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PhD thesis

How to overcome obstacles in contemporary implementation and utilization of Unicompartmental Knee Arthroplasty.

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Preface

This thesis is centered around medial Unicompartmental Knee Arthroplasty. I explore this treatment strategy's development through the last 20 years and evaluate the contemporary approach against Total Knee Arthroplasty. To this end, we use data on approximately 100,000 patients with end-stage osteoarthritis of the knee who had Knee Replacement surgery in Denmark or the UK between 1997 and 2018.

I hope you find this interesting and informative. If not, I do apologise.

Acknowledgements

First and foremost, this would never have come to be without my amazing supervisor and mentor, Anders Troelsen. Thank you for the opportunity and encouragement for me to do this. Thank you for being the best and most engaged supervisor one could ask for. You are truly a superhuman and an inspiration.

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Contents

1 List of studies

Registry studies

1. Circumstances for optimized medial Unicompartmental Knee Replacement outcome. Learning from 20 years of propensity score matched registry data. (*Under review at peer-reviewed journal*)

2. Does changes in Unicompartmental Knee Arthroplasty practice patterns influence reasons for revision? A study of 9639 cases from the Danish Knee Arthroplasty Register. (*Not submitted*)

Clinical studies

3. Comparison of two strategies in Knee Arthroplasty: Total Knee Arthroplasy only vs. Unicompartmental Knee Arthroplasty if possible (*Submitted to peer-reviewed journal*)

4. Total- vs. Unicompartmental Knee Arthroplasty: Is there something to gain from implementing medial Unicompartmental Knee Arthroplasty? (*Not submitted*)

2 Thesis at a glance

Paper	I	II
Aim	To determine: • Changes to revision risk over time. • Factors influencing revision risk and changes to these over time. • Revision risk for optimized contemporary UKA practice.	To determine: • How are the failure patterns and timing for TKA and UKA in DK? • If the revision indications for UKA depend on factors known to influence the overall risk of revision for UKA, such as the revision centres usage rates or the fixation mode of the primary implant.
Population	All UKA and TKA patients in DKR from 1997-2017	All UKA and TKA patients in DKR from 1997-2017
Methods	Surgeries due to primary OA were included and complex surgeries were excluded. For co-morbidity, mortality and emigration information, the data were linked to the NPR and CPR. TKAs were propensity score matched 4:1 to UKAs. Outcome was assessed using cox PH regression with a shared gamma frailty component	Cohort from study I. Revision indication were assessed as individual outcomes. The failure patterns were determined using cox PH regression with a shared gamma frailty component. Median time to revision determined the pattern for timing.
Conclusion	Risk of Revision for UKA has significantly decreased over the last 20 years, nearing that of TKA, with a 1.1 % difference between the two in 3-year survival probability.	UKAs were largely revised on unspecific indications, whereas TKAs are revised for severe indications such as infection. However, the unspecific revision indications are decreasing in incidence for UKA.

Paper	III	IV
Aim	To determine any differences in OKS at 1-year follow-up between optimized TKA and UKA in AMOA patients	To identify any potential performance drops in: OKS, FJS, readmission- and complication rates, LOS, and revisions during UKA implementation.
Population	300 UKAs from an experienced UKA centre and the last 200 TKA surgeries with AMOA prior to implementation of UKA at a none UKA centre	The first 100 UKA patients after UKA implementation and the last 100 TKA patients with AMOA prior to UKA implementation at the same centre.
Methods	TKAs were retrospectively evaluated for AMOA on pre-operative radiographs. UKA and TKA were propensity score matched 1:1 and compared for change in OKS at 1-year follow-up and the proportion achieving PASS.	The last 100 TKAs with AMOA from study III and the first 100 UKAs performed by two surgeons were compared using OKS at 3, 12 and 24 months as repeated measurements. LOS, 90 day readmission and, complications and 2-year mortality- and revision rates were compared.
Conclusion	UKA patients were more likely to reach the PASS at 1 year and had a higher change score than TKA with an adjusted mean difference of 3 points.	We found no performance drop on any of the parameters we investigated. The PROMs were similar, and there was an equal number of revisions. LOS, risk of complications and readmission were lower for UKA, immediately after implementation, thus making UKA beneficial for both patient and surgeon even during implementation.

3 Author Contributions

Paper I

Mette Mikkelsen	Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Visualization, Project administration, Writing - original draft, Writing - review & editing.
Andrew Price	Conceptualization, Methodology, Supervision, Writing - review & editing.
Alma Becic Pedersen	Conceptualization, Methodology, Supervision, Writing - review & editing.
Kirill Gromov	Conceptualization, Supervision, Writing - review & editing.
Anders Troelsen	Conceptualization, Methodology, Data curation, Project administration, Supervision, Resources, Writing - review & editing.

Paper II

Mette Mikkelsen	Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Visualization, Project administration, Writing - original draft, Writing - review & editing.
Andrew Price	Conceptualization, Methodology, Supervision, Writing - review & editing.
Lasse Enkebølle Rasmussen	Data curation, Writing - review & editing.
Alma Becic Pedersen	Conceptualization, Methodology, Supervision, Writing - review & editing.
Kirill Gromov	Conceptualization, Supervision, Writing - review & editing.
Anders Troelsen	Conceptualization, Methodology, Data curation, Project administration, Supervision, Resources, Writing - review & editing.

Paper III

Mette Mikkelsen	Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Visualization, Project administration, Writing - original draft, Writing - review & editing.
Hannah Wilson	Conceptualization, Data curation, Writing - original draft, Writing - review & editing.
Kirill Gromov	Conceptualization, Supervision, Writing - review & editing.
Andrew Price	Conceptualization, Methodology, Supervision, Writing - review & editing.
Anders Troelsen	Conceptualization, Methodology, Project administration, Supervision, Resources, Writing - review & editing.

Paper IV

Mette Mikkelsen	Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Visualization, Project administration, Writing - original draft, Writing - review & editing.
Kirill Gromov	Conceptualization, Supervision, Writing - review & editing.
Andrew Price	Conceptualization, Methodology, Supervision, Writing - review & editing.
Anders Troelsen	Conceptualization, Methodology, Project administration, Supervision, Resources, Writing - review & editing.

4 Abbreviations and terminology

AMOA	Anteromedial Osteoarthritis
BMI	Body Mass Index
CI	Confidence Intervals
CPR	Central Patient Registry
DKR	Danish Knee Arthroplasty Register
FJS	Forgotten Joint Score
HR	Hazard Ratio
IQR	Inter Quartile Range
MIC	Minimal Important Change
MID	Minimal Important Difference
NJR	National Joint Registry of England and Wales
NPR	National Patient Registry
OA	Osteoarthritis
OKS	Oxford Knee Score
OR	Odds Ratio
PASS	Patient Acceptable Symptom State
PH	Proportional Hazard
PROM	Patient Reported Outcome Measure
SD	Standard Deviation
SMD	Standardized Mean Difference
TKA	Total Knee Arthroplasty
UKA	Unicompartmental Knee Arthroplasty

Aims

5

5.1 General Aims

The overall aim of this thesis was to describe the UKA's performance in three scenarios; First, its development over time. Second, its performance in an optimized set-up, or what can be achieved if current recommendations for practice are followed. Third, to determine if there is a performance drop during implementation.

5.2 Specific aims

Paper I
To describe any changes to revision rates for UKA in a national registry over the last 20 years. To find correlations between implant, surgical- and patient factors, and the risk of revision for UKA. To describe any changes to frequency of said factors over the last 20 years, and to describe the short term risk of revision for the current UKA and TKA practice?

Paper II
To determine the patterns and timing of failure for TKA and UKA in Denmark, and how these have changed over time. If the failure patterns for UKA are correlated to factors known to be correlated to the overall risk of revision for UKA.

Paper III
To compare OKS for TKA and UKA as treatment strategies, from the initial consultation till the end of hospital follow-up at 1 year post-OP.

Paper IV
To describe what can be expected during implementation of UKA, in regards to LOS, adverse events and the knee specific PROMs OKS and FJS.

6 Summary

6.1 Dansk

Unikompartmentiel knæ alloplastik er en behandlingsmulighed for patienter med knæartrose isoleret til ét ledkammer. Den medial unikompartmentielle knæ alloplastik(UKA) står for over 90 % af alle unikompartmentielle knæ alloplastikker, og er emnet i denne afhandling. Internationalt laves over 90 % af alle UKAer pga. primær anteromedial artrose (AMOA). UKA blev introduceret i 70'erne, men har historisk kæmpet med en højere revisionsrisiko end total knæ alloplastik (TKA). Over de sidste 10 år har vi set den stige i popularitet, i takt med den publicerede evidens har øget vores forståelse af hvilke patienter, der har glæde af den, og hvilke kirurgiske aspekter der har indflydelse på resultaterne. Endvidere har den øgede fokus på andre mål end revision, gjort os opmærksomme på de fordele UKA har sammenlignet med TKA.
I Danmark ser det ud til, at den øgede evidens har medført en fordobling i brugen af UKA over de sidste 10 år. UKA udgør nu 20 % af alle primære knæ alloplastikker, der laves i Danmark årligt. Denne nationale implementering af UKA, som en del af standard kirurgisk behandlingen af AMOA, er grundlaget for denne afhandling. Formålet med afhandlingen har været at beskrive UKA i tre scenarier: Først, at beskrive udviklingen i revisionsrisiko over tid. Dernæst, at beskrive hvordan den klare sig under implementering. Til sidst tilstræbte vi at beskrive, hvad man kan opnå med UKA, hvis man optimerer den som strategi sammenlignet med den hidtil udførte strategi, TKA.

To register studier med 20 års national register data havde til formål at beskrive ændringer i UKA patienters revisionsrisiko over de sidste 20 år sammenlignet med TKA patienters. De 20 års dataindsamling gjorde det muligt at undersøge ændringer i revisionsrisikoen over tid, og at identificere faktorer der har haft en indvirkning på revisionsrisikoen for UKA. Studierne var propensity score matchede, og vi brugte competing risk cox proportional hazard regression til at teste for forskel mellem de to grupper, effekten af forklarende variable samt revisionsrisiko for individuelle revisionsårsager. For at lave en fair sammenligning af aktuel praksis for UKA og TKA plottede vi individualiserede overlevelsessandsynligheder for den mest almindelige UKA og TKA patient.
To yderligere kliniske studier blev udført på hospitalsniveau, og sammenlignede UKA

med TKA patienter med AMOA på deres præoperative røntgenbilleder. Det første monitorerede UKAs resultater, i forbindelse med implementeringen, og sammenlignede resultaterne med TKA patienter fra inden implementeringen. Vi evaluerede behandlingerne i flere domæner; længeden af primær indlæggelsen, uønskede resultater som komplikations- og genindlæggelsesrater samt revision. Forskel mellem grupperne blev testet med multiple lineær- og logistisk regression. Endeligt undersøgte vi i studiet også patienternes oplevelse af deres postoperative forløb ved at indsamle svar på de knæsymptom specifikke spørgeskemaer; Oxford Knee Score (OKS) og Forgotten Joint Score (FJS) ved 3, 12 og 24 måneders opfølgningerne. Vi brugte mixed model regression til at undersøge for signifikant forskel. Det andet studie var et 2-center studie, der sammenlignede optimeret UKA praksis med optimeret TKA praksis ved at måle ændring i OKS ved 1 års opfølgningen. Derudover undersøgte vi chancen for at nå det "patient acceptable symptom state" (PASS). UKA patienter blev inkluderet fra et erfarent UKA hospital og TKA patienter fra et erfarent TKA hospital der ikke tilbød UKA. Igen propensity score matchede vi patienterne, og brugte multiple lineær- og logistisk regression til at teste for forskelle.

Tilsammen blev der indhentet data på næsten 100.000 primære knæ alloplastikker udført fra 1997 til 2018. Vi fandt et signifikant fald i revisionsrisiko for UKA, også når vi sammenlignede med TKA patienters revisionrisiko over de sidste 20 år. Faldet var korreleret til hospitaler med en høj andel af UKA operationer samt brugen af ucementerede fiksation. Faldet i revisioner skyldes primært et fald i revisioner for smerte og aseptisk løsning. Implementeringsstudiet fandt bedre resultater for UKA end TKA. 2-center studiet fandt en større forskel i OKS end tidligere rapporteret og en signifikant større chance for at opnå en score hvor den gennemsnitslige patient føler sig rask 1 år efter operationen for UKA patienter.

Kort sagt fandt vi at UKA, er sikker at implementere og giver bedre resultater end TKA allerede under implementeringen. Revisionsrisikoen for UKA er faldene, og nærmer sig den vi kender fra TKA. Et fald der er korreleret til nylige ændringer i UKA praksis, og repræsentere et fald i antallet af revisioner udført på uspecifikke indikationer. Faldet i revision på uspecifikke revisioner indikerer, at kirurgerne støtter sig op af evidensen på området. Og når UKA som strategi er optimeret har UKA patienterne som gruppe større chance for at nå et symptomniveau hvor de føler sig raske end TKA patienterne. Derfor mener jeg der er basis for evidensbaseret implementering af UKA på andre hospitaler, og at den øgede brug af UKA i Danmark er til patienternes fordel, om de vælger den eller ej. Fordi den øgede brug giver flere patienter muligheden for nemt at få afgang til UKA, og derved øges både den information der gøres tilgængelig for dem, men også de valg der er tilgængelige for dem i den patient centrerede behandlingsstrategi.

6.2 English

The unicompartmental knee arthroplasty is a treatment option for end-stage single compartment knee osteoarthritis. Medial unicompartmental knee arthroplasty (UKA) accounts for more than 90 % and is the procedure this thesis explores. Internationally, primary anteromedial osteoarthritis (AMOA) is the main indication for more than 90 % of all UKA surgeries. The UKA was introduced in the 1970s, but has struggled with higher revision rates compared to the alternative; total knee arthroplasty (TKA). In the last decade we have seen its popularity grow as the published evidence increased our understanding of who benefit from it and which surgical practice factors influence the outcome. There has been an increased emphasis on outcomes other than revision which has drawn attention to the many benefits of UKA compared to TKA.
In Denmark it seems that the increased amount of evidence for UKA have led to a rapid increase in UKA usage in the last decade. UKA now accounts for 20 % of the annual primary knee replacements performed in Denmark. The nation wide implementation of UKA as a standard part of surgical treatment of end-stage AMOA, is the foundation for this thesis. The aim of this thesis was to describe the UKAs performance in three scenarios; First, its development over time. Secondly, how it is performing during the implementation both nationally and at a unit level. Thirdly, to describe its performance in an optimized set-up, and give us an indication of what can be achieved if current recommendations for practice is followed.

Two registry studies on 20 years of registry data aimed to describe development in UKA revision risk over the last 20 years compared to TKA. To identify any changes in practice patterns which could potentially be the cause of any potential changes to risk of revision, and to determine any correlation between these practice changes and changes to revision indication patterns for UKA. The studies were propensity score matched and competing risk cox proportional hazard regressions were used to determine differences in risk of revision between UKA and TKA, any changes to this relationship over time, and any effect modifying factors. The same statistical approach was used to determine differences in risk of revision due to specific revision indications. Individualized survival probabilities for current UKA and TKA practice were plotted to determine a fair comparison relevant for evaluating the current UKA practice.

Two additional clinical comparative studies were performed on a unit levels. They compared UKA patients to TKA patients with AMOA on pre-operative radiographs. The first study monitored the UKAs performance during the implants implementation, at a unit with no prior history of UKA usage, and compared it to that of TKA patients from prior to UKA implementation. Performance was evaluated in several domains;

length-of-stay (LOS), adverse events such as complication- and readmission rates and revisions. Differences were tested using multiple linear- and logistic regression. Finally we monitored the recovery trajectory by collecting the joint specific patient reported outcome measurements (PROMs); Oxford Knee Score and Forgotten Joint Score at 3, 12 and 24 months follow-up. Difference in trajectory were determined using mixed model regression. The second study was a 2-centre study comparing UKA and TKA as strategies in their optimal set-up, using change in OKS from baseline to 1 year follow-up as out primary outcome, and determined difference in likeliness of reaching the patient acceptable symptom state (PASS). We included UKA patients from an experienced UKA design centre and TKA patients with AMOA on preoperative radiographs from an experienced TKA centre with no history of UKA usage. Again we propensity score matched the patients and used multiple linear- and logistic regression to calculate our adjusted estimates.

In total data was collected from almost 100 000 (10 000 UKA) primary knee replacements performed from 1997 to 2018. UKA had higher revision risks compared to TKA. We found a significant decrease in UKA revision risk over the last 20 years, and a corresponding reduction in difference between UKA and TKA revision rates. The decrease was correlated to an increase in high usage units and the use of cementless fixation for UKA, and was due to a decrease in revisions for pain and aseptic loosening. The implementation study found significantly better outcome for UKA compared to TKA. Lastly, we found larger than previously reported difference OKS between UKA and TKA when investigated as optimized strategies and significantly larger likeliness for UKA patients of categorizing themselves as being well one year after surgery.

In summary, we found UKA to be safe to implement without any significant performance drop. The revision rates for UKA are decreasing significantly nearing those reported for TKA. A change which is correlated to the resent changes in practice. The decrease is primarily caused by fewer revision on unspecific indication, showing that surgeons are adhering to evidence based practice. Lastly, we found patients are more likely to categorize themselves as well after receiving a UKA rather than a TKA. Thus I argue there is basis for evidence based implementation at other centres, and that the rapid increase in UKA usage in Denmark benefits the patients, whether of not they choose the UKA. Because it makes the UKA more readily available to patients and thus increase, not only the information available to to them, but also their treatment options in the shared decision making process.

Introduction

7

7.1 Introduction to Unicompartmental Knee Arthroplasty

Unicompartmental knee arthroplasties (UKA) were the first knee arthroplasties. In the 1970s the total knee arthroplasty (TKA) was introduced, and soon became the preferred method for knee replacement surgery while the UKA struggled with higher revision rates[1]. In the late 1980s, Kozinn and Scott proposed a set of highly restrictive indications for UKA surgery, believing this would increase its success rate[2]. However, subsequent studies were unable to find correlations to risk of revision for UKA when examining the effect of these restrictions. Research from the last decade points in a more inclusive direction[3], [4], which increases the UKA appropriate cohort from 6 %[5] of all primary knee arthroplasties to somewhere between 25 % and 47 % [3], [6].

The current indications for UKA are anteromedial osteoarthritis (AMOA) or spontaneous osteonecrosis of the knee (SONK)[7]. To categorize a knee as AMOA, it needs to have bone-on-bone OA in the anteromedial part of the medial compartment, a functionally intact anterior cruciate ligament and a functionally intact medial collateral ligament. Lastly, severe damage to the lateral faces of the patellofemoral joint (PFJ) with grooving and subluxations should be avoided[8]–[10]. Factors related to the surgeon and unit which should also be satisfied when using UKA are a high surgical UKA volume and a UKA usage rate of at least 20 % - and ideally above 30 % [11]–[15].

The publications on UKAs mentioned above have completely changed the understanding of who UKA candidates are. Thus the UKA candidate today is older and heavier and shows closer resemblance to TKA patients[16], [17]. The literature also concludes that patients undergoing UKA surgery recover faster, experience less pain, thus needing less pain medication short term, have shorter lengths-of-stay (LOS), fewer complications and readmissions, better functional outcomes, lower mortality rates, and the procedure is more cost-effective [18]–[24]. These findings have culminated in a meta-analysis of 60 studies published in 2019 comparing UKA and TKA on multiple outcome domains. The authors found UKA to be inferior in regards to risk of revision, but to be superior or were unable to report differences between the two on all other investigated domains[20]. The only domain not covered in the paper was cost-effectiveness, which was expertly covered in the TOPKAT RCT from 2019. TOPKAT found UKA to be a more cost-effective treatment option for end-stage AMOA, also when taking the increased risk of revision for UKA into account[24]. Hence, the higher revision rates is the only drawback of UKA, and is likely the reason for most national registries reporting national UKA usage rates of approximately 10 % [25]–[28]. Regardless of the higher revision rates, UKA usage has increased by more than 100 % since 2015, and now accounts for 20.4 % of all primary knee arthroplasties in Denmark[29]. The increased usage indicates danish surgeons have chosen a different interpretation of the available information than surgeons internationally and deemed the increased risk of revision to be acceptable when comparing it to the benefits of UKA. Another interpretation could be that the survival probabilities reported in the registries do not offer a fair and true comparison of TKA and UKA and overestimate the UKA revision risk for the current practice. In conclusion, as pointed out by Beard et al. in 2012[30], there is no clear consensus on treatment of end-stage AMOA.

The rapid increase UKA usage has presented us with a unique opportunity to monitor its impact on the registry reported revision rates - but also to investigate the implementation phase locally at a unit level. The implementation and potential learning curve for UKA surgery is poorly described in the literature, with only one study describing the learning curve for the current practice for UKA. They used a CUSUM analysis[31] to determine the learning curve. The acceptable failure rate was achieved after 29 cases and never exceeded the unacceptable rate [32]. Others have described learning curves for changes in surgical technique. Hamilton et al.[33] followed 445 patients treated by 4 surgeons measuring revision and reoperation percentages, and compared the first half of the patients with the last after implementation of the minimally invasive surgical approach. They found no significant difference but a trend towards decreased revision numbers in the last half of the patients. These studies were published prior to the introduction of the current guidelines for UKA patient selection, including the radiographic decision aid[10] and the introduction of the cementless UKA.

7.2 The challenges we face when comparing Unicompartmental- with Total Knee Arthroplasty

This topic deserves a more prominent place in the discussion for or against UKA especially in the context of revision as an outcome. Revision has historically been the most important outcome, next to only mortality, when evaluating the performance of arthroplasties. However, the comparison of TKA and UKA using revision introduces a multitude of challenges. Registries most commonly report crude unadjusted outcomes where they pool all the data across a time period. This results in an extraordinary amount of bias if used to compare two different procedures rather than to monitor and compare one type of procedure over time. The most evident is selections bias due to differences in patient characteristics between the two groups. Further, bias due to changes to practice and design over time needs to be taken into account. Bias is also introduced from UKAs done on the wrong indications and/or by surgeons who do not have sufficient UKA usage rates and volume to ensure the best possible outcome[12], [13], [34]. UKAs are also very likely to be revised wrongly e.g. due to pain, which has been shown to yield no improvements for the patients [35]. Kennedy et al.[34] showed that only 20 % of revised UKA knees had the primary surgery due to the right indications, and their subsequent revisions were also done on appropriate indications. These findings ties well into publications which show UKAs revision threshold is significantly lower than that of TKAs[36], [37].

7.3 Outcome measures for comparison of Knee Arthroplasty

Having established that implant survival is not suitable to stand alone when determining treatment success, we have seen an increased focus on other outcome measurements to evaluate knee arthroplasty. Other adverse outcomes commonly used are complication- and readmission rates, postoperative length-of-stay (LOS) and socio-economic impact. Patient-reported outcome measures (PROM) have become key element when evaluating outcomes of knee arthroplasty, and have also been adopted into several national registries[38]. PROMs fit well into the patient-centered ideology in medicine today, as they are purely patient-perceived outcomes. They are commonly categorized into generic and specific surveys. In registries, EuroQol 5 dimension health outcome (EQ-5D) and SF-12/36 are the most used generic surveys, with EQ-5D being incorporated in 6 national registries. The Oxford Knee Score (OKS) is one of the most common knee-specific surveys[38]. These specific surveys can further be split into domains such as function, pain, quality of life, etc. The resulting scores generate rich, high resolution information on their domains, which however can be hard to interpret and convey to patients and non-healthcare professionals. To facilitate this communication, interpretive tools are being developed and studied to gain an understanding on what influences patient satisfaction and perceived transition [39]–[44]. They divide the scores into two or more categories defined either by distribution or by using an anchor question to define thresholds[43]. The most common interpretive tools are the minimal important difference (MID), the minimal important change (MIC) and the patient acceptable symptom state (PASS). In this thesis, the MID and PASS for OKS is used. The MID is a between-groups estimate of the clinically relevant difference in change. Kvien et al. [43] defined PASS as "the highest level of symptom beyond which patients consider themselves well". Thus this pertains to the final score and is time dependant [41].

Considering this entire complex of measurements gives a more nuanced picture of the arthroplasties' performances and makes it possible for both patients and surgeons to determine the relative importance of each factor of reach individual.

7.4 Why is this body of work needed

With the increased UKA usage in Denmark there is a need for evaluating the past to determine factors which can help us reduce the revision rates of UKA. With any changes to practice of this magnitude, it is also important to monitor and evaluate developments in connection with these changes at short intervals, to ensure safety. Knowledge of UKA performance during implementation is important, to further promote evidence base practice. It is also a subject which is poorly described in the literature. The increase in usage began less than a decade ago[45], meaning there is still a potential for optimization, and it is therefor essential to know the benchmark for what we can achieve if we continue to utilize UKA as a dominant treatment strategy for end-stage AMOA and adhere to the recommended best practice long term. Lastly, the prevalence of knee osteoarthritis (OA) is increasing and is expected to increase further in coming decade[46], [47]. The increased prevalence will likely result in an increase in demand for knee replacements, making cost-effect an even more prominent part of the discussion on UKA vs. TKA. If funding doesn't increase with demand the UKA will become even more attractive as an alternative to TKA in treatment of end-stage AMOA, because it is the more cost-effective option[24]. Thus, implementation and subsequent increase usage as seen in Denmark could become a necessity in other countries.

8 Methods and Materials

8.1 Study Designs

The two registry-based studies (Paper I and II) were non-randomized cohort studies. Paper III and IV were prospective longitudinal cohort studies. For the registry studies, we received data from the Danish Knee Arthroplasty Register (DKR) from its implementation in 1997 till December 4, 2017. The data were linked to the National Patient Registry (NPR) and the central persons registry (CPR) for comorbidity and death and immigration information. The study was approved by the Danish Data Protection Agency (J No P-2020-71). Paper III was a 2-centre study baseline patient characteristics and pre-operative and 1 year OKS questionnaires were obtained from the centres' local PROMs databases. The study was approved by the Danish Data Protection Agency (J No VD-2018-313, I-Suite No 6560). The longitudinal prospective study included data from the same local database as the TKA data from paper III, and collected 3 months, 1 year and 2 years follow-up questionnaires. Here we also accessed pre-operative radiographs for the TKA patients and monitored local medical records for any readmissions, complications revisions or deaths. The study was approved as a quality control study by the hospital management (WZ17038300-2018-96/WZ17038300-2018-97) and the database is approved by the Danish Data Protection Agency (J No HVH-2012-048). No ethical approval was required for any of these studies.

8.2 Participants and Data Collection

National Knee Arthroplasty Registry Cohort (Paper I and II)

The cohort included all primary TKA and UKA surgeries due to primary OA reported to DKR from 1997 to 2017. Patient characteristics, surgical information on primary and revision surgery were accessed from DKR, 10-year Charlson comorbidity index (CCI) was calculated using NPR data[48]–[50]. Mortality and immigration status were accessed from CPR. Patients were excluded if they could not be linked to NPR and

CPR. We excluded complex surgeries (bone grafts and/ or component supplements) and included bilateral cases.

2-Centre Cohort (Paper III)

Patients were included from 2 centres. Dept. of Orthopaedic surgery, Copenhagen University Hospital Hvidovre recruited TKA patients, and Nuffield Orthopedic Centre, Oxford University Hospitals recruited the UKA patients. 200 TKA with AMOA from 2013-2016 were identified through retrospective analysis of pre-operative radiographs. 300 UKAs were available in the second centre's database within the same time period. If a patient had bilateral knee replacements, one was excluded at random. Only patients with both baseline and 1-year OKS were included. Baseline questionnaires were filled out in the out-patient clinic with the help of an instructor. The follow-up questionnaires were answered either by letter or online by a link sent by e-mail. If the patient did not answer the follow-up questionnaire, an instructor made a follow-up phone call and helped the patient fill out the questionnaire over the phone.

Longitudinal Cohort (Paper IV)

We included the last 100 patients from the TKA cohort in paper III and added the first 100 UKA performed by two surgeons at Dept. of Orthopaedic surgery, Copenhagen University Hospital Hvidovre during UKA implementation. Bilateral cases were handled as in paper III. Only patients with baseline OKS were included. The PROM collection was as described above in paper III.

UKA Usage rates and surgical volume

As part of Paper I and II usage rates and surgical volume of UKA are two essential surgical factors which is investigated for correlation to risk of revision. They were calculated annually for each unit. Thus they could switch categories from year to year. Unit UKA Usage rates were cut into none (no UKA surgeries that year), low (< 20 %) and high (≥ 20 %) based on previous publications on surgeon level usage[12]. Surgical UKA volume was cut into three corresponding categories using the median UKA volume for the units as the cut between high and low volume. Thus, none (no UKA surgeries that year), low (< 52) and high (≥ 52)[16].

8.3 Outcomes

Adverse outcomes and LOS

Revision is the primary outcome in paper I and II and a secondary outcome in paper IV. Revision is defined as the removal or exchange of any of the arthroplasty parts. In paper I and II, the revision status has been collected by DKR, to whom it is mandatory to report all revision knee arthroplasties, including the revision indication and implant type prior to and after revision. Mortality was accessed from CPR, where all fatalities in Denmark are reported to electronically. In paper IV, revision and mortality information were collected at the end of the study by searching the regional medical records. This means any potential revisions done in the western part of Denmark were unknown to us. Mortality status was complete due to the use of the CPR system. Further adverse event outcomes in paper IV included 90-day readmissions and complications and 2-year revision rates. Complications were defined as any contact with the hospital outside of standard follow-up visits. Any overnight stays within 90 days of the surgery were regarded as a readmission. In paper IV, we also used LOS as an outcome. LOS was defined by the number of overnight stays.

PROMs

Patient-reported outcome measurements are questionnaires designed to best describe the patient perceived symptom burden in a certain domain. Here we investigated knee specific PROMs. They are mainly used to describe change in symptoms or final outcome after an interventions. They are increasing in popularity and have been introduced into several national registries[38] and used as main outcomes in RCTs[24]. To aid interpretation of the scores, interpretive tools are also being developed for differences(MID), changes(MIC) and final outcomes(PASS). The tools are either designed to interpret the patient perceived transition (change) or satisfaction (final outcome). The change score tools aims to describes the patient perceived improvements/worsening objectively. Final score tools asks the patient to evaluate their current symptom state and evaluate that, which introduces their expectations from prior to surgery. Thus final outcome tools can change significantly over time depending on where they are in the recovery[41], and change score tools are sensitive to recall bias. In this thesis, we use the PASS and the MID. The PASS is defined as the score at which the patients feel well at a group level[51], and is thus using the final score. The MID interprets change scores, specifically the between-group differences and it can be either improvement or worsening. It is a measure for clinical significance in comparative studies[42].

Oxford Knee Score
The OKS is a 12 item knee-specific questionnaire with 2 domains; pain and function. Each question has 5 response options from 0(severe problems) to 4(no pain or disability). It is a 0-48 score (48 indicating no pain or disability). The OKS was not calculated if more than two items were missing (maximum one from each construct). In paper III, we use 1-year PASS value for OKS, which Ingelsrud et al.[39] calculated to be OKS = 30.18. The MID value for OKS is 5 points[42]

Forgotten Joint Score
The FJS is a joint-specific awareness questionnaire with 12 items and 5 response options from 0 (never aware of the joint) to 4 (mostly aware of the joint). It is calculated as the mean of the scores, which is then multiplied by 25. This score is then subtracted from 100 for the final score. Resulting in the least joint awareness translates to a score of 100. The FJS was not calculated if more than four items were missing.

8.4 Statistics

Propensity score matching and multiple imputation

In all four studies we lack randomization, making them all liable to substantial selection bias from both known and unknown sources. There are a few ways of addressing the selection bias. The most used methods are, adjusting for confounders in regression analysis or by matching. In paper I, II and III our cohorts allowed for matching. We used propensity score matching, which if done properly produce no significant difference in estimates compared to RCTs in surgical research [52]. Propensity score matching demand complete data for all matching variables. There are generally two approaches to achieve this. The first is excluding any observations with missingness, the complete data approach. The second approach is imputing the missing variable with a best guess based on auxiliary variables, multiple imputation. Multiple imputation has been shown to reduce bias independently of the proportion of missingness, but to be dependant on the quality of the the auxiliary variables [53]. We had a large number of high quality auxiliary variables and chose to impute missing data[48]. To propensity score match a propensity score is calculated from the regression estimates of the matching variables' effects on the exposure. The matching itself can be done by a number of methods. We used the nearest neighbour method, a proximity search which locates the control patient closest to the treatment patient. The matching is seen as sufficient if matching variables have a standardized mean difference of 0.1 or less[54].

Survival analysis

In papers I and II, the primary outcome is time to revision for UKA and TKA, respectively. We investigated this using cox proportional hazard (PH) regression. Cox regression models are among the most commonly used survival analysis' and allows us to investigate the outcome adding multiple prognostic covariates. The model works under the PH assumption, which dictates that the effect of a variable is constant over time. Schoenfeld's Residuals were used to investigate the PH assumption[55], [56]. Interactions were investigated using likelihood ratio testing and added to the model when significant. To adjust for bilateral cases, a shared gamma frailty component was added as a random effect to the models, now being a model with two sources of variance, one fixed and one random[57]. Because of the competing risk from mortality, graphical presentations of the cumulative cause-specific incidence were done using the Nelson-Aalen estimator, a non-parametric estimator of the cumulative hazard function.

Multiple and Logistic Regression models

In paper III, the primary outcome is a continuous score. To adjust for residual bias from the propensity score matching we used multiple linear regression, which allows us to add confounders as fixed effects, to calculate the adjusted mean difference and OKS change score at 1 year follow-up[58]. Any difference in the likeliness of achieving PASS, a dichotomous outcome, was determined using logistic regression. These methods were also used in paper IV to calculate differences in LOS and the risk of complications. In paper IV, the inclusion of confounders was particularly important, since we did not propensity score match the groups.

Repeated measurements and mixed effects models

In paper IV OKS and FJS were collected as prospective longitudinal outcome at baseline, 3, 12 and 24 months follow-up. Making it possible to investigate the development over time. To handle the repeated measurements we did linear mixed modelling. The covariates gender, BMI, age and ASA scores were included as fixed effects. To account for the correlation of the repeated measurements and possible changes in variances over time we assumed an unstructured covariance pattern, and thus used an unstructured correlation matrix in the model[59]. This approach allows for the correlations between measurements on the same patient to change over time, while still adjusting for known confounders. Wald's test was used to test overall difference between the two treatments' score trajectories.

Table 8.1: Comparison of crude and matched data. Standardized mean difference (SMD) of 0.1 or less indicates balance between groups.

Matching variables		Crude Data TKA	Crude Data UKA	SMD	1:4 Matched Data TKA	1:4 Matched Data UKA	SMD
Matching variables	N	84738	9639		38556	9639	
	Sex (male)	31418(37.1)	4320 (44.8)	0.158	17241 (44.7)	4320 (44.8)	0.002
	Age at Surgery	69.53 (9.24)	65.68 (9.28)	0.448	66.15 (8.95)	65.68 (9.28)	0.084
	Weight	85.06 (18.63)	84.71 (17.54)	0.020	85.05 (16.84)	84.71 (17.54)	0.020
	Date at Surgery			0.368			0.125
	1997-2001	7131 (8.4)	194 (2.0)		1204 (3.1)	194 (2.0)	
	2002-2006	15648 (18.5)	1405 (14.6)		4287 (11.1)	1405 (14.6)	
	2007-2011	28685 (33.9)	2947 (30.6)		12605 (32.7)	2947 (30.6)	
	2011-2017	33274 (39.3)	5093 (52.8)		20460 (53.1)	5093 (52.8)	
	Alignment			0.625			0.125
	$\leq$ 4°(varus)	49306 (58.2)	7784 (80.8)		30905 (80.5)	7784 (80.8)	
	5-10°(neutral)	23240 (27.4)	1704 (17.7)		6986 (80.5)	1704 (17.7)	
	$\geq$ 11°(valgus)	11058 (13.0)	35 (0.4)		150 (0.4)	35 (0.4)	
	Not examined	1134 (1.3)	116 (1.2)		515 (1.3)	116 (1.2)	
	CCI			0.064			0.016
	0: None	51583 (60.9)	6120 (63.5)		24252 (62.9)	6120 (63.5)	
	1-2: Mild	19763 (23.3)	2094 (21.7)		8441 (21.9)	2094 (21.7)	
	3-4: Moderate	10465 (12.3)	1163 (12.1)		4739 (12.3)	1163 (12.1)	
	$\geq$ 5: Severe	2927 (3.5)	262 (2.7)		1124 (2.9)	262 (2.7)	
	Unit type (Public)	77921 (92.0)	8791 (91.2)	0.027	35165 (91.2)	8791 (91.2)	< 0.001
Non-Matching variables	AKSS-f	48.95 (18.84)	57.49 (17.08)		51.53 (17.95)	57.49 (17.08)	
	Usage rate						
	0 % None	26702 (31.5)	0 (0.0)		11518 (29.9)	0 (0.0)	
	1-20 % Low	48630 (57.4)	5033 (52.2)		22179 (57.5)	5033 (52.2)	
	> 20 % High	9406 (11.1)	4606 (47.8)		4859 (12.6)	4606 (47.8)	
	Surgical volume						
	0: None	26702 (31.5)	0 (0.0)		11518 (29.9)	0 (0.0)	
	1-51: Low	4277 (50.5)	4446 (46.1)		18838 (48.9)	4446 (46.1)	
	$\geq$: High	15264 (18.0)	4606 (47.8)		8200 (21.3)	4606 (47.8)	
	Fixation mode						
	Cemented	63043 (74.4)	7153 (74.2)		27675 (71.8)	7153 (74.2)	
	Cementless	5823 (6.9)	2393 (24.8)		2735 (7.1)	2393 (24.8)	
	Hybrid	15576 (18.4)	47 (0.5)		8015 (20.8)	47 (0.5)	
	NA	296 (0.3)	46 (0.5)		131 (0.3)	46 (0.5)	

Data is in number (%) or mean (standard deviation). CCI; Charlson Comorbidity Index, AKSS-f; American Knee Society Score (function)

Results

9

9.1 Cohorts

National Knee Arthroplasty Registry Cohort (Paper I and II)

There has been reported 129183 primary and revision knee arthroplasty surgeries to DKR from 1997 to 2017. After inclusion and exclusion criteria being applied to the cohort, a total of 94377 primary TKA and UKA procedures done due to primary OA were included in the cohort (Figure 9.1).

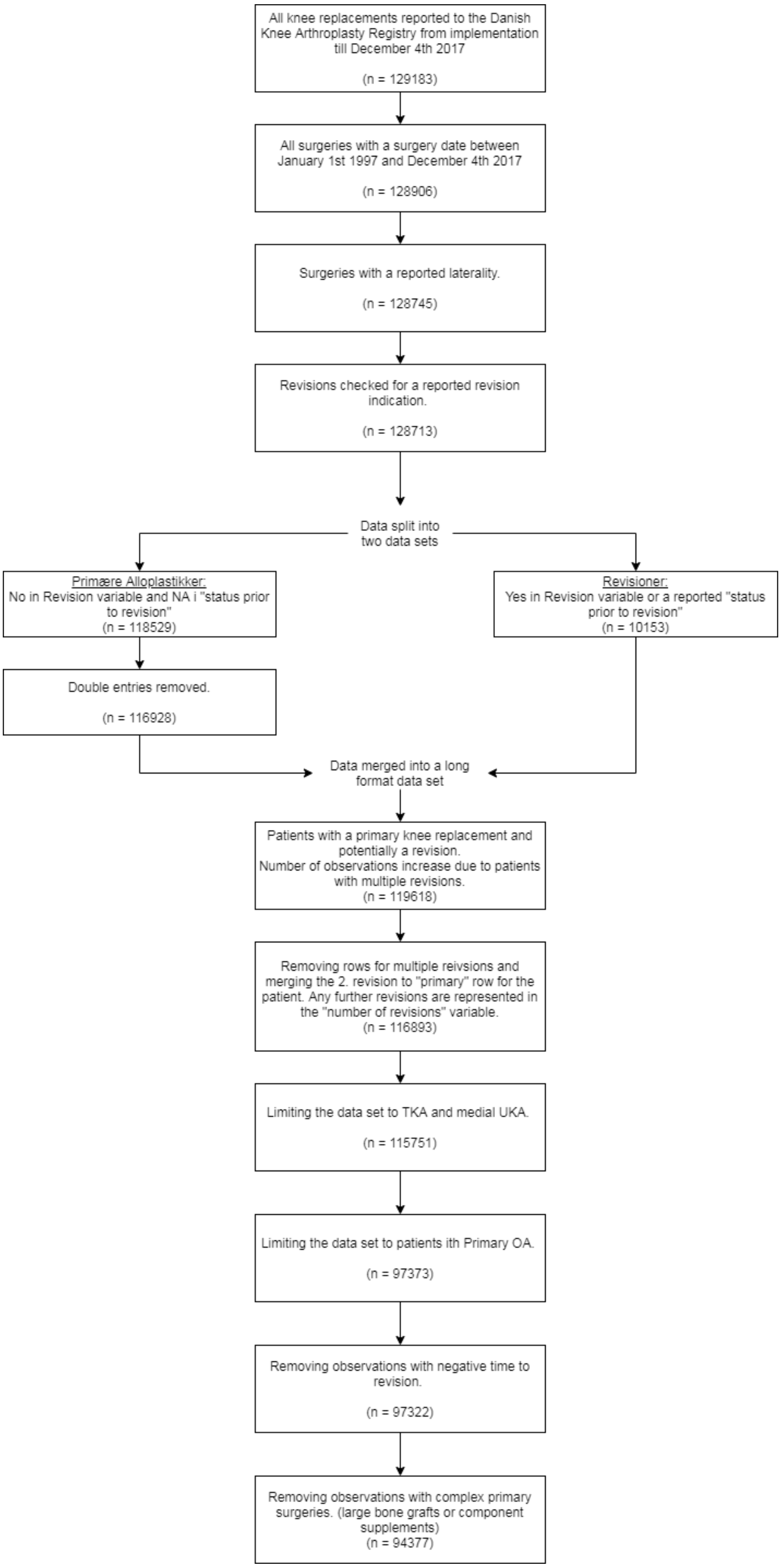
To limit selection bias, we propensity scored the cohort in a 1:4 ratio, resulting in a matched cohort of 48195 (9639 UKA) knees. Of these 8735 knees were bilateral cases. All matching variables except for date of surgery achieved balance between the two treatments. Date of surgery had a SMD of 0.125, which was a reduction of more than 100 % compared to before matching(Table 8.1).

Table 9.1: Paper III: Baseline (crude) and Propensity Score Matched demographics for patients having medial unicompartmental knee arthroplasty (UKA) or total knee arthroplasty (TKA). Changes in TKA from crude to matched data are due to multiple imputation of missing values.

	Crude Data			1:1 Matched Data		
	TKA	UKA	SMD	TKA	UKA	SMD
N	301	200		200	200	
Age	67.92 (9.94)	67.47 (9.21)	0.047	66.83 (9.87)	67.47 (9.21)	0.066
BMI	30.72 (5.65)	30.13 (5.34)	0.107	30.37 (5.72)	30.10 (5.33)	0.047
OKS	20.99 (7.33)	23.55 (6.53)	0.369	23.36 (6.87)	23.55 (6.53)	0.029
Sex (F)	147 (48.8)	107 (53.5)	0.093	106 (53.0)	107 (53.5)	0.010
ASA			0.154			0.045
1:	45 (15.0)	34 (17.4)		37 (18.5)	35 (17.5)	
2:	221 (73.4)	130 (66.7)		133 (66.5)	132 (66.0)	
3:	35 (11.6)	31 (15.9)		30 (15.0)	33 (16.5)	

Data is in number (%) or mean (standard deviation). SMD, standardized mean difference; BMI, body mass index; OKS, pre-operative Oxford Knee Score; F, Female; ASA, American Society of Anaesthesiologists.

Figure 9.1: Patient selection for Paper I and II



2-Centre Cohort (Paper III)

The 2 centres contributed with 501 patients (200 TKAs), which were then propensity score matched on age, sex, BMI, baseline OKS and ASA scores. Prior to matching, there were unbalance for BMI, baseline OKS and ASA, with the UKAs being heavier with lower baseline OKS and a larger proportion of ASA group II. After matching, balance was achieved for all variables (Table 9.1)

Longitudinal Cohort (Paper IV)

TKA inclusion was conditioned on having answered the preoperative PROM questionnaire (85,6%) and then having AMOA on preoperative radiographs (39.4%). All UKA patients filled out the preoperative questionnaire, and AMOA was assumed to be true for all UKA, since it determines a patients' eligibility for the UKA[10]. Baseline differences were present for age, ASA grade and Kellgren-Lawrence categories[60] (Table 9.2).

Table 9.2: Paper IV: Baseline demographics for TKA and UKA patients, including standardized mean difference.

	UKA	TKA	SMD	Missing (%)
N	100	100		
Sex (Female)	56 (56)	54 (54)	0.040	0 (0.0)
Age	63.94 (10.45)	67.57 (9.65)	0.361	0 (0.0)
Pre-OP OKS	23.18 (6.69)	22.74 (6.61)	0.067	0 (0.0)
Pre-OP FJS	20.25 (13.65)	20.40 (16.71)	0.010	0 (0.0)
BMI	30.04 (5.63)	30.73 (5.30)	0.126	1 (0.5)
ASA			0.222	2 (1.0)
1:	21 (21.2)	15 (15.2)		
2:	64 (64.6)	63 (63.6)		
3:	14 (14.2)	21 (21.2)		
Kellgren-Lawrence			0.500	34 (17.0)
1:	0 (0.0)	0 (0.0)		
2:	4 (4.3)	0 (0.0)		
3:	41 (44.1)	20 (27.4)		
4:	48 (51.6)	53 (72.6)		

Data is in number (%) or mean (standard deviation). SMD, standardized mean difference; OKS, Oxford Knee Score; FJS, Forgotten Joint Score; ASA, American Society of Anesthesiologists Classification

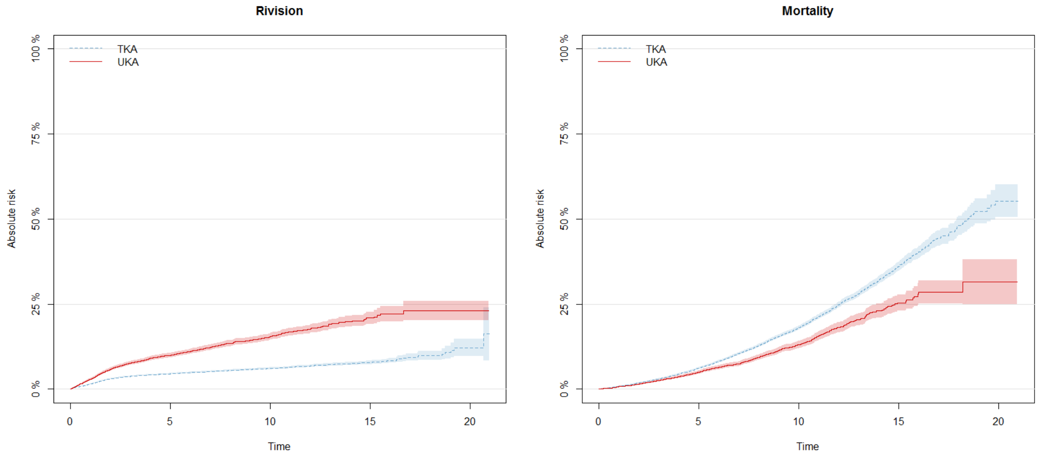


Figure 9.2: Overall Cumulative Incidence (Absolute risk) for Revision (left) and Mortality (right) for TKA and UKA.

9.2 Changes in revision rates over the last 20 years (Paper I)

The 20-year absolute risk of revision was higher for UKA(cumulative incidence 23.0, CI 95 % 20.2-25.9) than for TKA (cumulative incidence 11.9 ,CI 95 % (9.8-13.9)(Figure 9.2). To determine any changes over time, the cohort was cut into 4 groups based on the year of primary surgery; 1997-2001, 2002-2006, 2007-2011 and 2012-2017. Plotting the absolute risk of revision for the time intervals showed a decrease in risk of revision for UKA, but no visible development for TKA. To test if this is due to residual confounding or effect modifications, a cox PH regression for each time group was done, which showed a significant decrease in 3-year adjusted HR with the UKA revision risk nearing that of TKA (Figure 9.4).

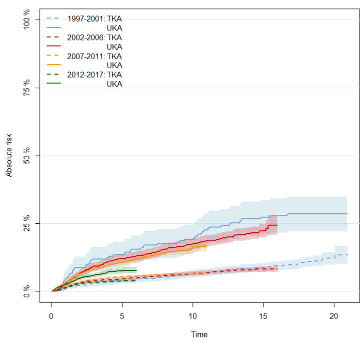


Figure 9.3: Cumulative Incidence (Absolute Risk) for revision of TKA and UKA categorized by year of surgery.

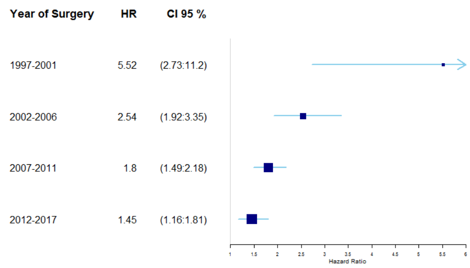


Figure 9.4: Forest plot for HR (CI 95 %) between TKA and UKA for different intervals of surgery year.

9.3 Factors influencing risk of Revision for UKA(Paper I)

Having shown a decrease in absolute risk of revision for UKA, we wanted to find factors that could be correlated to this decrease. To that end, we tested all known confounder and found fixation mode, surgical UKA volume and UKA usage rates at a unit level to be effect modifiers, making them the most likely targets. Patient-specific confounders had equal effects on UKA and TKA, thus in a propensity scored cohort, they are unlikely to be the main effects.

Fixation mode

The effect modification for fixation is large, with cementless TKA patients doing significantly worse compared to cemented TKA påtients (HR 1.65, CI 95 % 1.43-1.91). For UKA patients, the opposite it true, with cementless UKA patients doing significantly better (HR 0.60, CI 95 % 0.46-78)(Figure 9.5). This results in an effect modification with 20-year sub-HR 1.78 (CI 95 % 0.52-6.09) for cementless TKA vs. cementless UKA and sub-HR 4.87 (CI 95 % 1.55-15.3) for cemented TKA vs. cemented UKA.

UKA Usage Rates and Surgical Volume

High UKA usage rates significantly decreased the risk of revision for UKA (HR 0.72, CI 95 % 0.63-0.82). The TKA revision rates were not significantly correlated to UKA usage rates (HR 0.95, CI 95 % 0.81-1.13) (Figure 9.6). As an effect modifier, volume was similar to usage, with a significant effect on UKA(HR 0.68, CI 95 % 0.59-0.78), but no significant effect on TKA(HR 0.94, CI 95 % 0.82-1.07) (Figure 9.7).

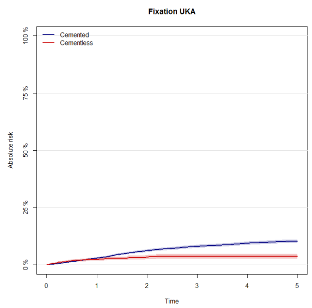


Figure 9.5: Risk of revision for UKA by fixation.

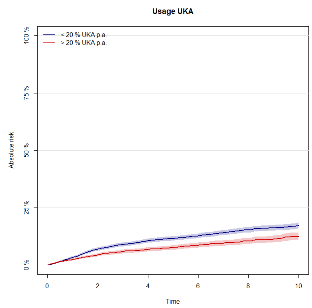


Figure 9.6: Risk of revision for UKA by usage.

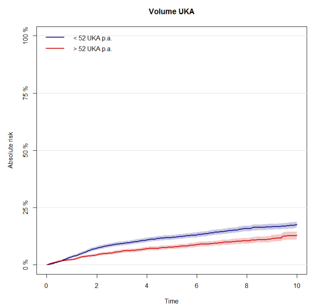


Figure 9.7: Risk of revision for UKA by volume.

Changes to effect modifiers over time.

Fixation, usage and volume were all correlated to the risk of revision for UKA, but for them to be a likely contributor to the decrease in risk of revision for UKA, the frequency of protective factors need to have increased over time parallel to the decreasing revision risk. Volume is influenced by the trend of merging smaller hospitals to bigger units over the years, meaning the number of small public units has decreased. Parallel to this decrease, there has been an increase in number of private units, which are all small volume units, making unit volume complex to interpret over time. What we have seen is a rapid introduction of the cementless UKA in 2014, with more than 80 % of UKAs being cementless in 2017 (Figure 9.8). For usage, the number of low usage units peaked in 2008 and have been decreasing since then. The number of high usage units has been increasing exponentially since the start of the 21st century, and is now the most common unit type(Figure 9.9).

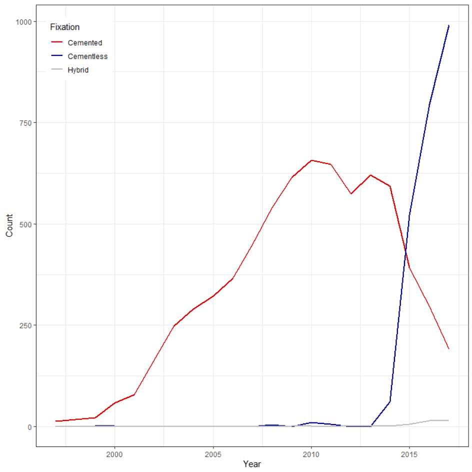


Figure 9.8: Unit frequency, Fixation.

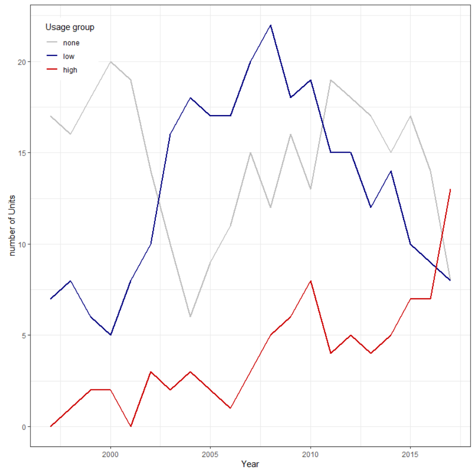
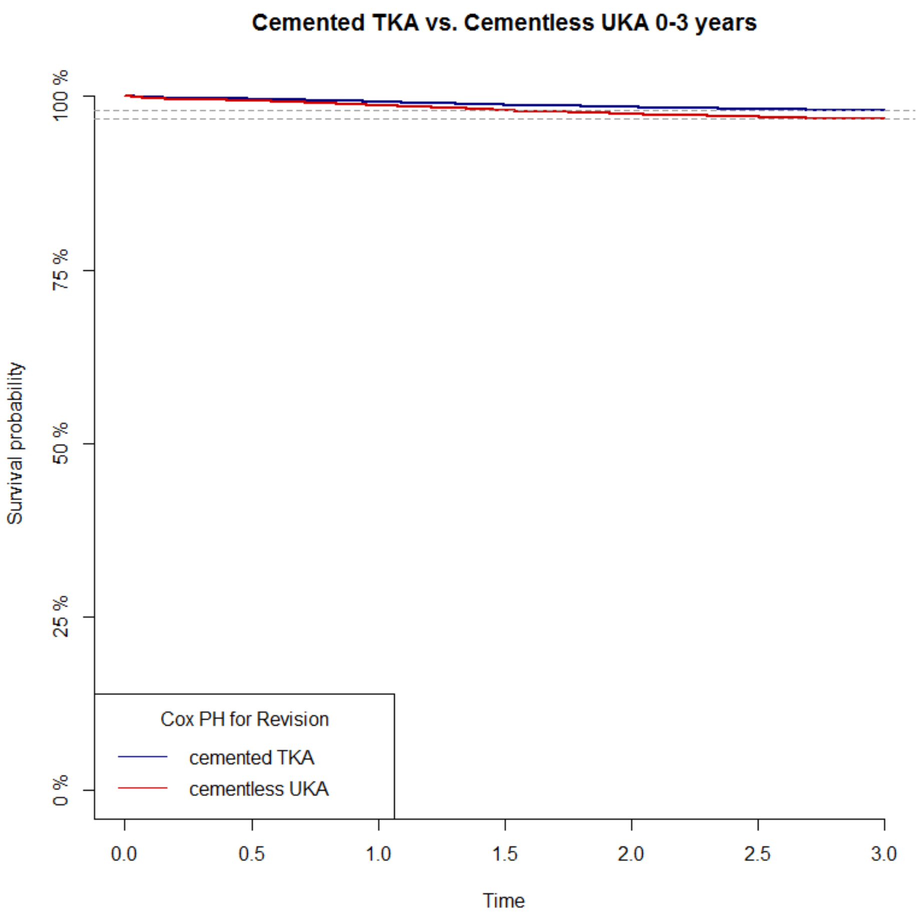


Figure 9.9: Unit frequency, Usage.

Current typical UKA and TKA practice.

With the recent changes to fixation mode and usage rates, we can plot the individualized survival probability for the current practice, and compare them to determine the revision rates to be expected from it. The most common practice for TKA is a cemented fixation at a high usage unit, resulting in a comparison of a 66 year old female with varus knee and CCI = 0, having cemented TKA vs. cementless UKA at a high usage unit. This showed a 1.1 % difference in 3-year survival probability between TKA and UKA(Figure 9.10).

Figure 9.10: Cox PH regression 3-year survival probability for revision for 66 year old female patients with varus knee and CCI = 0, having cemented TKA vs. cementless UKA at a high usage unit.



9.4 Revision Patterns and Timing (Paper II)

Overall TKA and UKA Revision Patterns and Timing.

DKR provides surgeons with 10 options as indications for the revision of the knee replacement. Using these, we calculated the HR for each indication, with death and all other revision indications as competing risks. Aseptic loosening was the most common indication for both treatments. For TKA patients infection was the second most common indication, showed that regardless of the overall higher risk of revision for UKA, the cause specific risk of revision due to infection was HR 0.53 (CI 95 % 0.39-0.72) in favour of UKA. For UKA patients the second most common indication was pain, something which was very rare for TKA, which is reflected in the HR of 5.92 (CI 95 % 4.90-7.14) (Table 9.3). Adding a patella component or having a bearing failure on the patella for UKA are very rare events, so is OA progression for TKA, making the HR for these categories less reliable and relevant.

Table 9.3: Ranked revision indication and 20-year hazard ratios for TKA vs. UKA.

	TKA		UKA		
	Rank	N (%)	Rank	N (%)	HR (CI 95 %)
Loosening	1	553 (29.5)	1	270 (26.7)	2.08 (1.79-2.41)
Infection	2	405 (21.6)	6	47 (4.7)	0.53 (0.39-0.72)
Instability	3	335 (17.9)	5	81 (8.0)	1.05 (0.82-1.35)
Pain	4	195 (10.4)	2	268 (26.5)	5.92 (4.90-7.14)
Other	5	142 (7.6)	4	129 (12.8)	3.89 (3.05-4.96)
Secondary Patella	6	102 (5.4)	10	2 (0.2)	0.08 (0.02-0.33)
Unknown	7	65 (3.5)	7	43 (4.3)	2.80 (1.89-4.14)
Bearing failure tibia	8	43 (2.3)	8	31 (3.1)	3.15 (1.97-5.04)
Bearing failure patella	9	26 (1.4)	9	3 (0.3)	0.50 (0.15-1.67)
OA Progression	10	7 (0.4)	3	136 (13.5)	85.0 (39.68-182.2)

The rankings show that TKA and UKA are revised on different indications, but does that mean that the timing is different as well? Overall, UKAs are revised 6 months later than TKA with median survival times of 1.55 (IQR 0.78-3.35) and 2.05 (IQR 0.95-5.08), respectively. But looking at cause-specific median time to revision we do not see clear differences apart from revision reasons which are exclusive to one type of implant.

Failure patterns for UKA depending on Fixation mode and usage rates.

In paper I we determined fixation mode and usage rates were correlated to risk of revision. They are also correlated to the revision indication pattern. For both fixation mode and usage rates, we see significant differences in the incidence of revisions due to pain and aseptic loosening(Table 9.4 and 9.5).

Table 9.4: Ranked revision indication and hazard ratios for Cemented vs. Cementless UKA.

	Cemented		Cementless		HR (CI 95 %)
	Rank	N (%)	Rank	N (%)	
Loosening	1	264 (28.2)	7	4 (6.2)	0.29 (0.10-0.81)
Pain	2	260 (27.8)	5	6 (9.4)	0.40 (0.17-0.94)
OA Progression	3	128 (13.7)	4	7 (10.9)	0.82 (0.36-2.00)
Other	4	105 (11.2)	1	23 (35.9)	1.43 (0.74-2.78)
Instability	5	71 (7.6)	2	9 (14.1)	1.13 (0.50-2.53)
Unknown	6	40 (4.3)	8	1 (1.6)	0.79 (0.09-7.13)
Infection	7	38 (4.1)	2	9 (14.1)	1.03 (0.09-12.00)
Bearing failure tibia	8	25 (2.7)	6	5 (7.8)	2.63 (0.51-13.53)
Bearing failure patella	9	3 (0.3)	9	0 (0.0)	NA
Secondary Patella	10	2 (0.2)	9	0 (0.0)	NA

Combining these factors correlation to revision indications (Table 9.4 and 9.5) with the increase in use of cementless fixation and the number of high usage unit, we are expecting to see an overall change in revision indication pattern. What we find are decreases in the number of revisions done due to pain and aseptic loosening, and stable numbers for all other indications.

Figure 9.11: Changes to number of revisions due to specific indications over time.

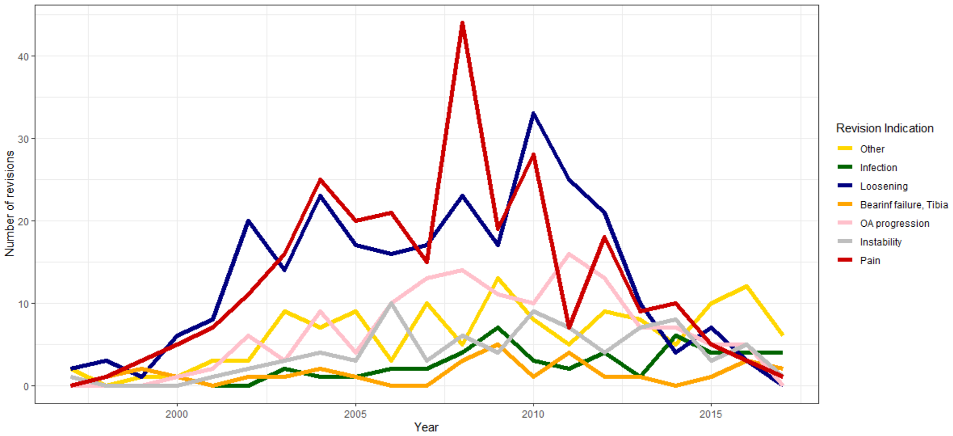


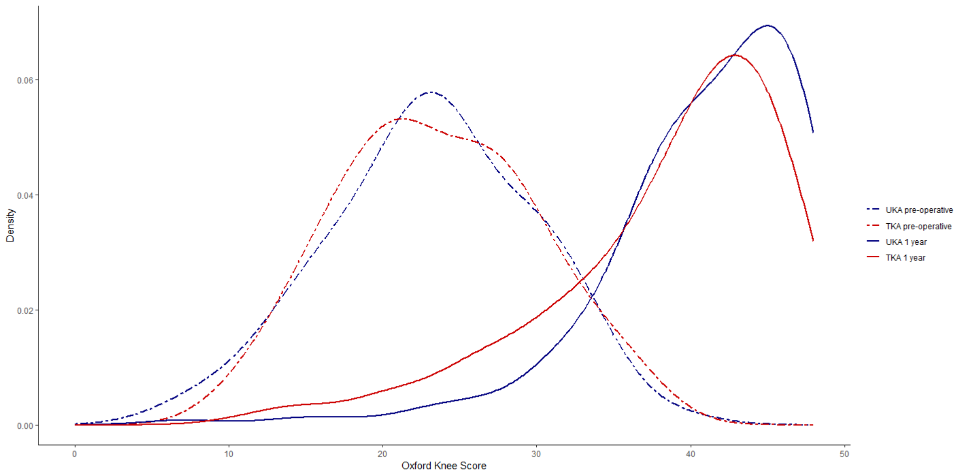
Table 9.5: Ranked revision indication for High, Low or No UKA usage at the revision unit. Hazard ratios comparing No and low usage to high usage units.

	None		Low		High		HR (CI 95 %)
	Rank	N (%)	Rank	N (%)	Rank	N (%)	
Overall		125 (12)		598 (59)		285 (28)	0.78 (0.68-0.90)
Loosening	1	45 (36.0)	2	172 (28.8)	3	53 (18.6)	0.51 (0.37-0.70)
Pain	2	32 (25.6)	1	179 (29.9)	2	56 (19.6)	0.67 (0.50-0.91)
OA Progression	3	18 (14.4)	3	72 (12.0)	4	46 (16.1)	0.74 (0.51-1.08)
Other	6	4 (3.2)	4	60 (10.0)	1	65 (22.8)	1.86 (0.96-3.61)
Instability	5	9 (7.6)	5	44 (7.4)	5	28 (9.8)	0.90 (0.55-1.49)
Unknown	4	13 (10.4)	7	18 (3.0)	6	12 (4.2)	0.87 (0.43-1.75)
Infection	7	2 (1.6)	6	33 (5.5)	6	12 (4.2)	0.36 (0.11-1.18)
Bearing failure tibia	7	2 (1.6)	8	16 (2.7)	6	12 (4.2)	1.24 (0.54-2.85)
Bearing failure patella	9	0 (0.0)	9	2 (0.3)	9	1 (0.4)	NA
Secondary Patella	9	0 (0.0)	9	2 (0.3)	10	0 (0.0)	NA

9.5 Difference in OKS between TKA and UKA in their optimal set-up (Paper III)

Plotting the pre-OP and 1-year OKS for the propensity score matched cohort we see similar baseline score distributions, but for the 1-year follow-up, we see a more extreme negative skewing for the UKA strategy's distribution, indicating a larger proportion of patients reaching very high OKS (Figure 9.12). The adjusted mean difference in change score at 1-year follow-up between the two treatments was 3.0 (CI 95 % 1.4 - 4.6, p < 0.001) points in favour of UKA. UKA patients reached a mean change score of 18.57 (10.42 - 26.72), and TKA patients reached OKS = 15.55 (7.39 -23.71). Patients treated with UKA were also significantly more likely to reach the PASS (OR = 3.67, CI 95 % 1.73 - 8.45, p = 0.00119) corresponding to 94.5 % of UKAs and 84.5 % of TKAs.

Figure 9.12: Paper III: Score distributions for baseline and 1 year follow-up OKS, stratified by treatment strategy.



9.6 Performance during implementation of UKA (Paper IV)

Adverse events and Length of stay.

LOS was significantly shorter for UKA patients with an adjusted mean difference of -0.93 days (CI 95 % -1.21:-0.64, p-value < 0.0001)). UKA patients stayed 1.13 (0.77) days and TKAs stayed 2.02 (1.04) days. Thus the likeliness of staying two or more nights was significantly larger for TKA (OR 12.4 (CI 95 %: 5.89-28.0, p-value = < 0.0001), corresponding to 74 % of TKA patients and 23 % of UKA patients.
Complications were also more common for TKA patients (OR 2.48, CI 95 %: 1.17 - 5.48, p-value 0.020)). Complications directly linked to the surgery were two incision infections and a deep vein thrombosis. Readmissions and revisions were rare, thus

only investigated descriptively (Table 9.6). Each group had 2 revisions, all between one and two years follow-up. The TKAs were both revised due to aseptic loosening. The UKAs were revised due to instability or progression of osteoarthritis in the lateral compartment.

Table 9.6: Paper IV: Adverse event counts. Readmissions and complications are included if within 90 days of the surgery. Complication severity is categoried using the Clavien-Dindo classification[61]. Revisions are 2-year follow-up.

		UKA	TKA
Number of patients		100	100
Readmissions		10	16
Readmission Indications			
	Surgical	1	5
	Medical	9	11
Complications		17	37
Complication severity			
	Grade I	13	28
	Grade II	3	7
	Grade III	1	2
	Grade IV	0	0
Revisions		2	2

PROMs 2-Year Trajectory

Forgotten Joint Score

UKA patients recover faster than TKA patients the first 3 months, after which the speed of improvement is similar for both groups. If we look at the mixed model regression, we see little to no difference at 3 months, but an increase after that and at 2 years, the difference is 5 points (Table 9.7).

Oxford Knee Score

The Oxford knee score's distribution is negatively skewed at both 12 and 24 months follow-up, why the plot shows the median OKS. Here we see a rapid increase in OKS for UKA compared to TKA. After that there are no further improvements for the UKA patients and at 24 months the TKAs have caught up, and the two are indistinguishable (Figure 9.13). The mixed effects model reports a statistically significant difference, which however never exceeds half a point(Table 9.7).

Figure 9.13: Paper IV: **Left:** Median OKS development over time. **Right:** Mean FJS development over time. Data collection at 3, 24 and 48 months follow-up.

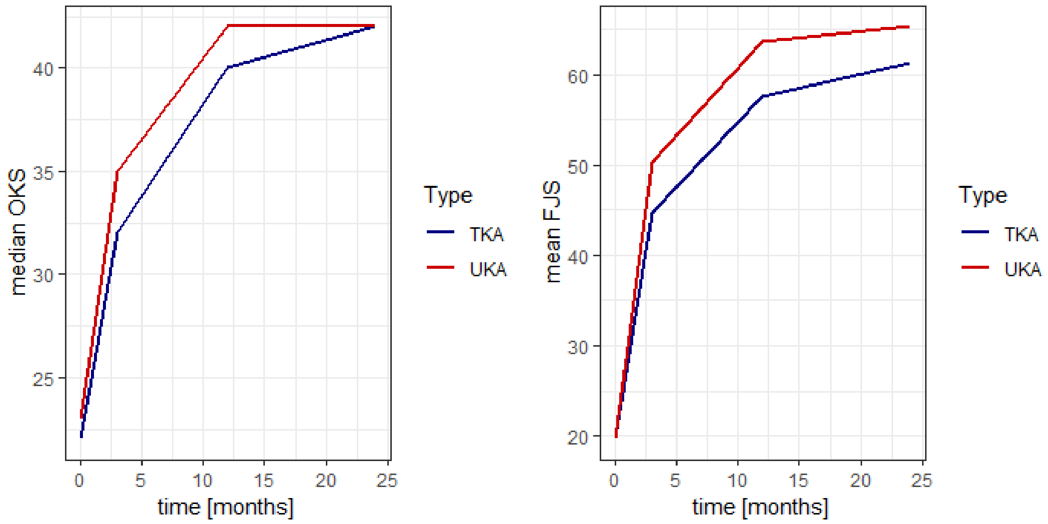


Table 9.7: Mixed model regression result for Oxford Knee Scores stratified by treatment. Presented as mean adjusted change score from pre-operative scores and corresponding CI 95 % . P-value is from multivariate Wald's test.

	Forgotten Joint Score		
	UKA (CI 95 %)	TKA (CI 95 %)	p-value
3 months	32.17 (26.63-37.72)	32.79 (24.51-41.07)	
12 months	41.97 (35.69-48.25)	37.42 (31.44-43.41)	
24 months	44.27 (37.76-50.78)	38.93 (32.98-44.89)	
			< 0.0001
	Oxford Knee Score		
	UKA (CI 95 %)	TKA (CI 95 %)	p-value
3 months	10.05 (8.30-11.81)	10.55 (7.91-13.19)	
12 months	15.34 (13.46-17.21)	14.87 (13.13-16.61)	
24 months	15.11 (12.90-17.32)	14.42 (12.38-16.45)	
			<0.0001

10 Discussion

The general aim of this thesis was, as described in chapter 5, "To describe the UKA's performance in three scenarios; First, its development over time. Second, its performance in an optimized set-up, or what can be achieved if current recommendations for practice are followed. Third, to determine if there is a performance drop during implementation."

10.1 Changes in UKA practice patterns, a potential reason for decreased UKA revision risk

In paper I, the registry study, we found an overall decrease in risk of revision for UKA over the last 20 years, but no significant development for TKA (Figure 9.3). This development has come in parallel to large changes in practice patterns. We found fixation mode, unit UKA volume and usage rates to be the most influential changes to the practice patterns when comparing revision rates for UKA to TKA. These factors are not new in the literature, and have repeatedly been reported to be protective factors of UKA's survival probability [10], [12], [21], [62], [63]. Whether these publications are the reason or not, we have seen an large shift in clinical practice in Denmark. What we did find was an almost complete shift to cementless fixation (Figure 9.8) and a large increase in high usage units (Figure 9.9). It is likely that these changes in practice are at least partly responsible for the improved short-term survival we report for UKA in Figure 9.4. We do not conclude that these factors are the reason for the decrease in risk of revision for UKA. The reason we are reluctant to do so, is the number of uncontrolled and unknown confounders. An partially uncontrolled confounder is fixation whose effect size theoretically can be overestimated due to the effect of high usage rates. The reason we are confident it is not the other way around is that Baker et al. found usage rates and surgical volume to influence revision rates in a cohort only containing cemented UKA[62], proving that the effect exists independently of fixation. We cannot reject the possibility of the effect of fixations is overestimated for fixation, since no publications comparing fixation modes while controlling adequately for usage rates. As for unknown confounders, Denmark is a small country with a large public healthcare system, which makes it easier to communicate end facilitate practice changes, making it possible that it was not the literature that caused the change in practice. Similarly, it is possible that unknown confounders have changed in parallel to fixation and usage, and its effect is measured in our known confounders. Regardless of the cause, the improved survival for UKA is still inferior to the survival for TKA. So why do we accept this?

10.2 Revision as an outcome for comparison of UKA and TKA

To propose a plausible explanation for the increase in UKA usage, when its revision rates are higher, we need to evaluate our outcome, revision. Liddle et al. showed that revision indications for TKA and UKA significantly differed in the NJR, with TKA patients being revised for specific reasons such as infection, and UKA patients for more unspecific indications such as pain [21], a pattern we also identified in the Danish registry(Table 9.3). Studies on both the New Zealand and UK registries have also shown that the threshold for revision is lower for UKA than TKA, with UKA patients being up to 5 times more likely to get revised than TKA patients with identical OKS[36], [37], [64]. Lastly, the definition of revision excludes reoperations, which TKA patients are significantly more likely to experience. Lastly, Kennedy et al. reported that only 20 % of all revised UKA patients had correct indications and appropriate technique for both primary and revision surgery [34]. Their analysis showed that one third of UKA knees had early stage OA, a contraindication for UKA[10]. This is data from the National Joint Registry (NJR), and we can therefore not directly transfer these numbers onto our cohort, but we must expect this phenomenon to be present in our cohort as well. They reported that as much as two-thirds of UKA revisions were due to unexplained pain. We found revisions due to pain to be declining in incidence in our danish cohort (Figure 9.11), and that most revisions due to pain were done at low or no UKA usage units (Table 9.5). Thus, the increase in high usage units and the consequent increased knowledge of the poor results for these revisions due to pain seem to have reduced this group considerably. Looking at indications for revision, we also found that the aseptic loosening, historically the most common reason for UKA revision, is declining. This seems to be linked to both usage and fixation (Table 9.5 and Table 9.4). For fixation, we are not alone in reporting this decrease in risk of getting revised due to aseptic loosening, Tay et al.[65] reported cemented fixation had a higher risk of revision due to aseptic loosening in their meta-analysis (relative risk 6.6, p-val < 0.001). The correlation between usage and aseptic loosening might be due to high usage hospitals using primarily the cementless fixation, but one could argue these surgeons are also more familiar with the UKA and more likely to recognize the difference between physiological and pathological radiolucency.

10.3 Patient reported outcome for comparison of optimized UKA and TKA strategies

Having established that revision as an outcome for comparison of UKA and TKA is complex, it is natural to conclude that revision cannot be a stand-alone measure for success of knee arthroplasty. To determine success, we need to acknowledge there are multiple domains which we need to take into consideration[20]. The first is the safety, i.e. mortality, revision, reoperation and medical complications, which is addressed in paper I, II and IV. The second is the patient-perceived outcome, both change and final outcome, which we investigated in paper III and IV. And lastly the socioeconomic costs or benefits, which was covered by Beard et al. in their RCT[24].

When looking at UKA performance in its optimal set-up, we chose to look at the patients' perceived change- and final outcome, using the OKS 1-year change score and 1-year PASS as our outcome. The literature and this thesis' paper I and II all point to the success of UKA being correlated to both correct patient selection and surgical practice, but also the health-care teams' knowledge of the implant and its recovery trajectory[3], [4], [13], [14], [34], [66]. Thus paper III aimed to compare UKA as a strategy for AMOA patients and compare it to TKAs for AMOA patients at a different unit, where TKA was the sole treatment option. We found a difference larger than previously reported, however the 3 point difference reported in chapter 9.5 still does not exceed the MID of 4 points [42].
An alternative to the MID as an interpretive tool in paper III would be interpreting the adjusted mean change score for each group, and determine if the two groups on average feel different levels of improvement. There are two tools available for interpreting change of OKS: The minimal important change (MIC), which describe the minimal change an average patient considers to be important [67]. The second interpretive tool is a four category tool which categorizes change into four categories; "much worse", "about the same", "a little better", "much better" based on an transition anchor question[68]. The four category interpretive tool is developed for 6-months change, limiting the strength of conclusion when we are using it on 1-year change [41]. However, paper III focused on the chances of achieving an excellent outcome, making MIC less the usefulness in this scenario, leaving us with the four category tool. The threshold for the "much better" group is a 16 points change score at 6-months - a threshold which our adjusted mean change score at 1 year for TKA does not meet, whereas the UKA group surpasses this with 2.57 points (chapter 9.5). We cannot conclude if the UKA score is also "much better" at 1 year, but it indicates a clinical difference in the patient-perceived magnitude of change between the two groups. Looking at the final score distributions in Figure 9.12, we see a more extreme negative skew for the UKAs, with almost no patients scoring under 30, whereas the TKA curve

has a larger proportion of patients scoring under 35. The distribution plot is very similar to that published on 14,076 NJR patients in 2015 on 6-months follow-up[22]. Testing this we used the PASS as a measure of patient satisfaction at that time point in the recovery. We found that UKA patients were significantly more likely to reach PASS, representing the point where an average patient categorizes their symptom burden as feeling well[51]. In conclusion, when both treatment strategies are used in their optimal set-up, UKA patients more likely feel well 1 year after surgery compared to TKA patients. The adjusted mean difference between the two groups not clinically significant, but UKAs achieved a adjusted mean change which can be interpreted as feeling much better, whereas TKA patients adjusted mean change was categorised as feeling a little better.

10.4 Evidence based implementation of UKA

Changing surgical practice and strategy today is expected to be evidence-based. As mentioned earlier, UKA is beneficial in several domains compared to TKA, with UKA experiencing fewer complications, readmissions and reoperations, achieve better functional outcome, and the procedure has lower mortality is more cost-effective[20], [23], [24], [69], [70]. As discussed earlier the only drawback is the higher revision risk[20], [21]. If the revision rate does not deter surgeons, the benefits of UKA are encouraging for UKA implementation. However, when searching the literature for publications pertaining to the implementation phase for UKA, we found only one true learning curve study describing implementation of the current UKA practice at a unit with no history of UKA usage[32]. Other publications describe changes from one UKA approach to another[33], [71]. Consequently, current implementation of UKA is largely based on evidence of what can be expected, once the implementation phase is passed. To increase our knowledge of UKA implementation paper IV focused on the performance during the implementation phase looking at several outcome domains. We found UKA patients to be less likely to experience complications and readmissions, to have shorter LOS and have statistically significant better PROM outcome than TKA at 2 year follow-up (Table 9.6 and Table 9.7). The differences between treatments in LOS and adverse events were comparable with previous publications on fully implemented treatments[6], [20], [70], [72]. Because of the small cohort revisions were recorded for safety, and reported descriptively to be equal between the two groups, but could not be tested for significance. However, if we include the nation-wide implementation investigated in papers I and II, the lack of increase in UKA revision risk for UKA (Figure 9.4) during the increase in usage, indicates implementation do not noticeable increase UKA revisions. In conclusion we found the benefits of UKA to set in already during implementation, without any short-term performance drop.

10.5 Strengths and limitations

We have looked at UKA as a treatment strategy using multiple different study designs and outcome domains. The registry data gave us 20 year of data, making it possible to evaluate UKA performance and revision patterns over time. The danish registries have high completeness, particularly for the last 10 years where it has consistently exceeded 95 %. We used a shared gamma frailty component in our analysis, making it possible for us to keep bilateral cases[57]. Bilateral cases is very common in knee arthroplasty, and excluding cases to remove the dependence increases attrition bias an decrease external validity. When we combine the high completeness and the handling of bilateral cases we do not expect high levels of attrition bias in the crude cohort[73]. Propensity score matching reduced selection bias from known confounders in paper I, II and III[55]. Paper III and IV further focused on limiting confounding by indication due to difference in pathology, by only including TKA patients with AMOA on pre-operative radiographs. Lastly, we limited selection bias in paper III and IV by limited TKA patient inclusion to TKAs performed prior to UKA implementation at the centre. To address performance bias and bias due to sub-par course of treatment paper III was done as a 2-center study, including only UKA cases from an experienced UKA centre and only include TKA cases from a high volume TKA centre, with no history of UKA usage. We aimed to limit bias due to personal preference from both healthcare personal and the patient by using the 2-centre design, and with blinding being impossible when comparing UKA and TKA, this design came closest to eliminating this type of bias. Over the course of four studies we investigated the UKA's performance and compared to it to TKA's performance, using a wide range of outcome from different domains. The importance of approaching comparison of UKA and TKA using different outcome domains is clear when put into the context of the patient centred treatment model. During the shared decision making process, it is the patient and surgeons responsibility to determine the relative importance of each domain to that individual patient, and make an evidence based decision on treatment base on this.

A common limitation for all four papers is the lack of randomization. In papers I, II and III, selection bias was reduced by propensity score matching. Propensity score matching always leave both known and unknown residual bias [55], [74], it also introduce attrition bias when you are unable to match all the controls to the treatment group[73]. The potential for attrition bias is most pronounced in the registry studies where 54.5 % of all TKAs were excluded after they satisfied the inclusion criteria. For paper IV the design was different and patients in the two groups were not recruited simultaneously, but one group after the other, to limit selection bias. This design could potentially introduce bias from factors which change over time. However, the inclusion periods were short making substantial bias unlikely.

The limitations specific for the registry studies are mainly due to unknown confounders. Because the registry is made for monitoring quality, the collected variables and data collection design are chosen for that purpose. Further, looking at development over time we can only measure changes to available variables, which makes it likely that known confounders effect include effect from unavailable or unknown confounders, making over-interpretation of their effect a risk. In paper III and IV TKA patients were included based on retrospectively assessing the radiographic wear pattern, thus we did not have the option of further imaging if needed increasing the risk of misclassification and selection bias. Further, the 2-centre design with patients from different countries made us vulnerable to undetected difference between the two populations both at baseline, but also any overall cultural differences in expectations and/or interpretations of the questionnaire.

11 Conclusion

In conclusion we found the risk of revision for UKA to be decreasing and nearing that of TKA over the last 20 years. High UKA usage rates and surgical volume, and cementless fixation have increased over the last decade and are all positively correlated to lower risk of revision for UKA. Further, our results indicate that the decreasing national UKA revision risk is primarily driven by a reduction of revisions due to pain and aseptic loosening. UKA usage rates and cementless fixation were also positively correlated to these revision indications. This all points to surgeons, especially at high UKA usage units, being more successful with the UKA, and to be more knowledgeable of appropriate use of the UKA and when revision is indicated and beneficial to the patient. The rapid increase in UKA usage did not increase the risk of revision for UKA, meaning implementation did not significantly increasing the amount early failures. Paper IV further showed no performance drop in other adverse events, LOS and joint specific PROMs during implementation, showing implementation to be safe and the benefits of UKA to be immediate. Lastly, paper III showed us that we can expect betters patient perceived improvements and a larger proportion of patients feeling well after optimizing UKA as a strategy compared to our previous strategy, TKA.

In summary, evidence based implementation of UKA is safe and will benefit both patient, health-care systems, but will possibly come at a cost of a slightly larger revision burden, which is steadily decreasing and nearing that of TKA.

12 Perspectives

Registry data is a great source of information for revision and mortality. They are created to detect unacceptable failure rates, not for comparison of treatment strategies. That being said, it is one of our most important sources for comparative studies on revision and mortality for arthroplasty. Because the data are not collected with this type of research in mind, we have a responsibility to do our best to make for a fair comparison, by limiting bias and being aware of changes over time. Paper I illustrated this point in the differences between the unadjusted and adjusted implant survivals. Further, it illustrated that we need to be careful with pooling data for UKA over time. In conclusion, we need to adhere to good practice for statistical analysis in registry studies[56], but we also need to acknowledge its limitations, and not over-interpret the results. Lastly, there is still a tendency towards over-interpretation of annual registry reports outcomes, using them for comparison of TKA and UKA. I don't think it feasible this will change, so we need to have a conversation about how to incorporate a fair comparison in the registries, to improve the quality of information available to all surgeons. Figure 9.10 compared current practice for UKA and TKA, which I argue is the most useful starting point for the a fair comparison.

My first point was using statistics appropriately in registry studies. In the field of RCTs, we have seen improvements of overall quality for RCTs after the CONSORT reporting guidelines were introduced[75]. Ranstam et al. published a corresponding guide for registry studies in 2011[56], which provides a solid foundation, from which the researchers can tailor the statistics to best answer their questions and limit bias. Further promotion of these guidelines could potentially do for registry studies what CONSORT did for RCTs.

The foundation for this thesis was the implementation of UKA at our department, at a time when we saw a large increase in UKA usage all over Denmark. This implementation happened after a series of high-quality publications showed us the advantages of, and pitfalls for UKA, leading the way to an evidence-based implementation. However, the implementation phase itself is poorly described in the literature, which is where this thesis was aimed to improve our knowledge. The only learning curve study published for the current practice showed implementation was safe and that in less than 30 cases, a surgeons reaches an acceptable outcome. Paper IV found immediate benefits of UKA, and no performance drop, further promoting the UKA as a viable alternative to TKA. Though this thesis adds to our understanding of the implementation phase there is a need for further studies, specifically more learning curve studies.

The Danish UKA usage rate have reached approximately 20 %, indicating we are far into the implementation phase. Papers I and II describe the short term effects of this large scale implementation. It is now important to monitor the mid- and long-term effects of both the change in fixation mode and the increased usage. Specifically for the cementless fixation, we do not expect to have seen the full effect here. Others have demonstrated lower revision rates for cementless UKAs[63]. We had 3-year follow-up (median follow-up 1.18 (IQR 0.68-2.04)) for cementless UKAs, and the overall median survival time for revised UKAs are 2.05 years (IQR 0.95-5.08).

The higher UKA usage rates also improve the shared decision-making process. With UKA taking such a prominent place in AMOA treatment, it becomes more readily available to the patients, and more natural for the surgeon to include in the conversation about treatment options. Having the research to back up the arguments in this conversation is essential for this process to be valid. Another important them in improving the shared decision making process is the focus on using a multitude of outcomes to evaluate knee arthroplasties[20], because allows the patient to decide the relative importance of each outcome domain individually. Especially PROMs has seen an increase in popularity in resent years [24], [38]. The interpretation and communication of PROM results can be challenging, as illustrated in paper III and IV. Thus, we have also briefly touched upon the importance of interpretive tools for PROM outcomes, which I argue is a necessity for these outcomes to be communicable to patients and non-healthcare professionals.

In conclusion UKA will likely always be compared to TKA, making it our responsibility to ensure this comparison is made fairly and communicated appropriately. Despite general disagreement on the merits of UKA, I argue that appropriate UKA usage improves the quality of treatment by enriching the shared decision-making process regardless.

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Papers

14

Paper I

Circumstances for optimized medial Unicompartmental Knee Arthroplasty outcome. *Learning from 20 years of propensity score matched registry data.*

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Abstract

Aims: The aims were to 1) investigate changes to revision risk for Unicompartmental Knee Arthroplasty (UKA) over the last 20 years compared to Total Knee Arthroplasty (TKA), 2) identify implant, surgery or patient factors that correlate to UKA revision risk and 3) describe the survival probability for current UKA and TKA practice.

Patients and Methods: All knee replacements reported to the Danish Knee Arthroplasty Register from 1997 to 2017 were linked to the National Patient Register and the Civil Registration System for information on comorbidities, emigration and mortality. We included all primary UKA and TKA performed due to primary osteoarthritis and propensity score matched TKA procedures to UKA procedures in a 4:1 ratio. Revision and mortality were analyzed using competing risk cox regression with a shared gamma frailty component.

Results: The matched cohort included 48,195 primary knee arthroplasties (9639 UKA). Difference in revision rates between UKA and TKA have significantly decreased over the last 20 years from 3-year hazard ratio 5.52 (CI 95 % 2.73-11.2) to 1.45 (CI 95 % 1.16-1.81) due to increased UKA survival. Fixation mode, UKA usage rates and surgical volume all significantly modified the revision risk for UKA, and changed parallel to the decreasing revision risks. Thus the current typical UKA practice using cementless fixation at high usage unit has increased the 3-year implant survival to 96.4 % (CI 95 % 97.4-95.4) which is 1.1 % lower than that of current TKA practice.

Conclusion: There has been a decrease in UKA revision risk over the last 20 years, reducing the difference in revision risk between UKA and TKA. High usage rates, surgical volume and the use of cementless fixation have increased during the study period and were all associated with lower UKA revision risks.

Word count: 289

Introduction

The medial unicompartmental knee arthroplasty (UKA) has been a part of knee arthroplasty for over four decades. In the last decade its relative use, in treatment of primary osteoarthritis (OA), has doubled in select countries, reaching up to 20 % of all primary knee replacements [1–3]. An increase in usage which has happened despite the registries reporting higher revision rates for UKA[4].
This is potentially a sign that surgeons are looking at multiple different outcomes when assessing the different types of knee replacements[5]. UKA has been shown to have fewer complications, lower mortality, and shorter length of stays and to be more cost-effective than Total Knee Arthroplasty (TKA)[6–8]. These advantages combined with the development of cementless fixation, which has been reported to decrease the risk of revision for UKA[9], seems to have changed the attitude towards the implant. In comparison to the revision rates in the registries, the latest clinical evidence including the RCT TOPKAT, has been unable to find a significant difference in risk of revision between the two[6,10,11].

Revision as an outcome for comparison of UKA and TKA is complex. It poses a multitude of challenges; difference in revision thresholds[12,13], the significant number of UKAs who's revision could have been avoided[14], and the of lack of inclusion of reoperations, when UKA are considerably less likely to have these[7,10].
Specific to registry data we are vulnerable to; confounders like fixation whose effect on revision is opposing depending on the type of arthroplasty[9]. Pooling of data across time regardless of changes to practice as seen with the less restrictive patient selection, introduction of minimal invasive surgery, emphasis on high usage rates and surgical volume and the switch to cementless fixation in the last decade is problematic[9,15–18]. And lastly registry studies are non-randomized and often not established with comparative research in mind, meaning handling confounding by indication correctly can significantly impact results[19,20] and you are limited to the variables which the registry collects. These factors combined are likely to blame for the differences in reported UKA revision rates between registries and the more resent prospective cohort studies where data collection and variables are decided by the study design[4,6,7,21]. Thus, the additional bias we have in registry studies, makes us vulnerable to mis and over interpretation of results and sometimes lead to sensational publications creating confusion for both surgeons and patients[22].
For all its limitations registry data is still an important source of data for research. And if used and interpreted respecting these limitations, it provides important information about rare events like revision and mortality we are otherwise unable or challenged to investigate. Because registries have collected data for 20 years now, we can investigate developments over time to further evaluate the association of potential confounders to revision. Giving us a better understanding of the effects of changes made to procedure during this time.

Thus, the primary aim of this study was to investigate if UKA revisions rates reported to a national Knee Arthroplasty Register has decreased compared to those for TKAs over the last 20 years. Secondly, we aimed to determine if patient, implant and surgical factors had significant associations to revision risk for UKA and TKA and to describe any changes in frequency for these variables over time. Thirdly, we aimed to compare the revision risk for the current typical UKA and TKA patient.

Method

Data

The data set consisted of all knee replacements reported to the Danish Knee Arthroplasty Register from its implementation in 1997 to December 4, 2017. This was linked to the Danish National Patient Registry (NPR) to obtain comorbidity information, and to the Danish Civil Registration System to obtain emigration and mortality data. The data link was done by The Danish Health Data Authority. NPR was established in 1976, and contains both inpatient (from 1977) and outpatient (from 1994) information[23]. We included all primary UKAs and TKAs with primary osteoarthritis as the sole indication, and excluded complex knee replacements. Complex surgeries were defined by the use of bone grafts or component supplements.

Statistics

UKA and TKA procedures were propensity score matched in a 1:4 ratio using; sex, age, weight, date of surgery, Charlson Comorbidity Index (CCI), alignment and unit type. Sex, age, weight, date of surgery and alignment were reported directly to the registry. CCIs were calculated from ICD-8 and -10 codes from any hospital contact within 10 years prior to the patients surgery[24–26]. The propensity score was calculated by estimating the effect of confounders on the implant type using logistic regression, and combining them into a propensity score, which was used to match UKA and TKA procedures using the nearest neighbor method. Standardized mean differences of 0.1 or less indicated sufficient balances between the treatment groups[20]. Missingness for matching variables (weight and alignment), were handled by multiple imputations, using predictive mean matching for weight and the polytomous logistic regression for alignment. Sensitivity analyses of imputed variables were done prior to propensity score matching.
Survival analyses were done using competing risk cox proportional hazard (PH) regression with a shared gamma frailty component added as a random effect, to account for bilateral cases[28]. Violations of the PH assumption were examined using Schoenfeld's residuals. If arthroplasty type violated the PH assumption, it was investigated in sections and reported as sub-hazard rates for each time-at-risk interval. Explanatory variables violating the PH assumption were stratified on the hazard. Effect modifications from covariates were investigated by likelihood ratio tests[29]. Cumulative incidence plots were done using the Nelson-Aalen estimator.
Usage rates and surgical volume were calculated per calendar year on a unit level. Usage was defined as the percentage of UKAs out of all primary knee replacement at a specific unit that calendar year. We categorized usage as high ≥ 20 %, low < 20 % or none 0 %. Surgical volume was defined as the total number of UKAs operated at a specific unit that calendar year, and categorized into high or low around the median volume of UKA (52 p.a.) and non-UKA units were categorized as none[15,17,18]. Thus, units could switch between categories for both volume and usage from year to year. The patients were assigned the category the unit had the year of their surgery.

All statistics were calculated using R version 4.0.3.

Ethics and funding

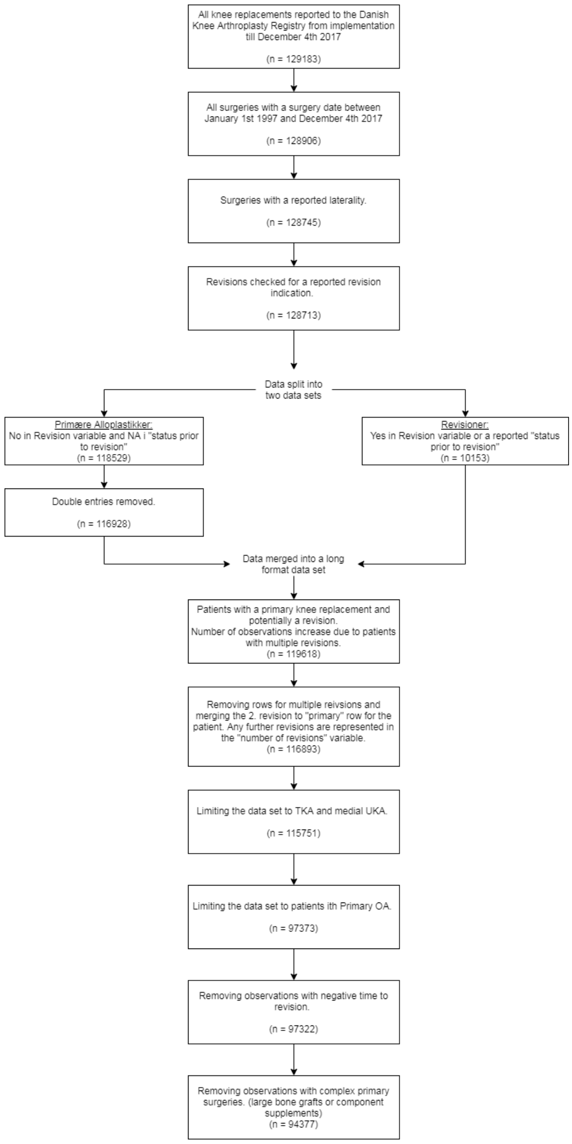
The study was approved by the Danish Data Protection Agency (J No 2012-58-0004). The author or one or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.

Results

Data

The database included 129,183 primary and revision knee replacement surgeries for all indications. After patient selection we had cohort of 94,377 knees with primary OA having primary UKA or TKA (Figure 1).

Figure 1: Flow chart of patient selection process.



Weight and alignment had missingness. Both were missing at random and were imputed. Propensity score matching yielded sufficient balance between the two groups on all matching variables except for date of surgery with SMD 0.125 (Table 1). The PH assumption for arthroplasty type was violated and the data was split into two sections around the 3-year mark.

Table 1: Comparison of crude and matched patient characteristics. Standardized mean difference (SMD) of 0.1 or less indicates balance between groups.

	Crude data			1:4 Matched data		
Matching variables	UKA	TKA	SMD	UKA	TKA	SMD
N	9639	84738		9639	38556	
Sex (male)	4320 (44.8)	31418(37.1)	0.158	4320 (44.8)	17241 (44.7)	0.002
Age at Surgery	65.7 (40.1-97.6)	69.5 (40.1-96.2)	0.448	65.7 (40.1-97.6)	66.2 (40.1-93.6)	0.084
Weight	84.7 (45-200)	85.1 (45-200)	0.020	84.7 (45-200)	85.1 (45-200)	0.020
Date of Surgery			0.368			0.125
1997-2001	194 (2.0)	7131 (8.4)		194 (2.0)	1204 (3.1)	
2002-2006	1405 (14.6)	15648 (18.5)		1405 (14.6)	4287 (11.1)	
2007-2011	2947 (30.6)	28685 (33.9)		2947 (30.6)	12605 (32.7)	
2012-2017	5093 (52.8)	33274 (39.3)		5093 (52.8)	20460 (53.1)	
Alignment			0.625			0.018
< 0-4° (varus)	7784 (80.8)	49306 (58.2)		7784 (80.8)	30905 (80.5)	
5-10° (neutral)	1704 (17.7)	23240 (27.4)		1704 (17.7)	6986 (80.5)	
> 11° (valgus)	35 (0.4)	11058 (13.0)		35 (0.4)	150 (0.4)	
Not examined	116 (1.2)	1134 (1.3)		116 (1.2)	515 (1.3)	
CCI			0.064			0.016
0: None	6120 (63.5)	51583 (60.9)		6120 (63.5)	24252 (62.9)	
1-2: Mild	2094 (21.7)	19763 (23.3)		2094 (21.7)	8441 (21.9)	
3-4: Moderate	1163 (12.1)	10465 (12.3)		1163 (12.1)	4739 (12.3)	
> 5: Severe	262 (2.7)	2927 (3.5)		262 (2.7)	1124 (2.9)	
Unit type (Public)	8791 (91.2)	77921 (92.0)	0.027	8791 (91.2)	35165 (91.2)	< 0.001
Non-Matching Variables						
Study Knee (left)	4942 (51.3)	40856 (48.2)		4942 (51.3)	19211 (49.8)	
AKSS (f)	57.5 (0-100)	49.0 (0-100)		57.5 (0-100)	51.5 (0-100)	
Usage rate						
0 % None	0 (0.0)	26702 (31.5)		0 (0.0)	11518 (29.9)	
0 - 20 % Low	5033 (52.2)	48630 (57.4)		5033 (52.2)	22179 (57.5)	
> 20 % High	4606 (47.8)	9406 (11.1)		4606 (47.8)	4859 (12.6)	
Surgical volume						
0: None	0 (0.0)	26702 (31.5)		0 (0.0)	11518 (29.9)	
0 - 51: Low	4446 (46.1)	4277 (50.5)		4446 (46.1)	18838 (48.9)	
> 52: High	4606 (47.8)	15264 (18.0)		4606 (47.8)	8200 (21.3)	
Fixation						
Cemented	7153 (74.2)	63043 (74.4)		7153 (74.2)	27675 (71.8)	
Cementless	2393 (24.8)	5823 (6.9)		2393 (24.8)	2735 (7.1)	
Hybrid	47 (0.5)	15576 (18.4)		47 (0.5)	8015 (20.8)	
NA	46 (0.5)	296 (0.3)		46 (0.5)	131 (0.3)	

Data is in number (%) or mean (range). CCI; Charlson Comorbidity Index, AKSS(f); American Knee Society Score (function)

Changes to risk of revision during the last 20 years.

The unadjusted revision- and mortality risk for the matched cohort, showed higher revision risk and lower mortality risk for UKA vs. TKA at all time points (Figure 2 and Table 2).

Figure 2: Overall Cumulative Incidence for Revision (left) and Mortality (right) for UKA and TKA.

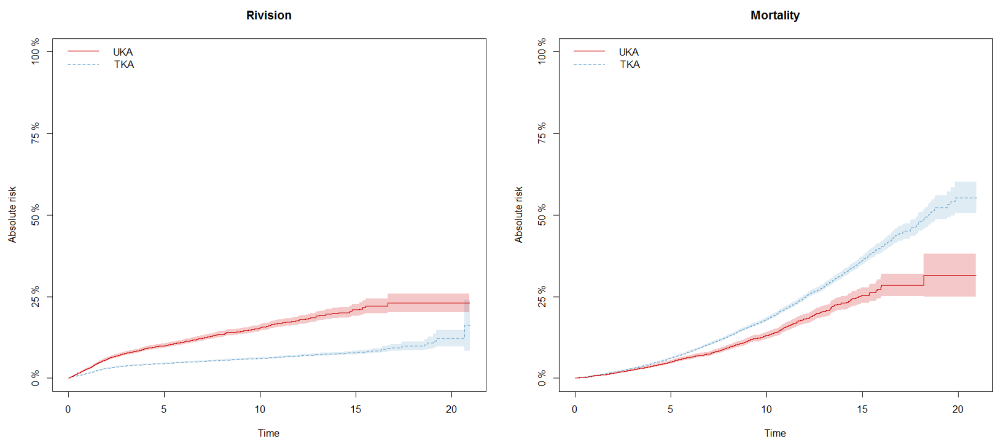
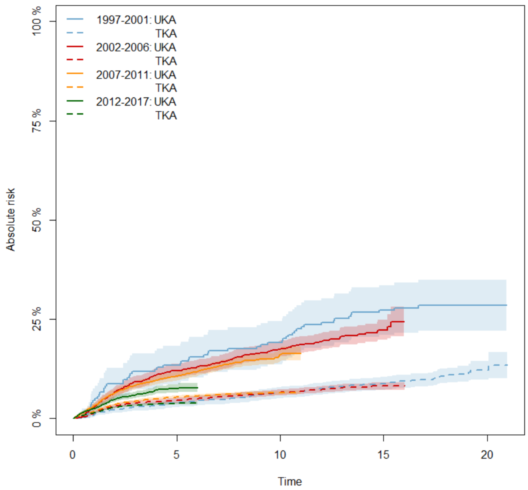


Table 2. Overall Cumulative Incidence (Cum. Inc.) and 95 % confidence intervals for Revision and Mortality.

	Revision		**Mortality**	
	UKA	TKA	UKA	TKA
3 years	7.6 (7.0-8.1)	3.8 (3.6-4.0)	2.5 (2.2-2.9)	3.1 (2.9-3.3)
10 years	12.8 (11.8-13.9)	6.2 (5.9-6.5)	12.8 (11.8-13.9)	17.9 (17.3-18.5)
20 years	23.0 (20.2-25.9)	11.9 (9.8-13.9)	31.5 (25.0-38.1)	50.5 (46.9-54.1)

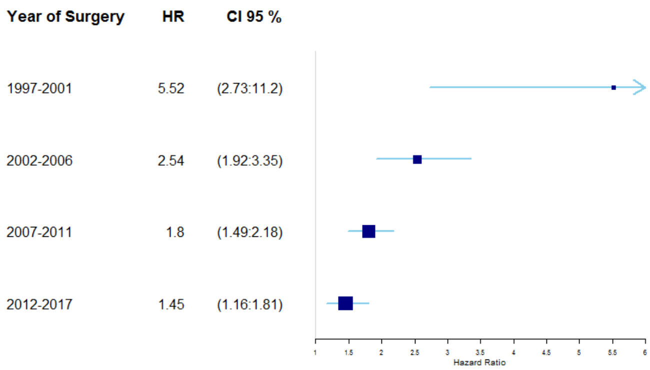
To investigating changes to revision risk over time we use the date of surgery intervals from the propensity score matching (Table 1). The cumulative incidences for these intervals indicate a significant decrease in absolute risk for UKA, and a stabile risk for TKA during the last 20 years (Figure 3).

Figure 3 Cumulative Incidence (Absolut Risk) for revision of UKA and TKA categorized by year of surgery.



3-year adjusted hazard ratios (HR) for each interval of surgery year shows significant decrease in revision risk difference between UKA and TKA (Figure 4).

Figure 4 Forest plot for HR (CI 95 %) between UKA and TKA for different intervals of surgery year. HR less than 1 favors UKA.



Fixation, usage rates and surgical volume:

Fixation:

Cementless UKA did significantly better than cemented UKA (HR 0.60, CI 95 % 0.46-78) and cementless TKAs did significantly worse than cemented TKA (HR 1.65, CI 95 % 1.43-1.91). Investigating the 20 year sub-hazard ratios including this interaction in the cox model it ranges from 1.78 (CI 95 % 0.52-6.09) for cementless UKA vs. cementless TKA to 4.87 (1.55-15.3) for cemented UKA vs. cemented TKA. The 5-year cumulative incidence for UKA depending on fixation was 10.3 (CI 95 % 9.6-11.1) for cemented and 3.8 (CI 95 % 2.7-4.8) for cementless fixations (Figure 5). Investigating this using the most common UKA type, the Oxford UKA (Zimmer Biomet, Swindon, UK) which accounts for 90.9 % of all UKAs we have 6274 cemented and 2408 cementless. The cemented Oxford (median follow-up: 7.33 (IQR 4.65-1016) had a cumulative incidence of 20.8 (CI 95 % 18.7-22.9) at maximum follow-up (15 years), and a 5-years cumulative incidence of 9.8 (CI 95 % 9.1-10.6). Cementless Oxfords (median follow-up 1.18 (IQR 0.68-2.04) had a cumulative incidence for revision of 3.7 (CI 95 % 2.7-4.7) at maximum follow-up (5 years).

Usage rates:

Usage rates were significantly correlated to UKA revision rates (HR 0.72, CI 95 % 0.63-0.82) in favor of high usage. 5-year cumulative incidence for high usage UKA was 7.6 (CI 95 % 6.6-8.6) and low usage was 11.5 (CI 95 % 10.6-12.5) (Figure 6). Usage were not significantly correlated to TKAs revision rates (HR 0.95, CI 95 % 0.81-1.13)

Surgical volume:

Surgical volume showed trends similar to usage, with UKAs being less likely to get revised if done at a high volume unit (HR 0.68, CI 95 % 0.59-0.78). 5-year cumulative incidence for high volume were 7.7 (CI 95 % 6.8-8.6) and 12.0 (CI 95 % 10.9-13.0) for low volume (Figure A3 in supplementary materials). Surgical volume was not significantly correlated to TKAs revision rates (HR 0.94, CI 95 % 0.82-1.07).

Figure 5: Cum. inc. for UKA by Fixation.

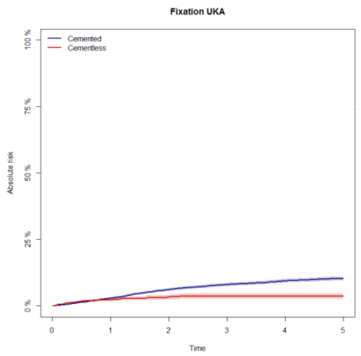
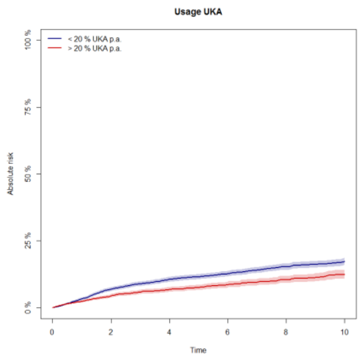


Figure 6: Cum. inc. for UKA by Usage.



Changes to fixation, usage rates and surgical volume over time

Cementless fixation was implemented in 2014 after the introduction of the cementless Oxford UKA, and now account for over 80 % of UKA procedures (Figure 7). The national usage rate of above 20 % UKA has been due to an increasing number of high usage and high volume units (Figure 8 and Figure A4 in supplementary materials).

Figure 7 UKA Fixation mode p.a.

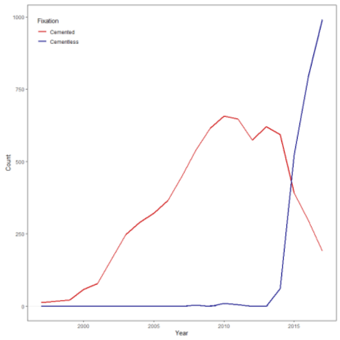
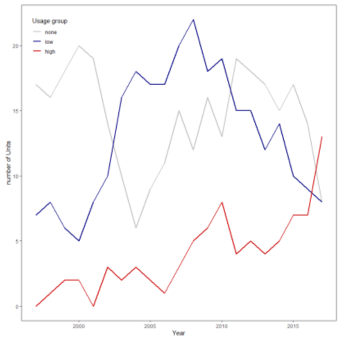


Figure 8 Units UKA usage rates p.a.



The survival probability for current typical UKA and TKA practice.

For a clinically relevant comparison of UKA and TKA, we compared current common practices. For UKA it is the combination of cementless fixation and a high usage unit. For TKA it is cemented fixation and a high usage unit. Thus, difference in 3-year survival probability for a typical patient (66 year old female, CCI = 0, varus knee) having the most common UKA vs. most common TKA was 1.1 % in favor of TKA (Figure 10 and Table 3). The 3-year survival probability for mortality was 99% for both groups (Figure A2 in supplementary materials).

Figure 10 Cox PH regressionv3-year Survival probabilities for revision for 66 year old female patients with varus knee and CCI = 0, having cemented TKA vs. cementless UKA.

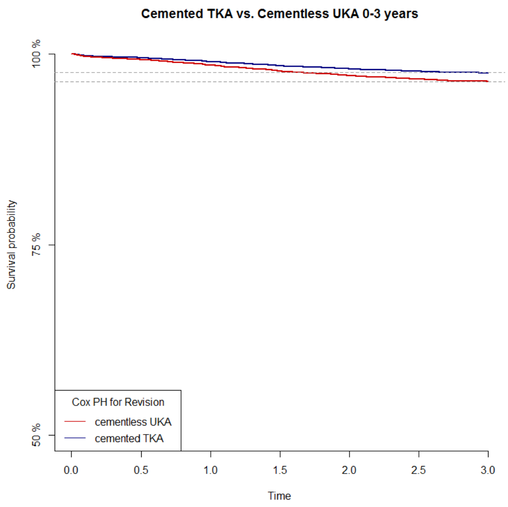


Table 3: 3-year survival probability and HR for 66 year old female patients with varus knee and CCI = 0, having cemented TKA or cementless UKA. HR less than 1 favors UKA.

	Survival Probability % (CI 95 %)		HR (CI 95 %)
	UKA	TKA	
3 years	96.4 (97.4-95.4)	97.5 (97.9-97.2)	1.46 (1.13-1.89)

Discussion

In a propensity matched registry based design, we observed the overall higher unadjusted risk of revision and lower mortality risk for UKA compared to TKA at all analyzed time points.

A pattern we have seen in multiple other publications[4,5,7]. However, we found a significant decrease in UKA revision risk over the last 20 years (Figure 3 and 4), meaning the 20 year survival tells us little of what to expect from the current practice.

These outcomes tell two very different stories from the same data. The unadjusted comparison is the closest to the annual registry reports and a few other publications, which found up to 6 % differences (double that of TKA) in 7-year revision risks[4,21], numbers that are comparable with our 10 year unadjusted outcome (Table 2). These estimates are however unadjusted for confounders like fixation, usage rates and surgical volume. All factors we have shown impact UKAs revision risk significantly and which has undergone resent changes[9,15,17,18]. Comparing our adjusted HR from the time analysis (Figure 4) to that of Liddle et al.[7] we find similar risks. They found a 4-year HR of 1.97 (CI 95 % 1.84-2.12) for patients operated in 2002-2013, we found 3-year HR 1.80 (CI 95 % 1.49-2.18). Their study also propensity score match and adjusted for, then known, confounders.

Since their publication in 2014 we have seen changes to implant design, and the literature has reported significant effect of usage rates and surgical volumes on revision risk. We found cementless fixation, high usage rates and surgical volume at a unit level had a protective effect on UKAs revision risks comparable to those previously reported on both surgeon and unit level[17,30,31]. What makes it plausible for these factors to be responsible for the decrease in revision risk for UKA is that the knowledge of their importance has resulted in a changed practice nationally. After the introduction of the cementless Oxford UKA in 2014[1] cementless fixation accounted for more than 80 % of all UKAs in 2017(Figure 7), and high usage unit are now the most common unit type (Figure 8).

Knowing that 20 year survival gives limited information on the current practice of UKA, we compared the two treatments short term using the current typical practice for each. The most influential modifier was fixation, where we found cementless to be superior for UKA and inferior for TKA. Thus, we investigated identical patients in regards to patient characteristics having cementless UKA vs. cemented TKA at a high usage unit. The survival probabilities at 3 years were in both cases over 96 % and the difference between the two was 1.1 % in favor of TKA. This analysis comes the closest to the TOPKAT design, and show similar revision risk to theirs (UKA 3 % and TKA 5 % revised at 5 years[6]). The analysis accounted for both patient characteristics, in the propensity score matching and as covariates in the cox regression, and the external factors; usage rates and fixation mode. Approaching the analysis this way halved the 3-year UKA revision risk from a cumulative incidence of 7.6 (CI 95 % 7.0-8.1) to a survival probability of 96.4 (CI 95 % 97.4-95.4). This illustrates the impact of adjusting for known confounders.

The main strengths of this study are the 20 year data collection and follow-up making investigation of time trends possible. The consistently high completeness of the registry and linking it to national patient registries minimizes attrition bias and makes propensity score matching on patient characteristics possible, reducing confounding by indication. Using registry data also offers us an unselected cohort, which we preserve by not excluding bilateral, but handling the random effect of this by using a shared gamma frailty component in our competing risk cox proportional hazard regressions, an approach we have been unable to find other knee arthroplasty registry studies using[28].

The main limitation is the lack of randomization. We partially adjust for it by propensity score matching, however there is residual confounding from both known and unknown confounders[19]. The effect of unknown confounders can also contribute to the effect of known confounder on our outcome making these appear more or less modifying. The matching excludes a large number of patients which increase the risk of attrition bias. Lastly, the data was extracted ultima 2017, making follow-up cementless UKA short and limited us from looking at fixations correlation to long term survival for UKA.

In conclusion we report a decrease in UKA revision risk over the last 20 years, nearing that of TKA. Cementless fixation, high usage and high volume were all associated to lower UKA revision risks, all factors which are being applied at the surgical units, where cementless fixation account for more than 80 % of all primary UKA and high usage units are now the most common unit type. Thus we are encouraging the knee arthroplasty registries to add survival curves for optimized use of UKA, thereby providing a report of outcome reflecting contemporary and appropriate practice strategies with the potential to stimulate future improvements in treatment quality.

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Supplementary materials

Figure A1 Cox PH regression 3 year Survival probability for revision

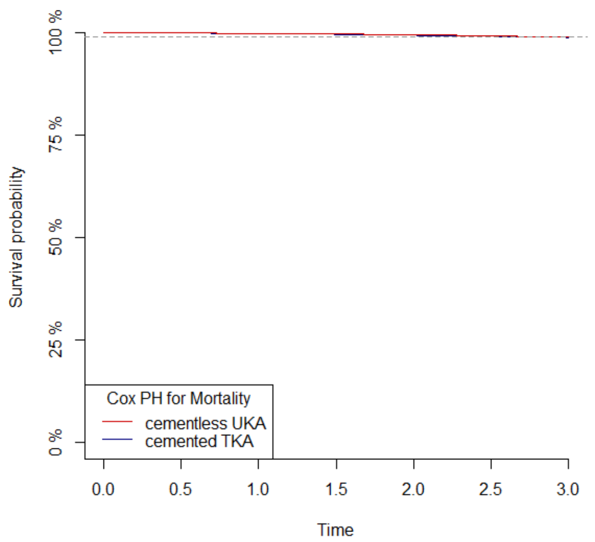


Figure A2 Cumulative Incidence (Absolut Risk) for mortality of TKA and UKA categorized by year of surgery.

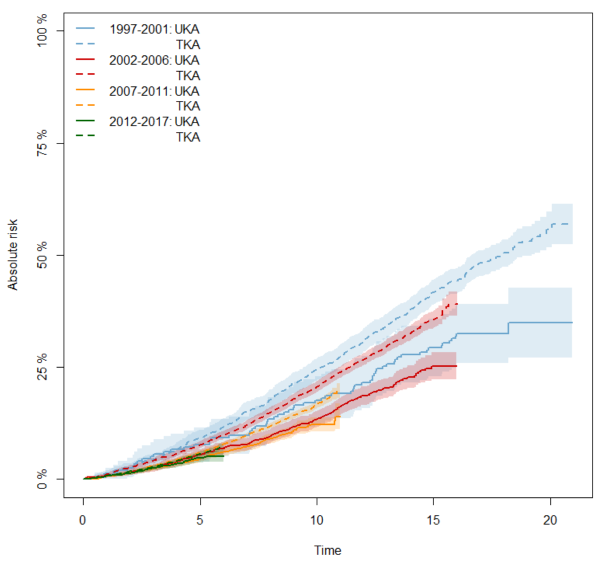


Figure A2 Cumulative incidence for UKA by Volume

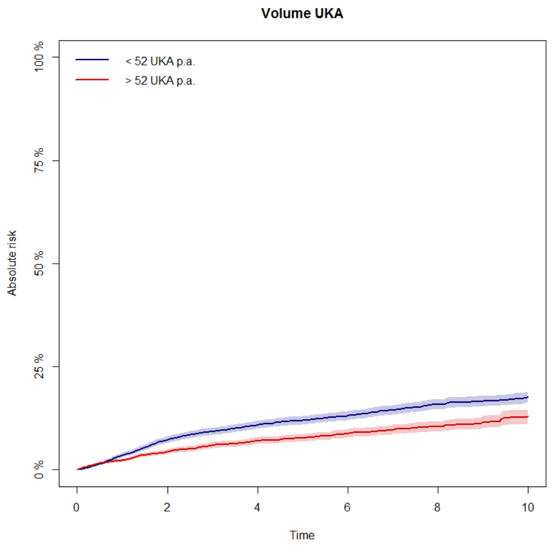
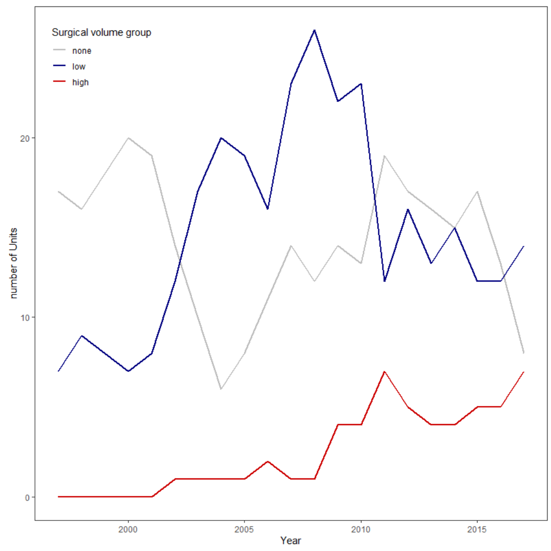


Figure A3 Units surgical UKA volume p.a



Paper II

Does changes in Unicompartmental Knee Arthroplasty practice pattern influence reasons for revision? *A study of 9639 cases from the Danish Knee Arthroplasty Register.*

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Abstract

Aims: We aimed to determine the national revision indication pattern and the timing for revision by indication for Unicompartmental Knee Arthroplasty (UKA) and Total Knee Arthroplasty (TKA). Further, we aimed to investigate any changes to the UKA revision indication pattern over time, and its' correlation to resent changes in surgical practice pattern.

Patients and Methods: All primary and revision knee replacement surgeries reported to the Danish Knee Arthroplasty Register from 1997 to 2017 performed due to primary OA were included. Complex surgeries were excluded. The data were linked to the National Patient Register and the Civil Registration System for comorbidity, mortality and emigration status. TKA procedures were then propensity score matched 4:1 to UKA procedures. Revision risks were investigated using competing risk cox proportional hazard regression with a shared gamma frailty component to account for bilateral cases.

Results: Aseptic loosening was the most common revision indication for both UKA (26.7 %) and TKA (29.5 %). For UKAs pain and OA progression accounted for 54.6 % of the remaining revisions, and for TKA infections and instability accounted for 56.1 % of the remaining revisions. TKA revisions were on average performed 6 months earlier than UKA revisions, due to the difference in revision indication patterns. The annual number of UKA revisions due to loosening or pain have noticeably decreased over the last decade and were in 2017 two of the three least common UKA revision indications. UKA patients getting a cementless UKA were less likely to get revised due to pain (HR 0.40, CI 95 % 0.17-0.94) or loosening (HR 0.29, CI 95 % 0.10-0.81) than if receiving a cemented UKA. UKA revisions due to pain (HR 0.67, CI 9 5% 0.50-0.91) and loosening (HR 0.51, CI 95 % 0.37-0.70) are also less likely at a high UKA usage unit.

Conclusion: The overall revision patterns for UKA and TKA for the last 20 years are similar to previous published patterns. There has been a large change in revision pattern for UKA in the last decade, and with the current surgical practice, revision due to pain or loosening are significantly less likely.

Research questions:

1. How are the failure patterns and the timing of revision for UKA and TKA in DK?
2. Does the failure patterns for UKA, depend on factors we know influence the overall risk of revision for UKA, such as the revision units UKA usage rates or the fixation mode of the primary implant.

Introduction

For patient with end-stage osteoarthritis (OA) of the knee, an arthroplasty is the natural choice ones conservative treatments have failed to preserve function and manage pain. However, for 25 % to 47 % of these patients their wear pattern is anteromedial, making them eligible for both total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA) [1,2]. Internationally, there seems to be a reluctance to use the UKA regardless of the many benefits it has compared to the TKA, with most national registries reporting UKA usage of approximately 10 % [3–6]. UKA has been shown to provide better function, lower mortality, faster recovery, lower risk of complications and readmissions and to be more cost-effective than TKA, but it is more likely to get revised[7–13].

Revision as a measure for comparison between TKA and UKA is a multi-factual discussion, but the primary discussion concerns the validity of revision as a comparative outcome measure. The main concerns are the difference in revision threshold and in the revision indications. There has been reported lower revision thresholds for UKA in two independent national registries[14,15]. The difference in failure pattern has been described previously, showing TKAs are commonly revised due to specific indications such as infections, whereas UKA has been revised for pain and loosenings[10,16].

Historically, the UKA are up to 6 times more likely to get revised compared to TKA[17], however when using appropriate guidelines for practice and patient selection this difference is significantly reduced[18,19]. In the last two decades there has been changes to design, instrumentation, fixation, patient selection and surgical practice, changes which are all associated with lower risk of revision[18–23], and can be seen in the significant decrease in UKA revision risk compared to TKA over the last 20 years [paper I]. However, if we want to get a complete picture of the difference between TKA and UKA with regards to revision, we also need to understand and account for differences in revision thresholds and revision indications when interpreting the our results.

We have seen a large increase in UKA usage in Denmark in the last decade and it now accounts for over 20 % of all primary knee arthroplasties[24]. Regardless of this increased UKA usage we are seeing an decrease in UKA revision risks[24]. We do not know if the decrease in revision risk is balanced between the revision indications, or it is linked to a reduction based on a few select indications, causing a change in revision indication pattern for UKA. Thus, the aim of this study was to determine if the revision pattern found in the Danish registry is comparable to those found in the literature, and to determine if the decrease in UKA revision risk has impacted the revision indication pattern for UKA in Denmark?

Method

Data

The cohort included all primary TKA and UKA surgeries performed due to primary OA from 1997 to December 4. 2017 reported to the Danish Knee Arthroplasty Register (DKR). All complex surgeries (bone grafts or component supplements) were excluded so were patients who could not be linked to the central patient register (CPR) to obtain mortality and emigration status. The data was further linked to the national patient register (NPR) to obtain comorbidity status. The data link was performed by the Danish Health Data Authority.

Surgeons are able to choose multiple indications for revision[24]. To determine the main indication for revision, two of the authors manually went through all 105 combinations of indications, and determined the main indication for each revision. To validate the consistency of these choices, a hierarchy was built (Table

A1 in supplementary materials). In choosing the revision indication, surgeons also have the option of choosing other indications, and write the indications in freehand. These were reclassified into an existing category if the text indisputably fit a category. If they did not fit a category, or there was a level of uncertainty as to the correct category, they were treated as “other indications” in the analysis, but categorized based on a best guess descriptively (Table A2 in supplementary materials).

The cohort has previously been published in Mikkelsen et al. [paper 1].

Statistics

After establishing the crude cohort four TKA procedures were propensity score matched to each UKA procedures using sex, age, weight, date of surgery, Charlson Comorbidity Index (CCI), alignment and unit type do calculate each patient’s propensity score using logistic regression. Sex, age, weight, date of surgery, alignment and unit type were reported to DKR. CCIs were calculated using the NPR data, which includes ICD-8 and 10 codes for every inpatient (from 1977) and outpatient (from 1994) visit[25]. We calculated a 10-year CCI, meaning any diagnoses from the 10 years prior to the date of surgery were included in the comorbidity index[26–28]. Surgeons can select multiple revision indications, to determine the main indication a hierarchy of the available indications were outlined by two of the authors by determining a main indication for all 105 combinations, and build a hierarchy from those to check for consistency (Table A1 in supplementary materials).

To address the lack of randomization we used propensity score matching. Propensity score matching is a method based on calculating a score from known confounders’ effect on the exposure using logistic regression. The matching base on the scores can then be done using a multitude of methods. Here we chose the nearest neighbor method, which is a proximity search method because it reduced the imbalance the most[29]. The matching was performed in a 1:4 ratio UKA to TKA. Since propensity score matching is unable to handle missingness for the confounders used to calculate the score, we used multiple imputation to calculate missing values for weight and alignment. Weight being continuous was calculated using predictive mean matching and alignment being categorical was calculated using polytomous logistic regression. Sensitivity analysis was done using plots and assessed by three of the authors individually before matching. Balance of the matching was determined by using standardized mean difference (SMD). A SMD over 0.1 indicated imbalance[30].

Survival analyses were done using competing risk cox proportional hazard (PH) regression with a shared gamma frailty component, where each revision indication was investigated as the outcome keeping all other revision indications and mortality as the competing risks. Violations of the PH assumption were examined using Schoenfeld’s residuals and effect modifications from covariates were tested using likelihood ratio tests[31,32]. The shared gamma frailty component was added to account for dependence of bilateral cases, thus the model became a mixed model containing both random and fixed variance[33].

Usage rates were calculated per calendar year on a unit level. High usage was defined as 20 % or more of all primary knee arthroplasty being UKA, low < 20 % or none 0 %. Thus, units could switch between categories from year to year. The patients were assigned the category the revision unit had the year of their surgery[23].

Statistical significance level was defined as p-values of < 0.01. All statistics were calculated using R version 4.0.3.

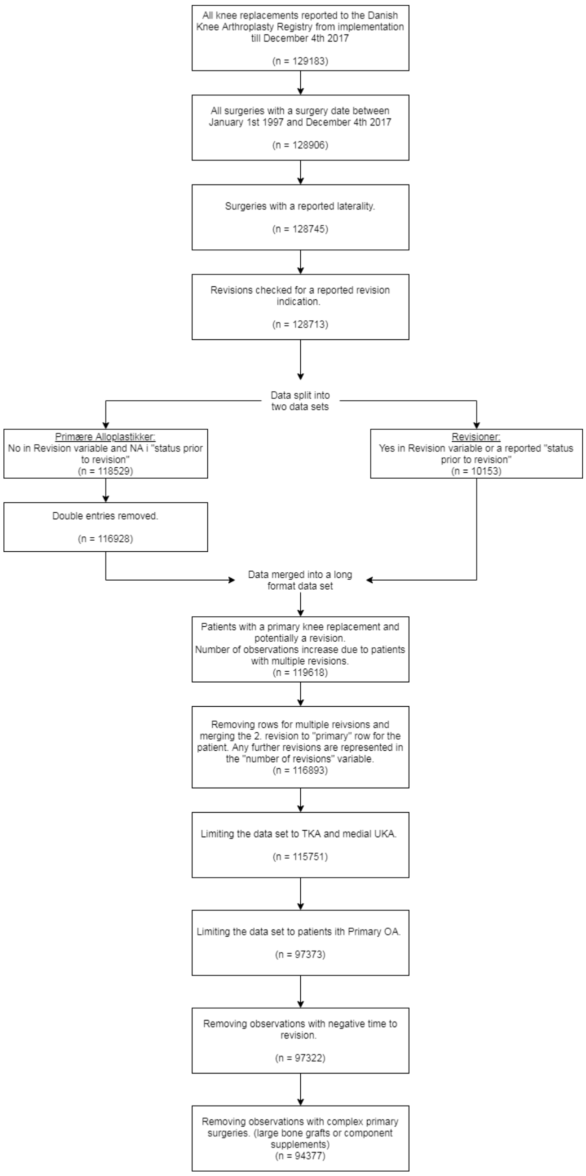
Ethics and funding

The study was approved by the Danish Data Protection Agency (J No 2012-58-0004). No funding was received for this specific study.

Results

The cohort received from the registry included 129,183 primary and revision knee replacement surgeries. After limiting the cohort to TKA and UKA surgeries performed due to primary OA and excluding complex surgeries, the cohort comprised of 94,377 primary knee surgeries (Figure 1).

Figure 1 Patient selection. This figure has previous been published [paper I].



Propensity score matching

Before propensity score matching, missingness for weight and alignment was handled using multiple imputations. Multiple imputation was performed after the missing values were concluded to be missing at random when examined over time, and in correlation with other explanatory variables. The propensity score matching resulted in a cohort of 48195 knee arthroplasties (Table 1). The matching insured balance for all matching variables except date of surgery (SMD 0.125).

Table 1 Patient Characteristics, before (crude) and after (matched) propensity score matching. Standardized mean difference (SMD) of 0.1 or less indicated balance between groups. This table has previously been published (paper I).

	Crude data			**1:4 Matched data**		
Matching variables	UKA	TKA	SMD	UKA	TKA	SMD
N	9639	84738		9639	38556	
Sex (male)	4320 (44.8)	31418(37.1)	0.158	4320 (44.8)	17241 (44.7)	0.002
Age at Surgery	65.7 (40.1-97.6)	69.5 (40.1-96.2)	0.448	65.7 (40.1-97.6)	66.2 (40.1-93.6)	0.084
Weight	84.7 (45-200)	85.1 (45-200)	0.020	84.7 (45-200)	85.1 (45-200)	0.020
Date of Surgery			0.368			0.125
1997-2001	194 (2.0)	7131 (8.4)		194 (2.0)	1204 (3.1)	
2002-2006	1405 (14.6)	15648 (18.5)		1405 (14.6)	4287 (11.1)	
2007-2011	2947 (30.6)	28685 (33.9)		2947 (30.6)	12605 (32.7)	
2012-2017	5093 (52.8)	33274 (39.3)		5093 (52.8)	20460 (53.1)	
Alignment			0.625			0.018
< 0-4° (varus)	7784 (80.8)	49306 (58.2)		7784 (80.8)	30905 (80.5)	
5-10° (neutral)	1704 (17.7)	23240 (27.4)		1704 (17.7)	6986 (80.5)	
> 11° (valgus)	35 (0.4)	11058 (13.0)		35 (0.4)	150 (0.4)	
Not examined	116 (1.2)	1134 (1.3)		116 (1.2)	515 (1.3)	
CCI			0.064			0.016
0: None	6120 (63.5)	51583 (60.9)		6120 (63.5)	24252 (62.9)	
1-2: Mild	2094 (21.7)	19763 (23.3)		2094 (21.7)	8441 (21.9)	
3-4: Moderate	1163 (12.1)	10465 (12.3)		1163 (12.1)	4739 (12.3)	
> 5: Severe	262 (2.7)	2927 (3.5)		262 (2.7)	1124 (2.9)	
Unit type (Public)	8791 (91.2)	77921 (92.0)	0.027	8791 (91.2)	35165 (91.2)	< 0.001
Non-Matching Variables						
Study Knee (left)	4942 (51.3)	40856 (48.2)		4942 (51.3)	19211 (49.8)	
AKSS (f)	57.5 (0-100)	49.0 (0-100)		57.5 (0-100)	51.5 (0-100)	
Usage rate						
0 % None	0 (0.0)	26702 (31.5)		0 (0.0)	11518 (29.9)	
0 - 20 % Low	5033 (52.2)	48630 (57.4)		5033 (52.2)	22179 (57.5)	
> 20 % High	4606 (47.8)	9406 (11.1)		4606 (47.8)	4859 (12.6)	
Surgical volume						
0: None	0 (0.0)	26702 (31.5)		0 (0.0)	11518 (29.9)	
0 - 51: Low	4446 (46.1)	4277 (50.5)		4446 (46.1)	18838 (48.9)	
> 52: High	4606 (47.8)	15264 (18.0)		4606 (47.8)	8200 (21.3)	
Fixation						
Cemented	7153 (74.2)	63043 (74.4)		7153 (74.2)	27675 (71.8)	
Cementless	2393 (24.8)	5823 (6.9)		2393 (24.8)	2735 (7.1)	
Hybrid	47 (0.5)	15576 (18.4)		47 (0.5)	8015 (20.8)	
NA	46 (0.5)	296 (0.3)		46 (0.5)	131 (0.3)	

Data is in number (%) or mean (range). CCI; Charlson Comorbidity Index, AKSS(f); American Knee Society Score (function)

Failure patterns and timing of revision for UKA and TKA

972 TKAs (52.9 %) and 629 UKAs (62.3 %) were revised at the same unit as the original knee replacement were performed at. The overall failure patterns for UKA and TKA over the last 20 years share aseptic loosening as the most common indications, after which TKAs were most at risk of revision due to infection or instability. UKAs were significantly less likely to get revised due to infection (HR 0.53, CI 95 % 0.39-0.72, $p < 0.0001$) but more likely to get revised due to pain (HR 5.92, CI 95 % 4.90-7.14, $p < 0.0001$)(Table 2).

Table 2 Ranked revision indication and hazard ratios (HR) for Total Knee Arthroplasty (TKA) vs. Unicompartmental Knee Arthroplasty (UKA). CI 95 %; 95 % confidence intervals.

Indication	TKA		UKA		HR (CI 95 %)	p-value
	Rank	N (%)	Rank	N (%)		
Loosening	1	553 (29.5)	1	270 (26.7)	2.08 (1.79-2.41)	< 0.0001
Infection	2	405 (21.6)	6	47 (4.7)	0.53 (0.39-0.72)	< 0.0001
Instability	3	335 (17.9)	5	81 (8.0)	1.05 (0.82-1.35)	0.664
Pain	4	195 (10.4)	2	268 (26.5)	5.92 (4.90-7.14)	< 0.0001
Other	5	142 (7.6)	4	129 (12.8)	3.89 (3.05-4.96)	< 0.0001
Secondary Patella	6	102 (5.4)	10	2 (0.2)	0.08 (0.02-0.33)	0.0005
Unknown	7	65 (3.5)	7	43 (4.3)	2.80 (1.89-4.14)	< 0.0001
Bearing failure, tibia	8	43 (2.3)	8	31 (3.1)	3.15 (1.97-5.04)	< 0.0001
Bearing failure, patella	9	26 (1.4)	9	3 (0.3)	0.50 (0.15-1.67)	0.26
OA progression	10	7 (0.4)	3	136 (13.5)	85.0 (39.68-182.2)	< 0.0001

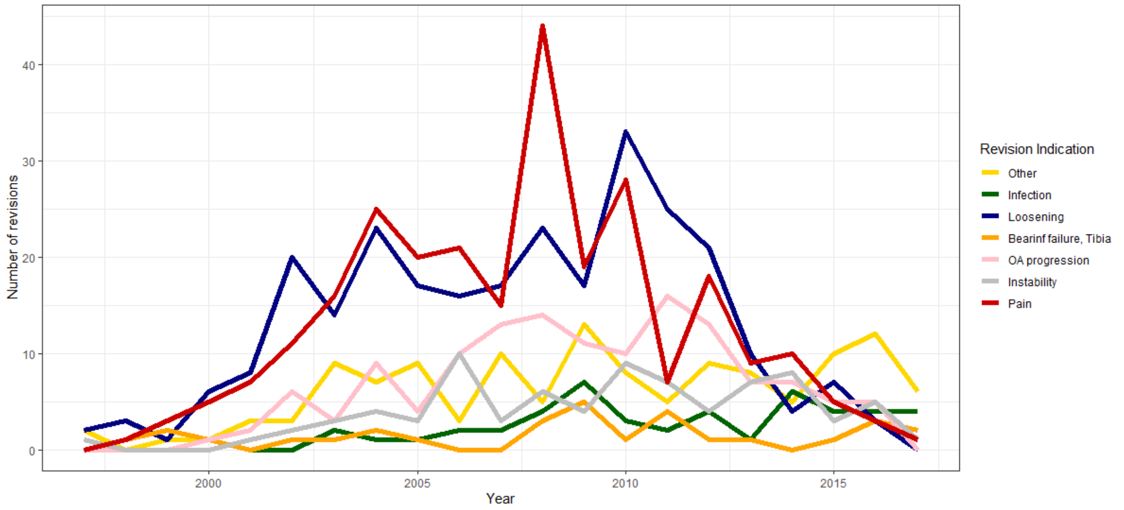
Overall TKAs were revised half a year earlier than UKAs. The timing of each indication is similar for infection, loosening and instability, and seems to differ for all other indications (Table 3).

Table 3 Median survival time by revision indication for Total Knee Arthroplasty (TKA) and Unicompartmental Knee Arthroplasty (UKA). Presented in years and interquartile ranges (IQR).

Indication	Median Survival Time [years (IQR)]	
	TKA	UKA
Infection	0.65 (0.10-2.06)	0.64 (0.11-2.60)
Loosening	2.50 (1.42-5.79)	2.48 (1.24-5.03)
Bearing failure, Tibia	5.79 (1.87-12.10)	2.75 (0.46-7.23)
Bearing failure, Patella	2.58 (1.37-5.55)	3.39 (1.80-6.34)
OA progression	2.15 (1.00-6.39)	6.02 (2.87-8.56)
Instability	1.53 (0.94-2.60)	1.78 (0.74-3.81)
Pain	1.49 (1.02-2.38)	1.73 (1.04-3.51)
Secondary Patella	1.46 (0.94-2.68)	1.96 (1.20-2.71)
Other	0.84 (0.23-1.82)	0.79 (0.27-2.69)
Unknown	1.50 (0.93-3.39)	2.35 (1.24-5.30)
All indications	1.55 (0.78-3.35)	2.05 (0.95-5.08)

Over time pain and loosening have been the most common indication for UKA revision(Table 2), but since 2010 they have both seen a fall in frequency and are now in the among the four less common reasons for UKA revision(Figure 2).

Figure 2 Frequency of Unicompartmental Knee Arthroplasty revisions by revision indication.



Failure patterns for UKA depending on usage rates and fixation mode

Overall the failure patters differed depending on the type of fixation. The difference was significant for loosening (HR0.29, CI 95 % 0.10‐0.81) and pain (HR 0.40, CI 95 % 0.17‐0.94). They were the most common indications for cemented UKAs accounting for 66 % of all revisions, whereas they accounted for less than 16 % of all cementless UKA revisions (Table 4). Cementless UKA had higher proportions of revisions due to instability and other indications, but not a significantly higher risk of revision for these reasons than cemented UKAs.

Table 4 Ranked revision indications and hazard ratios (HR) for cemented vs. cementless Unicompartmental Knee Arthroplasty. CI 95 %; 95 % confidence intervals.

Indication	Cemented		Cementless		HR (CI 95 %)
	Rank	N (%)	Rank	N (%)	
Loosening	1	264 (28.2)	7	4 (6.2)	0.29 (0.10‐0.81)
Pain	2	260 (27.8)	5	6 (9.4)	0.40 (0.17‐0.94)
OA progression	3	128 (13.7)	4	7 (10.9)	0.82 (0.36‐2.00)
Other	4	105 (11.2)	1	23 (35.9)	1.43 (0.74‐2.78)
Instability	5	71 (7.6)	2	9 (14.1)	1.13 (0.50‐2.53)
Unknown	6	40 (4.3)	8	1 (1.6)	0.79 (0.09‐7.13)
Infection	7	38 (4.1)	2	9 (14.1)	1.03 (0.09‐12.00)
Bearing failure, Tibia	8	25 (2.7)	6	5 (7.8)	2.63 (0.51‐13.53)
Bearing failure, Patella	9	3 (0.3)	9	0 (0.0)	NA
Secondary patella	10	2 (0.2)	9	0 (0.0)	NA

For usage rates we see a similar pattern, with significant difference between the no or low usage units and high usage units for pain and loosening (Table 5). Thus, UKA patients operated at a high usage unit had significantly lower risk of revision due to loosening (HR 0.51, CI 95 % 0.37‐0.70) and pain (HR, 0.67 CI 95 % 0.50‐0.91). Again, the “other” indications were a more common indication at a high usage unit, but with no significant increased risk compared to no or low usage units. Overall, there was a significantly lower risk of revision for UKA patients treated at high usage units (HR 0.78, CI 95 % 0.68-0.90). The other indications category predominantly contained OA progressions, bearing dislocations and periprosthetic fractures (Table A2 in Supplementary materials).

Table 5 Ranked revision indication for High, Low and None Unicompartmental Knee Arthroplasty (UKA) usage of the revision unit. Hazard ratios (HR) compare No and low usage to high usage units. CI 95 %; 95 % confidence intervals.

Indications	None		Low		High		HR (CI 95 %)
	Rank	N (%)	Rank	N (%)	Rank	N (%)	
Loosening	1	45 (36.0)	2	172 (28.8)	3	53 (18.6)	0.51 (0.37-0.70)
Pain	2	32 (25.6)	1	179 (29.9)	2	56 (19.6)	0.67 (0.50-0.91)
OA progression	3	18 (14.4)	3	72 (12.0)	4	46 (16.1)	0.74 (0.51-1.08)
Other	6	4 (3.2)	4	60 (10.0)	1	65 (22.8)	1.86 (0.96-3.61)
Instability	5	9 (7.6)	5	44 (7.4)	5	28 (9.8)	0.90 (0.55-1.49)
Unknown	4	13 (10.4)	7	18 (3.0)	6	12 (4.2)	0.87 (0.43-1.75
Infection	7	2 (1.6)	6	33 (5.5)	6	12 (4.2)	0.36 (0.11-1.18)
Bearing failure, Tibia	7	2 (1.6)	8	16 (2.7)	6	12 (4.2)	1.24 (0.54-2.85)
Bearing failure, Patella	9	0 (0.0)	9	2 (0.3)	9	1 (0.4)	NA
Secondary patella	9	0 (0.0)	9	2 (0.3)	10	0 (0.0)	NA
All indications		125 (12)		598 (59)		285 (28)	0.78 (0.68-0.90)

Discussion

Loosening is the most common revision indication in both groups, but the pattern differs much between the two treatments on all other indications. The overall pattern we find is very similar to that described by Liddle et al. in their registry study from 2014 (Table 2). For UKA loosening and pain account for 63.2 % of all UKA revision in Denmark over the last 20 years (Table 2). This difference means that a UKA patient has a much higher risk of revision due to pain than TKA (Table 2). Looking at infection, the second most common TKA revision indication, it is so much more common for TKA that even with the overall higher risk of revision for UKA, UKA patients are significantly less likely to get revised due to infection (Table 2). The HR for these indications are almost identical to those reported by Liddle et al.[10]. The second part of our comparison of TKA and UKA was to describe differences in revision timing. We found very similar timings for indications the two groups have in common (Table 3). Thus, the overall difference in timing is most likely due to the difference in revision indication pattern (Table 2).

Next we looked closer at the revision indications for UKA, and determined if the pattern had changed over time. We found a large reduction in the number of revisions done due to pain and loosening. The change in revision indication pattern looks to have started around 2010 (Figure 2) and coincides with the decrease in revision risk for UKA previously published on this cohort, making the decrease in revisions due to pain and loosening the reason for the overall decrease in revision risks. [paper 1].

From the literature we know fixation mode and UKA usage rates impact the results for UKA, thus we examined these factors relationship with the revision indication patterns. For fixation we found a significantly lower risk of revision due to loosening and pain compared for cementless fixations. Cementless UKAs had three times as many revisions with "other" as the indication than cemented UKAs. 70.7 % of this category is covered by OA progression, bearing dislocations and periprosthetic fractures (Table A2 in supplementary materials). Bearing dislocations and periprosthetic fractures are two indications others have also reported increases after introduction of the cementless UKA[20,34]. The increases in bearing dislocations are most likely due to more than 90 % of cementless UKAs in the cohort being the mobile bearing Oxford unicompartmental knee. Looking at unit UKA usage rates' correlation to revision indication pattern we found a similar pattern to that of fixation, with significant reduction in revisions due to pain and loosening and increase in the "other" category in high usage units (Table 5). In conclusion, there is a complex of increase in cementless fixation and high usage units over time which coincides with a decrease in risk of revision due to pain and aseptic loosening [study 1]. We generally interpret high usage as a measure of the surgeons' decision-making regarding patient selection in their UKA [18]., thus an interpretation of this could be that the increased usage and the use of cementless fixation has eliminated a large proportion of the UKA revisions which were done on inappropriate indications[16]. By inappropriate indications we are specifically looking at unexplained pain and at revisions performed due to physiological radiolucencies[35]. For unexplained pain there is a consensus to not revise TKA because it is unlikely to improve the symptoms[36]. The same is true for UKA, though there is less evidence for UKA[16,37].

The strengths of this study are, the large cohort from a registry with a consistently high completeness for both primary and revision surgeries. The large cohort and available comorbidity data makes it possible for us to propensity score match controls (TKA) to every available UKA procedure reducing confounding by indications[38]. The registry has consistently had a completeness above 90 % for both primary and revision surgery since 2007 which limits the amount of attrition bias[24]. The 20 year data collection permits us to look at changes in revision indication pattern over time, and gain an understanding of what may coincide with these changes. In the statistical approach we addressed dependent observations by adding a random effect to the cox model, limiting attrition bias considerably[33]. Further we treated the independent revision indications and mortality as competing risks[32].

The most important limitation is the lack of randomization. As mentioned in the strengths we address this by propensity score matching. Lonjon et al. [38] published a meta-analysis comparing propensity score matched studies to RCT in surgical research and were unable to find a significant difference in estimates between the two designs. However, we also know there always is a level of residual bias from both known and unknown confounders[39]. Another important limitation of this study is the revision indication categories available to the surgeons[24]. We have a large proportion of revisions which are marked as "other", especially for the cementless UKAs (Table 4). In this category we found a large proportion of bearing dislocations and periprosthetic fractures, for which there are no available categories in the registry form (Table A1 in supplementary materials). Thus, we are at risk of underestimating their numbers.

In conclusion, we found an overall revision pattern for TKA and UKA, which is similar to previous publications. We found a large decrease in revision for pain and loosening for UKA over the last 10 years, this decrease was correlated to cementless fixation and revisions being performed at high UKA usage units. There seems to have been a relative increase in revisions due to bearing dislocations and periprosthetic fractures for which there are no available categories in the registry. Thus, we urge the registry to include them as revision indication categories in the future.

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Supplementary materials

Table A1 Hierarchy for determining main revision indications

Indications
1. Infection
2. Loosening
3. Bearing failure, Tibia
4. Bearing failure, Patella
5. OA progression
6. Instability
7. Pain
8. Secondary patella
9. Other

Table A2 Revision indications for UKA, when revision indication "other" was chosen, and they could not be reclassified.

Indication	Count
OA progression	40
Bearing dislocation	28
Periprosthetic fracture	19
Text with no clear indication	10
Malalignment	5
Bearing exchange	4
SONK	4
Cementophytes	4
NA	4
Subsidence	3
Stiffness	2
Mechanical problems	2
Rheumatoid arthritis	2
Anterior Knee Pain	2
Traumatic loosening	1
Partial ACL rupture	1
Wound deficiency	1
Lateral compartment cartilage defect	1

Paper III

Comparison of two strategies in knee arthroplasty: Total Knee Arthroplasty only vs. Unicompartmental Knee Arthroplasty if possible.

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Abstract

Background Treatment of end-stage anteromedial osteoarthritis (AMOA) is commonly approached using one of two strategies: medial unicompartmental knee arthroplasty (UKA) versus total knee arthroplasty (TKA). We aimed to investigate difference between the two surgical strategies in Oxford Knee Score (OKS).

Methods 501 consecutive AMOA patients (301 UKA) operated in 2013-2016 from two centres. One centre did UKA whenever appropriate. Another did TKA regardless of wear pattern. Data was accessed from the centres' local databases. Our outcomes were change in OKS from baseline to 1 year follow-up and the proportion of patients achieving the patient acceptable symptom state (PASS) at 1 year. We did 1:1 Propensity score matching before regression models were used to investigate any significant difference.

Results The propensity score matched cohort included 400 patients (mean age 67, 53 % female, mean BMI 30.2, 84 % ASA $\leq$ 2). We found a mean adjusted difference in change score of 3.02 points (95 % CI 1.41 - 4.63, $p < 0.001$) and a significantly larger likeliness of achieving PASS, with odds ratio 3.67 (95 % CI 1.73 - 8.45, $p = 0.001$) both in favour of the UKA strategy.

Conclusion UKA and TKA are both good strategies for treating end-stage AMOA. However when compared UKA as a strategy achieved an average 3 points larger change in OKS at 1 year, and were significantly more likely to reach the PASS.

Keywords

Unicompartmental Knee Arthroplasty; Knee Replacement; Patient Reported Outcome Measurement; Oxford Knee Score; Anteromedial Osteoarthritis.

Introduction

Historically treatment of end-stage osteoarthritis has been total knee arthroplasty (TKA)[1]. However as many as 47 % of patients having knee replacements are suitable for a smaller partial replacement [2,3]. Medial unicompartmental knee arthroplasty (UKA) is a viable strategy for end-stage isolated anteromedial osteoarthritis (AMOA) and have lower mortality rates, shorter hospital admissions, lower infection rates, fewer complications and is more cost effective than the TKA[4–7].

Regardless of these advantages the strategy only accounts for 8.9 % of all primary knee replacements in the UK[8]. The reason for this is often explained by the higher revision rates reported in national registries[9]. Revision rates are frequently used to evaluate the performance of knee replacements, but using revision rates to compare UKA and TKA is insufficient as a stand-alone indicator for performance, as the threshold for revision is lower for partial replacements[12–14]. As a result a more multifactorial evaluation including Patient Reported Outcome Measures (PROM) to aid in both research and in the shared decision making process is gaining popularity[10,11]. This approach is supported by the introduction of joint specific PROMs into several large registries internationally[8,12,13].

In the last decade we have seen an increased focus on factors which influences the outcome of UKA. It has highlighted the importance of an optimal set-up for the UKA strategy to reach the best possible results, meaning high usage rates and correct patient selection[14–16]. Keeping that in mind we aimed to explore the difference between the two strategies; UKA whenever appropriate versus TKA only, in their optimal set-up.

Previous registry studies have shown a small but significant difference between TKA and UKA when measuring the knee specific PROM oxford knee score (OKS)[17,18]. Most of them are registry studies and do not have the option of selecting TKA patients with similar pathology to patients eligible for UKA. The only study we have been able to identify who have sufficiently overcome this obstacle is the English RCT published in 2019[19]. It followed 528 patients for 5 years at 27 UK sites randomly assigned to TKA or UKA, and they found no significant difference in OKS.

Our hypothesis was that insuring the optimal set-up would result in a larger difference between the two strategies than previously reported. Thus, we aimed to isolate the strategy even further and compare the UKA strategy of using UKA whenever it is possible and compare it to the common strategy of TKA regardless of wear pattern in their optimal set-up. To that end we chose a UKA centre with a long tradition for using UKA for all AMOA patients and chose a TKA centre which did not do UKA surgeries. In this way we aimed to limit the number of UKA done by low usage surgeons and to all the health care professionals included in the treatment were familiar with the trajectory of the recovery. Further it limited the risk of bias due to personal preference of the surgeon and other personal involved in the treatment. The last

Material and Methods

Participants and Study design

We designed a two centre retrospective cohort study with 501 (301 UKA) consecutive knee replacement patients included from two centres. Patients were included if they had OKS available at baseline and 1 year follow-up. UKA patients had primary AMOA as primary surgical indication and were all treated at centre one, where they got the cementless Oxford Phase 3 from April 4. 2014 to November 22. 2016. TKA patients were included if they had AMOA on their pre-operative radiographs[23] and were treated at centre two from January 1. 2013 to April 1. 2016. UKA was implemented at centre two in mid-2016 by which time the inclusion of TKAs for the study was concluded. The number of participants was controlled by how far back the databases went. Only patients with the most common indication for UKA, primary AMOA, were included to insure the patients were comparable in pathology [24]. Patient demographics included age, gender, BMI, ASA and date of surgery.

Source of data

Our outcome measure was the 12 item joint specific questionnaire OKS containing two domains; knee pain and function. Questions have 5 response options and is combined into a single score ranging from 0-48 with high scores indicating low disability [25,26]. The score was used to calculate the PASS, which is a dichotomous interpretive tool designed to evaluate the patients’ satisfaction with their symptoms at the specific time point after the intervention[27,28]. The outcome is collected at baseline and 1 year follow-up. Data was accessed from the two centres local databases, both with 100 % completeness. Response rates for OKS in the databases’ were 87.9 % for UKAs and 44.6 % for TKAs across the inclusion period.

Statistics

The propensity score was calculated using logistic regression to estimate the effect of the confounders (baseline OKS, age, gender, ASA and BMI) on our exposure and combine these into individual scores. The score were then used to match a UKA patient to each TKA patient using the nearest neighbour method. Standardized mean differences of 0.1 or less were used as a measure of sufficient balances between the treatment groups[29].

Missing values that were missing at random were handled by multiple imputation (Multivariate Imputation by Chained Equations) using the “mice” package[30]. Continuous variables were imputed using predictive mean matching and categorical variables were imputed by polytomous logistic regression. Sensitivity analysis using plots was done.

The primary outcome was change in OKS from baseline to 1 year follow-up (change score). The secondary outcome; likeliness of achieving the Patient Acceptable Symptom State (PASS) was calculated from the 1 year follow-up OKS. Multiple linear regression was used to investigate the difference in change score between UKA and TKA. To adjust for any residual imbalance between treatment groups age, gender, BMI and ASA grade were included in the analysis. To compare the proportion of patients achieving PASS after 1 year between the two strategies, we did logistic regression adjusted for age, gender, BMI, ASA grade and baseline OKS. To control the interaction between baseline OKS and 1 year follow-up OKS we stratified baseline OKS into three by range. The PASS at 1 year follow-up was defined as OKS above 30.18[31]. P-values less than 0.05 were considered statistically significant.

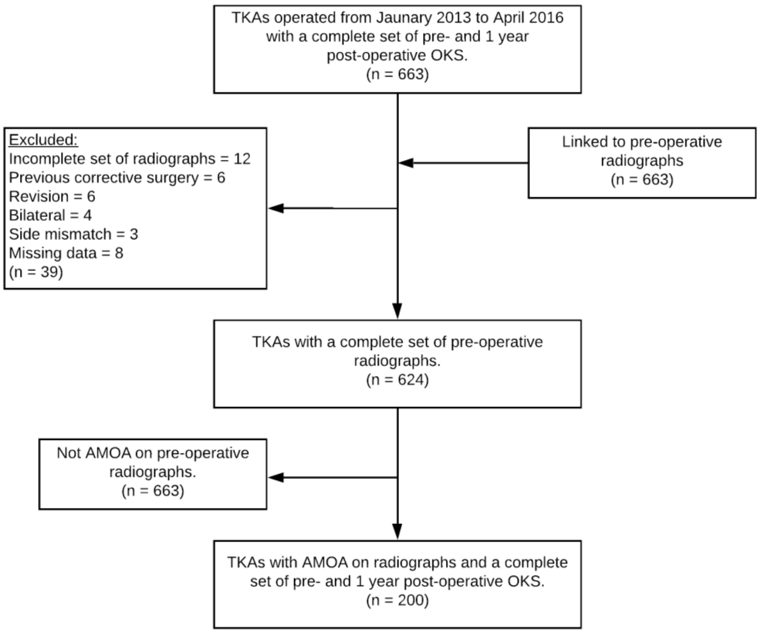
All statistics were calculated using R version 3.6.0.

Funding and Ethics

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. One or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.

The study was approved by the Danish Data Protection Agency under journal number; VD-2018-313.

Figure 1 Flowchart of selection process for Total Knee Arthroplasty (TKA) patients.



Results

The 200 TKA patients were selected as show in the flowchart (Figure 1). Our crude cohort thus comprised of 501 (301 UKA) patients, mean age 68 and 51 % female. After propensity score matching the cohort included 400 (200 UKA), mean age of 67, 53 % female, mean BMI of 30.23 and 66 % had ASA grade 2 (Table 1). Prior to matching the cohort had significant differences for pre-operative OKS and TKAs were performed 0.4 years earlier than UKA (CI 95 % 0.3 – 0.5, $p < 0.001$). Two patients had missing ASA grade and four had no BMI value, the values were missing at random and were imputed. Date of surgery had no interactions or significance in the regression analysis and was dropped from the analysis. Pre-OP OKS and 1 year post-OP OKS displayed a small positive interaction. Matching improved the balance between the two treatment groups by 68 %, and no significant difference was found after matching (Table 1).

Table 1. Baseline (crude) and Propensity Score Matched demographics for patients having medial unicompartmental knee arthroplasty (UKA) or total knee arthroplasty (TKS). Changes in TKA from crude to matched data are due to multiple imputation of missing values.

	Crude			1:1 Matched		
	UKA	TKA	SMD	UKA	TKA	SMD
n	301	200		200	200	
	Mean (s.d.)					
Age at Surgery	67.92 (9.94)	67.47 (9.21)	0.047	66.83 (9.87)	67.47 (9.21)	0.066
BMI	30.72 (5.65)	30.13 (5.34)	0.107	30.37 (5.72)	30.10 (5.33)	0.047
Pre-operative OKS	20.99 (7.33)	23.55 (6.53)	0.369	23.36 (6.87)	23.55 (6.53)	0.029
	N (%)					
Sex = Female	147 (48.8)	107 (53.5)	0.093	106 (53.0)	107 (53.5)	0.010
ASA			0.154			0.045
1	45 (15.0)	34 (17.4)		37 (18.5)	35 (17.5)	
2	221 (73.4)	130 (66.7)		133 (66.5)	132 (66.0)	
3	35 (11.6)	31 (15.9)		30 (15.0)	33 (16.5)	

SMD, standardized mean difference; s.d., standard deviation; BMI, body mass index; ASA, American Society of Anaesthesiologists.

At 1 year follow-up the UKA strategy achieved a statistically significant higher change score with a mean adjusted difference of 3.0 (CI 95 % 1.4 - 4.6, p < 0.001) points (Table 2).

Table 2. Predicted mean change in oxford knee score (OKS) at 1 year follow-up for unicompartmental knee arthroplasty (UKA) and total knee arthroplasty (TKA), and difference using multiple linear regression. Brackets indicate 95 % confidence intervals.

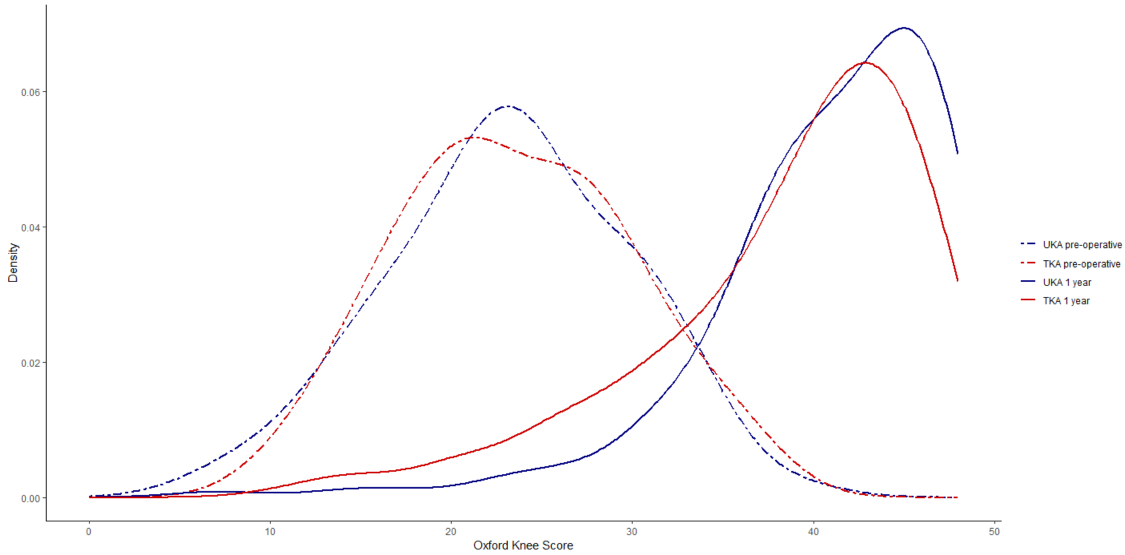
	UKA	TKA	Adjusted mean difference	Pr(> |t|)
OKS change	18.57 (10.42 - 26.72)	15.55 (7.39 -23.71)	3.02 (1.41 - 4.63)	< 0.001

The density plot in Figure 2 suggests a larger proportion of UKA patients reached an excellent 1 year OKS. This is supported by a statistically significant odds ratio (OR) of 3.67 (CI 95 % 1.73 - 8.45 p = 0.00119) (Table 3).

Table 3. Proportion of patients who achieved the patient acceptable symptom state (PASS) (oxford knee score > 30.18) as absolute number and percentage. Logistic regression results presented as odds ratio (OR) with 95 % confidence interval (CI) and p-value.

	UKA	TKA	OR (CI 95 %)	Pr(> |z|)
Achieved PASS	189(94.5 %)	169 (84.5 %)	3.67 (1.73 - 8.45)	0.001

Figure 2 Density plot showing the distribution of pre- and 1 year post-operative Oxford Knee Score (OKS) stratified by surgical strategy. UKA, unicompartmental knee arthroplasty; TKA, total knee arthroplasty.



Discussion

As expected, both strategies show substantial improvements at 1 year follow-up. The UKA strategy did significantly better with a mean adjusted difference in change score of 3.0 points and with 94.5 % compared to 84.5 % of patients achieving the PASS supporting the distributions seen in Figure 2.

The difference in change score presented in this study is statistical significant, the clinical significance is less certain. The 3 point difference we are reporting does not exceed the minimal important difference (MID) for OKS of 4.84 points[32], which marks the clinically significant difference.

Others have compared using a variety of other PROMs, collectively finding no significant difference[20–22]. Safe for Beard et al.[19] all randomised studies had small numbers of participants, making type 2 errors a valid concern. Though short of the MID, our estimate is noticeably large compared to previous studies [18,19,33]. We focused on the strategy from the decision of surgical treatment to the 1 year follow-up and did not isolate the investigation to the implant. Our design ensured not only the surgeon, but the entire healthcare personal involved in the treatment was familiar with the post-operative care and recovery trajectory. Further it limited the risk of bias due to personal preference. We measured change score whereas previous publications measured the final outcome. Lastly, the evaluation of baseline radiographs made inclusion of patients with similar pathology possible.

Except for RCTs we have been unable to find studies which are able to control the pathology. RCTs are the gold standard for original research and can be very successful in limiting a multitude of bias and confounding. Their main strength is limiting confounding by indication, but when treatment success partly relies on a surgeon's technical skill the RCT is vulnerable to performance bias. The same thing is true for the rest of the healthcare professionals involved in both pre- and post-operative care. Because the two treatments have different surgical approaches and post-operative care, the blinding of patients and healthcare personal is difficult, making the design vulnerable to the personal opinion and expectations of both patient and healthcare professionals. This is why we consider this body of work helpful in describe this area from a different perspective.

Our emphasis on the strategy and not the arthroplasty itself comes from our interpretation of resent year's research in UKA. It tells us the success of UKA as a strategy relies on not only the arthroplasty itself, but everything from correct patient selection and surgical skill to understanding its different recovery trajectory to the TKA[16,24,34]. The two centre design gave us an opportunity to insure all these factors were optimised for both strategies. It insured the surgeons were experienced and had high usage rates and volume for the strategy they followed, which limited the risk of subpar results[15] and limited performance bias. In exchange our design made us vulnerable to confounding by indication and selection bias. To address these limitations, we only included TKA patients with AMOA, and propensity score matched them. Thereby they would have been eligible for UKA had it been offered to them and any unbalance at baseline was controlled. Lastly we included our confounders in the regression analysis, thereby adjusting for any residual differences between the two groups.

The secondary outcome; PASS was chosen as a way of interpretation of the final score. It gave us an opportunity to illustrate the difference between the two strategies in a way easier to interpret and convey to patients as part of the shared decision making process. Communicating a 3 point difference in mean adjusted change score to a patient can be challenging, but communicating a OR and a percentage as in Table 3 is much more intuitive to patients and other non-health care professionals.

To gain the advantages of the two centre design we introduce bias, primarily selection bias as with the baseline difference in OKS seen in the crude data (Table 1), this we addressed by propensity score matching our cohort[35]. It is however likely there is residual selection bias from the two centre design on confounders we did not have the opportunity to include in the study. Our design relied on retrospective data from the two centres databases. The database at centre two had a low response rate, which was due to a low response rate in 2013 of 30 %. The study included 38 TKA patients (19%) from 2013. The low response rate was due to the implementation of the database, and we therefore worked under the assumption of the data being missing at random.

In conclusion we found a significant difference in change score in favour of the UKA strategy. This difference is larger than in previously published series. Additionally, patients from the UKA strategy were significantly more likely to achieve the PASS. We believe these findings further contextualise this area of research and are presented in a way which aids the further understanding of the UKAs potential.

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Paper IV

Total vs. Unicompartmental Knee Arthroplasty: *Is there something to gain from implementing Unicompartmental Knee Arthroplasty*

Running title: TKA vs. UKA: Implementation of the UKA

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Abstract

Background Medial unicompartmental knee arthroplasty (UKA) is gaining in popularity as treatment for primary anteromedial osteoarthritis (AMOA) of the knee, meaning implementation at new units. However, the literature contains little research focusing on this phase.

Purpose We aimed to describe the implementation phase. Specifically, to investigate potential differences between Total Knee Arthroplasty and UKA in length-of-stay, complication-, readmission-, and revision rates and in the Patient Reported Outcomes; Oxford Knee Score (OKS) and Forgotten Joint Score (FJS).

Method We included the last 100 TKA patients with AMOA prior to, and the first 100 UKA patients after implementation. Surgeries were performed 2015 to 2018. We collected Length-of-stay, 90-days complication- and readmission rates and 2 year revision rates. FJS and OKS were collected at baseline, 3 months, 1 year and 2 years follow-up.

Results UKA patients had shorter mean adjusted length-of-stay -0.93 days (CI 95 %: -0.64:-1.21, p-value < 0.0001), 14 % fewer complications and 5 % fewer readmissions. Both groups had 2 revisions during the study. Both FJS and OKS showed significantly larger improvements for UKA patients, p-value < 0.0001. **FJS**: UKAs improved by 44.27 points (CI 95 % 37.76-50.78) at 2 years. TKAs improved by 38.93 (CI 95 % 32.98-44.89). **OKS**: UKAs improved by 15.11 points (CI 95 % 12.90-17.32). TKAs improved by 14.42 (CI 95 % 12.38-16.45).

Conclusion UKAs had shorter admissions, fewer complications and readmissions and larger FJS improvements. The benefit of using UKA is achieved immediately after implementation and becomes clinically important when seen in the context of nationwide healthcare.

Introduction

When deciding to implement a new surgical procedure it is valuable to know whether to expect a performance drop during implementation or if the benefits of changing strategy are immediate. However, there are very few publications specifically focusing on the implementation of medial unicompartmental knee arthroplasty (UKA). The only learning curve study for UKA implementation showed a rapid decrease in failure rates after 16 cases and the acceptable failure rate was reached after 29 cases[30]. Another study looked at the implementation of the minimal invasive UKA from previously doing UKA with open access, they found a decreased risk of revision and reoperation for the second half of the of the patients[14]. Thus, we know very little about the implementation of UKA at a centre which has no previous experience with the UKA.

Previous publications show UKA has the potential of reducing the length-of-stay (LOS), lower mortality rates, yield fewer complications and readmission and is more cost-effective compared to TKA[3–5, 16, 20, 28, 29]. The only drawback is the increased risk of revision[17, 20].

Research from the last decade also found the success of UKA depends on appropriate usage rates and surgical volume[2, 13, 21]. This could indicate that UKA is a challenging procedure which could lead to a significant performance drop during implementation. However, their results has also alerted us to the importance of committing to UKA as a strategy and achieving high usage rates and surgical volume to be able to achieve appropriate outcomes.

Historically, the main argument against the UKA has been higher revision rates compared to the TKA[26, 29]. However, parallel to the increase in usage the Danish Knee Arthroplasty Register has reported a decrease in revision rates for UKA [7]. This decrease might be a reflection of surgeons adhering to the current consensus for appropriate UKA practice. Using the UKA in patients similar to the TKA patients with bone-on-bone anteromedial osteoarthritis and focusing on higher more appropriate usage rates and surgical volume for the surgeons[12, 13, 21]. The introduction of the cementless fixation is likely also part of the reason[24, 26]. Lastly, the absent of an increase in revision rates could be an indication of an implementation without a significant performance drop.

Regardless of the higher revision rates we have seen an increase in UKA usage in Denmark from 8.16 % prior to 2015 to 20 % in 2019[7]. Parallel to this we have seen a change in patient demographics towards those known from the TKA patient [15].

The purpose of this study was to investigate and describe the potential performance drop during implementation of UKA, using our previous strategy; TKA as the control treatment. Specifically we aimed to investigate potential differences in LOS, complication-, readmission-, and revision rates and the knee specific Patient Reported Outcome Measurements (PROM); Oxford Knee Score (OKS) and Forgotten Joint Score (FJS). Thus evaluate both the safety of the procedure, the patients' experience and the hospital impact.

Patients and Method

Study Design

We included the last 100 TKA patients with anteromedial osteoarthritis (AMOA) prior to, and the first 100 UKA patients after implementation in April 2016. TKA patients preoperative radiographs were evaluated retrospectively for AMOA to insure compatible pathology to that of the UKA patients [23]. TKAs were operated from January 2015 to March 2016. UKAs were operated from April 2016 to December 2018. The UKA surgeries were performed by two surgeons who throughout the study had usage rates above 30 %, as recommended[13]. TKAs were performed by nine experienced knee surgeons, including the two UKA surgeons. Patients were included if they had filled out the preoperatively PROM questionnaires. TKA patients were selected retrospectively and UKA patients were recruited prospectively. There were no difference in post-operative protocol between UKA and TKA at during implementation.

Measured Outcomes and Variables

Pre-operatively patient demographics included Sex, Age at Surgery, Body Mass Index (BMI), American Society of Anaesthesiologists physical status classification (ASA), and Kellgren-Lawrence classification. The knee specific PROMs; FJS and OKS were collected preoperatively and at 3 months, 1 year and 2 year follow-up. Patients' hospital records were searched to determine; LOS (defined as nights spent in the hospital), 90-days readmission- and complication rates and 2 year revision rates. Complications were categorised according to severity using the Clavien-Dindo classification[8, 18]. All presented patient demographics were adjusted for in the regression analyses.

Statistical Analysis

OKS and FJS were analysed using mixed model regression including sex, BMI, age and ASA scores as fixed effects and accounted for the correlation of the repeated measurements and possible changes in variances over time by using an unstructured correlation matrix in the model[10]. Overall significant difference between treatment groups was determined using a multivariate Wald's test. LOS was investigated as adjusted mean difference using multiple linear regression. The likeliness of staying 2 or more nights and complication rates were tested using logistic regression. Pre-operative differences between groups were investigated using standardized mean differences(SMD), balance was defined as SMD of 0.1 or less[1]. Sensitivity analysis on PROM missing values were done by comparing our results from the complete data analysis, to the same analysis done on a data set where missing values were managed by multiple imputations using "mice" package[6]. Difference was assessed qualitatively by the authors for change in overall conclusion.

All statistics were calculated using R version 3.6.0[27].

Conflict of interest statement:

One or more authors (KG, AP, AT) have consultancies with Zimmer-Biomet. One or more authors (KG, AP, AT) has directly received funding from Zimmer-Biomet independently of this study. The institution of one or more of the authors (MM, KG, AT) has received funding from Zimmer-Biomet independently of this study.

Ethical review committee statement:

This study was performed in accordance with the ethical standards in the 1964 Declaration of Helsinki. The study was approved as a quality assurance study by the hospital directors WZ number: WZ17038300-2018-96/97. Data was managed in accordance with the guidelines from the Danish Data Protection Agency. According to Danish law, there is no requirement for an ethical committee approval if the study does not include interventions and is performed as part of a quality assurance. The study was conducted at the Dept. of Orthopaedic Surgery, Clinical Orthopaedic Research Hvidovre (CORH), Copenhagen University Hospital Hvidovre.

Results

Data collection

Inclusion was conditioned on having filled out our preoperative PROM questionnaire and having AMOA, corresponding to 39.7 % of TKA surgeries during the time of inclusion. All UKA patients filled out the preoperative questionnaire. SMD on preoperative characteristics between treatment groups showed balance for pre-operative PROMs and sex, but imbalance for all other variables (Table 1). Testing balance for TKA patient selection between UKA and non-UKA surgeons showed the same pattern of imbalance as in Table 1, with UKA surgeons choosing older patients with lower pre-operative OKS for TKA patients (Supplementary Table A1). Sub-analysis of the UKA patients stratified by surgeon showed imbalance for all variables except pre-operative OKS and sex (Supplementary Table A2).

Table 1: Pre-operative patient demographics stratified by treatment type, including standardized mean difference (SMD).

		UKA	TKA	SMD	Missing (%)
N		100	100		
		Number			
Sex (Female)		56	54	0.040	0 (0.0)
		Mean (SD)			
Age		63.94 (10.45)	67.57 (9.65)	0.361	0 (0.0)
Pre-operative OKS		23.18 (6.69)	22.74 (6.61)	0.067	0 (0.0)
Pre-operative FJS		20.25 (13.65)	20.40 (16.71)	0.010	0 (0.0)
Body Mass Index		30.04 (5.63)	30.73 (5.30)	0.126	1 (0.5)
		Number (%)			
ASA grade				0.222	2 (1.0)
	1	21 (21.2)	15 (15.2)		
	2	64 (64.6)	63 (63.6)		
	3	14 (14.2)	21 (21.2)		
Kellgren-Lawrence				0.500	34 (17.0)
	1	0 (0.0)	0 (0.0)		
	2	4 (4.3)	0 (0.0)		
	3	41 (44.1)	20 (27.4)		
	4	48 (51.6)	53 (72.6)		

OKS, Oxford Knee Score; FJS, Forgotten Joint Score; ASA, American Society of Anesthesiologists Classification; NA, missing value; SD, standard deviation.

Length of Stay and Adverse Outcomes.

UKA had shorter admissions with a mean adjusted difference of -0.93 days (CI 95 % -1.21:-0.64, p-value < 0.0001)). 72 % of TKA patients were admitted 2 or more nights, compared to only 23 % UKA patients (Figure 1), corresponding to an odds ratio (OR) of 12.4 (CI 95 %: 5.89-28.0, p-value = < 0.0001). Complications were significantly more likely in the TKA treatment group with OR 2.48 (CI 95 %: 1.17 - 5.48, p-value 0.020) (Table 2). The TKA group had 2 major complications (grade III) within the first 90 days after surgery, both were diagnosed with cancer. The UKA group had one major complication; a polypectomy. Complications directly linked to the treatment were two incision infections and one deep vein thrombosis. All three received non-surgical treatment (grade II). Readmissions were rare, thus presented descriptively in Table 2.

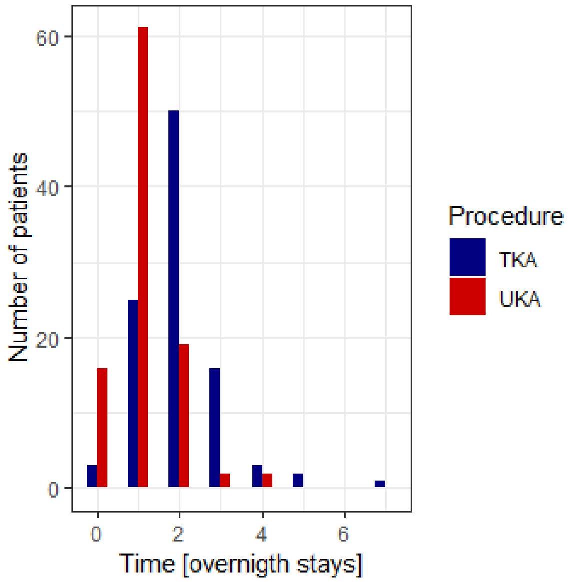
Table 2: Presents the mean length-of-stay, number of 90-day readmissions and complications, as well as number of revisions at 2 years follow-up. Complications have been categorized according to the type and severity[8, 18], for explanatory list see table A3 in the supplementary materials.

		UKA	TKA
N		100	100
		Adjusted Mean (SD)	
Length-of-stay		1.13 (0.77)	2.02 (1.04)
		Number	
Readmissions		10	16
Readmission indication			
	Surgical	1	5
	Medical	9	11
Complications		17	37
Complication severity			
	Grade I	13	28
	Grade II	3	7
	Grade III	1	2
	Grade IV	0	0
Revisions		2	2

Adjusted mean Length-of-stay is calculated using liniar regression and is adjusted for Sex, Body Mass Index, ASA grade and pre-operative OKS.

Both groups had 2 revisions within the first 2 years. All revisions occurred between the 1 and 2 year follow-up. The TKAs were both revised due to aseptic loosening. One UKA were revised due to instability, the other due to progression of osteoarthritis in the lateral compartment.

Figure 1: Histogram of Length-of-stay for the two treatment options.



Patient Reported Outcome Measures.

Oxford Knee Score:

The distribution of the OKS data indicates UKA patients did marginally better than TKA (Table A4 in supplementary materials). The mixed model analysis showed an overall significant difference, with UKA achieving higher change scores than TKA (Table 3). The median development over time in OKS is showing a more rapid recovery for UKAs at 3 months, but little or no difference at 1 and 2 years (Figure 2a). The sensitivity analysis warranted no change to the overall conclusion (Supplementary Table A5). It however supported the unadjusted 3 month results in Figure 1a and show the mixed model overestimates the TKAs improvement at 3 months by 0.5 points.

Table 2: Mixed model regression result for Oxford Knee Scores stratified by treatment. Presented as mean adjusted change score from pre-operative scores and corresponding 95 % confidence intervals (CI). P-value is from multivariate Wald's test.

	UKA (CI 95 %)	TKA (CI 95 %)	p-value
3 months	10.05 (8.30-11.81)	10.55 (7.91-13.19)	
12 months	15.34 (13.46-17.21)	14.87 (13.13-16.61)	
24 months	15.11 (12.90-17.32)	14.42 (12.38-16.45)	
			< 0.0001

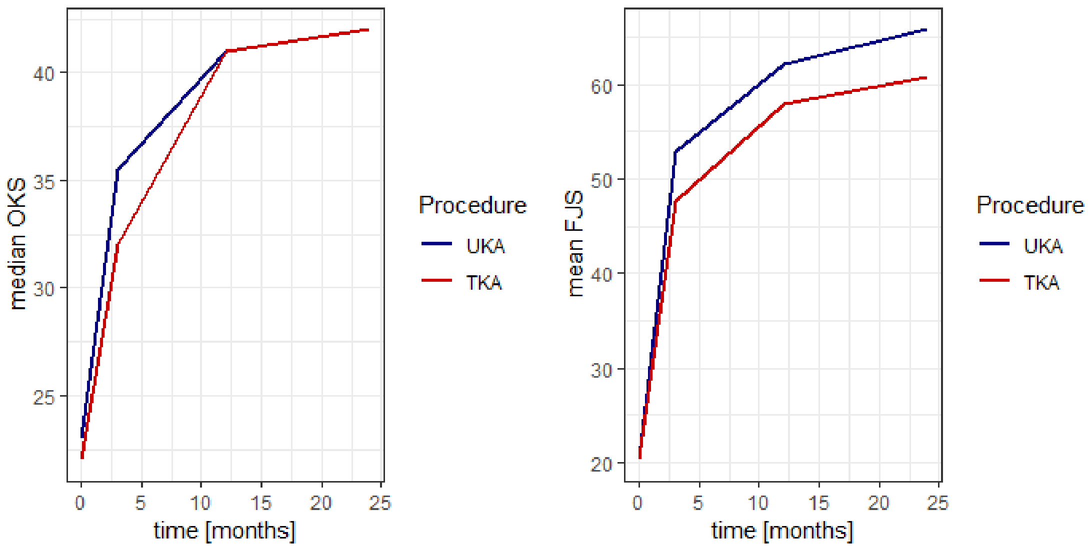
Forgotten Joint Score:

The unadjusted data show the UKA group consistently do better when measured as FJS (Figure 2b). The mixed model analysis showed a significantly larger improvement over the 2 years of follow-up with an end difference of 5.34 points (Table 4). The sensitivity analysis supports this showing our mixed model overestimate the TKAs with 1.4 points at the 3 month follow-up (Supplementary Table A4).

Table 3: Mixed model regression result for Forgotten Joint Scores stratified by treatment. Presented as mean adjusted change score from pre-operative scores and corresponding 95 % confidence intervals (CI). P-value is from multivariate Wald's test.

	UKA (CI 95 %)	TKA (CI 95 %)	p-value
3 months	32.17 (26.63-37.72)	32.79 (24.51-41.07)	
12 months	41.97 (35.69-48.25)	37.42 (31.44-43.41)	
24 months	44.27 (37.76-50.78)	38.93 (32.98-44.89)	
			< 0.0001

Figure 2 Left: Median development of Oxford Knee Score (OKS) for the treatment groups over time on crude data. Right: Mean development of Forgotten Joint Score (FJS) for the treatment groups over time on crude data.



Discussion

We set out to describe the implementation of UKA and determine if there is a performance drop during this phase. We measured performance as PROMs, LOS, complications, readmissions and revisions. Comparing LOS we saw UKA patients had significantly shorter admissions and were significantly less likely to stay 2 or more nights. Comparting this to the literature, publications show longer LOS for both groups but differences similar or slightly larger than we found here[9, 19, 29].
The references for LOS all found lower complication rates for UKA. We corroborate these results by finding that TKA patients were significantly more likely to experience complications. Descriptive statistics on severity in complications indicated no difference in pattern between the two treatments (Table 2). When looking at readmissions we saw a trend towards fewer readmissions for the UKA group (Table 2). Though we were unable to test for statistical significant difference in readmission rates, our findings support the findings of both Drager and Kulshrestha[9, 19]. An equal number of revisions were observed in each group with 2 in each group, TKAs for aseptic loosening, and UKAs for instability or progression of OA in the lateral compartment. All revisions occurred more than 1 year after the primary surgery. Aseptic loosening is the overall most common revision indication and OA progression is the 3rd most common reason for revision for UKA whereas instability is more rare and the 8th most common revision indication for UKA revisions[20].

We found a small but significant difference in OKS similar to that found by Beard et al.[3] and Liddle et al.[22]. Few have compared FJS in a similar set-up, but here we found a larger difference in change score between the two strategies in favour of UKA. It is possible the difference in focus of the two PROMs is responsible for the difference in trajectory and magnitude of difference between the two groups. Further the FJS operate on a larger scale and we do not know the MID for FJS, thus we cannot evaluate the clinical significance of the difference. The magnitude of difference however was not the focus of this study. What the PROM results show in this context is, that you do not have a performance drop when converting to the UKA strategy.

The strength of this study is the cross-over design for the unit, and the UKA surgeons also being part of the TKA surgeons prior to UKA implementation reducing selection bias. The TKAs were selected based on the pre-operative radiographic wear pattern, to insure the groups had similar pathology. The mixed model regression is a very robust method for handling missingness and the sensitivity analysis did not change our overall conclusion, that UKA achieve larger improvements than TKA when measured in PROMs even in the implementation phase. It showed a small overestimation for both PROMs for TKAs at 3 months corresponding to the large number of missing values in this category (Table A5 in supplementary materials).

The limitations were the retrospective radiographic analysis for the TKA patient making additional imaging impossible if needed. The lack of a randomized design resulted in baseline differences which we partially adjusted for in the statistical analysis by including the known confounders as covariates, however there will be residual selection bias from both known and unknown variables[11].

In conclusion our study indicates implementation of UKA gives us larger PROM improvements, shorter LOS and fewer complications compared to TKA. Further we observed an equal number of revisions in both groups. Thus, the benefit of using UKA is achieved immediately after implementation and becomes clinically important when seen in the context of nationwide healthcare.

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Supplementary materials

Table A1: Pre-operative patient demographics for TKA patients, stratified by surgeon type, and investigated by test of no difference (two one-sided tests (TOST)).

	UKA surg.	NonUKA surg.	SMD
N	10	77	
	Number (%)		
Gender (Female)	6 (60.0)	39 (50.6)	0.189
	Mean (SD)		
Age	70.50 (11.07)	67.45 (9.86)	0.291
Body Mass Index	30.20 (7.15)	30.38 (5.14)	0.289
Pre-operative OKS	20.90 (7.85)	22.97 (6.46)	0.121
Pre-operative FJS	18.97 (17.63)	21.08 (17.08)	0.029
	Number (%)		
ASA grade			0.414
1	2 (20.0)	11 (14.5)	
2	7 (70.0)	47 (61.8)	
3	1 (10.0)	18 (23.7)	
≥4	0 (0.0)	0 (0.0)	
Kellgren-Lawrence			0.446
4	7 (87.5)	39 (69.6)	

NA, Missing values; SD, standard deviation; OKS, Oxford Knee Score; FJS, Forgotten Joint Score; ASA, American Society of Anesthesiologists classification; Kellgren-Lawrence, Kellgren-Lawrence classification.

Table A2: Pre-operative patient demographics for UKA patients, stratified by surgeon, and investigated by test of no difference (paired two one-sided tests (TOST-P)).

		Surgeon 1	Surgeon 2	SMD
N		48	52	
Usage rate		47.53 %	35.66 %	
		Number (%)		
Sex (Female)		27 (56.2)	29 (55.8)	0.010
		Mean (SD)		
Age		65.79 (9.35)	62.23 (11.18)	0.345
Pre-operative OKS		23.47 (6.28)	22.82 (7.28)	0.095
Pre-operative FJS		22.14 (13.77)	18.20 (13.42)	0.290
Body Mass Index		31.67 (6.16)	28.55 (4.68)	0.571
		Number (%)		
ASA grade				0.162
	1	10 (21.3)	11 (21.2)	
	2	29 (61.7)	35 (67.3)	
	3	8 (17.0)	6 (11.5)	
Kellgren-Lawrence				1.205
	1	0 (0.0)	0 (0.0)	
	2	0 (0.0)	4 (8.7)	
	3	11 (23.4)	30 (65.2)	
	4	36 (76.6)	12 (26.1)	

NA, Missing values; SD, standard deviation; OKS, Oxford Knee Score; FJS, Forgotten Joint Score; ASA, American Society of Anesthesiologists classification; Kellgren-Lawrence, Kellgren-Lawrence classification.

Table A3: Distribution of diagnosis's in the complication categories.

Grade I	Grade II	Grade III
Percutaneous joint aspiration	Incision Defect/Infection	Unintended weight loss > 10 kg
Redness, swelling or fluid drainage from incision	Deep vein thrombosis	C. Mamma
Pain	Paracetamol poisoning	Polypectomy
Sounds from the knee	Urinary tract infection	
Baker's cyst	Urinary retention	
Synovitis	Erysipelas	
Vertigo		
Fall		
Cardiac outpatient treatment		
Kidney stone		
High creatinine		
Hyperglycemia		
Pericarditis		
Gastritis		
Eczema		
Thigh cramp		
Passing neurological symptoms (no treatment)		
Investigated for deep vein thrombosis (no treatment)		
Post-anesthesia shaking		
Chest pain (no ACS)		
Stiff knee		
Lack of mobilization		

Table A4: Distribution of the Oxford knee score (OKS), Forgotten Joint Score (FJS) and missingness at the 4 visits, stratified by treatment.

		Mean	1st quartile	Median	3rd quartile	NA (%)
Pre-OP OKS	UKA	23.2	19	23	27	24
	TKA	22.7	18	22	27	13
3 months OKS	UKA	33.3	28	35.5	38	22
	TKA	33.2	28	32	38	75
12 months OKS	UKA	38.1	34	41	44	24
	TKA	38.0	33	41	44	7
24 months OKS	UKA	39.4	36	42	45	34
	TKA	37.9	35	42	44	15
Pre-OP FJS	UKA	20.3	11	19	25	31
	TKA	20.4	8	15	30	11
3 months FJS	UKA	52.9	39	56	69	21
	TKA	47.7	27	40	78	76
12 months FJS	UKA	62.2	44	65	84	23
	TKA	58.0	35	60	81	14
24 months FJS	UKA	65.8	49	68	89	34
	TKA	60.7	41	65	86	16

Table A5: Sensitivity analysis of OKS and FJS missing values. Presented as difference between results and the same analysis done with multiple imputation for missing values. negative difference equal to underestimation.

	UKA	TKA
3 months OKS	0.14	0.52
12 months OKS	-0.13	0.00
24 months OKS	0.13	0.16
3 months FJS	-0.06	1.36
12 months FJS	0.90	0.09
24 months FJS	0.45	0.33