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VILLE TURPPO

VALIDITY OF THE FINNISH ARTHROPLASTY REGISTER AND OUTCOMES OF HIP AND KNEE ARTHROPLASTY

Validity of the Finnish Arthroplasty Register and Outcomes of Hip and Knee Arthroplasty

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ABSTRACT

Total hip and knee arthroplasties (THA, TKA) are common and cost-effective procedures in advanced osteoarthritis. The Finnish arthroplasty register (FAR) collects data from arthroplasty surgeries. In general, register data should have high coverage and validity that it can be used effectively in research and clinical decision-making. Previous studies on hip and knee prostheses have proven that they last a long time, even up to 30 years. Despite the long-term survival of prostheses, previous patient-reported outcome measure (PROM) studies have reported that up 10% of THA and up to 20% of TKA patients are dissatisfied with their surgery or with the long-term pain outcomes. However, PROM studies usually have follow-ups of just a few years, whereas prostheses last much longer.

The aim of the present thesis was to study how accurately THAs and TKAs can be identified from multiple sources including the FAR, the Finnish Care Register for Health Care (CRHC), patient self-reporting and the medical records of Kuopio University Hospital (KUH) (Study I). We also studied the long-term results of THA and TKA on patients self-reported physical capability (PC) and subjective well-being (SW) (Study II). We then investigated purchases of prescription analgesics by THA and TKA patients, prior to and after knee and hip arthroplasty (Study III).

In Study I data were collected from the FAR, CRHC and KUH medical records and the Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) study questionnaire. The information on THAs and TKAs from these databases was compared. The OSTPRE is a population-based prospective cohort study of 47–56 year-old-women from the Kuopio region, in Finland. The study started in 1989 and has continued ever since. It has collected detailed health information about the participants via postal questionnaires, including PC and SW. In Study II, data on THAs and TKAs were collected from the FAR and CRCH and the PC and SW self-reports were obtained from the OSTPRE questionnaires from 1994, 2004 and 2014. In Study III, data from THAs and TKAs and on purchases of pain medication were obtained from the PERformance, Effectiveness and Cost of Treatment episodes (PERFECT) project. The project was established in 2004 by the Finnish Institute for Health and Welfare (THL). It combines data from multiple sources (e.g. data from FAR, CRCH and social insurance institution of Finland (SII)).

The FAR had 94.5–96.1% data completeness for THAs and TKAs. The CRHC had 98.3–98.6% data completeness for THAs and TKAs, respectively. Patient self-reporting in order to identify the population with arthroplasty had 95.1% sensitivity and 92.9% positive predictive value (PPV) for THA and 94.6% sensitivity and 95.2% PPV for TKA. Sensitivity and PPV for self-reports in order to identify the actual date of THA or TKA were lower (62.9–65.3% sensitivity and 83.4 – 85.4% PPV).

In Study II, patients with THA or TKA maintained their self-reported PC and SW during 20-year epidemiological cohort study. The proportion of patients reporting good PC decreased by -1 percentage point (pp) (THA) and -4pp (TKA) in the first postoperative questionnaire (in 2004) compared with the questionnaire that was completed before arthroplasty in 1994. At the final 20-year follow-up in 2014 good PC reports by THA patients had decreased a total of -20pp (mean of 13 years postoperatively, 10-20 years) from the preoperative results. Good PC reports by TKA patients in 2014 had decreased by a total of -31pp (mean of 12 years postoperatively, 9–19). In participants without arthroplasty the same figures for good PC were -1pp (in 2004) and -25pp (in 2014), respectively.

The changes in good SW reports by the same THA/TKA patients were 0pp/ +9pp (in 2004) and -2pp/-5pp (in 2014, compared with the preoperative values). The changes in good SW reports by the participants without arthroplasty were +4pp and -5pp, respectively. However, during follow-up overall PC and SW were lower in those patients with arthroplasty compared to the participants without arthroplasty. Eventually in 2014, when compared to the control group, the THA/TKA patients reported lower results of -16pp/-27pp (good PC) and -12pp/-16pp (good SW).

In Study III, the proportion of THA and TKA patients purchasing paracetamol, NSAIDs or opioids steadily increased from three years preoperatively until three months preoperatively. From three months preoperatively to around the time of arthroplasty, the proportion of THA patients purchasing analgesics peaked to a level of 46% for paracetamol, 29% for NSAIDs and 17% for any opioids. After THA, the purchases decreased rapidly and they were: 19% (paracetamol), 11% (NSAIDs) and 6% (opioids) at six months postoperatively. Around the time of the TKA the purchases peaked at 56% for paracetamol, 33% for NSAIDs and 25% for opioids. Again, after a rapid decrease in purchases until six months postoperatively, TKA patients purchased 23% (paracetamol), 13% (NSAIDs) and 7% (opioids). All of these postoperative purchases further decreased by an additional 1–2pp until 12 months postoperatively and then remained at around the same level until the end of follow-up. Neuropathic pain medication had only a 4–5pp peak around the time of THA or TKA but seemed otherwise unaffected by arthroplasty.

In conclusion self-reports are suitable way of identifying people with THA or TKA. However, they do not perform as well in identifying the date of the actual arthroplasty event. The completeness of the FAR and the CRHC data is high, although the most optimal way to capture THAs and TKAs in Finland is to combine data from the FAR with data from the CRHC. Self-reported PC and SW are maintained by THA and TKA. However, when compared to control group without arthroplasty the overall PC and SW levels are lower in arthroplasty patients. The preoperative increases in the purchases of paracetamol, NSAIDs and opioids are reduced after THA and

TKA. After the first postoperative year, purchases of pain medications are close to the levels in the general Finnish population.

Keywords: THA, TKA, Arthroplasty, Osteoarthritis, Arthroplasty Register, Patient-reported outcome measure, PROM, Pain Medication, Physical Capability, Well-being

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TIIVISTELMÄ

Lonkan ja polven tekonivelleikkaukset ovat yleisiä ja kustannusvaikuttavia toimenpiteitä pitkälle edenneessä oireisessa nivelrikossa. Suomessa tekonivelleikkauksien tiedot kerätään Suomen tekonivelrekisteriin (FAR). Tekonivelrekistereiden tietojen hyödyntämiseksi tutkimuksissa ja kliinisessä päätöksenteossa tietojen on oltava kirjattu kaikkien leikkauksien osalta, ja tiedot on kirjattava oikein. Aiemmat tutkimukset ovat osoittaneet lonkka- ja polvi-implanttien kestävän pitkään, ja monet kestävät jopa noin 30 vuotta. Potilaiden itseilmoittamien hoitotulosten tutkimuksissa (PROM) on huomattu jopa 10 % lonkan ja 20 % polven tekonivelleikkauspotilaista olevan tyytymättömiä leikkaukseen tai kokevan riittämättöntä kivun lievitystä tekonivelleikkauksen jälkeen. Näissä PROM-tutkimuksissa seuranta-ajat ovat useimmissa tutkimuksissa yksittäisiä vuosia, vaikka proteesit kestävät jopa vuosikymmeniä.

Tämä väitöskirja koostuu kolmesta osatyöstä. Ensimmäisen tutkimuksen tavoitteena oli tutkia kuinka hyvin lonkan ja polven tekonivelleikkaukset ovat tunnistettavissa useista eri lähteistä, sisältäen FAR:n, Terveydenhuollon Hoitoilmoitusrekisterin (HILMO), Kuopion yliopistollisen sairaalan (KYS) potilastiedot ja potilaiden itseilmoitukset (Tutkimus I). Toiseksi tutkimme lonkan ja polven tekonivelleikattujen itseilmoitetun

liikuntakyvyn ja subjektiivisen terveydentilan muutoksia pitkällä aikavälillä (20 vuoden seurannassa) (Tutkimus II). Kolmanneksi tutkimme lonkan ja polven tekonivelleikattujen kipulääkkeiden ostoja ennen ja jälkeen leikkausten (Tutkimus III).

Tutkimuksen I aineisto perustuu FAR:n, HILMOn, KYS:n potilastietoihin ja potilaiden itseilmoittamiin tekonivelleikkaustietoihin Kuopion Osteoporoosin Vaaratekijät ja ehkäisy (OSTPRE) – tutkimuksessa. Näiden lähteiden sisältämiä tietoja lonkan ja polven tekonivelleikkauksien tapahtumatiedoista vertailtiin keskenään. OSTPRE on vuonna 1989 aloitettu väestöpohjainen tutkimus. Tutkimuksen kohteena olivat kaikki 47 – 56-vuotiaat naiset (n = 14 220), jotka asuivat tutkimuksen alun aikaan entisen Kuopion läänin alueella. Tutkimusta on jatkettu sittemmin 5 vuoden välein postitse lähetettävillä seurantakyselyillä. Kyselyissä on kartoitettu laajasti terveyteen liittyviä tietoja, kuten itseilmoitettua liikuntakykyä ja terveydentilaa. Tutkimuksessa II tiedot lonkan ja polven tekonivelleikkauksista kerättiin FAR:sta ja HILMO:sta. Tutkittavien itseilmoittamat liikuntakyky- ja terveydentilatiedot saatiin OSTPRE – tutkimuksesta vuosilta 1994, 2004 ja 2014. Tutkimuksen III tiedot tekonivelleikatuista ja heidän kipulääkkeiden ostoista saatiin Terveyden ja hyvinvoinnin laitoksen Performance, Effectiveness and Cost of Treatment episodes (PERFECT) –projektin tiedoista. 2004 aloitettu PERFECT keskittyy kustannuksiltaan ja potilasmäärältään merkittäviin toimenpiteisiin ja sairauksiin (kuten nivelrikko ja tekonivelleikkaukset). PERFECT:n aineistossa on yhdistetty tietoja useasta eri lähteestä, kuten FAR:sta, HILMO:sta ja Kansaneläkelaitokselta (reseptilääkkeiden toimitustiedot).

Tutkimuksessa I FAR:ssa löytyi tiedot 94.5–96.1 % lonkan ja polven tekonivelleikkauksista. Vastaavasti HILMO:sta löytyi tiedot 98.3–98.6 % leikkauksista. Itseilmoitetun lonkan tekonivelleikkauksen sensitiivisyys oli 95.1 % ja positiivinen ennustearvo (PPV) oli 92.9 %. Vastaavasti itseilmoitetun polven tekonivelleikkauksen sensitiivisyys oli 94.6 % ja PPV 95.2 %. Lonkan ja polven tekonivelleikkauksen ajankohdan itseilmoittamisen sensitiivisyys oli 62.9–65.3 % ja PPV 83.4–85.4 %.

Kaksikymmentä vuotta kestäneessä seurantatutkimuksessa (Tutkimus II) lonkan ja polven tekonivelleikatuilla itseilmoitettu liikuntakyky ja

terveydentila pysyivät useamman vuoden aiempaa vastaavalla tasolla, ja näiden muutokset olivat vastaavia kuin tutkituilla, joilla ei ollut tekoniveltä. Verrattuna tekonivelleikkausta edeltäneeseen tilanteeseen (1994 kysely) lonkan tekonivelleikatuilla hyvää liikuntakykyä ilmoittaneiden osuus laski -1 prosenttiyksikön (py) ja vastaavasti polvileikatuilla osuus laski -4 py ensimmäisessä leikkauksen jälkeisessä kyselyssä vuonna 2004. Vuonna 2014 (20-vuotisseurantakysely) hyvää liikuntakykyä ilmoittaneiden osuus oli laskenut kokonaisuudessaan -20 py lonkkapotilailla (keskimäärin 13 vuotta leikkauksen jälkeen, vaihteluväli 10–20 vuotta) ja polvipotilailla laskua oli kokonaisuudessaan -31 py (ka. 12 v. leikkauksen jälkeen, vaihteluväli 9–19 v). Verrokkiryhmässä (ei tekonivelleikkauksia) hyvää liikuntakykyä ilmoittaneiden osuuksien muutokset olivat vastaavissa pisteissä: -1 py (2004) ja -25 py (2014).

Samoilla lonkan / polven tekonivelleikatuilla hyvää terveydentilaa ilmoittaneiden osuudet muuttuivat 0 py / +9 py (vuonna 2004) ja -2 py / -5 py (vuonna 2014) verrattuna leikkausta edeltäviin tuloksiin. Verrokkiryhmässä leikkaamattomilla vastaavat muutokset olivat +4 py (2004) ja -5 py (2014). Kuitenkin verrokkiryhmässä hyvää liikuntakykyä ja terveydentilaa ilmoittaneiden osuudet olivat suuremmat läpi seuranta-ajan. Seurannan lopussa (vuonna 2014) erot olivat lonkan / polven tekonivelleikatuilla -16 py / -27 py liikuntakyvyn osalta ja -12 py / -16 py terveydentilan osalta verrattuna leikkaamattomiin verrokkiryhmässä.

Tutkimuksessa III lonkan ja polven tekonivelleikatuiden parasetamolin, tulehduskipulääkkeiden ja opioidien ostot kasvoivat tasaisesti alkaen kolme vuotta ennen tekonivelleikkausta. Leikkauksen aikana kaikkien lääkkeiden ostoissa tapahtui äkillinen nousu verrattuna kolme kuukautta ennen leikkausta olleeseen tilanteeseen. Tuolloin lonkan tekonivelleikatuista 46 % osti parasetamolia, 29 % tulehduskipulääkkeitä ja 17 % opioideja. Nopein väheneminen lääkeostoissa tapahtui ensimmäisten tekonivelleikkauksen jälkeisten kuukausien aikana. Lonkkaleikatuista 19 % osti parasetamolia, 11 % tulehduskipulääkkeitä ja 6 % opioideja 6 kuukautta leikkauksen jälkeen. Polven tekonivelleikkauksen aikaan parasetamolia osti 56 %, tulehduskipulääkkeitä 33 % ja opioideja 25 %. Myös polven tekonivelleikatuilla kipulääkkeiden ostot laskivat nopeasti

ensimmäisinä kuukausina, ja kuuden kuukauden kuluttua leikkauksesta 23 % osti parasetamolia, 13 % tulehduskipulääkkeitä ja 7 % opioideja. Kaikkien lääkkeiden ostot vähenivät vielä 1–2 py 12 kuukauteen asti leikkauksesta ja tämän jälkeen vakiintuivat lähes samalle tasolle seurannan loppuun asti. Neuropaattisen kivun hoitoon käytetyillä lääkkeillä oli myös hetkellinen 4–5 py nousu tekonivelleikkauksen aikana, mutta muuten näiden lääkkeiden ostot eivät vaikuttaneet muuttuvan leikkausten myötä.

Yhteenvetona voidaan todeta, että tutkittavien itseilmoituksella voidaan löytää kattavasti lonkan ja polven tekonivelleikatut, kuitenkaan leikkauksen ajankohdan selvittämiseksi itseilmoitukset eivät ole yhtä tarkkoja. Suomen tekonivelrekisterin ja Hoitoilmoitusrekisterin tiedot ovat kattavia, mutta kattavimmin lonkan ja polven tekonivelleikkaukset löytyvät yhdistämällä näiden rekistereiden tiedot. Lonkan ja polven tekonivelleikkaus ylläpitävät itseilmoitettua liikuntakykyä ja subjektiivista terveydentilaa. Tekonivelleikattujen tulokset ovat matalampia verrattuna verrokkeihin, joille ei ole tehty tekonivelleikkausta kliinisesti merkittävän oireisen nivelrikon vuoksi. Ennen tekonivelleikkausta parasetamolin, tulehduskipulääkkeiden ja opioidien ostot ovat kasvussa. Lonkan ja polven tekonivelleikkauksen jälkeen näiden kipulääkkeiden ostot vähenevät. Yksi vuosi tekonivelleikkauksen jälkeen kipulääkkeiden ostot ovat vakiintuneet ja ovat vastaavalla tasolla kuin yleisesti suomalaisessa väestössä.

Avainsanat: Tekonivelleikkaus, Lonkka, Polvi, Nivelrikko, Tekonivelrekisteri, Hoitoilmoitusrekisteri, PROM, Kipulääkitys, Liikuntakyky, Terveydentila

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LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Turppo V, Sund R, Sirola J, Kröger H, Huopio J. Cross-Validation of Arthroplasty Records Between Arthroplasty and Hospital Discharge Registers, Self-Reports, and Medical Records Among a Cohort of 14,220 Women. The Journal of Arthroplasty 2018;33:3649–3654.

II Turppo V, Sund R, Huopio J, Kröger H, Sirola J. Physical capability after total joint arthroplasty: long-term population-based follow-up study of 6,462 women. Acta Orthopaedica 2021;92:551–556.

III Turppo V, Sund R, Huopio J, Kröger H, Sirola J. Pain medication purchases before and after total hip and knee arthroplasty: a register study of 329,743 arthroplasties. Acta Orthopaedica 2022;93:534–541.

CONTENTS

ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical Classification System
ACR	American College of Rheumatology
AF	The Arthritis Foundation
CRHC	Care Register for Health Care (= FHDR)
FAR	Finnish Arthroplasty Register
FHDR	Finnish Hospital Discharge Register
THL	Terveyden ja hyvinvoinnin laitos / Finnish Institute for Health and Welfare
ISAR	International Society of Arthroplasty Registries
KL	Kellgren-Lawrence radiographic classification
NSAID	Non-Steroidal Anti-Inflammatory Drug
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OSTPRE	Kuopio Osteoporosis Risk Factor and Prevention study
PC	Physical capability
PP	Percentage point
PERFECT	Performance, Effectiveness, and Cost of Treatment episodes project
PROM	Patient-Reported Outcome Measure
SII	Social Insurance Institution of Finland (KELA)
SPSS	Statistical Package for the Social Sciences
SW	Subjective well-being
THA	Total hip arthroplasty
TKA	Total knee arthroplasty

1 INTRODUCTION

Osteoarthritis (OA) is the most common joint disease and it has been estimated that due to the ageing population and increased obesity OA will become even more common (Leifer et al., 2022). In a Finnish study, symptomatic OA of the hip was found in 20% of men and women over 75 year of age. Symptomatic OA of the knee was found from 16% of men and 32% of women of similar age (Aromaa and Koskinen, 2002). OA affects the whole joint. Its main symptom, which causes disability and restrictions for normal life, is pain. Other possible symptoms are stiffness, crepitus, joint effusion, restricted movement, malalignment and deformation of the joint. The symptoms persist as the disease progresses (Hunter and Bierma-Zeinstra, 2019).

Current treatments of OA aim to relieve the symptoms of OA, although they cannot stop or reverse the degenerative changes in the joint. Treatment includes conservative non-pharmacological treatment (e.g. physiotherapy, exercise, walking aids), conservative pharmacological treatment (e.g. paracetamol, NSAIDs, opioids, neuropathic pain medication and joint injections) and surgery (osteotomy and arthroplasty). Arthroplasty is the treatment of choice for patients who do not get sufficient relief for symptoms using conservative treatment methods (Bannuru et al., 2019; Hunter and Bierma-Zeinstra, 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018; Kolasinski et al., 2020). OA is also the main diagnosis resulting in total hip (THA) and knee (TKA) arthroplasties. Arthroplasty effectively treats pain and restores function in OA patients (Heath et al., 2021; Kamaruzaman et al., 2017; Räsänen et al., 2007).

Data on THAs and TKAs are collected to arthroplasty registries around the world. At least 34 countries have local or national registries. Arthroplasty registries have been established in order to improve the quality of arthroplasty and allow the post-market surveillance of prostheses. The registers usually collect a large amount of data from multiple institutions. This permits faster detection of poorly performing

prostheses and also the detection of rare outcomes. Finland was the second country in the world, after Sweden, to start its own nationwide arthroplasty register in 1980. The registries also show the positive results of arthroplasty. For example, up to 90% of the hip and knee prostheses can last at least 20 years (depending on joint, age at arthroplasty, sex, and model of the prosthesis) (AOANJRR, 2021; FAR, 2022; McKie et al., 2021).

Despite prosthesis survival and good pain and function outcomes, up to 10% of THA patients and 20% of TKA patients have long-term pain or dissatisfaction after arthroplasty (Beswick et al., 2012; Heath et al., 2021; Lau et al., 2012). This has been shown in patient-reported outcome measures (PROMs). Increased interest in the value that is provided by health care has led to the development of PROMs. PROMs are designed to capture patients' view of their health. They can be disease-specific (e.g. for osteoarthritis) or generic (covering more generally health-related quality of life issues). However, the follow-ups of the PROM studies are short, generally six to 12 months, whereas prostheses usually survive much longer than this (Ethgen et al., 2004).

As arthroplasties are intended to treat pain caused by OA, the consumption of analgesics can be considered to be an indirect outcome measure of success. We found only a few previous studies that reported both the pre- and postoperative consumption of various types of medications by THA and/or TKA patients (Blågestad et al., 2016; Jørgensen et al., 2018; Rajamäki et al., 2019). These studies have shown that arthroplasty reduces purchases of prescription drugs although there are still people who purchase all kinds of analgesics years after receiving arthroplasty. We found no studies with nationwide data that described the consumption of analgesics for several types of analgesics, by both THA and TKA patients with long-term pre- and postoperative follow-ups.

The aim of this thesis was to study the coverage of the FAR and the CRHC, the validity of self-reported arthroplasty, long-term pre- and postoperative self-reported physical capabilities and subjective well-being, as well as purchases of analgesics before and after THA and TKA, including several types of pain medication.

2 REVIEW OF THE LITERATURE

2.1 OSTEOARTHRITIS

Osteoarhtritis (OA) is the most common joint disease of the hip and knee. Its incidence increases with age due to the cumulation of exposure to a variety of different risk factors and age-related changes in the joint (Aromaa and Koskinen, 2002; Johnson and Hunter, 2014; Prieto-Alhambra et al., 2014). The development of OA is the result of inflammatory, mechanical and metabolic changes in the joint. OA affects the entire joint including the cartilage, subchondral bone, synovium, ligaments, capsule and periarticular bones (Hunter and Bierma-Zeinstra, 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018).
OA causes burden on individual patient and causes great health care costs. On an individual level, OA symptoms can result in reduced physical capability and inactivity (Palazzo et al., 2016). The costs relating to OA can be direct (e.g. healthcare visits, treatment, assistive devices) or indirect (e.g. lost wages and retirement due to disablity). The prevalence of OA is estimated to be increasing due to people living longer and being more obese (Leifer et al., 2022). This has caused the direct costs of OA to be as much as 1–2.5% of GNP in some developed countries (March and Bachmeier, 1997). In a Dutch study, hip and knee OA was estimated to cost EUR 40 milloin due to sickness absence from work alone. Knee OA caused twice the cost of sickness absence compared to hip OA (Hardenberg et al., 2022).

2.1.1 Epidemiology of hip and knee osteoarthritis

The incidence and prevalence of OA increases with age. OA can have many different stages and it may be that patients with the mildest symptoms are not identified or included in studies that investigate the prevalence of OA. Also, there is no consensus in the studies as to whether all cases should be doctor-diagnosed OA or whether also cases with only radiological OA

findings are included. Not all people with radiological OA changes have symptoms (Gwilym et al., 2008). Radiological OA has a higher prevalence than symptomatic OA and radiological findings are more often regarded as osteoarthritis in epidemiologic studies (Pereira et al., 2011). These factors make it harder to estimate the prevalence and incidence of OA.

In a Finnish study, 4–5% of women and men over 30 years of age had symptomatic physician-diagnosed hip OA. The same figure for over 75-year-olds was 20%. Symptomatic doctor-diagnosed knee OA was found in 5–7% of participants over 30 years of age. However, 32% of women over 75 years of age had knee OA, whereas only 16% of men over 75 years of age had knee OA (Aromaa and Koskinen, 2002). In a comprehensive review of prevalence studies around the world (Asia, Europe, North America), 10–27% of women 60 years and older had symptomatic OA of the knee and 4–11% of similar aged men also had symptomatic OA of the knee. Whereas in a Spanish study, 8%/7% of women/men of over 60 years of age had symptomatic OA of hip (Pereira et al., 2011). A few studies of small populations in the USA have reported 9% of over 45-year-olds with symptomatic hip OA, whereas 17% of over 45-year-olds had symptomatic knee OA (Lawrence et al., 2008). In the USA the incidence of symptomatic hip OA was 88/100,000 person-years and 240/100,000 person-years for symptomatic knee OA (Oliveria et al., 1995). In a Spanish study the incidence of hip OA was 2.1/1,000 person-years and the incidence of knee OA was 6.5/1,000. OA clusters to people, i.e. people with OA in one joint tend to have OA also in some other joint. Thus, the prevalence hip, knee or hand OA increases the incidence of hip and knee OA (Prieto-Alhambra et al., 2014).

2.1.2 Risk factors for hip and knee osteoarthritis

There are multiple risk factors for hip and knee OA. Many of the risk factors are shared, although some are joint-specific. Age is the greatest risk factor for OA in both joints. Incidence of symptomatic hip and knee OA start to increase after 50 years and peak at 75–80 years (Prieto-Alhambra et al., 2014). Other shared risk factors include obesity, previous joint trauma,

heavy sport activities, physically heavy work, genetics. Dysplasia of the acetabulum and cam deformity (deformity of the femoral head) are risk factors for hip OA. Women are at higher risk of knee OA. Also, knee malalignment (varus or valgus) and meniscectomy are risk factors for knee OA (Bijlsma et al., 2011; Hunter and Bierma-Zeinstra, 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018). Genetic components have been estimated to affect the development of OA in 40–80% of cases. There are multiple genetic variations that lead to OA (van Meurs, 2017). The genetics behind OA are complex and new discoveries are being made. For example, over 100 DNA polymorphic variants have been associated with OA (Aubourg et al., 2022).

2.1.3 Symptoms and diagnosis of osteoarthritis

Pain is the most disabling symptom of OA and is caused by tissue injury or inflammation of the joint. In the early stages of OA, pain is often related to heavy physical stress and is relieved by rest. Subsequent pain becomes more constant and the joint is also painfull when resting (Bijlsma et al., 2011). Many patients also suffer from neuropathic pain, which is caused by changes in the nervous system and joint innervation (Hunter and Bierma-Zeinstra, 2019). It is estimated that 23% of hip and knee patients suffer from neuropathic pain (French et al., 2017).

Other possible symptoms and clinical findings include joint stiffness, especially after resting for a long time. The stiffness usually lasts a few minutes. There can be also joint effusion, restricted movement, crepitus, malalignment, and deformation of the joint. Increased symptoms often lead to limitations in day-to-day life, e.g. walking, kneeling, climbing stairs, engaging in sports and household chores. Further, the symptoms and limitations caused by hip and knee OA can affect mental health and sleep (Bijlsma et al., 2011; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018).

There are no international diagnosis criteria for hip and knee OA. Diagnosis is based on complete history and clinical examination. In Finland, OA criteria include typical radiological findings in hip or knee radiographs.

Radiographs can also be used to rule out other conditions and for assessment of the severity of radiological OA findings in the joint (Hunter and Bierma-Zeinstra, 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018). Multiple radiological assessment tools for OA have been developed. As well as the scores developed by Kellgren and Lawrence (KL), Croft et al, Brandt, Ahlbäck, joint space width can also be used in the assessment of OA from radiographs (Brandt et al., 1991; Kellgren and Lawrence, 1957; Terjesen and Gunderson, 2012; Wright et al., 2014). The KL grading system is the oldest recognised rating scale for assessing the severity of OA from radiographs and the system is applicable to both hip and knee joint OA. The KL grading consideres the following to be evidence of OA in radiographs: osteophytes on the joint margins, periarticular ossicles (mainly in the interphalangeal joints in hands), subchondral bone sclerosis, joint space narrowing (JSN) via narrowing of joint cartilage, small pseudocysts with sclerotic walls in the subchondral bone and deformation of bone ends in the joint (Kellgren and Lawrence, 1957). The KL grading is described below in **Table 1.**

Table 1. Grading of osteoarthrosis from radiographs using Kellgren-Lawrence grading.

Grade	Description
0 (None)	Total absence of radiological OA changes
1 (Doubtful)	Possible JSN or osteophytes
2 (Minimal)	Definite radiological OA changes (JSN or osteophytes) but minimal level severity
3 (Moderate)	Definite JSN, moderate osteophytes, sclerosis, possible bone deformation
4 (Severe)	More severe changes as in Grade 3

Joint space narrowing (JSN). (Kellgren and Lawrence, 1957)

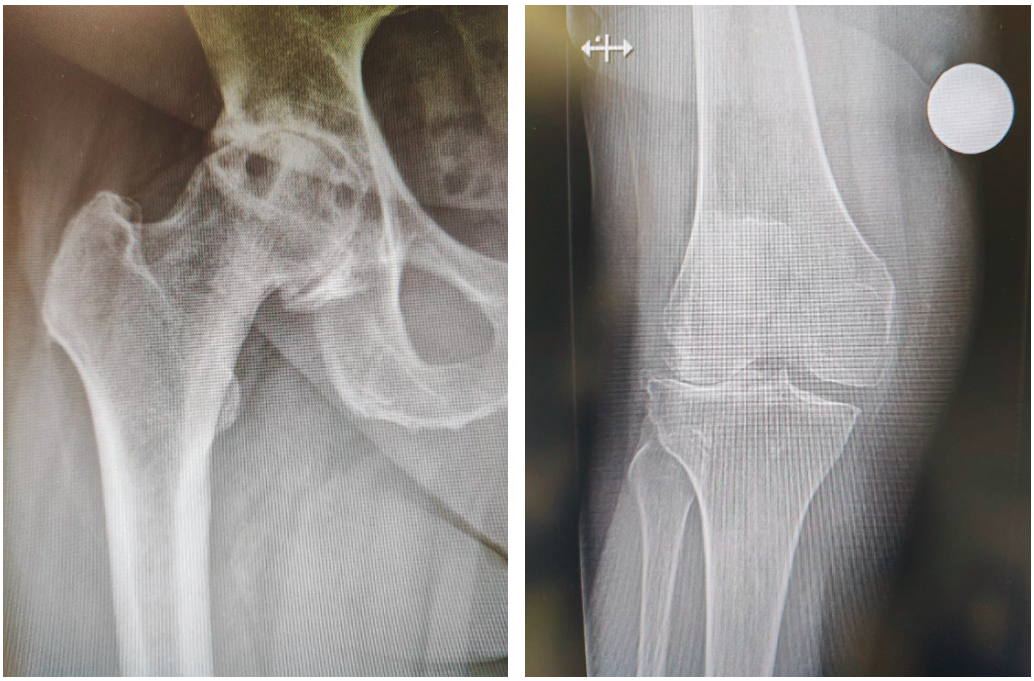


Figure 1.
KL 4 hip OA (on the left): Extreme JSN / bone contact, sclerosis, osteophytes (+ subchondral cysts)
KL 4 knee OA (on the right): Extreme JSN / bone contact, sclerosis, osteophytes

2.1.4 Treatment options

The treatment of hip and knee OA can be divided into three different modalities: conservative (non-pharmacological), conservative (pharmacological) and surgical. OA treatments aim to reduce both pain and stiffness and also to maintain functional capacity. Some patients may receive adequate help with only one intervention. However, many patients need a combination of different treatments.

Non-pharmacological treatments for both joints include education about osteoarthritis, physiotherapy, physical exercise, losing weight (for obese patients), walking canes, orthosis (knee OA), acupuncture **(Appendix 1)**. These treatments are mentioned in all of the following guidelines: Osteoarthritis Research Society International (OARSI), the American College of Rheumatology (ACR), the Arthritis Foundation (AF) and the Finnish

Current Care Guidelines for Knee and Hip OA (Bannuru et al., 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018; Kolasinski et al., 2020). Physiotherapy and physical exercise can include strength and aerobic exercises and exericses that increase the range of motion of the joint. There is no single exercise that is superior to others. However, it is important to implement an exercise program that is easy to reproduce at home and addresses the functional limitations of the individual patient (Fransen et al., 2015; Holden et al., 2022). Unlike the Finnish Current Care Guidelines, the ACR/AF recommendations strongly advise against the use of transcutaneous electrical stimulation (TENS) in hip and knee OA due to the lack of benefit. The OARSI and ACR/AF recommendations include mind-body interventions (yoga and Tai chi). They also have conditional recommendations for cognitive behavioural therapy (Bannuru et al., 2019; Kolasinski et al., 2020).

Pharmacological treatment usually starts with paracetamol. If paracetamol is not sufficient non-steroidal anti-inflammatory drugs (NSAIDs) are used. Topical NSAIDs are recommended for knee OA. Oral NSAIDs are recommended for both joints if there are no contraindications. The next step is mild opioids, including tramadol and codeine (only sold in combination products in Finland). The OARSI and ACR/AF recommendations only mention tramadol and it is recommended in preference to other opioids. However, opioids should only be used if other medications prove ineffective or cannot be used due to contraindications (Bannuru et al., 2019; Kolasinski et al., 2020). The Finnish recommendations also include codeine (Knee and Hip Osteoarthritis: Current Care Guidelines, 2018). Stronger opioids can be used in limited cases for example, when there is great pain, and the patient is unwilling to undergo or is not eligible for arthroplasty. Due to dependency potential and side effects of opioids, they should be used only with the minimal effective dose and they should be prescribed only for short-term use. (Benyamin et al., 2008). OA can cause pain sensitisation and widespread pain. In such cases, medication for neuropathic pain may be used. Due to the lack of studies on neuropathic pain medication in hip and knee patients, only duloxetine is recommended in appropriate cases in the

OARSI, ACR/AF and Finnish guidelines (Bannuru et al., 2019; Knee and Hip osteoarthritis: Current Care Guidelines, 2018; Kolasinski et al., 2020). Intra-articular (IA) corticosteroid injections are recommended for both joints. However, multiple injections at short intervals should be avoided. Repeated corticosteroid injections can increase the cartilage volume loss in OA joints (McAlindon et al., 2017). Ultrasound-guided application is needed for the hip joint. IA corticosteroids have a positive effect on pain and physical limitations (Bannuru et al., 2019; Knee and Hip osteoarthritis: Current Care Guidelines, 2018; Kolasinski et al., 2020). An IA hyaluronic acid injection for knee OA shows only limited evidence of benefits. At best, hyaluronic acid has had a modest reduction in symptoms and at worst has been as effective as a placebo. Recommendations for the use of IA hyaluronic acid are mainly conditional, even though, these injections are widely used (Bannuru et al., 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018; Kolasinski et al., 2020). Orally administered glucosamine and chondroitin sulphate are also widely used and there are many over the counter (OTC) products. These have been proved to be as effective as a placebo and there are recommendations against their use (Kolasinski et al., 2020).

If the aforementioned forms of medication fail to relieve the symptoms adequately and OA progression decreases the patient's physical capabilities and well-being, surgery is an option. Options for surgery include osteotomy and joint arthroplasty. The decision to undergo surgery is always made individually for every patient by an orthopaedic surgeon based on clinical findings, the severity of the symptoms and their effect on daily life.

An osteotomy is a surgical intervention in which bone is reshaped or realigned and the aim is to correct the malalignment of the joint and transfer physical stress to the healthy parts of the joint. Knee osteotomy can be used in unicondylar osteoarthritis and knee osteotomy is mainly performed on younger (usually <60-year-old) physically active patients with isolated medial knee OA. As patient's own joint is preserved, also better proprioception and physical capabilities are maintained compared with TKA. In knee osteotomy, usually the alignment of either proximal tibia or

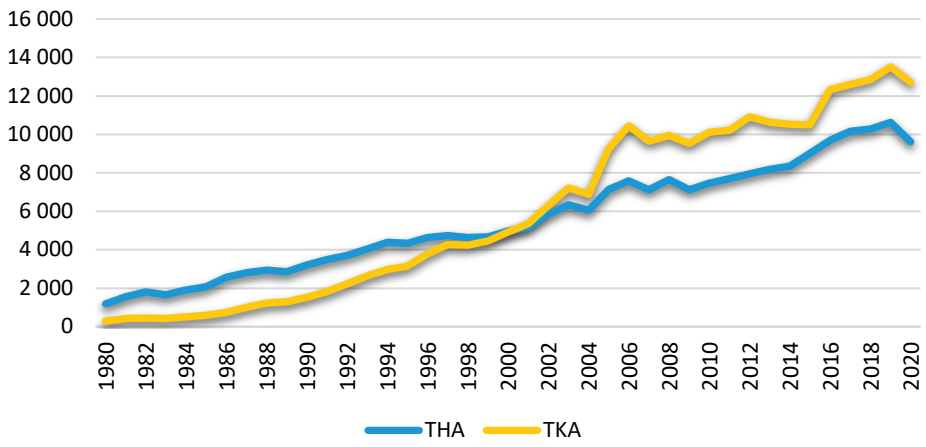
distal femur is corrected (Knee and Hip Osteoarthritis: Current Care Guidelines, 2018; Sillanpää et al., 2022). Osteotomy of the hip is mainly performed to prevent of OA in dysplastic hip joints. Hip osteotomy can be done by cutting and realigning either pelvic bones (acetabulum) or proximal femur (Knee and Hip Osteoarthritis: Current Care Guidelines, 2018; Sirola et al., 2022). Total hip and knee arthroplasty will be described below.

2.2 TOTAL HIP AND KNEE ARTHROPLASTY

The number of new THAs and TKAs per year has increased steadily every year and arthroplasty is now a common procedure. In Finland the peak year was 2019 and 10,625 primary THAs and 13,512 primary TKAs were performed. **(Figure 2)** In many countries, including Finland, 2020 was an exception and the number of new arthroplasties decreased, most probably due to COVID-19 pandemic (AOANJRR, 2021; FAR, 2022; W-Dahl et al., 2021). In Finland, in 2013 the lifetime risk for THA was estimated to be 15%/11% (women/men) and 23%/12% for TKA. Whereas the lifetime risk was estimated to be 12–16% (women)/8–11% (men) for THA and 10–21% (women) /6–15% (men) for TKA, in other countries (Australia, Denmark, Norway, Sweden), respectively (Ackerman et al., 2017b, 2017a). Recently, a Finnish register-based study revealed that the prevalence of TKA was 5% in women and 3% in men over 40 years or older. TKA prevalence in people aged 75 years or older was 12% (women)/8% (men) (Pamilo et al., 2022).

The following paragraphs describe the history of THA and TKA in short due to the nature of the present thesis, which is about epidemiological outcomes of THA and TKA

Figure 2. Number of primary arthroplasties in Finland from 1980 to 2020



Data for the figure was obtained from the Institute of Health and Welfare's FAR user interface. https://www.thl.fi/far/#index

2.2.1 The history of hip arthroplasty

The first attempts at treating OA with different materials and tissues inserted on or between articulating surfaces (interposition arthroplasty) started in the mid–late 19th century (Bota et al., 2021; Knight et al., 2011; Ollier, 1888) **(Figure 3)**. The first reported attempts at hip arthroplasty were by a German surgeon, Themistocles Gluck, in 1890. He designed and inserted artificial joints made from ivory (Brand et al., 2011; Glück, 1891). Mould arthroplasty was introduced in 1923 by Smith-Petersen. In this method, the femoral head was fitted with a new smooth glass surface. However, glass could not withstand the forces experienced by hip joints (Smith-Petersen, 1948). Philip Wiles developed the predecessor of modern hip implants and used bolts and screws to fit a stainless steel metal-on-metal (MoM) total hip prosthesis in 1938 (Wiles, 1958). The development of MoM implants continued. In the 1970s, there were some initial reports of adverse reactions to metal debris (ARMD) due to wear particles from MoM implants. However, in the 1990s, in order to avoid the osteolysis that had

been noted in MoP implants, MoM implants were used again in significant numbers. In the early 2010s, the use of MoM THA was ceased completely due to the high revision rates and complications (Hughes et al., 2018).

English orthopaedic surgeon, Sir John Charnley, can be considered the inventor of modern total hip arthroplasty. His invention in the early 1960s was a considerable improvement on previous inventions. He introduced low friction arthroplasty (using polyethylene as a bearing material) and using polymethylmethacrylate (PMMA) bone cement to fix the prosthesis to the bone (Charnley, 1961; Knight et al., 2011). The first low friction arthroplasty used polytetrafluoroethylene (PTFE) as bearing material. Due to the high level of wear of PTFE, ultra-high molecular weight polyethylene (UHMWPE) was subsequently introduced by Chranley in 1962. UHMWPE is a simple polymer which is created by the polymerisation of ethylene (Merola and Affatato, 2019; Sobieraj and Rimnac, 2009). However, even using UHMWPE components, wear still persisted (Wroblewski, 1997). Highly cross-linked polyethylene (XLPE) is a further development of UHMWPE to improve its mechanical characteristics and to decrease wear. The crosslinking is achieved by using radiation. The process produces free radicals (molecules with unpaired electrons) to the material, which need to be stabilised using heat or vitamin E (Merola and Affatato, 2019; Sobieraj and Rimnac, 2009).

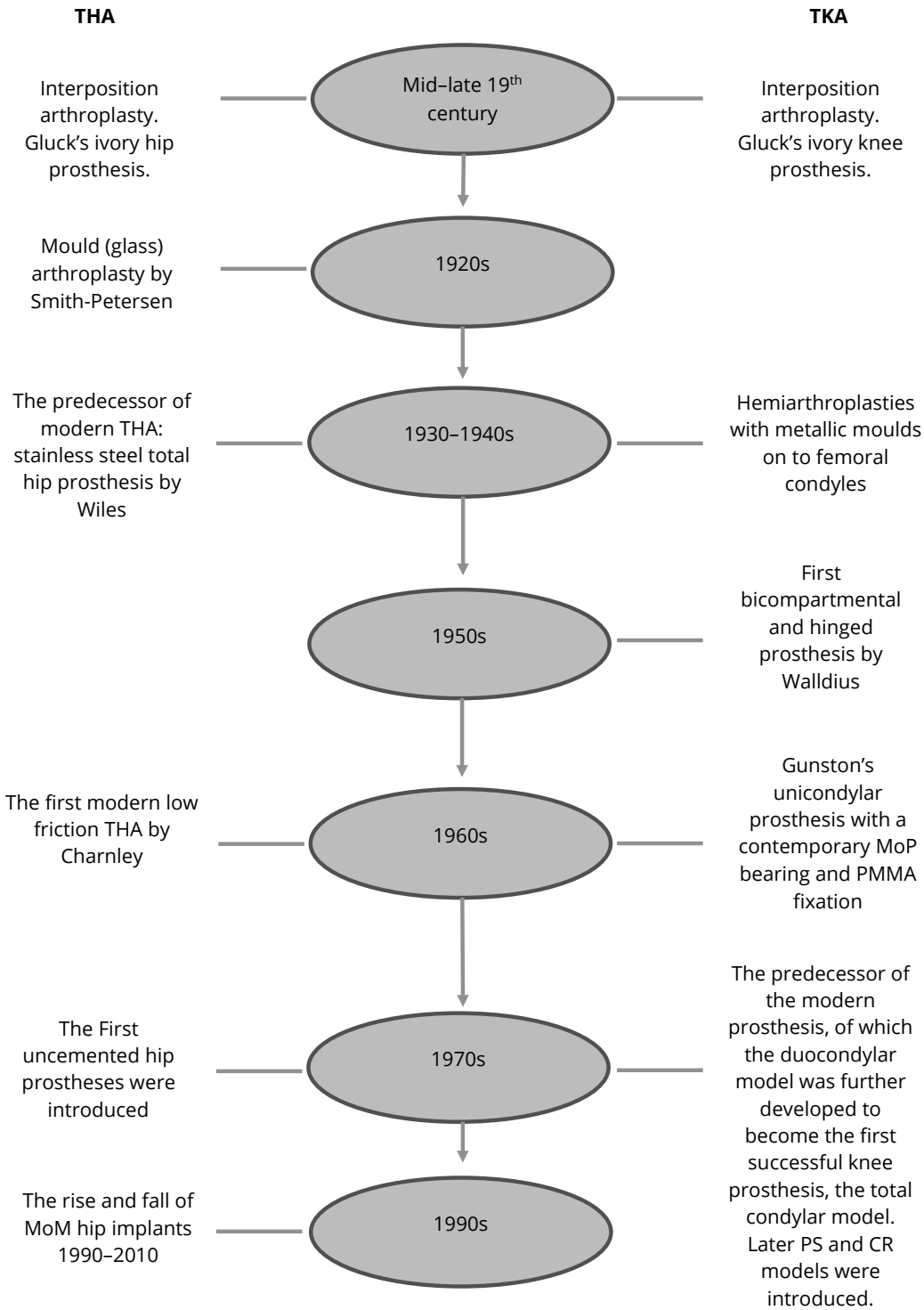
In the early 1970s, “cement disease” was described as being attributable to small PMMA particles that caused aseptic loosening of the prosthesis (Bota et al., 2021). This led to the development of porous-coated uncemented prostheses.

2.2.2 The history of knee arthroplasty

From the mid to late 19th century, interposition and resection arthroplasties were also tried in arthritic knees (Verneuil, 1860) **(Figure 3).** Themistocles Gluck was the first persons to report an attempted arthroplasty of the knee, in 1890 (Brand et al., 2011; Glück, 1891). Hemiarthroplasty was first attempted in the 1940s by Campbell, with metallic moulds inserted on both femoral condyles (Parcells, 2017). Later,

in 1950s first unicompartmental prostheses were inserted to isolated medial OA. (Mittal et al., 2020) In 1958, Walldius (from Sweden) introduced the first bicompartmental arthroplasty to replace both tibial and femoral surfaces of the joint. The prosthesis also included a hinge (Walldius, 1957). In 1968, Frank Gunston introduced the first bicompartmental knee arthroplasty without a hinge. It consisted of two separate unicondylar prostheses. The prostheses had metal-polyethylene articulating surfaces and PMMA cement was used to fix the prosthesis (Gunston, 1971). The predecessor of modern TKA was the bicompartmental prosthesis by Freeman and Swanson in the 1970s. This model prioritised joint function and stability over anatomy and the cruciate ligaments were sacrificed (Parcells, 2017; Swanson and Freeman, 1974). Concurrently with the Freeman-Swanson prosthesis, in 1971, Insall, Ranawat and Walker introduced their duocondylar knee prosthesis. The duocondylar model attempted to mimic anatomy and the cruciate ligaments were preserved. The duocondylar model was further developed towards a more functional approach (mechanical alignment) and the cruciate ligaments were subsequently sacrificed. These developments lead to a total condylar (all articulating surfaces replaced) model, which constitutes the first truly successful TKA (Insall et al., 1979; Parcells, 2017). In the late 1970s, the total condylar model was further developed and the first cruciate-retaining (CR) and posterior-stabilised designs (PS) were introduced (Insall et al., 1982; Parcells, 2017). Also, in the 1970s, Pappas and Buechel developed a mobile-bearing and rotating-platform prosthesis, which aimed to achieve more optimal joint movement and reduced prosthesis wear (Buechel and Pappas, 1986).

Figure 3. The development of THA and TKA



2.2.3 Total hip arthroplasty

Patients undergo THAs mainly because of OA of the hip. There is variation between countries. OA is the diagnosis for primary THA in 65–88% of cases. Other common diagnoses are femoral neck fracture, rheumatoid arthritis, osteonecrosis, tumour and developmental dysplasia. The mean age at the time of arthroplasty varies between 66–72 years depending on sex and country. 54–58% of primary THAs are performed to women (AOANJRR, 2021; FAR, 2022; McKie et al., 2021; W-Dahl et al., 2021). In Finland in 2019, the incidence of primary THA was 400/100,000 of inhabitants over 40 years of age. In Sweden, the incidence in the total population has been 146/100,000 inhabitants and it is estimated that 1.8% of the Swedish population has undergone a THA (FAR, 2022; W-Dahl et al., 2021).

Total hip arthroplasty consists of acetabular replacement, resection of the femoral head and neck, which are replaced with a stemmed femoral prosthesis and femoral head. In addition to polyethylene bearing materials (UHMWPE, XLPE), joint implants can be made of metallic and ceramic materials, for example titanium alloys, special high-strength alloys, alumina, zirconia, zirconia toughened alumina and stainless steel (Merola and Affatato, 2019). The bearing surfaces of acetabulum and femoral head can have several combinations. An acetabulum liner can be made of UHMWPE, XLPE, ceramic material or metal. The femoral head component can be made of metal, ceramacised metal or ceramic material. An XLPE liner combined with a metallic or ceramic head are the most commonly used THA bearing surfaces. The metal-on-polyethylene bearing is cost-effective and should perform well with all patiens (AOANJRR, 2021; Eskelinen et al., 2022). The reasons for the use of ceramic-on-polyethylene (CoP) prostheses could be e.g. suspected better wear resistance and less trunnionosis (local soft tissue reaction due to corrosion debris from the prosthesis) (Eskelinen et al., 2022; Gaudiani et al., 2018). In a review by Spir et al. with follow-ups up to six years, there was a little less wear in CoP than in metal-on-polyethylene (MoP) prostheses, however their revision rates and post-operative results were similar (Spir et al., 2022). Long-term 10- and 15-year results, in Australian arthroplasty registry show almost

identical results for CoP and MoP prostheses (AOANJRR, 2021). Ceramic on ceramic (CoC) prostheses have low wear rates and friction. Their drawbacks are price, possible squeaking noises and the risk of prosthesis breakdown (Zagra and Gallazzi, 2018). However, also CoC implants have excellent long-term results with up to 90% survival at 20 years (AOANJRR, 2021). Large head metal-on-metal (MoM) combinations should not be used due to their poor performance (Seppänen et al., 2018). The range of motion of joint implants and the risk of dislocation can be altered by adjusting the size and model of prosthesis components (especially the head of the femur). Fixation methods for THA include cemented, cementless, hydrid (cemented femur, cementless acetabulum) and inverse hybrid (cementless femur, cemented acetabulum) designs. In Finland in recent years, cementless fixation has been used in over 50% of primary THAs and hybrid fixation in around 40% of cases. A fully cemented design is currently used only in a minority of THAs, whereas it was used in around 50% of cases in the early 2000s (FAR, 2022). However, cemented THA implants seem to perform better in patients over 65 years of age. For patients under 65 years of age the survival rate is similar to cemented and uncemented THAs (Mäkelä et al., 2014).

2.2.4 Total knee arthroplasty

TKA is nearly always performed because of osteoarthritis. The mean age at time of surgery is 68–69 years internationally. In national arthroplasty registries, OA was reported for diagnosis in 95–97% of TKA cases. Other possible diagnoses could be rheumatoid arthritis/other inflammation of the joint, trauma, avascular necrosis and tumour (McKie et al., 2021; W-Dahl et al., 2021). In Finland, the incidence of TKA was 487/100,000 of inhabitants aged over 40 and the Swedish Arthroplasty Register reports an incidence of TKA 114/100,000 inhabitants with no age limitation. It is also estimated that 1.4% of the Swedish population has undegone TKA (FAR, 2022; W-Dahl et al., 2021). Internationally, more TKAs are performed on women (51–62%). Also, in Finland, there are more TKAs performed on

women compared to men (AOANJRR, 2021; FAR, 2022; McKie et al., 2021; W-Dahl et al., 2021).

Primary TKA has two competing prosthesis designs: the cruciate-retaining = CR (posterior cruciate ligament (PCL) retained) and posterior-stabilised = PS (both cruciate ligaments sacrficed) models. These models can be used in most cases, as soft tissue and ligament assymmetry can be balanced. CR models apply to the majority of cases. PS models should be considered if the range of movement of the knee joint is limited or there is remarkable malalignment before operation (Eskelinen et al., 2022; Parcells, 2017). The third and less used design, bicruciate-retaining (BCR-TKA), preserves both cruciate ligaments: the anterior cruciate ligament (ACL) and the PCL. Thus, it is more like a resurfacing procedure and has a more anatomic design than CR or PS. BCR-TKA prostheses had already been developed in the 1960s, yet in recent years there has been renewed interest interest in them. By also preserving ACL it is hypothesised that even better TKA results could be gained from more optimal knee kinematics and the proprioceptive qualities of ACL (Boese et al., 2021). During primary TKA there is rarely a need to use more stabilising prosthesis designs. Such designs are constrained implant (CCK = constrained condylar knee) and hinge prostheses. A CCK prosthesis includes a larger tibial post (compared to the PS model) and a larger femoral box. A stem is also often attached to a CCK prosthesis. A hinge prosthesis includes a hinge, stems and often a rotating platform. CCK and hinge models are used in the event of severe instability, laxity or malalignement that cannot be otherwise corrected (Eskelinen et al., 2022; Parcells, 2017). The patella can be resurfaced and is recommended if the arthroplasty is done for treating isolated patellofemoral OA (Eskelinen et al., 2022). Cobalt chrome metal is mainly used on the femoral bearing surface. Other materials, for example ceramacised metal, zirconia and titanium nitride are used with patients with metal allergy. UHMWPE and XLPE are used on the tibial bearing surface. In modern TKAs, XLPE is mainly used because it is more durable and has a lower revision rate than non-XLPE (AOANJRR, 2021; Civinini et al., 2017). The cemented fixation of all prosthesis components with polymethyl methacrylate (PMMA) is

considered the “gold standard” and in Finland it is used in the majority of cases (FAR, 2022). Other possible fixation methods are: hybrid (cemented tibia, cementless femur), inverse hybrid (cementless tibia, cemented femur) and uncemented prostheses. In Finland, cemented fixation is used in 90% of primary TKAs (FAR, 2022). In < 65-year-old patients, in addition to cemented models, also hybrid prosthesis have shown good mid-term results (Niemeläinen et al., 2020).

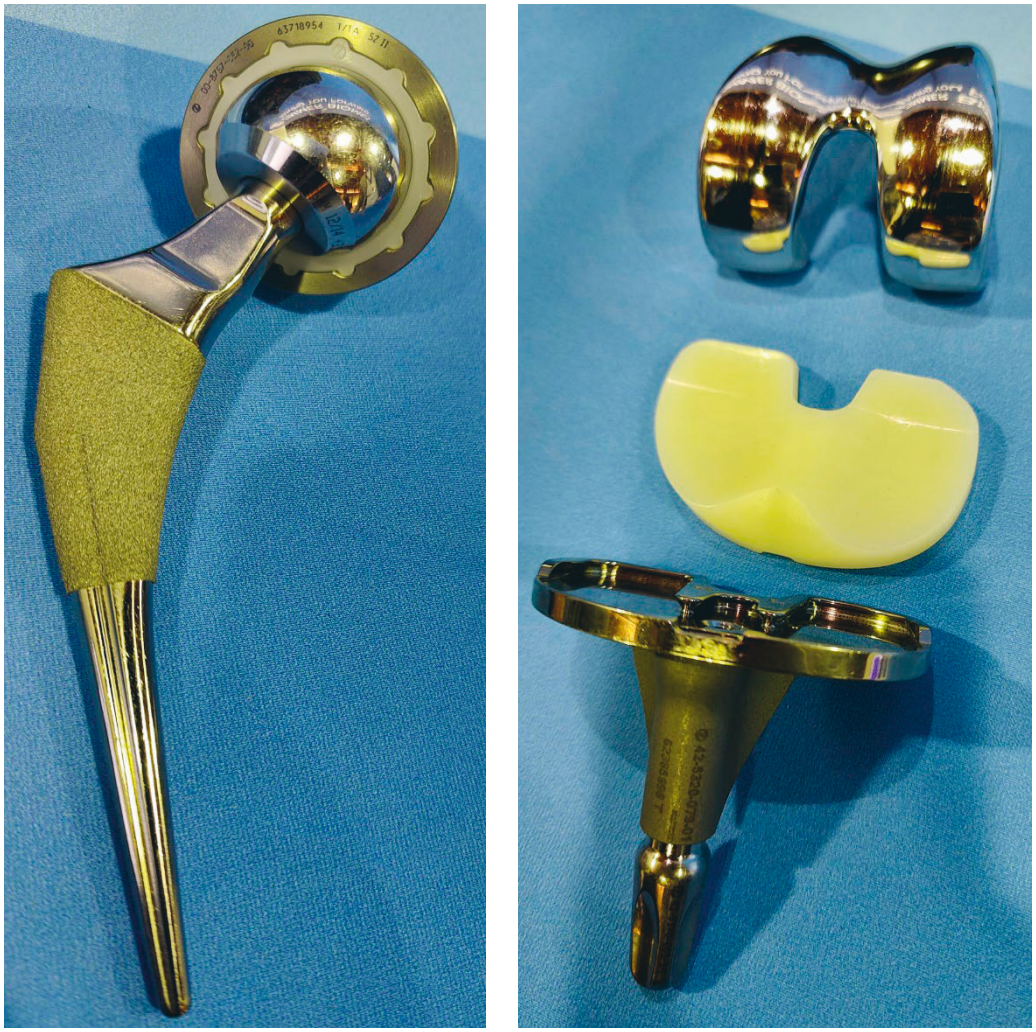


Figure 4. Contemporary prostheses for the hip (on the left) and knee (on the right).

2.2.5 Results of THA and TKA

Both THA and TKA are effective in treating symptoms of hip or knee OA and are also cost-effective procedures compared to non-surgical interventions in the treatment of OA. THA is more cost effective than TKA (Heath et al., 2021; Higashi and Barendregt, 2011; Kamaruzaman et al., 2017; Räsänen et al., 2007). In the case of severe OA of the hip or knee, arthroplasty appears to be the more cost-effective solution rather than prolonging the waiting time (Mather et al., 2014; Mota, 2013).

The annual reports of arthroplasty registries and previous studies have reported similar short-/medium-/long-term survival rates for THA. They report implant survival rates of around 96% at 10 years, around 85–90% at 15 years and 73–91% at 20 years for THA (Bayliss et al., 2017; FAR, 2022; McKie et al., 2021). The results can vary for example due to the fixation methods, implant models, age at the surgery. The annual reports from joint registries and previous studies have reported TKA implant survival rates of about 95% at 10 years, 91–94% at 15 years and 86–92% at 20 years (AOANJRR, 2021; Bayliss et al., 2017; FAR, 2022; McKie et al., 2021). Even though THA and TKA have good long-term survival rates, young patients in their early 50s or younger should be notified that there is up to a 35% probability that they will need a revision arthroplasty during their lifetime (Bayliss et al., 2017).

As arthroplasty registries have evolved, it has become evident that conclusions about the performance of prostheses and arthroplasty that are only based on the revision rates are not sufficient. For additional information on arthroplasty performance, collecting PROMs from arthroplasty patients has increased among joint registries. In quality studies, unfavourable pain outcome has been reported as being around 9% after THA and up to 20% after TKA (Beswick et al., 2012). The actual level of dissatisfaction reported by THA patients has been 10% or less, and 10–20% of TKA patients report dissatisfaction (Heath et al., 2021; Lau et al., 2012). A Finnish study by Niemeläinen et al. report 15% of knee arthroplasty patients (aged 65 years or younger) being dissatisfied with their operation and 7% of the patients had residual severe knee pain at

two years post-operatively (Niemeläinen et al., 2019). The New Zealand Joint Registry annual report includes PROMs (Oxford hip and knee scores) results for both THA and TKA (20% response rate). After surgery, at six months, good or excellent scores were reported by 84%/75% of THA/TKA patients, at five years 89%/84%, at ten years 87%/82%, at fifteen years 86%/79% and at 20 years 82%/77%. (McKie et al., 2021). Overall, THA patients are more satisfied with their surgery (Hamilton et al., 2012). However, multiple patient factors can affect satisfaction after total joint arthroplasty, such as preoperative expectations, satisfactory pain relief and comorbidities (e.g. depression) (Brander et al., 2007; Dunbar et al., 2004; Hamilton et al., 2013).

2.3 ARTHROPLASTY REGISTRIES

Arthroplasty registries are an important way of conducting post-market orthopaedic implant monitoring that aim to improve the quality of arthroplasty surgeries. Arthroplasty registries can detect early signs of major problems with certain implant models and surgical methods. A poorly performing prosthesis can cause considerable suffering. Also, all revision arthroplasties involve additional costs (Delaunay, 2015). As there can be publications from financially conflicted scientists, independent arthroplasty registries (non-commercial) offer financially unbiased real-world data (Hughes et al., 2017). The study results provided by the registries have even had a global impact on clinical practice. According to the International Association of Arthroplasty Registries (ISAR), there are arthroplasty registries in at least in 34 countries, although not all registries are national. Some countries have regional and institutional registries (ISAR, 2022) **(Appendix 2)**. If arthroplasty register data are to be used in high quality studies, the following should be taken into account: all orthopaedic departments report their arthroplasties to registries; all arthroplasties are reported; all variables are reported and variable values are accurate (Mäkelä et al., 2019).
Arthroplasty registries differ. This can lead to the misinterpretation of results, lack of clarity when comparing register data and problems with the

international use of arthroplasty register data. The ISAR encourages the registries and the scientific community to establish terminological consistency and the standardisation of statistical analysis. It has also published the summary of minimum dataset for all registries to use in data collection (ISAR, 2022).
The registries can be catogorised based on the type of data they collect. Level one data includes basic data on patient, type of surgery and prosthesis. Level two also includes comorbidity and demographic data. Level three includes PROMs. On the fourth and highest level, radiographic data are also collected. As the costs of the registers and data collection increase when a higher level of data is collected, most registries focus on level one data (Hughes et al., 2017).

2.3.1 The Finnish Arthroplasty Register (FAR)

The Finnish Arthroplasty Association soon followed its Swedish colleagues and the FAR was established in 1980 **(Appendix 2)**. Since 1989, the delivery of information on all arthroplasties became mandatory for all orthopaedic departments (National Institute for Health and Welfare, 2022a; Suomen Artroplastiayhdistys, 2022). The Finnish National Institute for Health and Welfare (THL) has been operating the register since the beginning of 2009. In the early 2010s, the FAR did not match the needs of a modern arthroplasty register. The modernisation of the FAR to match the requirements of modern registers started in 2011. The modernisation was quided by orthopaedic surgeons (Mäkelä, 2018; National Institute for Health and Welfare, 2022a). To improve the data collection for hip and knee arthroplasties, the register has collected the data online since 19 May 2014. Subsequently, data on shoulder (2019) and elbow (2021) arthroplasty have been collected online. However, they also include PROMs (The 15D generic instrument and the Western Ontario Osteoarthritis of the Shoulder (WOOS)) to be delivered to registries. The register collects wrist and ankle arthroplasty data using their own digital or paper forms (National Institute for Health and Welfare, 2022a). There is an online platform for the FAR data, which is open to the public. It was started in 2015.

https://www.thl.fi/far/#index. It is possible to search for basic information on hip, knee and shoulder arthroplasties.

Collecting THA and TKA operation data for the FAR can be conducted either via a commercial platform (the platform created by BCB Medical is mainly used in Finland by the hospital districts) or using a non-commercial platform created by the THL. https://www2.thl.fi/endo/. The platform for THA and TKA data requires the following information to be entered: joint, side, social security number, ASA (American Society of Anesthesiology) – classification, weight, height, antibiotic prophylaxis, antithrombotic medication, type of anaesthesia, surgery time and surgeon details (basic); diagnosis, operation codes, possible previous surgeries of the joint (operation classification and diagnosis codes); components, method of fixation, possible details about cementing, screws and bone grafts (components). In addition, PROMs (such as OHS or OKS) are collected and stored locally but are not yet routinely transferred to the FAR from THAs and TKAs. Other medical registries in Finland, for example, the Care Register for Health Care (CRHC) and register data from the Social Insurance Institution of Finland (SII) can be linked to the FAR for study purposes.

Currently, the FAR tests its data coverage by comparing recorded arthroplasties in the FAR to those found in the CRHC. The FAR reports its data coverage from 2003 to 2020 as 91.3–98.3% for primary THAs and 91.9–98.9% for primary TKAs. For revisions the data coverage is reported to be 84% for THAs and 85% for TKAs (FAR, 2022). Before Study I in 2018, there had not been previous actual validation studies of the FAR data. A few secondary results have been reported that compare FAR arthroplasty cases to CRHC data (Jämsen et al., 2009). These results are now available from the FAR user interface.

2.3.2 Swedish arthroplasty registries: SKAR, SHAR and their merging

The Swedish Knee Arthroplasty Register (SKAR) was the first ever national arthroplasty register and was established in 1975. The Swedish Hip Arthroplasty Register (SHAR) followed later in 1979 (Kärrholm, 2010; Robertsson et al., 2014). These registries have acted as role models for

many registries that were subsequently established. In 2021, SHAR and SKAR merged, and the Swedish arthroplasty register (SAR) was founded. The SAR reports its data completeness being 98% for both THAs and TKAs when the register data is compared with hospital admission data. (W-Dahl et al., 2021) **(Appendix 2)**.

The SKAR started collecting PROM data in 2008 and in 2020 over 50% of primary TKAs were covered. For TKAs, EQ-5D and KOOS, questionnaires are used (W-Dahl et al., 2021). The SHAR has included PROM data since 2002. PROMs are collected preoperatively and at one, six, and 10 years postoperatively. Since 2008, all primary THAs have been covered and EQ-5D is used as a questionnaire (Kärrholm, 2010).

2.3.3 Nordic Arthroplasty Register Association (NARA)

The Nordic countries have established high quality national arthroplasty registries and are all actively engaged in orthopaedic research. In 2007, the NARA was established by merging hip and knee arthroplasty registries from Norway, Sweden and Denmark. After a successful start, shoulder registries also joined the NARA (Mäkelä et al., 2019; Mäkelä and Hailer, 2021). Finland joined the NARA in 2010. Common for these countries is that they have uniform healthcare systems and unique personal identity numbers for all citizens. They have several national registries, including for example mortality, prescription and cancer data. Also, in the NARA countries, all orthopaedic department reports its arthroplasties to the registries. This enables registers to be linked and high quality studies. (Mäkelä et al., 2019). The quality of arthroplasty studies can be improved if larger number of patients are included. For example, certain small sub-groups of patients in individual registries can be merged to achieve more accurate statistical estimates. Not all the included arthroplasty registries are the same. The NARA register combines “minimal datasets” including certain common variables from each register. The NARA includes all primary hip arthroplasties since 1995, primary knee arthroplasties since 1997 and primary shoulder arthroplasties since 2004 from the participating countries (Mäkelä et al., 2019; Mäkelä and Hailer, 2021). There are also

differences in clinical practice in orthopaedics between the NARA countries. For example, in Finland and Denmark, uncemented THAs have been used more frequently than in Sweden and Norway. There are also differences in the approaches to THA, TKA fixation and frequency of patellar resurfacing (Mäkelä and Hailer, 2021).

2.3.4 Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR)

The AOANJRR was established in 1999 by the Australian Orthopaedic Association **(Appendix 2)**. Nation-wide data collection from hip and knee arthroplasties began in 2002. Since 2007, the AOANJRR has also collected data on ankle, wrist, elbow and shoulder arthroplasties. In 2017 the AOANJRR started collecting PROMs and is currently using EQ-5D, OHS, OKS, HOOS-12, KOOS-12 questionnaires. The PROMs are completed preoperatively and six months postoperatively by a proportion of THA, TKA and shoulder arthroplasty patients (Australian Orthopaedic Association National Joint Replacement Registry, 2022). The AOANJRR validates its data against health department data and the data completeness has been reported being 97% for all joint replacements in Australia (AOANJRR, 2021).

2.3.5 The National Joint Registry (NJR)

The NJR is based in the UK and includes arthroplasties from England, Wales, and Northern Ireland. Arthroplasties from the Isle of Man and Guernsey are also reported to the NJR **(Appendix 2)**. Before the NJR was established in 2002, there were two regional arthroplasty registries in the UK that were active from the early 1990s (Porter et al., 2019; The National Joint Registry, 2022). The NJR collects data on hip, knee, shoulder, elbow and ankle arthroplasties. In 2010, PROM data were included in the NJR. The following PROMs are collected: EQ-5D, VAS, OHS, OKS (The National Joint Registry, 2022). The registry also has an online platform which has both a public version and a restricted access version for surgeons https://surgeonprofile.njrcentre.org.uk/. The public version contains information about the number of arthroplasties performed by surgeons

and the outcomes of arthroplasties in certain hospitals. It also shows the mean gain in OHS or OKS. In the restricted access, version surgeons can view personal outcome data (Porter et al., 2019). The NJR reports data compliance rate for THAs and TKAs being 96% in England and in Wales. However, this compliance rate doesn't include private sector (The National Joint Registry, 2022).

2.3.6 Arthroplasty registries in the USA

The establishment of a single nationwide multi-institutional arthroplasty registry in the USA is challenging for both legal and financial reasons. The USA has several different national, institutional and regional arthroplasty registries (Hughes et al., 2017; ISAR, 2022).

The American Joint Replacement Registry (AJRR) is the largest national hip and knee arthroplasty register and has members in all 50 states. In addition to procedural data, it collects PROM data (The American Joint Replacement Registry, 2022).

Another significant yet smaller registry the Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement initiative (FORCE-TJR) was started in 2010 and it includes joint replacement data from 28 states. The FORCE-TJR defines PROMs as the primary outcome of total joint replacement (Ayers and Franklin, 2014). PROMs are collected from the patients via an online system that allows the analysis of the questionares immediately after reponse (Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement, 2022).

Other arthroplasty registries in the USA include the Mayo registry, Harris Joint Registry, Kaiser Permanente, Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) and the Hospital for Special Surgery Hip and Knee Joint Replacement Registry (Bohm et al., 2021; Malchau et al., 2018). The Mayo Registry is an institutional registry and is the oldest known arthroplasty registry. It was established in 1969 (Malchau et al., 2018) **(Appendix 2)**.

2.4 FINNISH HEALTH CARE REGISTRIES FOR ARTHROPLASTY RESEARCH PURPOSES

In addition to arthroplasty registries, administrative data (e.g. the Finnish CRHC and Social Insurance Institutions (SII = KELA) medication reimbursement data) can also be used in surgical outcome studies. Administrative healthcare data are collected for administrative or billing purposes but can be used to study the quality and costs of health care. Further, they can be used for steering purposes to allocate limited resources effectively and to compare the performance of health care providers (Peltola et al., 2011). Utilising administrative data in research has its benefits. The data are automatically collected on an ongoing basis every time a person contacts a healthcare system, for example, physician visits, hospital admissions, purchases of prescription drugs, thus they are cost and time effective (Sund, 2003). The results are usually more generalisable than the results from randomised clinical trials, which have very tight selection criteria for the study populations. Also, with large amounts of data, even rare findings can be studied with sufficient statistical power. Administrative data allows for large scale descriptive analyses, such as morbidity, mortality, reoperation rates, to be performed (Guller, 2006).

2.4.1 The Care Register for Health Care (CRHC)

The Finnish Hospital Discharge Register (FHDR) was in use from 1969 to 1993 and included data on patients discharged from hospital. Details of operations have been available since 1986. In 1994, the CRCH was established to replace the FHDR. The register is maintained by the THL. The CRCH includes more detailed information about healthcare services. In addition to hospital discharges, it collects data on outpatient surgeries, specialised outpatient care and the number of patients in inpatient care in health centres and hospitals. (Finnish Institute for Health and Welfare, 2022) In previous studies, CRHC/FHDR data completeness and accuracy have been studied to be from satisfactory to very good, depending on the disease. In research, the CRHC can be linked to other registries and offers

valuable additional information. (Sund, 2012) Data delivery to the CRHC is mandatory for all healthcare providers. Data must be delivered at least once per year. However, from 2019 it has been possible to deliver data automatically on a daily basis from medical record system, using a platform provided by the CRHC (National Institute for Health and Welfare, 2022b).

2.4.2 Social Insurance Institution of Finland (SII)

The SII of Finland offers reimbursement for medicine expenses. Medicines, clinical nutrients and emollient creams that are included in the reimbursement programme are determined by the Pharmaceutical Pricing Board. Reimbursements are available if these products are prescibed to treat an illness. In 2022, everyone (from the beginning of the year that they reach 19 years of age) has an initial deductible of EUR 50.00 that has to be reached before they become eligible for a reimbursement. There are then three classes of reimbursements: Basic rate (40% of the price reimbursed), lower special rate (65% of the price reimbursed) and higher special rate (100% of the price reimbursed, although EUR 4.50 is payable for each item of medication purchased). If the prescription medicine costs (covered by the reimbursement system) paid over one year reach EUR 592.16, only EUR 2.50 is payable for each item of medication purchased until the end of the calendar year. Reimbursable medicine can be purchased up to three months in advance (KELA, 2023). All prescription drug purchases are recorded in the SII's register. This data can be later combined with other register data. Public register data are also available ((KELA, 2019) until 31 December 2019 and (KELA, 2022) from 1 January 2020) for each item of medication delivered and for the number of people purchasing medication.

2.4.3 The PERformance, Effectiveness and Cost of Treatment episodes (PERFECT) – project

PERFECT was established in 2004 by the THL. The aim of the project was to create models for monitoring cost-effectiveness, quality and content of

treatment episodes in specialised medical care. In short, it aims to produce performance indicators that can be used for evaluating health policy actions at system level and also for comparison of quality of care at producer level. Medical procedures and disease groups with significant costs and the number of patients were included, for example, THA and TKA (Peltola et al., 2011). The project focuses on the entire treatment pathway of an individual. These disease-specific episodes of care were made by combining data from several existing registers. The episodes contain information from the beginning (e.g. THA/TKA) until the end of treatment (discharge home, or death). Further, there is at least one year of follow-up data for all patients. The observable events during follow-up include e.g. operations, admissions, discharges, deaths, medication purchases, outpatient visits. PERFECT dataset for arthroplasties combines data from e.g. the FAR, CRHC, the National Causes of Death Register and SII records on reimbursements for medicine expenses. SII's records provide data on reimbursements from 1994 and in PERFECT this data are used from 1997 onwards (Mäkelä et al., 2011). The data from different registers are linked using the unique identification numbers of the population. With these data it is possible to follow the daily events before and after the operation (Mäkelä et al., 2011; Peltola, 2022; Peltola et al., 2011).

2.5 PATIENT-REPORTED OUTCOME MEASURES (PROM)

A PROM is a measurement of any kind of participant's health status that is directly derived from the participant. A PROM is a way of measuring health effects and the results of medical interventions regarding how a patient functions or feels before and after interventions. There are several different PROM concepts. They can be specific (e.g. measuring the frequency of a phenomenon) or general (e.g. measuring well-being and physical capability) (U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research, 2006).

Traditionally, revision surgery is the endpoint in arthroplasty registries. However, revision arthroplasty may not be sufficient in measuring the total success of arthroplasty and the different kinds of prostheses. PROMs can

offer data on variables that are important for patients, e.g. restoration of function, pain relief, quality of life (I. Wilson et al., 2019). This data can impact the quality of care by offering both short- and long-term data on the performance of different joint implants and arthroplasty procedures. The recall of MoM hip implants in 2010 demonstrated the importance of capturing the patient's perspective of care. Many patients developed complications and symptoms without revision and the poor performance of some implants could not be detected at that point (Ayers and Franklin, 2014).

At least 17 arthroplasty registries collect PROM data **(Appendix 2)**. The most used disease-specific PROMs in the registries are, the Knee Injury and Osteoarthritis Outcome Score (KOOS), the Hip Disability and Osteoarthritis Outcome Score (HOOS), the Oxford Hip Score (OHS) and the Oxford Knee Score (OKS). Many registries also report the Visual Analogue Scale (VAS). The EuroQol 5 Dimension Health Outcome Survey (EQ-5D) from the general PROMs is used by many arthroplasty registries that collect PROM data (Bohm et al., 2021; Rolfson et al., 2016b).

The PROMs Working Group set by the International Society of Arthroplasty Registries (ISAR), recommends that PROMs are not collected on the day of arthroplasty, but 3–4 weeks before (Rolfson et al., 2016a). Postoperative PROM scores seem to increase until at least 12 months after THA and TKA. Differences have been noted between the hip and knee for the optimal time of postoperative PROMs (Browne et al., 2013; Rolfson et al., 2016a). However, in order to achieve better comparability between the registries, ISARs recommend postoperative PROMs at one year after THA or TKA (Rolfson et al., 2016a).

The FAR does not routinely currently collect PROM data. However, many orthopaedic departments collect PROMs to their health record data. In the future, PROM data collection should be part of the FAR data collection, as in several other national registries (AOANJRR, 2021; The American Joint Replacement Registry, 2022; The National Joint Registry, 2022; W-Dahl et al., 2021).

Table 2. Patient-reported outcome measures (PROM) presented in this thesis

PROM	Number of questions	Type: generic / disease-specific	Validated for (joint)
EQ-5D-5L (-3L)	5 + VAS	generic	THA, TKA [1]
HOOS	40	disease-specific	THA [2]
HOOS-12	12	disease-specific	THA [3]
KOOS	42	disease-specific	TKA [4]
KOOS-12	12	disease-specific	TKA [5]
OKS	12	disease-specific	TKA [6]
OHS	12	disease-specific	THA [6]
PROMIS	varying	generic	THA [7], TKA [8]
SF-36	36	generic	THA, TKA [9]
VAS	1	generic	THA, TKA [10]
WOMAC	12–24	disease-specific	THA, TKA [11]

[1] (Jin et al., 2019; Kang, 2021) [2] (Nilsdotter et al., 2003) [3] (Gandek et al., 2019a) [4] (Roos and Toksvig-Larsen, 2003) [5] (Gandek et al., 2019b) [6] (Kang, 2021) [7](Stephan et al., 2021) [8] (Shim and Hamilton, 2019) [9] (Clement et al., 2022; McGuigan et al., 1995; SooHoo et al., 2007) [10] (Danoff et al., 2018) [11] (Whitehouse et al., 2003)

2.5.1 Visual Analogue Scale (VAS)

The VAS is one of the simplest and oldest PROMs **(Table 2)**. It has been in use since 1921 and was introduced by Hayes and Patterson (Hayes and Patterson, 1921; Yeung and Wong, 2019). The 100 mm line scale can be used to measure the level of pain. The patient indicates the level of pain on the line. The following generalisations can be used when interpreting the results: 0–4 mm “no pain”, 5–44 mm “mild pain”, 45–74 mm “moderate pain” and 75–100 mm “severe pain” (Jensen et al., 2003). The VAS can be used to measure pain perioperatively during a hospital stay for arthroplasty. Danoff et al. report the minimal clinically important difference (MCID) values of VAS in THA and TKA patients. They reported MCID (for improving/worsening pain) of 15/–19 for THA and 16/–23 for TKA (Danoff et al., 2018). MCID is the smallest level of change in VAS that could be considered important by the patient or physician.

2.5.2 Oxford hip (OHS) and knee score (OKS)

Published in 1996–1998, the OHS and OKS are disease and joint-specific PROMs designed to assess the outcomes of THA and TKA (Oxford University Innovation, 2022) **(Table 2)**. They have been designed to be as simple to use as possible in order to encourage patients to participate. This has lead to the design of 12-item questionnaires that include questions about pain and actvities of daily living. Each question has five response options (Murray et al., 2007). OHS and OKS are widely used by arthroplasty registries. In Finland, many orthopaedic departments collect OHS and OKS data to their local health records pre- and post-operatively. Both OHS and OKS have shown good responsiveness in THA and TKA patients (Kang, 2021). Responsiveness refers to the ability of a questionnaire to detect actual clinical changes in patients health status (Rolfson et al., 2016b). The Finnish version of OKS has been tested to be valid, reliable and responsive when used pre- and post-operatively with Finnish speaking TKA patients (Reito et al., 2017).

2.5.3 Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC)

The WOMAC is an old (released in 1982) and widely used diasease-specific PROM tool for assessing symptoms and activity limitations in patients with osteoarthritis of the lower limbs **(Table 2)**. It comprises 24 questions from three different dimensions: pain, stiffness and physical function. Each question has five response options. The WOMAC has been evaluated as being responsive, valid and reliable when used with osteoarthritis patients (Bellamy et al., 1988). There is a short version of the questionnaire, which has 12 questions on pain and disability. Whitehouse et al. have studied the WOMAC and the short version has been proved practical and responsive when used with THA and TKA patients (Whitehouse et al., 2003). The disease-specific PROMs HOOS (hip) and KOOS (knee) are further developments of the WOMAC.

2.5.4 Knee Injury and Osteoarthritis Outcome Score (KOOS)

Knee injuries that cause cartilage or joint line damage frequently lead to the development of OA. Published in 1998, the KOOS is a PROM that has been specifically developed for the short- and long-term assessment of knee problems and for monitoring the symptoms of knee trauma patients **(Table 2)**. The questionnaire includes 42 questions in five different subscales and estimates both the short- and long-term consequences of knee injury (Roos and Lohmander, 2003). Also, the WOMAC index can be calculated from KOOS, since all WOMAC questions are included in the KOOS. In addition to the WOMAC, the KOOS has questions about sport and knee-related quality of life (Roos and Lohmander, 2003). The KOOS has been tested to be valid and to have good responsiveness as compared with WOMAC (Roos and Toksvig-Larsen, 2003). Validity refers to the ability of the questionnaire to measure the intended outcome (e.g. patient-relevant health measures after TKA or TKA) and the results also correlate with some other appropriate tool.

For the routine use of a questionnaire in clinical work or in registers, the KOOS might be considered too exhaustive. This has led to the development of shorter versions of the KOOS such as KOOS-PS (+ HOOS-PS), KOOS-JR (+ HOOS-JR) and KOOS-12 (HOOS-12). In order to achieve a significant reduction in respondent burden with still comprehensive measurements, the KOOS-12 and HOOS-12 were developed. Only three subscales are used in these questionnaires (pain, function, quality of life) and each subscale has four questions (Gandek et al., 2019c). The KOOS-12 has proven to be valid and reliable in the evaluation of TKA patients (Gandek et al., 2019b).

2.5.5 Hip Disability and Osteoarthritis Outcome Score (HOOS)

Good experiences of KOOS among TKA patients led to the development of the HOOS in 2003 (Nilsdotter et al., 2003; Roos and Lohmander, 2003) **(Table 2)**. The HOOS is a disease-specific PROM scoring system for assessing functional limitations and symptoms related to the hip. It can be used to evaluate THA results. It has been adapted from KOOS and all

WOMAC questions are also included in the HOOS. There are five subscales and 40 questions in the HOOS. The subscales are pain, symptoms, activity limitations in daily living, sport and recreation function and hip related quality of Life. Each question has five response options (no, mild, moderate, severe, extreme). The HOOS's responsiveness to clinical change is higher than the WOMAC's for evaluating the outcomes of THA (Nilsdotter et al., 2003). The background and aim of developing HOOS-PS, HOOS-JR and HOOS-12 is described above (Gandek et al., 2019c). HOOS-12 is a shortened version of the HOOS and has 12 questions in three different subscales (pain, function, quality of life). It has been validated for the assessment of THA patients (Gandek et al., 2019a).

2.5.6 EuroQol 5-dimension Health Outcome Survey (EQ-5D)

The EQ-5D is a generic PROM that was developed by the non-profit organisation EuroQol **(Table 2)**. The survey has been in use from 1990 and over a period of 30 years, three different versions have been released (EQ-5D-3L (original), EQ-5D-5L and EQ-5D-Y (young persons)) all of which collect data on five dimensions (mobility, self-care, activities, pain/discomfort, depression/anxiety). The 3L and Y versions describe severity using three levels and the 5L version using five levels. The VAS is also used for the assessment of overal health (EuroQol, 2022). The EQ-5D is widely used for measuring health-related quality of life in many different health conditions. It is the generic PROM that is most used by arthroplasty registries (Bohm et al., 2021). Both the 3L and 5L versions have been validated for use with THA and TKA patients. The longer 5L version has shown better performance and is recommended to be used in preference to the other versions (Jin et al., 2019; Kang, 2021).

2.5.7 Short form 36 (SF-36)

The SF-36 health survey is a generic PROM that was developed in 1992 **(Table 2)**. It has 36 questions and assesses three major health attributes (well-being, functional status, overall health) Later, in 1996, a shorter 12-item questionnaire (SF-12) was developed. Both of the questionnaires

provide physical and mental component scores by combining the original reponses (I. Wilson et al., 2019). The SF-12 has proven that it can be effectively used with less repondent burden compared to the SF-36. The results from the SF-36 or SF-12 are comparable (Ware et al., 1996). The Boston University School of Public Health has developed almost identical questionnaires with the SF-36 and SF-12: the Veterans Rand 36 (VR-36) and VR-12. It has made modifications to the original SF response options and added two items to the questionnaires (Boston University - School of Public Health, 2022; I. Wilson et al., 2019). The SF-36 seems to be resposive to the outcomes of THA and TKA. However, there may be limitations that prevent use of only the generic SF-36 questionnaire in the assessment of THA or TKA (Clement et al., 2022; McGuigan et al., 1995; SooHoo et al., 2007).

2.5.8 Patient-Reported Outcomes Measurement Information System (PROMIS)

The PROMIS is a generic patient-centered tool for self-reported health assessment **(Table 2)**. It measures physical, mental and social well-being. PROMIS data collection includes many items that have been gathered to different short form questionnaires. The questionnaires can be adapted based on the scope of the study. The number of questions in a short form varies. The PROMIS was developed by U.S. National Institutes of Health in 2004. Their aim was to create a PROM with generalisable, valid and reliable measures with no significant respondent burden for patients (Northwestern University, 2022). PROMIS has been increasingly used in arthroplasty registries, especially in North America (I. Wilson et al., 2019). PROMIS-10 version, with ten questions in five subscales, pain, fatigue, physical function, social health and emotional distress, has shown to be responsive with TKA patients (Shim and Hamilton, 2019). There is also evidence that the PROMIS short form for testing pain, pain intesity and pain interference can be used in the assessment of THA results. However. ceiling effect may lead to the underestimation of results (Stephan et al., 2021).

2.5.9 Harris Hip Score (HHS) and Knee Society Score (KSS)

The HHS and KSS are used by physicians for outcome assessment. They combine a PROM (physician interviews the patient) and a clinical assessment by the physician. The HHS was introduced in 1969 by Dr William H. Harris and has been used by physicians to evaluate the results of hip arthroplasty (Harris, 1969). It has also been used for hip OA. The original HHS included questions about activities of daily living, pain, and range of motion of the affected hip. In the modified HHS, the range of motion questions have been omitted and the remaining questions have been partially revised to allow the HHS to be used as PROM without physician input. A previous study has shown that patient self-reported HHS and HHS score based on physician assesment have a great level of agreement (Mahomed et al., 2001).

The KSS was introduced in 1989 and is a disease-specific tool for the assessment of knee joints before and after arthroplasty. It is also used by physicians and includes questions about daily functioning and pain. A clinical examination is also needed to score the range of motion, alignment and stability of the knee (Insall et al., 1989).

2.5.10 General PROMs: physical capability and subjective well-being

It is sometimes not feasible to use validated PROM tools, even their shorter versions. This could apply to large cohort studies using questionnaires that have many questions covering multiple aspects of life. For example, there were 52 items that needed to be answered in the OSTPRE 1994 questionnaire (the baseline questionnaire for Study II).
Using simple questions such as self-estimated physical capabilities and subjective well-being does not increase the respondent burden as much as full size validated PROMs. OSTPRE's question about subjective well-being is quite similar to the general health questions included in the SF-36/SF-12 questionnaires ("In general, would you say your health is" : excellent; very good; good; fair; poor?). SW is a broad concept and is determined by multiple factors, for example, person demographics, health and

functioning, socioeconomic status, social relationships, culture and personality (Das et al., 2020). SW is known to be affected by arthritis and the number of comorbidities. Age has had different effects on SW between nations. In rich English-speaking countries, SW has been reported improving towards elderly after a drop during middle age (Steptoe et al., 2015). Qazi et al. found that subjective health/well-being had a strong correlation with life satisfaction in the OSTPRE cohort. Further, an even stronger correlation was found between the SW and PC (Qazi et al., 2021).

OSTPRE's question on physical capability is similar to the distance walked question in the HHS. The OHS and OKS also include a question on walking duration. Multiple tests have been conducted to validate OSTPRE self-reports. It was recently shown that OSTPRE physical capability reports correlate with functional tests (Juopperi et al., 2021). However, OSTPRE PC or SW self-reports have not been validated using other validated PROMs such as OHS and OKS. It has also previously been shown that self-reported arthroplasties are sensitive in capturing women with a THA or TKA (Study I). In addition, self-reported wrist fractures are sensitive in finding actual fractures (Honkanen et al., 1999). However, self-reported hip fractures or minor fractures are not as sensitive (Honkanen et al., 1999; Sund et al., 2014).

3 AIMS OF THE STUDY

Study I

To study the coverage of the FAR and the CRHC data on THAs and TKAs.
And by using the complete register data as a reference, we examined how accurately 1) the population with THA/TKA and 2) the actual THA/TKA events can be identified using self-reports

Study II

To study patient self-reported physical capabilities and subjective well-being before and up to 20 years after THA or TKA in postmenopausal women aged 64–70 years.

Study III

To study the purchase of paracetamol, non-steroidal anti-inflammatory drugs (NSAID), opioids and neuropathic pain medication before and after THA or TKA in men and women aged 67–69 years.

4 SUBJECTS AND METHODS

Table 3. Summary of Studies I-III

Study	I	II	III
Design	Register-based study	Population-based follow-up study	Register-based study
Data	OSTPRE, FAR, CRHC	OSTPRE, FAR, CRHC	PERFECT
N	14,220 / 9,095	6,462	329,743
Females	100%	100%	57% (THA) / 67% (TKA)
Age	67–76 years	64–70 years *	67–69 years *
Follow-up time	23 years	0–20 years **	6 years
Study period	1987–2010	1994–2014	1997–2018

* Mean age at the time of THA or TKA; ** Depending on the time of THA or TKA; Kuopio Osteoporosis Risk Factor and Prevention – study (OSTPRE); Care Register for Health Care (CRHC); The Finnish Arthroplasty Register (FAR)

4.1 STUDY I

Study I subjects are from the Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) study population. It is a long-term population-based cohort study. OSTPRE started in 1989 and the first postal questionnaire was sent to all 47–56 year-old women (N = 14,220) in the former Kuopio Province in Finland. The study has been ongoing and follow-up questionnaires have been sent every fifth year to the participants. Originally, OSTPRE was used to investigate factors associated with bone loss, falls and fractures in the population. Subsequently, OSTPRE data have been merged with national register data which, has enabled validation studies of self-reports and has increased the opportunities to assess important health disorders and medical procedures (e.g. OA, arthroplasty and spinal surgeries) (Kuopio Musculoskeletal Research Unit, 2023).

The entire original OSTPRE population of 14,220 women was used in validation of the registers. For validating the self-reported THA and TKA, OSTPRE participants from 2009 follow-up questionnaire were used (N = 9,095) **(Figure 5)**.

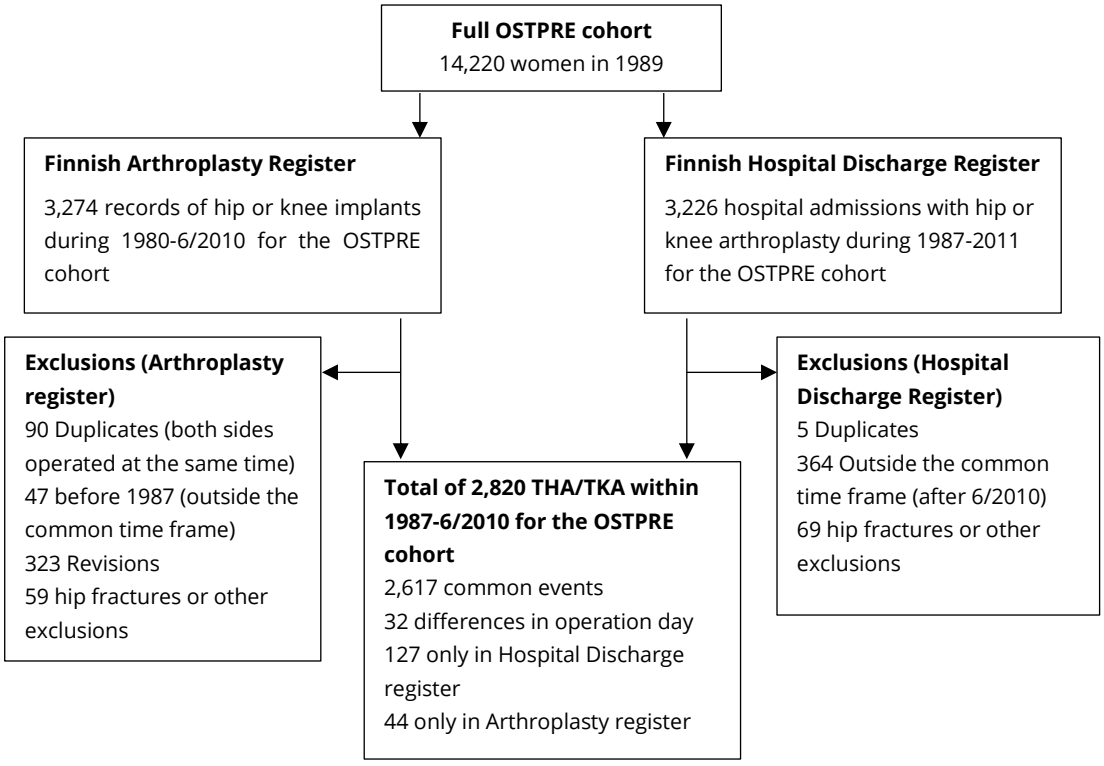
Available FAR data included information on THAs and TKAs from 1980 until June 2010 (at the time of Study I). The FAR collects THAs and TKAs as events and includes detailed data on the surgeries. The CRHC has collected data on inpatient hospital admissions since 1969 and more detailed data on operations since 1986. CRCH data were available until 31 December 2011. These registers and the OSTPRE questionnaire data were linked.

THAs and TKAs were identified using the operation codes 9293, 9294, 9313, and 9314 of the Finnish Hospital League operation classification (1987–1996) and codes NFB30, NFB40, NFB50, NFB60, NFB99, NGB10, NGB20, NGB30, NGB40, NGB50, NGB60 and NGB99 of the Finnish version of NOMESCO operation classification codes (in use from mid-1996). Codes for hemi-prostheses or revisions were not included. The joint (hip or knee) was determined from the operation code and the reason for the surgery from the main diagnosis. The operated side was deduced from the operation codes ZXA00 (right), ZXA05 (left) and ZXA10 (bilateral). All arthroplasty patients in the registers can be individually followed using a unique personal identity code. A personal identity code with information about hospital, operation date and joint operated on allowed us to compare THA and TKA cases in the FAR and the CRHC. In the event of any discrepancies, details were checked from patient records and radiographs.

For studying the validity of self-reports, we used the OSTPRE 20-year follow-up questionnaire from 2009 (n = 9,095). In this questionnaire participants were 67–76 years of age. They were asked the following questions: Have you experienced joint arthroplasty that was caused by osteoarthritis? In which joint and in which year? If the participant reported that she had undergone THA or TKA before the date they completed the questionnaire, this report was compared to the register data. To capture missing self-reports, arthroplasties in the register data were also compared to the self-report data. Further, the self-reported date of the surgery was compared with the register data (the date or at least the year of the new

arthroplasty was known from registries). Self-reports within +/- 1 year from the actual operation year were accepted as matches. The following statistics were calculated: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive agreement and kappa. Positive agreement estimates the conditional probability that if one of the randomly selected registers identifies an event, the other register will also recognise the event (Fleiss et al., 2003). Interrater reliability is a measurement of the extent to which raters give the same answer to the same variable (e.g. how well self-reports and register data agree on the number of arthroplasty operations / no arthroplasty) This can be measured using kappa statistics.

Figure 5. Study I. Flowchart for identifying THA and TKA from the FAR and the CRHC for the OSTPRE cohort.



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4.2 STUDY II

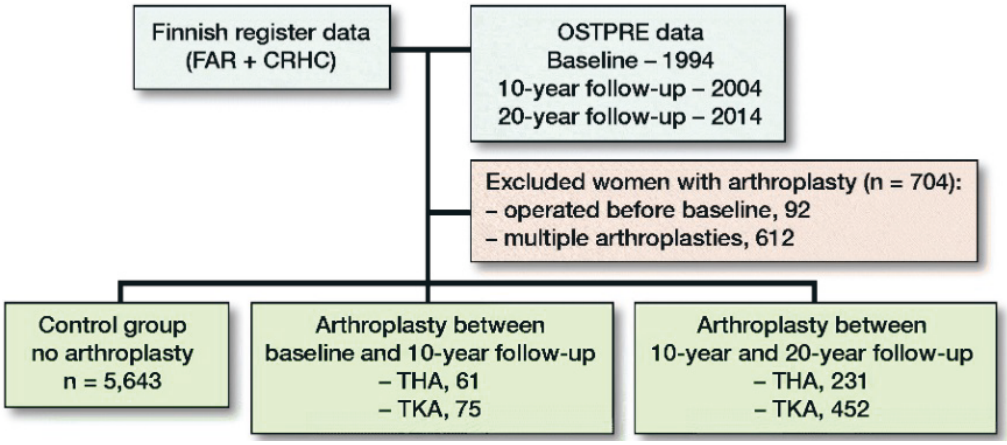
The OSTPRE cohort was also used in Study II. We used questions about physical capability (PC) and well-being (SW) and these questions have remained the same since the 1994 questionnaire. Thus, OSTPRE the 5-year questionnaire from 1994 (N = 11,954) was used as a baseline in this study. We used a 10-year interval between checkpoints and the next questionnaire was from 2004 (N = 10,912). At the time of the study, the most recent OSTPRE questionnaire available was from 2014, which was the end of follow-up (N = 7,765). OSTPRE participants who had returned all three questionnaires were included in the study **(Figure 6).**

The PC question in the questionnaire (originally in Finnish) was: How would you describe your current physical capability? The following response options were given 1: capable of moving without limitations; 2: no running, without other limitations; 3: cannot move more than 1,000 metres; 4: cannot move more than 100 metres independently; 5: can only move indoors; 6: I am temporarily immobilised; 7: I am permanently immobilised. For statistical purposes (group size), the following responses were combined into one: Responses 1 and 2 into “walking without limitations” and this group is later referred to as “good PC”. Responses 4–7 were combined into “cannot move more than 100 metres independently”. Since the capability to walk less than 1,000 metres supports the indication for arthroplasty, the grouping of responses also works in a clinical setting. The SW question was originally: “How would you describe your current well-being?” The response options were: 1: very good; 2: good; 3: moderate; 4: poor; 5: bad. For statistical purposes (group size), responses 1 and 2 were combined into “good” and responses 4 and 5 were combined into “poor”.

The common time frame for both the FAR and the CRHC in collecting arthroplasty dates back to 1987 (the CRHC started including detailed data on arthroplasties). Data on THAs and TKAs were collected from the registers until 31 December 2016. Any anomalies in the data were manually checked against the medical records and the OSTPRE questionnaire forms and corrected, where possible. 2,444 women (based

on register data) had had THA or TKA before the final return date for the 2014 questionnaire (31 December 2014). Eventually, after exclusions (failed to return any of the questionnaires, arthroplasty before baseline, mortality, multiple arthroplasties **Figure 6**) 819 women with THA or TKA were included in Study II. The following subgroups of women with arthroplasty were formed: 1 women with THA or TKA between the baseline and 10-year follow-up; 2 women with THA or TKA between the 10-year and 20-year follow-ups. 5,643 women without arthroplasties formed the control group. The self-reported PC and SW by these groups were followed. We also conducted additional analysis for a subgroup of participants. These women had undergone THA/TKA within one year (before or after) of any questionnaire. The preoperative results were compared to the postoperative results.

Figure 6. Study II. Flowchart of study population (n = 6,462)



4.3 STUDY III

In Study III, the PERFECT project, established by the THL, provided data on arthroplasties and purchases of precription drugs by patients. All THAs and TKAs from 1998–2018 were searched for in the PERFECT data. 149,158 THAs and 180,585 TKAs were found **(Figure 7)**. We then searched for purhases of prescription drugs by patients up to 15 years before and after each arthroplasty event, from the years (1997–2018) available in the reimbursement data. In addition, for the sensitivity analysis, we searched for other arthroplasties (revisions or arthroplasty of other joints) received by the same patients. If other arthroplasties were found, the follow-up of drug purchases was ceased before those arthroplasties. Eventually, at the time of arthroplasty, 104,045 THA and 117,203 TKA patients were included in the analysis.

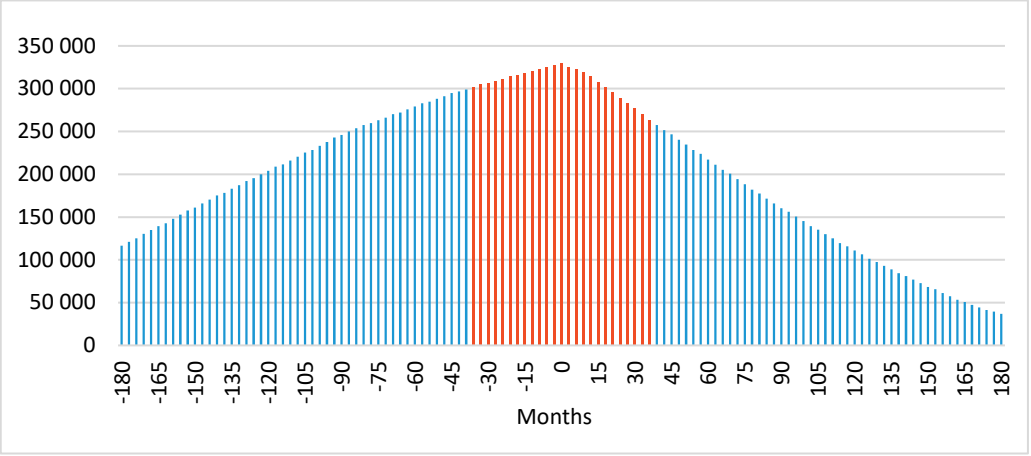
The drugs included in the study were divided into four groups: paracetamol, NSAIDs, opioids, and neuropathic pain medication, which is following the treatment recommendations for osteoarthritis (Hochberg et al., 2012; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018). The drugs of interest and their purchases were identified by using their Anatomical Therapeutic Chemical (ATC) Classification System codes. The following drugs were included in the study: paracetamol/acetaminophen (N02BE00), oral NSAIDs (M01A***, N02B*** excluding N02BE00), oral and transdermal opioids (N02A***, N07B***), antidepressants (venlafaxine/N06AX16, duloxetine/N06AX21, amitriptyline/N06AA09 and nortriptyline/N06AA10) and anticonvulsants (pregabalin/N03AX16 and gabapentin/N03AX12).

The individual data were processed into aggregate form for the purposes of this study. The aggregate form data included a matrix of the number of patients who had purchased drugs over a specific three-month time frame before and after arthroplasties and the total number of patients with follow-up in that time frame. Even though even longer follow-ups were often available, for the purposes of this study, we focused on the +/- 3 years since THA or TKA. The data were stratified by drug group, sex

and age at the time of arthroplasty (< 70 years, ≥ 70 years). This data allowed us to calculate the number of patients who purchased drugs for each three-month period.

Register data cannot reveal the purchases of non-prescription drugs, whether or not they were consumed or the indication for their use. In Finland, small packets of certain NSAIDs (ibuprofen, ketoprofen and acetylsalicylic acid) and paracetamol are sold over the counter on a prescription-free basis. However, in order to be reimbursed for the drugs, a prescription is needed. A maximum three-month supply of drugs can be purchased in advance. Continuous users will purchase drugs at least once every three months. This allows purchases of prescription drugs to be easily monitored.

Figure 7. The number of available THA and TKA events for the entire follow-up period. The red columns (+/- 36 months) represent the timeframe included to Study III.



4.4 STATISTICAL METHODS

In Study I, the statistical environment R with the extension package Survo R was used for data analysis. We calculated standard statistics of agreement, completeness, kappa, sensitivity, specificity, positive predictive value (PPV),

negative predictive value (NPV) and 95% confidence intervals where applicable.

In Study II, Chi-square test was used to examine the similarity of proportions of the population being in a certain state of physical capability / subjective wellbeing at different follow-up points between the control group and the different groups of women with THA or TKA. One-way analysis of variance (ANOVA) was used to compare means of weight, height and BMI for example. For additional analysis, propensity score matching was used to select the most suitable controls for THA or TKA operated women. The variables presented in **Table 6** were used as covariates. The Statistical Package for the Social Sciences (SPSS), version 27 (IBM Corp, Armonk, NY, USA), was used for statistical analysis.

In Study III, SPSS version 27 was also used for statistical analysis. A Chi-square test was used to compare whether purchases of certain drugs by a percentage of arthroplasty patients at different follow-up points were statistically significantly different. 95% confidence intervals (CI) for proportions of purchases for all drugs during follow-up were calculated. The results from all follow-up points (three-month intervals) from +/- 3 years since THA or TKA were included in this calculation.

4.5 ETHICS

For Studies I and II, all OSTPRE study participants gave their written consent. The Research Ethics Committee of the Northern Savo Hospital District granted permission for the OSTPRE study (3/11/2014//78/2004). The Finnish Institution for Health and Welfare granted permission to use the FAR and the CRHC data (THL/20/5.05.00/2016). There was a seperate permission for the PERFECT database (THL/538/6.02.00/2019). For Study III, aggregated data from the PERFECT was utilized.

5 RESULTS

5.1 VALIDITY OF ARTHROPLASTY EVENTS IN THE FAR AND THE CRHC

After 519 exclusions from the FAR data and 438 exclusions from the CRHC data **(Figure 5)**, the total number of primary arthroplasty events for the OSTPRE cohort included in Study I was 2,820 (including all diagnoses) from 1987 until June 2010. Both the FAR and the CRHC recorded 92.8% of cases. By relaxing operation date criteria, an additional 32 events could be matched, resulting in 93.9% common events. 127 (4.4%) events could only be found in the CRHC, of which around 95% could be confirmed from the medical records. 44 (1.7%) of the remaining events could be found in the FAR. Four of these events were completely missed by the CRHC and the remaining events could be identified as hospital admissions with a reasonable diagnosis, although the operation code was either missing or wrong. For the total of 1,019 THAs that were found, the completeness of the FAR data were 94.5% and 98.6% for the CRHC data. The positive agreement for THA events was 96.4%. For the 1,801 TKAs, the completeness of the FAR was 96.1% and 98.3% for the CRHC. The positive agreement for TKAs was 97.1% **(Table 4).**

The OSTPRE participants reported 80 events (37 THAs and 43 TKAs) that could not be confirmed by the registries or medical records. 18 of these events were among the excluded operations. For 36 of the events, some other surgical intervention was found (e.g osteotomy or arthroscopy), Two participants had received primary THAs before the common time frame and revisions in the registers confirmed this. For 24 THA or TKA reports, no reason for the report was found.

Table 4. Study I. Completeness of THA and TKA surgeries in the FAR and the CRHC

THAs, n = 1,019	
In both registers: 949 THA (93.1%) Missing from the CRHC: 14 THA (1.4%) • 0 Completely missing • 7 Missing operation code • 7 Wrong operation code	Missing from the FAR: 56 THA (5.5%) Positive agreement [1]: 96.4% (95% CI: 95.6–97.2%) Completeness of the FAR: 94.5% Completeness of the CRHC: 98.6%
TKAs, n = 1,801	
In both registers 1,700 TKA (94.4%) Missing from the CRHC: 30 TKA (1.7%) • 4 Completely missing • 11 Missing operation code • 15 Wrong operation code	Missing from the FAR: 71 TKA (3.9%) Positive agreement [1]: 97.1% (95% CI: 96.5–97.7%) Completeness of the FAR: 96.1% Completeness of the CRHC: 98.3%

FAR, Finnish Arthroplasty Register; CRHC, Care Register for Health Care

[1] Positive agreement estimates the probability that on the condition that one of the registers identifies an event the other register will also identify the event

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5.2 SELF-REPORTS IN IDENTIFYING THA AND TKA

Self-reported THAs/TKAs were compared to the register data. Also, THAs/TKAs confirmed by the registers or otherwise checked from the medical records were compared to self-reported arthroplasties. The OSTPRE 2009 questionnaire (n = 9,095) was used to determine the validity of self-reported arthroplasty in detecting the population with THA/TKA on the day of the questionnaire **Table 5**. The sensitivity of self-reports to detect THA (n = 512) was 95.1% (% of the THA population that could be identified using self-reports). The specificity was 99.6% (% of the study participants without THA identified), positive predictive value 92.9% (PPV, % of self-reported THA that really were THA) and negative predictive value 99.7% (NPV, % of participants not reporting THA who really did not have THA). For TKA (n = 909), the results were 94.6% (sensitivity)/99.5% (specificity)/ 95.2% (PPV)/99.4% (NPV). Kappa for THA 0.94 and TKA 0.94 indicate very good agreement between self-reports and the register data. The OSTPRE 2009 questionnaire was answered by 73.7% of the cohort (still alive at the median response date in 2009). This dropout was taken into account and mainly affected negatively to sensitivity and kappa. The results are presented in **Table 5**.

37 participants reported that they had undergone THA and 43 reported having undergone TKA but these reports could not be confirmed from the register data **Table 5**. 2 participants who self-reported THA had undergone the surgery before the time frame of the register data. Revision arthroplasties were found from the registers for these participants to confirm their THAs. 18 of these were among the excluded operations (e.g. necrosis or trauma). For 36 self-reports some other surgical intervention was found (e.g. osteotomy or arthroscopy). For 24 of these reports no explanation could be found.

OSTPRE self-reported arthroplasties were then assessed for detection of the time frame of THAs and TKAs (i.e. the dates or at least years of arthroplasties were correctly reported). For THAs, sensitivity was 65.3% (61.5–68.9%) and PPV was 85.4% (82.9–87.5%). For TKAs, sensitivity was 62.9% (60.1–65.6%) and PPV was 83.4% (81.8–84.9%).

Table 5. Study I. Comparison of OSTPRE questionnaire data and the Finnish register data for detecting women who have had THA or TKA before the response date

OSTPRE	Finnish Register Data	
THA	Confirmed arthroplasty [1]	No confirmed arthroplasty
Arthroplasty reported by patient	487	37
Arthroplasty NOT reported by patient	25	8,546
Non-respondents [2]	176	3,068
Respondents only		
Sensitivity: 95.1% (92.9–96.8%)		Kappa: 0.937 (0.921–0925)
Specificity: 99.6% (99.4–99.7%)		Positive predictive value: 92.9% (90.5–94.8%)
		Negative predictive value: 99.7% (99.6–99.8%)
All women including non-respondents [2]		
Sensitivity: 70.8% (67.2–74.2%)		Kappa: 0.794 (0.768–0.819)
Specificity: 99.7% (99.6–99.8%)		Positive predictive value: 92.9% (90.5–94.8%)
		Negative predictive value: 98.3% (98.1–98.5)
TKA		
Arthroplasty reported by patient	860	43
Arthroplasty NOT reported by patient	49	8,143
Non-respondents [2]	277	2,967
Respondents only		
Sensitivity: 94.6% (92.9–96.0%)		Kappa: 0.944 (0.932–0.955)
Specificity: 99.5% (99.3–99.6%)		Positive predictive value: 95.2% (93.7–96.4%)
		Negative predictive value: 99.4% (99.2–99.5%)
All women including non-respondents [2]		
Sensitivity: 72.5% (69.9–75.0%)		Kappa: 0.807 (0.788–0.826)
Specificity: 99.6% (99.5–99.7%)		Positive predictive value: 95.2% (93.7–96.4%)
		Negative predictive value: 97.2% (96.9–97.4%)

[1] Identical information on both registers (FAR and CRHC) or otherwise confirmed from medical records. [2] Still alive on the median response date of OSTPRE 2009 questionnaire (n = 3,244). (Turppo et al. 2018. The Journal of Arthroplasty/Study I) Reprinted by permission from Elsevier.

5.3 SELF-REPORTED PHYSICAL CAPABILITY AND SUBJECTIVE WELL-BEING BEFORE AND AFTER THA AND TKA

6,462 women answered all three OSTPRE questionnaires included in the Study II. 292 of them had THA and 527 had undergone TKA. Those women without arthroplasties were included in the control group. Women in the control group or with arthroplasties were similar in terms of the mean number of chronic diseases, the number of low-energy trauma fractures, osteoporosis, age and height **(Table 6)**.

Table 6. Study II Characteristics of the study population (n = 6,462)

	No arthroplasty during follow-up (n= 5,643)	Women with **THA** during follow-up (n = 292)	Women with **TKA** during follow-up (n = 527)	*P* [a]
Age at baseline	57 (52–62)	57 (52–62)	57 (52–62)	< 0.001
Height (cm)	161 (136–179)	162 (147–176)	162 (143–178)	0.005
Weight (kg)	69 (38–125)	70 (47–103)	74 (48–120)	<0.001
BMI (kg/m^2)	26 (16–53)	27 (19–40)	28 (20–48)	<0.001
The median number of chronic diseases (range)				
Baseline	1 (0–10)	1 (0–8)	1 (0–9)	0.002
End of follow-up	6 (0–36)	6.5 (0–26)	7 (0–26)	<0.001
Self-reported diseases at the end of the follow-up				p [b]
Osteoporosis/osteopenia	11%	8.6%	12%	0.3
Rheumatoid arthritis	4.1%	6.2%	8.3%	<0.001
Chronic back pain	24%	30%	29%	0.004
Ischaemic heart disease	18%	16%	19%	0.7
Hypertension	58%	59%	66%	0.002
Other heart disease	15%	18%	18%	0.01
Asthma	14%	15%	14%	0.9
Emphysema	2.6%	2.7%	2.5%	1.0
Diabetes	17%	14%	22%	0.006
Stroke	9.8%	9.6%	8.3%	0.6
Cancer	14%	13%	12%	0.6
Self-reported fractures at baseline/end of the follow-up				p [b]
Hip fractures	0.1 %/0.5 %	0.0 %/5.1 %	0.0 %/0.8 %	0.8/<0.001
Any low-energy trauma fracture	8.2 %/11.9 %	7.5 %/14.4 %	6.6 %/12.7 %	0.4/0.4

[a] One-way analysis of variance (ANOVA); [b] Pearson Chi-square test

Of the women who had THA or TKA between the baseline and 10-year follow-up, 80–84% reported good PC at the 10-year follow-up (first postoperative questionnaire). Thus, the level of good PC was within a few percentage points compared to the baseline **(Table 7, Figures 8 and 9)**. At the 20-year follow-up (second postoperative questionnaire), 64% of participants with THA and 53% with TKA reported good PC. The proportions of women with TKA in good PC state during the follow-up points were statistically significantly different (p=0.01) from the proportions of women in the control group in good PC state. But no statistically significant difference was found between the women with THA (p = 0.2) and the control group. The proportions of women reporting good SW were maintained or even improved after arthroplasty (first postoperative follow-up). The proportions of THA patients reporting good SW varied between 31–33% and for TKA the proportions of good SW were 27–41% during follow-up **(Table 8, Figures 8 and 9)**. The proportions of women with arthroplasty in good SW state during the follow-up points were statistically significantly different from the proportions of women in good SW state in the control group (p = 0.01 for both the THA and TKA groups). In these groups, the mean age at the time of THA was 64 years and the median follow-up time was 13 (10–20) years postoperatively. The same figures for TKA were 65 years (mean age) and the median follow-up time 12 (12–19) years, respectively. Only 6.7% of women with TKA underwent revision during follow-up. Among women with THA, 21% underwent revision. The proportion of good PC reports by the THA group that underwent revision, were similar to the original group of women with THA: 92% (baseline), 77% (first follow-up), 62% (second follow-up). However, the proportion reporting good SW were lower postoperatively: 46% (baseline), 15% (1st follow-up), 18% (2nd follow-up).

71–76% of women with either THA or TKA between the 10-year and 20-year follow-up reported good PC at the 20-year follow-up (their first postoperative follow-up). The Proportions of good PC reports had decreased from the 10-year follow-up (89–90%). Among these THA and TKA women, the proportions of good SW reports decreased steadily through the follow-up and at the 20-year follow-up the proportions of good SW

reports were 29–37%. **(Table 8, Figures 8 and 9)**. The mean age at the time of THA was 70 years and the median follow-up time was 3 (0–9) years. Among women with TKA, the mean age was also 70 years and the median follow-up time 3 (0–10) years, respectively. Revision arthroplasty was performed on only 3.0% of women with THA and on 2.2% with TKA.

In the control group that only included women without arthroplasty, the proportion of good PC reports was high 94–95% at baseline and at the 10-year follow-up. However, in the control group, there was also a decrease in good PC and the proportion reporting good PC was 80% at the 20-year follow-up **(Table 7, Figures 8 and 9)**. The SW reports for the control group remained almost the same throughout the follow-up and 43–52% of the women reported good SW **(Table 8, Figures 8 and 9)**.

In the additional analysis for the women who had THA or TKA within one year of any questionnaire. Good PC was reported by 54% of THA and 65% of TKA patients preoperatively. Of those women who returned the OSTPRE questionnaires within one year postoperatively, 62% (THA) and 69% (TKA) reported good PC.

Table 7. Study II. Self-reported **physical capability (PC)** assessed by walking ability, in the control group (women with no arthroplasty) and in women with THA or TKA at baseline, 10-year and 20-year follow-ups. Arthroplasties are stratified by the OSTPRE study follow-up periods (between baseline and 10-year FU, between 10-year and 20-year FU). (%)

Questionnaire	n [a]	Walking without limitations [b]	<1,000m [c]	< 100m [d]	P [e]
Control group					
Baseline	5,356	95	4.0	1.0	
10-year follow-up	5,557	94	4.0	2.0	
20-year follow-up	5,497	80	11	9.0	
Arthroplasty between baseline and 10-year follow-up					
THA					
Baseline	56	84	13	4.0	0.2
10-year follow-up	60	83	12	5.0	
20-year follow-up	59	64	12	24	
TKA					
Baseline	73	84	15	1	0.01
10-year follow-up	73	80	16	4	
20-year follow-up	73	53	27	19	
Arthroplasty between 10-year and 20-year follow-up					
THA					
Baseline	218	95	4	1	0.6
10-year follow-up	225	90	8	3	
20-year follow-up	222	76	12	12	
TKA					
Baseline	427	94	5	0	0.04
10-year follow-up	441	89	9	3	
20-year follow-up	431	71	17	12	

[a] Participants with a valid response at each individual follow-up point; [b] 'Good PC'; [c] Can move < 1,000m independently; [d] Can move < 100m independently; [e] A Chi-square test was used to examine similarity of proportions of the population being in "walking without limitations / good" PC state at different follow-up points between the control group and the different groups of women with THA/TKA

Table 8. Study II. **Subjective well-being (SW)** in the control (women with no arthroplasty) and in women with THA or TKA at baseline, 10-year and 20-year follow-ups. Arthroplasties are stratified by the OSTPRE study follow-up periods (between baseline and 10-year FU, between 10-year and 20-year FU). (%)

Questionnaire	n [a]	Good	Moderate	Poor	P [b]
Control group					
Baseline	5,520	48	42	10	
10-year follow-up	5,593	52	45	3	
20-year follow-up	5,577	43	50	7	
Arthroplasty between baseline and 10-year follow-up					
THA					
Baseline	60	33	50	17	0.01
10-year follow-up	60	33	62	5	
20-year follow-up	58	31	50	19	
TKA					
Baseline	73	32	51	18	0.005
10-year follow-up	74	41	55	4	
20-year follow-up	74	27	57	16	
Arthroplasty between 10-year and 20-year follow-up					
THA					
Baseline	227	45	46	9	0.004
10-year follow-up	227	38	56	5	
20-year follow-up	224	37	56	7	
TKA					
Baseline	435	40	49	11	<0.001
10-year follow-up	445	36	60	4	
20-year follow-up	449	29	61	10	

[a] Participants with a valid response at each individual follow-up point; [b] A Chi-square test was used to examine similarity of proportions of the population being in "good" SW state at different follow-up points between the control group and the different groups of women with THA/TKA

Figure 8. Study II. Proportion of women with **good** A) physical capability (PC) and B) subjective well-being (SW) after **THA**

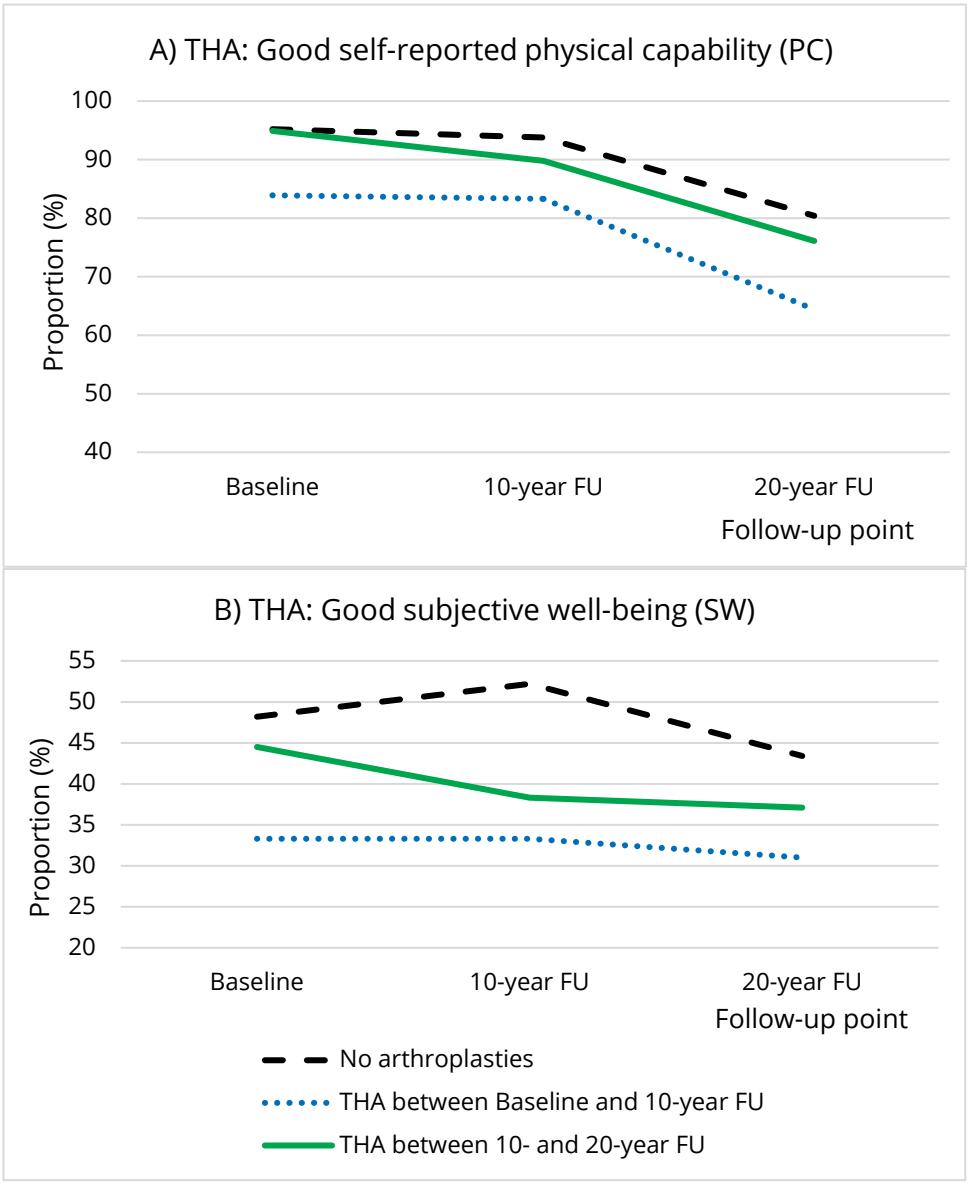
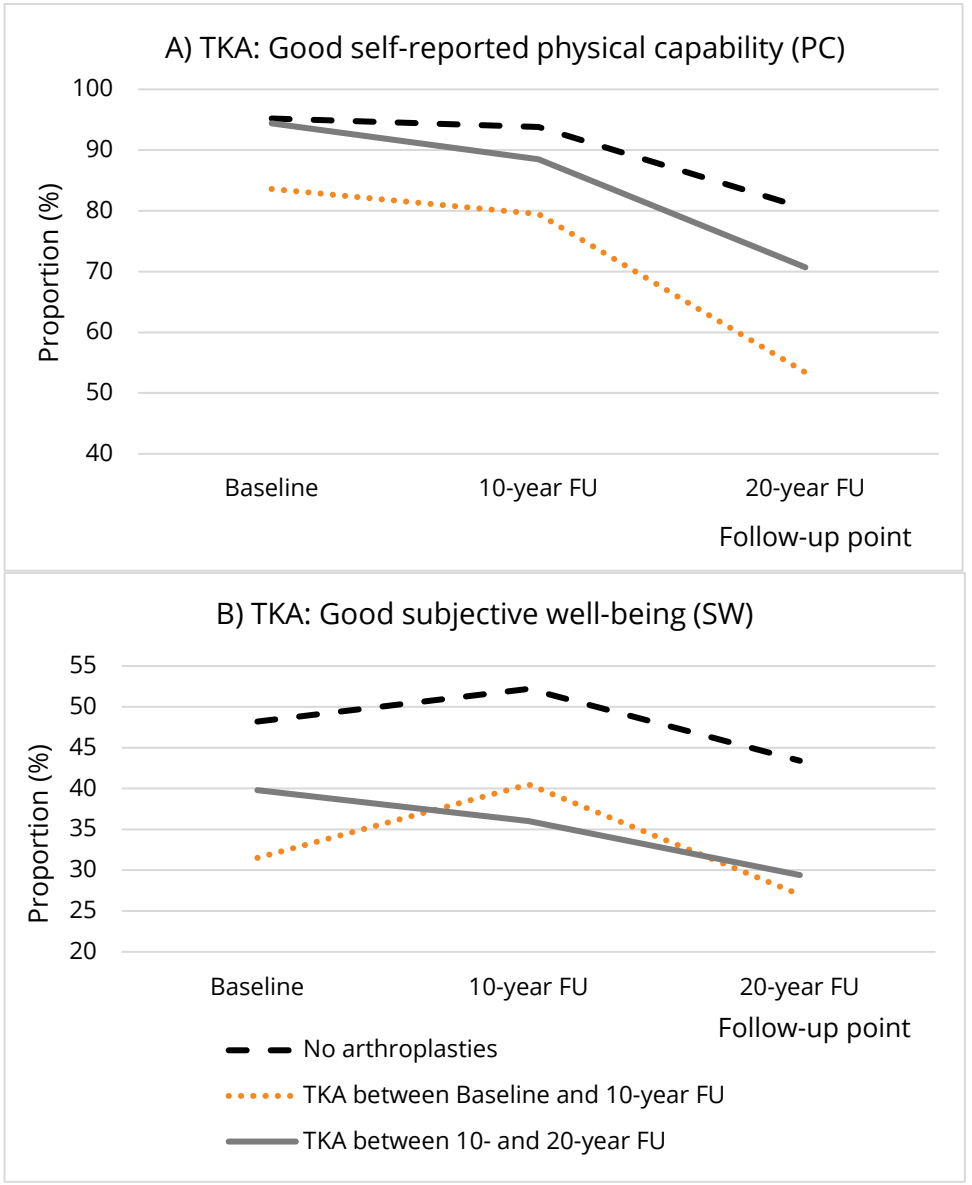


Figure 9. Study II. Proportion of women with **good** A) physical capability (PC) and B) subjective well-being (SW) after **TKA**



5.4 DRUG PURCHASES BEFORE AND AFTER THA AND TKA

Arthroplasties were retrieved from the PERFECT data from 1998–2018 and the data on dispensed prescriptions were available from 1997–2018. Each arthroplasty event had its own follow-up time and drug purchases could be monitored up to 15 years before or after THA or TKA. However, when arthroplasty was performed either near the start or the end of follow-up (1998–2018), the follow-up times for drug purchases either pre- or postoperatively could be short. We focused on follow-up of three years before and after arthroplasty in order to still include a high number of arthroplasties with long follow-ups **Figure 7**. The characteristics of arthroplasty patients are presented in **Table 9**.

Table 9. Study III Characteristics of arthroplasty patients

	THA		TKA
n	149,158		180,585
Mean age	67 years		69 years
		Co-morbidities	
Hypertension	46%		55%
Coronary artery disease	15%		16%
Atrial fibrillation	8%		9%
Heart failure	3%		4%
Diabetes	11%		15%
Hypercholesterolemia	15%		18%
Depression	11%		13%
Psychoses	4%		4%
Parkinson's disease	2%		2%
Dementia	1%		1%
Cancer	11%		11%
Chronic lung disease	13%		17%

Among both THA and TKA patients, the purchases of paracetamol, NSAID and opioids increased the closer the patients got to arthroplasty (**Figure 10 and Table 10)**. All groups of analgesics peaked around the time of arthroplasty. In turn, during the first postoperative months, purchases of all drugs decreased the most. Purchases of paracetamol, NSAIDs and opioids were even lower than they had been three-six months preoperatively. After the first postoperative months, the purchases remained quite constant and at the end of follow-up, 4–18% of patients were purchasing drugs depending on which joint was operated and the choice of drug.

Paracetamol was the most purchased drug and TKA patients purchased slightly more paracetamol than THA patients. Paracetamol purchases were also lower when the end of follow-up proportions of purchases (THA 15%, CI 15.1–15.5; TKA 18%, CI 17.9–18.3) were compared to purchases one year before arthroplasty ($p < 0.001$).

NSAIDs were the second most purchased drug by all patient groups. Early postoperative levels of NSAID purchases were lower than they were immediately before THA or TKA. However, at the end of follow-up the purchases (THA 11%, CI 11.1–11.5; TKA 14%, CI 13.9–14.3) remained higher than they had been one year before arthroplasty.

The proportion of purchases of the third most used drugs, opioids, decreased from the peak around the time of arthroplasty (THA 17%, CI 16.6–17.0; TKA 25%, CI 24.8–25.2) to the level of 5–6% of the patients purchasing opioids about one year after arthroplasty. The purchases remained on the same level until the end of follow-up.

Among THA and TKA patients, only a small proportion, mainly less than 5%, was purchasing neuropathic pain medication (antidepressants and anti-convulsants). Even though there was a peak around THA and TKA, the proportions of purchases did not appear to be affected by the arthroplasty. Instead, there was a slow but constant increase in purchases through the follow-up (total of 0.7–1.4%).

An additional sensitivity analysis was conducted. We assessed the effect of revision or arthroplasty of other joints on the original results. This analysis only included the first arthroplasty and if the patient underwent

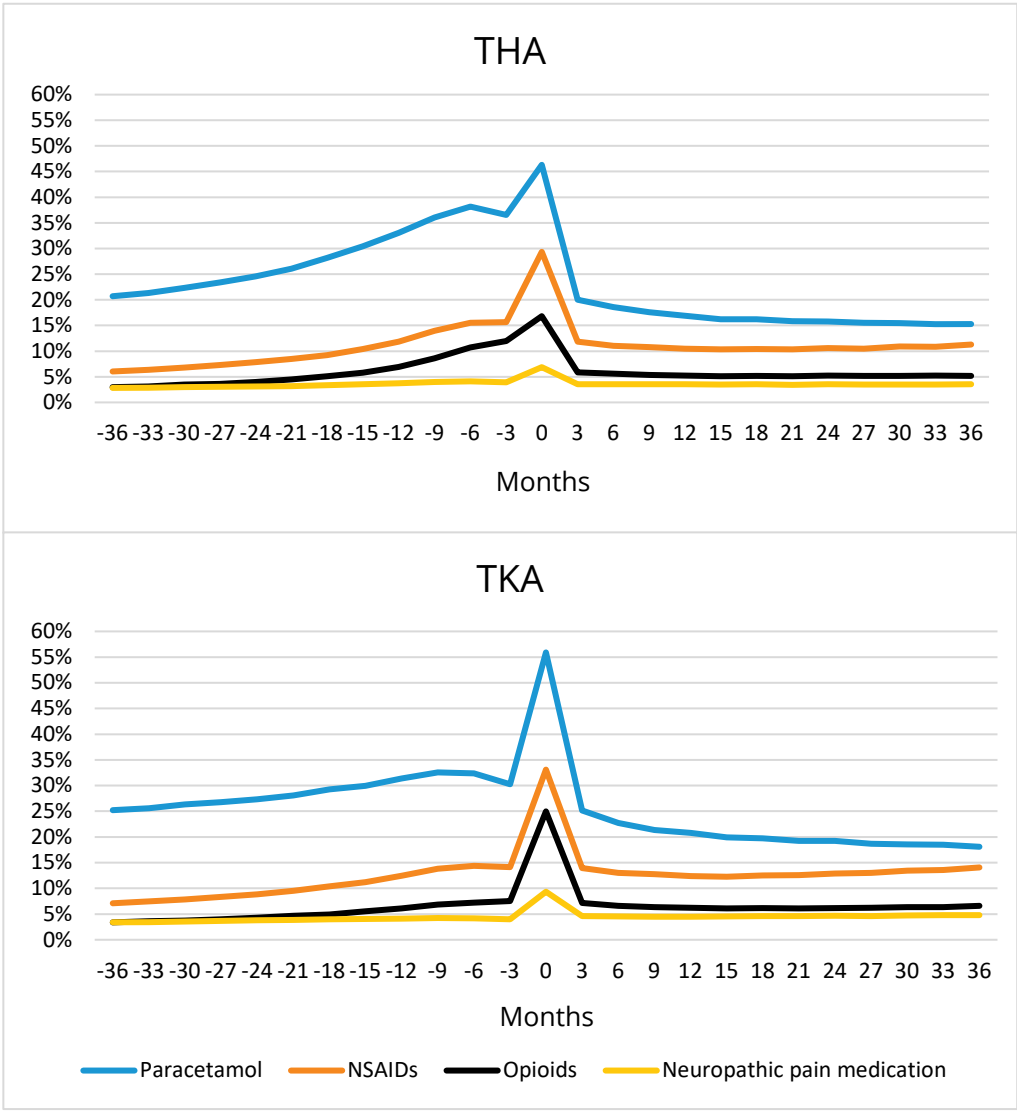
other arthroplasties, the follow-up was terminated immediately before them. The results were very similar to the original results shown in **Figure 10 and Table 10**. Differences of only a few percentage points could been seen in all drugs for both THA and TKA during follow-up. Eventually, 3–17% of THA and TKA patients were purchasing analgesics, depending on type of drug, at the end of follow-up.

Table 10. Study III. Proportion of patients (%) purchasing drugs during 90-day interval at certain time points.

	Paracetamol	NSAIDs	Opioids	Neuropathic pain medication
THA patients				
3 years preoperatively	21%	6%	3%	3%
2 years preoperatively	25%	8%	4%	3%
1 year preoperatively	33%	12%	7%	4%
Arthroplasty [c]	46%	29%	17%	7%
1 year postoperatively	17%	10%	5%	4%
2 years postoperatively	16%	11%	5%	4%
3 years postoperatively	15%	11%	5%	4%
95% confidence intervals [a]	[15–17%]	[9–11%]	[4–6%]	[2.9–3.4%]
TKA patients				
3 years preoperatively	25%	7%	3%	3%
2 years preoperatively	27%	9%	4%	4%
1 year preoperatively	31%	12%	6%	4%
Arthroplasty [c]	56%	33%	25%	9%
1 year postoperatively	21%	12%	6%	4%
2 years postoperatively	19%	13%	6%	5%
3 years postoperatively	18%	14%	7%	5%
95% confidence intervals [a]	[17–19%]	[11–14%]	[5–7%]	[3.7–4.3%]
The Finnish general population in 2018	15	26	8	4[b]

[a] Calculated using all follow-up points (three-month intervals). [b] Amitriptyline was not included in the calculations as prescription data could not be obtained. [c] 'Arthroplasty' includes the first 0-90 post-operative days and the post-operative follow-up points are X + 0-90 days from the surgery.

Figure 10. Study III. Proportions of patients purchasing drugs three years before and after THA and TKA



6 DISCUSSION

6.1 STUDY I

6.1.1 Completeness of THA and TKA events in the FAR and the CRHC

Both the FAR (94.5–96.1%) and the CRHC (98.3–98.6%) data had a high level of completeness of THA and TKA cases. Out of a total of 2,820 arthroplasties, the CRHC completely missed only 4 TKAs and the remaining missing arthroplasty records were due to inaccurate operation codes. The FAR missed 127 (4.5%) cases. This may have been due to the need to separately report arthroplasties to the FAR unless a link between the electronic health record system and the FAR was established. The validation studies of the national Dutch arthroplasty register and the Danish hip arthroplasty register show similar results. The Dutch register was shown to cover 98% of THAs and 96% of TKAs. (van Steenbergen et al., 2015) The Danish register covered 98% of THAs. (Gundtoft et al., 2016) Also, Norwegian arthroplasty register data have been compared to national patient register data and 98% of THAs and 99% of TKAs had been recorded in the arthroplasty register. (Espehaug et al., 2006) The FAR reached a high level of data completeness and the completeness is comparable internationally. Currently, the FAR reports its own estimate of data completeness (FAR, 2022). The FAR reports data completeness compared to the CHRC as being between 91.3–98.3% (mean 95.0%) for primary THAs and 91.9–98.8% (mean 95.9%) for primary TKAs. This is, close to our results regarding the FAR completeness.

6.1.2 Validation of self-reported arthroplasty

Arthroplasty is a major operation with significant health effects and it enables the patient's focus to shift from the disease (osteoarthritis) to other valuable aspects of life (Heath et al., 2021; Kamaruzaman et al., 2017). Thus, it may be that previous THAs or TKAs can be easily recalled. When self-reports were used to detect THA/TKA in the population (ie.

women who had at least one arthroplasty before the response date) they had high sensitivity, PPV and agreement with the register data.
However, the ability of self-reports to detect the dates (or at least the operation year) of THAs or TKAs was limited. This may be due to recall bias, as it may be difficult (especially for elderly people) to remember the exact date that the arthroplasty was performed. In this study, the time frame for the included arthroplasties was long, from 1980 to 2010 and the first surgeries were performed over 30 years ago.
Additional analysis focusing on arthroplasties during the last five years, increased sensitivity and PPV as expected. If both sides had undergone arthroplasties during the follow-up, it was common for only one of the surgeries to be reported (the main reason for low sensitivity). This may have been due to the way the questionnaire was formulated, as it was not clear how a bilateral operation should be reported. It seems that already recognised factors such as recall period, telescoping of landmark events (for informants the event is often more important rather than the date), formulation of survey questions and cognitive factors affected the accuracy of the self-reports. (Bhandari and Wagner, 2006; Gaskell et al., 2000; Sudman and Bradburn, 1973)
We found only one study with a similar study setting i.e. testing how well register confirmed arthroplasties are captured by self-reports. This study was conducted in Australia in a cohort of elderly women. Their self-reporting of arthroplasty (any joint) had 57–79% PPV, 100% NPV, 90–95% sensitivity and 99-100% specificity (Parkinson et al., 2013). In a Scottish study, the Million Women Study data were compared to national registers of hospital admission data. The study originally reported a high level of agreement between self-reports and the registries. However, the following data could be derived from their study. Their results for self-reports identifying register confirmed arhtroplasty events from last five years were as follows: THA (90.5% sensitivity, 99.8% specificity, 80.6% PPV and 99.9 NPV) and TKA (87.3% sensitivity, 100% specifity, 88.8% PPV and 99.9% NPV) (Liu et al., 2007).

6.1.3 Strengths and limitations of Study I

The strength of Study I is its use of several data sources including the FAR, the CRHC, self-reports, medical reports and radiographs in the validation of arthroplasty events. By utilising medical records in particular, we could conclusively distinguish whether the respondent had undergone THA or TKA. The study population was only from one local area of Finland, which may be a minor weakness. Also, as males were not included and may behave differently for some (unknown) reasons, the results related to self-reports are more applicable to female respondents.

6.2 STUDY II

Prior to the publication of Study II, there were a few studies investigating the long-term results of PROMs 10 or more years after THA or TKA (Butler et al., 2005; Gotze et al., 2006; Gould et al., 2012; Grazette et al., 2018; Mariconda et al., 2011; Meding et al., 2012; Ritter and Meneghini, 2010; Scott et al., 2019; Williams et al., 2013). These studies did not have a control group, did not measure preoperative PROMs, they only included one specific implant model in their analysis or they only measured PROMs at one point in time several years postoperatively. None of the above studies had a large number of THA and TKA patients compared to a control group without arthroplasty with both pre- and postoperative (multiple) checkpoints as we did in Study II.

6.2.1 Self-reported physical capability and subjective well-being

In Study II, elderly women who had undergone THA and TKA maintained their self-reported PC several years after arthroplasty. A decrease in results was noted 10 years after the surgery. Over 10 years of postoperative time seems to lead to a more rapid deterioration of PC and SW compared to the control group who did not receive surgery. However, those respondents who had THA or TKA later, between the 10- and 20-year follow-ups, also reported decreasing yet comparable results of PC and SW with the control group. Previous studies have shown joint scores deteriorating due to age

related changes in physical functioning, without experiencing any problems with implants (Ritter et al., 2004). Two previous studies on THAs report good yet poorer than control group patient-reported outcomes of physical functioning at 12 years postoperatively (Gould et al., 2012; Mariconda et al., 2011).

Regardless of possible age-related changes in self-reported PC. Those women who received arthroplasty between the baseline and 10-year follow-up had lower PC through the follow-up compared to the control group. It may be that these women were more affected by OA of the index joint or comorbidities. Changes in SW could also indicate that the younger patients felt more affected by OA, since at the time of the first postoperative questionnaire, their SW results had even improved or were at least the same, compared to a slight decrease after arthroplasty among the older patients. Those women with arthroplasty before the 10-year follow-up were around 4–6 years younger than the other arthroplasty patients. It is known that despite good clinical results, younger arthroplasty patients may have a poorer health-related quality of life and they report more residual symptoms compared to older patients (Gotze et al., 2006; Parvizi et al., 2014; Williams et al., 2013). Also, several patient level factors are known to affect the level of satisfaction after total joint arthroplasty, such as young age, preoperative expectations of the results, satisfactory pain relief and comorbities (e.g. depression), obesity and sex (Brander et al., 2007; Dunbar et al., 2004; Hamilton et al., 2013; Williams et al., 2013). It could be that younger patients live a more physically and socially demanding life and osteoarthrosis causes their PC and SW to deteriorate more, which is then restored after arthroplasty.

Overall, THA patients reported better results than TKA patients. This has previously been recognised by several studies (Ethgen et al., 2004; Hamilton et al., 2012; Heath et al., 2021; McKie et al., 2021; Räsänen et al., 2007). However, TKA patients had a 1–2 unit higher average body mass index compared to the control group and THA patients. Obesity is a more prominent risk factor for knee than hip OA but can also negatively affect the postoperative results (Hunter and Bierma-Zeinstra, 2019; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018; Williams et al., 2013).

The greatest improvement in pain and functioning observed from PROMs occurs during the first few months postoperatively (Ethgen et al., 2004). The observable PROM improvements continue up to 12 months for THA and perhaps even up to 24 months for TKA (Browne et al., 2013; Williams et al., 2013). ISAR recommends postoperative PROMs at 12 months for both joints after arthroplasty (Rolfson et al., 2016a). In our additional analysis, the women who had had THA or TKA a maximum of one year before the questionnaire reported better physical capability than those women who were going to receive arthroplasty during the following year. The short-term improvement of physical capabilities has been recognised both clinically and in studies reporting short-term PROMs (Browne et al., 2013; Peters et al., 2021; Rissanen et al., 1996; Williams et al., 2013). However, the proportions of THA and TKA patients reporting good PC were lower than in the groups with long follow-ups. It might be that they had not reached the full benefits of arthroplasty during the short follow-up postoperatively (Browne et al., 2013).

6.2.2 Strengths and limitations of Study II

The strenght of Study II are in its use of nationwide register data combined with the large cohort study. They provide long-term data on arthroplasties and on patient-reported outcomes. The weaknesses of the Study II are that we were unable to obtain comprehensive joint disease data in the population. Also, the results might not be generalisable to men. Further, as previously described in this thesis, no validated PROMs were used. However, the Harris Hip Score and Knee Society Score that are used in clinical settings to evaluate arthroplasty results include walking distance as a variable. Also, validated PROMs such as SF-36, OHS and OKS include walking distance/time variables. SF-36 also has questions on general health, similar to the SW question in OSTPRE. Thus, our end-point variables may be considered suitable in evaluating functional status. In addition, several previous studies have reported the validation of different OSTPRE self-reports. For example, self-reported fractures and hip fractures have been validated (Honkanen et al., 1999; Sund et al., 2014). More recently,

self-reported PC was validated using functional tests (Juopperi et al., 2021). There were many dropouts during the follow-up. The OSTPRE cohort is a rare population-based study with very long follow-up times for aging women. In an ageing population, it is obvious that there will natural reasons for “dropout”, such as mortality and long-term institutionalisation. This has been compensated in OSTPRE by linking records to national registers. PC and SW are not available in the registers. So without assuming the values for observable events such as long-term intitutionalization and mortality, we are forced to stick to the people who have returned the questionnaires. There might be selection bias due to the dropout. However, we are interested in people who can live an active life with THA or TKA. Some of the respondents who dropped out are not interesting at all, for example those respondents who ended up in an institution (10%) or have died (17%). They account for 27% of the population at the 20-year follow up (OSTPRE 25-year questionnaire). Excluding these women from the dropout makes the dropout rates much more tolerable. However, it is possible that women who are still participating are relatively healthier, although it is difficult to control for this kind of non-random bias.

6.3 STUDY III

6.3.1 Drug purchases by THA and TKA patients

Purchases of paracetamol, NSAIDs and opioids seemed to be reduced by THA and TKA when the perioperative period was studied. The greatest reduction in purchases occured during the first six months after arthroplasty. Reduction in drug purchases can be seen until 12 months postoperatively and after the first year, the proportion of patients purchasing drugs stabilised. Similar trends have been reported in PROMs after THA and TKA, indicating that the benefits of arthroplasty are gained at least up to one year after surgery (Browne et al., 2013). At three years postoperatively, depending on the anelgesic, approximately 4–18% of the patients were purchasing drugs. In their rewiev, Beswick et al. describe that in long-term follow-ups, up to 2–23% of THA and 10–34% of TKA patients

reported unfavourable pain outcomes (Beswick et al., 2012). When preoperative drug purchases from more than one year before THA or TKA were eventually compared to the postoperative results, only a reduction in paracetamol purchases was noted.

In 2018, in the Finnish population, prescription purchases of different analgesics were made in the following proportions: paracetamol 15%, NSAIDs 26% and opioids 8% (KELA, 2019). These proportions are close to the proportions of purchases by THA and TKA patients at the end of follow-up.

The most purchased drug in all groups was paracetamol. This is in line with the Finnish hip and knee OA current care guidelines, which state that paracetamol is the primary drug for OA (Knee and Hip Osteoarthritis: Current Care Guidelines, 2018). Paracetamol use in previous studies, close to the time of THA or TKA, has varied from 24% to 88% (Fuzier et al., 2014; Jørgensen et al., 2018; Rajamäki et al., 2019). In our study, the proportion of patients purchasing paracetamol was 46–56% around the time of arthroplasty. At 12 months postoperatively, Jørgensen et al. reported consumption of paracetamol by 24% of arthroplasty patients which, is similar to our results of 17–21% of patients purchasing paracetamol at the same point in time (Jørgensen et al., 2018).

The second most purchased group of drugs was NSAIDs by both THA and TKA patients. However, another Finnish study by Rajamäki et al. on drug use among THA and TKA patients had different results. NSAIDs were used the most purchased group of drugs by the patients in their study. Also, they recorded higher numbers of NSAID use by THA (> 50%) and TKA (>60%) patients at three months postoperatively. However, later at two years postoperatively they reported NSAID use that is comparable to the purchases reported in Study III (Rajamäki et al., 2019). Another study by Bolland et al. reported that at one year preoperatively, 21% of THA and TKA patients used NSAID, which is slightly more than in Study III for the same time frame. However, their conclusion that the reduction in NSAID use mostly occurred during the first postoperative year is also supported by our own conclusions.

Two previous studies reported very similar trajectories of opioid use among THA and TKA patients as us. In these studies, around 5% of patients used opioids years before the surgery and this increased to around 20% in THA and 20–35% in TKA patients at the time of arthroplasty or immediately postoperatively (Rajamäki et al., 2019; R. Wilson et al., 2019). However, the peak for opioid users (75%) reported by Wilson et al. during the first postoperative month was higher than the opioid purchases in our study. In previous studies, the proportion of THA and TKA patients with persistent opioid use stabilised at 12 months or more postoperatively and was 5–16% (Jørgensen et al., 2018; Kim et al., 2017; Rajamäki et al., 2019; R. Wilson et al., 2019).

The proportions of patients purchasing NSAIDs and opioids remained slightly higher than they had been one to three years preoperatively. However, they were comparable to purchases by the general population. This could mean that arthroplasty patients also had comorbidities that needed drugs for pain treatment. The patients also could have developed a habit of treating pain with opioids. Opioids have potential adverse effects and dependency potential (Benyamin et al., 2008). They need to be carefully considered in every patient group and physicians need to consider whether to prescribe opioids or to refer OA patiens for surgery, since preoperative opioid use increases the risk of their prolonged use (Benyamin et al., 2008; Jørgensen et al., 2018; R. Wilson et al., 2019). Also, the possible adverse effects of NSAIDs need special attention when treating older people, which OA patients often are, especially if they have comorbidities (Wongrakpanich et al., 2018).

The lowest proportions of purchases were constantly in the group of neuropathic pain medications. The purchases also remained constant throughout the follow-up, except for a small peak around the time of arthroplasty. The “base” level of purchases of these drugs is probably caused by the other indications of use, such as depression, fibromyalgia, and epilepsy. Rajamäki et al. reported constant neuropathic pain medication purchases of <5% by THA and TKA patients. In their study, this drug group did not peak even at the time of arthroplasty (Rajamäki et al., 2019). Jorgensen et al. also reported similar low proportions of

antidepressant/anticonvulsants (4%/3%) preoperatively and (5%/4%) postoperatively (Jørgensen et al., 2018). The low proportions of purchases of neuropathic pain medication by OA patients were predictable since the OA Current Care Guidelines have only conditionally recommended this type of medication (Bannuru et al., 2019; Hochberg et al., 2012; Knee and Hip Osteoarthritis: Current Care Guidelines, 2018). In addition to nociceptive and inflammatory pain, OA patients develop pain sensitisation and neuropathic pain affects OA patients in different levels of severity (Fu et al., 2018). In their review, French et al. estimated that neuropathic pain is present among at least 23% of OA patients (French et al., 2017). Based on this estimate the level of use of neuropathic pain medication is low among OA patients.

6.3.2 Strengths and limitations of Study III

We analysed the number of THA and TKA patients who purchased different drugs. The data and study design were limited and we were only able to see purchases of prescription drugs. As we used aggregated level data that does not support individual level analyses, it was not possible to monitor individual level drug purchases. Also, over-the-counter analgesics purchases were not captured. In this study, some of the patients with the longest follow-ups were six years older at the end of the follow-up compared to the start. In addition to OA, several other conditions can require pain medication use, especially in the elderly population. At three years postoperatively there were purchases in all drug groups. Purchases of drugs at this point may have been due to degenerative diseases in other joints, as well as in the spine. However, purchases of drugs by the general population were on a similar level. Also, in the sensitivity analysis, other arthroplasties and revisions were excluded and the results were similar to the original results during the entire follow-up period. The strengths of this study are its long follow-up times and nationwide registers. The registers contain all THAs and TKAs as well as the drug purchases made by these patients up to 15 years pre- and postoperatively.

7 CONCLUSIONS

7.1 STUDY I

I. In Finland, the most optimal way to identify all THAs and TKAs is to combine data from the FAR and the CRHC. The completeness of data in the FAR and the CRHC is high.
II. Self-reports are a suitable way of identifying the population with THA or TKA. Self-reports do not perform as well in identifying the actual dates of the surgery events.

7.2 STUDY II

I. THA and TKA maintain self-reported physical capability and subjective well-being. The overall self-reported physical capability and subjective well-being are lower in women with arthroplasty compared to women without arthroplasty during 20 years of follow-up

7.3 STUDY III

I. The preoperative increases in purchases of paracetamol, NSAIDs and opioids are reduced after THA and TKA.
II. After the first postoperative year, the purchases of pain medications by THA and TKA patients are similar to those in the general Finnish population.

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APPENDICES

Appendix 1. Conservative (non-surgical) treatment options for hip and knee osteoarthritis

Non-pharmacological conservative treatment options			
Treatment	Recommendation by A, B or C (strength of recommendation)		
	A	B	C
Osteoarthritis education	hip, knee	hip (1), knee (1)	hip (1), knee (1)
Exercise	hip, knee	hip (1), knee (1–3)	hip (1), knee (1)
Weight loss (for obese persons)	hip, knee	hip (4), knee (1)	hip (1), knee (1)
Cryo treatment	hip, knee	hip (4), knee (4)	hip (2), knee (2)
Thermal treatment	-	hip (4), knee (4)	hip (2), knee (2)
Ultrasound	hip, knee	knee (4)	-
TENS	hip, knee	-	hip (4), knee (4)
Acupuncture	hip, knee	hip (4), knee (4)	hip (2), knee (2)
Manual therapy	hip, knee	hip (4), knee (4)	hip (3), knee (3)
Cognitive behavioural therapy	-	hip (3–4), knee (3)	hip (2), knee (2)
Walking aids	hip, knee	hip (3), knee (3)	hip (1), knee (1)
Orthosis / braces	knee	knee (4)	knee (1-2)
Mind body exercises	-	hip (3), knee (1)	hip (1), knee (1–2)
Shoe insoles	knee	-	hip (3), knee (3)

Appendix 1. continues on the next page

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Pharmacological conservative treatment options			
Treatment	Recommendation by A, B or C (strength of recommendation)		
	A	B	C
Paracetamol	hip, knee	hip (4), knee (4)	hip (2), knee (2)
NSAIDs	hip, knee	hip (3), knee (3)	hip (1), knee (1)
Opioids	hip, knee	hip (4), knee (4)	hip (2), knee (2)
Neuropathic pain medication (the guidelines only mention Duloxetine)	hip, knee	hip (4), knee (3–4)	hip (2), knee (2)
IA corticosteroids [A]	knee	hip (4), knee (3)	hip (1), knee (1)
IA hyaluronic acid [A]	knee	hip (4), knee (3)	hip (4), knee (3)
Glucosamine	-	-	hip (4), knee (4)
Chondroitin	-	hip (4), knee (4)	hip (4), knee (4)

[A] intra articular (IA)

A) Finland: (Knee and Hip osteoarthritis: Current Care Guidelines, 2018)
The Finnish guidelines in this table only demonstrate the joints mentioned in the recommendations. The Finnish guidelines do not provide estimations on the strength of the recommendations.

B) International: Osteoarthritis Research Society International (OARSI) (Bannuru et al., 2019)
Strength of recommendations: (1) Strong; (2) Strong; conditional; (3) Conditional; (4) Conditional/Strongly against the use of treatment

C) USA: American College of Rheumatology (ACR) (Kolasinski et al., 2020)
Recommendation: (1) Strongly recommended; (2) Conditionally recommended; (3) Conditionally against; (4) Strongly against the use of treatment

Appendix 2. Arthroplasty registries around the world.

Established	Name (Country)	Joints	PROMs
1969	* The Mayo Registry (USA)	Hip, Knee, Shoulder, Elbow	-
1969	* Harris Joint Registry (USA)	Hip, Knee	EQ-5D, HHS, KOOS, UCLA
1975	Swedish Knee Arthroplasty Register = SKAR (Sweden)	Knee	EQ-5D, KOOS
1979	Swedish Hip Arthroplasty Register = SHAR (Sweden)	Hip	EQ-5D
2021	*SKAR and SHAR merged -> Swedish Arthroplasty Register (Sweden)*	*Hip, Knee*	*EQ-5D, KOOS, VAS*
1980	Finnish Arthroplasty Register (Finland)	Hip, Knee, Shoulder, Elbow	-
1987	Norwegian Arthroplasty Register (Norway)	Hip, Knee, Elbow, Shoulder, Ankle, Wrist, Finger	EQ-5D, HOOS, KOOS
1990	* Register of Orthopaedic Prosthetic Implants (Italy)	Hip, Knee, Shoulder	-
1995	Danish Hip Arthroplasty Register (Denmark)	Hip	-
1997	Danish Knee Arthroplasty Register (Denmark)	Knee	-
1997	New Zealand Orthopaedic Association Joint Registry (New Zealand)	Hip, Knee, Ankle, Shoulder, Elbow	OHS, OKS
1998	* Geneva Arthroplasty Registry (Switzerland)	Hip, Knee	HHS, WOMAC, SF-12
1999	Australian Orthopaedic Association National Joint Replacement Registry (Australia)	Hip, Knee, Shoulder, Elbow, Wrist, Ankle, Spinal disc	EQ-5D, OHS, OKS, HOOS-12, KOOS-12
1999	The Scottish Arthroplasty Project (Scotland, UK)	Hip, Knee	-
2001	Romanian Arthroplasty Register (Romania)	Hip, Knee	-
2001	Canadian Joint Replacement Registry (Canada)	Hip, Knee	EQ-5D, OHS, OKS
2001	* Kaiser Permanente (USA)	Hip, Knee	-
2002	The National Joint Registry (England, Wales, Northern Ireland, Isle of Man, Guernsey)	Hip, Knee, Shoulder, Elbow, Ankle	EQ-5D, VAS, OHS, OKS

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Established	Name (Country)	Joints	PROMs
2002	National Register of Joint Replacements (Czech Republic)	Hip	-
2002	* Valdoltra Arthroplasty Registry (Slovenia)	Hip, Knee	-
2003	Slovak Arthroplasty Register (Slovakia)	Hip, Knee	-
2005	* Catalan Arthroplasty Register (Spain)	Hip, Knee	-
2006	Japanese Arthroplasty Register (Japan)	Hip, Knee	-
2006	French Arthroplasty Register (France)	Hip	-
2007	Hungarian Arthroplasty register (Hungary)	Hip, Knee	-
2007	Dutch Arthroplasty Register (Netherlands)	Hip, Knee, Ankle, Shoulder, Elbow, Wrist, Finger	EQ-5D, NRS, HOOS-PS, OHS, Daily Functioning
2007	Egyptian Community Arthroplasty Register (Egypt)	Hip, Knee	-
2009	Portuguese National Arthroplasty Register (Portugal)	Hip, Knee, Shoulder	-
2009	Belgian National Arthroplasty Registry	Hip, Knee	-
2009	* California Joint Replacement Registry (USA) Part of AJRR since 2016	Hip, Knee	VR-12, WOMAC, UCLA
2010	American Joint Replacement Registry (AJRR) (USA)	Hip, Knee	HOOS-JR, KOOS-JR, VR-12, PROMIS-10
2010	* Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement (FORCE-TJR) (USA)*	Hip, Knee	HOOS-JR, KOOS-JR, VAS, SF-36
2011	Lithuanian Arthroplasty Register (Lithuania)	Hip, Knee	EQ-5D, KOOS, HOOS
2012	Swiss National Implant Register (Switzerland)	Hip, Knee	-
2012	German Arthroplasty Registry (Germany)	Hip, Knee	-
2012	* Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI)	Hip, Knee	PROMIS-10, HOOS-JR, KOOS-JR
2014	Irish National Orthopaedic Register (Ireland)	Hip, Knee	EQ-5D, OHS, OKS

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Appendix 2. Continued from the previous page

Established	Name (Country)	Joints	PROMs
2014	Pakistan National Joint Registry (Pakistan)	Hip, Knee	-
2016	Iranian Joint Registry (Iran)	Hip, Knee	-
2019	National Arthroplasty Registry (Slovenia)	Hip, Knee	-
2019	Indian Joint Registry (India)	Hip, Knee	-
?	JointCare (South Africa)	Hip, Knee	-
?	Turkish Arthroplasty Registry (Turkey)	Knee	-
?	* Hospital for Special Surgery Hip and Knee Joint Replacement Registry (USA)	Hip, Knee	-

(*) Regional or institutional register; (-) No PROMs are used, or status is not published in annual reports/websites of the registers

Data retrieved from: annual reports and websites of the registries and (EFORT, 2022; ISAR, 2022; Lübbeke et al., 2018; Rolfson et al., 2016a; I. Wilson et al., 2019).

8 ORIGINAL PUBLICATIONS (I-III)

I

Cross-Validation of Arthroplasty Records Between Arthroplasty and Hospital Discharge Registers, Self-Reports, and Medical Records Among a Cohort of 14,220 Women.

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Primary Arthroplasty

Cross-Validation of Arthroplasty Records Between Arthroplasty and Hospital Discharge Registers, Self-Reports, and Medical Records Among a Cohort of 14,220 Women

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ABSTRACT

Background: There are no actual validation studies of the Finnish Arthroplasty Register (FAR), and only a few studies about the accuracy of self-reported hip and knee arthroplasty exist. Therefore, we examine how reliably total hip (THA) and knee (TKA) arthroplasties can be identified from multiple data sources, including self-reports, the hospital discharge register, the arthroplasty register, and medical records.

Methods: Data from the FAR and from the Finnish Hospital Discharge Register (FHDR) during the years 1980-2010 were cross-checked to identify all THA and TKA events for the Kuopio Osteoporosis Risk Factor and Prevention Study cohort (n = 14,220). Unclear events were further checked from the medical records. After establishing a gold standard, by referring to confirmed THAs and TKAs, we examined the validity of self-reports in identifying the prevalent population with THA/TKA and in identifying incident THA/TKA.

Results: Completeness of 2820 total arthroplasty events was 96.1% in FAR and 98.3% in FHDR. The self-reports had 95.1% sensitivity and 92.9% positive predictive value (PPV) to identify population with THA and for TKA sensitivity was 94.6% and PPV 95.2%. Self-reports' sensitivity of finding the actual surgery events was 65.3% and PPV 85.4% for THA and for TKA sensitivity was 62.9% and PPV 83.4%.

Conclusion: The best way to identify THAs and TKAs in Finland is to combine data from the FAR and the FHDR. Self-reports can be considered as suitable to identify the prevalent population with THA/TKA, and they do not work as well to identify the actual surgery events.

Arthroplasty Registers

A worldwide interest in collecting data concerning arthroplasty surgeries has resulted in many arthroplasty registers [1,2]. Data in arthroplasty registers have been used mainly for the monitoring of operation volumes and for assessment of the effectiveness of implants. Arthroplasties can also be seen as outcomes that reflect when the osteoarthritis or other degenerative joint disease has exceeded a certain limit; in this sense, they are also interesting in various population health monitoring studies and cohort studies. National arthroplasty registers were first established in Sweden,

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where knee arthroplasties have been collected since 1975 and hip arthroplasties since 1979. The Finnish Arthroplasty Register (FAR) was founded in 1980 and it is the second oldest nationwide arthroplasty register in the world [3–5].

Fundamental criteria for any use of the data are data coverage (does the register capture all events of interest) and data accuracy (are the data recorded correctly). In Finland, data coverage of the FAR has been evaluated in terms of the proportion of events found in it of those with arthroplasties in the Finnish Hospital Discharge Register (FHDR). During 1997-2015, the coverage of recording primary operations has varied from 91.1% to 95.2% for hip and from 92.1% to 96.1% for knee [4]. There are no studies focusing primarily on validation of the FAR, but secondary results in some studies indicate that during 1988-1992, 5% of cases could not be linked between the FAR and the FHDR, while 3% had missing procedure codes [6]. During 1997-2003, 95.4% of primary or revision knee arthroplasties in the FAR could be supplemented with hospitalization data from the FHDR. For studying the outcomes of total knee arthroplasty (TKA), the end points should also be identified from the FHDR [7]. During 2003-2004, in one hospital, 25% of indications of reoperations of TKA were missing from the local hospital database and only about 80% of recorded indications were considered correctly forwarded to the FAR [8].

Self-Reported Arthroplasties

Although such good-quality arthroplasty registers are relatively common, they are not available everywhere. Even if the register exists, it may be impossible or infeasible to make linkages between the register and other research data because of, for example, strict privacy policies or different personal identification coding in the data sources. In such cases, information about arthroplasties can be sought directly from the study population with, for example, questionnaires. There are only a few prior studies about validation of self-reported arthroplasty [9–11].

Aims

The aims of the present study are 2-fold. First, we evaluate the coverage of register data on arthroplasties for a large population-based cohort. Specifically, we check how primary hip and knee arthroplasties can be identified from the FAR and from the FHDR, and in the case of discrepancies between the registers, details are checked in the patient records and radiology statements. Second, using the complete register data as a reference, we examine how well (1) the prevalent population with total hip arthroplasty (THA)/TKA and (2) actual incident THA/TKA events can be identified using self-reports.

Materials and Methods

OSTPRE Study

This study is based on data from the OSTPRE study launched in Kuopio Province, Eastern Finland, in 1989 [12]. The OSTPRE study focuses mainly on osteoporosis and fracture risk factors and included every woman aged 47-56 in the area of Kuopio Province (n = 14,220) in 1989. The study was conducted with postal questionnaires that have been renewed every fifth year.

Ethics and Permissions

The OSTPRE study has been approved by the ethics committee (3/11/2014//78/2004). All study subjects have provided written informed consent. Permissions to use the FAR and the FHDR data were applied for from the National Institute for Health and Welfare.

Register Data

The OSTPRE cohort was linked with data from the FHDR (until the final day of 2011) and the FAR (contained operations until June 2010 at the time of linkage). The FAR contains all hip and knee arthroplasties in Finnish hospitals since 1980 as events and records information concerning the joint, implant, fixation method, date, and reason for the surgery [3,4]. The FHDR contains linkable information about all inpatient admissions to public and private hospitals in Finland since 1969 [13]. Details of operations have been available since 1987. We identified hip and knee arthroplasties using the operation codes 9293, 9294, 9313, and 9314 of the Finnish Hospital League operation classification (1987-1996) and codes NFB30, NFB40, NFB50, NFB60, NFB99, NGB10, NGB20, NGB30, NGB40, NGB50, NGB60, and NGB99 of the Finnish version of Nomesco operation classification (in use from mid-1996). We did not include codes for semi-prostheses used in the treatment of hip fractures or any codes for revisions. The joint was determined from the operation code and reason for the operation from the main diagnosis. The operated side was detected from the operation codes ZXA00 (right), ZXA05 (left), and ZXA10 (bilateral).

Self-Reports

For the self-reported arthroplasties, we focused on the OSTPRE data collected at the 20-year follow-up in 2009 (N = 9095). In the 2009 survey, these women were 67-76 years old. The participants were asked about arthroplasties with the questions: “Have you experienced joint arthroplasty caused by osteoarthritis? In which joint and in what year?”

Data Analysis

The methodology flowchart is presented in Fig. 1. We compared register data from the FAR and the FHDR by matching using unique personal identity code, hospital, operation day, and joint. In the case of discrepancies, details were checked from the patient records and radiology statements. Self-reports were validated for 2 purposes. First, we checked how well the prevalent (participant had at least one THA or TKA implant on the questionnaire day, regardless of when the implant was installed) THA/TKA cases, at the time of 20-year questionnaire (known from register data), could be identified using self-reports. In other words, we compared (for hip and knee joints separately) the number of participants who reported at least one arthroplasty to those who had truly had arthroplasty on at least one side. Patient records, and all discharges from the FHDR, for participants who self-reported THA/TKA where there was no match from the registers, were checked in order to detect potential reasons for a (false-) positive report. Second, we assessed how incident THA/TKA events (meaning that the date or, at least, the year of the new implant

Methodology flowchart

1. Identification of THA/TKA from the FAR for the whole OSTPRE cohort
2. Identification of THA/TKA from the FHDR for the whole OSTPRE cohort
3. Cross-checking between the FAR/FHDR. All discrepancies checked from medical records.
4. Cross-checking between self-reported prevalent (existing implant no/yes) THA/TKA and combined FAR/FHDR. Discrepancies checked from medical records and all hospital discharge data.
5. Cross-checking between self-reported incident (implant year) THA/TKA and combined FAR/FHDR. Discrepancies checked from medical records and all hospital discharge data.

Fig. 1. Methodology flowchart. THA, total hip arthroplasty; TKA, total knee arthroplasty; FAR, Finnish Arthroplasty Register; FHDR, Finnish Hospital Discharge Register; OSTPRE, Kuopio Osteoporosis Risk Factor and Prevention Study.

was known) could be identified using self-reports. We considered self-reported events within ±1 year from the real operation year to be matches. We calculated standard statistics of agreement, completeness, kappa, sensitivity, specificity, positive predictive value (PPV), and negative predictive value with 95% confidence intervals where appropriate [14]. Statistical environment R with extension package Survo R was used for data analysis.

Results

Arthroplasties in Registers

When all possible causes for total joint arthroplasty of hip (THA) or knee (TKA) were included for the whole OSTPRE cohort of 14,220 women, the FAR identified 3274 implants during 1980-6/2010 and the FHDR identified 3226 hospital admissions with primary hip or knee arthroplasty operations during 1987-2011 (Fig. 2). As each implant was recorded separately in the FAR, simultaneous bilateral operations resulted in 2 records with virtually identical information, except for the side. These were recoded as bilateral operations and 90 records were excluded. Also, 323 obvious revisions identified from the FAR were excluded. Five duplicates and 364 admissions that occurred after June 2010 were excluded from the candidate list of the FHDR. There were 47 implants recorded in the FAR before 1987; these were outside the common time frame with the FHDR. Also, 59 operations for hip fractures, or for other reasons, which were treated with semi-prostheses were excluded from the FAR records. There were a total of 69 (7 of which were identifiable only from the FHDR) hip fractures treated with THA as well as other THA/TKAs resulting from special causes (osteonecrosis, cancer, developmental malformation) that were also excluded.

Matching Events in Registers

During the common time frame, 2820 total arthroplasty events were identified using the FAR and the FHDR. Of these, 2617 (91%) events had identical basic information in both registers. A further 32 events could be matched by relaxing the operation date criterion. Based on information in medical records, these operation dates were erroneously recorded in the FAR. An additional 127 (4.4%) events were found solely in the FHDR and virtually all could be confirmed from the medical records (that were retrievable for about 95% of these patients). Correspondingly, 44 (1.7%) events were identified only from the FAR. The FHDR missed 4 of these completely, 18 events had a hospital admission with reasonable diagnosis but without any recorded operation code, and for the remaining 26 events the recorded operation code was erroneous. About half of these operation codes were closely related ones, but not exactly primary THA or TKA operations.

Completeness of Registration

Completeness of the Finnish registers is reported in Table 1. During the common time frame, a total of 1019 THAs were found. The FAR identified 94.5% and the FHDR 98.6% of these surgeries. Individual surgeries were found in both registers in 93.1% of the cases. As TKAs were studied, 1801 surgeries were found. The completeness of data in the FAR was 96.1% and in the FHDR 98.3%. Both registers had reports from 94.4% of the individual surgeries. Positive agreement estimates the conditional probability that if one of the registers, randomly selected, identifies an event the other register will also do so [15]. Positive agreement on THAs was 96.4% and for TKAs was 97.1%.

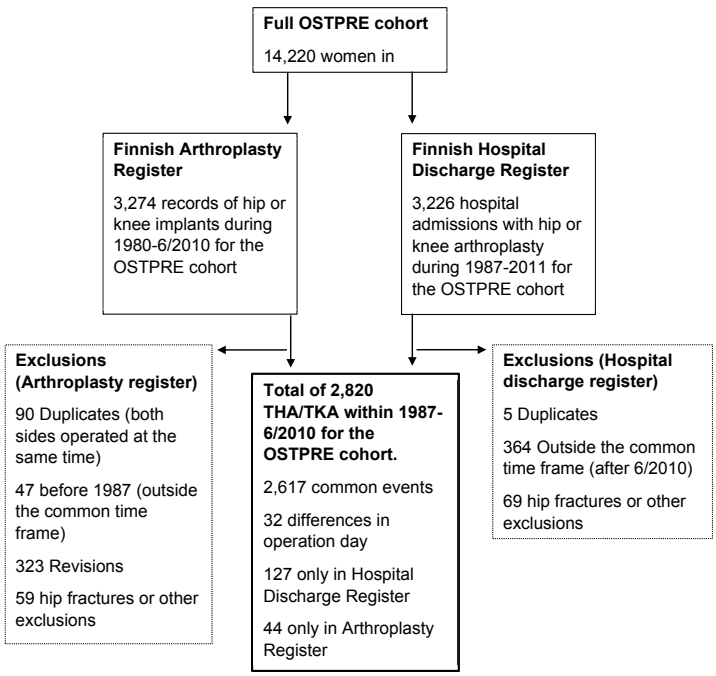

Fig. 2. Flowchart for identifying THA and TKA from the FAR and the FHDR for the OSTPRE cohort.

Table 1
Completeness of Total Hip (THA) and Knee (TKA) Arthroplasty Surgeries in the FAR and the FHDR.

THAs, N = 1019	
In both registers: 949 THA (93.1%) Missing from FHDR: 14 THA (1.4%) • 0 Completely missing • 7 Missing operation code • 7 Wrong operation code	Missing from FAR: 56 THA (5.5%) Positive agreement[a]: 96.4% (95% CI: 95.6%-97.2%) Completeness of FAR: 94.5% Completeness of FHDR: 98.6%
TKAs, N = 1801	
In both registers: 1700 TKA (94.4%) Missing from FHDR: 30 TKA (1.7%) • 4 Completely missing • 11 Missing operation code • 15 Wrong operation code	Missing from FAR: 71 TKA (3.9%) Positive agreement[a]: 97.1% (95% CI: 96.5%-97.7%) Completeness of FAR: 96.1% Completeness of FHDR: 98.3%

FAR, Finnish Arthroplasty Register; FHDR, Finnish Hospital Discharge Register; CI, confidence interval.
[a] Positive agreement estimates the probability that on the condition that one of the registers identifies an event the other register will also do so.

Self-Reports in Identifying Women With at Least One THA/TKA Before Response Date (Prevalent Population)

Self-reports of THA/TKA from the OSTPRE questionnaires are compared to the confirmed arthroplasties (found from both Finnish registers or otherwise checked from medical records) in Table 2. The results from the postal questionnaires from OSTPRE in 2009 included a total of 9095 returned paper forms by participants. The self-reports—while used to determine prevalent THA/TKA population, on the questionnaire day, among respondents—had 95.1% sensitivity (% of population with THA that could be identified using self-reports), 99.6% specificity, 92.9% PPV (% of self-reported that really were THA), and 99.7% negative predictive value for THAs (n = 512). Kappa statistics for THA were 0.937, indicating very good agreement. For TKAs (n = 909), the results were 94.6% sensitivity, 99.5% specificity, 95.2% PPV and 99.4% negative predictive value, and kappa 0.944. As only 73.7% of the cohort (alive at median response day in 2009) had actually responded to the questionnaire, we also calculated results taking this dropout into account; it mainly affected sensitivity and kappa, which dropped to 70.8% (only a bit more than 2/3 or true positives were identified) and 0.794, respectively (substantial agreement), for THA and 72.5% and 0.807, respectively, for TKA; other statistics remained of about the same magnitude (Table 3).

Only Self-Reported Arthroplasties

There were 37 THA and 43 TKA self-reports where the self-report could not be confirmed from the registers or medical records. Of these, 16 THAs and 2 TKAs were among the excluded operations (trauma or necrosis), for 13 THAs and 11 TKAs no reason was found to explain them, and for the rest some other surgical intervention (eg, arthroscopy, osteotomy) was found. Two self-reported primary THAs were found, from the time period before the registers, which were indirectly detectable from the registers, as reoperations were performed for both.

Self-Reports in Identifying the Events of (Incident) THA/TKA

Finally, we checked how well self-reports allowed for detection of the incident THA and TKA events, that is, the actual dates (or at least years) of the arthroplasty operations (Table 3). For THA, the sensitivity of finding the surgery events was 65.3% (61.5%-68.9%) and PPV 85.4% (82.9%-87.5%). For TKA, the corresponding sensitivity was 62.9% (60.1%-65.6%) and PPV 83.4% (81.8%-84.9%). For the identification of only recent surgeries (during the last 5 years), sensitivity was raised to 71.0% (65.7%-75.8%) and PPV to 92.7% (88.6%-95.5%) for THA and for TKA the sensitivity was 71.5% (67.8%-75.0%) and PPV 92.8% (90.1%-94.9%).

Table 2
Comparison of OSTPRE Questionnaire Data and the Finnish Register Data for Detecting Women Who Have Had THA or TKA Before Response Day (Prevalent Implant).

OSTPRE	Finnish Register Data	
THA	Confirmed Arthroplasty[a]	No Confirmed Arthroplasty
Arthroplasty informed by patient	487	37
Arthroplasty NOT informed by patient	25	8546
Nonrespondents[b]	176	3068
Respondents only	Kappa: 0.937 (0.921-0.952)	
Sensitivity: 95.1% (92.9%-96.8%)	Positive predictive value: 92.9% (90.5%-94.8%)	
Specificity: 99.6% (99.4%-99.7%)	Negative predictive value: 99.7% (99.6%-99.8%)	
All women including nonrespondents[b]	Kappa: 0.794 (0.768-0.819)	
Sensitivity: 70.8% (67.2%-74.2%)	Positive predictive value: 92.9% (90.5%-94.8%)	
Specificity: 99.7% (99.6%-99.8%)	Negative predictive value: 98.3% (98.1%-98.5%)	
TKA		
Arthroplasty informed by patient	860	43
Arthroplasty NOT informed by patient	49	8143
Nonrespondents[b]	277	2967
Respondents only	Kappa: 0.944 (0.932-0.955)	
Sensitivity: 94.6% (92.9%-96.0%)	Positive predictive value: 95.2% (93.7%-96.4%)	
Specificity: 99.5% (99.3%-99.6%)	Negative predictive value: 99.4% (99.2%-99.5%)	
All women including nonrespondents[b]	Kappa: 0.807 (0.788-0.826)	
Sensitivity: 72.5% (69.9%-75.0%)	Positive predictive value: 95.2% (93.7%-96.4%)	
Specificity: 99.6% (99.5%-99.7%)	Negative predictive value: 97.2% (96.9%-97.4%)	

OSTPRE, Kuopio Osteoporosis Risk Factor and Prevention Study; THA, total hip arthroplasty; TKA, total knee arthroplasty; FAR, Finnish Arthroplasty Register; FHDR, Finnish Hospital Discharge Register.
[a] Identical information in both registers (FAR and FHDR) or otherwise confirmed from medical records.
[b] Alive at median response day (n = 3244).

Discussion

Register Data

The completeness of data in THA and TKA events was high in both the FAR (94.5%-96.1%) and the FHDR (98.3%-98.6%). Yet, the FHDR seems to get closer to covering all THAs and TKAs conducted—only 4 TKAs were completely missing, the rest of the failed reports were due to an incorrect or missing operation code. The FAR had 127 (4.5%) surgeries missing, probably because the surgeries had to be separately reported to the register unless a special linkage between the Electronic Health Record system and the register was available. The completeness of the FHDR seems similar to the results from Norwegian studies about the Norwegian Arthroplasty Register, which had 99.6% agreement with national patient registers and local hospital data [16,17].

Table 3
Comparison of OSTPRE Questionnaire Data and the Finnish Register Data for Detecting the Events of (Incident) THA and TKA.

OSTPRE	Finnish Register Data		
THA	Confirmed Arthroplasty[a]	Year Does Not Match[b]	No Confirmed Arthroplasty
Arthroplasty informed by patient	431	46	28
Arthroplasty NOT informed by patient • Only 1 of 2 informed • Not any informed	153 30	Sensitivity 65.3% (61.5%-68.9%) Positive predictive value 85.4% (82.9%-87.5%)	
TKA			
Arthroplasty informed by patient	747	105	44
Arthroplasty NOT informed by patient • Only 1 of 2 informed • Not any informed	278 58	Sensitivity 62.9% (60.1%-65.6%) Positive predictive value 83.4% (81.8%-84.9%)	

OSTPRE, Kuopio Osteoporosis Risk Factor and Prevention Study; THA, total hip arthroplasty; TKA, total knee arthroplasty; FAR, Finnish Arthroplasty Register; FHDR, Finnish Hospital Discharge Register.

[a] Identical information in both registers (FAR and FHDR) or otherwise confirmed from medical records.

[b] Contributes to false positives as well as to false negatives.

Self-Reported Data

Kappa, sensitivity, and PPV for self-reported THAs and TKAs were very high for the prevalent cases (ie, women who had at least one THA or TKA before response day). This is probably because arthroplasty is a major invasive operation, usually with significant positive health effects, and the focus changes from the disease (osteoarthritis) to performance of the prosthesis [2,18]. However, self-reports did not perform as well in identifying the actual dates (or even years) of (incident) arthroplasty surgeries. This may be due to recall bias, as it may be difficult (for the elderly) to remember the exact date or year of the surgery afterward. In this study, the time frame for surgery dates to remember is wide as it ranges from 1980 to 2010, that is, the first surgeries were done over 30 years ago. Moreover, sensitivity analysis focusing only on recent (during the last 5 years) surgeries clearly increased sensitivity and PPV, as expected. Also, if both sides were operated on during the years, it was typical that only one of surgeries was reported (the main reason for low sensitivity). This may be due to the formulation of the questionnaire, as it was not obvious how to report more than one operation for the same level joint. In fact, recall period, telescoping of landmark events (it is often the event that is important, not when it happened), cognitive factors, and survey question formulation all seemed to have a role here; these are already recognized factors affecting the accuracy of self-reporting [19–21].

These results are in line with the few existing studies, but the number of arthroplasties is larger in our study. In Scotland, hospitals' admission data were compared to the Million Women study data. The women had self-reported 90.5% of the 220 confirmed incident hip arthroplasties and 87.3% of the 118 confirmed knee arthroplasties that had occurred within 5 years [9]. In the United States, Parimi et al [10] studied the accuracy of self-reported THAs in elderly white women and >95.0% of the self-reported THAs (prevalent cases from the past 8 years) could be confirmed with medical records or pelvis radiographs. Parkinson et al [11] found good agreement (sensitivity and specificity >80.0%) for self-reported arthritis-related procedures that had occurred within 3 years of the questionnaire date; inaccurate recall of the operation day instead of the actual procedure was a reason for differences between self-reports and inpatient hospital data.

Strengths and Limitations

The strength of this study is in the large number of arthroplasty events validated using several data sources including the FAR, the FHDR, self-reports, medical records, and radiographs. Especially by using medical records, we could conclusively tell whether the patient had undergone a THA or TKA surgery. A minor weakness may be that the study population is only from one local area of Finland, and not from the whole country. In addition, the results related to self-reporting are more applicable to female patients, because male patients may behave differently for some (unknown) reasons, but they were not included in this study.

Conclusions

By combining data from the FAR and the FHDR, we get an accurate information source for THAs and TKAs in Finland. This is the first actual validation study for the FAR. Self-reported arthroplasties can be considered as suitable for identifying the prevalent population with THA/TKA. Self-reports do not work as well to identify the incident event, the most likely reason for this is because of recall bias about the year of operation.

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II

Physical capability after total joint arthroplasty: long-term population-based follow-up study of 6,462 women.

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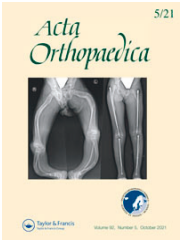

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Physical capability after total joint arthroplasty: long-term population-based follow-up study of 6,462 women

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Physical capability after total joint arthroplasty: long-term population-based follow-up study of 6,462 women

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Background and purpose — There is lack of knowledge concerning patient-reported long-time outcome after arthroplasty. Therefore, we investigated patient self-reported physical capabilities (PC) and subjective well-being (SW) up to 20 years after total hip (THA) or knee (TKA) arthroplasty.

Subjects and methods — The self-reports from postal questionnaires for study checkpoints (baseline, 10-year follow-up, 20-year follow-up) were provided by the Kuopio OSTPRE study including only women aged 52–62 years (n = 6,462). The Finnish Arthroplasty Register and Care Register for Health Care provided data on arthroplasties in the OSTPRE population. The results of women with THA/TKA were compared with women without arthroplasty (control group).

Results — In subjects with THA performed before the 10-year follow-up, the proportion of good PC was initially decreased by 0.6 percentage points (pp) at the 10-year follow-up and later by 19 pp at the 20-year follow-up. After TKA, the proportion of subjects with good PC decreased by 4.1 pp (10–year follow-up) and 27 pp (20-year follow-up), respectively. The proportion of controls reporting good PC decreased by 1.4 pp at the 10-year follow-up and 14 pp at the 20-year follow-up compared with the baseline. After THA, the proportion of subjects with good SW stayed on the same level at 10-year follow-up and decreased by 2.3 pp at 20-year follow-up. After TKA, the proportion of good SW increased by 9.0 pp (10-year follow-up) and decreased by 14 pp (20-year follow-up). The proportion of controls reporting good SW increased by 4.0 pp (10-year follow-up) and decreased by 8.8 pp (20-year follow-up).

Interpretation — THA and TKA maintain PC and SW. The overall PC and SW are lower in women with arthroplasty, in comparison with controls without arthroplasty. THA seems to outperform TKA in maintaining PC.

In recent years, more attention has focused on patient-reported outcomes after total hip (THA) and knee (TKA) arthroplasty. Most studies on patient-reported outcome measures (PROM) have relatively short follow-ups (Ethgen et al. 2004). As implants will usually survive longer, there is a need to investigate long-term patient satisfaction and functioning.

We found only a few PROM studies reporting long-term results on THA and/or TKA. THA seems to have high patient satisfaction and good functional outcomes, up to at least 16 years after operation (Mariconda et al. 2011, Gould et al. 2012). TKA seems to maintain patient functioning and activity up to 20 years postoperatively (Meding et al. 2012).

Patients often inquire about the performance of THA and TKA in activities of daily living. Also, the performance of THA and TKA is compared, by patients, with non-operated knees and hips. However, there are no studies available that have compared the physical capability and subjective well-being between THA and TKA patients and non-operated patients. Also, the long-term changes in PC and SW after THA and TKA remain largely unknown.

We assessed long-term patient self-reported physical capability (PC) and subjective well-being (SW) in women even up to 20 years after a primary THA or TKA. We compare THA/TKA patients with a control group and postoperative scores were compared with preoperative scores.

Subjects and methods

This study is based on the long-term follow-up of the female population in the Kuopio Osteoporosis Risk Factors and Prevention study (OSTPRE). The self-reports on participants' PC and SW were provided by OSTPRE. Supplementary data on all THAs and TKAs in the OSTPRE study population was

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obtained from the Finnish Arthroplasty Register (FAR) and the Care Register for Health Care (CRHC).

The original purpose of the OSTPRE study was to investigate osteoporosis in the female population in a prospective study setting. However, it has expanded from its start in 1989 into an overall health and subjective well-being cohort, still including only a female population (http://www.uef.fi/en/web/kmru/ostpre). The original study cohort included all 47–56-year-old women (n = 14,220) living in Kuopio Province in Eastern Finland in 1989. The study is based on self-reports via postal questionnaires, and it has been renewed every 5 years. In the current study, the OSTPRE 1994 questionnaire (n = 11,954) is used as baseline. Follow-ups are the 2004 (10-year follow-up, n = 10,912), and 2014 (20-year follow-up, n = 7,765) questionnaires. We chose these questionnaires to achieve long enough follow-up times for the participants. We focused on questions concerning self-reported PC and SW. These questions have basically remained the same since the questionnaire in 1994. Only those who had returned all 3 questionnaires were included in the study. The self-reported hip fractures in OSTPRE, also included in the present study, were complemented with the hip fractures found from the CRHC and all were also checked from the medical records.

The questions asked for self-reports in OSTPRE were as follows (originally in Finnish): "Describe your current physical capability?" and "How would you describe your current well-being?". Self-reported original PC included the following answer options: 1, capable of moving without limitations; 2, no running, without other limitations; 3, can move less than 1,000 meters; 4, can move less than 100 meters independently; 5, can move only indoors; 6, I'm temporarily immobilized; 7, I'm permanently immobilized. For statistical purposes (group size), answers 1 and 2 were combined as the group "walking without limitations" and are referred later as "good PC." Also, answers 4–7 were considered as one group, "can move less than 100 meters independently." This classification works well in clinical settings too, since being able to walk less than 1,000 meters supports the indication for arthroplasty. Originally, SW answers formed 5 groups: very good, good, moderate, poor, and bad. Again, for statistical purposes, very good and good were combined as "good." Poor and bad were combined as "poor."

THA/TKA register data was collected from the FAR and CRHC. We used 2 different data sources, since it has been previously found to more comprehensively cover all arthroplasties (Turppo et al. 2018). The CRHC records all special healthcare hospital admissions. It holds records of arthroplasty operations since 1987. The FAR has recorded data from arthroplasties since 1980 (National Institute of Health and W 2019). The data was collected until 31 December 2016. Any anomalies in data were manually checked from the questionnaire forms and medical reports and corrected when possible. There were 2,444 women with THA or TKA before the final return date of the 20-year follow-up questionnaire (December 31, 2014). 921 participants who failed to return any of the 3 questionnaires were excluded, of whom 293 had died during follow-up. 92 women underwent arthroplasty before baseline and 612 women had more than 1 operated joint. Eventually, there were 819 women with a THA or TKA who met the inclusion criteria. These women formed groups according to the time of their THA or TKA.

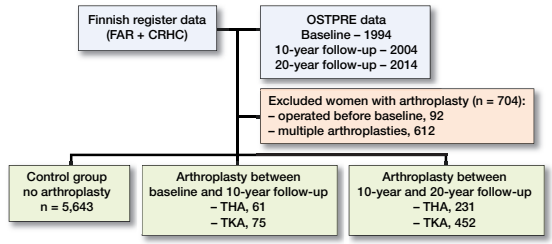

Figure 1. Flowchart of study population (N = 6,462).

The following subgroups of women were created (Figure 1, and see Tables 2 and 3): (1) the control group included all OSTPRE participants without arthroplasty until the end of follow-up; (2) women with hip or knee arthroplasty between baseline and 10-year follow-up; (3) women with hip or knee arthroplasty between 10-year and 20-year follow-up.

Statistics

We used the chi-square test to examine similarity of proportions of the population being in a certain physical capability state at different follow-up points between the control group and the different groups of women with THA/TKA. We used 1-way analysis of variance (ANOVA) to compare means of, e.g., height, weight, and BMI. We used propensity score matching to select the most suitable controls for women operated in with THA or TKA . The variables found in Characteristics (Table 1) were used as covariates. Statistical analysis was conducted with the Statistical Package for the Social Sciences (SPSS), version 27 (IBM Corp, Armonk, NY, USA).

Ethics, funding, and potential conflicts of interest

The Research Ethics Committee of the Northern Savo Hospital District has given permission for the OSTPRE study (3/11/2014//78/2004). Written consent has been provided by every study participant. The Finnish Institution for Health and Welfare has granted permission to use the CRHC and FAR data (THL/20/5.05.00/2016). This study was supported by the Finnish Arthroplasty Association, Päivikki and Sakari Sohlberg Foundation and Academy of Finland. The authors have no conflicting interests to report.

Results

The overall study population consisted of 6,462 women, 292 of whom had THA and 527 whom had TKA. Hip fracture was the indication for THA in 9 women.

Table 1. Characteristics of the study population (N = 6,462)

Factor	No arthroplasty during follow-up (n = 5,643)	Women with hip prostheses during follow-up (n = 292)	Women with knee prostheses during follow-up (n = 527)	p-value
Age at baseline (years)	57 (52–62)	57 (52–62)	57 (52–62)	< 0.001 [a]
Height (cm)	161 (136–179)	162 (147–176)	162 (143–178)	0.005 [a]
Weight (kg)	69 (38–125)	70 (47–103)	74 (48–120)	< 0.001 [a]
BMI	26 (16–53)	27 (19–40)	28 (20–48)	< 0.001 [a]
Mean number of chronic diseases at baseline	1.6 (0–10)	1.7 (0–8)	1.8 (0–9)	0.002 [a]
at end of follow-up	6.8 (0–36)	7.2 (0–26)	7.2 (0–26)	< 0.001 [a]
Self-reported diseases at end of follow-up (%) [b]				
Osteoporosis/osteopenia	11	8.6	12	0.3
Rheumatoid arthritis/ ankylosing spondylitis	4.1	6.2	8.3	< 0.001
Chronic back pain	24	30	29	0.004
Ischemic heart disease	18	16	19	0.7
Hypertension	58	59	66	0.002
Other heart disease	15	18	18	0.1
Asthma	14	15	14	0.9
Emphysema	2.6	2.7	2.5	1.0
Diabetes	17	14	22	0.006
Stroke	9.8	9.6	8.3	0.6
Cancer	14	13	12	0.6
Self-reported fractures (%) [b]				
Hip fracture				
at baseline	0.1	0.0	0.0	0.8
end of follow-up	0.5	5.1	0.8	< 0.001
Any low trauma energy fracture				
at baseline	8.2	7.5	6.6	0.4
end of follow-up	12	14	13	0.4

[a] One-way analysis of variance (ANOVA).
[b] Pearson's chi-square.

Among women with arthroplasty between baseline and 10-year follow-up, the mean age at the time of arthroplasty was 64 (THA)/65 (TKA) years. The median follow-up time for the groups was THA 13 (10–20)/TKA 12 (9–19) years. Good PC was reported by 83% of women with THA and 80% of women with TKA, at the 10-year follow-up (1st postoperative questionnaire). At the 20-year follow-up (2nd postoperative questionnaire), and good PC was reported by 64%/53% of women. The changes in good PC of women with a THA were not statistically significantly different from the control group (p = 0.2) whereas the changes in good PC in the TKA group were significantly different (p = 0.01) (Table 2 and Figures 2–3 and Table 5, see Supplementary data). Both THA and TKA women reported maintained or improved good SW after operation, at the 10-year follow-up 33% (THA)/41% (TKA). Later, at the 20-year follow-up, 31%/27% reported good SW. Again, there were statistically significant differences in good SW between THA (p = 0.01)/TKA (p = 0.005) and the control group (Table 3 and Figures 4–5, see Supplementary data). The proportion of women with revision arthroplasties until the end of follow-up was 21% for THA. Their results for good PC were: 92% (baseline), 77% (1st postoperative questionnaire) and 62% (2nd postoperative questionnaire). In this revised group, the proportion of women with good SW reports at the same follow-up points were 46%, 15%, and 18%. Only 6.7% of women with a TKA had revision arthroplasties.

Among women with THA or TKA between 10-year and 20-year follow-up, the mean age at the time of arthroplasty was 70 years for both THA and TKA. The median follow-up time for these women was THA 3 (0–9)/TKA 3 (0–10) years. Good PC was reported by 76% of women with THA and 71% with TKA at the 20-year follow-up (postoperative questionnaire) (Table 2 and Figures 2–3 and Table 5, see Supplementary data). The changes in good PC of women with THA were not significantly different (p = 0.6) when compared with the control group. For TKA there was a statistically significant difference (p = 0.04). During follow-up checkpoints participants reported a steady decrease of SW. Eventually, at the 20-year follow-up, good SW was reported by 37% (THA) and 29% (TKA) (Table 3 and Figures 4–5, see Supplementary data). Statistically the changes in proportion of women with good SW were significantly different from controls with THA (p = 0.004) and TKA (p < 0.001) women. Only 3.0% of the women with THA and 2.2% of women with TKA had experienced a revision arthroplasty by the end of follow-up.

Among OSTPRE participants without THA or TKA during follow-up, good PC was reported by 95% at baseline, 94% at 10-year follow-up, and 80% at 20-year follow-up (Table 2). SW remained almost the same throughout the follow-up (Table 3). At baseline 48% of these women reported good, 42% moderate, and 10% poor SW. The women in the control group and in the groups with a THA or TKA are similar in terms of age, height, number of low trauma energy fractures, osteoporosis/osteopenia, and the mean number of chronic diseases (Table 1). However, there are differences in the proportions of self-reports of some important groups of chronic diseases and in the amount of self-reported hip fractures by THA patients versus other participants.

Good PC was reported by 94–97% (baseline), 93–95% (10-year follow-up), and 80–81% (20-year follow-up) of the propensity score matched controls. Good SW was reported by 52–61% (baseline), 52–56% (10-year follow-up), and 47–53% (20-year follow-up) (Table 4).

Analysis for women with THA or TKA within a 1-year period of any questionnaire showed that preoperatively 54%

Table 2. Self-reported physical capability (PC) assessed by walking capability, in controls (women with no arthroplasty) and in women with total hip arthroplasty (THA) or total knee arthroplasty (TKA) at baseline, 10-year and 20-year follow-ups (%)

	n [a]	Walking without limitations [b]	< 1 km [c]	< 100 m [d]	p [e]
Control group					
Baseline	5,356	95	4.0	1.0	
10-year follow-up	5,557	94	4.0	2.0	
20-year follow-up	5,497	80	11	9.0	
THA between baseline and 10-year follow-up					
Baseline	56	84	13	4.0	0.2
10-year follow-up	60	83	12	5.0	
20-year follow-up	59	64	12	24	
TKA between baseline and 10-year follow-up					
Baseline	73	84	15	1	0.01
10-year follow-up	73	80	16	4	
20-year follow-up	73	53	27	19	
THA between 10-year and 20-year follow-up					
Baseline	218	95	4	1	0.6
10-year follow-up	225	90	8	3	
20-year follow-up	222	76	12	12	
TKA between 10-year and 20-year follow-up					
Baseline	427	94	5	0	0.04
10-year follow-up	441	89	9	3	
20-year follow-up	431	71	17	12	

Arthroplasties are stratified by OSTPRE study follow-up periods (between baseline and 10-year follow-up, between 10-year and 20-year follow-up).
[a] Participants with valid answer in each individual follow-up point.
[b] "Good PC."
[c] Can move < 1 km independently but > 100 m.
[d] Can move < 100 m independently.
[e] Chi-square was used to study the statistical significance of the changes in good PC during the follow-up between the control group and women with THA/TKA.

Table 3. Subjective well-being (SW) in controls (women with no arthroplasty) and in women with total hip arthroplasty (THA) or total knee (TKA) arthroplasty at baseline, 10-year, and 20-year follow-ups (%)

	n [a]	Good	Moderate	Poor	p-value [a]
Control group					
Baseline	5,520	48	42	10	
10-year follow-up	5,593	52	45	3	
20-year follow-up	5,577	43	50	7	
THA between baseline and 10-year follow-up					
Baseline	60	33	50	17	0.01
10-year follow-up	60	33	62	5	
20-year follow-up	58	31	50	19	
TKA between baseline and 10-year follow-up					
Baseline	73	32	51	18	0.005
10-year follow-up	74	41	55	4	
20-year follow-up	74	27	57	16	
THA between 10-year and 20-year follow-up					
Baseline	227	45	46	9	0.004
10-year follow-up	227	38	56	5	
20-year follow-up	224	37	56	7	
TKA between 10-year and 20-year follow-up					
Baseline	435	40	49	11	< 0.001
10-year follow-up	445	36	60	4	
20-year follow-up	449	29	61	10	

Arthroplasties are stratified by OSTPRE-study follow-up periods (between baseline and 10-year follow-up, between 10-year and 20-year follow-up).
[a] Participants with valid answer in each individual follow-up point.
[b] Chi-square was used to study the statistical significance of the changes in good SW during the follow-up between the control group and women with THA/TKA.

of THA and 65% of TKA participants reported good PC. Postoperatively good PC was reported by 62% of THA and 69% of TKA participants. Similarly, good SW was reported by 21% of THA and 24% of TKA participants preoperatively, but 37% (THA)/31% (TKA) postoperatively.

Discussion

Elderly women who had experienced THA or TKA maintained their self-reported PC approximately 10 years after the procedure. However, at the end of follow-up the PC and SW among women with arthroplasty generally seemed to decrease more than in women without arthroplasty. 2 prior studies reported worse physical functioning 12 years after THA than in a control group without arthroplasty (Mariconda et al. 2011, Gould et al. 2012). Another study reported good yet deteriorating results from TKA patients 20 years after TKA (Meding et al. 2012). The women with arthroplasty between baseline and 10-year follow-up may have been affected more by osteoarthritis or other comorbidities before the operation than those who underwent the operation later, because before operation there were notably fewer women reporting good PC than in the control group. Postoperatively, the THA group seemed to benefit more from the operation. Previous reports on THA outperforming TKA support this finding (Ethgen et al. 2004). SW was improved or maintained with both THA/TKA at the first postoperative follow-up (10-year follow-up). However, at the 20-year follow-up, SW deteriorated and was a little worse than at baseline. The exact cause for deteriorating results during the longer follow-up (about 13 years postoperatively) remains unclear. Age and comorbidities related to aging may be the main factors, as at the 20-year follow-up the results decreased in all other groups too. Women with arthroplasty may be more prone to these factors. Women who had arthroplasty between baseline and 10-year follow-up were 5–6 years younger than those with arthroplasty later in life. Previous studies have reported that younger patients may be less satisfied with their THA or TKA operation. Regardless of good clinical results, they report more residual symptoms and their health-related quality of life may be more impaired than amongst older patients (Gotze et al. 2006, Parvizi et al. 2014). It may be that arthrosis worsens physical capability in an otherwise more physically capable young population, and arthroplasty restores capability later. Furthermore, changing social demands, i.e.,

Table 4. PC and SW results (%) for propensity score matched controls (no arthroplasty) for women with THA (n = 61) and TKA (n = 75) between baseline and 10-year follow-up, and for women with THA (n = 231) and TKA (n = 452) between 10-year and 20-year follow-up

	PC				SW			
	Walking without limitations [a]	< 1 km [b]	< 100 m [c]	p-value [d]	Good	Moderate	Poor	p-value [d]
Baseline–10-year follow-up								
THA controls								
Baseline	95	6	0		61	31	9	
10-year follow-up	95	5	0	0.2	54	39	7	< 0.001
20-year follow-up	80	10	10		53	35	12	
TKA controls								
Baseline	94	6	0		59	32	9	
10-year follow-up	95	4	1	< 0.001	56	39	5	< 0.001
20-year follow-up	81	8	11		53	37	11	
10–20-year follow-up								
THA controls								
Baseline	97	3	0		54	38	8	
10-year follow-up	95	4	1	0.5	53	44	3	< 0.001
20-year follow-up	80	8	12		48	46	6	
TKA controls								
Baseline	97	3	1		52	40	9	
10-year follow-up	93	5	3	0.02	52	44	4	< 0.001
20-year follow-up	81	10	9		47	47	6	

[a] "Good PC."
[b] Can move < 1 km independently.
[b] Can move < 100 m independently.
[d] Chi-square was used to study the statistical significance of the changes in good PC and SW through the follow-up between the propensity score matched controls and women with THA or TKA.

during working life or doing sports without worrying about a prosthesis may have an influence on the improvement of PC. There are also patient-related factors that can influence postoperative patient-reported outcomes, e.g., comorbidities, obesity, psychological status, and expectations (Hofstede et al. 2016, Canovas and Dagneaux 2018).

Women who underwent THA/TKA later in life (between 10-year and 20-year follow-up) seemed to have a quite similar PC to the control group, 10 years prior to arthroplasty, at baseline. Before arthroplasty, at the 10-year follow-up, there was slight decrease in PC results, probably due to progression of osteoarthritis of the index joint. The postoperative scores in PC were close to those reported by the control group, and age-related factors may decrease patients' physical capabilities even more than arthrosis. However, neither THA nor TKA completely restored a person's ability to walk. The SW of these older women was good throughout the follow-up. Previous data has shown that age is not an obstacle for an effective THA or TKA and elderly people report improved quality of life scores after THA/TKA operations (March et al. 1999, Ethgen et al. 2004).

THAs' and TKAs' positive effects on pain, physical functioning and health are known to mostly increase from months to up to 2 years post-operatively (Ethgen et al. 2004, Williams et al. 2013). In our study, both PC and SW improved in participants with THA or TKA within 1 year of the questionnaire, when compared with results prior to operation.

At baseline, controls and women with arthroplasty had almost the same amount of doctor-diagnosed chronic diseases. At the end of follow-up, women with arthroplasty had a slightly higher average amount of chronic diseases. The greater burden of diseases may also affect PC and SW among women with THA or TKA. Furthermore, women with TKA had the highest average BMI as compared with controls and the THA group, which may have affected their PC negatively. Obesity has been shown to be strongly related to knee osteoarthritis but less to osteoarthritis of the hip (Hunter and Bierma-Zeinstra 2019).

We additionally performed propensity score matching, which gave PC results similar to the original control group. The difference in SW results between women with arthroplasty and propensity score matched controls was increased compared with the original control group.

Strengths of this study are the large cohort study combined with the national registers and with long-term data. Weaknesses of our study are that we did not have conclusive data on symptomatic joint diseases in the study population, and our results may not be generalizable to men. Also, no validated patient-reported outcome measures were used. However, scores used to evaluate clinical results of arthroplasty (e.g., Knee Society Score, Harris Hip Score, and Oxford Knee and Hip Score), include walking distance as a variable. Thus, our end point variable may be considered feasible for evaluation of the functional status. In addition, there are prior studies validating different self-reports in OSTPRE. Recently, we have reported the validity of self-reported physical capability with functional tests in the OSTPRE cohort (Juopperi et al. 2021). Also, self-reported fractures (Honkanen et al. 1999) as well as all hip fractures (Sund et al. 2014) have been validated. During follow-up there were many dropouts. The OSTPRE cohort is one of the rare true population-based cohorts of aging women with very long follow-up time and is also a part of the national roadmap infrastructure (Finnish Research Infrastructure for Population Based Surveys—FIRI-PBS). It is obvious that in the aging population there will be natural reasons for "drop-out" in the population answering questionnaires, such as mortality or long-term institutionalization. In the OSTPRE cohort

this has been compensated with record linkage to national registers. The PC or SW are not available in the registers, so without assuming some values for observable events (mortality, hospitalization, long-term institutionalization) we are forced to stick to the people who have answered the questionnaires. It is true that in this situation there may be some selection bias because of dropout. However, part of the dropout is not interesting at all, because we are interested in the population who can live a normal life with THA/TKA, not in those who have already died (17%) or ended up in an institution (10%), account for the 27% at the time of 20-year follow-up (i.e., at OSTPRE 25-year follow-up in 2014). Excluding women with these reasons from the dropout population makes the dropout rates much more tolerable. It is still possible and likely that the women who have answered are relatively healthier than the ones unwilling to participate anymore, but it is difficult to control for this kind of non-random bias.

In conclusion, THA and TKA maintain self-reported PC and SW. Yet, the overall PC and SW are lower in women with prior arthroplasty, in comparison with age-matched controls without arthroplasty. THA seems to outperform TKA in maintaining PC.

Supplementary data

Figures 2–5 and Table 5 are available as supplementary data in the online version of this article, http://dx.doi.org/10.1080/17453674.2021.1922039

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III

Pain medication purchases before and after total hip and knee arthroplasty: a register study of 329,743 arthroplasties

Turppo V, Sund R, Huopio J, Kröger H, Sirola J.
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Pain medication purchases before and after total hip and knee arthroplasty: a register study of 329,743 arthroplasties

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Background and purpose — Total hip (THA) and knee (TKA) arthroplasty are effective pain treatment in osteoarthritis; however, there are patients with long-term pain and in need of analgesics. We studied purchases of paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and neuropathic pain medication before and after THA or TKA.

Patients and methods — We searched all THA (n = 149,158) and TKA (n = 180,585) cases in Finland between the years 1998 and 2018 and the drug purchases made by patients during 1997–2018 using linked Finnish register data. Drug purchases were studied in 3-month periods.

Results — The purchases of all analgesics increased from 3 years before operation to 3 months before operation. Around the time of THA or TKA, the purchases of all analgesics spiked to 7–56%, depending on drug. The purchases of all analgesics decreased rapidly during the first 6 months postoperatively. Purchases of paracetamol, NSAIDs, and opioids at 6 months postoperatively (6–23%) were lower than they were at 3 months preoperatively. At 3 years postoperatively, only paracetamol purchases were lower (15–18%) postoperatively than they were 3 years before arthroplasty. NSAID, opioid, and neuropathic pain medication purchases remained higher (4–14%).

Interpretation — THA and TKA stop and reduce the preoperative increases in purchases of paracetamol, NSAIDs, and opioids. The purchases of pain medications by THA and TKA patients 1 year after operation are close to those in the general population.

According to Finnish Current Care treatment guidelines paracetamol is the primary analgesic for osteoarthritis (OA). The next step is to use non-steroidal anti-inflammatory drugs (NSAIDs). Opioids should be used only when pain cannot be controlled otherwise (1). Some patients may develop pain sensitization, and medication for neuropathic pain can then be used (e.g., antidepressants and anticonvulsants) (1-3).

When pain and disability of hip and knee OA cannot be controlled adequately by nonoperative means, the next treatment is usually total hip (THA) or knee arthroplasty (TKA). These surgical interventions have good long-term results for physical capability and well-being (4). However, prior studies have shown THA and TKA patients reporting unfavorable long-term pain outcomes from 2% to even over 20% (5,6).

Postoperative pain management includes the same medicines as before operation. Prior studies on perioperative pain management have mainly focused on opioid use, showing that preoperative opioid use is the strongest risk factor for long-term opioid use after THA or TKA (7,8). A few papers report pain medication consumption before and after THA or TKA and show an increase in analgesic use a few months before operation and then a decrease after operation, but a noticeable number of patients continue using analgesics long term (9-11). 1 study reports increased analgesic use after TKA (12).

As patients undergo THAs and TKAs to treat pain and disability caused by osteoarthritis, pain medication purchases and consumption can be considered an indirect outcome measure for arthroplasties. We hypothesize that pain medication purchases are reduced after THA and TKA and we studied the purchases of different types of analgesics (paracetamol/acetaminophen, NSAIDs, opioids, medication for neuropathic pain) in the years before and after THA and TKA.

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Table 1. Characteristics of the arthroplasty patients. Values are percent unless otherwise specified

Factor	THA n = 149,158	TKA n = 180,585
Mean age	67	69
Comorbidities		
Hypertension	46	55
Coronary artery disease	15	16
Atrial fibrillation	8	9
Heart failure	3	4
Diabetes	11	15
Hypercholesterolemia	15	18
Depression	11	13
Psychoses	4	4
Parkinson's disease	2	2
Dementia	1	1
Cancer	11	11
Chronic lung disease	13	17
Peak proportion of analgesics purchases around the time of arthroplasty		
Paracetamol	46	56
NSAIDs	29	33
Opioids	17	25
Neuropathic pain medication	7	9

Patients and methods

Data sources

The data is provided by the Finnish Institute for Health and Welfare and their PERFECT (PERFormance, Effectiveness, and Cost of Treatment episodes) project, which started in 2004. This was established to monitor specialized medical care treatment episodes, and it includes data on diseases and procedures with high costs and number of patients (e.g., arthroplasty). Data has been collected by combining data from multiple registers. In this study, we focus on data from the Care Register for Health Care (CRHC), the Finnish Arthroplasty Register (FAR), and the Social Insurance Institution of Finland (SII). The CRHC records all special healthcare hospital admissions. It holds records of arthroplasty operations since 1987. The FAR is maintained by the Finnish Institute for Health and Welfare, and it includes data on THAs and TKAs since 1980. SII's registers provide information on all dispensed prescriptions and reimbursements for medicine expenses since 1994, yet in PERFECT the prescription data starts from the year 1997 (13).

Included patients and analgesics

Using the CRHC and FAR data, we searched for all primary THAs and TKAs in Finland during 1998–2018. Eventually, 149,158 THAs and 180,585 TKAs were found (Table 1). Next, all purchases of prescription medication of interest during 1997–2018 for arthroplasty patients up to 15 years before and after arthroplasty were searched (Figure 1 and 2, see Supplementary data). For additional sensitivity analysis (Figure 3 and Table 2, see Supplementary data) we searched for other arthroplasties (revision or arthroplasty of other joint) for the patients in the original population. If other arthroplasties were found, the follow-up for drug purchases was ended directly before those. Eventually there were 104,045 THA and 117,203 TKA patients (at the time of arthroplasty) included in the analysis. The Anatomical Therapeutic Chemical (ATC) codes were used to identify prescriptions of interest, and the following analgesics were included: paracetamol/acetaminophen (N02BE00), oral NSAIDs (M01A***, N02B*** excluding N02BE00), oral and transdermal opioids (N02A***, N07B***), antidepressants (venlafaxine/N06AX16, duloxetine/N06AX21, amitriptyline/N06AA09, and nortriptyline/N06AA10), and anticonvulsants (pregabalin/N03AX16, gabapentin/N03AX12). We divided the drugs into 4 groups—paracetamol, NSAIDs, opioids, and neuropathic pain medication—following the treatment guidelines for osteoarthritis (1,2).

The available register data did not reveal non-prescription drugs, whether the pills were consumed after purchase, or the indication for use. In Finland, there are smaller packages of paracetamol, and some NSAIDs (ibuprofen, ketoprofen, and acetylsalicylic acid) that are prescription-free and sold "over the counter," and these are not captured by the register. However, a prescription is needed to get the reimbursed price for the drugs, and a maximum of three months' supply of pills can be purchased in advance. All this results in a practice whereby purchases of prescribed drugs can be followed easily, and for continuous users there will be purchases of drugs at least once every 3 months.

For the purposes of this particular study, the individual data was processed into aggregate form that included a matrix of the number of patients who had drug purchases in certain 3-month window before or after arthroplasties and the total number of patients with follow-up in that window. Time-windows covered periods up to about 15 years before and after the arthroplasty operation, but for the purposes of this study we focused only on the ±3 years since THA/TKA. The data was stratified by drug group, sex, year group of THA/TKA, and by age (< 70 years, ≥ 70 years). Such data allowed us to calculate the proportion of patients purchasing drugs for each 3-month period.

Statistics

The Statistical Package for the Social Sciences (SPSS), version 27 (IBM Corp, Armonk, NY, USA) was used for statistical analysis. A chi-square test was used to compare whether the proportions of patients purchasing certain pain medication at different follow-up points are statistically significantly different. We calculated 95% confidence intervals (CI) for proportions of purchases for all pain medications during the follow-up. For this calculation, results from all follow-up points (3-month intervals) from 3 years before until 3 years after THA or TKA were included. Also, 95% CIs were calculated for proportion of purchases of different pain medications at certain time points.

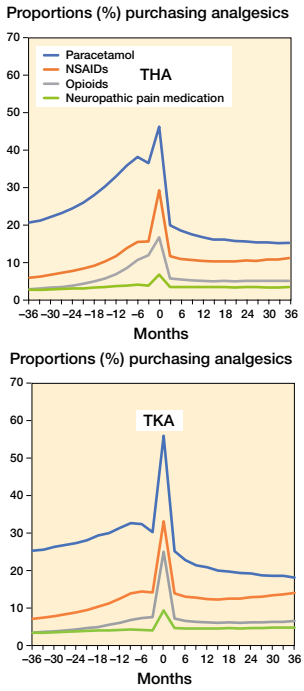

Figure 4. Proportions of patients purchasing analgesics from 3 years before to 3 years after THA/TKA.

Table 3. Proportion of patients (%) purchasing analgesics at 1-year intervals

	Para-cetamol	NSAIDs	Opioids	Neuropathic pain medication
THA patients				
3 years preoperative	21	6	3	3
2 years preoperative	25	8	4	3
1 year preoperative	33	12	7	4
Arthroplasty	46	29	17	7
1 year postoperative	17	10	5	4
2 years postoperative	16	11	5	4
3 years postoperative	15	11	5	4
95% confidence intervals [a]				
Lower limit	15	9	4	2.9
Upper limit	17	11	6	3.4
TKA patients				
3 years preoperative	25	7	3	3
2 years preoperative	27	9	4	4
1 year preoperative	31	12	6	4
Arthroplasty	56	33	25	9
1 year postoperative	21	12	6	4
2 years postoperative	19	13	6	5
3 years postoperative	18	14	7	5
95% confidence intervals [a]				
Lower limit	17	11	5	3.7
Upper limit	19	14	7	4.3
The Finnish general population in 2018	15	26	8	4 [b]

[a] Calculated using all follow-up points (3-month intervals).
[b] Amitriptyline was not included in the calculations, as prescription data could not be acquired.

Ethics, funding, potential conflicts of interest, and data sharing

The Finnish Institute for Health and Welfare has granted permission for the PERFECT project data (THL/538/6.02.00/2019). This work was supported by the Päivikki and Sakari Sohlberg Foundation and the North-Savo Regional Fund of the Finnish Cultural Foundation. The authors have no conflicting interests to report. Due to privacy regulations the original data cannot be shared. Anonymized summary tables can be shared on reasonable request.

Results

Time frame of follow-up

The complete register data included up to 15 years of pre- and postoperative follow-up data on dispensed prescriptions. Each THA and TKA had its own follow-up time, depending on when it was conducted during 1998–2018. Thus, the number of arthroplasties available at different follow-up points varied, as seen in Figure 1 (see Supplementary data). At the beginning and at the end of the follow-up, the number of arthroplasties was lower due to a lack of follow-up data (i.e., drug purchases before 1997 or after 2018), and we decided to focus on the follow-up of 3 years before and after arthroplasty.

Analgesics

Analgesics purchases before arthroplasty increase in all groups when getting closer to THA or TKA (Figure 4 and Table 3). The proportions of purchases for all analgesics and groups peaks around the time of arthroplasty. THA and TKA seemed to stop this rapid increase in analgesics purchases. The greatest decrease in purchases occurred during the 1st postoperative months, so that that the purchases of paracetamol, NSAIDs, and opioids decreased below the level they were 3–6 months before the arthroplasties. After that, the analgesics purchases stayed approximately on the same level until the end of follow-up. Eventually, 4–18% of arthroplasty patients were purchasing analgesics, depending on the group and analgesic, at the end of follow-up. Only paracetamol purchases decreased when postoperative proportions of purchases were compared with the proportions years before arthroplasty.

Paracetamol was the most purchased pain medication among both THA and TKA patients (Figure 4 and Table 3). After arthroplasty, paracetamol purchases were clearly reduced, and at 3 years postoperatively, the proportion of patients purchasing paracetamol (THA 15%, CI 15.1–15.5; TKA 18%, CI

Table 4. Chi-square statistics calculated between proportions of users and non-users at 1 year before arthroplasty and 3 years after arthroplasty

Factor	n	THA (%) yes	no	p-value	n	TKA (%) yes	no	p-value
Paracetamol								
1 year preoperative	144,529	33	67	< 0.001	176,322	31	69	< 0.001
3 years postoperative	118,997	16	84		144,649	18	82	
NSAIDs								
1 year preoperative	144,529	12	88	< 0.001	176,322	13	88	< 0.001
3 years postoperative	118,997	11	89		144,649	14	86	
Opioids								
1 year preoperative	144,529	7	93	< 0.001	176,322	6	94	< 0.001
3 years postoperative	118,997	5	95		144,649	7	93	
Neuropathic pain medication								
1 year preoperative	144,529	4	96	0.005	176,322	4	96	< 0.001
3 years postoperative	118,997	4	96		144,649	5	95	

17.9–18.3) was lower than 1 year before the operation in both joints ($p < 0.001$) (Table 4). TKA patients purchased a little more paracetamol postoperatively than THA patients.

NSAIDs were the second most purchased drug by all patient groups. Even though arthroplasty seemed to reduce NSAID purchases when the first postoperative months were compared with the final preoperative year, the proportions of patients purchasing NSAIDs at 3 years after THA (11%, CI 11.1–11.5) and TKA (14%, CI 13.9–14.3) were higher than the results from more than 1 year before arthroplasty (Figure 4, Tables 3 and 4).

Around the time of arthroplasty, the proportions of patients purchasing opioids were THA 17% (CI 16.6–17.0) and TKA 25% (CI 24.8–25.2) (Figure 4 and Table 3). The lowest level of purchases (5–6%) was reached approximately 12 months after arthroplasty, which was lower than during the final months preoperatively. After the 1st postoperative year, the purchases remained on the same level.

Neuropathic pain medication (antidepressants and anticonvulsants) had a low number of patients purchasing drugs through follow-up, mainly less than 5% (Figure 4 and Table 3). The purchases of these analgesics also peaked around the time of THA and TKA, as for the other analgesics. However, the proportion of purchases seemed not to be affected by arthroplasty. Purchases of these drugs increased steadily but by only 0.7–1.4% during the 6 years of follow-up. Eventually, 3.5% (CI 3.4–3.7) of THA and 4.8% (CI 4.7–4.9) of TKA patients were purchasing neuropathic pain medication.

Only one THA or TKA during follow-up

A sensitivity analysis was performed to determine the effect of arthroplasties of other joints or revisions on the primary results. Thus, in this analysis, only the 1st ever THA or TKA arthroplasties of the patients were included, and the follow-up was terminated if the THA or TKA patient had other THA or TKA arthroplasties or revisions. These THA and TKA cases also had a steady increase in purchases of all analgesics from 3 years until the final months before arthroplasty (Figure 3 and Table 2, see Supplementary data). The drug purchases then peaked around the time of arthroplasty. The greatest decrease in purchases of analgesics occurred during the 1st postoperative months, and then the proportion of patients purchasing drugs stabilized. At the end of follow-up, the proportion of patients purchasing analgesics was 3–17%, depending on the joint and drug. Paracetamol was the only drug with a lower proportion of purchases 3 years postoperatively compared with 3 years before the operation, among both THA and TKA patients.

Effect of age during arthroplasty on the results

The effect of age on purchases of pain medications was studied by dividing the patients into groups by the age at the time of arthroplasty (Table 5, see Supplementary data). Under 70-year-old patients purchased slightly more paracetamol (14–15% more at the time of arthroplasty) and a few less NSAIDs (3–6% less at the time of arthroplasty) throughout the follow-up compared with over 70-year-old THA and TKA patients. In opioids and neuropathic pain medication the younger patients purchased more drugs at the time of arthroplasty. Yet, during other follow-ups there were minimal or no differences between age groups.

Effect of time frame of the arthroplasty on results

Supplementary data 1 shows larger changes in the number of arthroplasties postoperatively than preoperatively. This is mainly due to short follow-up times of some arthroplasty events. Some arthroplasties were done close to the end of follow-up (2018) and they do not have long postoperative follow-ups. We studied whether the original results were affected by this phenomenon. We excluded arthroplasties from the last 6 years of follow-up (2012–2018). In this analysis the number of arthroplasties in the postoperative follow-up remained more stable, with 198,591 total (THA + TKA) events at the time of arthroplasty and 189,520 events at three years postoperatively. The patterns of medication purchases were similar to the original results and the proportion were within a few percentage points (maximum of 4 percentage points difference). NSAIDs were purchased a little less often than in the original results. During arthroplasty this was 11 and during the follow-up 2–6 percentage points less by both THA and TKA patients.

Discussion

Both THA and TKA seemed to reduce the purchases of paracetamol, NSAIDs, and opioids when the perioperative

purchases were studied. However, extending the follow-up time revealed that only the purchases of paracetamol were reduced after arthroplasty when compared with the results more than 1 year before arthroplasty. The greatest reduction in drug purchases occurred during the first 6 months after THA or TKA. Reduction in purchases continues until 12 months, after which the proportion of patients purchasing analgesics stabilizes. Approximately 4–18% of arthroplasty patients were purchasing different analgesics at 3 years postoperatively. Beswick et al., in their review of 14 articles, describe 2–23% of THA and 10–34% of TKA patients reporting unfavorable pain outcome during long-term follow-up (5).

Prescription analgesics purchases in the Finnish population

The proportions of patients purchasing drugs were close to that of drug purchases in the general population. In 2018, paracetamol was purchased by 15% (prescription purchases only), NSAIDs by 26%, and opioids by 8% of the population in Finland (SII's registers) (14).

Analgesics purchases compared with prior literature

Paracetamol was the most purchased drug in all groups, which is in line with care guidelines, with paracetamol being the primary drug recommended for osteoarthritis (1,3). Around the time of arthroplasty, the proportion of patients purchasing paracetamol was 46–56%. Prior studies have reported paracetamol use ranging from 24% to 88% at a point close to THA or TKA (9,10,12). At 12 months postoperatively, paracetamol was purchased by 17–21% of THA and TKA patients, which is close to the 24% reported by Jørgensen et al. (10). Paracetamol was the only drug with lower proportions of purchases postoperatively than 1–3 years before arthroplasty. At the end of follow-up, THA and TKA patients' paracetamol purchases were on the same level as in the general population. Prescription purchases of paracetamol were made by 15% of Finland's population (14).

NSAIDs were purchased second most among both THA and TKA patients. In a prior Finnish study by Rajamäki et al. (9) the results are different. In their study, NSAIDs were the most used single group of analgesics. They report higher numbers of use at 3 months postoperatively (> 50% THA and > 60% TKA). However, at 2 years postoperatively, the level of NSAID use was comparable to the proportion of NSAID purchases in our study. Bolland et al. (15) report 21% of THA and TKA patients being NSAID users 1 year preoperatively, which is a little more than the NSAID purchases in our study from the same time period. They also conclude that the decrease in NSAID use occurs during the 1st year postoperatively. Our results support this conclusion, with the decrease in purchases happening during the 1st postoperative year. In 2018 in Finland, NSAIDs were purchased by 26% of the general population, which is a little more than among arthroplasty patients at the end of follow-up (14).

In prior studies, the number of opioid users is close to the levels of opioid purchases in our study, with increasing use preoperatively and some residual users after the 1st postoperative year (9,10,12,16,17).

In our study, THA patients purchased more opioids than TKA patients before arthroplasty, if the peak of purchases perioperatively is excluded. After arthroplasty, TKA patients had a higher proportion of opioid purchases. Rajamäki et al. also report THA patients using more mild opioids preoperatively, whereas TKA patients used more opioids postoperatively. Also, the postoperative proportions of mild opioid users (5–8%) were similar to our study (9). Opioid purchases were made by 8% of the general population in Finland in 2018, which is a few percentage points higher than in our study at 3 years after arthroplasty.

Neither NSAID nor opioid purchases were reduced when postoperative results were compared with the results from 1 to 3 years before arthroplasty. However, the postoperative levels of NSAID and opioid purchases were on similar levels to those among the general population. This could indicate that the patients had other diseases causing drug purchases. However, they may also have developed an addiction or a habit of treating pain with opioids. The side effects of NSAIDs need special attention when treating older people with possible comorbidities (18). More importantly, opioids have side effects and dependency potential that need consideration in all patient groups and that clinicians need to consider thoroughly, whether prescribing opioids or referring the patient for surgery (19).

Medication for neuropathic pain had the fewest purchases and the purchases remained constant during follow-up, except around the time of arthroplasty. These drugs are also used for other conditions, such as depression, epilepsy, and fibromyalgia, which are likely to explain the "base" level of consumption. The proportions of purchases were close to the levels of neuropathic pain medication use reported by Jørgensen et al. (10) for THA and TKA patients, at 6.5% preoperatively and 8.6% postoperatively. Medication for neuropathic pain is only conditionally recommended by osteoarthritis current care guidelines, and thus the low level of purchases was a predictable outcome (1,2). However, prior literature estimates that at least 23% of THA and TKA patients have neuropathic pain (20). Osteoarthritis patients also develop pain sensitization in the affected joints and even peripheral sites (21).

Strengths and limitations

We analyzed the proportions of THA and TKA patients purchasing different drugs. The design and data were limited, so that we were able to see the prescription drug purchases only and were unable to consider doses or actual individual-level drug use. Also, over-the-counter pain medication purchases were not captured. In every class of drugs, there were patients purchasing drugs at the end of follow-up. During aging, several other medical conditions require pain medication. Some

patients with the longest follow-up were 6 years older at the end of study. The patients may have had degenerative diseases in other joints and in the spine, too, that required prescribed pain medication. However, the postoperative purchases were the same or close to those made by the general population. Also, as we compared patients based on age at the time of arthroplasty, only small differences between under- and over-70-year-old patients could be seen. Even more, the younger patients seemed to purchase more paracetamol, opioids, and neuropathic pain medication at the time of arthroplasty. In the sensitivity analysis, we excluded other arthroplasties and revisions, and the results were very similar to the primary results during the entire follow-up. We used aggregated-level data, which does not support individual-level analyses. In future studies, it will be interesting to study specific subgroups of arthroplasty patients (i.e., other medical conditions and fixation method of the implant) and their pain medication purchases. The strengths of this study are large nationwide registers and long follow-up times. The registers contain all THA and TKA cases and drug purchases made by the patients, enabling follow-up times up to 15 years before and after arthroplasty.

Conclusion

THA and TKA stop and reduce the preoperative increases in purchases of paracetamol, NSAIDs, and opioids. The purchases of pain medications by THA and TKA patients one year after operation are close to those in the general population

TV, SR, HJ, KH, SJ: writing the manuscript. TV, SR, SJ: data analysis and interpretation of the results. SR, HJ, KH, SJ: supervision of the study and proofreading.

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Supplementary data

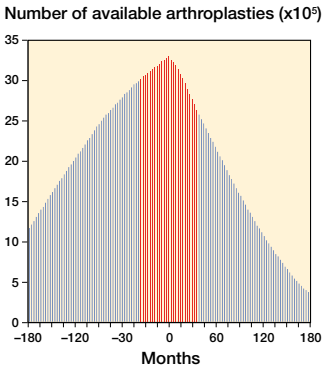

Figure 1. The number of available THAs and TKAs for entire follow-up time. The red columns (±36 months) represent the timeframe included in the study.

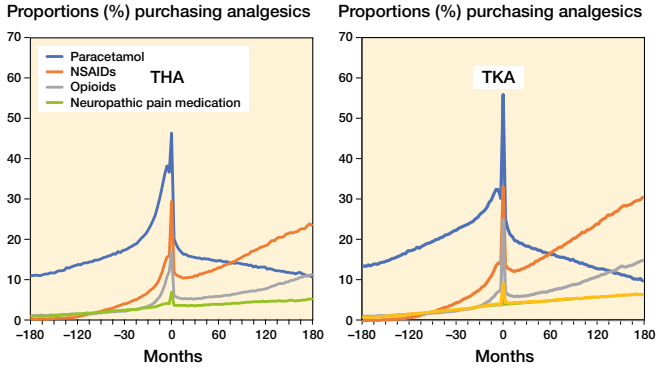

Figure 2. Proportions of patients purchasing analgesics for entire follow-up time available from the data.

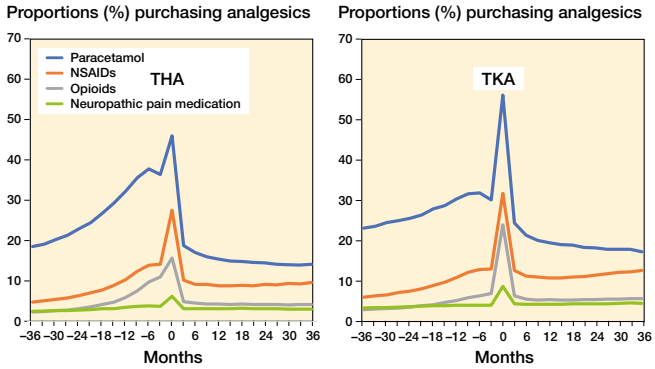

Figure 3. Proportions of patients purchasing analgesics for individuals with only 1 arthroplasty during follow-up.

Table 2. THA and TKA patients with only 1 arthroplasty during follow-up: proportions of patients (%) purchasing analgesics at 1-year intervals

	THA				TKA			
	Para-cetamol	NSAIDs	Opioids	Neuropathic pain medication	Para-cetamol	NSAIDs	Opioids	Neuropathic pain medication
3 years preoperative	19	5	2	3	23	6	3	3
2 years preoperative	23	6	3	3	25	7	3	4
1 year preoperative	32	10	6	3	30	11	5	4
Arthroplasty	46	28	16	6	56	32	24	9
1 year postoperative	15	9	4	3	19	11	5	4
2 years postoperative	15	9	4	3	18	11	5	4
3 years postoperative	14	10	4	3	17	13	6	4

Table 5. Proportions of patients (%) purchasing analgesics stratified by the age at the time of arthroplasty

	< 70-year old				≥ 70-year old			
	Para-cetamol	NSAIDs	Opioids	Neuropathic pain medication	Para-cetamol	NSAIDs	Opioids	Neuropathic pain medication
THA patients								
3 years preoperative	22	5	3	3	19	8	3	3
2 years preoperative	26	6	4	3	22	10	4	3
1 year preoperative	36	10	7	4	30	14	7	3
Arthroplasty	53	27	18	7	38	33	16	6
1 year postoperative	19	8	5	4	15	14	6	3
2 years postoperative	18	8	5	4	13	14	6	4
3 years postoperative	18	8	5	3	12	16	6	4
TKA patients								
3 years preoperative	27	6	4	4	23	8	3	3
2 years preoperative	30	7	5	4	25	10	4	3
1 year preoperative	35	11	7	5	28	14	6	4
Arthroplasty	63	32	28	11	49	35	22	8
1 year postoperative	24	10	7	5	18	14	6	4
2 years postoperative	23	11	6	5	16	15	6	4
3 years postoperative	22	11	7	5	14	17	7	4

VILLE TURPPO

The Finnish Arthroplasty Register offers objective data on implant performance. Patient-reported outcome measures (PROM) provide patient-specific subjective results of arthroplasties. This thesis examined the validity of the arthroplasty register data and self-reported arthroplasty. The PROMs of total hip and knee arthroplasty were studied using self-reported physical capability and well-being and purchases of pain medications. The results have impact on both clinical and research work.

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