjusting for increasing age per year, Charlson comorbidity index, sex, primary knee OA versus no primary knee OA, and single fracture (distal femur fracture versus patella fracture and proximal tibia fracture versus patella fracture), the HR of TKA and surgical treatment with external fixation versus ORIF and reduction only was 1.92 (95% CI 1.01 to 3.66; $p = 0.05$) during the 20-year period (Table 3). During the 20-year period, 9% (141 of 1518) of patients with knee fractures were treated with external fixation compared with 35% (1675 of 47,273) of patients with knee fractures treated with ORIF and reduction only. After adjusting for primary knee OA versus no primary knee OA, increasing age per year, sex, and Charlson comorbidity index, the HR of TKA in patients with knee fractures treated surgically versus that of patients treated non-surgically was also a risk factor in the first 5 years (HR 2.05 [95% CI 1.83 to 2.30]; $p < 0.01$) as well as after 5 years (HR 1.19 [95% CI 1.01 to 1.41]; $p = 0.04$) (Table 4). In the first 5 years after knee fracture, 4% (728 of 17,636) of patients with surgically treated knee fracture underwent TKA compared with 2% (508 of 31,155) of patients with knee fractures who were treated non-surgically (Table 4). After the first 5 years after knee fracture, 3% (258 of 10,321) of patients with knee fracture treated surgically underwent TKA while 2% (322 of 17,583) of patients with knee fractures treated non-surgically underwent TKA (Table 4).

Discussion

Background and Rationale

Knee injuries play a part in the rising rates of TKA procedures, which cannot be explained by increases in population size, longevity, and obesity rates alone [14]. Fractures of the distal femur, proximal tibia, and patella represent a substantial proportion of these injuries [10], often resulting in lower functional outcome [1, 3, 13, 27], lower work performance [23, 27], lower health-related quality of life [13, 23, 27], and post-traumatic knee

Table 4. Cox proportional hazards model with hazard ratios for TKA in surgically treated versus non-surgically treated knee fractures

	0-5 years from inclusion			More than 5 years from inclusion		
Variable	Hazard ratio (95% CI)	p value	Number of TKAs/number at risk	Hazard ratio (95% CI)	p value	Number of TKAs/number at risk
Non-surgically treated knee fracture	1		508/31,155 (2%)	1		322/17,583 (2%)
Surgically treated versus non-surgically treated knee fracture[a]	2.05 (1.83 to 2.30)	< 0.01	728/17,636 (4%)	1.19 (1.01 to 1.41)	0.04	258/10,321 (3%)

[a]Adjusted for primary knee OA versus no primary knee OA, increasing age per year, sex, and CCI. Primary knee OA = primary knee osteoarthritis.

osteoarthritis [7, 13, 16, 17, 20, 24, 26] with subsequent TKA in some patients [7, 17, 24, 26]. To date, secondary TKA for post-traumatic OA after knee fracture has been shown to have less successful results compared with primary TKA for primary knee OA in terms of functional outcome [15, 26], complication rates [8, 26], reoperations [8, 20], and survival rates [15]. Actual risk estimates of [12, 29] and risk factors for [29] TKA in patients with knee fractures compared with those of the general population remain largely unknown. Such knowledge would help establish the treatment burden and direct patient counseling after a patient sustains a knee fracture. We found that patients with knee fractures have a 3.7 times greater risk of TKA in the first 3 years after knee fracture, and the risk remains 1.6 times greater after 3 years and throughout their lifetimes. We found several independent risk factors that increased the chances of undergoing TKA over and above the risks posed by a history of knee fracture, including primary knee OA, surgical treatment of knee fractures, external fixation, proximal tibia fracture, and distal femur fracture.

This study has a number of limitations: First, there are the well-known limitations of administrative data, with potential incorrect use of diagnosis codes and incomplete registration of surgery codes. Second, there are no specific surgery codes for conversion of surgery to treat knee fractures to TKA, and because the study is a registry study, we did not have access to medical records. However, data in the Danish National Patient Registry are high quality, and the highest positive predictive value is found in orthopaedic diagnoses [22]. Third, laterality of knee fracture, TKA, amputation, and knee fusion were insufficiently registered in the Danish National Patient Registry and thus could not be used, possibly producing overestimations or underestimations of procedure rates as procedures could have been performed on the contralateral knee. Fourth, data on fracture severity, that is, ABC extensions of ICD-10 codes, and injury severity, such as trauma type, were incompletely registered; only a small percentage of the study population was registered with ABC extensions and trauma type, thus distributions of knee fracture subclassifications and trauma type could not be described [22]. Consequently, it was not possible to, for instance, differentiate between a high-energy comminuted proximal tibia fractures with intra-articular involvement and a low-energy simple fractures of the patella, possibly confounding the risk estimates presented. However, we still believe that this study provides insight into what a knee fracture entails in forms of both short-term and long-term TKA risk. It also provides insight into which general anatomic region of the knee is most vulnerable to undergoing TKA when fractured, including risk estimates of how much primary knee OA, surgical treatment versus non-surgical treatment of knee fracture, and external fixation are associated with TKA risk. Fifth, although a 20-year follow-up for the older proportion of patients in the study population would likely be sufficient, it may not be enough for the younger proportion of patients. Because our population consists of both age groups, we believe we have captured a high proportion of TKA events for the older population but may have captured a smaller proportion of TKA events for the younger population. However, given that we found a higher HR within the first 3 years after knee fracture and a lower HR in the remaining follow-up time, we assume it is unlikely that a HR beyond 20 years would drastically deviate from the long-term HR presented in our study, even for younger patients. In summary, the accumulated data comprised a large, representative nationwide sample during a 20-year study period from a relatively homogenous population, increasing external validity and thus providing results with high validity and generalizability with regards to Scandinavian countries. Of note is that international generalizability of the study results can only be assumed because the potential confounder of TKA accessibility in different healthcare systems could not be accounted for in our data analysis.

What Is the Short-term Risk of TKA After Knee Fracture?

We found that within the first 3 years after injury, patients with a knee fracture underwent TKA with much greater frequency than the control population. Larsen et al. [12] found an HR for TKA of 3.02 (95% CI 2.26 to 4.03) from 0 to 5 years after patella fracture compared with that of a matched cohort. This is comparable to the HR of 3.74 (95 % CI 3.44 to 4.07) in the first 3 years following knee fracture in our study. The results of Larsen et al. [12] can only be roughly compared with ours because they included only patellar fractures in patients from a single region in Denmark; however, their study described similar risk trends as our study, in which the critical TKA risk can be seen in the first few years after knee fracture.

What Is the Long-term Risk of TKA After Knee Fracture?

We found that the increased risk of subsequently undergoing TKA remained even after 3 years and in the long term, with a substantially higher proportion of patients with a history of knee fracture undergoing TKA surgery than patients in the matched control group, suggesting that the risk of secondary TKA for posttraumatic OA, pain, reduced function, and other complications after knee fracture is lifelong. Larsen et al. [12], found an HR for TKA of 1.56 [95% CI 1.17 to 2.07] at 5 to 10 years after patella fracture compared with that of a matched cohort. Because of differences in study design as discussed above, this can to some extent be compared with our results (HR 1.59 [95 % CI 1.46 to 1.71] after the first 3 years after knee fracture). Wasserstein et al. [29] compared the HR for TKA in patients with ORIF-treated tibial plateau fractures with that of a matched cohort without ORIF-treated tibial plateau fractures. During the 14-year study period, the comorbidity-adjusted HR for TKA in ORIF-treated tibial plateau fractures was 5.29 (95% CI 4.58 to 6.11), whereas in our study, the increasing age per year-, sex-, and Charlson comorbidity index-adjusted HR for TKA in patients with knee fractures versus that of population controls was 1.59 (95% CI 1.46 to 1.71) after the first 3 years and in the long-term. A total of 7% of patients with ORIF-treated tibial plateau fractures and 2% of patients in the matched cohort underwent TKA after 10 years in the study by Wasserstein et al. [29]. During the 20-year period in our study, 4% of patients with knee fractures and 1% of matched population controls underwent TKA, while 4% of patients with proximal tibia fracture underwent TKA. The variance in results might be explained by differences in knee fracture types, treatment types, comorbidity measures (use of aggregated diagnosis groups versus Charlson comorbidity index), data sources, inclusion and exclusion criteria, group matching criteria, coding systems, populations and length of the study period.

What Are the Risk Factors of TKA in Patients with Knee Fractures?

We found several independent risk factors that increased the chances of undergoing TKA over and above the risks posed by a history of knee fracture. Wasserstein et al. [29] found an HR of 1.25 ($p = 0.029$) for female sex versus male sex in patients with ORIF-treated tibial plateau fractures during their 14-year study period compared with a female sex versus male sex and knee fracture HR of 1.21 ($p = 0.17$) during our 20-year study of patients with knee fractures (Table 3). In their study, increasing age per year had an HR of 1.03 ($p < 0.01$) [29], which is comparable to the results of our study (HR 1.02; $p < 0.01$) (Table 3). Our results showed an association between external fixation versus ORIF and reduction only, with an HR for TKA of 1.92 ($p = 0.05$), and Wasserstein et al. [29] calculated an HR of 1.56 ($p < 0.20$) in preoperative external fixation in patients with ORIF-treated tibial plateau fractures. The studies are only partly comparable as Wasserstein et al. [29] studied conversion surgery in tibial plateau fractures whereas we studied external fixation, ORIF, and reduction index procedures. In other studies, TKA was found to be more prevalent in females and those with increasing age [9], and knee fractures were more prevalent in females and in those with increasing age [4, 5, 6, 11, 30]. Our HRs of 1.21 and 1.02 in patients with knee fractures mimic these findings, although the HR for female sex versus male sex was no different in our study ($p = 0.17$) and the increased HR for increasing age per year was only 1.02 in our study. TKA for primary knee OA is a well-established procedure; hence, the high HR in patients with knee fractures and primary knee OA is unsurprising. However, the HR of 9.57 provides insight into the level of hazard involved. The high HRs for TKA in patients with knee fractures that were surgically treated versus those that were non-surgically treated (2.05 in the first 5 years and 1.19 after 5 years) in our study indicate that because most surgically treated knee fractures are more complex than non-surgically treated knee fractures, the higher HR for TKA in patients with surgically treated knee fractures is to be expected. The high HRs for TKA in patients with knee fractures with the above-mentioned risk factors illustrate the importance of focusing research on further defining patient-, fracture-, and treatment-specific risk factors during the initial and long-term treatment of knee fractures. Focus should be placed on proximal tibia fractures because our 20-year study showed that proximal tibia fracture had the highest HR for TKA (1.75).

We found that patients with knee fractures have a 3.7 times greater risk of TKA in the first 3 years after knee fracture, and the risk remains 1.6 times greater after 3 years and throughout their lifetimes. Primary knee OA, surgical treatment of knee fractures, external fixation, proximal tibia fractures, and distal femur fractures are risk factors of TKA. This is important because these risk estimates and risk factors highlight the treatment burden of knee fractures, building a foundation for future studies to further counsel patients on their risk of undergoing TKA based on patient-, fracture-, and treatment-specific factors.

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Supplemental Digital Content 1. ICD-10 diagnosis codes and Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) surgery codes

ICD-10 diagnosis codes

Primary knee osteoarthritis (OA) ICD-10 codes include DM170 (primary bilateral knee OA), DM171 (primary unilateral knee OA) and DM179 (knee OA other, not otherwise specified).

Amputation ICD-10 codes include DS780 (traumatic amputation in hip joint), DS781 (traumatic amputation between hip and knee), DS789 (traumatic amputation in the hip region or thigh, not otherwise specified), DS880 (traumatic amputation in the knee joint), DS881 (traumatic amputation in the lower leg) and DT055 (traumatic amputation of both legs).

NOMESCO surgery codes

Knee arthroplasty NOMESCO codes include KNGB (primary prosthesis in the knee) and KNGC (secondary prosthesis in the knee).

Amputation NOMESCO codes include KNEQ (amputations in the pelvic area), KNFQ (amputations and other related surgeries on the hip and thigh) and KNGQ (amputations and other related surgeries on the knee and lower leg).

Knee fusion NOMESCO codes include KNGG (joint resections, arthroplasties and arthrodeses in the knee).

External fixation NOMESCO codes include KNFJ25 (external fixation of fracture in the distal femur), KNGJ20 (external fixation of fracture in the patella), KNGJ21 (external fixation of fracture in the proximal tibia) and KNGJ29 (external fixation of knee fractures, not otherwise specified).

Open reduction internal fixation (ORIF) including reduction NOMESCO codes include KNFJ0 (closed reduction of a femur fracture), KNFJ05 (closed reduction of a distal femur fracture), KNFJ1 (open reduction of a femur fracture), KNFJ15 (open reduction of a distal femur fracture), KNFJ3 (internal fixation with bio implants of a femur fracture), KNFJ35 (internal fixation with bio implants of a distal femur fracture), KNFJ4 (internal fixation with wires, rods, cerclage wiring or pins/needles of a femur fracture), KNFJ45 (internal fixation with wires, rods, cerclage wiring or pins/needles of a distal femur fracture), KNFJ5 (internal fixation with intramedullary nail of a femur fracture), KNFJ55 (internal fixation with intramedullary nail of a distal femur fracture), KNFJ6 (internal fixation with plate and screws of a femur fracture), KNFJ65 (internal fixation with plate and screws of a distal femur fracture), KNFJ7 (internal fixation with screws only of a femur fracture), KNFJ75 (internal fixation with screws only of a distal femur fracture), KNFJ8 (internal fixation with other or combined method of fracture in the femur), KNFJ85 (internal fixation with other or combined method of a distal femur fracture), KNFJ9 (other surgical fracture treatment in the femur), KNFJ95 (other surgical fracture treatment in the distal femur), KNGF2 (fixation of articular surface fragment in the knee), KNGJ0 (closed reduction of fracture in the knee), KNGJ00 (closed reduction of a patellar fracture), KNGJ01 (closed reduction of a proximal tibia fracture), KNGJ09 (closed reduction of fracture in the knee, not otherwise specified), KNGJ1 (open reduction of a knee fracture), KNGJ10 (open reduction of a patellar fracture), KNGJ11 (open reduction of a proximal tibia fracture), KNGJ19 (open reduction of a knee fracture, not otherwise specified), KNGJ3 (internal fixation with bio implants of a knee fracture), KNGJ30 (internal fixation with bio implants of a patellar fracture), KNGJ31 (internal fixation with bio implants of a proximal tibia fracture), KNGJ39 (internal fixation with bio implants of a knee fracture, not otherwise specified), KNGJ4 (internal fixation with wires, rods, cerclage wiring or pins/needles of a knee fracture), KNGJ40 (internal fixation with wires, rods, cerclage wiring or pins/needles of a patellar fracture), KNGJ41 (internal fixation with wires, rods, cerclage wiring or pins/needles of a proximal tibia fracture), KNGJ49 (internal fixation with wires, rods, cerclage wiring or pins/needles of a knee fracture, not otherwise specified), KNGJ5 (internal fixation with intramedullary nail of a knee fracture), KNGJ51 (internal fixation with intramedullary nail of a proximal tibia fracture), KNGJ59 (internal fixation with intramedullary nail of a knee fracture, not otherwise specified), KNGJ6 (internal fixation with plate and screws of a knee fracture), KNGJ60 (internal fixation with plate and screws of a patellar fracture), KNGJ61 (internal fixation with plate and screws of a proximal tibia fracture), KNGJ69 (internal fixation with plate and screws of a knee fracture, not otherwise specified), KNGJ7 (internal fixation with screws only of a knee fracture), KNGJ70 (internal fixation with screws only of a patellar fracture), KNGJ71 (internal fixation with screws only of a proximal tibia fracture), KNGJ79 (internal fixation with screws only of a knee fracture, not otherwise specified), KNGJ8 (internal fixation with other or combined method of a knee fracture), KNGJ80 (internal fixation with other or combined method of a patellar fracture), KNGJ81 (internal fixation with other or combined method of a proximal tibia fracture), KNGJ89 (internal fixation with other or combined method of a knee fracture, not otherwise specified), KNGJ9 (other surgical fracture treatment in the knee), KNGJ90 (other surgical fracture treatment in the patella), KNGJ91 (other surgical fracture treatment in the proximal tibia) and KNGJ99 (other surgical fracture treatment in the knee, not otherwise specified).

Supplementary Material

Study I

ICD-10 diagnosis codes and NOMESCO surgery codes

ICD-10 diagnosis codes

Concomitant near-knee fractures: DS720 (femoral neck fracture), DS721 (pertrochanteric femoral fracture), DS722 (subtrochanteric femoral fracture), DS723 (femoral shaft fracture), DS727 (multiple femoral fractures), DS728 (other femoral fracture), DS729 (femoral fracture, other, not otherwise specified), DS822 (tibial shaft fracture), DS823 (distal tibia fracture), DS824 (fibula shaft fracture), DS825 (medial malleolar fracture), DS826 (lateral malleolar fracture), DS827 (multiple fractures of the knee and lower knee), DS828 (fracture of other part of lower leg) and DS829 (fracture of lower leg, other, not otherwise specified).

Concomitant fractures: DS122 (fracture of cervical spine), DS127 (multiple fractures of cervical spine), DS22 (fracture of costae, sternum or thoracic spine), DS32 (fracture of lumbar spine or pelvis), DS42 (shoulder and/or upper arm fracture), DS52 (elbow and/or lower arm fracture), DS62 (wrist and/or hand fracture), DT021 (fractures in thorax, lumbar spine and pelvis), DT027 (fractures in thorax, lumbar spine, pelvis, upper and lower extremities) and DT08 (fracture of spine, not otherwise specified).

Lesions inside the knee: DS83 (luxation and distortion of joint and ligaments in knee).

Primary knee osteoarthritis (OA): DM170 (primary bilateral knee OA), DM171 (primary unilateral knee OA) and DM179 (knee OA other, not otherwise specified).

Osteoporosis: DM81 (osteoporosis without pathological fracture).

Proximal tibia fracture: DS821.

Patella fracture: DS820.

Distal femur fracture: DS724.

Femoral shaft fracture: DS723.

Tibial shaft fracture: DS822.

NOMESCO surgery codes

External fixation codes: KNFJ25 (external fixation of fracture in distal femur), KNGJ20 (external fixation of fracture in patella), KNGJ21 (external fixation of fracture in proximal tibia) and KNGJ29 (external fixation of fracture in knee, not otherwise specified).

Knee arthroplasty codes: KNGB (primary prosthesis in the knee), KNGC (secondary prosthesis in the knee) and KNGG (joint resections, arthroplasties and arthrodeses in knee joint).

Open reduction internal fixation (ORIF), external fixation and reduction codes:

Distal femur:

KNFJ0 closed reduction of femur fracture

KNFJ05 closed reduction of fracture in distal femur

KNFJ1 open reduction of femur fracture

KNFJ15 open reduction of fracture in distal femur

KNFJ2 external fixation of femur fracture

KNFJ25 external fixation of fracture in distal femur

KNFJ3 internal fixation with bio implants of femur fracture

KNFJ35 internal fixation with bio implants of fracture in distal femur

KNFJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of femur fracture

KNFJ45 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in distal femur

KNFJ5 internal fixation with intramedullary nail of femur fracture

KNFJ55 internal fixation with intramedullary nail of fracture in distal femur

KNFJ6 internal fixation with plate and screws of femur fracture

KNFJ65 internal fixation with plate and screws of fracture in distal femur

KNFJ7 internal fixation with screws only of femur fracture

KNFJ75 internal fixation with screws only of fracture in distal femur

KNFJ8 internal fixation with other or combined method of fracture in femur

KNFJ85 internal fixation with other or combined method of fracture in distal femur

KNFJ9 other surgical fracture treatment in femur

KNFJ95 other surgical fracture treatment in distal femur

KNGF2 fixation of articular surface fragment in knee joint

Patella/proximal tibia:

KNGJ fracture treatment in knee and lower leg

KNGJ0 closed reduction of fracture in knee

KNGJ00 closed reduction of fracture in patella

KNGJ01 closed reduction of fracture in proximal tibia

KNGJ09 closed reduction of fracture in knee, not otherwise specified

KNGJ1 open reduction of fracture in knee

KNGJ10 open reduction of fracture in patella

KNGJ11 open reduction of fracture in proximal tibia

KNGJ19 open reduction of fracture in knee, not otherwise specified

KNGJ2 external fixation of fracture in knee

KNGJ20 external fixation of fracture in patella

KNGJ21 external fixation of fracture in proximal tibia

KNGJ29 external fixation of fracture in knee, not otherwise specified

KNGJ3 internal fixation with bio implants of fracture in knee

KNGJ30 internal fixation with bio implants of fracture in patella

KNGJ31 internal fixation with bio implants of fracture in proximal tibia

KNGJ39 internal fixation with bio implants of fracture in knee, not otherwise specified

KNGJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee

KNGJ40 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in patella

KNGJ41 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in proximal tibia

KNGJ49 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee, not otherwise specified

KNGJ5 internal fixation with intramedullary nail of fracture in knee

KNGJ51 internal fixation with intramedullary nail of fracture in proximal tibia

KNGJ59 internal fixation with intramedullary nail of fracture in knee, not otherwise specified

KNGJ6 internal fixation with plate and screws of fracture in knee

KNGJ60 internal fixation with plate and screws of fracture in patella

KNGJ61 internal fixation with plate and screws of fracture in proximal tibia

KNGJ69 internal fixation with plate and screws of fracture in knee, not otherwise specified

KNGJ7 internal fixation with screws only of fracture in knee

KNGJ70 internal fixation with screws only of fracture in patella

KNGJ71 internal fixation with screws only of fracture in proximal tibia

KNGJ79 internal fixation with screws only of fracture in knee, not otherwise specified

KNGJ8 internal fixation with other or combined method of fracture in knee

KNGJ80 internal fixation with other or combined method of fracture in patella

KNGJ81 internal fixation with other or combined method of fracture in proximal tibia

KNGJ89 internal fixation with other or combined method of fracture in knee, not otherwise specified

KNGJ9 other surgical fracture treatment in knee

KNGJ90 other surgical fracture treatment in patella

KNGJ91 other surgical fracture treatment in proximal tibia

KNGJ99 other surgical fracture treatment in knee, not otherwise specified

Supplementary Material

Study II

ICD-10 diagnosis codes and NOMESCO surgery codes

ICD-10 diagnosis codes

Proximal tibia fracture: DS821.

Patella fracture: DS820.

Distal femur fracture: DS724.

NOMESCO surgery codes

External fixation codes: KNFJ25 (external fixation of fracture in distal femur), KNGJ20 (external fixation of fracture in patella), KNGJ21 (external fixation of fracture in proximal tibia) and KNGJ29 (external fixation of fracture in knee, not otherwise specified).

Knee arthroplasty codes: KNGB (primary prosthesis in the knee) and KNGC (secondary prosthesis in the knee).

Open reduction internal fixation (ORIF) and reduction codes:

Distal femur:

KNFJ0 closed reduction of femur fracture

KNFJ05 closed reduction of fracture in distal femur

KNFJ1 open reduction of femur fracture

KNFJ15 open reduction of fracture in distal femur

KNFJ3 internal fixation with bio implants of femur fracture

KNFJ35 internal fixation with bio implants of fracture in distal femur

KNFJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of femur fracture

KNFJ45 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in distal femur

KNFJ5 internal fixation with intramedullary nail of femur fracture

KNFJ55 internal fixation with intramedullary nail of fracture in distal femur

KNFJ6 internal fixation with plate and screws of femur fracture

KNFJ65 internal fixation with plate and screws of fracture in distal femur

KNFJ7 internal fixation with screws only of femur fracture

KNFJ75 internal fixation with screws only of fracture in distal femur

KNFJ8 internal fixation with other or combined method of fracture in femur

KNFJ85 internal fixation with other or combined method of fracture in distal femur

KNFJ9 other surgical fracture treatment in femur

KNFJ95 other surgical fracture treatment in distal femur

KNGF2 fixation of articular surface fragment in knee joint

Patella/proximal tibia:

KNGJ fracture treatment in knee and lower leg

KNGJ0 closed reduction of fracture in knee

KNGJ00 closed reduction of fracture in patella

KNGJ01 closed reduction of fracture in proximal tibia

KNGJ09 closed reduction of fracture in knee, not otherwise specified

KNGJ1 open reduction of fracture in knee

KNGJ10 open reduction of fracture in patella

KNGJ11 open reduction of fracture in proximal tibia

KNGJ19 open reduction of fracture in knee, not otherwise specified

KNGJ3 internal fixation with bio implants of fracture in knee

KNGJ30 internal fixation with bio implants of fracture in patella

KNGJ31 internal fixation with bio implants of fracture in proximal tibia

KNGJ39 internal fixation with bio implants of fracture in knee, not otherwise specified

KNGJ4 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee

KNGJ40 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in patella

KNGJ41 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in proximal tibia

KNGJ49 internal fixation with wires, rods, cerclage wiring or pins/needles of fracture in knee, not otherwise specified

KNGJ5 internal fixation with intramedullary nail of fracture in knee

KNGJ51 internal fixation with intramedullary nail of fracture in proximal tibia

KNGJ59 internal fixation with intramedullary nail of fracture in knee, not otherwise specified

KNGJ6 internal fixation with plate and screws of fracture in knee

KNGJ60 internal fixation with plate and screws of fracture in patella

KNGJ61 internal fixation with plate and screws of fracture in proximal tibia

KNGJ69 internal fixation with plate and screws of fracture in knee, not otherwise specified

KNGJ7 internal fixation with screws only of fracture in knee

KNGJ70 internal fixation with screws only of fracture in patella

KNGJ71 internal fixation with screws only of fracture in proximal tibia

KNGJ79 internal fixation with screws only of fracture in knee, not otherwise specified

KNGJ8 internal fixation with other or combined method of fracture in knee

KNGJ80 internal fixation with other or combined method of fracture in patella

KNGJ81 internal fixation with other or combined method of fracture in proximal tibia

KNGJ89 internal fixation with other or combined method of fracture in knee, not otherwise specified

KNGJ9 other surgical fracture treatment in knee

KNGJ90 other surgical fracture treatment in patella

KNGJ91 other surgical fracture treatment in proximal tibia

KNGJ99 other surgical fracture treatment in knee, not otherwise specified

Supplementary Material

Study III

ICD-10 diagnosis codes and NOMESCO surgery codes

ICD-10 diagnosis codes

Primary knee osteoarthritis (OA) ICD-10 codes include DM170 (primary bilateral knee OA), DM171 (primary unilateral knee OA) and DM179 (knee OA other, not otherwise specified).

Amputation ICD-10 codes include DS780 (traumatic amputation in hip joint), DS781 (traumatic amputation between hip and knee), DS789 (traumatic amputation in the hip region or thigh, not otherwise specified), DS880 (traumatic amputation in the knee joint), DS881 (traumatic amputation in the lower leg) and DT055 (traumatic amputation of both legs).

NOMESCO surgery codes

Knee arthroplasty NOMESCO codes include KNGB (primary prosthesis in the knee) and KNGC (secondary prosthesis in the knee).

Amputation NOMESCO codes include KNEQ (amputations in the pelvic area), KNFQ (amputations and other related surgeries on the hip and thigh) and KNGQ (amputations and other related surgeries on the knee and lower leg).

Knee fusion NOMESCO codes include KNGG (joint resections, arthroplasties and arthrodeses in the knee).

External fixation NOMESCO codes include KNFJ25 (external fixation of fracture in the distal femur), KNGJ20 (external fixation of fracture in the patella), KNGJ21 (external fixation of fracture in the proximal tibia) and KNGJ29 (external fixation of knee fractures, not otherwise specified).

Open reduction internal fixation (ORIF) including reduction NOMESCO codes include KNFJ0 (closed reduction of a femur fracture), KNFJ05 (closed reduction of a distal femur fracture), KNFJ1 (open reduction of a femur fracture), KNFJ15 (open reduction of a distal femur fracture), KNFJ3 (internal fixation with bio implants of a femur fracture), KNFJ35 (internal fixation with bio implants of a distal femur fracture), KNFJ4 (internal fixation with wires, rods, cerclage wiring or pins/needles of a femur fracture), KNFJ45 (internal fixation with wires, rods, cerclage wiring or pins/needles of a distal femur fracture), KNFJ5 (internal fixation with intramedullary nail of a femur fracture), KNFJ55 (internal fixation with intramedullary nail of a distal femur fracture), KNFJ6 (internal fixation with plate and screws of a femur fracture), KNFJ65 (internal fixation with plate and screws of a distal femur fracture), KNFJ7 (internal fixation with screws only of a femur fracture), KNFJ75 (internal fixation with screws only of a distal femur fracture), KNFJ8 (internal fixation with other or combined method of fracture in the femur), KNFJ85 (internal fixation with other or combined method of a distal femur fracture), KNFJ9 (other surgical fracture treatment in the femur), KNFJ95 (other surgical fracture treatment in the distal femur), KNGF2 (fixation of articular surface fragment in the knee), KNGJ0 (closed reduction of fracture in the knee), KNGJ00 (closed reduction of a patellar fracture), KNGJ01 (closed reduction of a proximal tibia fracture), KNGJ09 (closed reduction of fracture in the knee, not otherwise specified), KNGJ1 (open reduction of a knee fracture), KNGJ10 (open reduction of a patellar fracture), KNGJ11 (open reduction of a proximal tibia fracture), KNGJ19 (open reduction of a knee fracture, not otherwise specified), KNGJ3 (internal fixation with bio implants of a knee fracture), KNGJ30 (internal fixation with bio implants of a patellar fracture), KNGJ31 (internal fixation with bio implants of a proximal tibia fracture), KNGJ39 (internal fixation with bio implants of a knee fracture, not otherwise specified), KNGJ4 (internal fixation with wires, rods, cerclage wiring or pins/needles of a knee fracture), KNGJ40 (internal fixation with wires, rods, cerclage wiring or pins/needles of a patellar fracture), KNGJ41 (internal fixation with wires, rods, cerclage wiring or pins/needles of a proximal tibia fracture), KNGJ49 (internal fixation with wires, rods, cerclage wiring or pins/needles of a knee fracture, not otherwise specified), KNGJ5 (internal fixation with intramedullary nail of a knee fracture), KNGJ51 (internal fixation with intramedullary nail of a proximal tibia fracture), KNGJ59 (internal fixation with intramedullary nail of a knee fracture, not otherwise specified), KNGJ6 (internal fixation with plate and screws of a knee fracture), KNGJ60 (internal fixation with plate and screws of a patellar fracture), KNGJ61 (internal fixation with plate and screws of a proximal tibia fracture), KNGJ69 (internal fixation with plate and screws of a knee fracture, not otherwise specified), KNGJ7 (internal fixation with screws only of a knee fracture), KNGJ70 (internal fixation with screws only of a patellar fracture), KNGJ71 (internal fixation with screws only of a proximal tibia fracture), KNGJ79 (internal fixation with screws only of a knee fracture, not otherwise specified), KNGJ8 (internal fixation with other or combined method of a knee fracture), KNGJ80 (internal fixation with other or combined method of a patellar fracture), KNGJ81 (internal fixation with other or combined method of a proximal tibia fracture), KNGJ89 (internal fixation with other or combined method of a knee fracture, not otherwise specified), KNGJ9 (other surgical fracture treatment in the knee), KNGJ90 (other surgical fracture treatment in the patella), KNGJ91 (other surgical fracture treatment in the proximal tibia) and KNGJ99 (other surgical fracture treatment in the knee, not otherwise specified).