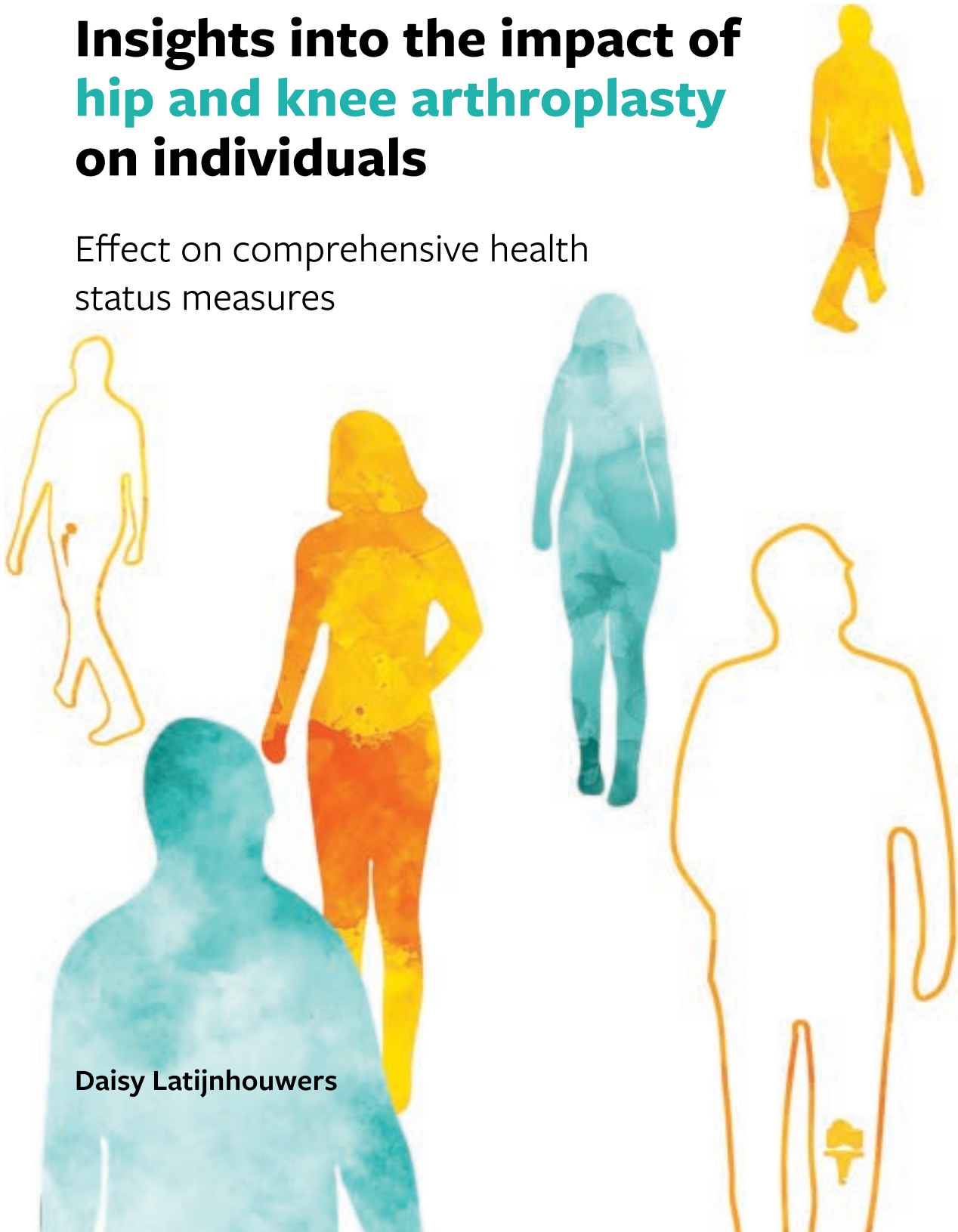


Insights into the impact of hip and knee arthroplasty on individuals

Effect on comprehensive health
status measures



Daisy Latijnhouwers

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Chapter 1

General introduction and thesis outline

Epidemiology of osteoarthritis

With an increasingly older and overweight population, osteoarthritis (OA) is becoming more prevalent. It is the most prevalent chronic disease in the Netherlands. Of all joints, the knee and joints are most often affected by OA [1, 2]. This thesis will therefore focus on hip and knee OA. The number of people suffering from hip and knee OA is increasing, with approximately 1.2 million people suffering from it in 2020. This number is projected to increase to 2.5 million by 2040 [3]. In the population aged sixty and older, approximately 10% of men and 18% of women have symptomatic OA [4, 5]. This prevalence increases to 33% among patients aged seventy-five and older [6-8]. OA is not only more often present in women than men, but it is often also more severe among women [1, 9-11].

The Pathophysiology

The pathogenesis of OA is multifactorial, involving metabolic, inflammatory, genetic, and mechanical factors [12-16]. OA is the result of a complex interaction between local and systemic inflammation, as well as mechanical stress, causing an imbalance between destruction and repair, leading to joint failure [17]. Furthermore, knee OA is associated with injury and mechanical load of the joint [18]. Also, OA progression in one joint is associated with progression of OA in other joints, significantly impacting patient's independence and social participation.

Overall, OA is more severe and / or more rapidly progressing in men than in women [19, 20]. However, there is no general agreement on what causes this difference in OA development or progression [21, 22]. Additionally, there is little evidence of sex differences in loading conditions of the lower extremity (i.e., biomechanics). Although anatomical differences are present between sexes in different races (1000 Africans, Caucasians and Asians compared with Computed Tomography data), it is unlikely that these morphological could explain the differences in development and progression of OA between sexes [23, 24].

Treatment

Treatment modalities for hip and knee OA are aimed at coping with OA symptoms or aimed at reducing OA symptoms, they can be divided into two categories: i)

non-surgical or conservative, and ii) surgical. Non-surgical treatment includes pharmacological treatment (such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and intra-articular corticosteroid injections) and non-pharmacological treatment (such as physical therapy, education, assistive devices (cane, crutches, brace), and weight loss) [6, 25]. When non-surgical management fails and no longer provides adequate relief, surgical management is the gold standard [16, 26]. The primary goal of a total hip and total knee arthroplasty (THA/TKA) is to alleviate pain and maintain or improve functionality.

Arthroplasty surgery

The number of performed elective THAs/TKAs has steadily grown in recent years [27]. In the Netherlands, the number of THA increased from 25.730 to 36.707 and of TKA from 21.727 to 26.708 between 2012 and 2022. The numbers in 2022 are likely still affected by the strain on elective healthcare due to the COVID-pandemic, as 37.000 THA and 34.000 TKA were performed in 2019, the year before the pandemic outbreak. The COVID-pandemic had a major direct impact on health care services worldwide and elective health care was particularly affected. Although the situation of patients awaiting arthroplasty surgery is not life threatening, the impact on the individual patient is significant, as limited mobility can lead to loss of independence, loss of participation in society and potential social isolation. In this thesis we evaluated the impact of the COVID-pandemic on changes in primary and revision arthroplasty rates in the Netherlands and Denmark for hip, knee, and shoulder arthroplasties ([Chapter 2](#)). We also investigated if certain patient groups were prioritized for surgery, which hospitals provided care and the impact on the waiting lists.

Indication for surgical treatment

Indications for arthroplasty surgery are currently provided by national guidelines. A systematic review by Gademan et al. [28] in 2016 presented all available guidelines and publications on THA and TKA indication criteria. The three most frequently mentioned criteria were pain, functional limitations, and radiological evidence for OA, with an inadequate response to conservative therapy as a prerequisite. Although Kellgren-Lawrence (KL) grade \geq III was reported as

threshold for radiographic changes, there were no specific cut-off values mentioned for pain or functional limitations. Additional criteria included limitations in quality of life and evident suffering due of pain, and achievable or realistic expectations.

Despite the availability of national guidelines the indications for THA and TKA are complex. They are determined by a multifactorial constellation of patient's symptoms in relation to a patient's overall health, social environment and perceived disability in presence of more objective radiological criteria and clinical examinations findings. Among orthopedic surgeons there seems to be consensus on which patients are suitable for THA and TKA [29]. Verra et al. [30] showed that old age and severe radiological OA in presence of severe pain were the most important variables in the decision to perform TKA, while the presence of mild pain and/or mild radiological OA were variables that made orthopedic surgeons more reluctant to perform TKA. Furthermore, when surgeons were asked, pain, functional limitations, failed conservative therapy and decrease in quality of life were criteria of overriding importance for THA and TKA [31, 32]. The latter shows that an individual approach of the complexity of perceived pain, disability, health, radiographic OA in each patient will be weighted differently in order to achieve an optimal outcome for these patients. Nevertheless, still 15-20% of arthroplasty patients are not satisfied with the results [33-35].

In the last decades, shared decision making has become increasingly implemented. Shared decision making is the engagement of the patient in the process of decisions regarding diagnosis and treatment. Previous research has shown many benefits of shared decision making, such as increase in patient knowledge and confidence, and an effect on treatment options that patients ultimately choose [36]. Literature also suggests that incorporating the patient's readiness and willingness to undergo TKA, and expectations regarding TKA into the decision-making process may improve the number of patients with a good match with their expectation on outcome [37]. Additionally, studies have shown that fulfillment of expectations after surgery is related to satisfaction, and that it is important to discuss the probability of fulfilment during the shared decision making process to increase postoperative satisfaction [38]. Although the latter is

mainly determined by managing expectations on outcome and on the psychological constitution of the patient [39].

Surgical approach

There are several different surgical approaches to performing a THA or TKA (Figure 1) [40]. The most often used approaches for THA are the direct lateral approach (DLA), direct anterior approach (DAA), and the posterior approach (PA) (Figure 1). In the Netherlands, the surgical approach for THA has shifted from direct lateral and anterolateral approaches to posterolateral (PLA) and direct anterior approaches (DAA) over the past decade [41]. The DAA claims to have less soft tissue damage and thus a more rapid recovery and rehabilitation, good functional outcomes and minimal risk for joint dislocation [42]. However, studies comparing complication and dislocation rates, clinical and patient-reported outcomes by approach have not been able to find superiority for any approach [43-47]. Thus, controversy exists although these data also stress the importance of surgical expertise when using a certain surgical approach, as changing to a new approach may lead to higher revision rates. Additionally, even experienced surgeons have learning curves when using a new surgical technique [48].

There are four approaches for a TKA but the median skin incision with a medial parapatellar approach is used in 97% of patients [49]. The subvastus, midvastus, or lateral parapatellar approach is used in selected cases due to severe deformity or skin problems (former scars).

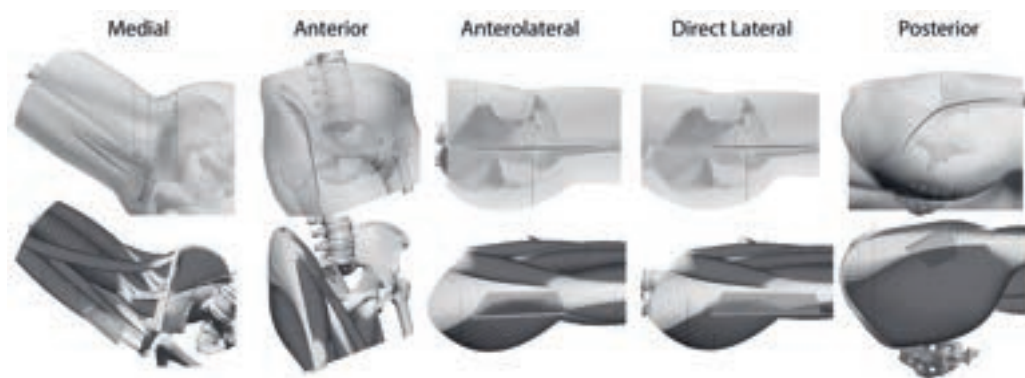


Figure 1 Surgical approaches for total hip arthroplasty

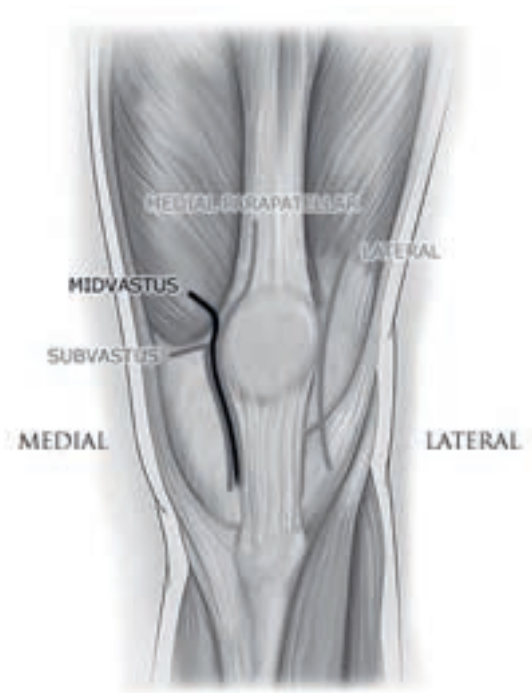


Figure 2 Surgical approaches for total knee arthroplasty [50]

Outcomes after hip and knee arthroplasties

Total joint arthroplasties (TJAs) are effective surgeries regarding surgeon-assessed outcomes, survival of the implant, and cost-effectiveness. Despite the success of TJAs in reducing pain and functional limitations, approximately 15% of THA and 20% of TKA patients are unsatisfied with the results of surgery [33, 34, 51, 52]. Although, postoperative outcomes show improvement in pain, function, physical activities, and quality of life in 80-90% of patients [53-57]. However, most research on outcome after TJA include patients with single joint arthroplasties. Nevertheless, a substantial proportion of patients suffer from multiple joint involvement. Patients with multiple joint involvement and usual multiple pain locations report more frequently worse pain, greater disability, reduced quality of life and increased healthcare utilization. Previous literature suggests that the 10-year risk of subsequent THA or TKA after a primary THA or TKA is approximately 35%, while the 20-year cumulative incidence ranges between 29% and 45% [58-60]. In this thesis, we investigated the impact of multiple joint involvement in patients. We estimated the incidence of multiple joint

involvement, assessed different trajectories of subsequent arthroplasties, and assessed the impact on patient outcomes ([Chapter 3](#)).

Patient reported outcome measures (PROMs)

The World Health Organization (WHO) developed the International Classification of Functioning, Disability and Health (ICF) to provide a standardized and comprehensive model for understanding health and health-related issues [61]. The biopsychosocial model of functioning and disability, as defined by the ICF, considers more than just a person's disease. The ICF has a main component, namely the Functioning and Disability domain, which focuses on the capabilities and limitations a patient experiences. Functioning relates to the human experience related to body functions, structures and activities and participation. It is conceptualized through its dynamic interaction between health conditions, personal and environmental factors. In contrast, Disability refers to the human experience of compromised physiological functions and structures, limitations in activity, and restrictions in participation, all within the context of interactions with health conditions, personal and environmental factors. The contextual factors considers the health condition, as well as the environmental and personal factors that might impact a patient's health. It is therefore recommended by the WHO, the Outcome Measures in Rheumatology Clinical Trials group (OMERACT) and the International Consortium for Health Outcomes Measurement (ICHOM) to use the different domains that are incorporated in the ICF model. These domains and factors form a dynamic interaction and relate to (Figure 3):

- i) Health conditions: Health conditions can affect the domains of body functions and structures, as well as activities and participation.
- ii) (impairments of) body function and structures of patients: Body function and structures focus on the physiological and anatomical aspects of the body. They include the functions and structures of the body systems, such as the nervous, musculoskeletal or cardiovascular system, and sensory organs. Impairment or damage in these functions and structures could be due to health conditions.
- iii) (experienced limitations in) activities of patients and (restricted) participation or involvement of patients in all areas of life: Activities and participation address the activities individuals perform in their daily lives

and the participation in societal roles and activities. This domain takes into consideration both the person's capacity and the actual performance. It is divided into several domains, such as mobility, self-care, community life and communication.

- iv) Environmental factors influencing patients: Environmental factors encompasses the physical, social, and attitudinal environment in which individuals live and interact. Factors that support and/or hinder a person's functioning and participation are included.
- v) Personal factors affecting patients: Personal factors (individual characteristics that can affect the ability of a person with regard to functioning, but that are not part of the health condition itself), such as age, gender and education

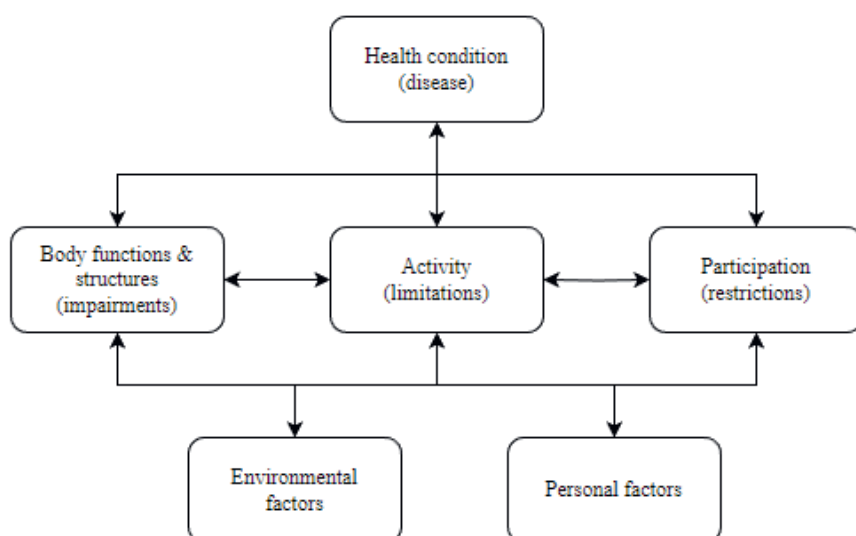


Figure 3 The International Classification of Function, Disability and Health (ICF) model

Overall, the ICF model is a comprehensive and holistic framework to understanding health and disability, taking into account the interaction between an individual and his or her environment, and it is widely recognized as a valuable tool in healthcare and disability studies. Specifically for people suffering from OA, measuring outcomes after arthroplasty in a broader sense is important. Patients with OA often suffer from debilitating pain and limited functionality, which can make it difficult to participate in activities and society. Therefore, two ICF Core

Set for OA were developed: Comprehensive ICF Core Set and a Brief ICF Core Set for osteoarthritis [62]. This globally agreed framework and classification allows to define the typical spectrum of problems in functioning of patients with OA. The Royal Dutch Society of Physical Therapy used his core set for hip and knee OA as a basis to optimize the clinical consultation [63]. Furthermore, the ICHOM developed a standardized set of PROMs for patients with OA [64], which covers the domains and factors of the ICF model, as well as an instruction on which specific instruments to use and at which moments during the course of a condition [61, 62]. This allows for the measurement of symptoms and health-related concepts in patients suffering from hip and/or knee OA. Furthermore, collecting such PROMs play a vital role in arthroplasty care by providing a patient-centered perspective, supporting clinical decision-making, promoting research, and improving the overall quality of care for patients undergoing joint replacement procedures [65, 66].

This thesis also covers the use of the ICF model in estimating i. the impact of the COVID-pandemic (**Chapter 2**) on arthroplasty care and the effect of multiple joint involvement in this population (**Chapter 3**). Furthermore, we assessed expectations of both female and male patients both before and after THA or TKA (**Chapter 4**). ii. Activities and participation to compare two surgical approaches for hip arthroplasty and the impact on activities and participation (**Chapter 5**), as well as adherence to the Dutch physical activity guideline both before and after THA and TKA (**Chapter 6**). iii. Body functions and structures to measure the impact of acute postoperative pain on the development of chronic pain after THA and TKA (**Chapter 7**).

All-encompassing ICF

Chapters 2 to 4 include more than one domain or factor of the ICF framework. Using several ICF components we determined the magnitude and impact of the COVID-pandemic, as well as MJA in OA patients and the differences between men and women on expectations. Using several ICF components allows for the inclusion of a wide variety of factors, from functional problems to environmental and personal factors that may impact the patients' health. This grants the possibility of obtaining a comprehensive assessment of the patients overall well-

being, as well as a multidimensional perspective, as OA is a complex condition that affects individuals in multiple ways.

Activities and participation

Previous studies comparing outcomes regarding surgical approaches for THA and TKA focused on pain and functional limitations in terms of hip or knee function. However, recent studies showed that outcomes in relation to aspects such as return to work and activities, and participation in social roles, leisure pursuits and community interactions are exceptionally relevant to patients receiving a THA or TKA. Especially due to the increasing age at which people retire and age at which patients receive a THA or TKA decreases, the population of working patients receiving arthroplasty surgery increases. Current literature comparing surgical approaches for THA in terms of activities and participation of the patient in society seems to be insufficient. We therefore performed a study including the comparison of two surgical approaches for THA, and its impact on activities and participation of these patients ([Chapter 5](#)).

Physical Activity

The evidence regarding the health benefits of physical activity is indisputable [67]. Several guidelines have been developed, recommending at least 150 minutes of moderate to vigorous PA for adults per week [68-70]. Nevertheless, patients suffering from OA of the lower extremities are facing difficulties to achieve and maintain a sufficient level of PA, because of severe joint pain, functional impairment or the fear of aggravating symptoms and worsening joint damage. Surgical intervention of OA might counteract some of these difficulties, as it aims to improve physical function and reduce pain. Nonetheless, large variability exists between patients during the first postoperative year [71, 72]. For this reason, we determined physical activity levels of patients both before and after THA and TKA ([Chapter 6](#)).

Pain

Pain can be classified into nociplastic (arises from a sensitized nervous system), neuropathic (arises from nerve injury/damage) and nociceptive (arises from tissue injury/damage) [73]. (Chronic) Pain is an often occurring, disabling

symptom of OA, and the main reason patients seek medical attention [74]. Furthermore, nearly 10% of THA and 20% of TKA patients report chronic pain after surgery [75]. The presence of chronic pain after THA or TKA has several unfavorable effects, thereby negatively impacting postoperative outcomes. However, it is unclear what causes chronic postoperative pain. In surgical patients' acute postoperative pain and pain sensitization (peripheral and central sensitization) have been postulated as risk factors for chronic pain [74, 76-79]. Chronic pain is associated with changes in the peripheral and central nervous system in response to acute injury, such as surgery or trauma. However, it is unclear what the effect of acute postoperative pain is in THA and TKA patients. In **Chapter 7** of this thesis, we assessed whether acute postoperative pain was associated with chronic postoperative pain.

Data sources

Within this thesis, data from the Dutch Arthroplasty Register (LROI) and the Leiden Orthopaedics Outcomes of Osteo-Arthritis study (LOAS) were used. Part I of this thesis includes research on the epidemiology and delivery of THA and TKA using data from the Dutch Arthroplasty Register (Landelijke Registratie Orthopedische Interventies (LROI)). The LROI is an initiative of the Netherlands Orthopaedic Association (NOV) and started in 2007 with the registration of implants of hip and knee. From 2014 onwards, the LROI also registers shoulder, ankle and elbow arthroplasties. In 2016, finger and wrist arthroplasties were added to the registry. The main goal of the LROI is to contribute to the traceability of orthopaedic implants in the Netherlands, as well as providing information on outcomes of orthopaedic implants to surgeons and manufacturers as part of a quality improvement cycle, as well as a public available annual report. The LROI collects information on the prosthesis, surgical and patient characteristics and PROMs. Based on the most recent annual report of the LROI, the registry has a completeness of 99% for all primary THA and TKA that are performed in the Netherlands [49].

In part II the aim was to evaluate outcomes after THA and TKA using data from the Longitudinal Leiden Orthopaedics Outcomes of Osteo-Arthritis study (LOAS), which is an ongoing multi-center, longitudinal prospective cohort study [52]. The department of Orthopaedics at Leiden University Medical Center (LUMC) initiated

the LOAS in 2012, as knowledge on the impact of THA and TKA on societal participation (physical activity, sports, and work) and health care usage, including rehabilitation was scarce and not available in hip and knee registries. The main aims of the LOAS are: (1) to describe the mid and long-term outcomes of THA and TKA in terms of health-status as a whole, including the levels of body functions and structures, daily activities, participation in society and health care usage; and (2) to determine which factors predict the outcomes of THA and TKA. Patients in need of arthroplasty surgery are included at 8 participating hospitals (Leiden University Medical Center, Leiden; Alrijne Hospital (former Diaconessenhuis and Rijnland Hospital), Leiden and Leiderdorp; Groene Hart Hospital, Gouda; Reinier de Graaf Hospital, Delft LangeLand Hospital, Zoetermeer; Waterlandziekenhuis, Purmerend and OCON Hospital, Hengelo). Patients are deemed eligible if aged 18 years or older, being listed for THA/TKA, and sufficient mental and physical capabilities to complete the questionnaires. Data is gathered using both paper and digital questionnaires prior to surgery, 3 (if THA), 6, 12, 24 months postoperative and every 2 years thereafter, until 10 years postoperative. The LOAS is still ongoing and actively recruiting patients.

Outline of this thesis

Aim of this thesis

The general aim of this thesis is to gain knowledge on the impact of THA and TKA on the patient's overall health status. Secondly, to provide insight into determinants that affect the outcome of the overall patient's health status. This research will inform orthopedic surgeons, and other stakeholders on the impact of "joint surgery" for the 'patient' as such. In the future, this information, in combination with new findings will contribute to better expectations on postoperative outcome. The latter enhances the discussion between surgeon and patient on expected values and expectations of elective joint replacement surgery, which is different between patients. This may also result in realising some expectations can not be met. Bridging the gap between orthopedic surgeons' and patients' expectations will improve patient experiences and outcomes.

This thesis is divided into two parts. **Part I** focusses on the need for arthroplasty in patients with hip and knee OA. **Chapter 2** presents the impact of the COVID-pandemic on arthroplasty surgery volumes and quality adjusted life years due to increased waiting times. **Chapter 3** assesses the impact of multiple joint involvement regarding the incidence of multiple joint arthroplasties, as well as the impact on patient outcomes.

Part II centers around the impact of osteoarthritis and arthroplasty surgery on the patients' well-being, including factors and determinants affecting the societal perspective. **Chapter 4** focuses on the difference in preoperative expectations and postoperative fulfillment of expectations between men and women. In **Chapter 5** we compare two different surgical approaches for THA (posterolateral and direct anterior approach) and their effect on the construct 'activity and participation' during the first postoperative year. **Chapter 6** investigates adherence to the Dutch physical activity guideline and different trajectories in hip and knee arthroplasty patients prior to and after surgery including potential predictors for non-adherence after surgery. **Chapter 7** examines whether severe acute pain, shortly after surgery, affects chronic pain during the first postoperative year after THA and TKA. **Chapter 8** contains the general discussion, including the main findings of this thesis, clinical implications, perspectives, and recommendations for future research on factors that affect arthroplasty patients.

References

1. (RIVM) RvVeM. Trendsscenario; Ziekten en aandoeningen 2020 [Available from: <https://www.volksgezondheidtoekomstverkenning.nl/c-vtv/trendsscenario-update-2020/ziekten-aandoeningen>].
2. Organization WH. Chronic rheumatic conditions [cited 2023 05-05-2023]. Available from: <https://www.who.int/chp/topics/rheumatic/en/>.
3. Safiri S, Kolahi AA, Smith E, Hill C, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis*. 2020;79(6):819-28.
4. Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *Jama*. 2021;325(6):568-78.
5. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. *J Rheumatol*. 2007;34(1):172-80.
6. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum*. 1987;30(8):914-8.
7. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393(10182):1745-59.
8. Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. *Annals of the Rheumatic Diseases*. 2014;73(9):1659-64.
9. Cho HJ, Chang CB, Yoo JH, Kim SJ, Kim TK. Gender differences in the correlation between symptom and radiographic severity in patients with knee osteoarthritis. *Clin Orthop Relat Res*. 2010;468(7):1749-58.
10. Hannan MT. Epidemiologic perspectives on women and arthritis: an overview. *Arthritis Care Res*. 1996;9(6):424-34.
11. Andrianakos AA, Kontelis LK, Karamitsos DG, Aslanidis SI, Georgountzos AI, Kaziolas GO, et al. Prevalence of symptomatic knee, hand, and hip osteoarthritis in Greece. The ESORDIG study. *J Rheumatol*. 2006;33(12):2507-13.
12. Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. *Radiol Clin North Am*. 2004;42(1):1-9, v.
13. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol*. 1988;128(1):179-89.
14. Felson DT. Risk factors for osteoarthritis: understanding joint vulnerability. *Clin Orthop Relat Res*. 2004(427 Suppl):S16-21.
15. Felson DT. Developments in the clinical understanding of osteoarthritis. *Arthritis Res Ther*. 2009;11(1):203.
16. Abramoff B, Caldera FE. Osteoarthritis: Pathology, Diagnosis, and Treatment Options. *Med Clin North Am*. 2020;104(2):293-311.
17. Hall M, van der Esch M, Hinman RS, Peat G, de Zwart A, Quicke JG, et al. How does hip osteoarthritis differ from knee osteoarthritis? *Osteoarthritis Cartilage*. 2022;30(1):32-41.

18. Long H, Liu Q, Yin H, Wang K, Diao N, Zhang Y, et al. Prevalence Trends of Site-Specific Osteoarthritis From 1990 to 2019: Findings From the Global Burden of Disease Study 2019. *Arthritis & Rheumatology*. 2022;74(7):1172-83.
19. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage*. 2005;13(9):769-81.
20. Perez BA, Slover J, Edusei E, Horan A, Anoushiravani A, Kamath AF, et al. Impact of gender and race on expectations and outcomes in total knee arthroplasty. *World J Orthop*. 2020;11(5):265-77.
21. Hussain SM, Cicuttini FM, Alyousef B, Wang Y. Female hormonal factors and osteoarthritis of the knee, hip and hand: a narrative review. *Climacteric*. 2018;21(2):132-9.
22. Stevens-Lapsley JE, Kohrt WM. Osteoarthritis in women: effects of estrogen, obesity and physical activity. *Womens Health (Lond)*. 2010;6(4):601-15.
23. Mahfouz M, Abdel Fatah EE, Bowers LS, Scuderi G. Three-dimensional Morphology of the Knee Reveals Ethnic Differences. *Clinical Orthopaedics and Related Research*®. 2012;470(1):172-85.
24. Budhiparama NC, Lumban-Gaol I, Ifran NN, de Groot PCJ, Utomo DN, Nelissen R. Mismatched knee implants in Indonesian and Dutch patients: a need for increasing the size. *Knee Surg Sports Traumatol Arthrosc*. 2021;29(2):358-69.
25. Richard MJ, Driban JB, McAlindon TE. Pharmaceutical treatment of osteoarthritis. *Osteoarthritis Cartilage*. 2023;31(4):458-66.
26. Mandl LA, Martin GM, Hunter D. Overview of surgical therapy of knee and hip osteoarthritis. UpToDate, Waltham, MA Accessed. 2018;4:16.
27. Rupp M, Lau E, Kurtz SM, Alt V. Projections of Primary TKA and THA in Germany From 2016 Through 2040. *Clin Orthop Relat Res*. 2020;478(7):1622-33.
28. Gademan MG, Hofstede SN, Vliet Vlieland TP, Nelissen RG, Marang-van de Mheen PJ. Indication criteria for total hip or knee arthroplasty in osteoarthritis: a state-of-the-science overview. *BMC Musculoskelet Disord*. 2016;17(1):463.
29. Richtlijnendatabase. Indicatiestelling voor plaatsen TKP: Federatie Medische Specialisten; 2014 [updated 03-10-2014. Available from: https://richtlijnendatabase.nl/richtlijn/totale_knieprothese/optimale_indicatiestelling_voor_plaatsen_tkp/indicatiestelling_voor_plaatsen_tkp.html#tab-content-substantiation.
30. Verra WC, Witteveen KQ, Maier AB, Gademan MG, van der Linden HM, Nelissen RG. The reason why orthopaedic surgeons perform total knee replacement: results of a randomised study using case vignettes. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(8):2697-703.
31. Frankel L, Sanmartin C, Hawker G, De Coster C, Dunbar M, Bohm E, et al. Perspectives of orthopaedic surgeons on patients' appropriateness for total joint arthroplasty: a qualitative study. *J Eval Clin Pract*. 2016;22(2):164-70.
32. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. Criteria used when deciding on eligibility for total knee arthroplasty--Between thinking and doing. *Knee*. 2016;23(2):300-5.
33. Keurentjes JC, Fiocco M, So-Osman C, Onstenk R, Koopman-Van Gemert AW, Pöll RG, et al. Patients with severe radiographic osteoarthritis have a better prognosis in physical functioning after hip and knee replacement: a cohort-study. *PLoS One*. 2013;8(4):e59500.
34. Tilbury C, Haanstra TM, Leichtenberg CS, Verdegaal SH, Ostelo RW, de Vet HC, et al. Unfulfilled Expectations After Total Hip and Knee Arthroplasty Surgery: There Is a Need

- for Better Preoperative Patient Information and Education. *J Arthroplasty*. 2016;31(10):2139-45.
35. Bourne RB, Chesworth BM, Davis AM, Mahomed NN, Charron KD. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? *Clin Orthop Relat Res*. 2010;468(1):57-63.
36. Stacey D, Légaré F, Col NF, Bennett CL, Barry MJ, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev*. 2014(1):Cd001431.
37. Hawker GA, Bohm E, Dunbar MJ, Faris P, Jones CA, Noseworthy T, et al. Patient appropriateness for total knee arthroplasty and predicted probability of a good outcome. *RMD Open*. 2023;9(2).
38. Hafkamp FJ, Gosens T, de Vries J, den Oudsten BL. Do dissatisfied patients have unrealistic expectations? A systematic review and best-evidence synthesis in knee and hip arthroplasty patients. *EFORT Open Rev*. 2020;5(4):226-40.
39. Haanstra TM, Tilbury C, Kamper SJ, Tordoir RL, Vliet Vlieland TP, Nelissen RG, et al. Can Optimism, Pessimism, Hope, Treatment Credibility and Treatment Expectancy Be Distinguished in Patients Undergoing Total Hip and Total Knee Arthroplasty? *PLoS One*. 2015;10(7):e0133730.
40. Moretti VM, Post ZD. Surgical Approaches for Total Hip Arthroplasty. *Indian J Orthop*. 2017;51(4):368-76.
41. Register DA. Annual Report of the Dutch Arthroplasty Register. 2016.
42. Moerenhout KG, Cherix S, Rüdiger HA. [Total hip arthroplasty through anterior "minimal invasive" approach]. *Rev Med Suisse*. 2012;8(367):2429-32.
43. van Steenbergen LN, de Reus IM, Hannink G, Vehmeijer SB, Schreurs BW, Zijlstra WP. Femoral head size and surgical approach affect dislocation and overall revision rates in total hip arthroplasty: up to 9-year follow-up data of 269,280 procedures in the Dutch Arthroplasty Register (LROI). *Hip Int*. 2023;11207000231160223.
44. Zijlstra WP, De Hartog B, Van Steenbergen LN, Scheurs BW, Nelissen R. Effect of femoral head size and surgical approach on risk of revision for dislocation after total hip arthroplasty. *Acta Orthop*. 2017;88(4):395-401.
45. Pincus D, Jenkinson R, Paterson M, Leroux T, Ravi B. Association Between Surgical Approach and Major Surgical Complications in Patients Undergoing Total Hip Arthroplasty. *Jama*. 2020;323(11):1070-6.
46. Peters RM, van Beers L, van Steenbergen LN, Wolkenfelt J, Ettema HB, Ten Have B, et al. Similar Superior Patient-Reported Outcome Measures for Anterior and Posterolateral Approaches After Total Hip Arthroplasty: Postoperative Patient-Reported Outcome Measure Improvement After 3 months in 12,774 Primary Total Hip Arthroplasties Using the Anterior, Anterolateral, Straight Lateral, or Posterolateral Approach. *The Journal of arthroplasty*. 2018;33(6):1786-93.
47. Jia F, Guo B, Xu F, Hou Y, Tang X, Huang L. A comparison of clinical, radiographic and surgical outcomes of total hip arthroplasty between direct anterior and posterior approaches: a systematic review and meta-analysis. *Hip Int*. 2019;29(6):584-96.
48. Peters RM, Ten Have B, Rykov K, Van Steenbergen L, Putter H, Rutgers M, et al. The learning curve of the direct anterior approach is 100 cases: an analysis based on 15,875 total hip arthroplasties in the Dutch Arthroplasty Register. *Acta Orthop*. 2022;93:775-82.
49. LROI. LROI Report 2022 2022 [Available from: <https://www.lroi-report.nl/>].
50. Cristea S, Predescu V, Dragosloveanu S, Cuculici S, N. M. Surgical Approaches for Total Knee Arthroplasty. 2016.

51. Martin SD, McManus JL, Scott RD, Thornhill TS. Press-fit condylar total knee arthroplasty. 5- to 9-year follow-up evaluation. *J Arthroplasty*. 1997;12(6):603-14.
52. Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br*. 1998;80(1):63-9.
53. Shields RK, Enloe LJ, Leo KC. Health related quality of life in patients with total hip or knee replacement. *Arch Phys Med Rehabil*. 1999;80(5):572-9.
54. Jones CA, Voaklander DC, Johnston DW, Suarez-Almazor ME. Health related quality of life outcomes after total hip and knee arthroplasties in a community based population. *J Rheumatol*. 2000;27(7):1745-52.
55. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. A Randomized, Controlled Trial of Total Knee Replacement. *N Engl J Med*. 2015;373(17):1597-606.
56. Hofstede SN, Gademán MG, Vliet Vlieland TP, Nelissen RG, Marang-van de Mheen PJ. Preoperative predictors for outcomes after total hip replacement in patients with osteoarthritis: a systematic review. *BMC Musculoskelet Disord*. 2016;17:212.
57. Tilbury C, Leichtenberg CS, Kaptein BL, Koster LA, Verdegaal SHM, Onstenk R, et al. Feasibility of Collecting Multiple Patient-Reported Outcome Measures Alongside the Dutch Arthroplasty Register. *J Patient Exp*. 2020;7(4):484-92.
58. Espinosa P, Weiss RJ, Robertsson O, Kärrholm J. Sequence of 305,996 total hip and knee arthroplasties in patients undergoing operations on more than 1 joint. *Acta orthopaedica*. 2019;90(5):450-4.
59. Lamplot JD, Bansal A, Nguyen JT, Brophy RH. Risk of Subsequent Joint Arthroplasty in Contralateral or Different Joint After Index Shoulder, Hip, or Knee Arthroplasty: Association with Index Joint, Demographics, and Patient-Specific Factors. *J Bone Joint Surg Am*. 2018;100(20):1750-6.
60. Sanders TL, Maradit Kremers H, Schleck CD, Larson DR, Berry DJ. Subsequent Total Joint Arthroplasty After Primary Total Knee or Hip Arthroplasty: A 40-Year Population-Based Study. *J Bone Joint Surg Am*. 2017;99(5):396-401.
61. Organization WH. How to use the ICF: A practical manual for using the International Classification of Functioning, Disability and Health (ICF). Exposure draft for comment Geneva: WHO. 2013;13.
62. Dreinhöfer K, Stucki G, Ewert T, Huber E, Ebenbichler G, Gutenbrunner C, et al. ICF Core Sets for osteoarthritis. *J Rehabil Med*. 2004(44 Suppl):75-80.
63. van Doormaal MCM, Meerhoff GA, Vliet Vlieland TPM, Peter WF. A clinical practice guideline for physical therapy in patients with hip or knee osteoarthritis. *Musculoskeletal Care*. 2020;18(4):575-95.
64. Rolfson O, Wissig S, van Maasakkers L, Stowell C, Ackerman I, Ayers D, et al. Defining an International Standard Set of Outcome Measures for Patients With Hip or Knee Osteoarthritis: Consensus of the International Consortium for Health Outcomes Measurement Hip and Knee Osteoarthritis Working Group. *Arthritis Care Res (Hoboken)*. 2016;68(11):1631-9.
65. Makhni EC. Meaningful Clinical Applications of Patient-Reported Outcome Measures in Orthopaedics. *J Bone Joint Surg Am*. 2021;103(1):84-91.
66. Makhni EC, Hennekens ME, Baumhauer JF, Muh SJ, Spindler K. AOA Critical Issues: Patient-Reported Outcome Measures: Why Every Orthopaedic Practice Should Be Collecting Them. *J Bone Joint Surg Am*. 2023;105(8):641-8.
67. Warburton DER, Bredin SSD. Health benefits of physical activity: a systematic review of current systematic reviews. *Curr Opin Cardiol*. 2017;32(5):541-56.

68. Ernstgård A, PirouziFard M, Thorstensson CA. Health enhancing physical activity in patients with hip or knee osteoarthritis - an observational intervention study. *BMC Musculoskelet Disord*. 2017;18(1):42.
69. Herbolzheimer F, Schaap LA, Edwards MH, Maggi S, Otero Á, Timmermans EJ, et al. Physical Activity Patterns Among Older Adults With and Without Knee Osteoarthritis in Six European Countries. *Arthritis Care Res (Hoboken)*. 2016;68(2):228-36.
70. Chang AH, Song J, Lee J, Chang RW, Semanik PA, Dunlop DD. Proportion and associated factors of meeting the 2018 Physical Activity Guidelines for Americans in adults with or at risk for knee osteoarthritis. *Osteoarthritis Cartilage*. 2020;28(6):774-81.
71. Vissers MM, Bussmann JB, de Groot IB, Verhaar JA, Reijman M. Physical functioning four years after total hip and knee arthroplasty. *Gait Posture*. 2013;38(2):310-5.
72. van Diemen MPJ, Ziagkos D, Kruizinga MD, Bénard MR, Lambrechtse P, Jansen JAJ, et al. Mitochondrial function, grip strength, and activity are related to recovery of mobility after a total knee arthroplasty. *Clin Transl Sci*. 2023;16(2):224-35.
73. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *Lancet*. 2021;397(10289):2082-97.
74. Fu K, Robbins SR, McDougall JJ. Osteoarthritis: the genesis of pain. *Rheumatology (Oxford)*. 2018;57(suppl_4):iv43-iv50.
75. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *BMJ Open*. 2012;2(1):e000435.
76. Fingleton C, Smart K, Moloney N, Fullen BM, Doody C. Pain sensitization in people with knee osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(7):1043-56.
77. Zolio L, Lim KY, McKenzie JE, Yan MK, Estee M, Hussain SM, et al. Systematic review and meta-analysis of the prevalence of neuropathic-like pain and/or pain sensitization in people with knee and hip osteoarthritis. *Osteoarthritis Cartilage*. 2021;29(8):1096-116.
78. Perrot S. Osteoarthritis pain. *Best Pract Res Clin Rheumatol*. 2015;29(1):90-7.
79. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. *J Pain*. 2009;10(9):895-926.



Part I

Epidemiology of arthroplasty surgery: nationwide studies



Chapter 2

No time to waste: the impact of the COVID-pandemic on hip, knee and shoulder arthroplasty surgeries in the Netherlands and Denmark

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ABSTRACT

Aims: This study aimed to investigate the estimated change in primary and revision arthroplasty rate in the Netherlands and Denmark for hips, knees, and shoulders during the COVID-19 pandemic in 2020 (COVID-period). Additional points of focus included the comparison of patient characteristics and hospital type (2019 vs COVID-period), and the estimated loss of quality-adjusted life years (QALYs) and impact on waiting lists.

Patients and methods: All hip, knee, and shoulder arthroplasties (2014 to 2020) from the Dutch Arthroplasty Register, and hip and knee arthroplasties from the Danish Hip and Knee Arthroplasty Registries, were included. The expected number of arthroplasties per month in 2020 was estimated using Poisson regression, taking into account changes in age and sex distribution of the general Dutch/Danish population over time, calculating observed/expected (O/E) ratios. Country-specific proportions of patient characteristics and hospital type were calculated per indication category (osteoarthritis/other elective/acute). Waiting list outcomes including QALYs were estimated by modelling virtual waiting lists including 0%, 5% and 10% extra capacity.

Results: During COVID-period, fewer arthroplasties were performed than expected (Netherlands: 20%; Denmark: 5%), with the lowest O/E in April. In the Netherlands, more acute indications were prioritized, resulting in more American Society of Anesthesiologists grade III to IV patients receiving surgery. In both countries, no other patient prioritization was present. Relatively more arthroplasties were performed in private hospitals. There were no clinically relevant differences in revision arthroplasties between pre-COVID and COVID-period. Estimated total health loss depending on extra capacity ranged from: 19,800 to 29,400 QALYs (Netherlands): 1,700 to 2,400 QALYs (Denmark). With no extra capacity it will take > 30 years to deplete the waiting lists.

Conclusion: The COVID-19 pandemic had an enormous negative effect on arthroplasty rates, but more in the Netherlands than Denmark. In the Netherlands, hip and shoulder patients with acute indications were prioritized. Private hospitals filled in part of the capacity gap. QALY loss due to postponed arthroplasty surgeries is considerable.

INTRODUCTION

Although the number of performed hip, knee and shoulder arthroplasty surgeries has been steadily growing in the past couple of years [1], the coronavirus disease 2019 pandemic (COVID-pandemic) and the admittance of COVID-patients in hospitals resulted in postponement of many arthroplasty surgeries worldwide [2, 3]. With an already growing need for arthroplasty surgery in the Western world, the COVID-pandemic may have an extra impact on extending waiting-lists for these patients.

Several countries drafted guidelines to prioritize patients with urgent indications. Especially in arthroplasty care, patients with high-priority indications, such as infection, progressive bone loss, loosening, fractures, dislocation and tumors were prioritized [4]. However, it is currently unclear whether prioritizing based on certain patient characteristics or patient groups, such as patients with increased morbidity or the frail elderly might have been impacted more negatively, as some guidelines postulated to operate healthy patients first [5, 6]. Although the situation of arthroplasty patients is not life threatening, awaiting arthroplasty surgery imposes a large impact on healthcare systems, patients and their families, and thus societies [7]. The overall burden in terms of disability is substantial. Several studies showed that deferring joint arthroplasties is detrimental with respect to pain, joint and physical function after the surgery, mental health, and results in substantial loss of quality-adjusted life years (QALYs) [8-14]. Clement et al. [15] showed that over one-third of hip and one-quarter of knee patients awaiting total hip or knee arthroplasty surgery during the COVID-pandemic are (according to the EuroQoL-5D score) in a disease-state “worse than death”, which is nearly twice the number compared to pre-COVID. Additionally, certain patient groups, such as the frail elderly might have been impacted more negatively as some guidelines postulated to operate healthy patients first [5, 6].

In both the Netherlands and Denmark, performance of arthroplasty surgeries has been affected due to the COVID-pandemic. However, decreases in surgical arthroplasty rates, while taking into account the expected growth in the number of arthroplasties, are unavailable and the impact from a societal perspective is unknown. Additionally, literature on whether prioritization actually occurred and information on the extent of loss of QALYs due to postponement of

surgeries is scarce.

As a results, this study has several aims: Firstly, we estimated the change in primary and revision arthroplasty surgery rate in the Netherlands and Denmark during the COVID-pandemic in 2020 (COVID-period). Secondly, we investigated whether prioritization occurred by comparing the distributions of patient-characteristics and hospital type differ between COVID-period and the pre-COVID year 2019. Lastly, we investigated the impact of the COVID-pandemic on disease burden by estimating the loss of QALYs within the primary arthroplasty population in COVID-period due to postponement of arthroplasty surgeries, and the impact on the waiting-lists and time needed to combat the backlog.

METHODS

This study was declared exempt by the Medical Research Ethics Committee Leiden Den Haag Delft, as they were of opinion that the Medical Research Involving Human Subjects act (Dutch abbreviation: WMO) did not apply to this study (G21.124). According to Danish law, an ethics committee approval is not required for registry-based studies. This study was reported to the Danish Data Protection Agency through registration at Aarhus University (record number: AU-2016-051-000001, sequential number 880). Additionally, both the Dutch Arthroplasty Register and the Danish Hip and Knee Arthroplasty Registries approved the use of their data.

Data sources

This population-based cohort study used different data sources. Primary and revision arthroplasties and their characteristics were collected from the Dutch Arthroplasty Register (Landelijke Registratie Orthopedische Interventies (LROI)); hip/knee/shoulder arthroplasties) and the Danish Hip and Knee Arthroplasty registries (DHR/DKR; no information regarding shoulder arthroplasties available). These registries have a high completeness (LROI primary arthroplasties: 99%, revision arthroplasties: 98%; DHR completeness 2020; primary arthroplasties: 95%, revision arthroplasties: 87%; DKR completeness 2020; primary and revision arthroplasties: 95%) [16,17]. Data on the entire general Dutch and Danish populations were collected from Netherlands Statistics and Statistics Denmark. Data regarding age and sex composition changes in the general population

between 2014 to 2020, as well as mortality numbers during this time, were extracted from these registries.

Study population

All hip, knee, and shoulder arthroplasties between 2014 and 2020 were extracted from the LROI/DHR/DKR, including both unilateral and bilateral procedures. Arthroplasties from January 2014 until March 2020 were categorized as ‘pre-COVID’, while arthroplasties between March 2020 and December 2020 were categorized as ‘COVID-period’. The lockdown periods in the Netherlands were 23 March 2020 to 11 May 2020 (first lockdown) and 13 October to December 2020 (second lockdown). In Denmark, the following lockdown periods were defined: 11 March 2020 to 15 April 2020 (first lockdown) and 16 December to December 2020 (second lockdown).

Demographic details

We gathered the following demographic information: age at the time of procedure (< 40 up to ≥ 105 years old, in five-year age categories), sex, BMI (underweight < 18.5 kg/m², normal weight 18.5 to 25 kg/m², overweight 25 to 30 kg/m², obese 30 to 40 kg/m², morbidly obese > 40 kg/m²), American Society of Anesthesiologists physical function (ASA) grade (I – normal health to IV – severe systemic disease that is a constant threat to life) [18] (not available in DKR), Charnley classification (A/B/C) [19], Walch score (A/B/C; only for Dutch shoulder arthroplasties) [20], and indication (osteoarthritis (OA)/other elective indications (rheumatoid or inflammatory arthritis, osteonecrosis, post-Perthes’ (hip), dysplasia (hip), cuff arthropathy (shoulder), irreparable cuff rupture (shoulder), other elective indications)/acute indications (fractures, tumours, post-traumatic)).

Arthroplasty

The following arthroplasty-related information was collected: date of procedure, type of procedure (primary/revision), type of hospital (general hospital/private or orthopaedic focus clinic), and fixation method (cemented/uncemented/hybrid).

Waiting list outcomes

Increased waiting time and QALY loss due to COVID-19 were estimated by modelling a virtual waiting list of patients who would otherwise already have had their primary arthroplasty [21]. Patients arrive at this virtual waiting list according to the expected numbers, as estimated from the pre-COVID-19 period with extrapolated time trend. Patients arriving with an acute indication are operated on immediately; other elective patients are operated on in order of arrival, depending on the available operating capacity. In 2020, the available operating capacity per country, joint, indication, and month is assumed equal to the actually observed number of operations in 2020. For 2021, only the total number of operations per country and joint was available, and we assumed the distribution over indications and months equal to 2020. For the first three months of 2022, available operating capacity was assumed equal to the first quarter of 2021. Starting from April 2022, we modelled three different scenarios to see how much additional capacity is needed to clear the backlog of patients that have arisen. The base-case scenario assumed 10% additional capacity for arthroplasty surgeries, as compared to the pre-COVID-19 trend. We also evaluated less optimistic scenarios with 5% and 0% additional capacity. While on the virtual waiting list, patients are assumed to die according to general Dutch and Danish mortality.

QALY loss was estimated by assuming that patients forgo the health benefit from arthroplasty for the duration they are on the virtual waiting list. This health benefit was estimated numerically by the difference in EQ-5D utility prior to arthroplasty compared to one year after arthroplasty, which was available for Dutch patients operated on from 2015 to 2019 [22]. Due to lack of Danish EQ-5D data, we estimated the Danish arthroplasty benefit by applying the Danish EQ-5D tariff to the Dutch patient questionnaires [23]. QALY loss per patient was then calculated as the country-specific benefit in EQ-5D utility from arthroplasty multiplied by the average time on the virtual waiting list.

Statistical analysis

All analyses were stratified by country and joint (hip/knee/shoulder). Means with standard deviations (SDs) or frequencies with proportions were used to describe the different populations at baseline. First, we estimated the change in surgery rate by comparing the number of observed arthroplasties in 2020 per month with

the expected number of arthroplasties. We used Poisson regression to estimate individual rates of primary hip, knee, and shoulder arthroplasty and revision within three months. The expected number of arthroplasties per month was based on the number of arthroplasties between 2014 and 2019, and change in composition of the general populations (age (< 40 and up to ≥ 105 years old, in five-year age categories) and sex). The calculated observed/expected (O/E) rates were then used to predict the total expected incidence of hip, knee, and shoulder arthroplasties in 2020. As revision surgery within the first three months is dependent on primary arthroplasty surgery, these extrapolations were based on the incidence rates of revision from the year 2014 to 2019.

We used descriptive statistics to investigate if patient characteristics and hospital type for arthroplasty surgery were different between the pre-COVID-19 period and COVID-period. Here, we compared the distribution of proportion per characteristic within 2019 (these proportions were assumed to be a closer representation of the 2020 proportions than those of the prior years) with the proportions per characteristic per month in 2020, stratified based on indication (OA/other elective/acute). All analyses were performed using R (R Foundation for Statistical Computing, Austria).

RESULTS

Observed and expected primary arthroplasties during 2020 in the Netherlands and Denmark

During 2020, at least 40,791 hip arthroplasties were expected in the Netherlands, but 33,664 arthroplasties were actually performed. As such, 7,127 (18%) surgeries were not observed. In Denmark, 618 (6%) of the 11,196 expected hip arthroplasties in 2020 were not performed. In both populations the largest decrease in O/E ratio was observed in April (Netherlands: 0.25; Denmark: 0.30) (Figure 1a). For knee arthroplasties in the Netherlands, a total of 31,772 were expected in 2020, but 24,445 knee arthroplasties were performed, resulting in 7,327 (23%) unperformed knee arthroplasties. In Denmark, 372 (4%) of the expected 9,963 knee arthroplasties were not performed. Similar to the hip arthroplasty population, the largest decrease in O/E ratio was seen in April (Netherlands: 0.03; Denmark: 0.24) (Figure 1b). In the Netherlands, 3,603 shoulder arthroplasties were expected in 2020 of which 809 (22%) shoulder arthroplasties

were not performed. Again, the largest decrease in O/E ratio was found in April (0.23) (Figure 1c).

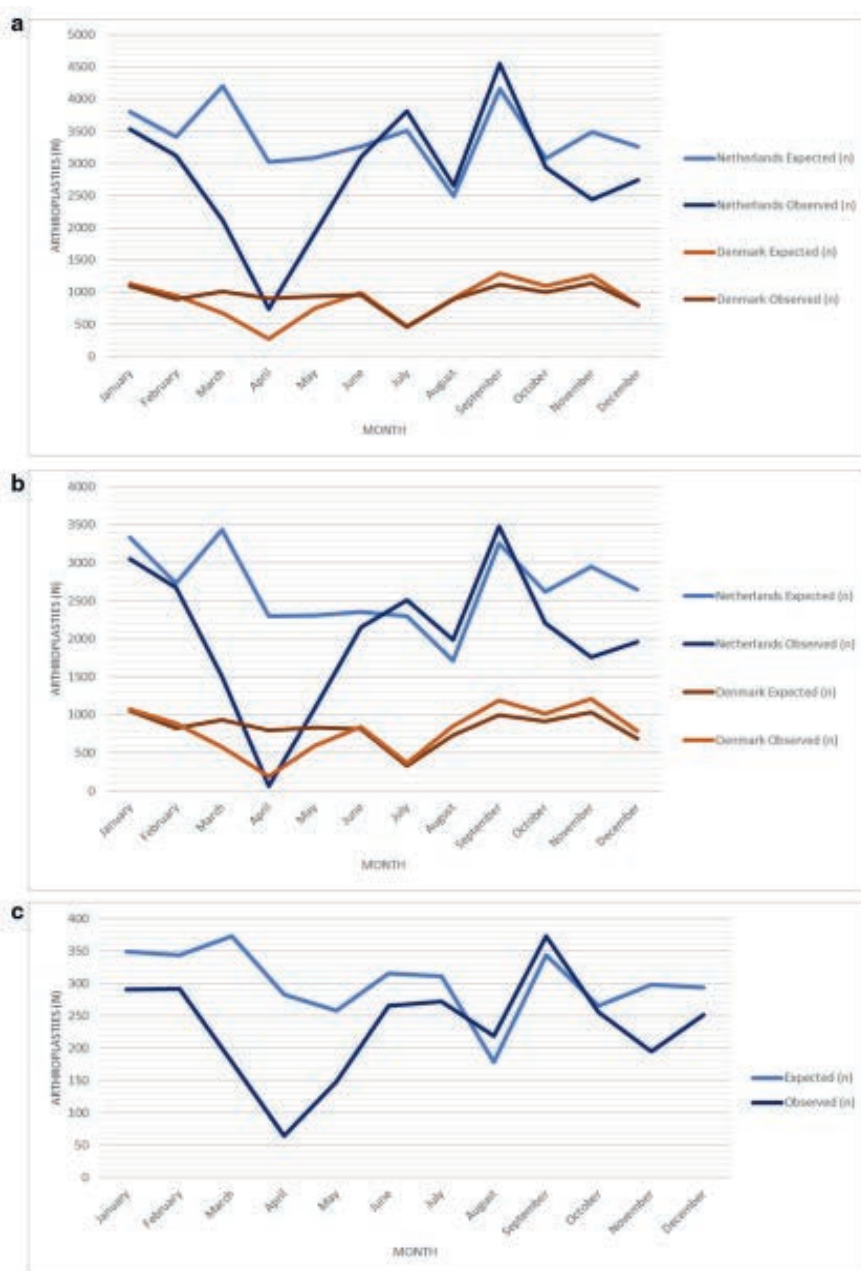


Figure 1 a) Observed versus expected number of primary hip arthroplasties in 2020 in the Netherlands and Denmark. b) Observed versus expected number of primary knee arthroplasties in 2020 in the Netherlands and Denmark. c) Observed versus expected number of primary shoulder arthroplasties in 2020 in the Netherlands

Observed and expected revision arthroplasties during 2020 in the Netherlands and Denmark

In the Netherlands, overall the expected and observed proportions of hip, knee, and shoulder revisions within three months in 2020 were relatively similar, namely 1.3% expected versus 1.3% observed, 0.6 versus 0.5% and 1.0% versus 1.2%, respectively (Supplementary Figure a to c). In Denmark, the observed proportion of hip revisions within three months in 2020 was slightly lower compared to the expected proportion (observed: 1.5% vs expected: 1.8%), with almost similar proportions for knee revisions (observed: 0.9% versus expected: 0.8%) (Supplementary Figure a to c).

Differences in patient and primary arthroplasty characteristics

We found several differences in patient characteristics between the pre-COVID-19 and COVID-period population. In the Netherlands, the proportion of patients undergoing hip and shoulder surgery due to osteoarthritis decreased during the COVID-period (hip: 74% E/68% O; shoulder: 44% E/42% O) (Table 1A/B). Overall, more patients were operated with ASA III to IV, and more uncemented and hybrid knee and shoulder arthroplasties were inserted in the COVID-period. In Denmark, results were rather similar to the Dutch population (Table 1A/B). Slightly more ASA III to IV patients received hip surgery in the COVID-period compared to the pre-COVID-19 period. More uncemented knee arthroplasties were performed in the COVID-period. In both countries, more patients received surgery in private hospitals (i.e. focus clinics without intensive care unit) in COVID-period.

Table 1A Patient and prosthesis characteristics of primary arthroplasty patients in the Netherlands

Characteristic	Hip Pre-COVID* (n = 223,198)	COVID (n = 25,148)	Knee Pre-COVID* (n = 179,726)	COVID (n = 17,161)	Shoulder Pre-COVID* (n = 17,216)	COVID (n = 2,050)
Age (%)						
<40	2,103 (0.9)	253 (1.0)	368 (0.2)	32 (0.2)	102 (0.6)	5 (0.2)
40-45	1,800 (0.8)	182 (0.7)	867 (0.5)	44 (0.3)	96 (0.6)	6 (0.3)
45-50	4,732 (2.1)	442 (1.8)	3,324 (1.8)	259 (1.5)	251 (1.5)	26 (1.3)
50-55	8,909 (4.0)	995 (4.0)	9,851 (5.5)	926 (5.4)	496 (2.9)	44 (2.1)
55-60	14,902 (6.7)	1,688 (6.7)	18,848 (10.5)	1,921 (11.2)	953 (5.5)	119 (5.8)
60-65	24,853 (11.1)	2,684 (10.7)	28,569 (15.9)	2,763 (16.1)	1,718 (10.0)	215 (10.5)
65-70	36,593 (16.4)	3,668 (14.6)	36,204 (20.1)	3,335 (19.4)	2,842 (16.5)	348 (17.0)
70-75	41,432 (18.6)	4,853 (19.3)	35,990 (20.0)	3,722 (21.7)	3,810 (22.1)	513 (25.0)
75-80	36,617 (16.4)	4,174 (16.6)	26,915 (15.0)	2,535 (14.8)	3,720 (21.6)	405 (19.8)
80-85	27,842 (12.5)	3,237 (12.9)	14,234 (7.9)	1,244 (7.2)	2,344 (13.6)	269 (13.1)
85-90	15,860 (7.1)	2,018 (8.0)	4,081 (2.3)	341 (2.0)	779 (4.5)	89 (4.3)
90-95	6,224 (2.8)	761 (3.0)	441 (0.2)	37 (0.2)	100 (0.6)	11 (0.5)
95-100	1,224 (0.5)	176 (0.7)	29 (0.0)	1 (0.0)	5 (0.0)	-
100-105	105 (0.0)	17 (0.1)	4 (0.0)	1 (0.0)	-	-
≥105	2 (0.0)	-	1 (0.0)	-	-	-
Female, yes (%)	146,067 (65.4)	16,126 (64.1)	113,096 (62.9)	10,323 (60.2)	12,831 (74.5)	1,532 (74.4)
BMI (%)						
Underweight	3,508 (1.6)	411 (1.6)	274 (0.2)	23 (0.1)	158 (0.9)	14 (0.7)
Normal weight	78,346 (35.1)	9,415 (37.4)	30,068 (16.7)	3,156 (18.4)	4,623 (26.9)	571 (27.9)
Overweight	86,741 (38.9)	9,318 (37.1)	72,946 (40.6)	7,037 (41.0)	6,576 (38.2)	761 (37.1)
Obese	44,599 (20.0)	4,528 (18.0)	66,834 (37.2)	6,161 (35.9)	4,963 (28.8)	566 (27.6)
Morbidly obese	2,295 (1.0)	239 (1.0)	6,110 (3.4)	477 (2.8)	513 (3.0)	62 (3.0)
Missing	7,709 (3.5)	1,237 (4.9)	3,450 (1.9)	304 (1.8)	383 (2.2)	76 (3.7)
ASA (%)						
I	33,210 (14.9)	3,290 (13.1)	25,246 (14.0)	2,317 (13.5)	1,383 (8.0)	140 (6.8)
II	131,471 (58.9)	13,600 (54.1)	120,632 (67.1)	11,038 (64.3)	10,314 (59.9)	1,207 (58.9)
III-IV	57,685 (25.8)	8,206 (32.6)	33,312 (18.5)	3,779 (22.0)	5,248 (30.5)	697 (34.0)
Charnley classification (%)						
A	90,275 (40.4)	8,404 (33.4)	75,620 (42.1)	6,768 (39.4)		
B	95,011 (42.6)	10,299 (40.9)	94,800 (52.7)	9,665 (56.3)		
C	5,731 (2.6)	634 (2.5)	5,312 (3.0)	538 (3.1)		
Walch score (%)						
A1					7,869 (45.7)	784 (38.2)
A2					3,732 (21.7)	465 (22.7)
B1					1,730 (10.0)	157 (7.7)
B2					876 (5.1)	131 (6.4)
B3					260 (1.5)	49 (2.4)
C					160 (0.9)	30 (1.5)
Indication (%)						
OA			172,806 (96.1)			
Other elective	164,493 (73.7)	17,015 (67.7)	3,485 (1.9)	16,510 (96.2)	7,501 (43.6)	866 (42.2)
Acute	11,740 (5.3)	1,265 (5.0)	2,627 (1.5)	343 (2.0)	5,552 (32.2)	579 (28.2)
Missing	44,766 (20.1)	6,566 (26.1)		245 (1.4)	4,055 (23.6)	597 (29.1)
Type of hospital (%)						
Public	208,864 (93.6)	21,809 (86.7)	156,210 (86.9)	13,414 (78.1)	16,336 (94.9)	1,884 (91.9)
Private	14,334 (6.4)	3,339 (13.3)	23,516 (13.1)	3,747 (21.8)	880 (5.1)	166 (8.1)
Fixation (%)						
Cemented	72,184 (32.3)	8,268 (32.9)	156,631 (87.1)	14,065 (82.0)	1,681 (9.8)	99 (4.8)
Uncemented	129,817 (58.2)	14,568 (57.9)	16,643 (9.3)	2,520 (14.7)	10,127 (58.8)	1,242 (60.6)
Hybrid	21,197 (9.5)	2,312 (9.2)	6,452 (3.6)	576 (3.3)	1,012 (31.4)	709 (65.4)
Other/unknown	-	-	-	-	-	-
Missing	-	-	-	-	-	-
EQ-5D (mean (SD))	0.533 (0.192)	0.522 (0.214)	0.566 (0.184)	0.561 (0.200)	0.527 (0.213)	0.520 (0.239)

Legend of Table 1A continues on the next page

Continuation of Table 1A

Dichotomous characteristics are presented as percentages, and continuous variables are presented as mean \pm standard deviation (SD) for normally distributed variables

**: 2014 – March 2020*

Abbreviations: BMI, Body Mass Index; ASA-score: American Society of Anaesthesiologists; OA: Osteoarthritis; EQ-5D: EuroQol-5D.

Table 1B Patient and prosthesis characteristics of primary arthroplasty patients in Denmark

Characteristic	Hip Pre-COVID* (n = 62,648)	COVID (n = 14,993)	Knee Pre-COVID* (n = 52,780)	COVID (n = 13,484)
Age (%)				
<40	865 (1.4)	216 (1.4)	Masked	37 (0.3)
40-45	902 (1.4)	177 (1.2)	414 (0.8)	92 (0.7)
45-50	1,899 (3.0)	476 (3.2)	1,386 (2.6)	300 (2.2)
50-55	3,446 (5.5)	894 (6.0)	3,464 (6.6)	874 (6.5)
55-60	4,874 (7.8)	1,347 (9.0)	5,432 (10.3)	1,599 (11.9)
60-65	7,184 (11.5)	1,615 (10.8)	7,439 (14.1)	2,071 (15.4)
65-70	10,550 (16.8)	2,235 (14.9)	9,737 (18.4)	2,197 (16.3)
70-75	12,670 (20.2)	2,841 (18.9)	11,263 (21.3)	2,689 (19.9)
75-80	10,229 (16.3)	2,649 (17.7)	8,166 (15.5)	2,188 (16.2)
80-85	6,405 (10.2)	1,590 (10.6)	3,993 (7.6)	1,104 (8.2)
85-90	2,691 (4.3)	694 (4.6)	1,133 (2.1)	299 (2.2)
90-95	796 (1.3)	210 (1.4)	143 (0.3)	33 (0.2)
95-100	121 (0.2)	45 (0.3)	<5 (.)	<5 (.)
100-105	16 (0.0)	<5 (.)	-	Masked
≥105	-	Masked	-	Masked
Female, yes (%)	35,759 (57.1)	8,488 (56.6)	30,377 (57.6)	7,608 (56.4)
BMI (%) **				
Underweight	562 (0.9)	251 (1.7)	161 (0.3)	34 (0.3)
Normal weight	12,568 (20.1)	4,963 (33.1)	10,114 (19.2)	2,458 (18.2)
Overweight	14,276 (22.8)	5,699 (38.0)	20,388 (38.6)	5,216 (38.7)
Obese	8,495 (13.6)	3,518 (23.5)	18,896 (35.8)	5,034 (37.3)
Morbidly obese	752 (1.2)	295 (2.0)	2,895 (5.5)	726 (5.4)
Missing	25,995 (41.5)	267 (1.8)	326 (0.6)	16 (0.1)
ASA (%)***				
I	7,227 (20.3)	2,620 (17.9)		
II	21,581 (60.6)	8,891 (60.7)		
III-IV	6,794 (19.1)	3,146 (21.5)		
Charnley classification (%)				
A	38,581 (61.6)	9,528 (63.5)	21,948 (41.6)	6,096 (45.2)
B	22,818 (36.4)	5,316 (35.5)	11,972 (22.7)	2,962 (22.0)
C	1,041 (1.7)	120 (0.8)	18,691 (35.4)	4,411 (32.7)
Indication (%)				
OA	51,364 (82.0)	12,281 (81.9)	44,760 (84.8)	11,302 (83.8)
Other elective	4,802 (7.7)	1,215 (8.1)	7,465 (14.1)	2,057 (15.3)
Acute	6,347 (10.1)	1,487 (9.9)	555 (1.1)	125 (0.9)
Missing	135 (0.2)	10 (0.1)	-	-
Type of hospital (%)				
Public	58,707 (93.7)	11,861 (79.1)	48,854 (92.6)	10,105 (74.9)
Private	3,941 (6.3)	3,132 (20.9)	3,926 (7.4)	3,379 (25.1)
Fixation (%)				
Cemented	5,297 (8.5)	1,227 (8.2)	30,313 (57.4)	6,465 (47.9)
Uncemented	43,485 (69.4)	10,182 (67.9)	9,824 (18.6)	4,347 (32.2)
Hybrid	13,042 (20.8)	3,389 (22.6)	11,858 (22.5)	2,459 (18.2)
Other/unknown	15 (0.0)	0 (0.0)	785 (1.5)	213 (1.6)
Missing	809 (1.3)	195 (1.3)	-	-

Dichotomous characteristics are presented as percentages, and continuous variables are presented as mean \pm standard deviation (SD) for normally distributed variables

*: 2014 – March 2020

** : BMI available in DHR/DKR from 2016 onwards

***: No ASA-score available for knee arthroplasty patients in Denmark

Abbreviations: BMI, Body Mass Index; ASA-score: American Society of Anaesthesiologists; OA: Osteoarthritis.

In both the Netherlands and Denmark, no differences were found regarding patient characteristics within the different indication categories (OA/other elective/acute) (Supplementary Tables i to iii). The only difference observed was a shift in hospital type during the COVID-period towards more OA procedures performed in private hospitals.

Differences in patient and revision arthroplasty characteristics

In the Netherlands, more ASA III to IV hip (40% E/49% O) and knee (27% E/42% O) patients and more ASA II shoulder patients (52% E/60% O) received revision surgery within three months. Additionally, more hip patients with an acute indication for primary arthroplasty received revision surgery during the COVID-period (hip: 25% E/7% O) (Table 2A/B). Infection was more often the reason for revision during COVID-period (hip: 40% E/46% O; knee: 60% E/62% O; shoulder: 24% E/32% O). Similar to primary arthroplasties, a shift was seen to private hospitals to perform revision arthroplasties during COVID-period (hip: 4% E/7% O; knee: 9% E/14% O; shoulder: 4% E/8% O). No differences were found in the revision population of Denmark when comparing the pre-COVID-19 and COVID-period, apart from the proportion of women receiving knee revision surgery (pre-COVID-19: 52% E/44% O).

Table 2A Patient and prosthesis characteristics revision arthroplasty patients in the Netherlands

Characteristic	Hip Pre-COVID* (n = 2979)	COVID (n = 339)	Knee Pre-COVID* (n = 958)	COVID (n = 91)	Shoulder Pre-COVID* (n = 193)	COVID (n = 25)
Age (%)						
<40	26 (0.9)	3 (0.9)	4 (0.4)	-	1 (0.5)	-
40-45	23 (0.8)	2 (0.6)	6 (0.6)	-	1 (0.5)	-
45-50	59 (2.0)	3 (0.9)	14 (1.5)	1 (1.1)	2 (1.0)	1 (4.0)
50-55	98 (3.3)	10 (2.9)	49 (5.1)	4 (4.4)	2 (1.0)	1 (4.0)
55-60	162 (5.4)	27 (8.0)	83 (8.7)	11 (12.1)	10 (5.2)	3 (12.0)
60-65	300 (10.1)	36 (10.6)	124 (12.9)	14 (15.4)	29 (15.0)	3 (12.0)
65-70	473 (15.9)	49 (14.5)	177 (18.5)	21 (23.1)	34 (17.6)	2 (8.0)
70-75	566 (19.0)	73 (21.5)	167 (17.4)	18 (19.8)	51 (26.4)	8 (32.0)
75-80	521 (17.5)	63 (18.6)	178 (18.6)	7 (7.7)	33 (17.1)	6 (24.0)
80-85	400 (13.4)	40 (11.8)	113 (11.8)	12 (13.2)	24 (12.4)	-
85-90	246 (8.3)	27 (8.0)	38 (4.0)	3 (3.3)	6 (3.1)	1 (4.0)
90-95	88 (3.0)	6 (1.8)	5 (0.5)	-	-	-
95-100	16 (0.5)	-	-	-	-	-
100-105	1 (0.0)	-	-	-	-	-
≥105	-	-	-	-	-	-
Female, yes (%)	1,783 (59.9)	196 (57.8)	501 (52.3)	46 (50.5)	104 (53.9)	13 (52.0)
BMI (%)						
Underweight	48 (1.6)	4 (1.2)	4 (0.4)	-	6 (3.1)	-
Normal weight	908 (30.5)	108 (31.9)	177 (18.5)	17 (18.7)	32 (16.6)	6 (24.0)
Overweight	1,103 (37.0)	109 (32.2)	354 (37.0)	32 (35.2)	71 (36.8)	13 (52.0)
Obese	755 (25.3)	90 (26.5)	340 (35.5)	36 (39.6)	70 (36.3)	4 (16.0)
Morbidly obese	81 (2.7)	10 (2.9)	57 (5.9)	4 (4.4)	7 (3.6)	2 (8.0)
Missing	84 (2.8)	18 (5.3)	26 (2.7)	2 (2.2)	7 (3.6)	-
ASA (%)						
I	232 (7.8)	17 (5.0)	110 (11.5)	8 (8.8)	8 (4.1)	2 (8.0)
II	1,527 (51.3)	145 (42.8)	580 (60.5)	45 (49.5)	100 (51.8)	15 (60.0)
III-IV	1,187 (39.8)	167 (49.3)	258 (26.9)	38 (41.8)	79 (40.9)	8 (32.0)
Indication primary arthroplasty (%)	2,019 (67.8)	190 (56.0)	898 (93.7)	85 (93.4)	46 (23.8)	6 (24.0)
OA	211 (7.1)	24 (7.1)	18 (1.9)	2 (2.2)	60 (34.8)	9 (36.0)
Other elective indication	749 (25.1)	125 (36.9)	57 (4.4)	4 (4.4)	76 (39.3)	10 (40.0)
Acute indication						
Reason revision (%)**						
Aseptic loosening	369 (12.4)	37 (10.9)	67 (7.0)	5 (5.5)	27 (14.0)	1 (4.0)
Infection	1,176 (39.5)	155 (45.7)	574 (59.9)	56 (61.5)	47 (24.3)	8 (32.0)
Fracture	609 (20.4)	61 (18.0)	89 (9.3)	7 (7.7)	12 (6.2)	-
Dislocation	824 (27.7)	79 (23.0)	23 (2.4)	1 (1.1)	-	-
Pain only	-	-	7 (0.7)	-	-	-
Other reason	388 (13.0)	75 (22.1)	307 (32.0)	27 (29.7)	130 (67.4)	16 (64.0)
Missing	-	-	-	-	-	-
Type of hospital (%)						
Public	2,871 (96.4)	315 (92.9)	958 (91.3)	78 (85.7)	186 (96.4)	23 (92.0)
Private	108 (3.6)	24 (7.1)	91 (8.7)	13 (14.3)	7 (3.6)	2 (8.0)

*: 2014 – March 2020

**: In the LROI it is possible to mark multiple reasons for revision, therefore the sum of proportions exceeds 100%

Abbreviations: BMI, Body Mass Index; ASA-score: American Society of Anaesthesiologists; OA: Osteoarthritis.

Table 2B Patient and prosthesis characteristics revision arthroplasty patients in Denmark

Characteristic	Hip Pre-COVID* (n =1,225)	COVID (n = 134)	Knee Pre-COVID* (n =410)	COVID (n =66)
Age (%)				
<40	Masked	<5 (.)	-	-
40-45	12 (1.0)	<5 (.)	<5 (.)	0 (0.0)
45-50	30 (2.4)	<5 (.)	8 (2.0)	<5 (.)
50-55	50 (4.1)	<5 (.)	19 (4.6)	<5 (.)
55-60	90 (7.3)	6 (4.5)	31 (7.6)	7 (10.6)
60-65	125 (10.2)	13 (9.7)	45 (11.0)	<5 (.)
65-70	208 (17.0)	15 (11.2)	66 (16.1)	8 (12.1)
70-75	235 (19.2)	34 (25.4)	97 (23.7)	18 (27.3)
75-80	232 (18.9)	25 (18.7)	80 (19.5)	15 (22.7)
80-85	148 (12.1)	21 (15.7)	43 (10.5)	8 (12.1)
85-90	60 (4.9)	7 (5.2)	Masked	<5 (.)
90-95	21 (1.7)	<5 (.)	-	-
95-100	<5 (.)	<5 (.)	-	-
100-105	-	-	-	-
≥105	-	-	-	-
Female, yes (%)	701 (57.2)	81 (60.4)	215 (52.4)	29 (43.9)
BMI (%) **				
Underweight	8 (0.7)	5 (3.7)	<5 (.)	Masked
Normal weight	208 (17.0)	45 (33.6)	78 (19.0)	12 (18.2)
Overweight	251 (20.5)	49 (36.6)	143 (34.9)	17 (25.8)
Obese	216 (17.6)	29 (21.6)	135 (32.9)	35 (53.0)
Morbidly obese	33 (2.7)	<5 (.)	Masked	<5 (.)
Missing	509 (41.6)	<5 (.)	13 (3.2)	0 (0.0)
ASA (%) ***				
I	56 (7.7)	7 (5.3)		
II	416 (57.5)	74 (56.5)		
III-IV	252 (34.8)	50 (38.2)		
Indication primary arthroplasty (%)	1,047 (77.0)	102 (76.1)		61 (92.4)
OA	Masked	Masked	366 (89.3)	5 (7.6)
Other elective indication	202 (14.9)	18 (13.4)	38 (9.3)	-
Acute indication			6 (1.5)	
Reason revision (%)				
Aseptic loosening	Masked	<5 (.)	19 (4.6)	6 (9.1)
Infection	484 (39.5)	50 (37.3)	245 (59.8)	36 (54.5)
Fracture	282 (23.0)	36 (26.9)	-	-
Dislocation	308 (25.1)	29 (21.6)	-	-
Pain only	6 (0.5)	0 (0.0)	6 (1.5)	-
Other reason	91 (7.4)	14 (10.4)	11 (2.7)	-
Missing	<5 (.)	<5 (.)	129 (31.5)	24 (36.4)
Type of hospital (%)				
Public	1,219 (99.5)	132 (98.5)	408 (99.5)	66 (100.0)
Private	6 (0.5)	Masked	2 (0.5)	-

*: 2014 – March 2020

**: BMI available in DHR/DKR from 2016 onwards

***: No ASA-score available for knee arthroplasty patients in Denmark

Abbreviations: BMI, Body Mass Index; ASA-score: American Society of Anaesthesiologists; OA: Osteoarthritis.

Waiting list outcomes

Figures 2a and 2b show the evolution of the virtual waiting lists due to COVID-19 assuming 10%, 5%, and 0% extra capacity (regardless of whether these patients are actually registered or not; additional insight into these models is provided in Supplementary Figure b). The waiting list outcome numbers are depicted in Table 3. Assuming 10% extra capacity from April 2022 onwards, additional waiting times due to COVID-19 will last until 2025 or 2026 in the Netherlands and until 2023 or 2024 in Denmark (Table 3). Average additional waiting times over this entire period are then estimated at 2.4 months in the Netherlands and 1.1 months in Denmark (and about double that time by the end of 2021). The mean forgone utility gain of arthroplasty was 0.24 and 0.26, respectively, resulting in a mean QALY loss of 0.049 (SD 0.031) and 0.024 (SD 0.014) per patient, respectively. When assuming 10% extra capacity, total QALY loss was estimated at 19,800 in the Netherlands and 1,500 in Denmark. Assuming a less optimistic scenarios with 5% additional post-COVID-19 capacity, the backlog will last until 2027 to 2029 in the Netherlands and until 2024 to 2026 in Denmark. If no additional post-COVID-19 capacity is available, the backlog will last for more than 30 years to come (> 2050).

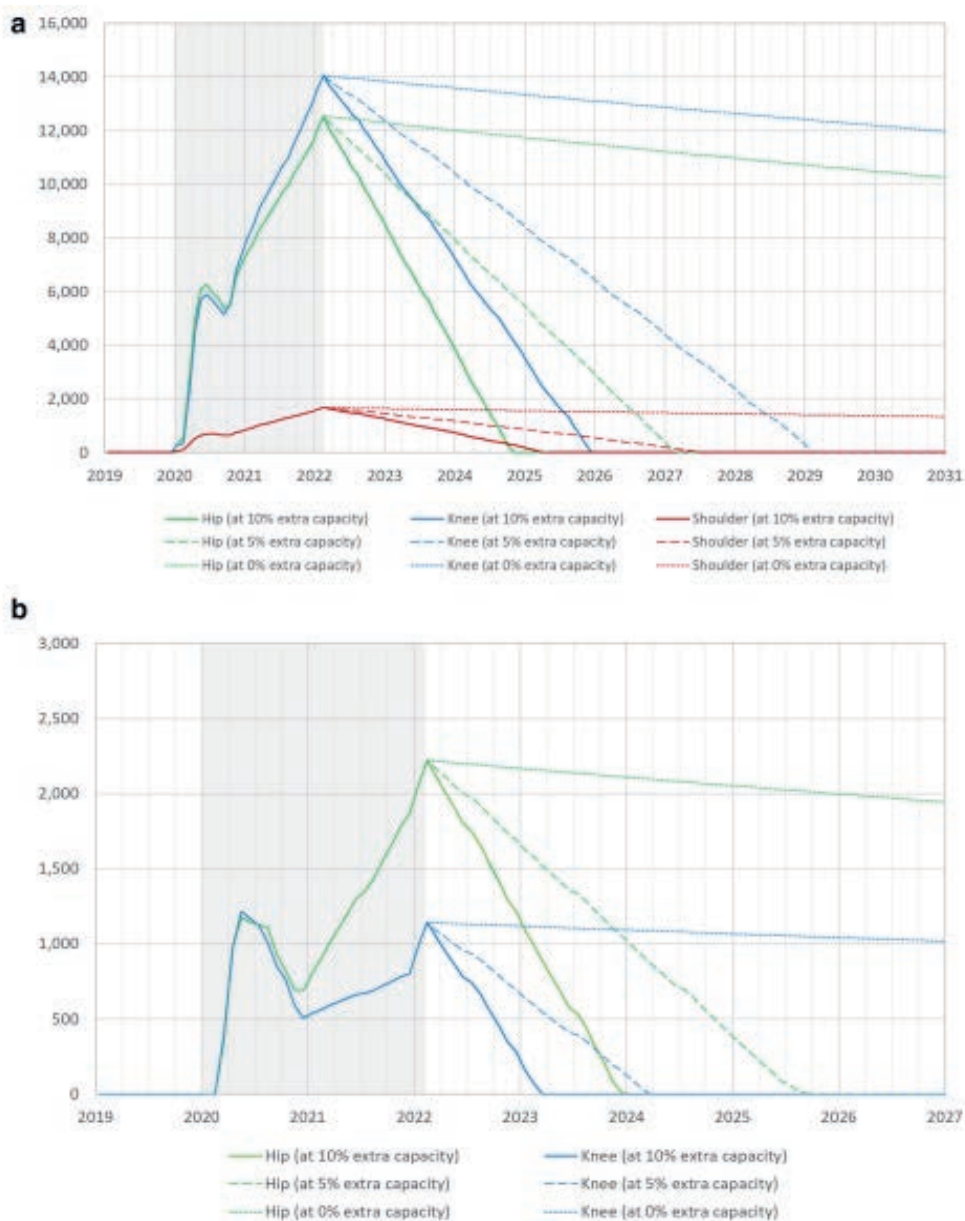


Figure 2 a) Dutch virtual waiting lists due to COVID-19 by joint, depending on the post-COVID-19 extra capacity (0%, 5%, or 10%). b) Danish virtual waiting lists due to COVID-19 by joint, depending on the post-COVID-19 extra capacity (0%, 5%, or 10%)

Table 3A Waiting-list outcomes among elective patients assuming 10% additional capacity

	End of virtual waiting-list	Number of patients involved	Average additional waiting time per patient	Average QALY Loss per patient	Total QALY loss
The Netherlands					
– Hip	2025	173,000	2.3 months	0.052	9,000
– Knee	2026	209,000	2.5 months	0.047	9,900
– Shoulder	2025	19,000	3.0 months	0.047	900
– Total	2026	401,000	2.4 months	0.049	19,800
Denmark					
– Hip	2024	42,000	1,3 months	0.029	1,200
– Knee	2023	32,000	0.8 months	0.016	500
– Total	2024	74,000	1.1 months	0.024	1,700

Legend: QALY: Quality-adjusted-life-years

Table 3B Waiting-list outcomes among elective patients assuming 5% additional capacity

	End of virtual waiting-list	Number of patients involved	Average additional waiting time per patient	Average QALY Loss per patient	Total QALY loss
The Netherlands					
– Hip	2027	269,000	2.1 months	0.049	13,100
– Knee	2029	335,000	2.4 months	0.045	15,000
– Shoulder	2027	30,000	2.6 months	0.043	1,300
– Total	2029	634,000	2.3 months	0.046	29,400
Denmark					
– Hip	2026	62,000	1,2 months	0.028	1,700
– Knee	2024	43,000	0.8 months	0.016	700
– Total	2026	105,000	1.0 months	0.023	2,400

Legend: QALY: Quality-adjusted-life-years

Table 3C Waiting-list outcomes among elective patients assuming 0% additional capacity

	End of virtual waiting-list*	Number of patients involved	Average additional waiting time per patient	Average QALY Loss per patient	Total QALY loss
The Netherlands					
– Hip	>2050	1,739,000	1.9 months	0.045	77,700
– Knee	>2050	1,604,000	2.5 months	0.047	74,900
– Shoulder	>2050	573,000	0.8 months	0.012	7,000
– Total	>2050	3,916,000	2.0 months	0.041	159,000
Denmark					
– Hip	>2050	451,000	1,2 months	0.029	12,900
– Knee	>2050	445,000	0.7 months	0.014	6,400
– Total	>2050	896,000	1.0 months	0.022	19,300

Legend: QALY: Quality-adjusted-life-years

*: outcome only up to 2050; waiting lists go beyond 2050

DISCUSSION

This study evaluated the impact of the COVID-19 pandemic on arthroplasty care in the Netherlands and Denmark. We showed that the impact of the pandemic in 2020 on primary arthroplasty surgeries was larger in the Netherlands compared to Denmark. In the Netherlands, 20% fewer primary arthroplasties than expected were performed, while in Denmark a 5% decrease was seen. The largest decrease was seen in the primary knee arthroplasty population in the Netherlands (23%).

During the pandemic, proportionally more acute primary hip and shoulder arthroplasties were performed, whereas the OA arthroplasty numbers dropped. No prioritizing took place based on age or patient comorbidity (ASA and Charnley) scores within each of the surgical indication categories (OA, other elective and acute surgery). However, within the total population in the Netherlands, an increase in ASA III to IV patients was observed. This was due to the prioritization of more acute non-OA indications, such as fractures and bone tumours (primary and metastases). We found an increase in uncemented primary knee arthroplasties during the COVID-period, which are generally (pre-COVID-19) performed in approximately 10% of the cases. No differences were found in

fixation method in the primary hip and shoulder arthroplasty population.

Within the hip and knee revision populations, we found a shift towards a more comorbid population (i.e. more ASA III to IV patients) during the COVID-period. Conversely, patients in need of shoulder revision arthroplasty during the COVID-period were more often less comorbid (ASA II). Revision surgery for periprosthetic joint infection was relatively more common during the COVID-period, possibly due to the urgency of this indication. With regard to the delivery of care, a shift occurred towards private hospitals for both primary and revision surgery during the COVID-period.

Finally, if we assume that after COVID-19 the available operating capacity can be increased by 10% compared to the pre-COVID-19 trend, then it will take three to four years to clear the backlog of patients in the Netherlands and one to two years in Denmark. In that case, the estimated total health loss in the Netherlands and Denmark will be 19,800 and 1,700 QALYS, respectively. With an additional capacity of only 5%, it will take about double the time before the backlogs are cleared (i.e. five to seven years in the Netherlands and two to four years in Denmark).

Although the numbers differ by country, worldwide orthopaedic care and arthroplasty surgical volume have been negatively affected by the COVID-19 pandemic [24]. Other countries mentioned major effects of the pandemic on hip and knee arthroplasty procedures, with drops ranging from 20% to 61% [25-28]. Similar to our results, these studies also observed the most significant decrease during April and May of 2020. Furthermore, a survey administered within the European Hip Society (EHS) and Knee Associates (EKA) showed that primary total joint replacements (TJR), alongside with aseptic revisions, were impacted most, while septic revisions and periprosthetic fractures were still performed [3].

Previous studies suggested prioritizing patients during the COVID-19 pandemic [5,24], Which could possibly worsen existing healthcare disparities. Our results indicate that no prioritizing based on patients' health seemed to have occurred within surgical indication categories in the Netherlands and Denmark. However, during the first lockdown more acute indications were prioritized over elective OA patients, thereby explaining the shift towards higher ASA grades in the total population in the Netherlands [29]. The shift towards higher ASA grades was not apparent in the Danish population, which could be due to the fact that

fewer arthroplasties were postponed and the DHR does not include hemi hip arthroplasties.

Although no prioritization occurred, a shift in healthcare delivery (i.e. arthroplasty surgery) towards private hospitals occurred during the COVID-period in both countries. Due to the absence of an intensive care unit (ICU), private hospitals generally perform surgery on patients with lower ASA grades. During the COVID-19 pandemic, several guidelines were suggested to postpone these patients first when healthcare capacities were impacted. However, private hospitals were able to fill in part of the capacity gap, thereby minimizing the impact on patients with lower ASA grades in the Netherlands and Denmark. Similar to the Netherlands and Denmark, the independent sector in the UK also helped reduce the burden on the elective care during the pandemic [28]. The independent sector lowered the elective workload, using a 'lift and shift' service, thereby decreasing the overall impact of the COVID-19 pandemic.

Due to the decline in surgical volume, as a consequence of anaesthesia personnel working at ICUs and recovery rooms in hospitals that were transformed into ICUs, the waiting lists increased. The backlog, caused by postponing arthroplasty surgery, occurred in many countries [26]. Oussedik et al. [30] showed that elective orthopaedic waiting lists in England were approximately three times the pre-COVID-19 average in November 2020. Similarly to other studies, we estimate that the effect of the pandemic is long lasting, and will be cumulative if no extra surgical capacity can be created [21,25,31,32]. Several strategies have been proposed to combat the backlog, such as increased operating theatre schedules, risk stratification, and the use of outpatient and ambulatory surgical centres [24], while others suggest that reducing the waiting lists should not solely rely on the length of time the patient has been waiting, but should also include the level of need of the patient [9].

Due to the extended wait on the waiting list, the patient's health status could be negatively affected, thereby making them more susceptible to other health problems and also affecting rehabilitation after surgery [10]. Green et al. [33] showed that time to surgery and length of stay in the hospital increased due to the pandemic, thereby possibly contributing to radiological and clinical deterioration of arthritis and general musculoskeletal conditioning. This in turn could affect patient rehabilitation, as well as increase the length of stay. Based on the scenarios described in this study, even with a 10% increase in capacity

(including operating theatre personnel, hospital beds, nursing staff, and surgeons), compared to the pre-pandemic capacity in hospitals, it will take anywhere between one and four more years to reduce the extended waiting lists to their pre-COVID-19 length. Wilson et al. [21] showed similar results regarding the long-term impact of the pandemic on the backlog in arthroplasty surgeries. Due to the elective case ban, the surplus of surgical volume is significant. Both the results from the current study and the study of Wilson et al. [21] emphasize the value of anticipatory planning to lessen the impact of the pandemic.

Increase in waiting lists also significantly impacts patients' health status and quality of life [9,14,34]. However, previous studies did not mention the actual impact of the pandemic regarding QALY loss. Nevertheless, due to restricted possibilities in providing additional capacity for orthopaedic care, drastic changes within this field are needed, possibly resulting in a change of focus from surgical interventions towards prevention or non-surgical interventions for OA that can relieve pressure on orthopaedic healthcare. As a result, research aimed at improving patients' health status during the period between diagnosis and surgery, to facilitate their quality of life and health status to remain stable, seems a necessity. This study has several strengths. First, we obtained data from national registries from two countries, which both have a completeness of 97% to 98%. Second, we took into account the expected number of arthroplasties for 2020, based on the growth in arthroplasty numbers and changes in the general population over the years. A possible limitation is the fact that some patients received bilateral arthroplasties during one procedure, which could result in an overestimation of the number of expected surgeries. However, only a small percentage of patients received this type of surgery. Furthermore, the DHR only contains information regarding total hip arthroplasties. No information regarding partial hip arthroplasties was available in the DHR, which could affect estimates regarding the switch towards acute surgeries in Denmark. In addition, within the DHR and DKR registers no EQ-5D scores are available, so the Danish health gain and QALY calculations were extrapolated from the Dutch arthroplasty population. Unfortunately, we had no information on the number of TJRs performed per month for 2021, and no information on the number of actual procedures performed after 2021. Additionally, we were not able to account for factors affecting the backlog during the ongoing COVID-19 pandemic, such as relative shortage of operating theatre capacity, other specialties also attempting

to combat the backlog, and the unpredictable future course. As a result, it is difficult to determine whether healthcare systems are able to accommodate an increase in arthroplasty surgery volumes. Moreover, we did not include whether a patient's willingness to undergo elective surgery changed during the pandemic, thereby impacting the calculation of the procedure backlog. Although some studies showed that a proportion of patients were reluctant to undergo surgery during the pandemic, the majority wished to proceed with the planned surgery [35-37]. Furthermore, studies showed that elective surgery can safely be resumed during the pandemic [38-40]. Although it is possible that willingness decreased during this time, it is also likely that reluctance decreases and an influx of new patient referrals will increase again when the pandemic eases.

The COVID-19 pandemic had a huge impact on patients in need of hip, knee, or shoulder arthroplasty. Within the first wave in the Netherlands, patients with more acute indications were prioritized. However, within the indication categories, no prioritization based on patient characteristics occurred. Relatively more surgeries were performed in private hospitals compared to pre-COVID-19. The QALY loss in the Netherlands and Denmark has been considerable, and will last for years to come. Although both the Netherlands and Denmark were affected by the pandemic, the impact on hip and knee arthroplasty volumes was greater in the Netherlands than Denmark. This could be explained by the relatively low rate of COVID-19 infections and related deaths in Denmark [41]. Furthermore, Denmark was one of the first European countries to partially reopen society [41,42], most likely due to rapid interference by the Danish government, and a high level of trust and confidence in the government by the public [41]. In the future, there will be additional strain on the healthcare system, especially in orthopaedic departments, based on the reduced surgical rate throughout the pandemic. It is necessary to investigate which possible measures can be taken to eliminate the extended waiting lists. Evaluating interventions that provide patients with a way to cope with their symptoms or avoid aggravation of symptoms could benefit those awaiting surgery.

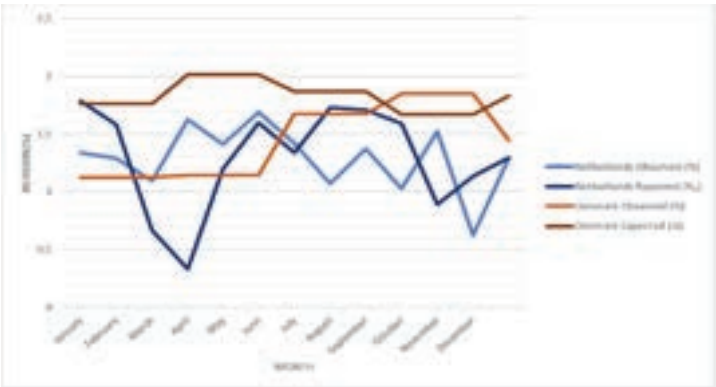
References

1. Rupp M, Lau E, Kurtz SM, Alt V. Projections of primary TKA and THA in Germany from 2016 through 2040. *Clin Orthop Relat Res*. 2020;478(7):1622–1633. 10.1097/CORR.0000000000001214
2. Bedard NA, Elkins JM, Brown TS. Effect of COVID-19 on hip and knee arthroplasty surgical volume in the United States. *J Arthroplasty*. 2020;35(7S):S45–S48. 10.1016/j.arth.2020.04.060
3. Thaler M, Khosravi I, Hirschmann MT, et al.. Disruption of joint arthroplasty services in Europe during the COVID-19 pandemic: an online survey within the European Hip Society (EHS) and the European Knee Associates (EKA). *Knee Surg Sports Traumatol Arthrosc*. 2020;28(6):1712–1719. 10.1007/s00167-020-06033-1
4. Rizkalla JM, Gladnick BP, Bhimani AA, Wood DS, Kitziger KJ, Peters PC. Triaging total hip arthroplasty during the COVID-19 pandemic. *Curr Rev Musculoskelet Med*. 2020;13(4):416–424. 10.1007/s12178-020-09642-y
5. Parvizi J, Gehrke T, Krueger CA, et al.. Resuming elective orthopaedic surgery during the COVID-19 pandemic: Guidelines developed by the International Consensus Group (ICM). *J Bone Joint Surg Am*. 2020;102-A(14):1205–1212. 10.2106/JBJS.20.00844
6. Mouton C, Hirschmann MT, Ollivier M, Seil R, Menetrey J. COVID-19 - ESSKA guidelines and recommendations for resuming elective surgery. *J Exp Orthop*. 2020;7(1):28. 10.1186/s40634-020-00248-4
7. The Lancet Rheumatology . Too long to wait: the impact of COVID-19 on elective surgery. *Lancet Rheumatol*. 2021;3(2):e83. 10.1016/S2665-9913(21)00001-1
8. Ostendorf M, Buskens E, van Stel H, et al.. Waiting for total hip arthroplasty: avoidable loss in quality time and preventable deterioration. *J Arthroplasty*. 2004;19(3):302–309. 10.1016/j.arth.2003.09.015
9. Morris JA, Super J, Huntley D, Ashdown T, Harland W, Anakwe R. Waiting lists for symptomatic joint arthritis are not benign: prioritizing patients for surgery in the setting of COVID-19. *Bone Jt Open*. 2020;1(8):508–511. 10.1302/2633-1462.18.BJO-2020-0112.R1
10. Cisternas AF, Ramachandran R, Yaksh TL, Nahama A. Unintended consequences of COVID-19 safety measures on patients with chronic knee pain forced to defer joint replacement surgery. *Pain Rep*. 2020;5(6):e855. 10.1097/PR9.0000000000000855
11. Endstrasser F, Braitto M, Linser M, Spicher A, Wagner M, Brunner A. The negative impact of the COVID-19 lockdown on pain and physical function in patients with end-stage hip or knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc*. 2020;28(8):2435–2443. 10.1007/s00167-020-06104-3
12. Fahy S, Moore J, Kelly M, Irwin S, Kenny P. Assessing the attitudes, awareness, and behavioral alterations of patients awaiting total hip arthroplasty during the COVID-19 crisis. *Geriatr Orthop Surg Rehabil*. 2020;11:2151459320969377. 10.1177/2151459320969377
13. Knebel C, Ertl M, Lenze U, et al.. COVID-19-related cancellation of elective orthopaedic surgery caused increased pain and psychosocial distress levels. *Knee Surg Sports Traumatol Arthrosc*. 2021;29(8):2379–2385. 10.1007/s00167-021-06529-4
14. Pietrzak JRT, Maharaj Z, Erasmus M, Sikhuli N, Cakic JN, Mokete L. Pain and function deteriorate in patients awaiting total joint arthroplasty that has been postponed due to the COVID-19 pandemic. *World J Orthop*. 2021;12(3):152–168. 10.5312/wjo.v12.i3.152
15. Clement ND, Scott CEH, Murray JRD, Howie CR, Deehan DJ, IMPACT-Restart Collaboration . The number of patients “worse than death” while waiting for a hip or

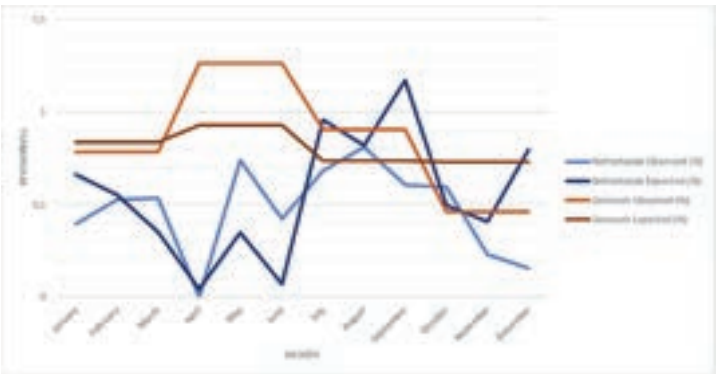
- knee arthroplasty has nearly doubled during the COVID-19 pandemic. *Bone Joint J.* 2021;103-B(4):672–680. 10.1302/0301-620X.103B.BJJ-2021-0104.R1
16. No authors listed . DHR Report 2021. *Dansk Høftealloplastik Register.* 2021. https://www.sundhed.dk/content/cms/98/4698_dhr-aarsrapport-2021_offentliggørelse.pdf (date last accessed 23 November 2022).
17. No authors listed . DKR report 2021. *Dansk Knæalloplastik Register.* 2021. https://www.sundhed.dk/content/cms/99/4699_dkr_aarsrapport_2021.pdf (date last accessed 23 November 2022).
18. Saklad M. Grading of patients for surgical procedures. *Anesthesiol.* 1941;2(3):281–284. 10.1097/00000542-194105000-00004
19. Charnley J. The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. *J Bone Joint Surg Br.* 1972;1:61–76.
20. Vo KV, Hackett DJ, Gee AO, Hsu JE. Classifications in brief: Walch Classification of primary glenohumeral osteoarthritis. *Clin Orthop Relat Res.* 2017;475(9):2335–2340. 10.1007/s11999-017-5317-6
21. Wilson JM, Schwartz AM, Farley KX, Roberson JR, Bradbury TL, Guild GN. Quantifying the backlog of total hip and knee arthroplasty cases: Predicting the impact of COVID-19. *HSS J.* 2020;16(Suppl 1):85–91. 10.1007/s11420-020-09806-z
22. Lamers LM, McDonnell J, Stalmeier PFM, Krabbe PFM, Busschbach JJV. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. *Health Econ.* 2006;15(10):1121–1132. 10.1002/hec.1124
23. Wittrup-Jensen KU, Lauridsen J, Gudex C, Pedersen KM. Generation of a Danish TTO value set for EQ-5D health states. *Scand J Public Health.* 2009;37(5):459–466. 10.1177/1403494809105287
24. Chen AZ, Shen TS, Bovonratwet P, Pain KJ, Murphy AI, Su EP. Total joint arthroplasty during the COVID-19 pandemic: A scoping review with implications for future practice. *Arthroplast Today.* 2021;8:15–23. 10.1016/j.artd.2020.12.028
25. Yapp LZ, Clarke JV, Moran M, Simpson AHRW, Scott CEH. National operating volume for primary hip and knee arthroplasty in the COVID-19 era: a study utilizing the Scottish arthroplasty project dataset. *Bone Jt Open.* 2021;2(3):203–210. 10.1302/2633-1462.23.BJO-2020-0193.R1
26. Levašič V, Savarin D, Kovač S. The impact of COVID-19 on the orthopaedic patient in Slovenia: Hip and knee replacement surgery, 90-day mortality, outpatient visits and waiting times. *Zdr Varst.* 2022;61(3):155–162. 10.2478/sjph-2022-0021
27. Czubak-Wrzosek M, Czubak J, Grzelecki D, Tyrakowski M. The effect of the COVID-19 pandemic on total hip and knee arthroplasty surgical volume in 2020 in Poland. *Int J Environ Res Public Health.* 2021;18(16):16. 10.3390/ijerph18168830
28. Hampton M, Riley E, Garneti N, Anderson A, Wembridge K. The orthopaedic waiting list crisis: two sides of the story. *Bone Jt Open.* 2021;2(7):530–534. 10.1302/2633-1462.27.BJO-2021-0044.R1
29. Bonsel JM, Groot L, Cohen A, et al.. Impact of the COVID-19 lockdown on patient-reported outcome measures in Dutch hip and knee arthroplasty patients. *Acta Orthop.* 2022;93:808–818. 10.2340/17453674.2022.4856
30. Oussedik S, MacIntyre S, Gray J, McMeekin P, Clement ND, Deehan DJ. Elective orthopaedic cancellations due to the COVID-19 pandemic: where are we now, and where are we heading? *Bone Jt Open.* 2021;2(2):103–110. 10.1302/2633-1462.22.BJO-2020-0161.R1

31. Jain A, Jain P, Aggarwal S. SARS-CoV-2 impact on elective orthopaedic surgery: Implications for post-pandemic recovery. *J Bone Joint Surg Am*. 2020;102-A(13):13. 10.2106/JBJS.20.00602
32. Howlett NC, Wood RM. Modeling the recovery of elective waiting lists following COVID-19: Scenario projections for England. *Value Health*. 2022;S1098-3015(22)02071-X. 10.1016/j.jval.2022.06.016
33. Green G, Abbott S, Vyrides Y, Afzal I, Kader D, Radha S. The impact of the COVID-19 pandemic on the length of stay following total hip and knee arthroplasty in a high volume elective orthopaedic unit. *Bone Jt Open*. 2021;2(8):655–660. 10.1302/2633-1462.28.BJO-2021-0022.R1
34. Johnson NR, Odum S, Lastra JD, Fehring KA, Springer BD, Otero JE. Pain and anxiety due to the COVID-19 pandemic: A survey of patients with delayed elective hip and knee arthroplasty. *Arthroplast Today*. 2021;10:27–34. 10.1016/j.artd.2021.05.013
34. Johnson NR, Odum S, Lastra JD, Fehring KA, Springer BD, Otero JE. Pain and anxiety due to the COVID-19 pandemic: A survey of patients with delayed elective hip and knee arthroplasty. *Arthroplast Today*. 2021;10:27–34. 10.1016/j.artd.2021.05.013
35. Chang J, Wignadasan W, Kontoghiorghe C, et al.. Restarting elective orthopaedic services during the COVID-19 pandemic: Do patients want to have surgery? *Bone Jt Open*. 2020;1(6):267–271. 10.1302/2046-3758.16.BJO-2020-0057
36. Madanipour S, Al-Obaedi O, Ayub A, Iranpour F, Subramanian P. Resuming elective hip and knee arthroplasty in the COVID-19 era: a unique insight into patient risk aversion and sentiment. *Ann R Coll Surg Engl*. 2021;103(2):104–109. 10.1308/rcsann.2020.7012
37. Wignadasan W, Mohamed A, Kayani B, Magan A, Plastow R, Haddad FS. Restarting elective orthopaedic surgery as COVID-19 lockdown restrictions are reduced: have patient perceptions towards surgery changed? *Bone Jt Open*. 2021;2(10):865–870. 10.1302/2633-1462.210.BJO-2021-0076.R1
38. Chuntamongkol R, Meen R, Nash S, Ohly NE, Clarke J, Holloway N. Resuming elective orthopaedic services during the COVID-19 pandemic: our experience. *Bone Jt Open*. 2021;2(11):951–957. 10.1302/2633-1462.211.BJO-2021-0080.R1
39. Asopa V, Sagi A, Bishi H, et al.. The safe resumption of elective orthopaedic services following the first wave of the COVID-19 pandemic: a review of 2,316 consecutive cases and implications for recovery following further waves. *Bone Jt Open*. 2022;3(1):42–53. 10.1302/2633-1462.31.BJO-2021-0138
40. Jabbal M, Campbell N, Savaridas T, Raza A. Careful return to elective orthopaedic surgery in an acute hospital during the COVID-19 pandemic shows no increase in morbidity or mortality. *Bone Jt Open*. 2021;2(11):940–944. 10.1302/2633-1462.211.BJO-2021-0114.R1
41. Olganier D, Mogensen TH. The Covid-19 pandemic in Denmark: Big lessons from a small country. *Cytokine Growth Factor Rev*. 2020;53:10–12. 10.1016/j.cytogfr.2020.05.005
42. Mishra S, Scott JA, Laydon DJ, et al.. Comparing the responses of the UK, Sweden and Denmark to COVID-19 using counterfactual modelling. *Sci Rep*. 2021;11(1):16342. 10.1038/s41598-021-95699-9

APPENDICES



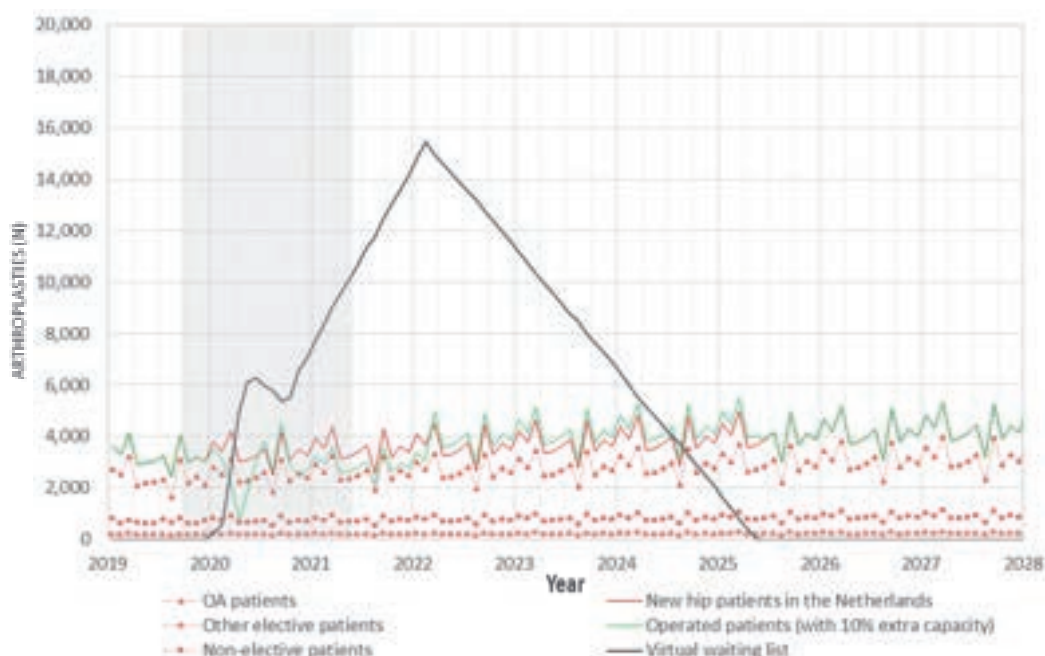
Supplementary Figure 1A Observed/Expected ratios of proportions of revision hip arthroplasties within 3 months in 2020 in the Netherlands and Denmark



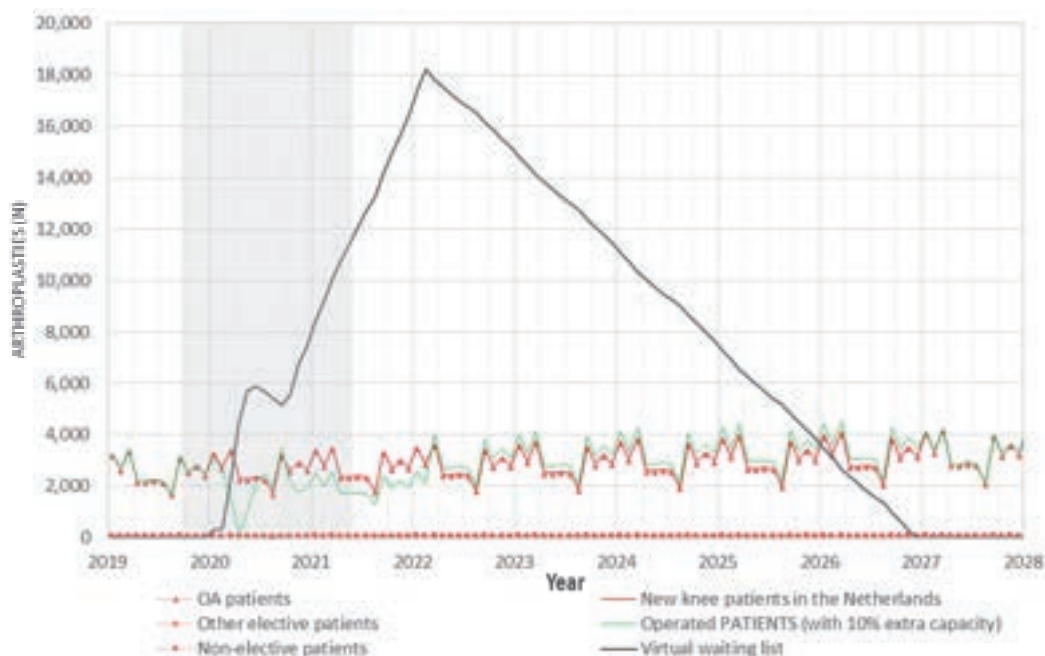
Supplementary Figure 1B Observed/Expected ratios of proportions of revision knee arthroplasties within 3 months in 2020 in the Netherlands and Denmark



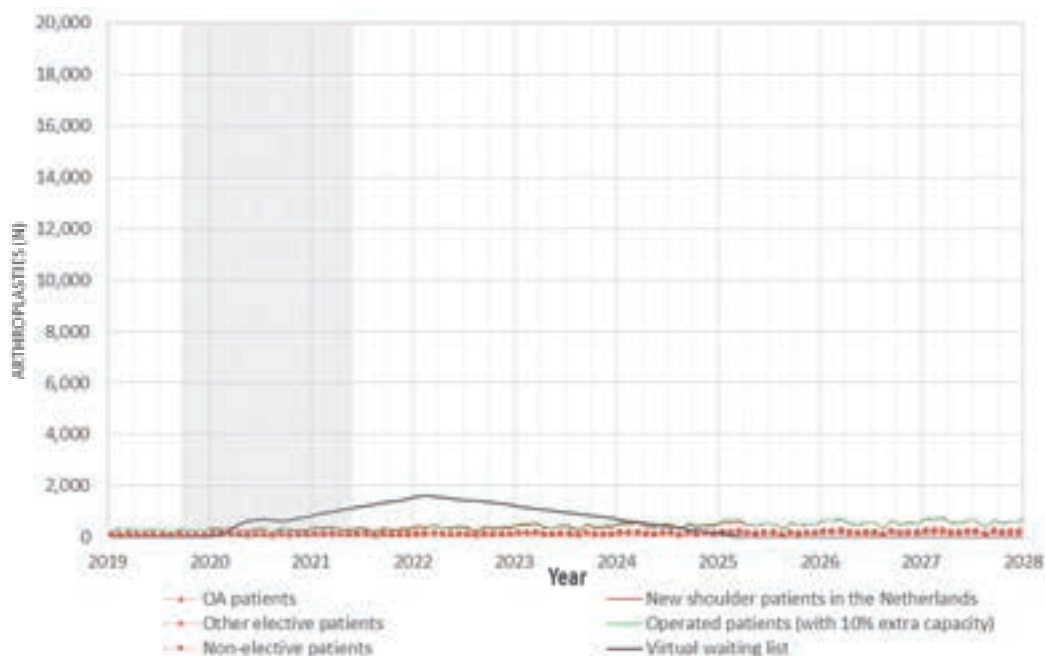
Supplementary Figure 1C Observed/Expected ratios of proportions of revision shoulder arthroplasties within 3 months in 2020 in the Netherlands



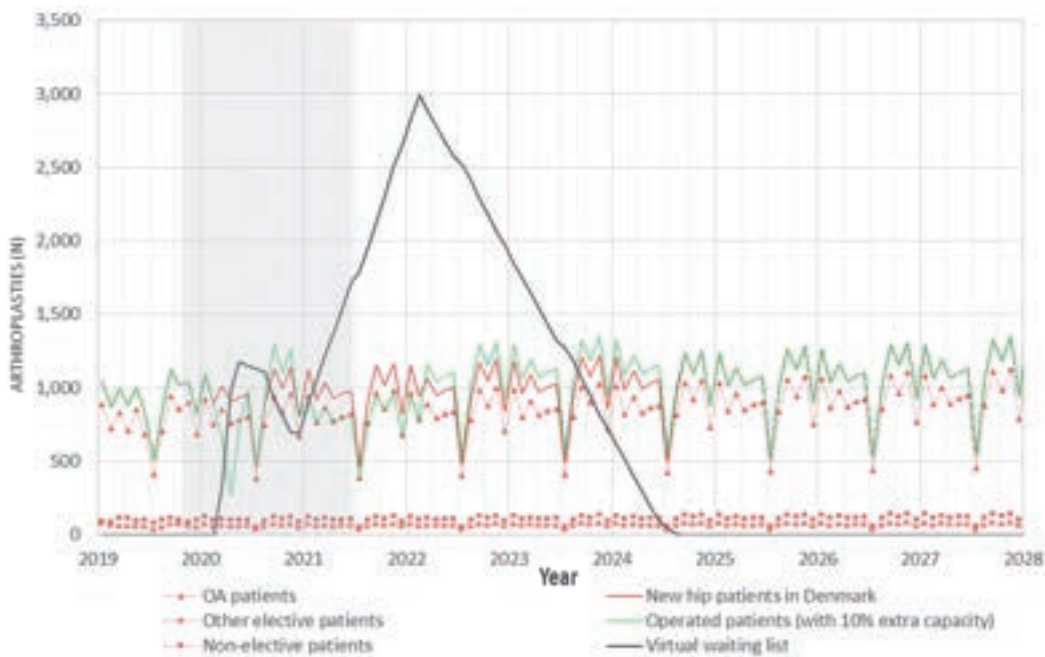
Supplementary Figure 2A Virtual waiting list for the Dutch hip population, including operated and arriving numbers of patients by indication



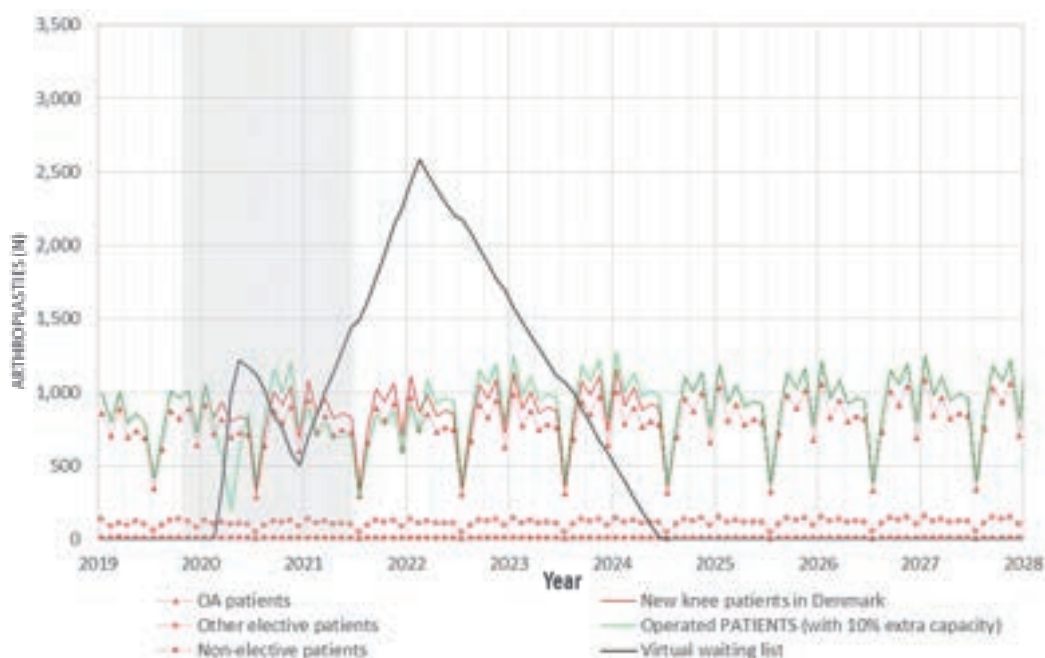
Supplementary Figure 2B Virtual waiting list for the Dutch knee population, including operated and arriving numbers of patients by indication



Supplementary Figure 2C Virtual waiting list for the Dutch shoulder population, including operated and arriving numbers of patients by indication



Supplementary Figure 2D Virtual waiting list for the Danish hip population, including operated and arriving numbers of patients by indication



Supplementary Figure 2E Virtual waiting list for the Danish knee population, including operated and arriving numbers of patients by indication

Supplementary tables made digitally accessible



Chapter 3

Multiple Joint Arthroplasties in Hip and Knee Osteoarthritis Patients: a national longitudinal cohort study

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P.J. Marang – van de Mheen, S.C. Cannegieter, S.H.M. Verdegaal, R.G.H.H.
Nelissen, and M.G.J. Gademan

ABSTRACT

Background: Many patients suffer from osteoarthritis in multiple joints, possibly resulting in multiple joint arthroplasties (MJA). Primarily, we determined the cumulative incidence (C_{in}) of MJA in hip and knee joints up to 10 years. Secondly, we calculated the mean time between the first and subsequent joint arthroplasty and evaluated the different MJA-trajectories. Lastly, we compared patient characteristics and outcomes (functionality and pain) after surgery between MJA-patients and single hip or knee arthroplasty (HA and KA) patients.

Methods: Primary index (first) HA or KA for osteoarthritis were extracted from the Dutch Arthroplasty Register. The 1, 2, 5 and 10-year C_{in} (including competing risk death) of MJA, mean time-intervals and MJA-trajectories were calculated and stratified for primary index HA or KA. Sex, and preoperative age and BMI were compared using ordinal logistic regression. Outcomes, measured preoperatively, 3, 6, and 12 months postoperatively (function: Hip Disability or Knee Injury and Osteoarthritis Outcome Score; Pain: Numerical Rating Scale), were compared using linear regression.

Results: A total of 140,406 HA-patients and 140,268 KA-patients were included. One, 2, 5, and 10-year C_{in} for a second arthroplasty were respectively 8.9% [95% confidence interval (CI): 8.7 to 9.0], 14.3% [95%CI: 14.1 to 14.5], 24.0% [95%CI: 23.7 to 24.2], and 32.7% [95%CI: 32.2 to 33.1] after index HA, and 9.5% [95%CI: 9.4 to 9.7], 16.0% [95%CI: 15.9 to 16.2], 26.4% [95%CI: 26.1 to 26.6], and 35.8% [95%CI: 35.4 to 36.3] after index KA. The 10-year C_{in} for > 2 arthroplasties were small in both the index HA and KA groups. Time-intervals from first to second, third, and fourth arthroplasty were 26 [95%CI: 26.1 to 26.7], 47 [95%CI: 46.4 to 48.4], and 58 [95%CI: 55.4 to 61.1] months after index HA, and 26 [95%CI: 25.9 to 26.3], 52 [95%CI: 50.8 to 52.7], and 61 [95%CI: 58.3 to 63.4] months after index KA. There were 83% of the second arthroplasties placed in the contralateral cognate joint (i.e., knee or hip). Differences in postoperative functionality and pain between MJAs and single HAs and KAs were small.

Conclusion: The 10-year C_{in} showed that about one-third of patients received a second arthroplasty after approximately 2 years, with the majority in the contralateral cognate joint. Few patients received > 2 arthroplasties within 10

years. Being a women, having a higher BMI, and being younger increased the odds of MJA. Postoperative outcomes were slightly negatively affected by MJA.

INTRODUCTION

Osteoarthritis (OA) often affects multiple joints within an individual [1, 2]. As such, a considerable number of OA patients are at risk of multiple joint arthroplasties (MJAs). Hip and knee arthroplasties are indicated for end stage OA when patients have severe joint pain and limited mobility and when conservative treatments such as pain medication or physical therapy no longer suffice. Previous studies reported a MJA prevalence of 27% at 5 to 8 years after first joint arthroplasty, while the 10 and 20-year cumulative incidences range between 29% and 45% [3-9], showing that many OA patients receive MJA.

Within MJA patients, the timeframe between arthroplasty procedures may affect the outcome after primary joint arthroplasty [10]. For instance, if a patient receives a second arthroplasty within the first year of the index (i.e. first) arthroplasty it is likely that patient reported outcomes (PROs) in the first year after surgery reflect the continued symptoms of the second arthroplasty rather than recovery after the first arthroplasty. The literature on the impact of MJA on postoperative outcomes is limited, as the majority of studies reporting outcomes after arthroplasty are performed in patients who have single joint arthroplasty (SJA), include small numbers of patients, or present information on the safety of bilateral joint arthroplasty during one single procedure. Previous studies showed that patients who have MJA or multiple joint pain sites more frequently reported worse pain, greater disability, reduced quality of life, and increased health care utilization prior to surgery [11-17]. Outcomes based on single joint arthroplasty (SJA) patients provide an over-optimistic impression of the severity of OA, and are likely not directly transferable. Therefore, not including the number of affected joints or the number of arthroplasties performed over time in an individual patient, might provide biased results [18]. Additionally, patients who have MJA have to be distinguished from patients who have single joint arthroplasty, since they are likely to belong to different phenotypes of OA.

Thus, it is important to evaluate the possibility and outcomes of additional successive arthroplasties in different joints during the follow-up of the index primary arthroplasty and to identify patient characteristics predictive of MJA. The identification of patients who have increased risks of MJA helps to provide better fitting expectation management and informed decision-making for both the individual patient and orthopaedic surgeon.

Currently, valid estimates of the yearly incidence, trajectories and time intervals between index and successive joint arthroplasties are lacking. Additionally, it is unclear whether patient characteristics and PROs differ between patients who have MJA and SJA. Therefore, the primary aim of this study was to determine the 1, 2, 5 and 10-year cumulative incidences (C_{in}) of MJA in hip and knee joints. Secondly, we calculated the mean time between index arthroplasty and subsequent arthroplasties and the (frequency of) MJA trajectories. Furthermore, we compared patient characteristics and postoperative PROs regarding function and pain between MJA and SJA patients.

MATERIALS AND METHODS

Data source

This population-based cohort study included data on primary hip and knee arthroplasties from the Dutch Arthroplasty Register (Landelijke Registratie Orthopedische Interventies (LROI)). The LROI contains data on the procedure, prosthesis, and patient characteristics of primary and revision arthroplasties. To ascertain the accurate lifespan of an arthroplasty, the death of a patient is documented in the registry through integration with Vektis (the care information center, collecting and analyzing data on costs and quality of care in the Netherlands). The registry includes arthroplasty patients from 2007 onwards and has a completeness of 99% for primary hip arthroplasties (HA) and knee arthroplasties (KA) [19].

Study population

The study population consisted of primary hip or knee arthroplasty patients in the Dutch Arthroplasty Register (LROI) between 2011 and 2020 who had a diagnosis of OA. To correctly identify index (i.e., first) joints between 2011 and 2020, the data available in the LROI between 2007 and 2011 were used. If an index joint (either hip and/or knee) was present between 2007 and 2011, patients were excluded. Furthermore, we increased the certainty of identified index joints by first verifying the index joint with the Charnley classification (A, B1, B2, C, n/a) obtained from the LROI and secondly by the record of revision surgery as the first surgery in the LROI. Using these verification methods, we increased the reliability and validity of the estimated C_{in} of MJA.

Subpopulations to investigate patient characteristics and patient-reported outcomes

To allow for sufficient follow-up time to have a MJA (i.e., 5 years), while minimizing the likelihood of a previous arthroplasty being missed in the LROI data, we used a subset of the study population to examine differences in patient characteristics and patient reported outcomes (PROs) between patients who have MJA and patients who have SJA. In this subpopulation we included all index arthroplasty joints registered in the LROI in 2015 (Figure 1). Selecting all index arthroplasties performed in 2015, patients had 5 years to ‘develop’ MJA. This time span was chosen based on previous literature in which time periods between a first and second arthroplasty of the lower extremity were assessed [3, 4].

Included population

From 2007 until 2020, 596,083 patients were registered with a primary hip or knee arthroplasty in the LROI. A total of 129,793 patients who have a previously registered arthroplasty (between 2007 and 2011) were excluded. Of the remaining 466,290 patients, 16,495 were excluded based on self-reported previous arthroplasty according to the Charnley classification. This resulted in 365,267 index arthroplasty patients who had an indication for OA (Figure 1). The mean age of the patients in the HA population was 69 (standard deviation (SD): 9.9) years old; 65% of the patients were women and had a mean BMI of 27 (SD: 4.5) (Table 1). The mean age in the knee population was 67 (SD: 9.3) years, with 62% women and a mean BMI of 29 (SD: 4.9) (Table 2).

Patient characteristics

Patients’ characteristics that were collected at the time of primary surgery were age, sex, Body Mass Index (BMI; available from 2014 onwards), current smoking status (yes/no; available from 2014 onwards), and the American Society of Anesthesiologists physical function (ASA) score as an assessment of the patient’s overall health (I – normal health to IV- severe systemic disease; considering surgery in patients who have ASA I to IV).

PROs

Data on PROs were collected using questionnaires that were filled out before surgery and postoperatively at three (HA) or six (KA) months, and one year (both HA and KA). These questionnaires included the Hip Disability and Osteoarthritis Outcome Score Short Form (HOOS-PS; 0 best to 100 worst), and the Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS; 0 best to 100 worst) and Numerical Rating Scales (NRS) for pain during rest and activities during the past 7 days, both ranging from 0 (no pain) to 10 (worst pain) [20-22]. Minimal Clinical Important Difference (MCID) for HOOS-PS and KOOS-PS was set at 10 points [23, 24]. Minimal Clinical Significant Difference for the NRS pain scores was set at 1.4 points [25].

Data analyses

All analyses, except the ordinal logistic regression on risk factors, were stratified by index joint (hip or knee). To assess the 1, 2, 5, and 10-year Cin based on the index joint, we calculated the occurrence of subsequent arthroplasties while accounting for the competing risk of death. To visualize the results, a Kaplan-Meier was plotted, and event-free survival probabilities using additional arthroplasty as the event were calculated. Furthermore, for each individual patient, the time between subsequent arthroplasties was calculated to determine the mean time intervals between arthroplasties. In addition, the number of patients who have a certain sequence of arthroplasties (e.g., left hip followed by a right hip, followed by the left knee) was calculated to assess the frequency of different MJA trajectories. Ordinal logistic regressions were performed to investigate if certain patient characteristics were associated with the number of arthroplasties. Sex (men as the reference category), age (continuous), BMI (continuous), and index joint were used as independent factors. To compare postoperative PROs in the first year after the index joint regarding function and pain between patients who had MJA and SJA, linear mixed models including a random intercept and interaction term (Timing PRO assessment * presence or absence of MJA) were performed, while adjusting for possible confounders (age, sex, BMI). All analyses were performed in R (version 3.6.3) (Posit PBC, Boston, Massachusetts, United States).

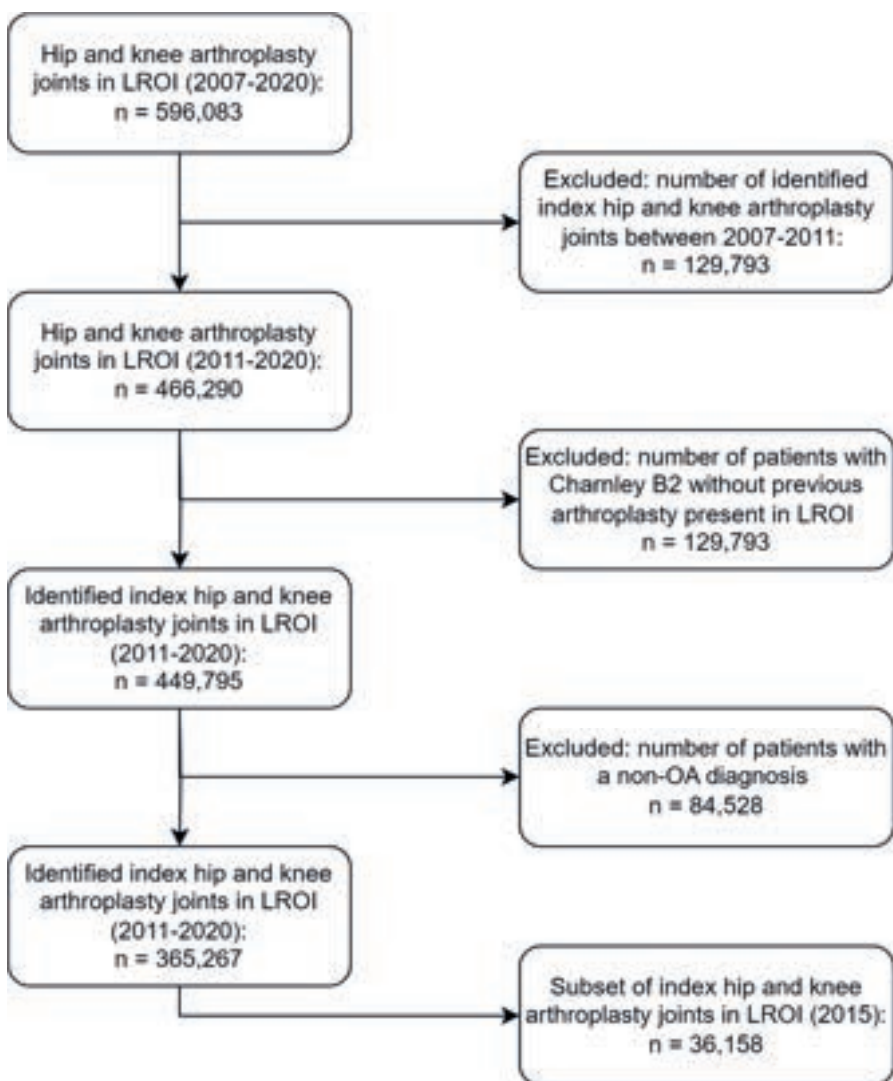


Figure 1 Flowchart of patient inclusion and exclusion

HA: Hip Arthroplasty, KA: Knee Arthroplasty, LROI: Dutch Arthroplasty Register, OA: Osteoarthritis, Charnley score B2 = presence of a self-reported previous arthroplasty

Table 1 Patient demographics of patients who have a primary index hip arthroplasty

Demographics	Number of joint arthroplasties (N = number of joint arthroplasties)				
	1 (N = 140,406)	2 (N = 37,245)	3 (N = 2,350)	4 (N = 326)	Total (N = 180,327)
Sex (%)					
Woman	88,454 (63.1)	25,763 (69.2)	1,790 (76.2)	260 (79.8)	116,267 (64.5)
N-missing	169	24	1	0	194
BMI					
Mean (SD)	27.2 (4.4)	27.5 (4.5)	29.2 (4.8)	29.0 (4.5)	27.3 (4.5)
N-missing	34708	12815	1141	182	48,846
BMI categories (%)*					
Under weight (<=18.5)	763 (0.7)	152 (0.6)	1 (0.1)	0 (0.0)	916 (0.7)
Normal weight (18.5-25)	35,885 (34.0)	7,743 (31.7)	238 (19.7)	25 (17.4)	43,891 (33.4)
Over weight (25-30)	45,129 (42.7)	10,489 (42.9)	526 (43.5)	66 (45.8)	56,210 (42.8)
Obese (30-40)	22,840 (21.6)	5,764 (23.6)	405 (33.5)	51 (35.4)	29,060 (22.1)
Morbid obese (>40)	1,081 (1.0)	282 (1.2)	39 (3.2)	2 (1.4)	1,404 (1.1)
N-missing	34708	12815	1141	182	48,846
Age					
Mean (SD)	69.5 (10.1)	67.7 (9.3)	68.0 (8.0)	66.6 (7.9)	69.1 (9.9)
N-missing	131	21	1	0	153

Legend: * BMI = Body mass index (kg/m²); BMI was recorded from 2014 onwards

SD; Standard Deviation

Table 2 Patient demographics of patients who have a primary index knee arthroplasty

Demographics	Number of joint arthroplasties (N = number of joint arthroplasties)				
	1 (N = 140,268)	2 (N = 41,802)	3 (N = 2,513)	4 (N = 357)	Total (N = 184,940)
Sex (%)					
Woman	84,274 (60.2)	27,307 (65.4)	1,851 (73.8)	272 (76.2)	113,704 (61.6)
N-missing	278	57	5	0	340
BMI					
Mean (SD)	29.3 (4.8)	30.2 (5.2)	29.6 (4.8)	29.6 (5.1)	29.4 (4.9)
N-missing	31,609	13,768	1,275	205	46,857
BMI categories (%)*					
Under weight (<=18.5)	175 (0.2)	30 (0.1)	1 (0.1)	0 (0.0)	206 (0.1)
Normal weight (18.5-25)	20,118 (18.5)	4,149 (14.8)	211 (17.0)	26 (17.1)	24,504 (17.7)
Over weight (25-30)	46,657 (42.9)	11,172 (39.9)	509 (41.1)	64 (42.1)	58,402 (42.3)
Obese (30-40)	38,779 (35.7)	11,440 (40.8)	481 (38.9)	56 (36.8)	50,756 (36.8)
Morbid obese (>40)	2,930 (2.7)	1,243 (4.4)	36 (2.9)	6 (3.9)	4,215 (3.1)
N-missing	31,609	13768	1275	205	46,857
Age					
Mean (SD)	67.6 (9.5)	66.7 (8.8)	68.3 (8.3)	66.7 (7.8)	67.4 (9.3)
N-missing	122	23	0	0	145

Legend: * BMI = Body mass index (kg/m²); BMI was recorded from 2014 onwards

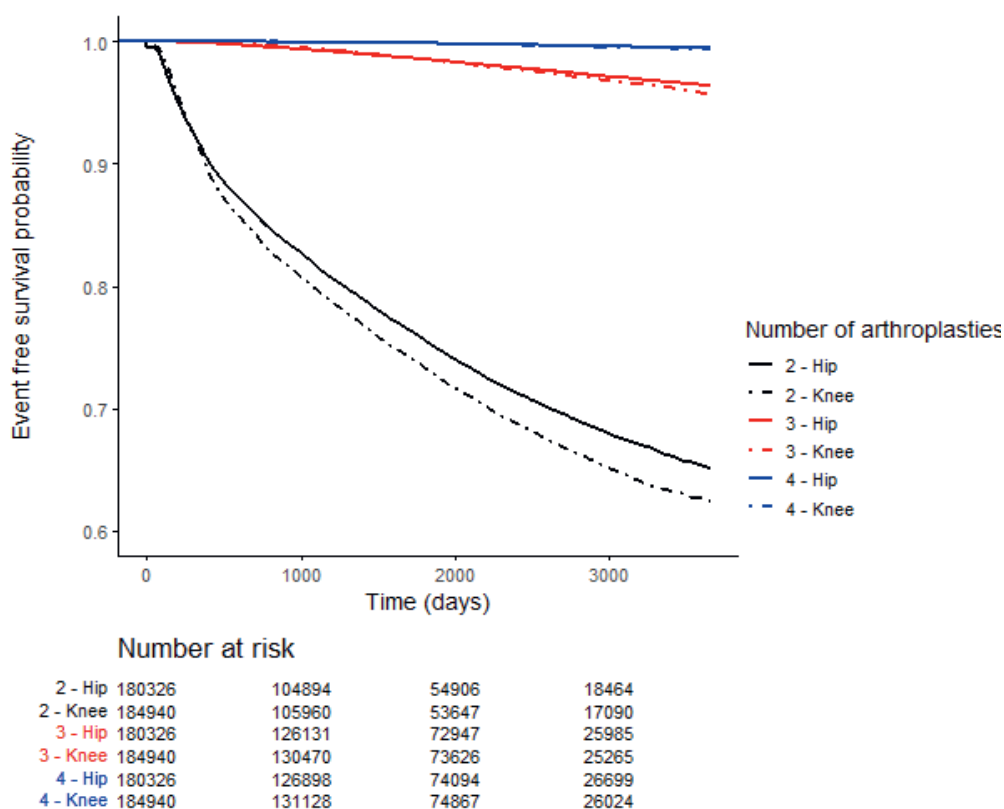
SD; Standard Deviation

RESULTS

Cumulative incidence

The 1, 2, 5, and 10-year Cin for MJA are depicted in Figure 2 and Table 3. The 10-year Cin for a second arthroplasty was 32.7% (95% CI [32.2 to 33.1]) after an index hip arthroplasty and 35.8% (95% CI [35.4 to 36.3]) after index knee arthroplasty (Figure 2 and Table 2). The 10-year Cin for > 3 and > 4 joint arthroplasties were <4% after both index hip and knee arthroplasty.

Figure 2 Cumulative incidence for 2, 3 and 4 arthroplasties



Stratified for initial joint (Hip = solid, Knee = dotdash). The 95% confidence interval was not visually distinguishable from the probability lines, it was therefore not plotted

Table 3 Multiple joint arthroplasties cumulative incidence with competing risk of death

Hip (index joint)	2+ arthroplasties	3+ arthroplasties	4 arthroplasties
Time (days)	Risk (95% CI)	Risk (95% CI)	Risk (95% CI)
1 Year (365)	8.9% (8.7% - 9.0%)	0.1% (0.1% - 0.1%)	0.01% (0% - 0.01%)
2 Years (730)	14.3% (14.1% - 14.5%)	0.4% (0.4% - 0.4%)	0.02% (0.02% - 0.03%)
5 Years (1825)	24.0% (23.74% - 24.2%)	1.4% (1.4% - 1.5%)	0.14% (0.12% - 0.16%)
10 Years (3650)	32.7% (32.2% - 33.1%)	3.2% (3.0% - 3.3%)	0.47% (0.41% - 0.54%)
Knee (index joint)	2+ arthroplasties	3+ arthroplasties	4 arthroplasties
Time (days)	Risk (95% CI)	Risk (95% CI)	Risk (95% CI)
1 Year (365)	9.5% (9.4% - 9.7%)	0.1% (0.1% - 0.1%)	0.00% (0.00% - 0.00%)
2 Years (730)	16.0% (15.9% - 16.2%)	0.3% (0.3% - 0.3%)	0.01% (0.01% - 0.02%)
5 Years (1825)	26.4% (26.1% - 26.6%)	1.5% (1.4% - 1.5%)	0.15% (0.13% - 0.17%)
10 Years (3650)	35.8% (35.4% - 36.3%)	3.8% (3.6% - 4.1%)	0.57% (0.48% - 0.65%)

Legend: 2+ arthroplasties (and 3+) is defined so that all patients receiving a second or more (and 3 or more) arthroplasties after their initial hip or knee arthroplasty are classified as having the event with a time at risk from first to subsequent arthroplasty

CI = Confidence interval

Mean time-intervals

For hip arthroplasty patients, the mean time intervals between the first and subsequent second, third, and fourth arthroplasty were 26.3 (95% CI: 26.1 to 26.7), 47.4 (95% CI: 46.4 to 48.4), and 58.3 (95% CI: 55.4 to 61.1) months, respectively. For knee arthroplasty patients these numbers were 26.1 (95% CI: 25.9 to 26.3), 51.7 (95% CI: 50.8 to 52.7), and 60.9 (95% CI: 58.3 to 63.4) months (Table 4).

Table 4 Mean time interval between arthroplasties in months

Joints	Time interval between arthroplasties (months)		
	first and second	first and third	first and fourth
Hip (index joint)			
Mean (95% CI)	26.3 (26.1 – 26.7)	47.4 (46.4 – 48.4)	58.3 (55.4 – 61.1)
Median (range)	17.5 (0 – 119.5)	44.1 (0 – 117.8)	58.7 (3.1 – 113.5)
Knee (index joint)			
Mean (95% CI)	26.1 (25.9 – 26.3)	51.7 (50.8 – 52.7)	60.9 (58.3 – 63.4)
Median (range)	16.8 (0 – 119.5)	49.9 (0.1 – 118.1)	60.3 (8.3 – 116.3)

Legend: CI = Confidence Interval

Arthroplasty trajectories

A total of 84,593 (43%) of index hip and knee patients received a second arthroplasty. Of the patients receiving a second arthroplasty, 83% received a second arthroplasty in the contralateral cognate joint (Figure 3). The group that received an arthroplasty in the contralateral cognate joint as a second arthroplasty had the lowest risk of receiving a third arthroplasty (1.53% for index HA and 1.82% for index KA). The most often followed sequence was index (e.g., HA right), cognate (e.g., HA left), noncognate contralateral (e.g., KA left), noncognate ipsilateral (e.g., KA right), or a shorter version of this path, if < 4 joint arthroplasties. Percentages for the complete path were low (0.05% for index hip and 0.02% for the index knee). Other trajectories showed no clear patterns.

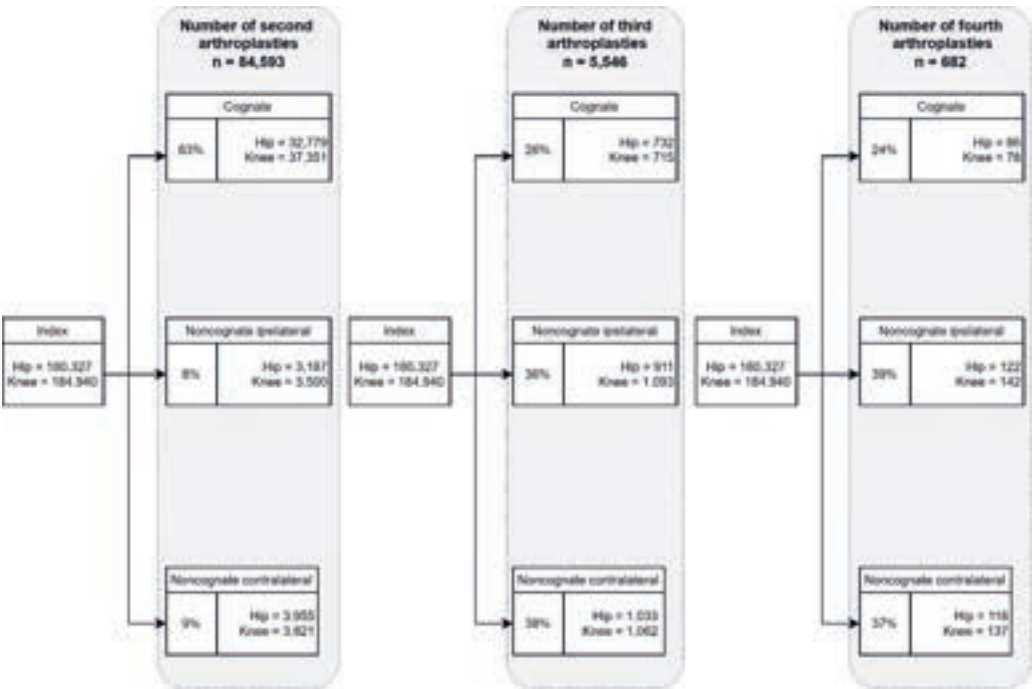


Figure 3 Arthroplasty-trajectories

Numbers in boxes represent absolute numbers of patients and percentages represent the total number of the box divided by the total number of patients who had a second, third or fourth MJA.

Patient characteristics

After analysing the patient’s characteristics, the odds of MJA significantly increased among women (OR 1.33, 95%-CI [1.3-1.4]), patients with a higher BMI (OR 1.02, 95%-CI [1.02 – 1.03]) and younger patients (OR 0.99, 95%-CI [0.98-0.99]) (Table 5).

Table 5 Association between patient characteristics and multiple joint arthroplasties

Factors	OR (95% CI)
Women	1.33 (1.3 – 1.40)
BMI	1.02 (1.02 – 1.03)
Age	0.99 (0.98 – 0.99)
Knee index joint	1.01 (1.0-1.1)
Intercepts	
1->2	2.2
2->3	41.8
3->4	381.1

Legend: OR = Odds Ratio; CI = Confidence Interval; BMI = Body Mass Index (kg/m²)

Subset 2015 subset, n = 36,158; SJA n = 26,042, MJA n = 10,116)

Patient Reported Outcomes (PROs)

A total of 36,158 joints were included in this analysis (Supplementary Table 1). Functional scores in the hip population were lower in MJA patients at 3 months (-3.3, 95% CI [-4.5 to -2.1]) and 12 months (-2.4, 95% CI [-3.6 to -1.3]) compared to SJA (Table 6). Additionally, the model including the pain scores showed that MJA patients scored lower on the NRS pain scales during activity (3 months: -0.4, 95% CI [-0.6 to -0.3]; 12 months: -0.4, 95% CI [-0.5 to -0.2]) and in rest (3 months: -0.4, 95% CI [-0.5 to -0.2]; 12 months: -0.4, 95% CI [-0.5 to -0.2]). Similar outcomes were found in the index knee population. The PROs postoperatively significantly differed between patients who had MJA and SJA; the differences were small and not clinically relevant based on the MCID.

Table 6 Difference in patient reported outcome measures (PROMs) between single and multiple joint arthroplasty patients*

		Crude		Adjusted*	
PROMs	N	Coefficients (95%CI)		N	Coefficients (95%CI)
Hip patients					
HOOS-PS	7662			7607	
Baseline		2.5 (1.6 – 3.3)			2.1 (1.3 – 3.0)
3 months postoperative		-3.3(-4.5 – -2.1)			-3.3 (-4.5 – -2.1)
12 months postoperative		-2.5 (-3.6 – -1.3)			-2.4 (-3.6 – -1.3)
Pain during activity	7844			7787	
Baseline		0.2 (0.1 – 0.3)			0.16 (0.1 – 0.3)
3 months postoperative		-0.4 (-0.6 – -0.3)			-0.4 (-0.6 – -0.3)
12 months postoperative		-0.4 (-0.5 – -0.2)			-0.4 (-0.5 – -0.2)
Pain during rest	7826			7769	
Baseline		0.3 (0.2 – 0.4)			0.2 (0.1 – 0.4)
3 months postoperative		-0.4 (-0.5 – -0.2)			-0.4 (-0.5 – -0.2)
12 months postoperative		-0.4 (-0.5 – -0.2)			-0.4 (-0.5 – -0.2)
Knee patients					
KOOS-PS	5029			5019	
Baseline		2.3 (1.2 – 3.4)			1.7 (0.6 – 2.8)
6 months postoperative		-3.5 (-5.0 – -1.9)			-3.5 (-5.0 – -1.9)
12 months postoperative		-1.8 (-3.2 – -0.4)			-1.8 (-3.2 – -0.5)
Pain during activity	3972			3962	
Baseline		0.2 (-0.0 – 0.4)			0.12 (-0.1 – 0.3)
6 months postoperative		-0.6 (-0.8 – -0.3)			-0.6 (-0.8 – -0.3)
12 months postoperative		-0.2 (-0.5 – 0.0)			-0.2 (-0.5 – -0.0)
Pain during rest	3970			3960	
Baseline		0.2 (0.0 – 0.4)			0.1 (-0.1 – 0.3)
6 months postoperative		-0.4 (-0.7 – -0.1)			-0.5 (-0.7 – -0.2)
12 months postoperative		-0.3 (-0.5 – 0.0)			-0.3 (-0.5 – -0.0)

Legend: *Adjusted for sex, age and body mass index (kg/m²) measured for index joint, with an interaction term between timing of the Patient Reported Outcome and presence or absence of MJA

CI = Confidence Interval; HOOS-PS: Hip Disability and Osteoarthritis Outcome Score Short Form

KOOS-PS: Knee Injury and Osteoarthritis Outcome Score Short Form

DISCUSSION

We investigated the cumulative incidence of MJA. We also assessed the time between the first lower joint arthroplasty and subsequent lower joint arthroplasty and the frequency of MJA trajectories. Furthermore, we compared patient characteristics and postoperative PROs between MJA and SJA patients. The results of this study showed that the 10-year cumulative incidence for a second arthroplasty (HA or KA) was 33% after an index primary HA and 36% after an index primary KA. Only a few patients received more than two arthroplasties during a 10-year period. If a patient received a second arthroplasty, it was most often the contralateral cognate joint (83%). Furthermore, the intervals between the first and second, third, and fourth arthroplasty were approximately 2 years, 4 years, and 5 years, respectively. We found that women patients who have a higher BMI and younger patients were at greater risk of receiving MJA. Also, postoperative patient-reported outcomes seemed clinically comparable between patients who have MJA and SJA.

Previous literature reported prevalence or used other time periods to assess the cumulative incidence, which makes comparison of results difficult. Espinosa et al. [3] reported that the average time interval for a second arthroplasty was 3.1 years after index knee arthroplasty and 4.0 years after index hip arthroplasty. This study showed that on average 2.2 years were between the first and subsequently second arthroplasty. Furthermore, previous studies reported 20-year cumulative incidences between 29% and 45% [3-5]. The 10-year cumulative incidences for subsequent hip and knee arthroplasty in this study were 33% in index hip and 36% in index knee patients. This corresponds to the findings of previous studies [6-9] regarding the 10-year risk of subsequent arthroplasty. Regarding the patient characteristics associated with MJA as compared to SJA, our study is in accordance with previous studies that identified various risk factors for a second arthroplasty, such as younger age, being more obese, and women [3-5, 26]. Different from this study, these studies also found that an index TKA joint was a risk factor for MJA.

Although THA and TKA are known to alleviate symptoms associated with OA, about 15 to 20% of these arthroplasty patients do not improve as expected or are unsatisfied with the results after this elective surgical procedure [27-29]. A multitude of factors have been mentioned for this, varying from preoperative

incapacitating pain with little radiological OA, to expectations on the effect of arthroplasty [28, 30, 31]. Despite the fact that multiple joint involvement in the lower extremities alongside the single joint indicated for surgery seems like an obvious factor, only a few patients have MJA. Thus, multiple joint-affected OA patients throughout a follow-up may constitute different phenotypes of patients who have a different, more inflammatory genotype of OA. Nevertheless, literature on the difference between MJA and SJA in OA patients is scarce [15, 16]. Singh et al. [15] showed that ipsilateral involvement of another lower extremity joint increases the risk of poor pain and function outcomes after THA or TKA. The study by Singh et al. [15] stresses the importance of including multiple joint involvements of the lower extremities. Although it was expected that MJA would affect outcomes, the current study only shows significantly worse outcomes in MJA patients compared to SJA patients during the first postoperative year. Nevertheless, these differences were not clinically relevant. Within the LROI, patients receive postoperative questionnaires until one year after surgery. This might explain the findings of this current study. Additionally, the present study showed that, on average, patients receive their second arthroplasty approximately 2 years after their index joint. As a result, symptoms regarding the second joint might not significantly impact the PROs of the index joint at 1-year postoperatively.

We identified the following potential limitations based on the study design: Within this study, MJA patients were identified in retrospect. Therefore, patients had to survive until their subsequent joint arthroplasty to be identified as MJA patients. This might have introduced immortal time bias, which could have diluted our results. Additionally, we did not address planned staged bilateral arthroplasty separately, as this information is not available in the Dutch Arthroplasty Register. Planned staged bilateral arthroplasties could have affected the outcomes of the PROs in the MJA group. It is therefore important that information regarding these procedures be included in future research on this topic. Also, no information was available on the stage of OA disease in the hip and knee joints, and as such, we were not able to quantify the severity of OA in the index joint and the other joints at the time of surgery.

This study provides estimates of the yearly incidence, different MJA-trajectories, and time intervals between index and successive joint arthroplasties in patients who have a HA or KA. Knowledge of these numbers is warranted to

estimate whether MJA involvement affects postoperative outcomes in registers. Taking into consideration the increased risk of successive joint arthroplasties in women, patients who have a higher BMI, and at a younger age, this provides orthopaedic surgeons and patients who have additional information regarding the possible progression of OA in the lower extremities. Hence, this information can be used in clinical practice to provide necessary information for orthopaedic surgeons as well as improve health outcomes and care processes for the patient. It aids in expectation management, thereby leading to improved postoperative outcomes, satisfaction, and quality of care.

Conclusion

The MJA patients occupy a considerable proportion of the population receiving HA or KA. Irrespective of the index joint arthroplasty, the odds of receiving MJA significantly increased among women, patients who had a higher BMI and younger age, and postoperative outcomes were slightly negatively affected by MJA. With the results of this large nationwide study, patients and physicians can be more accurately informed about the probability and possible prospects of MJA.

References

1. Hassett G, Hart DJ, Doyle DV, March L, Spector TD. The relation between progressive osteoarthritis of the knee and long term progression of osteoarthritis of the hand, hip, and lumbar spine. 2006;65(5):623-8.
2. Bijsterbosch J, Meulenbelt I, Watt I, Rosendaal FR, Huizinga TW, Kloppenburg M. Clustering of hand osteoarthritis progression and its relationship to progression of osteoarthritis at the knee. *Annals of the rheumatic diseases*. 2014;73(3):567-72.
3. Espinosa P, Weiss RJ, Robertsson O, Kärrholm J. Sequence of 305,996 total hip and knee arthroplasties in patients undergoing operations on more than 1 joint. *Acta orthopaedica*. 2019;90(5):450-4.
4. Lamplot JD, Bansal A, Nguyen JT, Brophy RH. Risk of Subsequent Joint Arthroplasty in Contralateral or Different Joint After Index Shoulder, Hip, or Knee Arthroplasty: Association with Index Joint, Demographics, and Patient-Specific Factors. *J Bone Joint Surg Am*. 2018;100(20):1750-6.
5. Sanders TL, Maradit Kremers H, Schleck CD, Larson DR, Berry DJ. Subsequent Total Joint Arthroplasty After Primary Total Knee or Hip Arthroplasty: A 40-Year Population-Based Study. *J Bone Joint Surg Am*. 2017;99(5):396-401.
6. McMahon M, Block JA. The risk of contralateral total knee arthroplasty after knee replacement for osteoarthritis. *J Rheumatol*. 2003;30(8):1822-4.
7. Sayeed SA, Sayeed YA, Barnes SA, Pagnano MW, Trousdale RT. The risk of subsequent joint arthroplasty after primary unilateral total knee arthroplasty, a 10-year study. *The Journal of arthroplasty*. 2011;26(6):842-6.
8. Sayeed SA, Trousdale RT, Barnes SA, Kaufman KR, Pagnano MW. Joint arthroplasty within 10 years after primary charnley total hip arthroplasty. *Am J Orthop (Belle Mead NJ)*. 2009;38(8):E141-3.
9. Sayeed SA, Johnson AJ, Jaffe DE, Mont MA. Incidence of contralateral THA after index THA for osteoarthritis. *Clin Orthop Relat Res*. 2012;470(2):535-40.
10. van der Pas SL, Nelissen RGHH, Fiocco M. Patients with Staged Bilateral Total Joint Arthroplasty in Registries: Immortal Time Bias and Methodological Options. *JBJS*. 2017;99(15):e82.
11. Iijima H, Fukutani N, Aoyama T, Fukumoto T, Uritani D, Kaneda E, et al. Clinical Impact of Coexisting Patellofemoral Osteoarthritis in Japanese Patients With Medial Knee Osteoarthritis. *Arthritis Care & Research*. 2016;68(4):493-501.
12. Collados-Maestre I, Lizaur-Utrilla A, Martinez-Mendez D, Marco-Gomez L, Lopez-Prats FA. Concomitant low back pain impairs outcomes after primary total knee arthroplasty in patients over 65 years: a prospective, matched cohort study. *Archives of Orthopaedic and Trauma Surgery*. 2016;136(12):1767-71.
13. Raja R, Dube B, Hensor EM, Hogg SF, Conaghan PG, Kingsbury SR. The clinical characteristics of older people with chronic multiple-site joint pains and their utilisation of therapeutic interventions: data from a prospective cohort study. *BMC musculoskeletal disorders*. 2016;17(1):194.
14. Felson DT, Niu J, Quinn EK, Neogi T, Lewis C, Lewis CE, et al. Multiple Nonspecific Sites of Joint Pain Outside the Knees Develop in Persons With Knee Pain. *Arthritis & Rheumatology*. 2017;69(2):335-42.
15. Singh JA, Lewallen DG. Ipsilateral lower extremity joint involvement increases the risk of poor pain and function outcomes after hip or knee arthroplasty. *BMC Med*. 2013;11:144.

16. Ayers DC, Li W, Oatis C, Rosal MC, Franklin PD. Patient-reported outcomes after total knee replacement vary on the basis of preoperative coexisting disease in the lumbar spine and other nonoperatively treated joints: the need for a musculoskeletal comorbidity index. *The Journal of bone and joint surgery American volume*. 2013;95(20):1833-7.
17. Perruccio AV, Power JD, Evans HM, Mahomed SR, Gandhi R, Mahomed NN, et al. Multiple joint involvement in total knee replacement for osteoarthritis: Effects on patient-reported outcomes. *Arthritis Care Res (Hoboken)*. 2012;64(6):838-46.
18. Bryant D, Havey TC, Roberts R, Guyatt G. How many patients? How many limbs? Analysis of patients or limbs in the orthopaedic literature: a systematic review. *The Journal of bone and joint surgery American volume*. 2006;88(1):41-5.
19. LROI. Research report 2021 (<https://www.lroi-rapportage.nl/>).
20. Perruccio AV, Lohmander LS, Canizares M, Tennant A, Hawker GA, Conaghan PG, et al. The development of a short measure of physical function for knee OA KOOS-Physical Function Shortform (KOOS-PS)–an OARSI/OMERACT initiative. *Osteoarthritis and cartilage*. 2008;16(5):542-50.
21. Davis A, Perruccio A, Canizares M, Tennant A, Hawker G, Conaghan P, et al. The development of a short measure of physical function for hip OA HOOS-Physical Function Shortform (HOOS-PS): an OARSI/OMERACT initiative. *Osteoarthritis and cartilage*. 2008;16(5):551-9.
22. McCaffery M. Using the 0-to-10 pain rating scale. *Am J Nurs*. 2001;101(10):81-2.
23. Çelik D, Çoban Ö, Kılıçoğlu Ö. Minimal clinically important difference of commonly used hip-, knee-, foot-, and ankle-specific questionnaires: a systematic review. *J Clin Epidemiol*. 2019;113:44-57.
24. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. A randomized, controlled trial of total knee replacement. *New England Journal of Medicine*. 2015;373(17):1597-606.
25. Kendrick DB, Strout TD. The minimum clinically significant difference in patient-assigned numeric scores for pain. *Am J Emerg Med*. 2005;23(7):828-32.
26. Santana DC, Anis HK, Mont MA, Higuera CA, Piuze NS. What is the Likelihood of Subsequent Arthroplasties after Primary TKA or THA? Data from the Osteoarthritis Initiative. *Clin Orthop Relat Res*. 2020;478(1):34-41.
27. Keurentjes JC, Fiocco M, So-Osman C, Onstenk R, Koopman-Van Gemert AW, Poll RG, et al. Patients with severe radiographic osteoarthritis have a better prognosis in physical functioning after hip and knee replacement: a cohort-study. *PloS one*. 2013;8(4):e59500.
28. Tilbury C, Haanstra TM, Leichtenberg CS, Verdegaal SH, Ostelo RW, de Vet HC, et al. Unfulfilled Expectations After Total Hip and Knee Arthroplasty Surgery: There Is a Need for Better Preoperative Patient Information and Education. *The Journal of arthroplasty*. 2016;31(10):2139-45.
29. DeFrance MJ, Scuderi GR. Are 20% of Patients Actually Dissatisfied Following Total Knee Arthroplasty? A Systematic Review of the Literature. *The Journal of arthroplasty*. 2023;38(3):594-9.
30. Tilbury C, Holtslag MJ, Tordoir RL, Leichtenberg CS, Verdegaal SH, Kroon HM, et al. Outcome of total hip arthroplasty, but not of total knee arthroplasty, is related to the preoperative radiographic severity of osteoarthritis. A prospective cohort study of 573 patients. *Acta orthopaedica*. 2016;87(1):67-71.
31. van de Water RB, Leichtenberg CS, Nelissen R, Kroon HM, Kaptijn HH, Onstenk R, et al. Preoperative Radiographic Osteoarthritis Severity Modifies the Effect of Preoperative Pain on Pain/Function After Total Knee Arthroplasty: Results at 1 and 2 Years

Postoperatively. The Journal of bone and joint surgery American volume. 2019;101(10):879-87.

Appendix

Supplementary Table 1 Demographics of the 2015 subset of patients who have single joint arthroplasty and multiple joint arthroplasties

Demographics	Count TJA (N%)* of patients			
	1 (N=26,042)	2 (N=9,470)	3 (N=578)	4 (N=68)
Sex				
Female	15805 (61%)	6300 (67%)	429 (74%)	49 (72%)
N-missing	14	4	0	0
BMI				
Mean (SD)	28.24 (5)	28.96 (5)	29.41 (5)	29.8 (5)
N-missing	297	104	14	1
BMI categories				
Under weight (<=18.5)	132 (1%)	34 (0%)	1 (0%)	0 (0%)
Normal weight (18.5-25)	6713 (26%)	2084 (22%)	98 (17%)	12 (18%)
Overweight (25-30)	11095 (43%)	3868 (41%)	242 (43%)	25 (37%)
Obese (30-40)	7283 (28%)	3092 (33%)	210 (37%)	28 (42%)
Morbid obese (>40)	522 (2%)	288 (3%)	13 (2%)	2 (3%)
N-missing **	297	104	14	1
Age				
Mean (SD)	68.41 (10)	67.23 (9)	68.48 (8)	66.2 (9)
N-missing **	15	2	0	0
Joint				
Hip	12981 (50%)	4380 (46%)	269 (47%)	33 (49%)
Knee	13061 (50%)	5090 (54%)	309 (53%)	35 (52%)
Type of prosthesis				
Total joint arthroplasty	24378 (94%)	8840 (93%)	553 (96%)	66 (97%)
Hemi-/ Uni prosthesis	1545 (6%)	600 (6%)	23 (4%)	2 (3%)
Resurfacing prosthesis	11 (0%)	2 (0%)	0 (0%)	0 (0%)
Patellofemoral prosthesis	103 (0%)	23 (0%)	0 (0%)	0 (0%)
Other	5 (0%)	1 (0%)	0 (0%)	0 (0%)
N-missing	0	4	2	0
Baseline HOOS-PS				
Mean (SD)	48.2 (18)	50.5 (18)	52.4 (19)	49.4 (26)
N-missing	21438	7849	472	56
Baseline KOOS-PS				
Mean (SD)	50.7 (15)	52.9 (15)	53.6 (16)	70.2 (31)
N-missing	23957	8682	529	66
Baseline pain during activities				
Mean (SD)	7.1 (2)	7.3 (2)	7.4 (2)	7.6 (2)
N-missing	19148	7019	416	52
Baseline pain at rest				
Mean (SD)	4.9 (3)	5.2 (3)	5.4 (3)	4.9 (3)
N-missing	19164	7026	416	52

* Or otherwise as indicated

** BMI was recorded from 2014 onwards

BMI = Body mass index (kg/m²); SD = Standard deviation; HOOS-PS = Hip Disability and Osteoarthritis Outcome Score short form; KOOS-PS = Knee Injury and Osteoarthritis Outcome Score short form



Part II

Impact of osteoarthritis and arthroplasty surgery on patients wellbeing: a regional study on associations between arthroplasty surgery and patient-perceived outcomes



Chapter 4

Perceived expectations of the outcome of total hip and knee arthroplasties and their fulfillment: differences between men and women

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ABSTRACT

The effect of sex on preoperative expectations and their fulfillment following total hip and knee arthroplasty (THA/TKA) remains unexplored. We investigated differences between men and women in perceived preoperative expectations on the outcome of THA/TKA and their fulfillment 1 year postoperatively. We performed a cohort study. Expectations were collected preoperatively and 1 year postoperatively using the Hospital for Special Surgery Hip/Knee Replacement Expectations Surveys (HSS-HRES/KRES; not applicable = 0, applicable: back to normal = 1, much = 2/moderate = 3/slight improvement = 4). Fulfillment of expectations was calculated by subtracting preoperative from postoperative scores (score < 0: unfulfilled; score ≥ 0: fulfilled). We included patients with “applicable” expectations. Chi-square and ordinal regression were used to compare expectations and fulfillment regarding sex. 2333 THA (62% women) and 2398 TKA (65% women) patients were included. 77% of THA and 76% of TKA patients completed the HSS-HRES/HSS-KRES both preoperatively and 1 year postoperatively. Men more often perceived items as “applicable”, with differences in 9/20 (HSS-HRES) and 9/19 (HSS-KRES) preoperative items and, respectively, 12/20 (HSS-HRES) and 10/19 (HSS-KRES) postoperative items. The largest differences (> 10%) were found in sexual activity and working ability. 16/20 (HSS-HRES) and 14/19 (HSS-KRES) items showed an increased probability of having higher preoperative expectations of ≥ 10%, in favor of men. In all items, 60% of the respondents indicated that their expectation was fulfilled. Differences were observed in 16/20 (HSS-HRES) and 6/19 (HSS-KRES) items in favor of men. Sex differences were present in expectations and fulfillment, with higher applicability of items, preoperative expectations and fulfillment in men, especially on items related to functional activities.

INTRODUCTION

Studies have shown that women more often suffer from hip or knee osteoarthritis (OA), and in general are known to experience more functional limitations and pain before total hip or knee arthroplasty (THA/TKA) compared to men [1, 2]. While previous literature has reported that women show similar or greater postoperative improvements in function and pain than men, women do not seem to achieve the same postoperative levels in function and pain [3–6]. Therefore, Karlson et al. [7] suggested that women might receive THA/TKA at a more advanced stage of OA.

Several explanations for sex differences in preoperative disease state and arthroplasty utilization have been explored. Possible causes could be gender bias in informed decision making, or differences in referral and recommendation of arthroplasty surgery by sex [8, 9]. Additionally, differences in perceptions and expectations between men and women could also be an underlying explanation for the differences found between men and women before and after arthroplasty surgery [7, 10].

Studies investigating to what extent sex affects preoperative expectations and their fulfillment after hip and knee arthroplasty surgery are scarce. Previous literature suggests that female sex is a predictor of lower preoperative expectations on treatment outcomes [7, 11, 12]. Although studies on hip and knee arthroplasties did not investigate differences in specific expectation domains or items between men and women, one study on shoulder arthroplasty did [13]. They found that men were more focused on participation in sports and maintaining their employment, while women valued the ability to independently perform household chores and daily routine most. Studies in joint arthroplasty surgery population show that men mainly focus on activities achievable after surgery, while women are more concerned about the inability to perform basic functional activities after surgery [7, 11–14].

With regard to the fulfillment of the preoperative expectations, Harmsen et al. [15] and Tilbury et al. [16] showed that almost 50% of THA/TKA patients had unfulfilled expectations of certain functional outcomes, but did not go into detail whether sex affected these expectations. Two other studies indicate that male sex is associated with higher fulfillment of expectations [17, 18]. However, none of the studies specified the areas in which preoperative expectations or fulfillment differ

between men and women. When orthopedic surgeons want to target expectations and fulfillment in expectations, focusing on differences as a result of sex can be helpful in educating and managing expectations [19].

Since available evidence on sex differences on expectations and fulfillment after THA/TKA is scarce, we performed a large observational cohort study. The aim of this study was to investigate differences between men and women in perception of preoperative expectations on outcome of THA/TKA and their fulfillment 1 year postoperatively. Insight into the perception of men and women could improve the preoperative expectation management and shared decision-making process, thereby improving clinical outcomes.

MATERIALS AND METHODS

Study design

Consecutive patients undergoing primary THA/TKA as a result of OA were included (June 2012-December 2018) from the ongoing multicenter cohort [Longitudinal Leiden Orthopaedics and Outcomes of OsteoArthritis Study (LOAS), Trial-ID NTR3348] [20]. Patients with an indication for THA/TKA in seven hospitals were included (Leiden University Medical Center; Alrijne Hospital Leiden/Leiderdorp; Waterland Hospital; Albert Schweitzer Hospital; LangeLand Hospital; Groene Hart Hospital; Reinier de Graaf Hospital).

Patient recruitment

Patients eligible for the LOAS were 18 years or older and able to read and complete the Dutch questionnaires. Patients were excluded if the index procedure was revision hip/knee arthroplasty or if the patient had a diagnosis other than OA. Patients receiving a revision of their primary index arthroplasty within the first year were not excluded. After providing informed consent, questionnaires were filled out preoperatively and 1 year after surgery. The current study population consisted of patients who answered at least one item of the validated Dutch versions of the Hospital for Special Surgery Hip or Knee Replacement Expectations Survey (HSS-HRES/HSS-KRES) prior to surgery. Missing information in any of the other questionnaires was not an exclusion criterion.

Sociodemographic and clinical characteristics

The following preoperative sociodemographic characteristics were extracted from medical files: sex, age (years), body mass index (BMI) and current smoking status (yes/no). Prior to surgery, information regarding living situation (living alone (yes/no)) and work status (paid work (yes/no); among patients below the Dutch retirement age of 67 years old) was collected using questionnaires. To describe clinical characteristics of the patients, patient-reported outcome measures (PROMs) were gathered preoperatively. Validated Dutch versions of the Hip disability or Knee injury and Osteoarthritis Outcome Score (HOOS/KOOS) were used to assess OA-related problems on five domains: pain, symptoms, function in daily living, function in sports and recreation, and hip or knee-related quality of life (QoL) (score of 100 representing the best possible outcome, 0 meaning the worst outcome; with minimal clinical important differences ranging between 6 and 9) [21, 22]. The Physical and Mental Component Summary of the Short Form-12 (PCS-12 and MCS-12) were used to collect information on the physical and mental health status of the patient (ranging from 0 to 100, with higher scores representing better health) [23]. Preoperative information on comorbidity was collected using the comorbidity questionnaire of the Dutch Central Office of Statistics (CBS) [24]. Both musculoskeletal and non-musculoskeletal comorbidities were dichotomized (yes/no).

Expectations

Expectations were measured preoperatively and 1 year postoperatively using validated Dutch versions of HSS-HRES and HSS-KRES. Validated Dutch versions of the questionnaires are included in Supplement A [25]. The HSS-HRES contains 20 items and the HSS-KRES 19 items, obtaining patients' expectations regarding postoperative pain, function, activities and psychological well-being (item is expected: to get back to normal = 1, show much = 2/moderate = 3/slight improvement = 4, or not applicable = 0). One year postoperative, patients received the HSS-HRES/KRES and were asked to report the perceived actual outcome of the items from the preoperative questionnaire (went back to normal = 1, much = 2/moderate = 3/slight improvement = 4, and not applicable = 0). Both not applicable (NA) and missing values were coded as 0. An item was "applicable" if a patient reported 'back to normal' or

‘much/moderate/slight improvement’. Only patients that reported an item as “applicable” were included in the analysis to compare expectations. Fulfillment of expectations was determined 1 year postoperative based on the methods used in the study of Tilbury et al. [16]: subtracting the preoperative score from the postoperative score (score < 0: unfulfilled; score ≥ 0: fulfilled; patients with exceeded expectations were also categorized as ‘fulfilled’). When a patient answered “not applicable”(NA) or did not answer an item in either the preoperative or postoperative questionnaire or both, a fulfillment of expectation score was not calculated for that item.

Additionally, preoperative scores were transformed to a ‘total expectation score’, ranging from 0 to 76, which was recoded to a 0–100 scale (lowest to highest expectations, respectively). To calculate a total score, ≤ 2 items were allowed to be NA/missing. If more than 2 items were NA/missing, we did not calculate a total score for that patient.

Statistics

All analyses were stratified by joint (hip/knee). Descriptive statistics were used for the patients’ preoperative characteristics. To assess the presence of potential bias due to dropout, baseline characteristics of patients with and without preoperative expectations were compared by the independent Student’s T test (if continuous) or Chi-square test (if categorical) (Supplementary table 1-A). The same tests were performed to identify possible differences in patient characteristics between men and women. After calculating postoperative fulfillment of expectations for each item, frequencies were reported for both THA and TKA patients. “Applicability” of items and postoperative fulfillment of expectations was compared by Chi-square tests to study the similarity of proportions between men and women. Preoperative expectations were compared using ordinal regression, presented as odds ratios (OR) with corresponding 95% confidence intervals (CI; CI lower limit; upper limit) with sex as the determinant and the different items on the HSS-HRES or HSS-KRES as outcome. To our knowledge variables causing both sex and affecting expectations are non-existent. Therefore, in case of our research question, all adjustments would lead to non-preferable adjustments within the causal pathway (Supplement B). As such, analyses performed in this study were not

adjusted. Currently, there are no proportions defined for the HSS-HRES and HSS-KRES to discriminate differences between populations. However, to be able to indicate differences between men and women in this study, apart from statistical testing, we reported all differences of $\geq 5\%$ and $\geq 10\%$ between men and women for all items among applicability and fulfillment of expectations to provide additional guidance while reading the most important results. Additionally, we defined $OR \geq 1.1$ (indicating a difference in probability of $\geq 10\%$ between men and women) to indicate larger differences in preoperative expectations between men and women. $OR > 1$ indicated lower preoperative expectations among women, as the highest score represents the lowest value in the HSS-HRES/KRES. Analyses were performed using SPSS version 25.0 (Chicago, IL).

RESULTS

Response

Of the 2570 THA and 2592 TKA patients who were eligible for participation in the study period, 2333 THA (91%) and 2398 TKA (93%) patients filled in the HSS-HRES/KRES questionnaire before surgery and were included. 1878 THA (73%) and 1887 TKA (73%) patients completed both the preoperative and 1 year postoperative questionnaires and were included in the analysis of fulfillment of expectations (Fig. 1). Both the THA and TKA study populations were on average slightly younger, with more comorbidities and better mental health compared to patients without preoperative HSS-HRES/KRES. Additionally, the THA study population was more likely to be employed (Supplementary Table 1-A). We did not find any clinically relevant differences between the populations with HSS-HRES/KRES measurements at both time points compared to the population with only a preoperative HSS-HRES/KRES measurement (Supplementary Table 1-B).

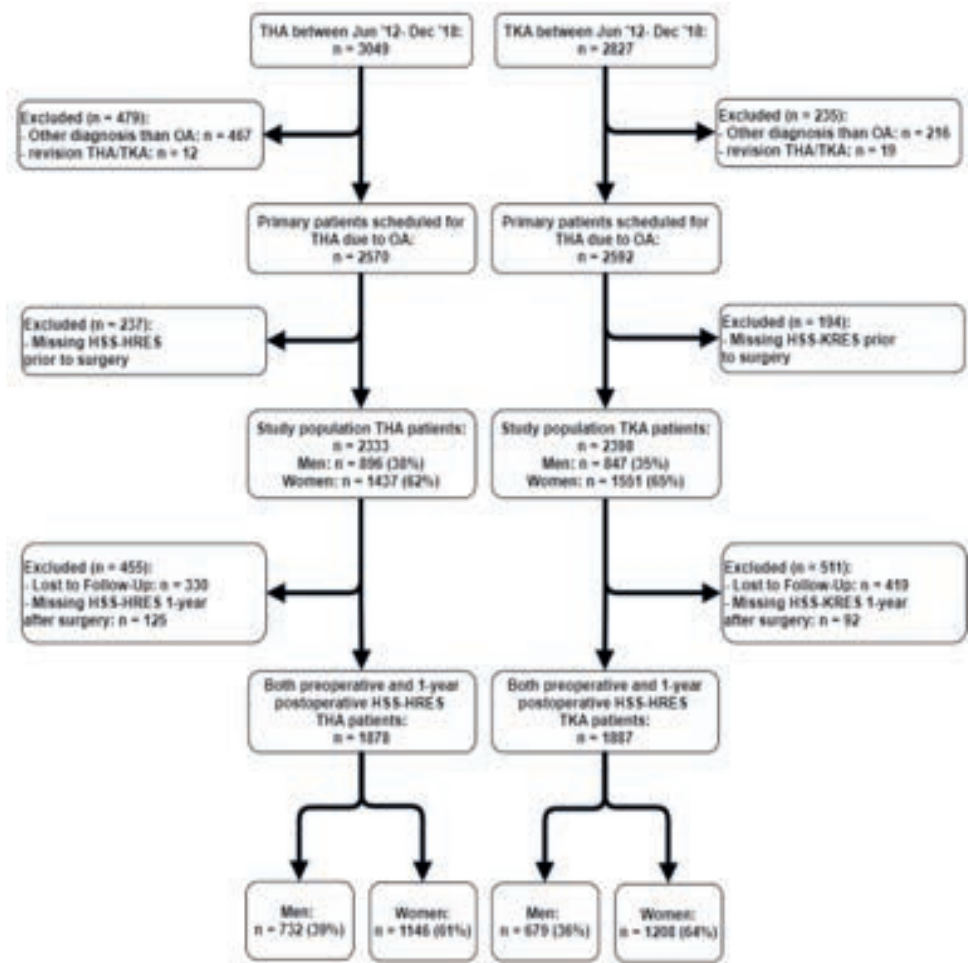


Figure 1 Flowchart of patient selection. Legend: THA total hip arthroplasty, TKA total knee arthroplasty, OA osteoarthritis, HSS-HRES Hospital for Special Surgery Hip Replacement Expectations Survey, HSS-KRES Hospital for Special Surgery Knee Replacement Expectations Survey

The characteristics of the study population stratified by sex are shown in Table Table1. Both the THA and TKA groups have a higher proportion of women (62% of THA and 65% of TKA group). Women were slightly older, suffered more often from comorbidities, reported significantly, but not clinically relevant more OA-related problems (based on lower scores on the HOOS/KOOS subscales), more often lived alone, and were less often employed compared to men. Additionally, women in the TKA population had higher BMI scores than men (30 (5) versus 29 (5)).

Table 1 Preoperative characteristics of patients

		THA		TKA	
		Men (n = 896)	Women (n = 1,437)	Men (n = 847)	Women (n = 1,551)
Age, mean (SD) (years)		68 (9)	69 (9)	67 (8)	68 (9)
BMI, mean (SD)		28 (4)	27 (5)	29 (5)	30 (5)
Smoking, yes, n (%)		58 (7)	78 (5)	53 (6)	78 (5)
Missing		201 (22)	345 (24)	188 (22)	384 (25)
Comorbidities, n (%)	Non-musculoskeletal	294 (33)	395 (28)	353 (42)	533 (34)
	Musculoskeletal	107 (12)	183 (13)	79 (9)	135 (9)
	Both	295 (33)	569 (40)	208 (25)	564 (36)
	None	81 (9)	86 (6)	114 (14)	131 (8)
	Missing	119 (13)	204 (14)	93 (11)	188 (12)
Work status, employed, n (%)		299 (34)	259 (18)	275 (32)	282 (18)
Missing		8 (1)	17 (1)	10 (1)	18 (1)
Type of work, n (%)	Physical	50 (174)	55 (21)	67 (24)	73 (26)
	Mental	105 (25)	90 (35)	83 (30)	67 (24)
	Both	122 (41)	107 (41)	115 (42)	139 (49)
	Missing	22 (7)	7 (3)	10 (4)	3 (1)
Living alone, yes, n (%)		96 (11)	406 (30)	85 (10)	428 (28)
Missing		44 (5)	97 (7)	53 (6)	105 (7)
Preoperative HOOS/KOOS Score, mean (SD)**	Pain	43 (18)	36 (18)	43 (17)	37 (17)
	Symptoms	44 (19)	38 (18)	54 (18)	48 (18)
	Daily Living	45 (19)	38 (19)	50 (19)	43 (18)
	QoL	20 (20)	16 (19)	29 (16)	25 (15)
	Sports	31 (17)	27 (16)	15 (17)	8 (13)
SF-12, mean (SD)	PCS	33 (10)	31 (9)	34 (9)	31 (9)
	Missing, n (%)	67 (7)	151 (11)	57 (60)	170 (11)
	MCS	55 (10)	53 (11)	56 (9)	54 (10)
	Missing, n (%)	67 (7)	151 (11)	57 (6)	170 (11)
Preoperative expectations, mean (SD)		82 (19)	78(19)	72 (18)	69 (18)
Missing, n (%)		30 (3)	77 (5)	10 (1)	26 (2)

Legend: **: HOOS/KOOS scores are complete for approximately 75% of patients, as it was replaced with the HOOS-PS/KOOS-PS after January 2017

Note: THA: total hip arthroplasty; TKA: total knee arthroplasty; HOOS: Hip Disability and Osteoarthritis Outcome Score; KOOS: Knee Injury and Osteoarthritis Outcome Score; SF-12: Short form-12 survey; PCS: component score for physical health score; MCS: component score for mental health score

Comparisons of preoperative expectations

The proportion of patients scoring individual items as applicable varied considerably. Expectations related to work, sexual activity, psychological well-being and no need for a cane, crutch or walker were relatively less often considered as “applicable” (Supplementary Tables 2-A and 2-B) in both hip and

knee populations. As for THA patients, men and women showed a differences in proportions of $\geq 5\%$ in “applicability” on four items, with only the item eliminate the need for pain relief medication higher among women (Supplementary Table 2-A). Nevertheless, only the items sexual activity and return to work showed a difference in the proportion of $\geq 10\%$ in reporting an item as “applicable”, in favor of men. 9/20 items showed a difference between men and women regarding applicability. Overall, we found differences of $\geq 10\%$ (OR ≥ 1.1) in the probability of having higher preoperative expectations, in favor of men in 16/20 HSS-HRES items (Table 2).

In the TKA population, men and women showed a difference in the proportions of $\geq 5\%$ in five items regarding “applicable” (Supplementary Table 2-B). Similar to the THA population, expectations of sexual activity and return to work showed differences in proportions of $\geq 10\%$ in favor of men. On 9/19 items, applicability was different between men and women. Overall, we found differences of $\geq 10\%$ (OR ≥ 1.1) in the probability of having higher preoperative expectations, in favor of men in 14/19 HSS-KRES items (Table 3). In general, men had higher expectations compared to women.

Table 2 Total Hip Arthroplasty (THA): Preoperative Expectations using the HSS-HRES

	Applicable†		Back to normal (%)		Much Improved (%)		Moderately Improved (%)		Slightly Improved (%)		OR [95% CI]*
	♂, n	♀, n	♂	♀	♂	♀	♂	♀	♂	♀	
Relief of pain during the day	749 (98)	1,230 (99)	65	64	31	31	3	4	1	1	1.1 [0.9 – 1.4]
Relief of pain during sleeping	807 (93)	1,304 (96)	74	69	21	27	3	4	2	1	1.3 [1.0 – 1.5]
Improve walking ability											
Short distances (in house)	829 (98)	1,262 (98)	73	70	23	26	3	4	2	1	1.2 [1.0 – 1.5]
Middle-long distances (<1.5 km)	826 (97)	1,252 (97)	52	59	33	32	13	7	3	2	1.2 [1.0 – 1.4]
Long distances (>1.5 km)	808 (94)	1,206 (93)	52	49	33	33	13	13	3	6	1.2 [1.0 – 1.4]
No need for cane, crutch or walker	624 (72)	987 (71)	88	84	8	9	3	4	1	2	1.4 [1.0 – 1.8]
Ability to stand better	833 (95)	1,320 (94)	78	75	18	20	3	5	1	1	1.2 [0.9 – 1.4]
Getting rid of limp	813 (92)	1,258 (90)	77	77	21	18	2	4	1	1	1.0 [0.8 – 1.2]
Walking stairs	837 (95)	1,318 (94)	73	70	23	23	4	5	1	2	1.2 [1.0 – 1.4]
Getting out of bed, chair or car	851 (97)	1,388 (99)	72	71	23	24	3	5	1	1	1.1 [0.9 – 1.3]
Eliminate need for pain relief medication	662 (75)	1,175 (84)	87	81	10	14	2	4	2	1	1.5 [1.1 – 1.9]
Be able to put on shoes and socks	797 (90)	1,236 (88)	81	80	15	15	2	4	2	2	1.0 [0.8 – 1.3]
Be able to do paid work	319 (37)	282 (21)	88	89	9	7	2	3	2	2	1.1 [0.7 – 1.7]
Join recreational activities (dancing, going out on trips)	703 (80)	1,087 (78)	73	70	21	23	4	6	2	1	1.2 [1.0 – 1.5]
Improve ability to perform daily activities in and around the house	828 (94)	1,346 (96)	73	71	22	21	3	6	1	2	1.2 [1.0 – 1.5]
Improve ability to do sports	749 (85)	1,116 (84)	56	59	36	31	6	9	2	2	0.9 [0.8 – 1.1]
Ability to cut toenails	773 (88)	1,190 (85)	67	69	24	22	6	6	3	3	1.0 [0.8 – 1.2]
Social life	746 (85)	1,128 (81)	76	71	18	21	6	6	1	2	1.4 [1.1 – 1.6]
Sexual activity	640 (73)	820 (59)	79	76	13	16	5	6	3	1	1.2 [0.9 – 1.5]
Psychological well-being	610 (70)	853 (61)	83	78	11	14	4	5	2	3	1.5 [1.1 – 1.9]

Legend: ‡ Preoperative expectations proportions based on patients that reported preoperative items as “applicable”; more information on preoperative “Not Applicable”/“Applicable” population in Supplementary table 2-A *Comparison of preoperative expectations in men and women by means of ordinal logistic regression (presented as Odds Ratio (OR) with corresponding 95% Confidence Interval (95% CI); men as reference category); with OR>1 indicating lower preoperative expectations among women as a higher HSS-HRES score indicates a lower expectation

Note: HSS-HRES: Hospital For Special Surgery Hip Replacement Expectations Survey; ♂: Men; ♀: Women

Table 3 Total Knee Arthroplasty (TKA): Preoperative Expectations using the HSS-KRES

	Applicable†		Back to normal (%)		Much Improved (%)		Moderately Improved (%)		Slightly Improved (%)		OR [95% CI]*
	♂, n	♀, n	♂	♀	♂	♀	♂	♀	♂	♀	
Relief of pain during the day	823 (99)	1,479 (99)	49	50	46	44	4	6	1	1	1.0 [0.9-1.2]
Improve walking ability											
Short distances (in house)	740 (98)	1,320 (99)	58	58	37	35	3	6	2	1	1.0 [0.9 – 1.2]
Middle-long distances (<1.5 km)	746 (98)	1,318 (97)	48	44	42	42	9	12	2	2	1.2 [1.0 – 1.4]
Long distances (>1.5 km)	764 (96)	1,272 (92)	38	37	45	43	12	15	5	6	1.2 [1.0 – 1.4]
No need for cane, crutch or walker	530 (65)	1,036 (70)	86	83	10	12	2	4	1	2	1.1 [0.9 – 1.5]
Be able to stretch the knee	773 (93)	1,426 (95)	65	62	30	30	4	7	2	1	1.1 [1.1 – 1.3]
Improve walking upstairs	810 (97)	1,465 (97)	59	56	34	34	5	9	2	2	1.2 [1.0 – 1.4]
Improve walking downstairs	808 (97)	1,459 (97)	58	56	36	34	5	8	1	2	1.1 [1.0 – 1.4]
Being able to kneel down	794 (96)	1,390 (92)	31	30	46	37	16	19	7	15	1.3 [1.1 – 1.6]
Being able to squat	791 (96)	1,388 (93)	29	28	45	37	19	21	7	15	1.3 [1.1 – 1.6]
Being able to travel by public transportation (bus, tram or train)	569 (69)	1,128 (75)	74	67	21	22	4	8	1	3	1.4 [1.1 – 1.7]
Be able to do paid work	287 (36)	342 (24)	79	81	15	14	2	3	3	2	0.8 [0.6 – 1.2]
Join recreational activities (dancing, going out on trips)	688 (83)	1,185 (79)	57	55	33	33	8	8	2	3	1.0 [0.9 – 1.3]
Improve ability to perform daily activities in and around the house	743 (89)	1,361 (90)	74	71	19	21	5	7	2	2	1.2 [1.0 – 1.4]
Improve ability to do sports	720 (86)	1,223 (81)	40	42	44	41	13	14	2	4	1.0 [0.8 – 1.1]
Being able to change positions (getting up, sitting down)	797 (95)	1,450 (96)	59	57	34	33	5	9	2	2	1.1 [0.9 – 1.3]
Social life	679 (82)	1,212 (80)	61	58	32	31	6	8	1	3	1.2 [1.0 – 1.4]
Sexual activity	557 (68)	751 (51)	72	68	17	20	7	9	4	3	1.2 [0.9 – 1.5]
Psychological well-being	516 (62)	872 (58)	73	69	17	20	7	7	4	5	1.3 [1.0 – 1.6]

Legend: ‡ Preoperative expectations proportions based on patients that reported preoperative items as “applicable”; more information on preoperative “Not Applicable”/“Applicable” population in Supplementary table 2-B *Comparison of preoperative expectations in men and women by means of ordinal logistic regression (presented as Odds Ratio (OR) with corresponding 95% Confidence Interval (95% CI); men as reference category); with OR>1 indicating lower preoperative expectations among women as a higher HSS-HRES score indicates a lower expectation

Note: HSS-KRES: Hospital For Special Surgery Knee Replacement Expectations Survey; ♂: Men; ♀: Women

Fulfillment of expectations

Tables 4 and 5 show an overview of the applicability and fulfillment of expectations 1 year after surgery. In the THA population, 7/20 HSS-HRES items showed $\geq 5\%$ difference in the proportions of “applicability” between men and women, of which 6 items had higher proportions among men than women (Table 4). Similar to the preoperative results, the item ability to do work showed a difference in prevalence of $\geq 10\%$ in favor of men (83% vs 70%). 12/20 items showed a difference between men and women regarding applicability. All items were fulfilled in $\geq 60\%$ of men, and on 18/20 HSS-HRES items, $\geq 60\%$ of women reported fulfilled expectations. The following expectations were most often fulfilled: be able to do paid work (men: 91%; women: 88%) and no need for a cane, crutch or walker (men: 85%; women: 78%). Although the majority of all patients had fulfilled their expectations on the HSS-HRES items, the proportion of men with fulfilled expectations was higher on all items. 18/20 HSS-HRES items showed a difference in proportions of $\geq 5\%$, in favor of men, in the proportion of fulfilled expectations, and $\geq 10\%$ differences in walking stairs and sexual activity (Table 4).

In the TKA population, 7/19 HSS-KRES items showed $\geq 5\%$ difference in proportion “applicable” when comparing men and women, with higher proportion of “applicable” rates among men, which included mainly functionally related expectations (Table 4). On 10/19 items, applicability was different between men and women. The majority of items of the HSS-KRES had a proportion of $\geq 60\%$ with fulfilled expectations: 17/19 items among men and 15/19 among women. In accordance with the THA population, the items be able to do paid work (men: 85%; women: 78%) and no need for a cane, crutch or walker (men: 85%; women: 80%) were most often fulfilled expectations. Overall, men had a larger proportions of fulfilled expectations on 15 items than women. Additionally we found $\geq 5\%$ difference, in favor of men, in the proportion of fulfilled expectations on ten items between men and women, which were mainly functionally related (Table 5).

Table 4 Total Hip Arthroplasty (THA): Fulfillment of preoperative expectations 1 year after surgery

	Applicable†				95% CI*	Fulfilled		95% CI*
	♂, n	♀, n	♂, n (%)	♀, n (%)		♂, %	♀, %	
Relief of pain during the day	579	907	552 (95)	860 (95)	0.69 – 1.49	74	68	0.60 – 0.96
Relief of pain during sleeping	594	903	559 (94)	853 (95)	0.97 – 1.70	76	70	0.57 – 0.92
Improve walking ability								
Short distances (in house)	645	928	629 (98)	891 (96)	0.50 – 1.13	77	71	0.55 – 0.88
Middle-long distances (<1.5 km)	638	901	604 (95)	806 (90)	0.40 – 0.75	72	65	0.60 – 0.94
Long distances (>1.5 km)	624	872	558 (89)	731 (84)	0.50 – 0.80	68	61	0.58 – 0.93
No need for cane, crutch or walker	477	717	338 (68)	488 (68)	0.75 – 1.08	85	78	0.43 – 0.88
Ability to stand better	648	983	617 (95)	892 (93)	0.59 – 1.05	76	68	0.53 – 0.83
Getting rid of limp	629	937	577 (92)	921 (87)	0.43 – 0.77	74	68	0.43 – 0.67
Walking stairs	655	982	627 (96)	814 (91)	0.52 – 0.83	72	59	0.61 – 0.97
Getting out of bed, chair or car	660	1,044	640 (97)	985 (94)	0.69 – 1.41	68	62	0.63 – 0.96
Eliminate need for pain relief medication	513	880	313 (61)	591 (67)	1.22 – 1.77	84	76	0.42 – 0.86
Be able to put on shoes and socks	621	931	585 (94)	866 (93)	0.59 – 0.95	71	67	0.67 – 1.06
Be able to do paid work	319	283	264 (83)	199 (70)	0.30 – 0.46	91	88	0.42 – 1.38
Join recreational activities (dancing, going out on trips)	556	827	451 (81)	605 (73)	0.56 – 0.82	74	69	0.58 – 1.00
Improve ability to perform daily activities in and around the house	652	1,021	610 (94)	929 (91)	0.69 – 1.19	72	63	0.53 – 0.82
Improve ability to do sports	589	847	490 (83)	666 (79)	0.56 – 0.82	68	64	0.67 – 1.09
Ability to cut toenails	600	910	532 (89)	750 (82)	0.52 – 0.79	64	55	0.55 – 0.86
Social life	599	850	517 (86)	701 (83)	0.55 – 0.82	79	72	0.53 – 0.91
Sexual activity	504	631	403 (80)	477 (76)	0.45 – 0.64	83	72	0.38 – 0.73
Psychological well-being	477	637	417 (87)	524 (83)	0.51 – 0.73	83	75	0.43 – 0.83

Legend:

† Fulfillment of preoperative expectations proportions based on patients that reported both preoperative and postoperative items as “applicable”

*Comparison of fulfillment of expectations in men and women by means of Chi-square test, with corresponding 95% Confidence Interval(CI)

Note: HSS-HRES: Hospital For Special Surgery Hip Replacement Expectations Survey; ♂: Men; ♀: Women

Table 5 Total Knee Arthroplasty (TKA): Fulfillment of preoperative expectations 1 year after surgery

	Applicable†				95% CI*	Fulfilled		95% CI*
	♂, n	♀, n	♂, n (%)	♀, n (%)		♂, %	♀, %	
Relief of pain during the day	629	1,102	603 (96)	1,053 (96)	0.72 – 1.55	67	65	0.72 – 1.10
Improve walking ability								
Short distances (in house)	560	925	545 (97)	896 (97)	0.80 – 1.75	73	66	0.59 – 0.94
Middle-long distances (<1.5 km)	564	930	531 (94)	843 (91)	0.49 – 0.91	67	63	0.66 – 1.04
Long distances (>1.5 km)	579	910	518 (90)	771 (85)	0.43 – 0.70	66	61	0.65 – 1.03
No need for cane, crutch or walker	377	750	220 (58)	461 (62)	1.04 – 1.54	85	80	0.45 – 1.06
Be able to stretch the knee	598	1,070	573 (94)	1,015 (95)	0.86 – 1.48	75	77	0.91 – 1.46
Improve walking upstairs	624	1,106	597 (96)	1,040 (94)	0.60 – 1.14	66	58	0.57 – 0.87
Improve walking downstairs	629	1,101	601 (96)	1,025 (93)	0.56 – 1.04	62	56	0.62 – 0.94
Being able to kneel down	607	1,024	524 (86)	760 (74)	0.37 – 0.58	49	42	0.60 – 0.94
Being able to squat	611	1,033	526 (86)	792 (77)	0.42 – 0.66	54	49	0.65 – 1.01
Being able to travel by public transportation (bus, tram or train)	429	834	346 (81)	631 (76)	0.90 – 1.30	80	76	0.57 – 1.08
Be able to do paid work	287	342	224 (78)	244 (71)	0.42 – 0.64	85	78	0.68 – 1.93
Join recreational activities (dancing, going out on trips)	529	879	436 (82)	669 (76)	0.57 – 0.84	76	63	0.42 – 0.72
Improve ability to perform daily activities in and around the house	573	1,009	539 (94)	965 (96)	0.87 – 1.42	78	73	0.59 – 0.97
Improve ability to do sports	559	933	442 (79)	702 (75)	0.60 – 0.88	67	65	0.70 – 1.15
Being able to change positions (getting up, sitting down)	616	1,103	581 (94)	1,038 (94)	0.76 – 1.35	65	64	0.78 – 1.19
Social life	522	919	449 (86)	757 (84)	0.68 – 1.01	73	68	0.63 – 1.06
Sexual activity	429	570	330 (77)	419 (74)	0.43 – 0.62	76	77	0.75 – 1.49
Psychological well-being	401	646	337 (84)	510 (79)	0.61 – 0.88	80	77	0.62 – 1.22

Legend: † Fulfillment of preoperative expectations proportions based on patients that reported both preoperative and postoperative items as “applicable”

*Comparison of fulfillment of expectations in men and women by means of Chi-square test, with corresponding 95% Confidence Interval(CI)

Note: HSS-KRES: Hospital For Special Surgery Knee Replacement Expectations Survey; ♂: Men; ♀: Women

DISCUSSION

The most important finding of this study was that men and women have different perceptions of preoperative expectations regarding outcome of THA or TKA. One year after THA or TKA, they differ in their fulfillment of expectations. More items are perceived as applicable to men than women, in particular in terms of sexual activity and ability to work (difference in prevalence > 10%). Other items showed only small differences in the score “applicable”. Men reported higher preoperative expectations related to the ability to perform functional activities compared to women, and men more often fulfilled their preoperative expectations 1 year after THA and TKA than women.

As previously reported, men more often report that the item regarding sexual activity applies to them [15]. In addition, men more often report that the item being able to do paid work applied to them. In our population, women more often live alone and are less often employed, which could partly explain these differences. Elderly people who live alone more often tend to report a lower frequency of sexual activity and consider it less important than people living with a spouse [26]. In addition, men and women have different preoperative expectations on several items of the HSS-HRES and HSS-KRES. Men are more likely to expect to return to normal in terms of pain relief and the ability to perform basic functional activities, while women expect moderate to much improvement in these items. The latter is in accordance with the results of other studies in OA patients after a THA or TKA [11, 12]. Some authors suggest that these differences in preoperative expectations could be related to the fact that women are more likely to opt for OA treatment at a later stage of the disease, possibly because they are more afraid of TKA/THA surgery and suffer from OA pain for longer than men [7].

Our findings on the fulfillment of expectations in terms of sex are in line with other studies [16, 17]. The high proportion of fulfilled expectations on the item no need for a cane, crutch or walker could be explained by the improved functional status and walking ability in many patients after THA and TKA [27]. Furthermore, many patients are fulfilled with the expectation be able to do paid work. This can be explained by the previously established association between patients’ beliefs and preoperative expectations and return to work after surgery [28]. With regard to unfulfilled expectations, we find that the expectation of the

ability to cut toenails is often unfulfilled after THA, with percentages ranging from 64 to 55% in men and women. Items with a high proportion of unfulfilled expectations among TKA patients were: the ability to kneel or squat, and walking up and downstairs [16]. Studies addressing the effect of sex on fulfillment of expectations after THA or TKA are scarce. Previous studies [17, 29] show that women less often experience fulfillment in expectations 1 year postoperatively, but failed to include the specific items in which differences are present. Furthermore, unfulfilled expectations are known to be a principal source of patient dissatisfaction [30]. In addition to this finding, other specialties within medicine have identified sex as an independent predictor for unsatisfactory outcomes 1 year after surgery, such as patients with sciatica [31].

Our findings are in accordance with previous studies that suggest women have a worse preoperative disease state. For instance they score worse on function and pain [3]. Differences between preferences and expectations prior to THA and TKA could be possible explanations for the difference in disease state preoperatively. Lower expectations of surgical interventions, such as THA or TKA, can lead to postponing surgery. Contrary to this, others suggest that worse preoperative disease state can lead to lower preoperative expectations and explain a difference between men and women [32].

Based on our findings, we suggest to take these sex specific differences into account when informing patients in a shared decision-making process for THA or TKA. Also future research should focus on the underlying reasons that could explain the differences found in this study, such as differences in life situations which could influence needs and demands. Patient-specific education provides more realistic information about expectations of outcomes, which could lead to better postoperative outcomes, patient satisfaction, and increased fulfillment of preoperative expectations [33]. Hence, it has also been shown that sex disparities in postoperative TKA expectations can be targeted with a decision aid [34].

Despite the prospective nature of this study for both preoperative and postoperative fulfillment scores, there are some limitations. First, for the assessment of expectations and fulfillment we used standardized expectation surveys, which do not include the patient's own individual expectations regarding other activities or aspects of life. Second, with regard to the option "not applicable" of the HSS-HRES/HSS-KRES, patients might have different reasons to

score “not applicable”. Possible explanations can be: unable to respond, not doing a certain activity or having expectations that were lower than the available scoring options. We are not able to specify these different reasons. Nevertheless, this study showed that men reported the item on sexual activity and ability to do paid work more often as “applicable”, and were more often employed and less often lived alone, compared to women. This supports our reasoning that reporting an item as “not applicable”, is identical to ‘not doing’ the activity, and is less related to the severity of the hip/knee complaints. Although the questionnaires were specifically developed for THA/TKA outcomes, the meaning of “back to normal” could have been interpreted differently by patients, as no detailed description of this response option was provided (i.e., before OA-related symptoms started, or before THA/TKA). Furthermore, not being able to indicate expectations such as ‘no improvement’ or ‘worsening’, although not a desirable outcome of elective surgery, could have resulted in an overestimation in preoperative expectations and an underestimation in fulfillment. We did not include ‘exceeded’ as a separate category, as there is a potential ceiling effect in this questionnaire when calculating exceeded expectations: if a patient preoperatively expects an item to go back to normal, this patient will not have the ability to exceed his/her expectations after surgery, as there is no category above ‘back to normal’. As the proportion of patients reporting an item as ‘back to normal’ before surgery is large (> 50% on almost all items), we categorized exceeded expectations alongside fulfilled expectations.

Men had higher expectations and more often fulfilled their expectations 1 year after THA and TKA surgery compared to women. Men’s expectations were mainly related to the ability to perform functional activities, while women were more concerned with the performance of activities of daily living. A deeper understanding of the impact of sex on expectations, both before and after THA/TKA, helps informing patients and the shared decision-making process. As a result, orthopedic surgeons and other health-care providers are able to more specifically target expectations in both men and women and to provide a more tailored expectation management, which finally could diminish sex disparities. Our recommendation for future research is to evaluate whether such tailored shared decision-making process, in which the specific expectations of men and women are included, indeed diminishes differences in fulfillment of expectations, thereby aiming at an optimal balance between preoperative expectations and

fulfilled expectations after a THA/TKA. In addition, future research should focus on the underlying reasons of the sex differences found.

References

1. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage*. 2005;13(9):769–781. doi: 10.1016/j.joca.2005.04.014.
2. Perez BA, Slover J, Edusei E, Horan A, Anoushiravani A, Kamath AF, et al. Impact of gender and race on expectations and outcomes in total knee arthroplasty. *World J Orthop*. 2020;11(5):265–277. doi: 10.5312/wjo.v11.i5.265.
3. Rolfson O, Kärrholm J, Dahlberg LE, Garellick G. Patient-reported outcomes in the Swedish Hip Arthroplasty Register: results of a nationwide prospective observational study. *J Bone Joint Surg Br*. 2011;93(7):867–875. doi: 10.1302/0301-620x.93b7.25737.
4. Parsley BS, Bertolusso R, Harrington M, Brekke A, Noble PC. Influence of gender on age of treatment with TKA and functional outcome. *Clin Orthop Relat Res*® 2010;468(7):1759–1764. doi: 10.1007/s11999-010-1348-y.
5. Lavernia CJ, Alcerro JC, Contreras JS, Rossi MD. Patient perceived outcomes after primary hip arthroplasty: does gender matter? *Clin Orthop Relat Res*. 2011;469(2):348–354. doi: 10.1007/s11999-010-1503-5.
6. Mehta SP, Perruccio AV, Palaganas M, Davis AM. Do women have poorer outcomes following total knee replacement? *Osteoarthritis Cartilage*. 2015;23(9):1476–1482. doi: 10.1016/j.joca.2015.05.007
7. Karlson EW, Daltroy LH, Liang MH, Eaton HE, Katz JN. Gender differences in patient preferences may underlie differential utilization of elective surgery. *Am J Med*. 1997;102(6):524–530. doi: 10.1016/S0002-9343(97)00050-8.
8. Borkhoff CM, Hawker GA, Kreder HJ, Glazier RH, Mahomed NN, Wright JG. Influence of patients' gender on informed decision making regarding total knee arthroplasty. *Arthritis Care Res (Hoboken)* 2013;65(8):1281–1290. doi: 10.1002/acr.21970.
9. Borkhoff CM, Hawker GA, Wright JG. Patient gender affects the referral and recommendation for total joint arthroplasty. *Clin Orthop Relat Res*® 2011;469(7):1829–1837. doi: 10.1007/s11999-011-1879-x.
10. Gandhi R, Razak F, Davey JR, Rampersaud YR, Mahomed NN. Effect of sex and living arrangement on the timing and outcome of joint replacement surgery. *Can J Surg*. 2010;53(1):37.
11. Tolk JJ, Janssen RPA, Haanstra TM, van der Steen MMC, Bierma Zeinstra SMA, Reijman M. Outcome expectations of total knee arthroplasty patients: the influence of demographic factors, pain, personality traits, physical and psychological status. *J Knee Surg*. 2019 doi: 10.1055/s-0039-1692632.
12. Lavernia CJ, Contreras JS, Parvizi J, Sharkey PF, Barrack R, Rossi MD. Do patient expectations about arthroplasty at initial presentation for hip or knee pain differ by sex and ethnicity? *Clin Orthop Relat Res*® 2012;470(10):2843–2853. doi: 10.1007/s11999-012-2431-3.
13. Jawa A, Dasti U, Brown A, Grannatt K, Miller S. Gender differences in expectations and outcomes for total shoulder arthroplasty: a prospective cohort study. *J Shoulder Elbow Surg*. 2016;25(8):1323–1327. doi: 10.1016/j.jse.2016.03.003.
14. Mancuso CA, Altchek DW, Craig EV, Jones EC, Robbins L, Warren RF, et al. Patients' expectations of shoulder surgery. *J Shoulder Elbow Surg*. 2002;11(6):541–549. doi: 10.1067/mse.2002.126764.
15. Harmsen RTE, Haanstra TM, Den Oudsten BL, Putter H, Elzevier HW, Gademan MGJ, et al. A high proportion of patients have unfulfilled sexual expectations after TKA: a

- prospective study. *Clin Orthop Relat Res*. 2020;478(9):2004–2016. doi: 10.1097/corr.0000000000001003.
16. Tilbury C, Haanstra TM, Leichtenberg CS, Verdegaal SH, Ostelo RW, de Vet HC, et al. Unfulfilled expectations after total hip and knee arthroplasty surgery: there is a need for better preoperative patient information and education. *J Arthroplasty*. 2016;31(10):2139–2145. doi: 10.1016/j.arth.2016.02.061.
 17. Deakin AH, Smith MA, Wallace DT, Smith EJ, Sarungi M. Fulfilment of preoperative expectations and postoperative patient satisfaction after total knee replacement. A prospective analysis of 200 patients. *Knee*. 2019;26(6):1403–1412. doi: 10.1016/j.knee.2019.07.018.
 18. Lützner C, Postler A, Beyer F, Kirschner S, Lützner J. Fulfillment of expectations influence patient satisfaction 5 years after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(7):2061–2070. doi: 10.1007/s00167-018-5320-9.
 19. Hung NJ, Wong SE. Gender influences on shoulder arthroplasty. *Curr Rev Musculoskelet Med*. 2022;15(1):21–26. doi: 10.1007/s12178-021-09737-0.
 20. Tilbury C, Leichtenberg CS, Kaptein BL, et al. Feasibility of collecting multiple patient-reported outcome measures alongside the Dutch Arthroplasty Register. *J Patient Exp*. 2020;7(4):484–492. doi: 10.1177/2374373519853166.
 21. De Groot IB, Favejee MM, Reijman M, Verhaar JA, Terwee CB. The Dutch version of the Knee Injury and Osteoarthritis Outcome Score: a validation study. *Health Qual Life Outcomes*. 2008;6(1):16. doi: 10.1186/1477-7525-6-16.
 22. De Groot I, Reijman M, Terwee C, Bierma-Zeinstra S, Favejee M, Roos E, et al. Validation of the Dutch version of the Hip disability and Osteoarthritis Outcome Score. *Osteoarthritis Cartilage*. 2007;15(1):104–109. doi: 10.1016/j.joca.2006.06.014.
 23. Mols F, Pelle AJ, Kupper N. Normative data of the SF-12 health survey with validation using postmyocardial infarction patients in the Dutch population. *Qual Life Res*. 2009;18(4):403–414. doi: 10.1007/s11136-009-9455-5.
 24. Reeuwijk KG, de Rooij M, van Dijk GM, Veenhof C, Steultjens MP, Dekker J. Osteoarthritis of the hip or knee: which coexisting disorders are disabling? *Clin Rheumatol*. 2010;29(7):739–747. doi: 10.1007/s10067-010-1392-8.
 25. van den Akker-Scheek I, van Raay JJ, Reininga IH, Bulstra SK, Zijlstra W, Stevens M. Reliability and concurrent validity of the Dutch hip and knee replacement expectations surveys. *BMC Musculoskelet Disord*. 2010;11:242. doi: 10.1186/1471-2474-11-242.
 26. Flynn TJ, Gow AJ. Examining associations between sexual behaviours and quality of life in older adults. *Age Ageing*. 2015;44(5):823–828. doi: 10.1093/ageing/afv083.
 27. Bączkiewicz D, Skiba G, Czermer M, Majorczyk E. Gait and functional status analysis before and after total knee arthroplasty. *Knee*. 2018;25(5):888–896. doi: 10.1016/j.knee.2018.06.004.
 28. Hoorntje A, Leichtenberg CS, Koenraadt KLM, van Geenen RCI, Kerkhoffs G, Nelissen R, et al. Not physical activity, but patient beliefs and expectations are associated with return to work after total knee arthroplasty. *J Arthroplasty*. 2018;33(4):1094–1100. doi: 10.1016/j.arth.2017.11.032.
 29. Yapp LZ, Clement ND, Macdonald DJ, Howie CR, Scott CEH. Patient expectation fulfilment following total hip arthroplasty: a 10-year follow-up study. *Arch Orthop Trauma Surg*. 2020;140(7):963–971. doi: 10.1007/s00402-020-03430-6.
 30. Husain A, Lee GC. Establishing realistic patient expectations following total knee arthroplasty. *J Am Acad Orthop Surg*. 2015;23(12):707–713. doi: 10.5435/jaaos-d-14-00049.

31. Peul WC, Brand R, Thomeer R, Koes BW. Influence of gender and other prognostic factors on outcome of sciatica. *Pain*. 2008;138(1):180–191. doi: 10.1016/j.pain.2007.12.014.
32. Jain D, Nguyen LL, Bendich I, Nguyen LL, Lewis CG, Huddleston JI, et al. Higher patient expectations predict higher patient-reported outcomes, but not satisfaction, in total knee arthroplasty patients: a prospective multicenter study. *J Arthroplasty*. 2017;32(9s):S166–S170. doi: 10.1016/j.arth.2017.01.008.
33. O’ Reilly M, Mohamed K, Foy D, Sheehan E. Educational impact of joint replacement school for patients undergoing total hip and knee arthroplasty: a prospective cohort study. *Int Orthop*. 2018;42(12):2745–2754. doi: 10.1007/s00264-018-4039-z.
34. Volkmann ER, FitzGerald JD. Reducing gender disparities in post-total knee arthroplasty expectations through a decision aid. *BMC Musculoskelet Disord*. 2015;16(1):16. doi: 10.1186/s12891-015-0473-x.

APPENDICES

Supplementary table 1-A Preoperative characteristics of THA and TKA patients with and without response to the preoperative expectations questionnaire

		THA population		TKA population	
		With (n = 2333)	Without (n = 237)	With (n = 2398)	Without (n = 194)
Age (years), mean (SD)		69 (9)	71 (9)	68 (9)	70 (9)
BMI, mean (SD)		27 (4)	28 (4)	30 (5)	30 (5)
Smoking, yes, n (%)		136 (6)	18 (8)	131 (6)	17 (9)
Comorbidities (%)	Non-musculoskeletal	549 (24)	14 (7)	447 (34)	13 (7)
	Musculoskeletal	534 (23)	23 (10)	283 (12)	14 (7)
	Both	525 (23)	7 (6)	824 (27)	21 (11)
	None	476 (20)	17 (3)	568 (19)	13 (7)
	Missing	249 (11)	176 (74)	276 (12)	133 (69)
Work status, employed, n (%)		558 (24)	5 (2)	557 (23)	13 (7)
	Missing	25 (1)	176 (74)	28 (1)	131 (68)
Living alone, yes, n (%)		502 (23)	16 (7)	513 (21)	19 (10)
	Missing	141 (6)	163 (69)	158 (7)	123 (63)
Preoperative	Pain	38 (19)	46 (22)	39 (18)	36 (18)
HOOS/KOOS, mean	Symptoms	41 (19)	47 (25)	50 (18)	49 (16)
(SD)*	Daily Living	41 (19)	47 (20)	45 (19)	40 (21)
	QoL	29 (17)	40 (23)	26 (16)	27 (18)
	Sports	18 (19)	13 (20)	10 (15)	10 (17)
SF-12, mean (SD)	PCS	32 (9)	32 (10)	32 (9)	34 (11)
	MCS	54 (10)	48 (11)	55 (10)	50 (12)

Legend: *: HOOS/KOOS scores are complete for approximately 75% of patients, as it was replaced with the HOOS-PS/KOOS-PS after January 2017 Note: THA: total hip arthroplasty; TKA: total knee arthroplasty; HOOS: Hip Disability and Osteoarthritis Outcome Score; KOOS: Knee Injury and Osteoarthritis Outcome Score; SF-12: Short form-12 survey; PCS: component score for physical health score; MCS: component score for mental health score.

Supplementary table 1-B Preoperative characteristics of THA and TKA patients with and without follow-up

		THA population		TKA population	
		With (n =1878)	Without (n = 2333)	With (n =1887)	Without (n = 2398)
Age (years), mean (SD)		69 (9)	69 (9)	68 (8)	68 (9)
BMI, mean (SD)		27 (4)	27 (4)	29 (5)	30 (5)
Smoking, yes, n (%)		93 (5)	136 (6)	95 (6)	131 (5)
Comorbidities	Non-musculoskeletal	458 (24)	549 (24)	633 (34)	447 (34)
(%)	Musculoskeletal	414 (22)	534 (23)	219 (12)	283 (12)
	Both	398 (21)	525 (23)	433 (23)	824 (27)
	None	385 (21)	476 (20)	346 (18)	568 (19)
	Missing	224 (12)	249 (11)	257 (14)	276 (12)
Work status, employed, n (%)		437 (23)	558 (24)	426 (23)	557 (23)
	Missing	15 (2)	25 (1)	21 (2)	28 (1)
Living alone, yes, n (%)		378 (20)	502 (23)	384 (20)	513 (21)
	Missing	135 (7)	141 (6)	162 (9)	158 (7)
Preoperative	Pain	39 (19)	38 (19)	39 (17)	39 (18)
HOOS/KOOS,	Symptoms	41 (19)	41 (19)	50 (18)	50 (18)
mean (SD)*	Daily Living	41 (19)	41 (19)	46 (18)	45 (19)
	QoL	30 (17)	29 (17)	27 (15)	26 (16)
	Sports	18 (19)	18 (19)	11 (15)	10 (15)
SF-12, mean	PCS	32 (9)	32 (9)	32 (9)	32 (9)
(SD)	MCS	54 (10)	54 (10)	55 (10)	55 (10)

Legend: *: HOOS/KOOS scores are complete for approximately 75% of patients, as it was replaced with the HOOS-PS/KOOS-PS after January 2017. Note: THA: total hip arthroplasty; TKA: total knee arthroplasty; HOOS: Hip Disability and Osteoarthritis Outcome Score; KOOS: Knee Injury and Osteoarthritis Outcome Score; SF-12: Short form-12 survey; PCS: component score for physical health score; MCS: component score for mental health score.

Supplementary table 2-A Total Hip Arthroplasty (THA): Preoperative Expectations using the HSS-HRES

			Applicable†		95% CI*
	Men, n (%)	Women, n (%)	Men, n (%)	Women, n (%)	
Relief of pain during the day	763	1,240	749 (98)	1,230 (99)	0.17 – 0.15
Relief of pain during sleeping	868	1,364	807 (93)	1,304 (96)	0.39 – 0.87
Improve walking ability					
Short distances (in house)	843	1,286	829 (98)	1,262 (98)	0.50 – 2.86
Middle-long distances (<1.5 km)	848	1,294	826 (97)	1,252 (97)	0.73 – 2.55
Long distances (>1.5 km)	856	1,301	808 (94)	1,206 (93)	0.92 – 2.17
No need for cane, crutch or walker	872	1,382	624 (72)	987 (71)	0.82 – 1.25
Ability to stand better	880	1,399	833 (95)	1,320 (94)	0.62 – 1.42
Getting rid of limp	881	1,393	813 (92)	1,258 (90)	0.74 – 1.78
Walking stairs	879	1,397	837 (95)	1,318 (94)	0.88 – 1.76
Getting out of bed, chair or car	880	1,406	851 (97)	1,388 (99)	0.16 – 0.64
Eliminate need for pain relief medication	881	1,400	662 (75)	1,175 (84)	0.44 – 0.70
Be able to put on shoes and socks	884	1,405	797 (90)	1,236 (88)	0.82 – 1.50
Be able to do paid work	867	1,348	319 (37)	282 (21)	1.86 – 2.87
Join recreational activities (dancing, going out on trips)	874	1,392	703 (80)	1,087 (78)	0.90 – 1.46
Improve ability to perform daily activities in and around the house	878	1,406	828 (94)	1,346 (96)	0.41 – 1.03
Improve ability to do sports	880	1,391	749 (85)	1,116 (84)	1.04 – 1.75
Ability to cut toenails	880	1,404	773 (88)	1,190 (85)	0.85 – 1.49
Social life	879	1,394	746 (85)	1,128 (81)	1.18 – .99
Sexual activity	875	1,387	640 (73)	820 (59)	1.47 – 2.23
Psychological well-being	877	1,398	610 (70)	853 (61)	1.19 – 1.79

Legend: † Preoperative expectations proportions based on applicable population

*Comparison of preoperative expectations in men and women by means of Chi-square test, with corresponding 95% Confidence Interval (CI)

Note: HSS-HRES: Hospital For Special Surgery Hip Replacement Expectations Survey

Supplementary table 2-B Total Knee Arthroplasty (TKA): Preoperative Expectations using the HSS-KRES

	Men, n (%)	Women, n (%)	Applicable		95%CI*
	Men, n (%)	Women, n (%)	Men, n (%)	Women, n (%)	
Relief of pain during the day	830	1,490	823 (99)	1,479 (99)	0.18 – 1.76
Improve walking ability					
Short distances (in house)	756	1,335	740 (98)	1,320 (99)	0.26 – 1.32
Middle-long distances (<1.5 km)	760	1,360	746 (98)	1,318 (97)	0.75 – 2.92
Long distances (>1.5 km)	796	1,385	764 (96)	1,272 (92)	1.26 – 3.16
No need for cane, crutch or walker	822	1,481	530 (65)	1,036 (70)	0.58 – 0.88
Be able to stretch the knee	834	1,509	773 (93)	1,426 (95)	0.47 – 1.00
Improve walking upstairs	835	1,514	810 (97)	1,465 (97)	0.49 – 1.45
Improve walking downstairs	832	1,506	808 (97)	1,459 (97)	0.44 – 1.33
Being able to kneel down	831	1,506	794 (96)	1,390 (92)	1.04 – 2.46
Being able to squat	828	1,500	791 (96)	1,388 (93)	0.89 – 2.08
Being able to travel by public transportation (bus, tram or train)	824	1,497	569 (69)	1,128 (75)	0.57 – 0.87
Be able to do paid work	801	1,405	287 (36)	342 (24)	1.31 – 2.03
Join recreational activities (dancing, going out on trips)	834	1,500	688 (83)	1,185 (79)	0.95 – 1.56
Improve ability to perform daily activities in and around the house	831	1,512	743 (89)	1,361 (90)	0.68 – 1.25
Improve ability to do sports	836	1,502	720 (86)	1,223 (81)	1.00 – 1.71
Being able to change positions (getting up, sitting down)	835	1,511	797 (95)	1,450 (96)	0.43 – 1.07
Social life	832	1,508	679 (82)	1,212 (80)	0.77 – 1.26
Sexual activity	822	1,482	557 (68)	751 (51)	1.57 – 2.35
Psychological well-being	828	1,501	516 (62)	872 (58)	1.05 – 1.56

Legend: ‡ Preoperative expectations proportions based on applicable population

* Comparison of preoperative expectations in men and women by means of Chi-square test, with corresponding 95% Confidence Interval (CI)

Note: HSS-KRES: Hospital For Special Surgery Knee Replacement Expectations Survey

Supplement A

Expectations questionnaire

The versions of the HSS-HRES and HSS-KRES developed by van den Akker-Scheek et al. (van den Akker-Scheek, I., van Raay, J. J., Reininga, I. H., Bulstra, S. K., Zijlstra, W., & Stevens, M. (2010). Reliability and concurrent validity of the Dutch hip and knee replacement expectations surveys. *BMC musculoskeletal disorders*, 11(1), 1-8.) were used in this study. The developer of the questionnaires was informed and gave consent to a Dutch translation of the Expectations Surveys (Carol Mancuso, MD, Hospital for Special Surgery, personal communication, 2008). The studies of Mancuso et al. (mentioned below) include a detailed description of the English version of the questionnaires.

References for English versions:

Mancuso CA, Wentzel CH, Ghomrawi HMK, Kelly BT. Hip Preservation Surgery Expectations Survey: A New Method to Measure Patients' Preoperative Expectations. Arthroscopy 2017; 33: 959-968.

Mancuso CA, Sculco TP, Wickiewicz TL, Jones EC, Robbins L, Warren RF, et al. Patients' expectations of knee surgery. JBJS 2001; 83: 1005-1012.

Reference for Dutch version:

van den Akker-Scheek I, van Raay JJ, Reininga IH, Bulstra SK, Zijlstra W, Stevens M. Reliability and concurrent validity of the Dutch hip and knee replacement expectations surveys. *BMC Musculoskelet Disord* 2010; 11: 242

Validated Dutch of the Hospital for Special Surgery Hip Replacement Expectations Survey

Vragenlijst Verwachtingen van een Totale Heupvervangning

Wilt u alstublieft het nummer omsirkelen dat uw antwoord op de vraag het beste omschrijft.

Hoeveel verlichting of verbetering verwacht u op de volgende gebieden als gevolg van uw totale heupvervangning?

	Terug naar normaal of totale verbetering	Niet terug naar normaal, maar ...			Ik heb deze verwachting niet of deze verwachting is niet op mij van toepassing
		Veel verbetering	Middelmatige verbetering	Een kleine verbetering	
Verlichting van pijn die overdag optreedt	1	2	3	4	5
Verlichting van pijn tijdens slapen	1	2	3	4	5
Verbeteren van het loopvermogen	1	2	3	4	5
Verbeteren van het vermogen te staan	1	2	3	4	5
Niet langer mank lopen	1	2	3	4	5
Het niet meer nodig hebben van een stok of andere hulpmiddelen	1	2	3	4	5
Verbeteren van het vermogen trappen op te lopen	1	2	3	4	5
Verbeteren van het vermogen in of uit bed, stoel of auto te komen	*	2	3	4	5
Verbeteren van het vermogen dagelijkse activiteiten rond het huis te verrichten (bijvoorbeeld, huishoudelijke klusjes, tuinieren)	1	2	3	4	5
Verbeteren van het vermogen dagelijkse activiteiten buiten het huis te verrichten (bijvoorbeeld, winkelen, vrijwilligerswerk)	1	2	3	4	5
Het niet langer nodig hebben van medicijnen	1	2	3	4	5
Betaald werk kunnen doen	1	2	3	4	5
Verbeteren van seksuele activiteit	1	2	3	4	5
Verbeteren van het vermogen lichamelijk actief te zijn of deel te nemen aan sport	1	2	3	4	5
Verbeteren van het vermogen deel te nemen aan sociale of recreatieve activiteiten	1	2	3	4	5
Verbeteren van het vermogen schoenen en sokken aan te trekken	1	2	3	4	5
Verbeteren van het vermogen teennagels te knippen	1	2	3	4	5
Verbeteren van psychologisch welzijn	1	2	3	4	5

*: divided in the following subquestions: i) korte afstanden (binnenshuis, een huizenblok), ii) middellange afstanden (een stukje lopen, tot 1,5 km), iii) lange afstanden (meer dan 1,5 km)

Vragenlijst Verwachtingen van een Totale Knievervanging

Wilt u alstublieft het nummer omcirkelen dat uw antwoord op de vraag het beste omschrijft.

Hoeveel verlichting of verbetering verwacht u op de volgende gebieden als gevolg van uw totale knievervanging?

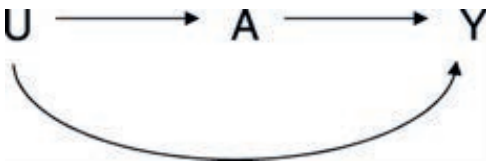
	Terug naar normaal of totale verbetering	Niet terug naar normaal, maar ...			Ik heb deze verwachting niet of deze verwachting is niet op mij van toepassing
		Veel verbetering	Middelmatige verbetering	Een kleine verbetering	
Verlichting van pijn	1	2	3	4	5
Verbeteren van het loopvermogen op: ** korte afstanden (binnenshuis, een huizenblok)	1	2	3	4	5
** middellange afstanden (een stukje lopen, tot 1,5 km)	1	2	3	4	5
** lange afstanden (meer dan 1,5 km)	1	2	3	4	5
Het niet meer nodig hebben van een stok, kruk of rollator	1	2	3	4	5
Het strekken van knie of been	1	2	3	4	5
Verbeteren van het vermogen trappen op te gaan	1	2	3	4	5
Verbeteren van het vermogen trappen af te gaan	1	2	3	4	5
Verbeteren van het vermogen om te knielen	1	2	3	4	5
Verbeteren van het vermogen te hurken	1	2	3	4	5
Verbeteren van het vermogen om van het openbaar vervoer gebruik te maken of te rijden	1	2	3	4	5
Betaald werk kunnen doen	1	2	3	4	5
Verbeteren van het vermogen deel te nemen aan recreatieve activiteiten (bijvoorbeeld dansen, plezierreisjes)	1	2	3	4	5
Verbeteren van het vermogen dagelijkse activiteiten uit te voeren (bijvoorbeeld huishoudelijke werkzaamheden, dagelijkse routine)	1	2	3	4	5
Verbeteren van het vermogen lichamelijk actief te zijn of deel te nemen aan sport	1	2	3	4	5
Verbeteren van het vermogen om van positie te veranderen (bijvoorbeeld van zitten naar staan of van staan naar zitten)	1	2	3	4	5
Verbeteren van het vermogen om te gaan met anderen (bijvoorbeeld voor iemand zorgen, spelen met kinderen)	1	2	3	4	5
Verbeteren van seksuele activiteit	1	2	3	4	5
Verbeteren van psychologisch welzijn	1	2	3	4	5

Supplement B

Explanation regarding our unadjusted analysis approach

Hernán (2008) provided the following definitions for a confounding variable: “can be used to block a backdoor path between exposure and outcome”, “any variable that can be used to reduce [confounding] bias” and “any variable that is necessary to eliminate the bias in the analysis” (Hernán MA. *Confounding*. In: Everitt B, Melnick E, editors. *Encyclopedia of Quantitative Risk Assessment and Analysis*. John Wiley & Sons Chichester, United Kingdom: 2008. pp. 353–362.)

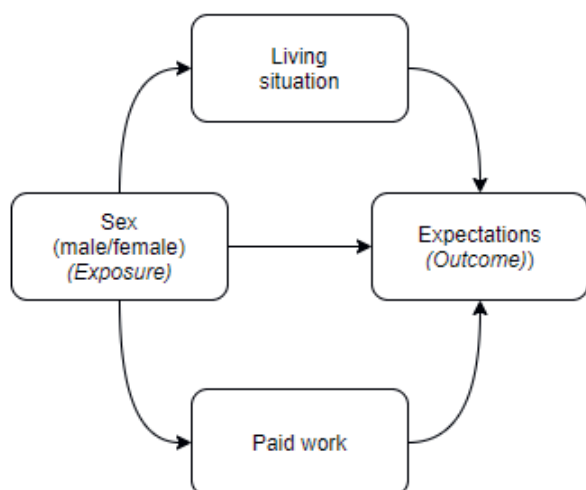
Below we have created a Directed Acyclic Graph (DAG) to explain why we have not adjusted for additional covariates (*Supplementary figure 1*). DAGs represent causal relationships among variables, and can be used to determine the variables on which it is necessary to condition to control for confounding in the estimation of causal effects.



Supplementary figure 1 Example illustrating confounding by health status. Y indicates disease; A, exposure; U, health status

(VanderWeele, Tyler J.a; Hernán, Miguel A.b; Robins, James M.b,c *Causal Directed Acyclic Graphs and the Direction of Unmeasured Confounding Bias*, *Epidemiology*: September 2008 - Volume 19 - Issue 5 - p 720-728 doi: 10.1097/EDE.0b013e3181810e29)

We investigated if sex affects expectations, indicated by the arrow between “Sex (male/female)”/exposure and “Expectations”/outcome (or dependent variable) in *Supplementary figure 2*. Indeed there could be other factors, alongside sex, that affect expectations, such as living situation and having paid work. However, these factors are a result of sex and are therefore not a “cause” of sex. Hence, being female could affect your living situation and having paid work, and therefore indirectly via living situation/paid work affect expectations. Nevertheless, as made visible using the DAG below, these ‘covariates’ are within the causal pathway between “sex” and “expectations”, or so-called ‘mediators’. Therefore, adjusting for these covariates/mediators would lead to non-preferable adjustments within the causal pathway. To our knowledge there are no covariates ‘causing’ sex, that could affect expectations.



Supplementary figure 2: Directed Acyclic Graph



Chapter 5

Activities and participation after primary total hip arthroplasty; posterolateral versus direct anterior approach in 860 patients

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ABSTRACT

Background and purpose: In the past decade, a shift occurred in surgical total hip arthroplasty (THA) approaches to the posterolateral (PLA) and direct anterior approach (DAA). Comparisons of postoperative activities and participation between surgical approaches for THA are sparse. We therefore investigated the association between PLA and DAA for THA regarding the construct “activity and participation” (ICF model) during the first postoperative year.

Patients and methods: This was an observational cohort study on osteoarthritis patients scheduled for primary THA in 2 hospitals. Questionnaires to assess the ICF domain “activity and participation” were completed preoperatively, and 3/6/12 months postoperatively (HOOS Activities of daily living (ADL) and Sport and Recreation Function (SR), Hospital for Special Surgery Hip Replacement Expectations Survey, and questions regarding return to work). Each hospital exclusively performed one approach (PLA [Alloclassic-Zweymüller stem] or DAA [Taperloc Complete stem]) for uncemented THA. Hospital was included as instrumental variable, thereby addressing bias by (un)measured confounders. Adjusted mixed-effect models were used, stratified by employment.

Results: Total population: 238 PLA (24% employed) and 622 DAA (26% employed) patients. At 12 months, the PLA group had a lower ADL score (7, 95% CI -12; -2 points). At 6 months, significantly fewer PLA patients had fulfillment of the expectation *sports-performance* (OR = 0.3, CI 0.2; 0.7]. Other outcomes were comparable.

Employed population: At 6 and 12 months, PLA patients scored clinically lower on ADL (respectively 10, CI -19; 0 and 9, CI -19; 0 points) and SR (respectively 13, CI -21; -4 and 9, CI -18; -1 points). At 6 months, fewer PLA patients fulfilled the expectation *joining recreational activities* (OR = 0.2, CI 0.1; 0.7]. Fulfillment of other expectations was comparable between groups. PLA patients less often returned to work within 3 months (31% vs. 45%), but rates were comparable at 12 months (86% vs. 87%).

Interpretation: Overall, functional recovery regarding “activity and participation” was comparable for PLA and DAA. Among employed patients, DAA

resulted in better functional recovery and more fulfillment of expectations compared with PLA patients. DAA might also facilitate faster return to work.

INTRODUCTION

During the past decade, the surgical approach for THA has shifted in the Netherlands from direct-lateral and anterolateral approaches to posterolateral (PLA) and direct-anterior-approach (DAA) [1]. Studies comparing complication and dislocation rates, clinical and patient-reported outcomes by approach were unable to find superiority for any approach [2,3].

Previously, comparison of DAA and PLA mainly focused on hip function and a limited number of activities (mobility and walking). According to the International Classification of Functioning, Disability and Health (ICF), conditions such as osteoarthritis (OA) may have more consequences. Moreover, OA patients in need of THA are increasingly becoming concerned about their return to work and participation in society [4]. Nevertheless, the majority of studies comparing surgical approaches for THA have focused on mobility, but overall functioning of the patient, as defined within ICF, has been little addressed [5]. For that matter the ICF domain “activity and participation” also comprises other aspects, currently underemphasized in this population, such as “Major life areas,” especially concerning “community, social and civic life,” in particular recreation, leisure, and work/employment [3,6,7].

A study assessing the effect of DAA and PLA on recreational activities after THA showed that DAA patients were more likely to return to sporting activities [7]. However, it was a small study, using unvalidated questionnaires on sport and recreational activities. Additionally, information on fulfillment of expectations regarding “activity and participation,” an intricate part of shared decision-making, has not been studied either. Moreover, expectations are likely to be determined by social context (social engagement) and/or employment [8]. We therefore hypothesized that participation might differ in employed patients.

Hence, we evaluated the association between self-reported outcomes, return to work and fulfillment of expectations regarding the ICF domain “activity and participation” during the first postoperative year between two surgical approaches for THA (PLA/DAA).

MATERIALS AND METHODS

Study design

Data from patients scheduled for primary THA between January 2014 and December 2018 in 2 participating teaching hospitals, located in South Holland, the Netherlands were obtained from the ongoing, multicenter, observational cohort Longitudinal Leiden Orthopaedic Outcome of Osteo-Arthritis Study (LOAS, TRIAL ID: Trial NL3197 [NTR3348]). The study includes patients undergoing THA or total knee arthroplasty, to describe mid-term and long-term outcomes of these surgeries in terms of health status as a whole. Questionnaires included were based on the obligatory set of patient-reported outcome measures for THA by the Dutch Orthopaedic Society, complemented by specific research questions of the LOAS steering group (i.e., return to work, sports) [9].

Both hospitals exclusively performed one surgical approach (LangeLand Hospital, Zoetermeer—PLA; four surgeons, Alrijne Hospital, Leiderdorp/Leiden—DAA; five surgeons). Both hospitals performed their surgical approach during sufficient time (at least 6 months) before the start of this study, therefore avoiding possible learning curve effects.

Patient recruitment

Patients were eligible if: scheduled for primary THA due to OA, ≥ 18 years old, and mentally and physically capable of completing the Dutch questionnaires. Patients were excluded if they received TKA or contralateral THA in the 6 months prior to surgery, or lived outside the catchment area, or within overlapping catchment areas, avoiding inclusion based on preference for a specific procedure. Patients lacking information on employment status were excluded.

Intervention

Preoperatively, patients received information regarding surgical procedures and the postoperative rehabilitation protocol. Surgical technique was specific to hospital. PLA provides good exposure of the acetabulum and femur, but involves the release and repair of the external hip rotators, possibly affecting the strength of these rotators [10]. PLA was performed in lateral decubitus position, using uncemented Alloclassic® Zweymüller® femoral stem, hemispherical uncemented Allofix® acetabular component (Zimmer-Biomet Inc, Warsaw, IN,

USA), and Biolog® ceramic femoral head with cross-linked polyethylene liner. In comparison, DAA is performed through an internervous and intermuscular plane, causing less soft tissue damage. The DAA gained interest as it is promoted as a minimally invasive approach. Nevertheless, DAA is technically more demanding, with limited exposure to the femur [11]. DAA was performed in supine position, using uncemented titanium porous sprayed Taperloc Complete distal reduced femoral stem, hemispherical uncemented Allofit® acetabular component (Zimmer-Biomet Inc), and Biolog® femoral head with a cross-linked polyethylene liner.

All patients received a similar standardized postoperative pain and rehabilitation protocol, full weight-bearing, but use of crutches for 2–4 weeks to stimulate normal gait during ambulation. All patients were allowed to resume activities within the limits of comfort. Patients receiving THA using PLA were instructed not to hyperflex, adduct, and internally rotate during the first 6 weeks. DAA patients were not given specific restrictions on range of motion, but were instructed on hyperextension and external rotation during the first 6 weeks. Both hospitals had the same policy on return to work.

Data collection

Activities and participation

Preoperatively, and 3, 6, and 12 months postoperatively, the domain “activity and participation” was captured by validated, Dutch versions of the Hip Disability and Osteoarthritis Outcome Score (HOOS) Activities of daily living (ADL) and Sport and Recreation Function subscales, which show good content and construct validity [12]. Item description of ADL subscale: descending and ascending stairs, rising from sitting, sitting, standing, bending to the floor/pick up an object, walking on a flat surface, getting in/out of car, going shopping, putting on socks/stockings, taking off socks/stockings, rising from bed, lying in bed, getting in/out of bath, getting on/off toilet, heavy domestic duties, light domestic duties. Item description of Sport and Recreation Function subscale: squatting, running, twisting/pivoting on loaded leg, walking on uneven surface. For both subscales, the scores were summed and converted to a 0–100 score (0 = worst possible outcome). Minimal clinical important differences for the HOOS ADL, and Sport

and Recreation Function subscales have been reported between 6–9 and 9–10 points, respectively.

Expectations regarding “activity and participation”

Preoperative expectations and fulfillment at 6 and 12 months regarding the domain “activity and participation” [13] were collected using a validated Dutch version of the Hospital for Special Surgery Hip Replacement Expectations Survey (HSS-HRES) [14]. The following items were included: *Join recreational activities*, *Social life* and *Improve ability to do sports*. Expectations were obtained using a 5-point Likert scale (back to normal, much/moderate/slight improvement, or not applicable). Fulfillment at 6 and 12 months was dichotomized into two scales (unfulfilled/fulfilled). Patients were excluded if they answered “not applicable,” either before and/or after surgery.

Employed population

Preoperatively, patients reported their current employment status (paid work yes/no). If employed, additional aspects regarding their working situation were recorded: working hours per week, physical workload (light, medium, heavy), employment status (employed, self-employed), limitations at work, or sick leave due to hip complaints. In employed patients, return to work (yes/no; months between surgery and return), number of working hours per week, and experienced limitations at work due to hip complaints (yes/no) were collected both before and after surgery. Additionally, questions from the validated Dutch Short-Form 12-Item Health Survey (SF-12) regarding work and HSS-HRES pre- and postoperative expectations regarding work ability were included.

Secondary assessments

The following routinely registered preoperative patient characteristics were extracted from medical files: age (years), sex, BMI, current smoking status (yes/no), and ASA class. Preoperatively, self-reported comorbidities were collected using the comorbidity questionnaire of the Dutch Central Bureau of Statistics, in which the presence of comorbidities in the previous year was determined (yes/no) for the following comorbidities: elbow, wrist, hand, or back pain; other rheumatic diseases, chronic lung, cardiac, or coronary disease;

arteriosclerosis; hypertension; [consequences of] stroke; severe bowel disorder; diabetes mellitus; migraine; psoriasis; chronic eczema; cancer; urine incontinence. Comorbidities were afterwards categorized based on the ASA classification. Preoperatively, the Oxford Hip Score (OHS) was used to assess function and pain (range: 0–42; 0 = greatest disability). Additionally, the validated Dutch Short-Form 12-Item Health Survey (SF-12) was collected to assess health-related quality of life, and to calculate the Physical and Mental Component Summary (PCS/MCS) (range: 0–100; 0 = worst health).

Statistics

Power calculation

Based on the available sample as at December 2018 (PLA: $n = 238$; DAA: $n = 622$), we would be able to show an effect size of 0.18 in the current study ($\alpha=0.05$, 80% power).

Patient characteristics and outcomes regarding “activity and participation” were compared between PLA and DAA patients using either independent t-tests (continuous data), chi-square tests (categorical data), or Fisher’s exact tests (categorical data; if cell count < 5), to assess whether observed differences are generalizable to the larger patient population of interest, in both the total population and stratified groups by employment status. We compared postoperative work-related factors within the returned population at each timepoint (e.g., only patients who returned to work within the timeframe were compared).

Mixed-effect models

As all surgeons at LangeLand Hospital exclusively used PLA, and all surgeons at Alrijne hospital exclusively performed DAA, hospital acted as an instrumental variable. With an instrumental variable approach (IVA), a pseudo-random assignment of the exposure (surgical approach) was introduced. Thus, exchangeability of concerning (un)measured confounding is possible. IVA was used to estimate the effect of approach, in the presence of unmeasured confounding. The instrumental variable should meet the following conditions: it (hospital) is (i) associated with treatment (approach), (ii) unrelated to

confounders, (iii) unrelated to the outcome (activity and participation), other than by association with the actual treatment (THA) [15]. Mixed-effect models (including subject-specific intercepts) were fitted (linear) models (if continuous) with corresponding effect estimates, or logistic models (if binary) with corresponding odds ratios (OR), including corresponding 95% confidence intervals, to estimate the effect of THA approach on postoperative “activity and participation.” The models included an interaction term between the time of measurement and hospital, alongside adjustments for ASA and smoking status, based on baseline imbalances. Fit of the statistical models was assessed using residual plots and examination of the goodness-of-fit statistics. All statistical analyses were performed using R (version 2.15.2; R Foundation for Statistical Computing, Vienna, Austria).

Ethics, registration, funding, and potential conflicts of interest

Ethical approval was obtained from the Medical Ethics Committee of Leiden University Medical Center (LUMC) (Protocol Number: P12.047 [March 27, 2012]). All included patients provided informed consent. This work was supported by the Dutch Arthritis Foundation (grant number LLP13) and the Department of Orthopaedics from Leiden University Medical Center. The study sponsors had no involvement in the interpretation of data, the writing of the manuscript or the decision to submit the manuscript for publication.

RESULTS

Study population

Of the 1,109 eligible patients, 860 patients were included in the study population (238 PLA and 622 DAA patients) (Figure 1, Table 1). Preoperatively, 221 patients were employed (PLA = 58 (24%) versus DAA = 163 (26%)). Within the total population, the majority of patients were female, whereas among employed patients sex was more equally divided. At the time of surgery, the average age in the total population was 68 (SD 9.6) years, while for the employed population the average age was 58 (7.4) years. In the PLA population, smoking (PLA = 14% vs. DAA = 6%) and higher ASA classification and comorbidity score were more common than in the DAA group (Table 1).

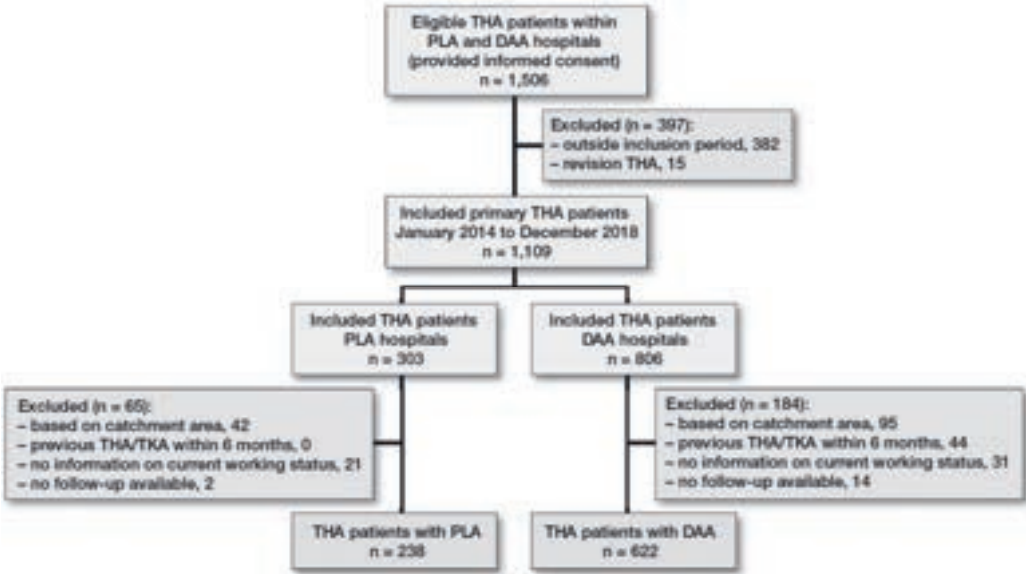


Figure 1 Flowchart of inclusion of participants in the study

THA: total hip arthroplasty; PLA: posterolateral approach; DAA: direct anterior approach

Table 1 Preoperative patient characteristics of study population receiving total hip arthroplasty: comparison based on preoperative employment status

Factor	Total population		Not employed *		Employed *	
	PLA (n = 238)	DAA (n = 622)	PLA (n = 180)	DAA (n = 59)	PLA (n = 58)	DAA (n = 163)
Female sex, n (%)	146 (61)	386 (62)	118 (65)	311 (68)	28 (48)	75 (46)
Age (years), mean (SD)	68 (10)	68 (10)	71 (8)	71 (8)	56 (8)	58 (7)
BMI, mean SD)	28 (4)	27 (4)	27 (4)	27 (4)	28 (4)	27 (4)
Currently smoking, yes, n (%)	29 (12)	31 (5)	18 (10)	20 (4)	11 (20)	11 (7)
ASA, n (%):						
I	24 (10)	117 (19)	15 (8)	70 (15)	9 (16)	47 (29)
II	169 (71)	405 (65)	125 (69)	307 (70)	44 (76)	98 (60)
III	46 (19)	55 (9)	41 (23)	47 (10)	5 (9)	8 (5)
Comorbidity, n (%): ‡						
I	76 (32)	240 (39)	56 (31)	152 (33)	20 (35)	88 (54)
II	141 (59)	313 (50)	108 (60)	250 (55)	33 (57)	63 (39)
III	22 (9)	69 (11)	17 (9)	57 (12)	5 (9)	12 (7)
Living alone, n (%):	47 (20)	127 (20)	41 (23)	111 (24)	6 (10)	16 (10)
OHS (0–42), mean (SD)	24 (9)	24 (8)	24 (9)	24 (9)	24 (7)	24 (8)
SF-12 (0–100), mean (SD)						
MCS	56 (9)	57 (7)	56 (8)	56 (8)	53 (10)	58 (5)
PCS	42 (10)	43 (10)	42 (10)	43 (10)	33 (10)	44 (10)
HOOS, mean (SD):	45 (22)	41 (19)	44 (22)	42 (19)	47 (21)	40 (18)
Subscale Activities in Daily living	16 (21)	20 (20)	16 (20)	20 (20)	14 (21)	19 (18)
Subscale Sports and Recreation Function						
HSS-HRES, back to normal, n (%):						
Join recreational activities	134 (56)	338 (54)	95 (53)	234 (51)	39 (67)	104 (65)
Social life	160 (67)	412 (66)	118 (65)	300 (65)	42 (72)	112 (69)
Ability to do sports	116 (49)	293 (47)	85(47)	214 (47)	31 (5)	79 (49)
Do paid work					41 (71)	109 (67)

Legend: * Employment status (paid work no = not employed; yes = employed)

‡ Comorbidity: comorbidities based on ASA classification (I: Normal Health; II: Mild Systemic Disease; III: Severe Systemic Disease). PLA: posterolateral approach; DAA: direct anterior approach; BMI: body mass index; ASA: American Society of Anesthesiologists; OHS: Oxford Hip Score; SF-12: Short Form-12; MCS: Mental Component Summary; PCS: Physical Component Summary; HOOS: Hip Disability and Osteoarthritis Outcome Score; FU: follow-up; HSS-HRES: New York Hospital for Special Surgery Hip Replacement Expectations Survey

Activity and participation

For all groups, outcomes on ADL, and Sport and Recreation improved postoperatively (Figures 2 and 3, Supplementary Table 1, see Supplementary data). For instance, ADL scores improved by 40 points (CI 38; 42) in the DAA group and 34 points in the PLA group (Supplementary Table 1, see Supplementary data: Estimate of “3 months FU + Approach*3months FU”: 39.6+5.3). Compared with the DAA group, the PLA group only scored clinically worse on ADL at 12 months (12-month FU: 7; CI -12; -2.4; Supplementary Table 1, see Supplementary data). 7.1 represents a clinically relevant difference between the DAA and PLA population, but the 95% confidence interval of this difference is big. No other clinically relevant differences were found in the total population. We found no clinical or statistically significant differences in the not-employed population. The employed PLA group scored clinically worse on both ADL (6-month FU: 10; CI -19; 0.1, 12-month FU: 9; CI -19; 0.4), and Sport and Recreation scores (6-month FU: -13; CI -21; -4.3, 12-month FU: 9; CI -18; 0.5) at both 6 and 12 months postoperatively, compared with the employed DAA group (Table 2, see Supplementary data). Similar to the total population, the differences are clinically relevant, but the 95% confidence intervals are big. To provide insight into the individual measurements over time, we included spaghetti plots of the ADL and Sport and Recreation scores (Figures 4 and 5).

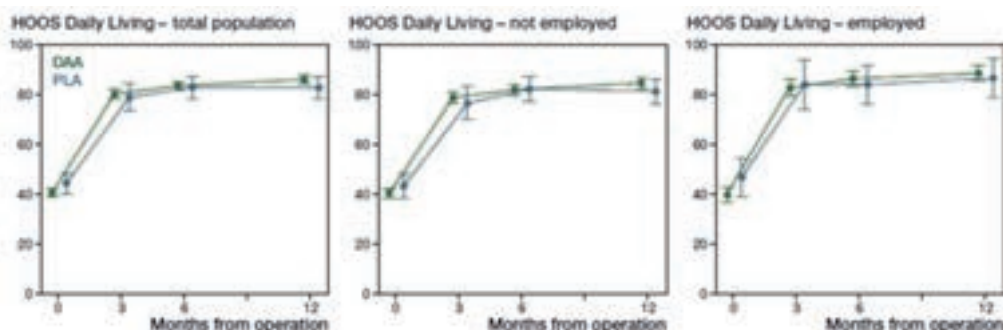


Figure 2 Score over time of the Hip Disability and Osteoarthritis Outcome Score (HOOS) subscale “activities of daily living”. Based on mixed-effect model analyses. 0 indicating preoperative measurement; 3, 6, 12 indicating measurement months postoperatively

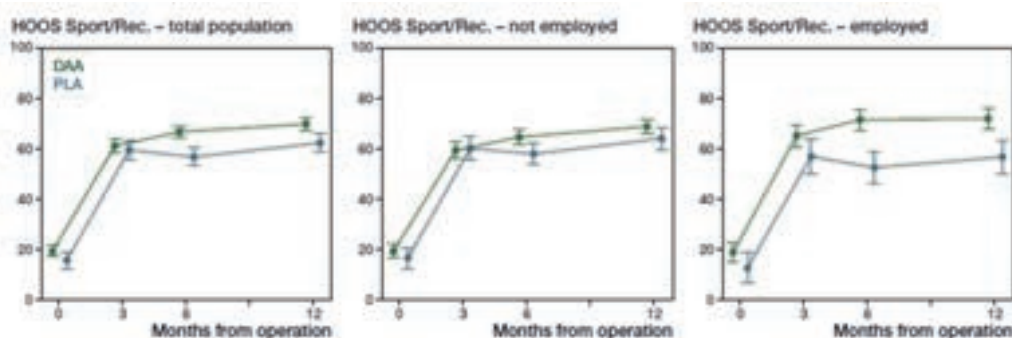


Figure 3. Score over time of the Hip Disability and Osteoarthritis Outcome Score (HOOS) subscale “Sport and recreation function.” Based on mixed-effect model analysis. 0: indicating preoperative measurement; 3, 6, 12: measurement months postoperatively.

Figure 3 Score over time of the Hip Disability and Osteoarthritis Outcome Score (HOOS) subscale “sport and recreation function”. Based on mixed-effect model analyses. 0 indicating preoperative measurement; 3, 6, 12 indicating measurement months postoperatively

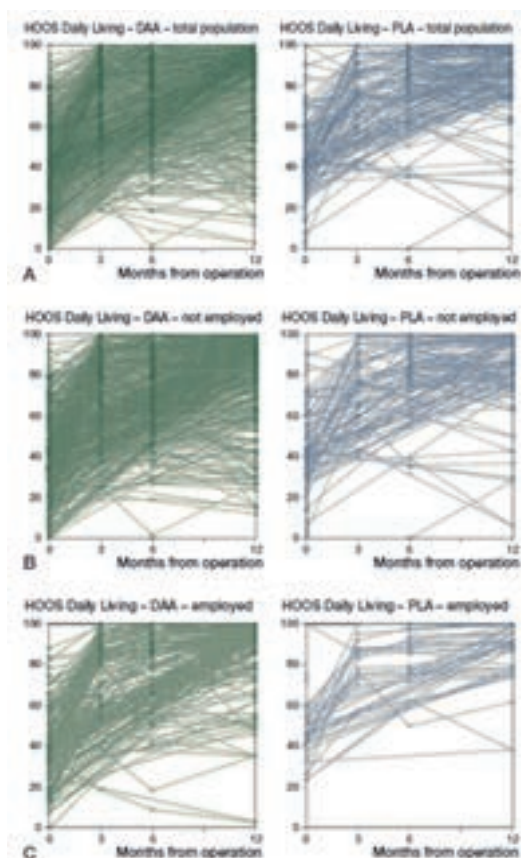


Figure 4. HOOS daily living scores in the total population (A), in the not-employed population (B), and in the employed population (C).

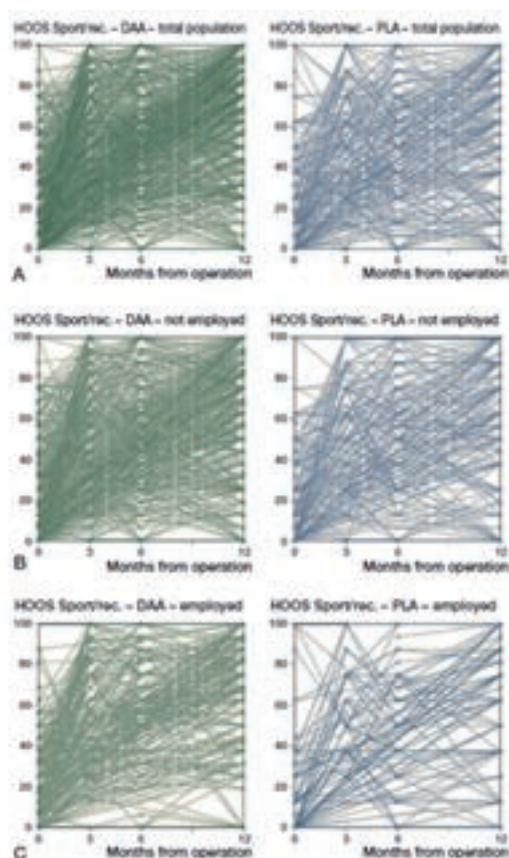


Figure 5. HOOS sport and reaction scores in the total population (A), in the not-employed population (B), and in the employed population (C).

Expectations regarding activity and participation

Preoperatively, PLA and DAA groups reported comparable preoperative expectations (Supplementary Table 2, see supplementary data). 6 months postoperatively, the PLA group had lower odds (70%; OR = 0.3; CI 0.2; 0.7) to fulfill the expectation on *sports performance*. At 12 months no difference between the 2 groups was present (Figure 6, Supplementary Table 2, see Supplementary data). We found no statistically significant differences in fulfillment of *joining recreational activities* or *social life* (Figure 6).

In the employed population, the PLA population had lower odds at 6 (80%; OR = 0.2; CI 0.1; 0.7) and 12 (30%; OR = 0.7; CI 0.2; 2.5) months regarding fulfillment of *joining recreational activities* (Figure 6, Supplementary Table 2, see Supplementary data). No statistically significant differences were present in the not-employed population.

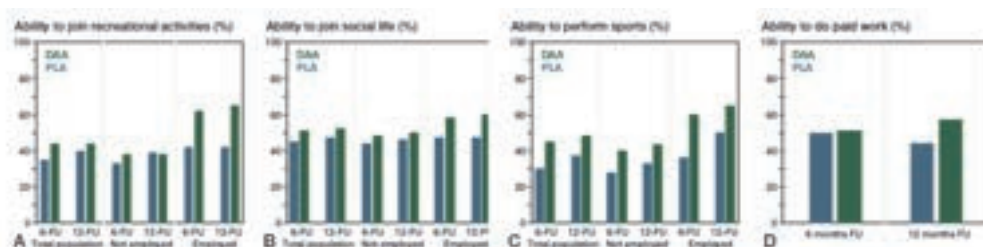


Figure 6 Fulfillment of expectations regarding activities and participation at 6 and 12 months after total hip arthroplasty A. Fulfillment of the preoperative expectation ‘ability to join recreational activities’. B. Fulfillment of the preoperative expectation ‘ability to join social life’. C. Fulfillment of the preoperative expectation ‘ability to perform sports’. D. Fulfillment of the preoperative expectation ‘ability to do paid work’ in the employed population. PLA = posterolateral approach; DAA = direct anterior approach; FU = follow-up

Work participation

Preoperatively, no statistically significant differences for type of work and hours worked were found between the PLA and DAA groups (Supplementary Table 3, see supplementary data). Although return to work within the first year postoperative was comparable (PLA = 85%; DAA = 86%), a larger proportion of DAA patients returned to work earlier (within 3 months: 45% vs 31%, $p = 0.07$; Supplementary table 4, see Supplementary data). Other postoperative work-related factors were similar (Supplementary table 4, see Supplementary data). Less than half of the employed population fulfilled their expectations on ability to do paid work at 6 (PLA = 44%; DAA = 45%) and 12 months (PLA = 39%; DAA = 50%) (Figure 6), but were similar between the groups (Supplementary table 2, see Supplementary data).

DISCUSSION

We assessed the association of “activity and participation” as well as expectations regarding the latter between 2 surgical approaches for THA (PLA and DAA) during the first postoperative year. As a secondary goal we evaluated these outcomes in employed and not-employed patients. At 12 months, patients with a DAA approach showed more improvement in ADL compared with the patients with a PLA. Patients with a PLA less often fulfilled their expectations regarding *sports performance* at 6 months postoperatively, but at 12 months results were comparable. Overall, functional recovery defined by the ICF domain “activity and participation” was comparable between both groups. The employed DAA group scored better on ADL and Sport and Recreation at 6 and 12 months postoperatively, and more often fulfilled their expectations regarding recreational activities at 6 months, and needed less time to return to work.

In line with previous studies, we found only small differences in the total population at 6 and 12 months postoperatively [2,3,16]. In the employed subgroup, surgical approach affected recovery of “activity and participation”, as well as fulfillment of expectations. The employed group was younger, healthier (less smoking, fewer comorbidities), and had higher preoperative expectations regarding “activity and participation” than the not-employed group. Previous research showed that younger patients recovered faster with respect to function and pain, allowing a positive effect on participation [17]. Additionally, younger and more active patients considering THA view improvement of activity levels, ability to return to work, and social role participation as more important [18,19]. Hence, the combination of these differences in preoperative factors, recovery (less muscle damage and improved function after DAA), as well as a more prominent view on return to work and social participation, might explain why we found more favorable results for DAA in the employed group.

Concerning work participation, the average return to work within the first year is in accordance with a systematic review [20]. Within the first 3 postoperative months, a larger proportion of employed DAA patients returned to work (45% versus 31%). This might be related to less muscle damage during DAA, resulting in faster gait training and thus earlier functional independence and return to work, but literature is lacking on this assumption. A faster return to work coincides with substantial financial benefits. Additionally, DAA is less expensive

per patient than PLA [21]. Therefore, there might also be a financial consideration to use DAA, especially with increasing numbers of working-age patients undergoing THA. Nevertheless, the results should be interpreted with caution, as the number of patients included in the employed PLA population is rather small. Therefore, a prospective randomized trial, including both surgical approaches for THA, is needed to validate the findings in this study, whilst also including objectively measured outcomes of functional recovery. Previous literature also reported short-term favorable outcomes regarding return to sporting activities and functional outcomes for DAA patients [7,22]. Although studies with longer follow-up were unable to show superiority for any approach based on patient-reported outcomes, others reported higher risks of femoral failure, complications, and revision surgery after DAA after mid- and long-term follow-up [2,22–24].

The main strength of this study is the large cohort design, assessing “activity and participation” pre- and postoperatively. Additionally, avoiding inclusion based on patients’ preference for a certain surgical approach can be viewed as an instrumental variable, as both hospitals exclusively performed one of the approaches. All arthroplasties were performed using uncemented techniques, therefore the results of this study are not generalizable to the patient population that received cemented THA. We did not include information on implant-related differences. However, implant-related differences will probably not affect short-term outcomes observed in this study. The presence of surgical complications was unavailable for this study, but the literature showed higher complication rates for DAA. Due to the IVA, possible disturbing effects of confounding are less of an issue here. Baseline imbalances in smoking and ASA were accounted for using adjustment in the statistical analyses. In addition, we tried to avoid the occurrence of selection bias (healthier patients choosing a certain approach) by including only patients from the hospital’s own catchment area, thereby ruling out a large part of the preference for a specific surgical approach. Additionally, both hospitals are of similar type (teaching hospitals) in the Netherlands, and both approaches are covered by health insurance. Furthermore, we stratified based on employment, but were unable to distinguish between having a non-paid job/volunteer work and no employment at all. It should be noted that, despite the large cohort, we also performed a large number

of statistical tests, which might have resulted in significant differences by random chance.

Conclusion

In this THA population, functional recovery related to “activity and participation” was comparable between the two surgical approaches. However, in the employed patient group, the DAA group had better functional recovery regarding “activity and participation” and had better fulfillment of expectations regarding activities and participation. Additionally, DAA might also facilitate faster return to work.

References

1. Register D A. Annual Report of the Dutch Arthroplasty Register; 2016.
2. Jia F, Guo B, Xu F, Hou Y, Tang X, Huang L. A comparison of clinical, radiographic and surgical outcomes of total hip arthroplasty between direct anterior and posterior approaches: a systematic review and meta-analysis. *Hip Int* 2019; 29: 584-96.
3. Peters R M, van Beers L, van Steenbergen L N, Wolkenfelt J, Ettema H B, Ten Have B, et al. similar superior patient-reported outcome measures for anterior and posterolateral approaches after total hip arthroplasty: postoperative patient-reported outcome measure improvement after 3 months in 12,774 primary total hip arthroplasties using the anterior, anterolateral, straight lateral, or posterolateral approach. *J Arthroplasty* 2018; 33: 1786-93.
4. Gignac M A, Backman C L, Davis A M, Lacaille D, Mattison C A, Montie P, et al. Understanding social role participation: what matters to people with arthritis? *J Rheumatol* 2008; 35: 1655-63.
5. Stucki G, Kostanjsek N, Ustün B, Cieza A. ICF-based classification and measurement of functioning. *Eur J Phys Rehabil Med* 2008; 44: 315-28.
6. Amlie E, Havelin L I, Furnes O, Baste V, Nordsletten L, Hovik O, et al. Worse patient-reported outcome after lateral approach than after anterior and posterolateral approach in primary hip arthroplasty: a cross-sectional questionnaire study of 1,476 patients 1–3 years after surgery. *Acta Orthop* 2014; 85: 463-9.
7. Mead P A, Bugbee W D. Direct anterior approach to total hip arthroplasty improves the likelihood of return to previous recreational activities compared with posterior approach. *J Am Acad Orthop Surg Glob Res Rev* 2022; 6.
8. Lee H Y, Jang S-N, Lee S, Cho S-I, Park E-O. The relationship between social participation and self-rated health by sex and age: cross-sectional survey. *Int Nurs Stud* 2008; 45: 1042-54.
9. Tilbury C, Leichtenberg C S, Kaptein B L, Koster L A, Verdegaal S H M, Onstenk R, et al. Feasibility of collecting multiple patient-reported outcome measures alongside the Dutch Arthroplasty Register. *J Patient Exp* 2020; 7: 484-92.
10. Rathod P A, Orishimo K F, Kremenic I J, Deshmukh A J, Rodriguez J A. Similar improvement in gait parameters following direct anterior & posterior approach total hip arthroplasty. *J Arthroplasty* 2014; 29: 1261-4.
11. Palan J, Manktelow A. Surgical approaches for primary total hip replacement. *Orthopaedics and Trauma* 2018; 32: 1-12.
12. Nilsson A K, Lohmander L S, Klässbo M, Roos E M. Hip disability and osteoarthritis outcome score (HOOS): validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord* 2003; 4: 10.
13. Dreinhöfer K, Stucki G, Ewert T, Huber E, Ebenbichler G, Gutenbrunner C, et al. ICF core sets for osteoarthritis. *J Rehabil Med* 2004; 10.1080/16501960410015498: 75-80.
14. van den Akker-Scheek I, van Raay J J, Reininga I H, Bulstra S K, Zijlstra W, Stevens M. Reliability and concurrent validity of the Dutch hip and knee replacement expectations surveys. *BMC Musculoskelet Disord* 2010; 11: 242.
15. Greenland S. An introduction to instrumental variables for epidemiologists. *Int J Epidemiol* 2000; 29: 722-9.
16. Fagotti L, Falotico G G, Maranho D A, Ayeni O R, Ejnisman B, Cohen M, et al. Posterior versus anterior approach to total hip arthroplasty: a systematic review and meta-analysis of randomized controlled trials. *Acta Ortop Bras* 2021; 29: 297-303.

17. Dolata J, Pietrzak K, Manikowski W, Kaczmarczyk J, Gajewska E, Kaczmarek W. Influence of age on the outcome of rehabilitation after total hip replacement. *Pol Orthop Traumatol* 2013; 78: 109-13.
18. Gignac M A, Backman C L, Davis A M, Lacaille D, Cao X, Badley E M. Social role participation and the life course in healthy adults and individuals with osteoarthritis: are we overlooking the impact on the middle-aged? *Soc Sci Med* 2013; 81: 87-93.
19. Takeuchi K, Hashimoto S, Matsumoto T, Hayashi S, Takayama K, Kuroda R. Recovery of activity level following total hip arthroplasty in patients less than 60 years of age. *Hip Int* 2020; 10.1177/1120700020911911: 1120700020911911.
20. Hoorntje A, Janssen K Y, Bolder S B T, Koenraadt K L M, Daams J G, Blankevoort L, et al. The effect of total hip arthroplasty on sports and work participation: a systematic review and meta-analysis. *Sports Med* 2018; 48: 1695-1726.
21. Joseph N M, Roberts J, Mulligan M T. Financial impact of total hip arthroplasty: a comparison of anterior versus posterior surgical approaches. *Arthroplast Today* 2017; 3: 39-43.
22. Zijlstra W P, De Hartog B, Van Steenberghe L N, Scheurs B W, Nelissen R. Effect of femoral head size and surgical approach on risk of revision for dislocation after total hip arthroplasty. *Acta Orthop* 2017; 88: 395-401.
23. Hoskins W, Bingham R, Lorimer M, Hatton A, de Steiger R N. Early rate of revision of total hip arthroplasty related to surgical approach: an analysis of 122,345 primary total hip arthroplasties. *J Bone Joint Surg Am* 2020; 10.2106/jbjs.19.01289.
24. Sun X, Zhao X, Zhou L, Su Z. Direct anterior approach versus posterolateral approach in total hip arthroplasty: a meta-analysis of results on early post-operative period. *J Orthop Surg Res* 2021; 16: 69

APPENDICES

Supplementary Table 1 Association between surgical approach and the subscales of the Hip Disability and Osteoarthritis Outcome Score

	Total population	Not employed population	Employed population
	Adjusted Model 1	Adjusted Model 2	Adjusted Model 3
	Estimates (95% CI)	Estimates (95% CI)	Estimates (95% CI)
Activities in daily living:			
Approach at baseline	3.9 (-0.6 to 8.4)	2.9 (-2.4 to 8.2)	7.1 (-1.2 to 15.5)
3-month FU	40 (38 to 42)	38 (36 to 41)	43 (39 to 47)
Approach*3-month FU	-5.3 (-11 to 0.7)	-5.2 (-12 to 1.8)	-5.7 (-17.0 to 5.7)
6-month FU	43 (41 to 45)	42 (40 to 44)	47 (43 to 50)
Approach*6-month FU	-4.4 (-9.2 to 0.4)	-2.6 (-8.2 to 2.9)	-9.5 (-19 to 0.1)
12-month FU	46 (44 to 47)	44 (42 to 46)	49 (45 to 52)
Approach*12-month FU	-7.1 (-12 to -2.4)	-6.3 (-12 to -0.9)	-9.1 (-19 to 0.4)
Sport and recreation function:			
Approach at baseline	-3.5 (-7.7 to 0.6)	-2.8 (-7.7 to 2.2)	-6.3 (-14 to 1.1)
3-month FU	42 (39 to 45)	40 (38 to 43)	47 (42 to 52)
Approach*3-month FU	1.9 (-3.1 to 7.0)	3.5 (-2.6 to 9.5)	-2.1 (-11 to 6.9)
6-month FU	48 (45 to 50)	45 (42 to 49)	53 (49 to 58)
Approach*6-month FU	-6.5 (-11 to -1.8)	-4.0 (-9.6 to 1.6)	-13 (-21 to -4.3)
12-month FU	51 (48 to 53)	50 (46 to 53)	54 (49 to 58)
Approach*12-month FU	-4.0 (-8.7 to 0.8)	-2.0 (-7.7 to 3.7)	-9.1 (-18 to -0.5)

Legend: Model 1 presents the analysis in the study population; Model 2 presents the analysis in the not-employed population; Model 3 presents the analysis in the employed population. Approach coded as: 0 = direct anterior approach (DAA) vs 1 = posterolateral approach (PLA). 95% CI = 95% confidence intervals; FU = follow-up. "Approach at baseline" = Difference in HOOS subscale score between PLA and DAA at baseline (preoperative). "# month FU" = increase/decrease (if negative score) in HOOS subscale between baseline score and score at # months of follow-up. "Approach*month FU" = interaction term between approach and follow-up measurement; difference in HOOS subscale score between PLA and DAA at # month of follow-up. Adjusted model 1, 2, 3: adjusted for American Society of Anesthesiologists' physical status classification and smoking status.

Supplementary Table 2 Association between surgical approach and fulfillment of expectations after total hip arthroplasty

	Total population	Not-employed population	Employed population
	Adjusted Model 1	Adjusted Model 2	Adjusted Model 3
	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)
Join recreational activities:			
Approach at 6-month FU	0.6 (0.3 to 1.2)	0.9 (0.4 to 2.0)	0.2 (0.1 to 0.7)
12-month FU	1.3 (0.9 to 1.8)	1.2 (0.8 to 1.9)	1.5 (0.7 to 3.2)
Approach*12-month FU	1.1 (0.5 to 2.2)	1.3 (0.6 to 3.0)	0.7 (0.2 to 2.5)
Ability to join social activities:			
Approach at 6-month FU	0.8 (0.4 to 1.5)	1.0 (0.4 to 2.4)	0.3 (0.1 to 1.2)
12-month FU	1.3 (0.9 to 2.0)	1.2 (0.8 to 2.0)	1.7 (0.8 to 3.9)
Approach*12-month FU	0.7 (0.4 to 1.5)	0.8 (0.3 to 1.9)	0.5 (0.1 to 2.2)
Ability to perform sports:			
Approach at 6-months FU	0.3 (0.2 to 0.7)	0.5 (0.2 to 1.2)	0.1 (0.0 to 0.5)
12-month FU	1.4 (0.9 to 2.1)	1.4 (0.9 to 2.3)	1.5 (0.6 to 3.7)
Approach*12-month FU	1.1 (0.5 to 2.3)	0.9 (0.4 to 2.2)	1.6 (0.3 to 7.4)
Ability to return to work :			
Approach at 6-month FU			0.6 (0.1 to 2.8)
12-month FU			1.9 (0.9 to 4.3)
Approach*12-month FU			0.3 (0.1 to 1.5)

Legend: Model 1 presents the analysis in the study population; Model 2 presents the analysis in the not-employed population; Model 3 presents the analysis in the employed population. Approach coded as: 0 = direct anterior approach (DAA) vs. 1 = posterolateral approach (PLA). 95% CI = 95% confidence intervals; FU = follow-up. "Approach at 6-month FU" = difference in odds of fulfillment of expectations between PLA and DAA at 6 months postoperatively. "12-month FU" = increase (if positive)/decrease (if negative) in odds of fulfillment of expectations between 6-month score and score at 12 months of follow-up. "Approach*12-month FU" = interaction term between approach and follow-up measurement; difference in odds of fulfillment of expectations between PLA and DAA at 12 months of follow-up. Adjusted model 1, 2, 3: adjusted for American Society of Anesthesiologists' physical status classification and smoking status.

Table 3 Preoperative work characteristics of the employed population receiving total hip arthroplasty

	PLA (n = 58)	DAA (n = 166)
Working hours	32 (12)	31 (12)
Physical workload, n (%):		
Light	27 (47)	64 (40)
Medium	17 (30)	66 (41)
Heavy	13 (23)	31 (19)
Work status, n (%):		
Employed	53 (91)	134 (82)
Self-employed	5 (9)	29 (18)
Sick leave due to hip complaints, yes, n (%)	14 (25)	40 (24)
Limited at work due to hip complaints, yes n (%)	52 (95)	130 (88)
SF-12		
Problems with work or other regular daily activities as a result of physical health? n (%):		
Accomplished less, yes	42 (74)	133 (81)
Limited in kind of work or other activities, yes	41 (71)	129 (78)
Pain interference with normal work (including work outside the home and housework)? n (%):		
Not at all/A little bit	38 (64)	79 (48)
Moderately	6 (10)	47 (29)
Quite a bit/Extremely	15 (26)	39 (24)
Expected working hours 12 months postoperatively	32 (14)	31 (13)
Compared with current situation, n (%):		
More hours	6 (12)	22 (15)
Less hours	2 (4)	4 (3)
Equal hours	43 (84)	126 (83)
Expected return to work (weeks)	8 (5)	8 (5)

Legend: Values are count (%) unless otherwise specified

PLA: posterolateral approach; DAA: direct anterior approach; SF-12: Short Form-12

Table 4 Postoperative work characteristics in the employed population receiving total hip arthroplasty

	PLA (n = 58)	DAA (n = 163)	p-value *
Return to work, yes (%):			
3-month FU	18 (31)	74 (45)	0.1
6-month FU	41 (72)	128 (79)	0.3
12-month FU	50 (86)	141 (87)	0.8
Working hours at follow-up:			
3-month FU	13.6 (11)	15.9 (10)	0.6
6-month FU	15.9 (11)	16.2 (11)	0.9
12-month FU	29.9 (15)	29.7 (14)	0.9
Limited at work due to complaints, yes, n (%):			
3-month FU	11 (61)	38 (51)	0.3
Missing	-	-	
6-month FU	18 (44)	50 (39)	0.7
Missing	-	2 (2)	
12-month FU	12 (24)	28 (20)	0.8
Missing	11 (22)	41 (29)	
SF-12			
Problems with work or other regular daily activities as a result of physical health? Yes, n (%):			
Accomplished less			
3-month FU	6 (33)	18 (24)	0.5
Missing	-	1 (1)	
6 month FU	12 (29)	29 (23)	0.5
Missing	-	1 (1)	
12 month FU	6 (12)	33 (23)	0.04
Missing	-	-	
Limited in kind of work or other activities			
3-month FU	8 (44)	26 (35)	0.5
Missing	-	1 (1)	
6 month FU	11 (27)	27 (21)	0.6
Missing	-	2 (2)	
12 month FU	11 (22)	31 (22)	0.9
Missing	1 (2)	2 (1)	
Pain interference with normal work (including work outside the home and housework)? n (%):			
3-month FU			
Not at all/A little bit			0.7
Moderately	-	2 (1)	
Quite a bit/Extremely	2 (11)	6 (8)	
Missing	15 (83)	63 (85)	
6-month FU	1 (6)	3 (4)	
Not at all/A little bit			0.7
Moderately	2 (5)	3 (2)	
Quite a bit/Extremely	4 (10)	11 (9)	
Missing	35 (85)	105 (82)	
12-month FU	-	9 (7)	
Not at all/A little bit			0.6
Moderately	33 (66)	87 (62)	
Quite a bit/Extremely	1 (2)	20 (14)	
Missing	1 (2)	5 (4)	
	15 (30)	29 (21)	

Legend: Values are count (%) unless otherwise specified *Comparison of PLA and DAA patients by means of independent sample t-test for continuous variables; chi-square test or Fisher's exact test for categorical variables.

PLA: posterolateral approach; DAA: direct anterior approach; FU: follow-up; SF-12: Short Form-12



Chapter 6

Adherence to the Dutch recommendation for physical activity: prior to and after primary THA and TKA

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Vliet Vlieland, and M.G.J. Gademán, on behalf of the LOAS study group

ABSTRACT

Purpose: The course of adherence to physical activity(PA) recommendation in hip/ knee osteoarthritis patients before and after hip/knee arthroplasty(THA/TKA). Moreover, we explored predictors for non-adherence 12-months postoperatively.

Materials and methods: Primary THA/TKA included in a multicenter observational study. Preoperatively and 6/12 months postoperatively, patients reported engagement in moderate-intensity PA in days/week in past 6 months(PA-recommendation(≥ 30 minutes of moderate-intensity ≥ 5 days/week)). We included predictors stratified by preoperative adherence: sex, age, BMI, comorbidities, smoking, living/working status, season, mental health, HOOS/KOOS subscales before and 6 months postoperatively, and 6-month adherence.

Results: (1005 THA/972 TKA) Preoperatively, 50% of the populations adhered. Adherence increased to 59% at 6 and 12 months. After 12 months, most patients remained at their preoperative PA-level, 11% of the preoperative adherers decreased, while 20% of the preoperative non-adherers increased their PA-level. In all different groups, adherence to the PA-recommendation at 6 months was identified as a predictor(OR-range:0.16-0.29). In addition, BMI was identified as predictor in the THA adherent (OR=1.07;95%-CI[1.02-1.15]) and TKA non-adherent group(OR=1.08;95%-CI[1.03-1.12]). THA non-adherent group not having paid work(OR=0.53;95%-CI[0.33-0.85]), and in the TKA adherent group a lower KOOS subscale symptoms(OR=1.03;95%-CI[1.01-1.05]) was associated with non-adherence.

Conclusion: Majority of patients remained at their preoperative PA-level. Non-adherence at 6 months was highly predictive for 12-month non-adherence.

INTRODUCTION

Physical inactivity, or sedentary behavior, increases mortality risk by 20-30% compared to active individuals [1,2]. Additionally, the evidence supporting health benefits of physical activity (PA) is irrefutable [3]. To experience health benefits from PA, various national and international guidelines regarding PA recommend at least 150 minutes of moderate to vigorous PA for adults per week [4-6]. In patients with end-stage OA of the lower extremity, achieving and maintaining a sufficient level of PA is particularly difficult, since they often experience severe joint pain, functional impairment, or fear of aggravating symptoms and increasing joint damage [7,8].

Since both THA and TKA surgery aim to relieve pain and decrease functional impairment, these patients should have the ability to become more physically active after surgery and reach a sufficient PA level to enhance their health [9,10]. However, Vissers et al. [9] showed that even though perceived physical function increased, patients do not adopt a more active lifestyle after THA or TKA. Several studies have demonstrated a difference in self-reported and objectively measured PA after surgery. While self-reported PA-levels tend to show higher PA-levels after surgery, PA-levels remain at or below pre-surgical levels when measured objectively [11-20]. Unraveling the differences between pre- and postoperative PA-levels is important, not only in the preoperative consultation and indication for surgery process of these elective surgeries, but also to identify patients eligible for interventions aimed at improving PA after surgery.

Previous studies identified risk factors for lower PA-levels after surgery: female gender, older age, higher body mass index (BMI), smoking, lower educational level, unemployment, number of comorbidities, OA pain in multiple sites, lower quality of life, sedentary behavior, and preoperative inadequate PA [4,5,11-13,21]. However, most studies only included risk factors either preoperative or postoperative, while noting the change in the physical activity score is essential.

Thus, the primary aim of this study was to assess the prevalence of adherence to the Dutch PA-recommendation, preoperatively and 6 and 12 months following primary THA or TKA. Secondly, we explored which patient characteristics (measured prior to surgery and/or at 6 months postoperatively) were associated with non-adherence to the PA-recommendation at 12 months. As preoperative PA-level is a strong predictor for postoperative PA-levels, we

stratified our population based on preoperative adherence level. This latter may enable the identification of patients at risk of non-adherence to the PA-recommendation after THA or TKA.

MATERIALS AND METHODS

Study design

This study included a subset of patients scheduled for THA or TKA, as a result of OA (October 2013–December 2018), from the ongoing Longitudinal Leiden Orthopaedics Outcomes of Osteo-Arthritis Study (LOAS) (Trial ID NTR3348) [22] (Level of Evidence II). Ethical approval was obtained from the regional Medical Research Ethics Committee (METC) (protocol number: P12.047). Patients treated with primary THA or TKA at one of the seven participating hospitals in the Netherlands were aimed to be included. After obtaining informed consent, patients received a paper or digital LOAS-questionnaire before surgery and at 6 and 12 months after surgery, containing a questionnaire regarding self-reported physical activity.

Patient selection

Patients were eligible if scheduled for a primary THA or TKA as a result of OA, were 18 years or older, and physically and mentally able to complete questionnaires in Dutch. Patients were excluded if the PA-level was missing at any of the time points after surgery.

Assessments

Patients' baseline characteristics

The following patient characteristics were collected preoperatively: sex, age (years), BMI, current smoking status (yes/no), living arrangements (alone/with others), and work status (paid work; yes/no).

The Dutch recommendation for health enhancing physical activity

The Dutch recommendation for health-enhancing physical activity (PA-recommendation) was used to evaluate patients' perceived PA. In September 2017 the Dutch Health Council launched new Physical Activity Guidelines [23,24]. According to the new guidelines for adults, a minimum of 150 minutes of moderate-intensity PA/week, divided over several days, is considered health

enhancing. Besides, muscle and bone strengthening activities are recommended at least twice a week, and for the elderly, combined with balance exercises. The LOAS-questionnaire included the Dutch PA-recommendation based on the guidelines before 2017, which states that at least 30 minutes of moderate-intensity PA/day, for a minimum of 5 days/week, is considered health-enhancing for adults, based on international guidelines [25]. PA of moderate intensity is defined as all kinds of PA with the same intensity as brisk walking or cycling. Prior to surgery and at 6 and 12 months postoperatively, patients answered how often they engaged in PA of such kind (days/week), for at least 30 minutes per day, in the past 6 months. Patients classified as “adherent” if they reportedly engaged on 5 or more days/week. As a result, patients who were active for more than 150 minutes/week, but not on 5 or more days/week, were classified as “non-adherent”.

Other assessments

Additionally, Patient Reported Outcome Measures (PROMs) were collected using several validated Dutch questionnaires. To gain insight into changes in disease state of patients, the questionnaires were collected prior to surgery and 6 and 12 months postoperatively. Validated Dutch versions of the Hip disability and Knee Injury and Osteoarthritis Outcome Score (HOOS/KOOS) were used to assess hip/knee associated problems (Pain, Function in daily living (ADL), Symptoms, Sports and Recreation Function and Quality of Life) [26-28], ranging from 0-100(0 representing the worst outcome and 100 representing the best outcome). Patient's general health and health-related quality of life were evaluated using the Short Form Health Survey (SF-12) [29], calculating summary scores for the Physical Component Summary (PCS) and Mental Component Summary (MCS), with a range from 0-100 (higher score indicating better health). To determine the presence of comorbidities before surgery, a comorbidity questionnaire from the Dutch Central Bureau of Statistics (CBS) [30] was used, analyzing whether comorbidities were present in the previous year, categorized into either musculoskeletal or non-musculoskeletal comorbidities.

Statistical analysis

All analyses were stratified by joint(hip/knee) and preoperative adherence level. To determine nonresponse bias, we performed unpaired T-tests(continuous,

normally distributed data) and Chi-squared tests (categorical data) to compare patient characteristics between the included and excluded patients. We visualized adherence trajectories over time. Subsequently, we calculated proportions of patients with increased, decreased, or equal PA-levels 12 months postoperatively.

To be able to identify patient-related predictors for PA-adherence (yes/no) 12 months postoperatively, we performed multiple multivariable logistic regression analyses with backward elimination (Level of significance for removing variables in the backward elimination was set at $P < 0.20$): A model including variables collected both before and 6 months postoperatively, stratified by joint and preoperative adherence. Decisions on the variables to be examined were based on previous studies and our own knowledge about PA after arthroplasty [12,21]. Included variables were: sex, age, BMI, comorbidities, smoking, living and working status, seasons, MCS and HOOS/KOOS scores (both before and 6 months after surgery), and 6-month adherence. Missing values in covariates (assumed to be missing at random (MAR)) were imputed using the Multivariate Imputation by Chained Equations (MICE) algorithm in R, while including all other variables available in the model [31]. Imputed data were visually inspected to determine if the data seemed reasonable, and were then pooled to obtain within- and between-imputation variance. The effect estimates were depicted as Odds Ratios (OR) with corresponding 95% Confidence Intervals (lower limit, upper limit). All analyses were performed using R (Version R 3.6.1).

RESULTS

Included patients

1596 THA and 1588 TKA patients answered the question regarding PA-levels prior to surgery. In total, 1005 (63%) THA and 972 (61%) TKA patients had preoperative and 6 and 12 month postoperative data (Figure 1). Compared to THA patients without postoperative PA information, the included THA patients were younger, more often female (60% in the group without PA information vs 65% among included patients), had lower BMI scores, more often had non-musculoskeletal comorbidities (21% in the group without PA information vs 31% among included patients), were less often smokers (9% in the group without PA information vs 4% among included patients), and had lower preoperative HOOS and SF-12 scores (Appendix table 1).

Similar to the THA population, compared to TKA patients without postoperative PA information, the included TKA patients were younger, less often smoker (8% in the group without PA information vs 5% among included patients) and more often had not only musculoskeletal comorbidities (respectively, no musculoskeletal comorbidities: 9% in the group without PA information vs 13% among included patients and only musculoskeletal comorbidities 8% in the group without PA information vs 10% among included patients, with better KOOS Sports and Recreation Function, MCS and PCS scores. Additionally, the TKA included patients more often had a paid job (19% in the group without PA information vs 27% among included patients) (Appendix table 1).

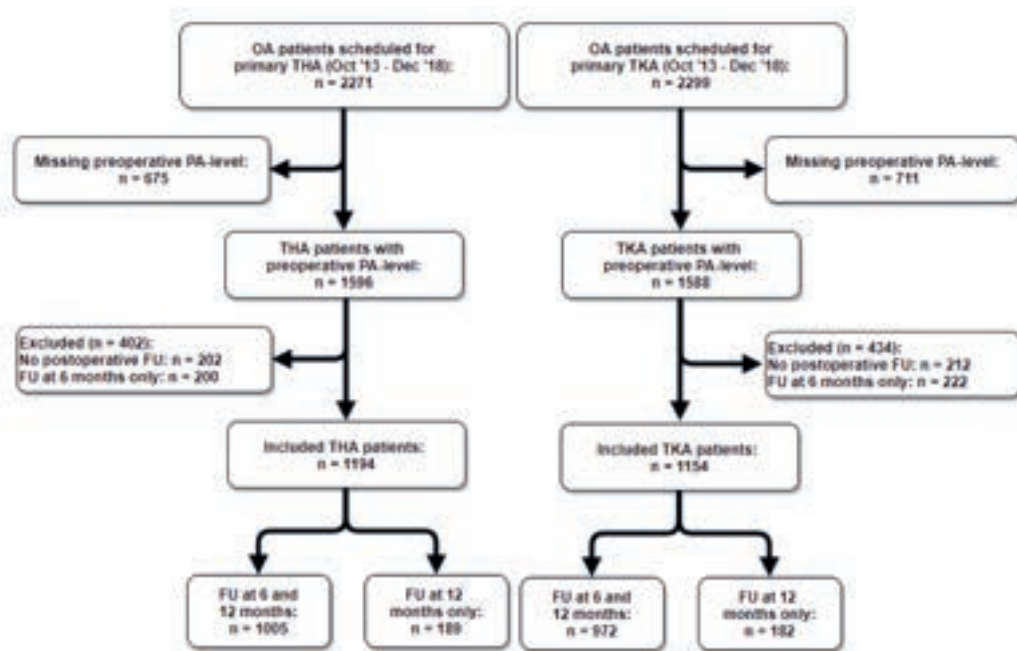


Figure 1 Flowchart patient selection

Legend: Included patients with data at all assessments

THA: Total Hip Arthroplasty; TKA: Total Knee Arthroplasty; OA: Osteoarthritis; PA-level: Physical Activity level; FU: Follow-up

Table 1 Preoperative characteristics of patients based on preoperative adherence to the Dutch PA-recommendation*

	THA		TKA	
	Adherent (n = 497)	Non- adherent (n = 508)	Adherent (n = 465)	Non- adherent (n = 507)
Sex, Female (%)	281 (56.5)	323 (63.6)	274 (58.9)	334 (65.9)
Age (years)	68.0 (8.3)	68.2 (9.1)	67.0 (8.2)	67.4 (8.0)
BMI	26.6 (3.8)	27.7 (4.4)	28.4 (4.3)	30.2 (5.1)
Smoking, yes (%)	18 (3.6)	21 (4.1)	22 (4.7)	25 (4.9)
Missing (%)	99 (19.9)	101 (19.9)	85 (18.3)	87 (17.2)
Comorbidities, (%)				
Non-musculoskeletal	145 (29.2)	162 (31.9)	161 (34.6)	166 (32.7)
Musculoskeletal	63 (12.7)	59 (11.6)	57 (12.3)	43 (8.5)
Both	163 (32.8)	196 (38.6)	128 (27.5)	180 (35.5)
None	67 (13.5)	45 (8.9)	67 (14.4)	59 (11.6)
Missing	59 (11.9)	46 (9.1)	52 (11.2)	59 (11.6)
HOOS/KOOS scores				
Symptoms	42.3 (18.9)	40.0 (17.7)	51.3 (17.7)	48.5 (17.8)
Pain	41.2 (18.3)	37.4 (17.9)	40.4 (17.5)	38.0 (16.6)
ADL	44.8 (19.2)	39.2 (18.2)	48.8 (18.0)	43.4 (17.7)
Sport and Recreation	23.6 (21.0)	16.5 (17.0)	12.9 (15.8)	10.5 (14.6)
Quality of life	32.1 (15.7)	27.2 (16.2)	28.8 (15.0)	25.2 (14.6)
Living arrangement, (%)				
Alone	95 (19.1)	102 (20.1)	80 (17.2)	106 (20.9)
With others	365 (73.5)	375 (73.8)	347 (74.6)	356 (70.2)
Missing	37 (7.4)	31 (6.1)	38 (8.2)	45 (8.9)
SF-12 scores				
MCS	55.1 (9.6)	53.3 (10.3)	55.9 (9.0)	54.7 (9.8)
PCS	34.2 (9.2)	30.8 (9.1)	34.7 (9.5)	30.7 (8.8)
Work				
Paid job, yes (%)	135 (27.2)	110 (21.7)	135 (29.0)	125 (24.7)
Missing	3 (0.6)	2 (0.4)	5 (1.1)	1 (0.2)
PA-recommendation, (days)	6.2 (0.9)	1.8 (1.5)	6.3 (0.9)	2.0 (1.5)

Legend: All continuous variables are depicted as mean (SD) *The Dutch recommendation for health enhancing physical activity

Note: THA = Total Hip Arthroplasty; TKA = Total Knee Arthroplasty; n = number of patients; SD = Standard Deviation; BMI = Body Mass Index; HOOS = The Hip disability and Osteoarthritis Outcome Score; KOOS = The Knee injury and Osteoarthritis Outcome Score; MCS = Mental Component Summary of the Short-Form-12; PCS = Physical Component Summary of the Short-Form-12

Preoperative physical activity

Preoperatively, 497 (49%) THA and 465 (48%) TKA patients adhered to the PA-recommendation. Adhering THA patients performed 30 minutes of moderate-intensity PA on 6 (SD:0.9) days/week, compared to 2 (SD:1.5) days/week in the non-adhering THA patients. Comparison of the adherent and non-adherent THA populations showed lower BMI scores, better HOOS subscales Pain, ADL, Sport and Recreation Function, and Quality of Life scores, MCS and PCS scores, and higher employment percentage (adherent: 27% vs non-adherent: 22%).

Moreover, in the adherent group the proportion of women was lower (adherent: 57% vs non-adherent: 64%) (Table 1). Overall, we found similar results in the TKA population, with on average lower BMI and better scores on all KOOS subscales and PCS in the adherent population. Additionally, the adherent TKA population consisted of less females (adherent: 59% vs non-adherent: 66%), compared to the non-adherent group.

When comparing PA in men and women within the adherent THA group, no differences were found (men: 6 (SD:0.9) days/week; women: 6 (SD:0.9) days/week), nor within the non-adherent group found (men: 2 (SD:1.5) days/week; women: 2 (SD:1.5) days/week).

Outcomes after surgery

PA-trajectories

With respect to PA-levels prior to surgery, 6 months, and 12 months postoperatively, we identified eight different trajectories over time (Figure 2/3). Overall, PA-adherence in both the THA and TKA population increased to 59% 12 months after surgery. Within the THA population, the group adhering to the PA-recommendation at 12 months consisted of 65% preoperative adherers and 35% preoperative non-adherers. Furthermore, 11% of patients decreased their PA-level, while 22% increased their PA-level at 12 months. Almost similar to the THA population, the adherent TKA group at 12 months of 64% preoperative adherers 36% preoperative non-adherers. Similar changes in adherent levels were found in the TKA population: 11% decreased, while 20% increased their PA-level. In total, 69% of THA and TKA patients remained at their preoperative adherence-level.

Approximately 70% of the THA and TKA patients reached their final PA-level at 6 months. Additionally, the PA-level had changed in 12% of THA and 13% of TKA patients at 12 months, while being consistent at preoperative and 6 months. Furthermore, 13% of THA and 7% of TKA patients switched at 6 months, to return to their preoperative level at 12 months.

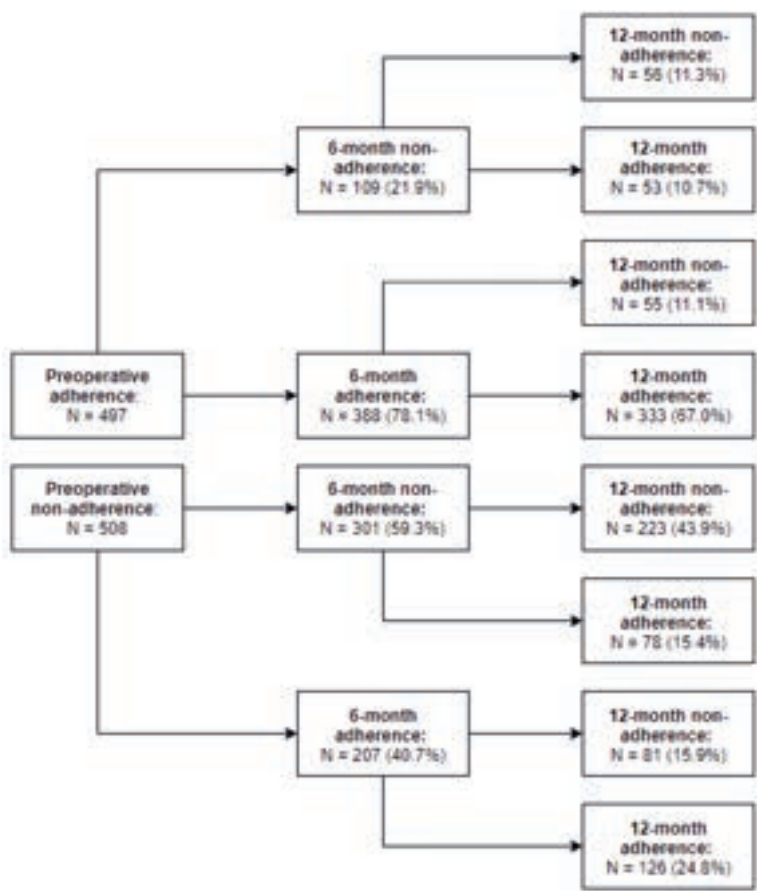


Figure 2 PA-recommendation trajectories after total hip arthroplasty

Legend: The eight different trajectories patients could follow regarding meeting the PA-recommendation preoperative, 6 and 12 months postoperative. All percentages are with respect to preoperatively meeting the PA-recommendation.

Complete cases: patients with data at both 6 and 12 months postoperative

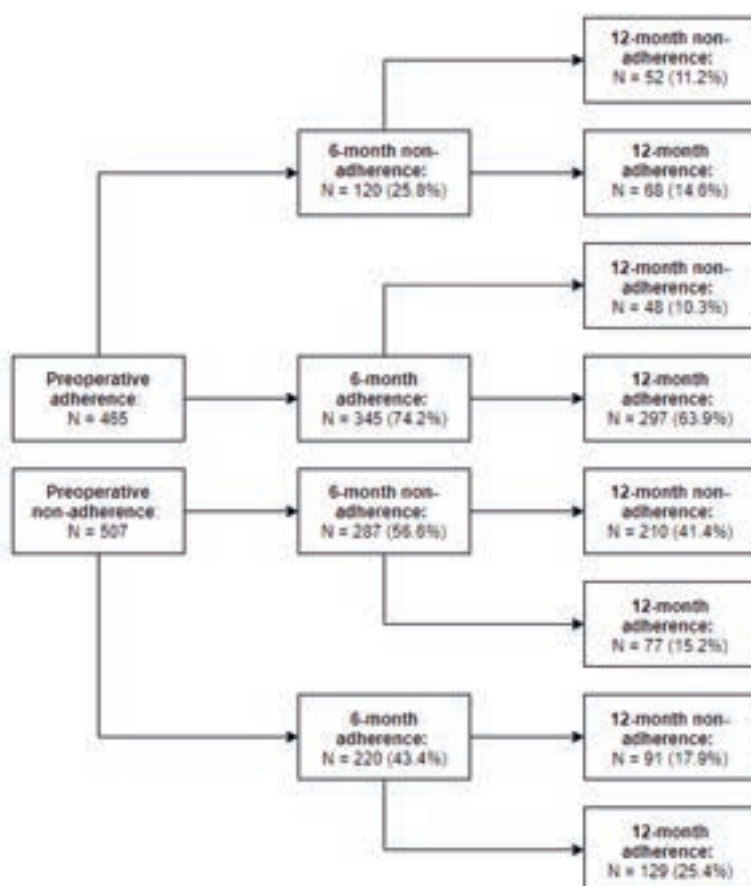


Figure 3 PA-recommendation trajectories after total knee arthroplasty

Legend: The eight different trajectories patients could follow regarding meeting the PA-recommendation preoperative, 6 and 12 months postoperative. All percentages are with respect to preoperatively meeting the PA-recommendation.

Complete cases: patients with data at both 6 and 12 months postoperative

Pain and functional outcomes

We did not find significant nor clinical differences in the preoperative adherent and non-adherent THA population when comparing changes in pain (preoperative–6 month FU; non-adherent: 49 (SD:22.0), adherent: 47 (SD:22.5) and changes in ADL (preoperative–6 month FU; non-adherent: 43 (SD:21.6), adherent: 41 (SD:21.9). We found similar results in the TKA population: changes in pain (preoperative–6 month FU; non-adherent: 42 (SD:23.3), adherent: 41 (SD:23.2) and changes in ADL (preoperative–6 month FU; non-adherent: 36 (SD:21.5), adherent: 33 (SD:20.8)).

Table 2 Associated predictors (Preoperative and 6 months after surgery) for adherence 12 months after surgery

	Total Hip Arthroplasty population		Total Knee Arthroplasty population	
	<i>Adherent (n = 497) OR [95% CI]</i>	<i>Non-adherent (n = 508) OR [95% CI]</i>	<i>Adherent (n = 465) OR [95% CI]</i>	<i>Non-adherent (n = 507) OR [95% CI]</i>
6-month follow-up model				
Age	-	-	1.03 [1.00 – 1.06]	1.03 [1.00 – 1.05]
BMI	1.07 [1.02 – 1.15]	-	1.06 [1.00 – 1.12]	1.08 [1.03 – 1.12]
Comorbidities	-	-	-	-
Musculoskeletal comorbidities (yes)		2.33 [0.96 – 5.68]		
Non-musculoskeletal comorbidities (yes)		1.03 [0.50 – 2.14]		
Both types (yes)		1.69 [0.80 – 3.57]		
MCS	-	-	-	0.97 [0.95 – 0.99]
Preoperative work status	-	0.48 [0.29 – 0.80]	-	-
Preoperative HOOS/KOOS subscales	-	-	-	-
Pain		-	0.99 [0.96 – 1.02]	-
ADL		0.99 [0.98 – 1.01]	0.99 [0.96 – 1.02]	-
Symptoms		1.02 [1.00 – 1.03]	1.03 [1.01 – 1.05]	-
Quality of life		-	-	1.02 [1.00 – 1.03]
6-month FU HOOS/KOOS subscales				
Pain	0.99 [0.97 – 1.00]	-	-	-
ADL	-	0.99 [0.97 – 1.00]	-	0.99 [0.98 – 1.00]
Quality of life			0.99 [0.98 – 1.00]	-
Meeting 6-month PA-recommendation	0.16 [0.10 – 0.27]	0.23 [0.15 – 0.35]	0.22 [0.13 – 0.36]	0.29 [0.19 – 0.42]

Legend:

Multivariable logistic regression with imputed values and backward elimination; If a variable was identified as a predictor for that time point and population, an Odds Ratio and corresponding 95% Confidence Interval is included in the table above.

*Stratification based on meeting the PA-recommendation prior to total hip or knee arthroplasty surgery; this was coded as event

Note: OR = Odds Ratio; 95% CI = 95% Confidence Interval; BMI = Body mass index; HOOS = The Hip disability and Osteoarthritis Outcome Score; KOOS = The Knee injury and Osteoarthritis Outcome Score; MCS-12 = Mental Component Summary of the Short-Form-12

Identified predictors for adherence to Dutch PA-recommendation

In table 2 we depicted the predictors, stratified for THA and TKA, for PA-adherence 12 months postoperatively. In all different groups, adherence to the PA-recommendation at 6 months was identified as a predictor. In addition, BMI was also identified as predictor in the THA adherent group (OR=1.07; 95%-CI[1.02-1.15]) and TKA non-adherent group (OR=1.08; 95%-CI[1.03-1.12]). In the THA non-adherent group we also identified not having paid work (OR=0.53; 95%-CI[0.33-0.85]), and in the TKA adherent group a lower KOOS subscale symptoms (OR=1.03; 95%-CI[1.01-1.05]) to be significantly associated with non-adherence.

DISCUSSION

We assessed the prevalence of adherence to the Dutch PA-recommendation, preoperative and 6 and 12 months postoperative primary THA or TKA. Secondly, we identified patient-related predictors both before and 6 months after surgery for non-adherence to the Dutch PA-recommendation 12 months postoperatively. Although 40% of the preoperative non-adherers became adherers 12 months after surgery, PA-adherence decreased in 22% of THA and TKA patients adherent before surgery. The majority of the patients remained at their preoperative PA-level. Several patient characteristics were associated with PA-adherence 12 months after THA and TKA, but 6-month non-adherence was the most common predictor among all groups and highly predictive for non-adherence at 12 months.

Preoperative, about 50% of THA and TKA patients adhered to the Dutch PA-recommendation, which is comparable, and even slightly higher than the general Dutch population (45% adherence) [32]. 12 months after surgery, 59% of the THA and TKA populations adhered in our study, which is comparable with, and also slightly higher than two other Dutch studies reporting 51% adherence after THA [33] and 55% adherence after TKA [34]. However, in those studies adherence to the PA-recommendation was measured with the Short QQuestionnaire to ASsess Health-enhancing physical activity (SQUASH), which has 11 items and includes questions on multiple activities people perform during a normal week in recent months, compared to the use of a one-item questionnaire in our study. Even though the majority of patients adhered to the Dutch PA-recommendation, with even greater numbers than the general Dutch population, there is still a large proportion of patients that remained below the adherence-

level or even decreased their PA-level. As said before, performing PA at a sufficient level is important to improve overall health status [35].

To the best of our knowledge, this is the first study reporting the proportion of patients with increased, decreased or equal PA-levels 12 months after THA/TKA in a larger cohort setting. A small study reported improved PA at 6 months after THA/TKA surgery in 72% of patients, while PA decreased in 10% of patients [11]. In comparison, our results were somewhat less positive at 12 months as the majority of patients that were non-adherent prior to surgery remained at their level(60%), and 11% of patients no longer adhered 12 months postoperative, while they adhered before surgery. Nevertheless, 22% of non-adherent patients increased their PA-level. Therefore, THA or TKA could offer preoperative non-adherent patients an opportunity to increase their PA-level [36]. Additionally, it is known that physical activity after THA or TKA has health enhancing benefits on bone quality, better muscle strength and coordination [3,37,38].

With regard to predictors for postoperative PA, Hodges et al. [12] found that inadequate PA before TKA was strongly predictive of inadequate PA 12 months postoperatively. Furthermore, previous studies identified older age, female gender, higher BMI, lower educational level, number of comorbidities, and lower quality of life after surgery to be associated with physical inactivity after surgery [12,21]. After stratification based on preoperative PA-adherence, we identified that whether or not patients adhered to the PA-recommendation at 6 months to be the only consistent predictor in all groups, with large odds ratios. None of the models showed a significant effect of pain or function, preoperatively or 6 months after surgery. Thus improved pain and function does not always result in a more active lifestyle, indicating that possibly a behavioral change is needed to gain a more active lifestyle after surgery.

On average, 40% of all patients did not adhere to the PA-recommendation 12 months after surgery. Webber et al.[39] showed that patients are often unaware of the health risks associated with high levels of sedentary behavior, and lack concern and familiarity with increasing PA in order to meet the recommended guidelines. Although PA-adherence after surgery is somewhat higher compared to the general population, clinicians could pay more attention to patient education as PA health benefits are substantial in this population. Furthermore, given the pervasive nature of sedentary behavior, there could also

be a potential role for behavior change interventions to increase PA after THA/TKA [21]. With our trajectories of patient flow, and identified characteristics of patients at risk of decreased PA-level after THA or TKA, orthopedic surgeons and physical therapist may be able to anticipate the behavior of their patients and intervene prior to and 6 months after surgery, to increase PA in these patients.

Strengths and limitations

This study has several strengths. First, it is a large, multicenter cohort study, assessing PA prior to surgery and 6 and 12 months after surgery. By including preoperative PA we could assess predictors for non-adherence for preoperative adherers and non-adherers. Limitations of the present study include the risk of bias: The PA level was assessed using a one-item question on PA behavior during the last 6 months. First, this is quite a long period, which could have resulted in recall bias, and such a long period is also likely to be influenced by the seasons. Furthermore, the use of self-reported physical activity has been shown to differ from objectively measured physical activity, as patient tend to overestimate their physical activity levels [11-20]. However, the use of objective measures (e.g. accelerometers) for physical activity levels in such a large population and both prior to and after surgery was not deemed feasible for the current study. Regarding subjective measurement instruments on PA, the literature reports that the validity of single-item questionnaires shows notable similarities to device-based measures and multiple-item measures for PA [40,41]. In that sense, the assessment method used can be considered as a strength. Moreover, previous studies show that single-item questions are valuable measurements in older adults and adolescents, as well as in settings where resources and time are limited [41]. Patients might have several reasons to refuse answering the PA-recommendation question, resulting in the introduction of self-selection. To evaluate this risk of bias, we compared characteristics of the included patients and excluded population, but we expect that no self-selection was introduced, as differences were not clinically relevant. Furthermore, we did not include all previously identified predictors for postoperative PA-level, such as educational level (this information was not recorded) and physical therapy (PT). The latter was excluded as 95% of our population used postoperative PT [42]. Lastly, due to the cutoff point (Adherence=PA \geq 5 days/week), misclassification may have occurred, as a patient's PA-level fluctuates over time around 5 days/week, they

could be included in the adherent group prior to surgery, while being included in the non-adherent group after surgery, indicating a decreased PA-level. Within the new guideline of the Dutch recommendation for health enhancing PA, the cut-off point of 5 days has been amended to 'a minimum of 150 minutes of moderate-intensity PA/week, divided over several days' thereby some participants in our study may adhere to the new recommendation but are classified as non-adheres in our current study. As such the numbers reported could be an underestimation of the new Dutch recommendation for health enhancing PA.

We presented trajectories of patient flow and identified predictors associated with adherence 12 months postoperatively. Non-adherence to the PA-recommendation at 6 months was found to be highly predictive for non-adherence at 12 months.

References

1. Organization WH. Physical activity 2018 [11 December 2019]. Available from: <https://www.who.int/news-room/fact-sheets/detail/physical-activity>
2. Lavie CJ, Ozemek C, Carbone S, et al. Sedentary Behavior, Exercise, and Cardiovascular Health. *Circulation research*. 2019 Mar;124(5):799-815.
3. Warburton DER, Bredin SSD. Health benefits of physical activity: a systematic review of current systematic reviews. *Current opinion in cardiology*. 2017 Sep;32(5):541-556.
4. Chang AH, Song J, Lee J, et al. Proportion and Associated Factors of Meeting the 2018 Physical Activity Guidelines for Americans in Adults with or at Risk for Knee Osteoarthritis. *Osteoarthritis and cartilage*. 2020 Mar 18.
5. Ernstgard A, PirouziFard M, Thorstensson CA. Health enhancing physical activity in patients with hip or knee osteoarthritis - an observational intervention study. *BMC musculoskeletal disorders*. 2017 Jan 25;18(1):42.
6. Herbolzheimer F, Schaap LA, Edwards MH, et al. Physical Activity Patterns Among Older Adults With and Without Knee Osteoarthritis in Six European Countries. *Arthritis care & research*. 2016 Feb;68(2):228-36.
7. Nuesch E, Dieppe P, Reichenbach S, et al. All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ (Clinical research ed)*. 2011 Mar 8;342:d1165.
8. Fransen M, McConnell S. Land-based exercise for osteoarthritis of the knee: a metaanalysis of randomized controlled trials. *The Journal of rheumatology*. 2009 Jun;36(6):1109-17.
9. Vissers MM, Bussmann JB, de Groot IB, et al. Physical functioning four years after total hip and knee arthroplasty. *Gait & posture*. 2013 Jun;38(2):310-5.
10. Jüni P, Reichenbach S, Dieppe P. Osteoarthritis: rational approach to treating the individual. *Best Pract Res Clin Rheumatol*. 2006 Aug;20(4):721-40.
11. Harding P, Holland AE, Delany C, et al. Do activity levels increase after total hip and knee arthroplasty? *Clinical orthopaedics and related research*. 2014 May;472(5):1502-11.
12. Hodges A, Harmer AR, Dennis S, et al. Prevalence and determinants of physical activity and sedentary behaviour before and up to 12 months after total knee replacement: a longitudinal cohort study. *Clinical rehabilitation*. 2018 Sep;32(9):1271-1283.
13. Issa K, Jauregui JJ, Given K, et al. A Prospective, Longitudinal Study of Patient Activity Levels Following Total Knee Arthroplasty Stratified by Demographic and Comorbid Factors. *The journal of knee surgery*. 2015 Aug;28(4):343-7.
14. Meessen JM, Peter WF, Wolterbeek R, et al. Patients who underwent total hip or knee arthroplasty are more physically active than the general Dutch population. *Rheumatology international*. 2017 Feb;37(2):219-227.
15. Hammett T, Simonian A, Austin M, et al. Changes in Physical Activity After Total Hip or Knee Arthroplasty: A Systematic Review and Meta-Analysis of Six- and Twelve-Month Outcomes. *Arthritis care & research*. 2018 Jun;70(6):892-901.
16. Arnold JB, Walters JL, Ferrar KE. Does Physical Activity Increase After Total Hip or Knee Arthroplasty for Osteoarthritis? A Systematic Review. *The Journal of orthopaedic and sports physical therapy*. 2016 Jun;46(6):431-42.
17. Paxton RJ, Melanson EL, Stevens-Lapsley JE, et al. Physical activity after total knee arthroplasty: A critical review. *World journal of orthopedics*. 2015 Sep 18;6(8):614-22.
18. Mills K, Falchi B, Duckett C, et al. Minimal change in physical activity after lower limb joint arthroplasty, but the outcome measure may be contributing to the problem: a systematic review and meta-analysis. *Physiotherapy*. 2019 Mar;105(1):35-45.

19. Kahn TL, Schwarzkopf R. Does Total Knee Arthroplasty Affect Physical Activity Levels? Data from the Osteoarthritis Initiative. *The Journal of arthroplasty*. 2015 Sep;30(9):1521-5.
20. Jeldi AJ, Deakin AH, Allen DJ, et al. Total Hip Arthroplasty Improves Pain and Function but Not Physical Activity. *The Journal of arthroplasty*. 2017 Jul;32(7):2191-2198.
21. Naylor JM, Pocovi N, Descallar J, et al. Participation in Regular Physical Activity After Total Knee or Hip Arthroplasty for Osteoarthritis: Prevalence, Associated Factors, and Type. *Arthritis care & research*. 2019 Feb;71(2):207-217.
22. Tilbury C, Leichtenberg C, Kaptein B, et al. Feasibility of Collecting Multiple Patient-Reported Outcome Measures Alongside the Dutch Arthroplasty Register. *Journal of Patient Experience*. 2019 06/04:237437351985316.
23. Klein Kd. De beweegrichtlijnen per september 2017: Kenniscentrum Sport & Bewegen; 2020 [updated 19-02-2020]. Available from: <https://www.allesoversport.nl/artikel/hoeveel-moet-je-bewegen-volgens-de-beweegrichtlijnen/>
24. Bernaards C. Bewegen in Nederland 2000-2013. Leiden 2014.
25. Gezondheidsraad. Beweegrichtlijnen 2017 2017. Available from: <https://www.gezondheidsraad.nl/documenten/adviezen/2017/08/22/beweegrichtlijnen-2017>
26. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health and quality of life outcomes. 2003 Nov 3;1:64.
27. de Groot IB, Favejee MM, Reijman M, et al. The Dutch version of the Knee Injury and Osteoarthritis Outcome Score: a validation study. Health and quality of life outcomes. 2008 Feb 26;6:16.
28. Nilsdotter AK, Lohmander LS, Klassbo M, et al. Hip disability and osteoarthritis outcome score (HOOS)--validity and responsiveness in total hip replacement. *BMC musculoskeletal disorders*. 2003 May 30;4:10.
29. Gandhi SK, Salmon JW, Zhao SZ, et al. Psychometric evaluation of the 12-item short-form health survey (SF-12) in osteoarthritis and rheumatoid arthritis clinical trials. *Clinical therapeutics*. 2001 Jul;23(7):1080-98.
30. Statistiek CBvd. Gezondheid, leefstijl, zorggebruik; 2000-2009 2016. Available from: <https://opendata.cbs.nl/statline/> \l "/CBS/nl/dataset/03799/table?fromstatweb"
31. Buuren Sv, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in R. *Journal of statistical software*. 2010:1-68.
32. RIVM. Gestandaardiseerde trend voldoen aan beweegrichtlijnen: Volksgezondheidzorg.info; 2019 [updated 18 April 2019;17 April 2020]. Available from: <https://www.volksgezondheidzorg.info/onderwerp/bewegen/cijfers-context/trends>
33. Wagenmakers R, Stevens M, Zijlstra W, et al. Habitual physical activity behavior of patients after primary total hip arthroplasty. *Physical therapy*. 2008 Sep;88(9):1039-48.
34. Kersten RF, Stevens M, van Raay JJ, et al. Habitual physical activity after total knee replacement. *Physical therapy*. 2012 Sep;92(9):1109-16.
35. Kokkinos P. Physical activity, health benefits, and mortality risk. *ISRN Cardiol*. 2012;2012:718789.
36. Ponzio DY, Rothermel SD, Chiu YF, et al. Does Physical Activity Level Influence Total Hip Arthroplasty Expectations, Satisfaction, and Outcomes? *The Journal of arthroplasty*. 2021 Aug;36(8):2850-2857.
37. Warburton DE, Gledhill N, Quinney A. Musculoskeletal fitness and health. *Canadian journal of applied physiology = Revue canadienne de physiologie appliquee*. 2001 Apr;26(2):217-37.

38. Kuster MS. Exercise recommendations after total joint replacement: a review of the current literature and proposal of scientifically based guidelines. *Sports medicine (Auckland, NZ)*. 2002;32(7):433-45.
39. Webber SC, Ripat JD, Pachu NS, et al. Exploring physical activity and sedentary behaviour: perspectives of individuals with osteoarthritis and knee arthroplasty. *Disability and rehabilitation*. 2020 Jul;42(14):1971-1978.
40. Bauman AE, Richards JA. Understanding of the Single-Item Physical Activity Question for Population Surveillance. *Journal of physical activity & health*. 2022 Oct 1;19(10):681-686.
41. O'Halloran P, Kingsley M, Nicholson M, et al. Responsiveness of the single item measure to detect change in physical activity. *PloS one*. 2020;15(6):e0234420.
42. Groot L, Latijnhouwers D, Reijman M, et al. Recovery and the use of postoperative physical therapy after total hip or knee replacement. *BMC musculoskeletal disorders*. 2022 Jul 13;23(1):666.

APPENDIX

Supplementary table 1 Characteristics of included and excluded patients

	THA			TKA		
	Included (n=1005)	Excluded (n=1266)	P - value	Included (n= 972)	Excluded (n=1327)	P - value
Sex, Female (%)	604 (60.1)	822 (64.9)	0.018	608 (62.6)	879 (66.2)	0.057
Age (years)	68.1 (8.7)	69.4 (9.4)	0.001	67.2 (8.1)	68.7 (8.7)	<0.001
BMI (mean (SD))	27.1 (4.2)	27.7 (4.4)	0.001	29.4 (4.8)	29.7 (4.9)	0.073
Smoking, yes (%)	39 (3.9)	109 (8.6)	<0.001	47 (4.8)	101 (7.6)	0.028
Comorbidities, (%)			<0.001			0.033
None	112 (11.1)	54 (4.3)		126 (12.5)	115 (8.7)	
Non-musculoskeletal	307 (30.5)	260 (20.6)		327 (32.5)	433 (32.6)	
Musculoskeletal	122 (12.1)	162 (12.8)		100 (10.0)	110 (8.3)	
Both	359 (35.7)	465 (36.7)		308 (30.6)	419 (31.6)	
HOOS/KOOS scores						
Symptoms	39.3 (18.2)	36.8 (19.0)	0.012	39.2 (17.0)	39.0 (18.2)	0.879
Pain	41.1 (18.4)	40.4 (19.4)	0.449	49.8 (17.8)	49.9 (18.2)	0.987
ADL	42.0 (18.9)	38.3 (19.6)	<0.001	45.9 (18.1)	44.7 (19.5)	0.188
Sport and Recreation	20.0 (19.4)	14.1 (19.0)	<0.001	11.6 (15.2)	9.2 (14.6)	<0.001
Quality of life	29.6 (16.1)	27.1 (17.4)	0.006	26.9 (14.9)	26.2 (16.4)	0.398
Living arrangement, (%)			0.056			0.470
Alone	197 (19.6)	253 (20.0)		186 (19.1)	268 (20.2)	
With partner	634 (63.1)	662 (52.3)		590 (60.7)	727 (54.8)	
With partner and children	94 (9.4)	94 (7.4)		98 (10.1)	110 (8.3)	
Alone with children	12 (1.2)	18 (1.4)		13 (1.3)	22 (1.7)	
With others	0	5 (0.4)		2 (0.2)	3 (0.2)	
SF-12 scores						
MCS	54.2 (10.0)	52.9 (10.8)	0.007	55.3 (9.4)	54.0 (10.4)	0.004
PCS	32.5 (9.3)	30.5 (9.2)	<0.001	32.6 (9.3)	31.7 (9.2)	0.024
Paid job, yes (%)	245 (24.4)	249 (19.7)	0.475	260 (26.7)	255 (19.2)	0.001

Legend: All continuous variables are depicted as mean (SD)

THA = Total Hip Arthroplasty; TKA = Total Knee Arthroplasty; n = number of patients; SD = Standard Deviation; BMI = Body Mass Index; HOOS/KOOS = The Hip disability and Knee injury and Osteoarthritis Outcome Score; MCS = Mental Component Summary of the Short-Form-12; PCS = Physical Component Summary of the Short-Form-12



Chapter 7

Acute pain after total hip and knee arthroplasty does not affect chronic pain during the first postoperative year: observational cohort study of 389 patients

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ABSTRACT

Chronic pain is frequently reported after total hip and knee arthroplasties (THA/TKA) in osteoarthritis (OA) patients. We investigated if severity of acute postoperative pain following THA/TKA in OA patients was associated with pain during the first postoperative year. From an observational study, OA patients scheduled for primary THA/TKA (June 2012–December 2017) were included from two hospitals in the Netherlands. Acute postoperative pain scores were collected within 72 h postoperatively and categorized as no/mild ($\text{NRS} \leq 4$) or moderate/severe ($\text{NRS} > 4$). Pain was assessed preoperatively, 3, 6 and 12 months postoperatively using the HOOS/KOOS subscale pain. With Multilevel Mixed-effects-analyses, we estimated associations between acute and chronic pain until one year postoperative, adjusted for confounders and including an interaction term ($\text{Time} \times \text{Acute pain}$). 193 THA and 196 TKA patients were included, 29% of THA and 51% of TKA patients reported moderate/severe pain acutely after surgery. In the THA group, the difference in pain at 3 months between the no/mild and moderate/severe groups, was approximately six points, in favor of the no/mild group (95% CI $[-12.4 \text{ to } 0.9]$) this difference became smaller over time. In the TKA group we found similar differences, with approximately four points (95% CI $[-9.6 \text{ to } 1.3]$) difference between the no/mild and moderate/severe group at 6 months, this difference attenuated at 12 months. No association between severity of acute postoperative pain and pain during the first postoperative year was found. These findings suggest that measures to limit acute postoperative pain will likely not impact development of chronic pain.

INTRODUCTION

Approximately 20% of the general adult population suffers from OA of the knee, hip or hand, with increasing numbers due to age and obesity, resulting in increasing numbers of patients in pain due to OA [1]. Pain is a pervasive symptom in osteoarthritis (OA) patients, more often occurring than functional limitations [1], and the main reason that patients seek medical attention [2]. A previous study including patients with knee OA, showed that 41% of patients experience mild pain, 40% experienced moderate pain and 20% experienced severe pain [3]. Additionally, Zolio et al. [4] described the prevalence of neuropathic-like pain and/or pain sensitization in patients with knee and hip OA, using self-administered questionnaires, and showed that the prevalence of these types of pain ranged between 20 and 40% in knee OA and 9–29% in hip OA patients. Nevertheless, it is difficult to provide a pain prevalence number in these patients, given the variation in pain experienced by patients, as well as pain scores obtained and heterogeneity of the studied populations [5].

Apart from the fact that patients often suffer from pain prior to surgery, chronic pain after total hip and knee arthroplasty (THA/TKA) is an often reported unfavorable outcome [6, 7], with chronic pain defined as recurring or being present for more than 3 months [8]. The presence of chronic postoperative pain after arthroplasty surgery could have substantial unfavorable effects, including delayed postoperative rehabilitation [9], a negative impact on quality of life [10], decreased postoperative satisfaction [11] and increased the risk of revision surgery and additional healthcare costs [12, 13]. Therefore, new treatments targeting the prevention of the development of chronic postoperative pain after total joint arthroplasties are of utmost importance.

In surgical patients, (intensity of) acute postoperative pain has been postulated as a risk factor for chronic postoperative pain, although results are somewhat heterogeneous. [14]. Nevertheless, the effect of acute postoperative pain may be different in hip and knee arthroplasty patients compared to other surgical fields, as the majority of OA patients experienced pain for years before arthroplasty surgery [15]. Hence, one of the main indications for joint arthroplasty is chronic preoperative pain [16]. The few studies on the effect of acute postoperative pain in THA and TKA patients did not provide unequivocal evidence of the effect of acute postoperative pain on chronic postoperative pain

in patients with OA [17–21]. This may be due to several reasons: the use of a cross-sectional study design, recall bias in the intensity of acute postoperative pain (reported months after surgery) or end-points analysis at 6 months, while THA and TKA patients are known to show improvements later than 6 months after surgery [22, 23]. Additional research to gain further insight into the association between acute and chronic postoperative pain in THA and TKA patients is therefore needed. If the intensity of acute postoperative pain is associated with chronic postoperative pain, prevention of severe acute postoperative pain could be a treatment target to improve chronic postoperative pain.

Consequently, we performed a longitudinal, multi-center study to investigate if severity of acute postoperative pain, following THA or TKA in OA patients, is associated with chronic pain during the first postoperative year.

MATERIALS AND METHODS

Patients

This study was part of the ongoing cohort Longitudinal Leiden Orthopaedics and Outcomes of Osteoarthritis Study (LOAS) (Trial ID NTR3348) [24]. In short, ethical approval for the LOAS was obtained prior to patient recruitment from the Medical Ethics Committee of Leiden University Medical Center (LUMC; P12.047, date: 27th of March, 2012). Patients with OA and scheduled for a primary THA or TKA at two hospitals (i.e., Leiden University Medical Center (LUMC) or Alrijne Hospital) between June 2012 and December 2017 were included in the LOAS, after informed consent was obtained, which is in compliance with the Helsinki Declaration. For the present study, patients without an acute postoperative pain score or without any follow-up measurements were excluded.

Pain assessments

Acute pain scores were assessed by a nurse and reported in the medical file, every three hours within 72 h after surgery (during hospitalization), using the Numeric Rating Scale (NRS) at rest. This was part of standard care in both hospitals. The NRS provides a number between 0 and 10, with 0 meaning no pain and 10 meaning the worst pain possible [25]. An average acute pain score was calculated based on the two highest pain scores of all available pain scores within 72 h after surgery and afterwards categorized into ‘no/mild’ if $\text{NRS} \leq 4$ and

‘moderate/severe’ if NRS > 4 [26, 27]. If patients reported pain score > 4 points, additional analgesia were provided, as an NRS > 4 is seen as postoperative pain in need of intervention in the hospitals included in this study. Additionally, NRS > 4 served as a contraindication for discharge from recovery. Even more, a pain score of NRS 4 in postoperative patients is used as an upper limit (i.e. benchmark) in quality measure assessments.

Analgesic treatment

Patients for THA received spinal, combined spinal-epidural or general anesthesia during surgery. Postoperative pain relief was achieved by a combination of paracetamol, NSAID and morphine subcutaneously. Patients were discharged with oral oxycodone. TKA was performed under spinal, combined spinal-epidural or general with epidural anesthesia. Postoperatively, patients received a combination of paracetamol, NSAID and a patient controlled epidural anesthesia (PCEA) pump or an intravenous patient controlled anesthesia (PCA) pump with either morphine or fentanyl in case of spinal anesthesia. After epidural anesthesia was terminated, morphine was subcutaneously administered. Patients were discharged with oral oxycodone. Using questionnaires, patients were asked to report the use of acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) in the past six months before surgery, because of hip or knee complaints ((almost) daily, few days per week, few days per month), and indicate the persistence of hip or knee joint symptoms (< 1 year, 1–5 years, 5–10 years and > 10 years). Additionally, duration of surgery (minutes) and hospitalization (days) were collected from the medical records as possible proxies for complications during and after surgery [28].

Prior to surgery, and at 3 (if THA), 6, and 12 months after surgery patients received questionnaires to obtain pain scores using validated Dutch versions of the Hip disability of Knee injury and Outcomes of Osteoarthritis Score (HOOS/KOOS) [29]. These questionnaires contain 40 and 42 items, respectively, categorized into five subscales. We used the HOOS/KOOS pain subscale, with scores ranging from 0 to 100, with 0 indicating ‘extreme pain’ and 100 indicating ‘no pain’.

Secondary outcome measurements

The following sociodemographic characteristics were collected: age, sex, Body Mass Index (BMI (kg/m²)), type of anesthesia (i.e., local, general, or combination), living arrangement (household composition; i.e., living alone (yes/no)) and working status (i.e., employed or unemployed). To indicate the mental health status of the patient, the subscale Mental Component Summary of the Short-Form-12 (MCS-12) (ranging from 0 to 100, with higher scores representing better health) was used [30]. Information on existing comorbidities was collected with the comorbidity questionnaire of the Dutch Central Bureau of Statistics (CBS) [31], asking for the presence or absence of comorbidities in the previous year (yes/no). Comorbidities were classified into three domains: musculoskeletal comorbidities (severe elbow, wrist, hand or back pain and other rheumatic diseases), non-musculoskeletal comorbidities (chronic lung, cardiac, or coronary disease; arteriosclerosis; hypertension; stroke; severe bowel disorder; diabetes mellitus; migraine; psoriasis; chronic eczema; cancer; incontinence; hearing or vision impairments; and dizziness in combination with falling) and comorbidities that could cause chronic pain syndromes (diabetes mellitus; migraine; back pain, other rheumatic diseases).

Sample size calculation

We anticipated a correlation of 0.2 between severity of acute postoperative pain and pain within the first year after surgery. The sample size calculation with alpha equal to 0.05 and 80% power, resulted in a required sample size of 193 patients for the THA and TKA group. First, we assessed all 265 patients included in the LUMC between July 2012 and December 2017 (THA: n = 125; TKA: n = 140). Of these patients, 23 had no follow-up data, and 74 had no acute pain scores available, resulting in 168 LUMC patients (THA: n = 81; TKA: n = 87) to be included (Fig. 1). Then, we included a random sample from the Alrijne Hospital THA and TKA population to reach a minimum of 193 THA patients and 196 TKA patients (Fig. 1).

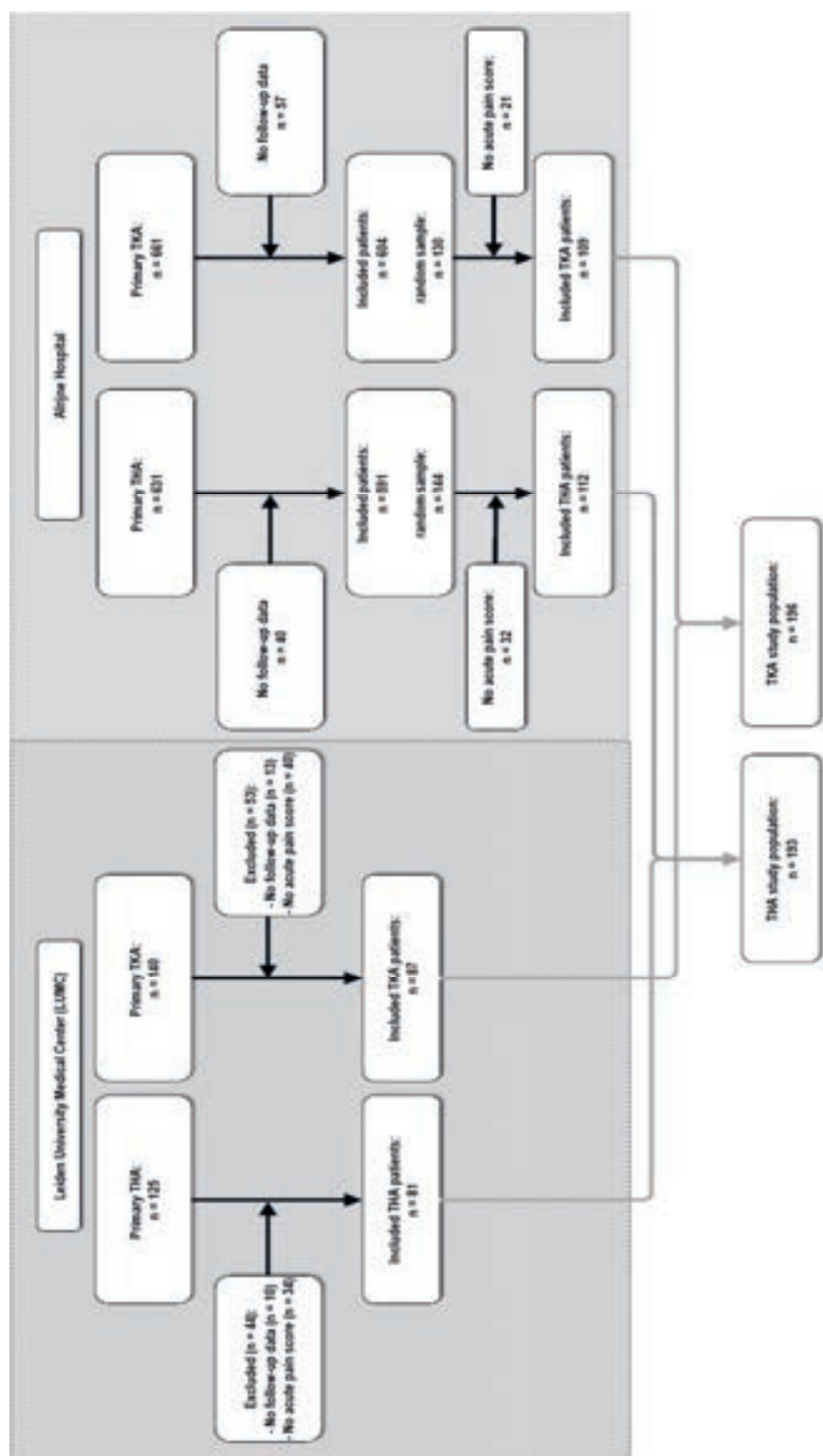


Figure 1 Flowchart of included total hip and knee arthroplasty patients.
THA Total Hip Arthroplasty, TKA Total Knee Arthroplasty

Statistical analyses

All analyses were performed while stratified by joint (hip or knee). Patients were grouped according to their acute postoperative score (i.e., no/mild NRS ≤ 4 , moderate/severe NRS > 4). To compare the characteristics of patients with no/mild and moderate/severe acute postoperative pain, we performed Mann–Whitney U tests (after check for normality, non-parametric tests were performed for continuous variables) and Chi-Square tests (for proportions). Baseline characteristics of included and excluded patients were compared to assess for selection bias. Although not statistically tested to avoid multiple testing, no clinically important differences were found between included and excluded patients (Supplementary Table 1).

We used multilevel mixed-effects-analyses to assess whether severity of acute postoperative pain was associated with pain during the first postoperative year, because it takes the between-patient correlation into account. The models included a group variable based on acute postoperative pain (i.e., no/mild or moderate/severe) and a time variable (i.e., 3 months, 6 months, 12 months). The models included subject-specific intercepts and a random effect to account for the correlation between repeated measures over time in the same patient, while correcting for originating hospital as patient population could vary between both hospitals. By including an interaction term between acute postoperative pain and timing of postoperative pain measurement (evaluated at 3 (if THA), 6 and 12 months postoperatively), we were able to assess whether acute postoperative pain affected postoperative pain during the first year after surgery. Further, we corrected for several confounders: age, sex, BMI, preoperative HOOS/KOOS pain score, preoperative MCS-12 score, surgery duration, hospitalization duration/length and type of anesthesia [18, 32]. Missing values in preoperative pain (1.6% in THA-group and 5.6% in TKA-group) and MCS-12 (2.6% in THA-group and 3.6% in TKA-group) (assumed to be missing at random (MAR)) were imputed using the Multivariate Imputation by Chained Equations (MICE) algorithm in R, based on variable available in the final model. Crude versus imputed models did not show differences in associations (data not shown). Sensitivity analyses were performed while including a continuous value for acute pain instead of acute pain based on the cut off value, to test the robustness of our exposure assessment. The

effect estimates were depicted as coefficients with 95% Confidence Intervals (95%-CI). All analyses were performed using R (Version R 3.6.1).

RESULTS

A total of 193 THA (57% female, mean age 67 (SD 10.4)) and 196 TKA patients (63% female, mean age 66 (SD 8.4)) were included in the present study (Fig. 1, Table Table1). The median number of acute postoperative pain measurements per patient was 5 [range 1–13] in THA and 6 [range 1–17] in TKA patients. In 15 THA and 14 TKA patients, only one NRS measurement was recorded. Overall, the mean acute postoperative pain scores were 4 (SD 1.7) in THA patients and 5 (SD 2.0) in TKA patients. Almost a third of the THA patients reported moderate/severe pain (NRS > 4 = 29%), compared to half of the TKA patients (NRS > 4 = 51%). THA patients reporting moderate/severe pain scored worse on preoperative pain and MCS-12, had increased duration of surgery and hospitalization period, and more often received a cemented arthroplasty compared to the no/mild acute pain group (Table1). TKA patients reporting moderate/severe pain scored worse on preoperative pain, used more acetaminophen 6 months prior to surgery, had lower MCS scores, and had a longer duration of surgery and hospitalization period compared to the no/mild acute pain group (Table 1).

Table 1 Comparison of preoperative patient characteristics and peri and postoperative treatment information: stratified for mild (NRS<5) and moderate/severe (NRS≥5) acute pain and joint*

Total population	THA			TKA		
	Total population (n = 193)	Mild (n = 137)	Moderate/ Severe (n = 56)	Total population (n = 196)	Mild (n = 97)	Moderate/ Severe (n = 99)
Sex, Female, n (%)	109 (57)	76 (56)	33 (59)	124 (63)	58 (60)	33 (67)
Age, median (IQR) (years)	66.0 (12)	66.5 (13)	66.0 (12)	66.0 (11)	65.0 (10)	66.0 (12)
BMI, median (IQR)	26.3 (6)	26.3 (6)	26.7 (6)	28.4 (6)	28.4 (6)	28.3 (7)
HOOS/KOOS, median (IQR)	35.0 (28)	37.5 (27)	27.5 (27)	36.1 (19)	40.4 (19)	33.3 (19)
Preoperative pain (0-100)						
Acetaminophen, n (yes (%))	119 (62)	81 (59)	38 (70)	143 (73)	60 (62)	39 (80)
NSAIDs, n (yes (%))	76 (39)	55 (40)	21 (38)	87 (44)	35 (36)	21 (43)
Duration of complaints, n (%)						
<1 year	28 (15)	17 (12)	17 (12)	10 (5)	3 (3)	7 (7)
1-5 years	106 (55)	76 (56)	76 (53)	87 (44)	45 (46)	42 (42)
5-10 years	28 (15)	19 (14)	19 (14)	39 (20)	18 (19)	21 (21)
>10 years	16 (8)	13 (10)	13 (10)	44 (22)	21 (22)	23 (23)
MCS-12, median (IQR) (0-100)	54.2 (14)	54.8 (13)	52.6 (16)	53.7 (10)	56.8 (10)	52.5 (9)
Work, n (yes (%))	56 (29)	41 (30)	15 (27)	63 (32)	32 (33)	31 (31)
Comorbidities, n (%)						
Non-musculoskeletal	47 (24)	33 (24)	10 (18)	51 (26)	26 (27)	25 (25)
Musculoskeletal	1 (1)	1 (1)	14 (25)	-	-	-
Chronic pain syndrome related	38 (20)	28 (20)	10 (18)	32 (16)	14 (14)	18 (18)
All	66 (34.2)	43 (31)	23 (41)	69 (35)	31 (32)	38 (38)
None	21 (10.9)	17 (12)	4 (7)	17 (9)	8 (8)	9 (9)
Living arrangement, n (%)						
Alone	49 (25)	31 (23)	18 (32)	39 (20)	13 (13)	26 (26)
Type of anesthesia, n (%)						
General	37 (19)	21 (15)	16 (28)	25 (13)	9 (9)	16 (16)
Local	31 (16)	26 (19)	5 (9)	86 (44)	40 (41)	46 (47)
Combination	125 (65)	90 (66)	35 (63)	85 (43)	48 (50)	37 (37)

Table 1 continues on the next page

Continuation of table 1

	Total population (n=193)	THA Mild (n = 137)	THA Moderate/ Severe (n = 56)	THA p-value ^a	TKA Total population (n = 196)	TKA Mild (n = 97)	TKA Moderate/ Severe (n = 99)	TKA p-value ^a
Fixation, n (%)								
Cementless	133 (69)	103 (75)	30 (54)		9 (5)	6 (6)	3 (3)	0.21
Hybrid	8 (4)	5 (4)	3 (5)		2 (1)	2 (2)	-	
Cemented	51 (26)	29 (21)	22 (39)		180 (92)	88 (91)	92 (93)	
Missing	1 (1)	-	1 (2)		5 (3)	1 (1)	4 (4)	
Duration surgery, median (IQR) (min)	72 (50)	70 (51)	88 (40)	0.004	77 (34)	68 (30)	82 (36)	<0.001
Hospitalization, median (IQR) (days)	3 (2)	2 (2)	3 (4)	<0.001	3 (2)	2 (2)	3 (3)	<0.001
Acute pain NRS, median (IQR) (0-10)	4 (2)				5 (3)			

Legend:

a: All continuous variables are depicted as median (Interquartile Range (IQR))

b: Comparison of patients with mild and moderate/severe acute pain by means of Mann-Whitney U tests (for continuous variables) or Chi Square test (for categorical variables)

NRS = Numeric Rating Scale

THA = Total Hip Arthroplasty

TKA = Total Knee Arthroplasty

n = number of patients

BMI = Body Mass Index

HOOS = The Hip disability and Osteoarthritis Outcome Score

KOOS = The Knee injury and Osteoarthritis Outcome Score

NSAID = Non-steroidal Anti-inflammatory Drugs

MCS-12 = Mental Component Summary of the Short-Form 12

Association acute postoperative pain

To evaluate if acute pain severity was associated with pain during the first postoperative year, an interaction term (Acute pain*Time of measurement) was added to the models. In the THA group, the difference between the no/mild and moderate/severe groups, was approximately 6 points (95%-CI [-12.4 to 0.9], on a 0–100 scale) at 3 months in favor of the no/mild group, and the difference became smaller over time. In the TKA group we found similar differences, with approximately 4 points (95%-CI [-9.6 to 1.3], on a 0–100 scale) difference between the no/mild and moderate/severe group at 6 months. The differences attenuated at 12 months. None of the coefficients showed clinically or statistically significant differences between no/mild and moderate/severe acute postoperative pain and postoperative pain during the first postoperative year (Table2). There were also no postoperative differences present between the no/mild and moderate/severe groups when compared in patients with complete follow-up (Fig. 2A and B).

Table 2 Estimated effects of the association between severity of acute postoperative pain and postoperative pain over time in total hip and knee arthroplasty patients^a

	THA Coefficient [95% CI] ^b	TKA Coefficient [95% CI] ^b
Adjusted Model ^c		
Moderate/Severe acute pain	-5.7 [-12.4 – 0.9]	-4.1 [-9.6 – 1.3]
6 months	5.5 [0.5 – 10.5]	
Acute pain*6 months	1.5 [-4.5 – 7.5]	
12 months	-1.7 [-6.8 – 3.3]	2.5 [-2.2 – 7.2]
Acute pain*12 months	4.8 [-1.2 – 10.8]	1.2 [-3.7 – 6.1]

Legend: a: Mixed model including interaction term hospital*time and acute pain*time; mild acute pain as reference category

b: 95% CI=95% Confidence Interval

c: Adjusted for Sex, Age, BMI, Preoperative pain, MCS-12, Duration of surgery and Hospitalization, Type of Anesthesia.

THA = Total Hip Arthroplasty, TKA = Total Knee Arthroplasty

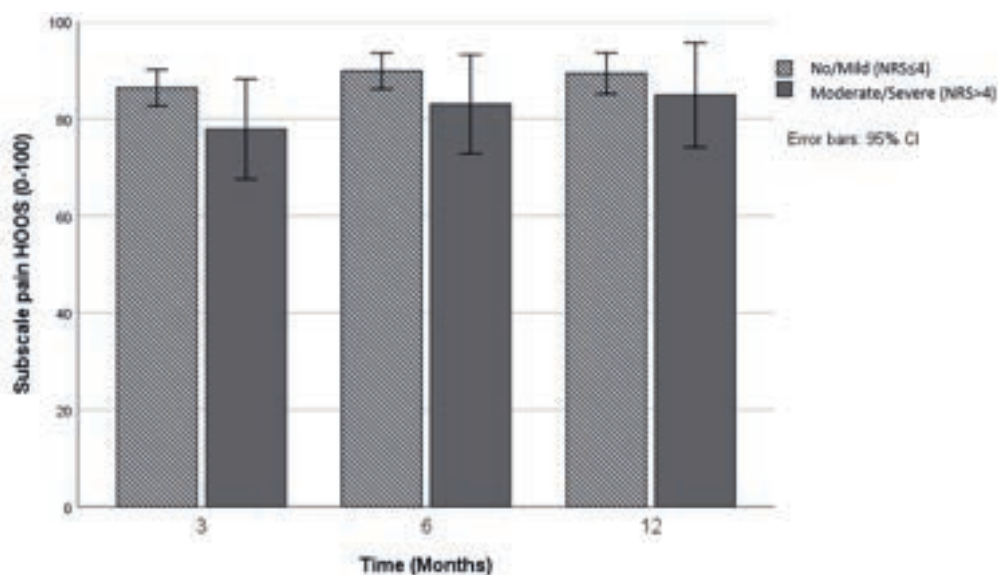


Figure 2-A Mean HOOS pain scores at 3, 6 and 12 months postoperatively in THA patients reporting no/mild or moderate/severe acute pain (0 = extreme pain, 100 = no pain) (n = 83)

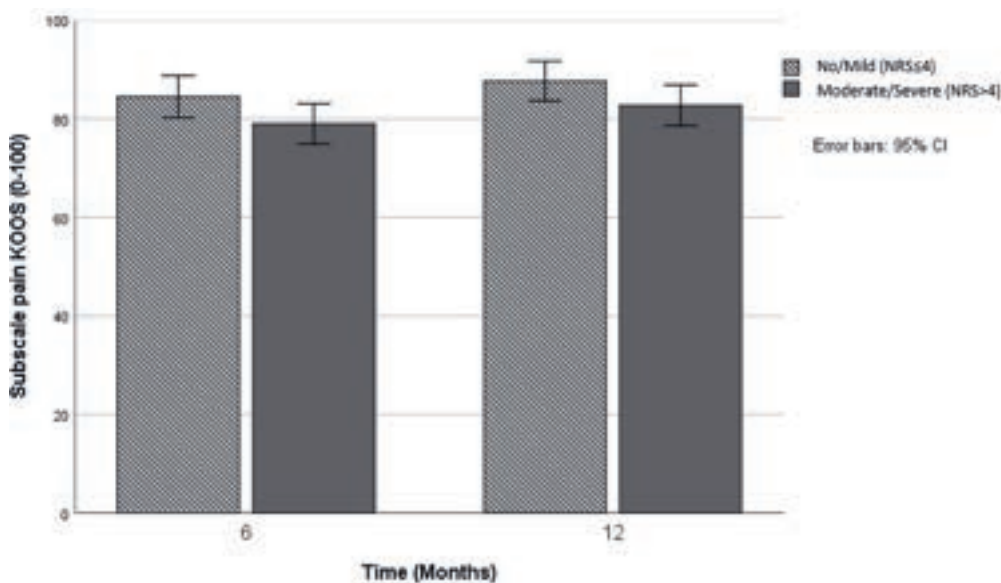


Figure 2-B Mean KOOS pain scores at 6 and 12 months postoperatively in TKA patients reporting no/mild or moderate/severe acute pain (0 = extreme pain, 100 = no pain) (n = 148)

Sensitivity analyses

In supplementary Table 2 the findings from the sensitivity analyses are shown. Including acute pain as a continuous measure in our model instead of including acute pain as category ($\text{NRS} \leq 4$ or $\text{NRS} > 4$) yielded similar results.

DISCUSSION

In this study we investigated if severity of acute postoperative pain, following THA or TKA in OA patients, was associated with pain during the first postoperative year. Almost one-third of THA, and more than half of TKA patients reported moderate/severe acute postoperative pain. Nevertheless, our findings indicated that severity of acute postoperative pain after THA or TKA was not associated with postoperative pain during the first postoperative year in this population.

Our findings are consistent with previous studies that were unable to show an association between acute and chronic postoperative pain in THA and TKA patients [17, 20, 21]. Similar to our study these studies collected acute postoperative pain scores shortly after surgery (within the first two postoperative days). In contrast to our study, both studies were smaller and assessed postoperative pain only up to 6 months after surgery, which is similar to the duration of follow-up in the study of Buvanendran et al. [18], who did find an effect of acute pain on postoperative pain. In comparison with Buvanendran et al. [18], we had a longer follow-up, included postoperative pain as a continuous measure, and applied less strict inclusion criteria. The study of Nikolajsen et al. [19] also found an effect of acute pain on postoperative pain, but patients had to recall their acute postoperative pain 12–18 months postoperatively, thereby possibly introducing recall bias. Our study collected acute postoperative pain from the medical files, reported during their hospitalization within 72 hours after surgery.

While our study is in concordance with some studies that assessed the effect of acute pain in OA patients after THA and TKA, our findings are inconsistent with other surgical fields that consider intensity of acute postoperative pain as a risk factor for the development of chronic pain [33]. A possible explanation could be that the type of injuries or diseases in these surgical fields have a more acute onset compared to patients suffering from OA, as patients with OA often suffer from (chronic) pain prior to surgery. This pain is the main reason that OA patients

seek medical attention [2]. Previous research showed that OA pain is the result of the involvement of both peripheral and central processes [2]. Nevertheless, the mechanism of pain is complex and not fully understood in OA patients, and neither is the development of chronic pain in patients after THA and TKA.

It is known that chronic pain is associated with changes in the peripheral and central nervous system in response to acute injury, such as surgery or trauma. This could result in hypersensitivity of the nervous system and if persistent, lead to central sensitization [34]. Several studies showed that central sensitization is related to the most consistent risk factors for the development of chronic postoperative pain in OA patients: preoperative and subacute (within 4–12 weeks after surgery) postoperative pain [32, 35–37]. Additionally, subacute pain triggers peripheral sensitization, which could result in central sensitization [38]. According to previous studies, the development of chronic postoperative pain may be prevented by preventing the development of central sensitization preoperatively or identify patients already suffering from central sensitization before surgery, as patients with central sensitization often experience less benefits after joint arthroplasties [33, 39].

As chronic pain could be the result of either chronic preoperative pain or (sub)acute postoperative pain, it is difficult to differentiate whether chronic postoperative pain is the result of (sub)acute postoperative pain from the surgery or ongoing preoperative pain. Future cohort studies including more extensive measurements for study purposes on preoperative and (sub)acute postoperative pain, preoperative data on endogenous pain modulation and quantitative sensory testing including central sensitization [40], should be carried out to contribute to the knowledge on modifiable factors of chronic postoperative pain after THA and TKA. Understanding the multifactorial components of OA pain and identifying possible causes of pain in these patients could result in more appropriate and effective treatments to help decrease the prevalence of chronic pain.

Pain experience in OA has a multidimensional nature, which causes the underlying etiology of OA-pain also to be multifactorial. Several modifiable risk factors have been reported that could reduce pain before surgery: losing weight, healthier dietary choices, levels of physical activity, use of assistive devices (i.e. insoles), decrease the number of medical comorbidities, pain catastrophizing and coping, and psychological factors, such as anxiety, distress and depression might

also affect postoperative pain [5, 32, 41, 42]. Sorel et al. [42] showed that perioperative interventions targeting psychological distress resulted in improved pain scores or decreased opioid or other types of pain medication prescriptions after TKA. Lastly, decreasing preoperative pain could result in better postoperative outcomes regarding pain in this population, as preoperative pain is mentioned as one of the main risk factors of pain postoperatively.

This study has several strengths and limitations: We imputed missing values in confounders, therefore refraining from exclusion of patients with missing values. After comparing the current population with the excluded patients we found no clinically relevant differences (Supplementary Table 1). Therefore we expect that no selection bias has occurred. A possible limitation could be the method of acute postoperative pain collection from medical records, which was part of standard care. Hence, acute pain was not collected with the intention to use for study purposes, and were therefore not regularly recorded by the same nurse, which could have affected the consistency. Furthermore, there is no consensus on cut-off points for NRS pain, which might affect generalizability [27, 43–46]. However, we additionally performed a sensitivity analysis while including acute pain as a continuous exposure, which yielded similar results. Nor did this study collected subacute pain (lasting 4–12 weeks post operatively) after surgery, to measure the effect on chronic pain. Subacute pain has been identified as risk factor for chronic pain after orthopedic surgeries, especially TKA [35]. We were unable to include specific information on analgesic treatment during hospitalization. However, we aimed to investigate the effect of perceived acute pain on chronic pain, making the underlying analgesic treatment less important. Additionally, we did not exclude or include patients based on their anti-inflammatory drug therapy before surgery. Lastly, some relevant patient characteristics were not available, such as the amount of pain catastrophizing, pain elsewhere in the body and presence of central sensitization in patients.

We found that a substantial group of THA and TKA patients reported moderate/severe acute postoperative pain, but no association between severity of acute postoperative pain and chronic pain during the first postoperative year was found. Although it is important to limit the presence of acute postoperative pain as much as possible, acute postoperative pain does not seem to be associated with postoperative pain. Therefore, efforts to reduce the presence of

chronic pain should be focused elsewhere, such as reduction of preoperative pain, or psychological well-being of the patient.

References

1. Trouvin AP, Perrot S. Pain in osteoarthritis. Implications for optimal management. *Joint Bone Spine*. 2018;85(4):429–434. doi: 10.1016/j.jbspin.2017.08.002.
2. Fu K, Robbins SR, McDougall JJ. Osteoarthritis: the genesis of pain. *Rheumatology (Oxford)* 2018;57(suppl_):iv43–iv50. doi: 10.1093/rheumatology/kex419.
3. Collins JE, Katz JN, Dervan EE, Losina E. Trajectories and risk profiles of pain in persons with radiographic, symptomatic knee osteoarthritis: data from the osteoarthritis initiative. *Osteoarthritis Cartilage*. 2014;22(5):622–630. doi: 10.1016/j.joca.2014.03.009.
4. Zolio L, Lim KY, McKenzie JE, Yan MK, Estee M, Hussain SM, et al. Systematic review and meta-analysis of the prevalence of neuropathic-like pain and/or pain sensitization in people with knee and hip osteoarthritis. *Osteoarthritis Cartilage*. 2021;29(8):1096–1116. doi: 10.1016/j.joca.2021.03.021.
5. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*. 2013;21(9):1145–1153. doi: 10.1016/j.joca.2013.03.018.
6. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *BMJ Open*. 2012;2(1):e000435. doi: 10.1136/bmjopen-2011-000435.
7. Boye Larsen D, Laursen M, Simonsen O, Arendt-Nielsen L, Petersen KK. The association between sleep quality, preoperative risk factors for chronic postoperative pain and postoperative pain intensity 12 months after knee and hip arthroplasty. *Br J Pain*. 2021;15(4):486–496. doi: 10.1177/20494637211005803.
8. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11) *Pain*. 2019;160(1):19–27. doi: 10.1097/j.pain.0000000000001384.
9. Ibrahim MS, Khan MA, Nizam I, Haddad FS. Peri-operative interventions producing better functional outcomes and enhanced recovery following total hip and knee arthroplasty: an evidence-based review. *BMC Med*. 2013;11:37. doi: 10.1186/1741-7015-11-37.
10. da Silva RR, Santos AAM, Júnior JSC, Matos MA. Quality of life after total knee arthroplasty: systematic review. *Revista Brasileira de Ortopedia (English Edition)* 2014;49(5):520–527. doi: 10.1016/j.rboe.2014.09.007.
11. Scott C, Howie C, MacDonald D, Biant L. Predicting dissatisfaction following total knee replacement: a prospective study of 1217 patients. *J Bone Jt Surg Br Volume*. 2010;92(9):1253–1258. doi: 10.1302/0301-620X.92B9.24394.
12. Khan M, Osman K, Green G, Haddad F. The epidemiology of failure in total knee arthroplasty: avoiding your next revision. *Bone Jt J*. 2016;98(1_Supple_A):105–112. doi: 10.1302/0301-620X.98B1.36293.
13. Pinto PR, McIntyre T, Ferrero R, Almeida A, Araújo-Soares V. Predictors of acute postsurgical pain and anxiety following primary total hip and knee arthroplasty. *J Pain*. 2013;14(5):502–515. doi: 10.1016/j.jpain.2012.12.020.
14. Gilron I, Vandenkerkhof E, Katz J, Kehlet H, Carley M. Evaluating the association between acute and chronic pain after surgery: impact of pain measurement methods. *Clin J Pain*. 2017;33(7):588–594. doi: 10.1097/ajp.0000000000000443.
15. Liu SS, Buvanendran A, Rathmell JP, Sawhney M, Bae JJ, Moric M, et al. Predictors for moderate to severe acute postoperative pain after total hip and knee replacement. *Int Orthop*. 2012;36(11):2261–2267. doi: 10.1007/s00264-012-1623-5.

16. Gademan MG, Hofstede SN, Vliet Vlieland TP, Nelissen RG, Marang-van de Mheen PJ. Indication criteria for total hip or knee arthroplasty in osteoarthritis: a state-of-the-science overview. *BMC Musculoskelet Disord*. 2016;17(1):463. doi: 10.1186/s12891-016-1325-z.
17. Clarke H, Kay J, Mitsakakis N, Katz J. Acute pain after total hip arthroplasty does not predict the development of chronic postsurgical pain 6 months later. *J Anesth*. 2010;24(4):537–543. doi: 10.1007/s00540-010-0960-z.
18. Buvanendran A, Della Valle CJ, Kroin JS, Shah M, Moric M, Tuman KJ, et al. Acute postoperative pain is an independent predictor of chronic postsurgical pain following total knee arthroplasty at 6 months: a prospective cohort study. *Region Anesth Pain Med*. 2019;44(3):e100036. doi: 10.1136/rapm-2018-100036.
19. Nikolajsen L, Brandsborg B, Lucht U, Jensen T, Kehlet H. Chronic pain following total hip arthroplasty: a nationwide questionnaire study. *Acta Anaesthesiol Scand*. 2006;50(4):495–500. doi: 10.1111/j.1399-6576.2006.00976.x.
20. Pinto PR, McIntyre T, Ferrero R, Araújo-Soares V, Almeida A. Persistent pain after total knee or hip arthroplasty: differential study of prevalence, nature, and impact. *J Pain Res*. 2013;6:691. doi: 10.2147/JPR.S45827.
21. Rice DA, Kluger MT, McNair PJ, Lewis GN, Somogyi AA, Borotkanics R, et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. *Br J Anaesth*. 2018;121(4):804–812. doi: 10.1016/j.bja.2018.05.070.
22. Vissers MM, Bussmann JB, Verhaar JA, Arends LR, Furlan AD, Reijman MJP. Recovery of physical functioning after total hip arthroplasty: systematic review and meta-analysis of the literature. *Phys Thera*. 2011;91(5):615–629. doi: 10.2522/ptj.20100201.
23. Vissers M, Bussmann J, De Groot I, Verhaar J, Reijman MJG. Physical functioning four years after total hip and knee arthroplasty. *Posture*. 2013;38(2):310–315. doi: 10.1016/j.gaitpost.2012.12.007.
24. Tilbury C, Leichtenberg CS, Kaptein BL, Koster LA, Verdegaal SHM, Onstenk R, et al. Feasibility of collecting multiple patient-reported outcome measures alongside the Dutch arthroplasty register. *J Patient Exp*. 2019;7:484–492. doi: 10.1177/2374373519853166.
25. Farrar JT, Young JP, Jr, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*. 2001;94(2):149–158. doi: 10.1016/s0304-3959(01)00349-9.
26. Mei W, Seeling M, Franck M, Radtke F, Brantner B, Wernecke KD, et al. Independent risk factors for postoperative pain in need of intervention early after awakening from general anaesthesia. *Eur J Pain (London, England)* 2010;14(2):149.e1–7. doi: 10.1016/j.ejpain.2009.03.009.
27. Gordon DB, Dahl JL, Miaskowski C, McCarberg B, Todd KH, Paice JA, et al. American pain society recommendations for improving the quality of acute and cancer pain management: American Pain Society Quality of Care Task Force. *Arch Intern Med*. 2005;165(14):1574–1580. doi: 10.1001/archinte.165.14.1574.
28. Yasunaga H, Tsuchiya K, Matsuyama Y, Ohe K. Analysis of factors affecting operating time, postoperative complications, and length of stay for total knee arthroplasty: nationwide web-based survey. *J Orthop Sci*. 2009;14(1):10–16. doi: 10.1007/s00776-008-1294-7.
29. de Groot IB, Reijman M, Terwee CB, Bierma-Zeinstra SM, Favejee M, Roos EM, et al. Validation of the Dutch version of the Hip disability and Osteoarthritis Outcome Score. *Osteoarthritis Cartilage*. 2007;15(1):104–109. doi: 10.1016/j.joca.2006.06.014.

30. Mols F, Pelle AJ, Kupper N. Normative data of the SF-12 health survey with validation using postmyocardial infarction patients in the Dutch population. *Qual Life Res.* 2009;18(4):403–414. doi: 10.1007/s11136-009-9455-5.
31. CBS. Gezondheid, leefstijl, zorggebruik 2009 [cited 2018 June 6]. Available from: <http://www.cbs.nl/>
32. Kim DH, Pearson-Chauhan KM, McCarthy RJ, Buvanendran A. Predictive factors for developing chronic pain after total knee arthroplasty. *J Arthroplasty.* 2018;33(11):3372–3378. doi: 10.1016/j.arth.2018.07.028.
33. Katz J, Seltzer Z. Transition from acute to chronic postsurgical pain: risk factors and protective factors. *Expert Rev Neurotherapeutics.* 2009;9(5):723–744. doi: 10.1586/ern.09.20.
34. McGreevy K, Bottros MM, Raja SN. Preventing chronic pain following acute pain: risk factors, preventive strategies, and their efficacy. *Eur J Pain Suppl.* 2011;5(2):365–376. doi: 10.1016/j.eujps.2011.08.013.
35. Veal FC, Bereznicki LRE, Thompson AJ, Peterson GM, Orlikowski C. Subacute pain as a predictor of long-term pain following orthopedic surgery: an australian prospective 12 month observational cohort study. *Medicine (Baltimore)* 2015;94(36):1. doi: 10.1097/md.0000000000001498.
36. Lindberg MF, Miaskowski C, Rustøen T, Cooper BA, Aamodt A, Lerdal A. Preoperative risk factors associated with chronic pain profiles following total knee arthroplasty. *Eu J Pain (London, England)* 2020 doi: 10.1002/ejp.1703.
37. Lewis G, Rice D, McNair P, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. *Br J Anaesth.* 2014;114(4):551–561. doi: 10.1093/bja/aeu441.
38. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. *Pain.* 2011;152(3 Suppl):S2–s15. doi: 10.1016/j.pain.2010.09.030.
39. Wylde V, Sayers A, Odutola A, Gooberman-Hill R, Dieppe P, Blom AW. Central sensitization as a determinant of patients' benefit from total hip and knee replacement. *Eur J Pain (London, England)* 2017;21(2):357–365. doi: 10.1002/ejp.929.
40. Damien J, Colloca L, Bellei-Rodriguez CE, Marchand S. Pain modulation: from conditioned pain modulation to placebo and nocebo effects in experimental and clinical pain. *Int Rev Neurobiol.* 2018;139:255–296. doi: 10.1016/bs.irn.2018.07.024.
41. Georgiev T, Angelov AK. Modifiable risk factors in knee osteoarthritis: treatment implications. *Rheumatol Int.* 2019;39(7):1145–1157. doi: 10.1007/s00296-019-04290-z.
42. Sorel JC, Overvliet GM, Gademan MGJ, den Haan C, Honig A, Poolman RW. The influence of perioperative interventions targeting psychological distress on clinical outcome after total knee arthroplasty. *Rheumatol Int.* 2020;40(12):1961–1986. doi: 10.1007/s00296-020-04644-y.
43. Gordon DB, de Leon-Casasola OA, Wu CL, Sluka KA, Brennan TJ, Chou R. Research gaps in practice guidelines for acute postoperative pain management in adults: findings from a review of the evidence for an American Pain Society Clinical Practice Guideline. *J Pain.* 2016;17(2):158–166. doi: 10.1016/j.jpain.2015.10.023.
44. Gerbershagen HJ, Rothaug J, Kalkman CJ, Meissner W. Determination of moderate-to-severe postoperative pain on the numeric rating scale: a cut-off point analysis applying four different methods. *Br J Anaesth.* 2011;107(4):619–626. doi: 10.1093/bja/aer195.
45. Boonstra AM, Stewart RE, Köke AJ, Oosterwijk RF, Swaan JL, Schreurs KM, et al. Cut-off points for mild, moderate, and severe pain on the numeric rating scale for pain in patients with chronic musculoskeletal pain: variability and influence of sex and catastrophizing. *Front Psychol.* 2016;7:1466. doi: 10.3389/fpsyg.2016.01466.

46. Cho S, Kim YJ, Lee M, Woo JH, Lee HJ. Cut-off points between pain intensities of the postoperative pain using receiver operating characteristic (ROC) curves. *BMC Anesthesiol.* 2021;21(1):29. doi: 10.1186/s12871-021-01245-5.

APPENDICES

Supplementary table 1 Comparison of study population and patients not included: stratified by joint^a

	THA		TKA	
	Study population (n = 193)	Not included (n = 563)	Study population (n = 196)	Not included (n = 605)
Sex, Female; n (%)	109 (57)	335 (60)	124 (63)	379 (63)
Age (years)	66.0 (12)	68.0 (13)	66.0 (11)	66.5 (12)
BMI	26.3 (6)	26.6 (5)	28.4 (6)	28.4 (6)
HOOS/KOOS, pain (0-100)	35.0 (28)	37.5 (20)	36.1 (19)	38.9 (23)
Acetaminophen, n (yes (%))	119 (62)	363 (70)	143 (73)	397 (71)
NSAIDs, n (yes (%))	76 (39)	232 (45)	87 (44)	255 (46)
MCS-12 (0-100)	54.2 (14)	56.3 (12)	56.8 (10)	56.6 (11)
Work, n (yes (%))	56 (29)	151 (27)	63 (32)	194 (33)

Legend:

a: All continuous variables are depicted as median (Interquartile Range (IQR))

THA = Total Hip Arthroplasty

TKA = Total Knee Arthroplasty

n = number of patients

BMI = Body Mass Index

HOOS = The Hip disability and Osteoarthritis Outcome Score

KOOS = The Knee injury and Osteoarthritis Outcome Score

NSAID = Non-steroidal Anti-inflammatory Drugs

MCS-12 = Mental Component Summary of the Short-Form-12

Supplementary Table 2 Estimated effects of the association between acute postoperative pain and postoperative pain over time in total hip and knee arthroplasty patients^a

	THA Coefficient [95% CI] ^b	TKA Coefficient [95% CI] ^b
Adjusted Model ^c		
Acute pain	-1.2 [-3.0 – 0.7]	-1.5 [-3.9 – 5.8]
6 months	2.7 [-5.2 – 10.6]	
Acute pain*6 months	0.9 [-0.8 – 2.5]	
12 months	-5.4 [-13.5 – 2.7]	-0.7 [-8.0 – 6.7]
Acute pain*12 months	1.4 [-0.3 – 3.1]	0.8 [-0.5 – 2.0]

Legend:

a: Mixed model including interaction term hospital*time and acute pain*time;

b: 95% CI=95% Confidence Interval

c: Adjusted for Sex, Age, BMI, Preoperative pain, MCS-12, Duration of surgery and Hospitalization, Type of Anesthesia.

THA = Total Hip Arthroplasty

TKA = Total Knee Arthroplasty



Chapter 8

Summary and general discussion, clinical implications and future perspectives

This thesis aims firstly to gain knowledge on the impact of total hip and knee arthroplasty (THA and TKA) on the patients' health status in terms of body functions and structures, activities and participation. Secondly to provide insight into determinants that affect outcomes of the patient's health. This chapter discusses the results and their implications.

Part I

This part, encompassing **chapters 2 and 3**, focused on the epidemiology and need of arthroplasties in people with hip or knee OA. The study in **chapter 2** is based on data of three national arthroplasty registers, the Dutch Arthroplasty Register (LROI) and the Danish Hip and Knee Arthroplasty registers (DHR and DKR). **Chapter 3** includes data collected from the LROI. The pandemic's surge in COVID-19 hospitalizations led to the postponement of elective surgeries [1, 2]. We therefore quantified the negative impact of the COVID-pandemic on the number of arthroplasty surgeries in the Netherlands and Denmark in **chapter 2**. The study aimed to investigate the estimated change in primary and revision arthroplasty rates for hips, knees and shoulders. Additional points of focus included the comparison of patient characteristics and hospital type, and the estimated loss of quality-adjusted life years and impact on the waiting lists. Using the LROI, DHR and DKR, information on arthroplasty surgeries between 2014 and 2020 was collected. Based on observed/expected ratios, we concluded that both countries performed fewer arthroplasty surgeries due to the COVID-pandemic expected (Netherlands: 20%; Denmark: 5%). As such, the Netherlands experienced a more pronounced impact of the COVID-pandemic on the number of performed arthroplasties compared to Denmark. Patients awaiting arthroplasty surgery due to OA were particularly impacted, as proportionally more acute arthroplasties, such as THA for a fracture, were performed during the pandemic. Nevertheless, within each indication category for arthroplasty, prioritization based on patient characteristics did not occur. Additionally, the patient characteristics for those receiving an arthroplasty for OA were similar in 2020 compared to previous years. Notably, private hospitals (i.e. no intensive care) were found to have partially compensated for the reduced capacity in public hospitals. Estimated total health loss depending on additional capacity ranged from: 19,800 – 29,400 QALYs Netherlands; 27,000; 1,700 – 2,400 QALYs Denmark.

With no additional capacity it will take more than 30 years to deplete the waiting-lists. Extended waits on the waiting list have a negative effect on patients' health status, making them more susceptible to other health problems, reducing their quality of life, and complicating rehabilitation [3-5]. The COVID-pandemic significantly increased the waiting lists for arthroplasty procedures, which had already been growing due to an increasing number of patients undergoing arthroplasty surgery in recent decades. As highlighted in the study, many patients endured loss of life years due to extended waiting for hip and knee arthroplasty surgery. Moreover, the lack of additional capacity to address the backlog resulting from the pandemic will place an added strain on the healthcare system for years to come. Without an increase in surgical capacity, the backlog is projected to persist for over 30 years. Future research contributing to the evidence-based personalized treatment recommendations, focusing on possible ways to prevent worsening of OA or helping patients cope with OA symptoms while awaiting arthroplasty surgery are needed.

In **chapter 3** we investigated the cumulative incidences of multiple joint arthroplasties (MJA). We also assessed the time between first lower joint arthroplasty and subsequent lower joint arthroplasty, and the (frequency of) MJA trajectories. Furthermore, we compared patient characteristics and postoperative PROs between MJA and single joint arthroplasty patients. We evaluated our aims with data of 140.406 primary index (i.e. first) hip arthroplasty patients and 140.268 knee arthroplasties patients with an OA indication from the LROI. We found that a considerable proportion of OA patients are at risk of MJA. The 10-year cumulative incidences of MJA for hip and knee arthroplasty patients was approximately 30%. During a 10 year period, relatively few patients (less than 4%), received more than two arthroplasties. The mean time intervals between the first and the second, third and fourth arthroplasty were 26 [95%-CI: 26.1 - 26.7], 47 [95%-CI: 46.4 - 48.4], and 58 [95%-CI: 55.4 - 61.1] months after index hip arthroplasty. For index knee arthroplasty, the mean time intervals were 26 [95%-CI: 25.9 - 26.3], 52 [95%-CI: 50.8 - 52.7], and 61 [95%-CI: 58.3 - 63.4] months. If patients received a second arthroplasty it was most often performed in the contralateral cognate joint. Thus, patients who received a hip as index arthroplasty most often received a contralateral hip arthroplasty as second arthroplasty and patients with a knee as first arthroplasty most often received a

contralateral knee arthroplasty. Female sex, higher BMI and younger age were associated with MJA. Patients with MJA reported slightly worse outcomes within the first year after their index arthroplasty than patients with a single arthroplasty.

The considerable proportion of patients with MJAs stresses the importance of including them in studies regarding postoperative outcomes, alongside single joint arthroplasty patients. In current research on outcomes after arthroplasties this is often not the case. In some cases this may lead to biased results, for instance when outcomes of different types of prostheses are compared and a certain prosthesis is more or less often used in MJA patients [6]. Furthermore, from a patient's perspective, as well as an orthopaedic surgeon's perspective, knowing the likelihood of multiple joint surgery within a certain time span after the index surgery, will be addressed different than patients with one joint affected by OA. This may ultimately result in more realistic patient expectations on the effect of arthroplasty surgery on existing symptoms.

Part II

The second part of this thesis focused on the impact of OA and THA or TKA on patients' health status. Specifically focusing on the identification of determinants affecting patients' perspectives regarding their health status. The research centered on the associations between arthroplasty surgery and the outcomes perceived by the patients. All the studies in this section are based on data from the Leiden Orthopaedics Outcomes of Osteo-Arthritis Study (LOAS).

All-encompassing International Classification of Functioning, Disability, and Health (ICF) domains

Addressing patient expectations regarding the outcome after arthroplasty surgery is a crucial part in the preoperative consultation of arthroplasty care. Patient expectations play a pivotal role in establishing realistic objectives and enabling patients to make informed decisions regarding the surgical procedure or even refraining from arthroplasty surgery. Notably, unrealistic expectations have the potential to lead to post-operative dissatisfaction. The research conducted in **chapter 4** investigated the differences between men and women in perceived preoperative expectations on the outcome of THA/TKA and their

fulfillment 1 year postoperatively. Expectations were collected preoperatively and 1 year postoperatively using the Hospital for Special Surgery Hip/Knee Replacement Expectations Surveys (HSS-HRES/KRES). We included 2333 THA (62% women) and 2398 TKA (65% women) patients. Results from this study revealed notable sex disparities in the way men and women perceive preoperative expectations and their corresponding fulfillment of expectations postoperatively. Men, in particular, reported higher preoperative expectations related to the ability to perform functional activities compared to women. The results also indicated that a larger number of items in the HSS-HRES and HSS-KRES questionnaires were considered applicable to men compared to women. Specifically, items such as sexual activity and the ability to engage in paid work were more often applicable to Dutch men. This result may be attributed to the fact that women in this study more frequently lived alone and were less likely to be employed at the age of THA or TKA. Furthermore, men exhibit a higher likelihood of fulfilling their postoperative expectations within one year of surgery. Although the majority of all patients had fulfilled their expectations on the HSS-HRES items, the proportion of men with fulfilled expectations was higher on all items.

Previous studies already identified sex as a predictive factor for unsatisfactory postoperative outcomes, with women being less likely to have their expectations met. Research also showed that women are at a disadvantage in various aspects of arthroplasty care compared to men. These disparities include differences in preoperative disease states, arthroplasty utilization rates, and gender biases that affect informed decision-making, referrals, and recommendations for arthroplasty surgery [7-9]. Disparities in perceived expectations may be associated with the presence of gender bias in arthroplasty care. Although available evidence on this subject is limited, studies suggest that this could be attributed to the timing at which women with OA seek medical treatment and the stage at which they present at the consultation [10]. Consequently, women often present with more pronounced functional limitations and pain, potentially seeking medical care at a more advanced stage of OA. However, it remains unclear whether lower expectations prompt the delay in seeking medical care or whether the delay in seeking medical care causes lower expectations.

Improving our comprehension of the effect of sex on expectations, both

prior to and following THA and TKA, holds significant value for both patients and their orthopedic surgeons. Providing patients with the necessary information prior to seeking surgical intervention, will lead to better-informed decisions, thereby additionally improving the shared decision-making process. For health care providers, such as orthopedic surgeons, a heightened awareness and knowledge of potential postoperative outcomes due to sex allows for more individualized expectation management. Consequently, related to a more patient-centered approach, outcomes and patient satisfaction may improve, and contributes to the reduction of gender disparities. Subsequently, future research should concentrate on assessing the efficacy of a tailored expectation management program, taking into account the results of the study in [chapter 4](#).

Activities and participation

Chapter 5 of this thesis is dedicated to the comparison of two surgical approaches for THA: the posterolateral approach (PLA) and the direct anterior approach (DAA). The comparison primarily focused on postoperative activities and participation within the "activity and participation" domain of the ICF during the initial year following surgery, as well as the associated expectations. To facilitate this comparison, we used the ICF domains of "activity" and "participation" [11]. Furthermore, we assessed whether outcome differed between patients who were employed and those who were not, given the growing number of relatively young patients with debilitating osteoarthritis (OA) opting for THA [12].

This study was conducted in a subpopulation of the LOAS study. We included 238 patients of the LangeLand Hospital in whom the PLA was used and 622 patients of the Alrijne Hospital in whom the DAA was performed. Approximately 25% of these patients were employed at the time of surgery. Overall our analysis yielded minimal differences between the two surgical approaches. At 6 months, significantly fewer PLA patients (Odds Ratio = 0.3, 95% Confidence Interval [0.2–0.7]) had fulfillment of the expectation sports-performance and at 12 months. Furthermore, the PLA group had a 7 point lower score on activities of daily living (ADL) than the DAA group. Other outcomes in terms of recovery within the ICF domain of "activity and participation" were comparable. However, when we analyzed the two approaches based on

employment status, the DAA group showed better scores in ADL (6 months: 10 point difference; 12 months: 9 point difference) and sports and recreation (6 months: 13 point difference; 9 point difference) post-surgery. Additionally, they more frequently fulfilled their expectations regarding recreational activities at the 6-month postoperative milestone and returned to work at a faster rate following surgery. PLA patients less often returned to work within 3 months (31% vs. 45%), but rates were comparable at 12 months (86% vs. 87%). A faster return to work aligns with both societal and financial advantages, particularly in light of the increasing number of working-age patients opting for THA. As previously noted, a growing number of younger patients are now undergoing THA, and this patient demographic has demonstrated quicker recovery in terms of pain alleviation and functional improvement [13]. Furthermore, younger, more active patients awaiting THA are more concerned about improvements in activities and participation [14]. To provide further clarity and insight, future research should be directed toward comparing the DAA and PLA approaches in specific populations to ascertain potential superiority within those contexts.

Physical activity

Physical activity and exercise constitute crucial components of healthy aging [15]. However, maintaining an adequate level of physical activity can be particularly challenging for patients suffering from OA, given its adverse impact on lower extremity performance and its status as the leading cause of activity limitations [16]. **Chapter 6** of this study sought to evaluate the effect of arthroplasty surgery on patients' physical activity levels according to the Dutch recommendations for health-enhancing physical activity. Preoperatively and at 6 and 12 months postoperatively, patients reported engagement in moderate-intensity physical activity in days per week in the past 6 months. Patients met the recommendation if they performed at least 30 minutes of moderate-intensity physical activity on 5 or more days per week. A total of 1005 THA and 972 TKA patients were included in this study. Preoperatively, 50% of the population adhered to these recommendations. In addition we found that the majority (69%) of patients remained at their preoperative physical activity levels. Approximately 20% of patients who were not adhering to the recommended activity levels before surgery demonstrated improvements, aligning with the recommendations

one year after surgery. However, in 11% of patients who adhered to the recommendations preoperatively the physical activity levels decreased below the recommended level one year after the surgical procedure. Although the results underscore that arthroplasty surgery can enable patients to enhance their physical activity levels, a significant proportion of patients experienced a decrease in physical activity levels after the surgery. Given that THA and TKA are elective procedures and considering the pivotal role of physical activity in the context of healthy aging, it is imperative to identify patients who may be at risk of diminished physical activity levels one year post-surgery.

The present study revealed that several patient characteristics were associated with post-surgery physical activity levels. However, the most critical risk factor for non-adherence to the recommended activity levels 12 months after surgery was the individual's adherence to the recommendation at the 6-month postoperative mark. Non-compliance at this stage may be linked to various factors. For example, patients who encountered postoperative complications may find it challenging to engage in the required level of physical activity as recommended. Furthermore, patients who had low physical activity levels before surgery due to a sedentary lifestyle were more likely to continue having low physical activity levels following the surgery. Notably, while certain patient characteristics influenced adherence, the study did not identify a significant impact of pain or function on postoperative physical activity levels. This indicates that improvements in pain or function after surgery do not guarantee an increase in active behavior. The identified patterns and predictive patient characteristics for non-adherence within this population allow orthopedic surgeons and other healthcare providers involved in rehabilitation following THA and TKA to anticipate and address changes in physical activity levels. This proactive approach enables intervention prior to or shortly after surgery. It is also linked to the recommendations included in the ICHOM. This recommendation includes the measurement of physical activity in the outcome measures set. Including this measurement after surgery, allows for the assessment of physical activity in patients after THA or TKA. This allows for anticipation on sedentary behavior by the caregiver, either by providing information/education on the risks of sedentary behavior, providing physical activity programs, or a referral to the physical therapist. Nevertheless, additional research regarding this topic is needed to provide the appropriate care if physical activity levels are lacking.

In **chapter 7**, the research focused on determining whether acute pain following THA and TKA has an impact on chronic pain experienced within the first year postoperatively. Patients with OA frequently endure chronic pain both before and after undergoing arthroplasty surgery. The persistence of chronic postoperative pain is a commonly reported adverse outcome [17-19]. Numerous studies have underscored the significance of chronic pain after joint arthroplasty, affecting approximately 2% to 8% of THA patients and 7% to 20% of TKA patients [20-25]. Prior research among surgical patients had hypothesized that (the intensity of) acute pain could serve as a risk factor for the development of chronic pain [26]. Nevertheless, the findings from these studies have remained inconclusive and do not offer direct applicability to THA or TKA patients.

Within this study, acute postoperative pain scores were collected within 72 hours after surgery and categorized as no/mild ($\text{NRS} \leq 4$) or moderate/severe ($\text{NRS} > 4$) acute pain. Additionally, pain was assessed preoperatively, 3, 6 and 12 months postoperatively. This study included 193 THA and 196 TKA patients. Our study revealed that roughly 30% of THA patients and 50% of TKA patients experienced moderate to severe acute postoperative pain. However, the intensity of acute postoperative pain did not demonstrate an association with pain experienced during the first postoperative year within this patient population. This lack of association might be attributed to the distinction in the onset of pain, given that OA patients frequently suffer from chronic pain before surgery. The development of postoperative chronic pain could potentially be related to pain sensitization, which may be present prior to surgery [27-30]. Consequently, focusing on the prevention of pain sensitization in OA patients before surgery may be a viable target for averting chronic postoperative pain. Furthermore, alternative explanations for the lack of association may pertain to the multifaceted nature of pain in OA patients. Modifiable risk factors, such as physical fitness, the presence of comorbidities, and mental and psychological factors, have been identified. Therefore, strategies aimed at reducing or preventing chronic postoperative pain are important. Additionally, strategies focusing on different aspects than acute postoperative pain, including the management of postoperative pain and the psychological well-being of the patient could be beneficial.

Methodological considerations

Results presented in this thesis are based on national arthroplasty registers and a prospective cohort study including hip and knee OA patients. Studies based on registers and studies based on prospective cohorts both have strengths and limitations. Both allow for the collection of longitudinal data of large samples, as well as the ability to track the natural history of the disease over time and long-term effectiveness and safety of arthroplasties. Additionally, both types allow for the collection of information on complications and provide generalizable evidence. The main difference between a registry and cohort study is that a prospective cohort study is designed to address specific research questions. The study is set up with these questions in mind, which means that the most important data to address the research hypothesis have to be collected. This is not necessarily the case with a registry. Nevertheless, bias and confounding in cohort studies provide difficulties when analyzing the data.

The first part of this thesis contains data from registers, the Dutch Arthroplasty Register (LROI) and the Danish Hip and Knee Arthroplasty Register (DHR/DKR). The LROI is a nationwide register in the Netherlands including a wide range of information regarding arthroplasty surgeries, with currently about 1.1 million implants (www.LROI.nl). From 2007 onwards, the LROI started the registration of hip and knee arthroplasties, and corresponding patient, surgical and prosthetic characteristics, as well as Patient Reported Outcome Measures (PROMs). The overall completeness and quality of data of the LROI is high for a national registry. The DHR and DKR are Danish national clinical databases on THA and TKA. Ever since the start of the DHR in 1995 and DKR in 1997, completeness has been high, assuring high quality of prospectively collected data with long-term follow up [31, 32]. There are several benefits associated with the use of register data while conducting research. The LROI, DHR and DKR data provide a large and representative sample of high quality data, providing the opportunity to perform longitudinal analysis to examine trends, outcomes and changes over time. Additionally, register data often contain well-documented and maintained information, allowing other researchers to replicate and validate findings. However, there are primary sources of bias when using register data, such as selection bias, information bias, missing data and misclassification [33]. We expect that selection bias was not a big issue in the studies mentioned in

chapters 2 and 3. Nonetheless, a limitation in the use of the data is the limited information available. Registers do not allow for the opportunity to collect additional information if needed for a specific study. Due to the lack of information regarding waiting lists for arthroplasties in **chapter 2**, we therefore had to provide an estimation of the impact of the COVID-pandemic on the waiting lists. Additionally, another limitation of register data in general is truncation of data, as collection of data will always start and end at a certain timepoint. In **chapter 3** the data truncation resulted in challenges in the analyses of the data. The LROI started collecting surgical and prosthetic characteristics in 2007, while the registration of PROMs and patient characteristics was initiated in 2014. Therefore, we were unable to determine with certainty that patients did not receive a previous arthroplasty before their first registered arthroplasty in the LROI.

The second part of the thesis contains studies performed using data from the prospective, cohort Leiden Orthopaedics Outcome of OsteoArthritis Study (LOAS). This study collects a comprehensive set of patient characteristics and PROMs, such as social participation and health care usages. In comparison with the LROI, the set of PROMs collected in the LOAS is more extensive, and their follow up in time is longer (LOAS up to 10 years versus 1 year postoperative in the LROI). The LOAS allows researchers to study multiple outcomes of THA and TKA over time. This is key for the assessment of trends, patterns and developmental trajectories. Other benefits of a prospective study design in general are that it allows for the collection of accurate exposure information. Additionally, the LOAS provides a more holistic understanding of OA by considering multiple data points with respect to the ICF model at patient level and their interaction over time. Nevertheless, the prospective and longitudinal study design poses some limitations. Firstly, the costs and time it takes to collect information regarding long-term outcomes in this patient population, as patients need to be followed for a considerable amount of time. Secondly, prospective studies are prone to bias. The major types of bias that occur in these studies is selection and information bias. The first type, selection bias, is present since loss to follow-up can occur. To minimize the presence of bias in the LOAS, efforts were made to maximize participation rates by remaining in close contact with the participating hospitals, minimizing barriers to participate and be available for questions or concerns patients may have. Additionally, we performed non-response analysis

and sensitivity analyses to assess whether systematic differences were present between patients that were lost to follow up and those who remained in the study. As such, we were able to estimate the impact of selection bias. The second type is information bias, which refers to systematic errors or inaccuracies in the measurement or assessment, thereby distorting the relationship between the exposure and outcome. This type of bias can distort the relationship between exposure and outcome. Information bias can manifest in different ways, such as misclassification bias, recall bias and observer or measurement bias. We used objective, standardized, and validated measurement tools in the questionnaires. Furthermore, we minimized the presence of recall bias by using prospective data collection methods, maintaining participant confidentiality, and strategies to enhance participant cooperation. To ensure that patients feel adequately involved in the LOAS study and are willing to participate throughout the follow-up period, commitment is established by interesting patients and creating commitment by sending out newsletters and Christmas cards, but also by remaining in close contact with the participating hospitals. The LOAS underscores the pivotal role of patients in the development of recommendations for the management of OA. As a result, the LOAS installed a patient panel, consisting of several patient representatives, herewith ensuring patient involvement in the study. These patients representatives were involved in inclusion of relevant questions and topics in the questionnaires, as well as feedback on results.

Lastly, confounding might result in inaccurate estimates of the association between an exposure and outcome through mixing of effects. The analyses were controlled for possible confounding factors that might be a common cause of both exposure and the outcome of interest of the studies performed. However, residual confounding can still be an issue here. We performed instrumental variable (IV) analysis in [chapter 5](#). IV analysis allows to make causal claims about the relationship between an independent variable and a dependent variable, even in the presence of unobservable confounding factors if certain conditions are fulfilled.

Although prospective research designs offer various benefits, they also present challenges, including the requirement for extended follow-up periods, the possibility of participant attrition, and the resource-intensive nature of data collection. To leverage their advantages and tackle potential limitations,

researchers must meticulously strategize, execute, but also analyze prospective studies.

Conclusion

Overall, this thesis contributed to the body of knowledge on the impact of THA/TKA for patients and provided insight into determinants affecting outcome at the level of the patient's overall health status. The second and third chapter of this thesis elaborated on the epidemiology of hip and knee arthroplasty procedures in the Netherlands and Denmark during the COVID-pandemic, as well as in patients with multiple joint arthroplasties. Due to the COVID-pandemic, the strain on orthopedic health care has exponentially grown in the Netherlands, which will last a few decades if no additional elective THA and TKA capacity can be realized. Before the COVID-pandemic, there was already a growing need of (multiple) arthroplasty surgeries. This need is increasing due to several reasons: there are more younger patients in need of THA or TKA, people are more often overweight and there is a growing elderly population. These factors also contribute to the growing number of MJA, due to multiple joint involvement by OA in these patients. Chapters 4-7 elaborate on the impact of OA and arthroplasty surgery on the patient's overall health-status. These chapters focused on determinants that affect the societal perspective of these patients, rather than only focusing on the patients' health status with regard to their arthroplasty surgery. This allows for the possibility to evaluate the association between arthroplasty surgery and patient-perceived outcomes in a broader perspective like participation in society in its broadest sense. The latter is essential for people in general, thus meeting up with these expectations of the patient is a must and will have an effect on outcome of arthroplasty surgery, which is more than just dealing with the affected joint, but dealing with a humanbeing.

References

1. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. *Br J Surg*. 2020;107(11):1440-9.
2. Diaz A, Sarac BA, Schoenbrunner AR, Janis JE, Pawlik TM. Elective surgery in the time of COVID-19. *Am J Surg*. 2020;219(6):900-2.
3. Desmeules F, Dionne CE, Belzile E, Bourbonnais R, Frémont P. The burden of wait for knee replacement surgery: effects on pain, function and health-related quality of life at the time of surgery. *Rheumatology (Oxford)*. 2010;49(5):945-54.
4. Desmeules F, Dionne CE, Belzile É L, Bourbonnais R, Frémont P. The impacts of pre-surgery wait for total knee replacement on pain, function and health-related quality of life six months after surgery. *J Eval Clin Pract*. 2012;18(1):111-20.
5. Seddigh S, Lethbridge L, Theriault P, Matwin S, Dunbar MJ. Association between surgical wait time and hospital length of stay in primary total knee and hip arthroplasty. *Bone Jt Open*. 2021;2(8):679-84.
6. van der Pas SL, Nelissen R, Fiocco M. Patients with Staged Bilateral Total Joint Arthroplasty in Registries: Immortal Time Bias and Methodological Options. *J Bone Joint Surg Am*. 2017;99(15):e82.
7. Bawa HS, Weick JW, Dirschl DR. Gender Disparities in Osteoarthritis-Related Health Care Utilization Before Total Knee Arthroplasty. *J Arthroplasty*. 2016;31(10):2115-8.e1.
8. Moretti B, Spinarelli A, Varrassi G, Massari L, Gigante A, Iolascon G, et al. Influence of sex and gender on the management of late-stage knee osteoarthritis. *Musculoskelet Surg*. 2022;106(4):457-67.
9. Borkhoff CM, Hawker GA, Wright JG. Patient gender affects the referral and recommendation for total joint arthroplasty. *Clin Orthop Relat Res*. 2011;469(7):1829-37.
10. Karlson EW, Daltroy LH, Liang MH, Eaton HE, Katz JN. Gender differences in patient preferences may underlie differential utilization of elective surgery. *Am J Med*. 1997;102(6):524-30.
11. Dreinhöfer K, Stucki G, Ewert T, Huber E, Ebenbichler G, Gutenbrunner C, et al. ICF Core Sets for osteoarthritis. *J Rehabil Med*. 2004(44 Suppl):75-80.
12. Kurtz SM, Lau E, Ong K, Zhao K, Kelly M, Bozic KJ. Future young patient demand for primary and revision joint replacement: national projections from 2010 to 2030. *Clin Orthop Relat Res*. 2009;467(10):2606-12.
13. Williams DP, Price AJ, Beard DJ, Hadfield SG, Arden NK, Murray DW, et al. The effects of age on patient-reported outcome measures in total knee replacements. *Bone Joint J*. 2013;95-b(1):38-44.
14. Witjes S, van Geenen RC, Koenraadt KL, van der Hart CP, Blankevoort L, Kerkhoffs GM, et al. Expectations of younger patients concerning activities after knee arthroplasty: are we asking the right questions? *Qual Life Res*. 2017;26(2):403-17.
15. Eckstrom E, Neukam S, Kalin L, Wright J. Physical Activity and Healthy Aging. *Clin Geriatr Med*. 2020;36(4):671-83.
16. Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *Jama*. 2021;325(6):568-78.
17. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *BMJ Open*. 2012;2(1):e000435.
18. Boye Larsen D, Laursen M, Simonsen O, Arendt-Nielsen L, Petersen KK. The association between sleep quality, preoperative risk factors for chronic postoperative pain and

- postoperative pain intensity 12 months after knee and hip arthroplasty. *Br J Pain*. 2021;15(4):486-96.
19. Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. *Pain*. 2011;152(3):566-72.
 20. Baker PN, van der Meulen JH, Lewsey J, Gregg PJ. The role of pain and function in determining patient satisfaction after total knee replacement. Data from the National Joint Registry for England and Wales. *J Bone Joint Surg Br*. 2007;89(7):893-900.
 21. Brander VA, Stulberg SD, Adams AD, Harden RN, Bruehl S, Stanos SP, et al. Predicting total knee replacement pain: a prospective, observational study. *Clin Orthop Relat Res*. 2003(416):27-36.
 22. Puolakka PA, Rorarius MG, Roviola M, Puolakka TJ, Nordhausen K, Lindgren L. Persistent pain following knee arthroplasty. *Eur J Anaesthesiol*. 2010;27(5):455-60.
 23. Wylde V, Blom AW, Whitehouse SL, Taylor AH, Pattison GT, Bannister GC. Patient-reported outcomes after total hip and knee arthroplasty: comparison of midterm results. *J Arthroplasty*. 2009;24(2):210-6.
 24. Nikolajsen L, Brandsborg B, Lucht U, Jensen TS, Kehlet H. Chronic pain following total hip arthroplasty: a nationwide questionnaire study. *Acta Anaesthesiol Scand*. 2006;50(4):495-500.
 25. Singh JA, Lewallen D. Predictors of pain and use of pain medications following primary Total Hip Arthroplasty (THA): 5,707 THAs at 2-years and 3,289 THAs at 5-years. *BMC Musculoskelet Disord*. 2010;11:90.
 26. Gilron I, Vandenkerkhof E, Katz J, Kehlet H, Carley M. Evaluating the Association Between Acute and Chronic Pain After Surgery: Impact of Pain Measurement Methods. *Clin J Pain*. 2017;33(7):588-94.
 27. Wylde V, Sayers A, Odutola A, Gooberman-Hill R, Dieppe P, Blom AW. Central sensitization as a determinant of patients' benefit from total hip and knee replacement. *Eur J Pain*. 2017;21(2):357-65.
 28. Fu K, Robbins SR, McDougall JJ. Osteoarthritis: the genesis of pain. *Rheumatology (Oxford)*. 2018;57(suppl_4):iv43-iv50.
 29. Fingleton C, Smart K, Moloney N, Fullen BM, Doody C. Pain sensitization in people with knee osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(7):1043-56.
 30. Zolio L, Lim KY, McKenzie JE, Yan MK, Estee M, Hussain SM, et al. Systematic review and meta-analysis of the prevalence of neuropathic-like pain and/or pain sensitization in people with knee and hip osteoarthritis. *Osteoarthritis Cartilage*. 2021;29(8):1096-116.
 31. Gundtoft PH, Varnum C, Pedersen AB, Overgaard S. The Danish Hip Arthroplasty Register. *Clin Epidemiol*. 2016;8:509-14.
 32. Pedersen AB, Mehnert F, Odgaard A, Schröder HM. Existing data sources for clinical epidemiology: The Danish Knee Arthroplasty Register. *Clin Epidemiol*. 2012;4:125-35.
 33. Bots SH, Groenwold RHH, Dekkers OM. Using electronic health record data for clinical research: a quick guide. *Eur J Endocrinol*. 2022;186(4):E1-e6.



Chapter 9

Summary in Dutch (Nederlandse samenvatting)

Artrose is de meest voorkomende chronische aandoening in Nederland. Het is de verwachting dat door de toenemende vergrijzing en overgewicht van de bevolking, de prevalentie van artrose nog verder zal toenemen. De knie-, heup-, nek- en handgewrichten zijn het vaakst aangedaan. Er is niet één enkele oorzaak aan te wijzen voor artrose, aangezien zowel metabole, inflammatoire, genetische en mechanische factoren hier een rol spelen. Daarnaast komt artrose vaker en in ernstigere vormen voor bij vrouwen.

Wanneer conservatieve behandelingen, zoals pijnstilling en fysiotherapie niet langer verlichting geven van pijn en functionele klachten verminderen, kan een operatie overwogen worden. Voor mensen met een heupartrose is dit vaak een totale heup prothese en voor mensen met knieartrose een totale knie prothese. Het aantal totale heup- en knieprothese operaties neemt in Nederland toe. In totaal kregen 36.707 mensen een totale heupprothese en 26.708 mensen een totale knieprothese in 2022. Om postoperatieve uitkomsten van een totale heup- of knieprothese te meten, kan onder andere gebruik gemaakt worden van patiënt gerapporteerde uitkomstmaten (PROMs). Mede door de meer patiëntgerichte zorg in de orthopedische praktijk zijn patiënt gerapporteerde uitkomsten (PROs) in toenemende mate belangrijk geworden in de zorg van mensen met een THP en TKP. Door middel van PROs kan inzicht geboden worden in het resultaat van de behandeling, vanuit het perspectief van de patiënt.

De 'International Classification of Functioning, Disability and Health (ICF)' heeft een allesomvattend raamwerk ontwikkeld om de algehele gezondheidstoestand van een patiënt te beschrijven. Dit raamwerk bevat onder andere het bio psychosociale model van functioneren en invaliditeit, waardoor het rekening houdt met meer dan alleen de ziekte van een persoon. Het behandelt multidimensionale concepten en benoemt functionele en invaliderende problemen, maar includeert daarnaast ook persoonlijke of omgevingsfactoren die van invloed kunnen zijn op de gezondheid. Het ICF-raamwerk kan zowel voor de patiënt als de behandelaar nuttig zijn bij het stellen van doelen. Voor artrose heeft de ICF een basis set opgesteld met aspecten van de algehele gezondheidstoestand van de patiënt en de behandelaar die als het meest relevant worden beschouwd. Deze basis set is gebruikt in dit proefschrift om de algehele gezondheidstoestand van patiënten met artrose te meten.

Doelstellingen van dit proefschrift:

Dit proefschrift heeft twee hoofddoelen. In de eerste plaats onderzoeken we de impact van een totale heup- en knieprothese op de algehele gezondheidstoestand van de patiënt. Vervolgens onderzoeken we de factoren die van invloed kunnen zijn op deze algehele gezondheidstoestand.

DEEL I

Het eerste deel van dit proefschrift richt zich op de vraag naar een totale heup- en/of knieprothese bij mensen met artrose. Hiervoor hebben we gebruikgemaakt van gegevens verzameld in de Nederlandse Landelijke Registratie van Orthopedische Interventies (LROI). Daarnaast hebben we voor **hoofdstuk 2** ook gebruik gemaakt van de Deense heup en knie registers (Danish Hip and Knee arthroplasty Registers (DHR/DKR)). Beide registers verzamelen informatie omtrent orthopedische implantaten.

In **hoofdstuk 2** wordt onderzocht in hoeverre de COVID-pandemie heeft geleid tot een afname van heup-, knie- en schouderprothesen operaties in Nederland en Denemarken. Ook onderzoeken we de effecten van parallelle langere wachttijden op de kwaliteit van leven. Dit onderzoek is uitgevoerd met data van de LROI en DHR/DKR over de periode 2014 en 2020. De COVID-pandemie leidde tot uitstel van geplande ingrepen. In Nederland werden 20% minder heup- en knieprothese operaties uitgevoerd, vergeleken met een daling van slechts 5% in Denemarken tijdens de COVID-pandemie. Het effect van de COVID-pandemie op het aantal heup- en knieprothesen was dus veel groter in Nederland dan in Denemarken. Mensen met artrose, die wachtten op een prothese, werden persoonlijk (pijn en minder zelfstandig) en sociaal (isolement) harder getroffen dan mensen met acute indicaties voor een prothese, zoals een fractuur. Er vond ook geen prioritering plaats op basis van patiëntkenmerken binnen de verschillende indicatiecategorieën. Opvallend was dat focusklinieken de verminderde capaciteit van andere ziekenhuizen slechts deels konden compenseren door extra productie. Doordat deze extra productie gering was, heeft de COVID-pandemie de wachtlijsten voor orthopedische implantaten aanzienlijk verlengd. Zonder uitbreiding van de capaciteit voor heup en

knieprothesen zal het naar verwachting meer dan 30 jaar duren om de aanvullende wachttijd volledig weg te werken. Deze langere wachttijd heeft ook een grote impact op het aantal jaren dat mensen in volledige gezondheid doorbrengen, dus toenemend minder mobiel worden (lopen met krukken of rolstoel afhankelijk, traplift), waardoor zelfstandigheid afneemt (zoals boodschappen doen) en het sociaal isolement toeneemt. Veel mensen kiezen voor gewricht vervangende operaties om chronische pijn en functionele beperkingen te verlichten. De langere wachttijden zorgen er voor dat patiënten langer moeten wachten op deze verbeteringen qua pijn, mobiliteit (lees: zelfstandigheid in sociale context). Toekomstig onderzoek zou zich moeten richten op manieren om verergering van artrose-gerelateerde klachten tijdens de wachttijd te verminderen, maar ook patiënten met gerichte, niet pijn provocerende oefeningen toch een goede spierconditie te laten hebben, om zodoende niet ook de revalidatie na deze operaties te bemoeilijken. Daarnaast kunnen hulpmiddelen de progressieve klachten verminderen en patiënten toch enigszins mobiel te houden.

In **hoofdstuk 3** wordt de cumulatieve incidentie van het krijgen van meerdere heup en/of knie prothesen onderzocht, evenals de impact van meerdere prothesen op PROs. We hebben onderzocht hoeveel tijd er gemiddeld zit tussen de eerste prothese en de daaropvolgende prothesen. Ook hebben we de verschillende volgordes voor meerdere prothesen in kaart gebracht. Daarnaast hebben we patiëntkenmerken en PROs vergeleken tussen patiënten met meerdere prothesen en patiënten met één prothese. We vonden dat een aanzienlijk deel van de mensen die vanwege artrose een heup- of knieprothese krijgen uiteindelijk meerdere prothesen krijgt. De cumulatieve incidentie voor meerdere heup- en/of knieprothesen over 10 jaar bedroeg ongeveer 30%, waarbij relatief weinig mensen (minder dan 4%) meer dan twee prothesen kregen. De gemiddelde tijd tussen de eerste en de tweede, derde en vierde prothese was respectievelijk 26 maanden, 50 maanden en 60 maanden. Meestal werd bij een tweede prothese hetzelfde gewricht aan de andere zijde vervangen.

We vonden dat vrouwelijk geslacht, een hoger BMI en jongere leeftijd geassocieerd zijn met het krijgen van meerdere prothesen. Een jaar na de eerste prothese rapporteerden mensen met meerdere prothesen iets minder goede resultaten in vergelijking met mensen met slechts één prothese. Momenteel

worden mensen met meerdere prothesen vaak niet meegenomen in onderzoek. Wij raden aan dit wel te doen aangezien dit een groot deel is van de groep patiënten met heup- en knieprothesen. Dit zal ook bijdragen aan een betere informatieverstrekking aan patiënten over mogelijke vooruitzichten over mogelijke betrokkenheid van meerdere gewrichten en het aantal benodigde prothese operaties. Hierdoor worden realistischere verwachtingen gecreëerd voor zowel de patiënt als de zorgverlener tijdens een spreekuur.

DEEL II

Deel II van het proefschrift richt zich op het effect van een totale heup- of knieprothese op de algehele gezondheid bij patiënten met artrose. Waarbij rekening wordt gehouden met de factoren die hierop van invloed zijn. Voor dit onderzoek hebben we gebruikgemaakt van gegevens van de Longitudinal Leiden Orthopaedics Outcomes of Osteo-Arthritis Study, oftewel de LOAS. Dit is een multicenter longitudinale cohortstudie waaraan verschillende ziekenhuizen deelnemen, waaronder het Leids Universitair Medisch Centrum (LUMC) (Leiden), Alrijne Ziekenhuis (Leiden/Leiderdorp), Groene Hart Ziekenhuis (Gouda), 't Lange Land Ziekenhuis (Zoetermeer), Reinier de Graaf Groep (Delft), Albert Schweitzer ziekenhuis (Dordrecht), Waterlandziekenhuis (Purmerend) en OCON Orthopedische Kliniek (Hengelo). Het doel van deze studie is om inzicht te verkrijgen in het dagelijks functioneren, de tevredenheid en de kwaliteit van leven van mensen die een totale heup- en knieprothese ondergaan.

Hoofdstuk 4 richt zich op de verschillen in preoperatieve verwachtingen en de postoperatieve vervulling hiervan bij mannen en vrouwen na een totale heup- of knieprothese. In totaal werden 2333 totale heupprothese patiënten, waarvan 62% vrouw, en 2398 totale knieprothese patiënten, waarvan 65% vrouw, geïnccludeerd. Patiënten ontvingen voorafgaand aan de operatie en 1 jaar na de operatie een vragenlijst waarin onder andere hun verwachtingen werden gemeten met de Hospital for Special Surgery Hip and Knee Replacement Expectations Survey.

Wij vonden dat meer items van de gebruikte vragenlijst meer door mannen relevant gevonden werden dan door vrouwen. Bijvoorbeeld, items

betreffende seksuele activiteit en het vermogen om betaald werk te verrichten werden door mannen vaker relevant bevonden. Dit kan mogelijk verklaard worden doordat vrouwen vaker alleen wonen en minder vaak betaald werk verrichten. Daarnaast speelden verwachtingen met betrekking tot het uitvoeren van functionele activiteiten een belangrijkere rol bij mannen. Ook werden verwachtingen bij mannen vaker na de operatie vervuld dan in de groep vrouwen.

Het is nog steeds niet duidelijk waarom vrouwen minder vaak hun verwachtingen lijken te vervullen na deze grote operaties dan mannen. Het vergroten van inzicht in de invloed van geslacht en daarmee samenhangend de persoonlijke en sociaal maatschappelijke context op verwachtingen, zowel vóór als na een totale heup- en knieprothese, is van groot belang voor zowel patiënten als orthopedische chirurgen. Dit begrip kan helpen beter geïnformeerde beslissingen te nemen en daarmee het gedeelde besluitvormingsproces verbeteren.

Hoofdstuk 5 is gewijd aan de vergelijking van twee chirurgische benaderingen voor een totale heupprothese, de posterolaterale en directe anterieure benadering. De vergelijking richt zich met name op postoperatieve activiteiten en participatie (gebaseerd op het concept "activiteit en participatie" van de ICF) gedurende het eerste jaar na de operatie. Ook werden verwachtingen betreffende activiteiten en participatie onderzocht. Het deel over activiteiten richt zich op onderdelen van iemands handelen en de mogelijke beperkingen of moeilijkheden die iemand ervaart bij het uitvoeren van activiteiten. Het deel over participatie richt zich op iemands deelname aan het maatschappelijk leven en participatieproblemen die iemand ervaart. Aangezien we verwachtten dat er verschillen zouden bestaan in activiteiten en participatie tussen de werkzame populatie en de niet-werkzame populatie, hebben we de uitkomsten ook apart in deze twee groepen onderzocht. Het is van belang om deze subgroepen van elkaar te onderscheiden gezien het groeiende relatieve aantal werkenden die een totale heupprothese ondergaan.

Deze studie werd uitgevoerd in een subpopulatie van de LOAS. We includeerden 238 totale heupprothese patiënten van het LangeLand Ziekenhuis en 622 totale heupprothese patiënten van het Alrijne Ziekenhuis. In het LangeLand Ziekenhuis is de posterolaterale benadering de standaard chirurgische benadering, terwijl in het Alrijne Ziekenhuis gebruik werd gemaakt

van de direct anterieure benadering. Doordat beide ziekenhuizen een andere standaard hadden was er sprake van pseudorandomisatie van de chirurgische benadering. Op het moment van de operatie had 25% van de patiënten een betaalde baan. De resultaten lieten minimale verschillen zien tussen de groepen, bij patiënten na een direct anterieure heupoperatie werd zes maanden na de operatie net iets vaker aan verwachtingen met betrekking tot sportprestaties voldaan. Daarnaast vertoonden zij meer verbetering in dagelijks functioneren een jaar na de operatie dan de posterolaterale groep. De sub analyse onder patiënten met betaald werk toonde aan dat de direct anterieure groep betere scores behaalde in dagelijks functioneren en sport- en recreatieactiviteiten na de operatie. Bovendien werden bij deze groep vaker verwachtingen met betrekking tot recreatieve activiteiten zes maanden na de operatie vervuld en keerde de groep sneller terug naar werk. Dit laatste is belangrijk omdat steeds meer jongere, werkende patiënten een totale heupprothese operatie ondergaan. Uit onderzoek blijkt dat deze patiëntengroep een snellere verbetering vertoont wat betreft pijnverlichting en functionele verbetering. Jongere, actievere patiënten die wachten op een totale heupprothese hechten ook meer waarde aan verbeteringen in activiteiten en participatie. Voor een diepgaander begrip van de impact van deze benaderingen op het herstel van deze specifieke patiëntengroep op het gebied van "activiteiten en participatie", is het van belang dat toekomstig onderzoek zich richt op het vergelijken van de benaderingen om mogelijke superioriteit binnen die contexten vast te stellen.

Fysieke activiteiten en sport vormen essentiële elementen van gezond ouder worden. Echter, het naleven van richtlijnen met betrekking tot fysieke activiteit kan bijzonder uitdagend zijn voor mensen met artrose. Heup- en knieartrose heeft namelijk een nadelige impact op het functioneren van de onderste extremiteiten. Dat leidt er toe dat dit de belangrijkste oorzaak is van ervaren beperkingen in activiteiten binnen deze patiëntpopulatie. **Hoofdstuk 6** van dit proefschrift heeft tot doel om het effect van een totale heup- en knieprothese op de mate van fysieke activiteit van patiënten te onderzoeken, op basis van de Nederlandse Norm Gezond Bewegen (NNGB). Voorafgaand aan en 6 en 12 maanden na de totale heup- en knieprothese operatie rapporteerden patiënten hoeveel dagen per week ze gedurende het laatste half jaar matig intensieve lichamelijke activiteit. Patiënten voldeden aan de NNGB als ze op 5 of meer dagen

per week ten minste 30 minuten matig intensieve lichamelijke activiteit uitvoerden. In totaal werden 1005 mensen met een totale heupprothese en 972 mensen met totale knieprothese patiënten geïnccludeerd in dit onderzoek.

Ongeveer 50% van de studiepopulatie voldeed voorafgaand aan de operatie aan de NNGB. Daarnaast bleek dat een meerderheid (69%) van de patiënten hun preoperatieve niveau van fysieke activiteit behielden na de operaties. Ongeveer 40% van de patiënten die vóór de operatie niet voldeden aan de NNGB, verbeterden hun fysieke activiteit en voldeden wel aan de richtlijn één jaar na de operatie. Echter, bij ongeveer 20% van de patiënten was het activiteitsniveau één jaar na de operatie afgenomen. Dit is een fors percentage, dus ondanks dat een totale heup- of knieprothese de patiënt in staat kan stellen het niveau van fysieke activiteit te verhogen, ondervond een aanzienlijk deel van de patiënten een afname in fysieke activiteit na de operatie. Een totale heup- en knieprothese operatie is een electieve ingreep met als doel pijn vermindering en hierdoor activiteiten in haar ruimste zin te kunnen verhogen. Dit in het kader van de cruciale rol van fysieke activiteit bij gezond ouder worden, geeft het essentiële belang aan om patiënten te identificeren die mogelijk een risico hebben op vermindering van lichamelijke activiteit één jaar na de operatie.

Dit onderzoek toonde aan dat verschillende patiëntkenmerken geassocieerd waren met de niveaus van fysieke activiteit na de operatie. De belangrijkste risicofactor voor het niet voldoen aan de NNGB één jaar na de operatie was of de patiënt al dan niet aan deze richtlijnen voldeed zes maanden na de operatie. Het niet naleven van de NNGB zes maanden na de operatie kan verschillende oorzaken hebben, zoals postoperatieve complicaties of het sedentaire gedrag en leefstijl van de patiënt voorafgaand aan de operatie. Opvallend is dat, pijn of functie geen invloed op de niveaus van fysieke activiteit na de operatie leken te hebben. Dit suggereert dat verbeteringen in pijn of functie na de operatie geen garantie zijn voor een toename in fysieke activiteit. In dit onderzoek zijn patronen en voorspellende kenmerken van patiënten geïdentificeerd die er toe kunnen leiden dat patiënten de NNGB niet naleven. Dit stelt orthopedisch chirurgen en andere zorgverleners in staat te anticiperen op veranderingen in de niveaus van fysieke activiteit. Deze proactieve benadering maakt interventie mogelijk voorafgaand aan of kort na de operatie.

Patiënten met artrose ervaren vaak chronische pijn, zowel voor als na een totale heup- en knieprothese. Het aanhouden van chronische postoperatieve pijn is een veelvoorkomende negatieve uitkomst binnen deze patiëntpopulatie. Ongeveer 10-20% van de patiënten ervaart persisterende pijn na de operatie. In eerdere onderzoeken onder mensen die operatie hebben ondergaan is (de intensiteit van) acute pijn geïdentificeerd als mogelijke risicofactor voor de ontwikkeling van chronische pijn. Desalniettemin bieden deze onderzoeken geen directe toepasbaarheid op artrose patiënten, aangezien de patiënten in bovenstaande onderzoeken geen chronische pijn ervaarden voorafgaand aan de operatie. In **hoofdstuk 7** onderzochten we of acute pijn na een totale heup- en knieprothese van invloed is op chronische pijn die ervaren wordt binnen het eerste jaar na de operatie. Acute pijn werd gemeten middels pijnscores in de eerste 72 uur na de operatie. Deze pijnscores werden gecategoriseerd als geen/milde ($\text{NRS} \leq 4$) of matige/ernstige ($\text{NRS} > 4$) acute pijn. Daarnaast werd de pijn voorafgaand aan de operatie en op 3, 6 en 12 maanden na de operatie beoordeeld middels een vragenlijst. Aan dit onderzoek namen 193 totale heup- en 196 totale knieprothese patiënten deel uit het LUMC en Alrijne Ziekenhuis.

Ongeveer 30% van de patiënten met een totale heupprothese en 50% van de patiënten met een totale knieprothese ervaarden matige tot ernstige acute postoperatieve pijn. De intensiteit van de acute postoperatieve pijn was niet geassocieerd de pijn die deze patiëntenpopulatie gedurende het eerste postoperatieve jaar ervaarden. Dit kan mogelijk verklaard worden doordat patiënten met artrose al vaak voor de operatie chronische pijn ervaren. Een andere oorzaak van postoperatieve chronische pijn zou pijnsensitisatie kunnen zijn. Doordat pijn langdurig aanwezig is, kan een patiënt overgevoelig raken voor pijnsignalen. Het pijnsysteem reageert sneller en/of heftiger op het signaal. Dit wordt pijnsensitisatie genoemd. Hierdoor zou de nadruk van het klinisch handelen met betrekking tot pijn kunnen liggen op het voorkomen van de ontwikkeling van pijn-sensitisatie vóór de operatie.

Conclusie

Dit proefschrift heeft bijgedragen aan de kennis over de impact van totale heup- en knieprothesen op de uitkomsten van de algehele gezondheid van de patiënt en tevens inzicht geboden in factoren die van invloed zijn op deze uitkomsten. De

hoofdstukken 2 en 3 van dit proefschrift belichten specifiek de impact en epidemiologie van totale heup- en knieprothesen tijdens de COVID-pandemie, evenals bij patiënten met meerdere gewrichtsprothesen. Ze tonen een toenemende druk op de orthopedische gezondheidszorg en op de persoonlijke leefwereld van de patiënt aan als gevolg van het uitstellen van geplande ingrepen tijdens de COVID-pandemie, maar ook een groeiende vraag naar (meerdere) gewrichtsprothesen. Deze vraag stijgt om verschillende redenen, waaronder patiënten die op jongere leeftijd een totale heup- of knieprothese nodig hebben en een vergrijzende bevolking met zwaardere belasting op de gewrichten. Dit draagt ook bij aan het groeiende aantal meervoudige prothesen, door betrokkenheid van meerdere gewrichten bij artrose. Hoofdstukken 4-7 bieden verdere inzichten in de impact van artrose en gewricht vervangende operaties op het algehele welzijn van de patiënt. Deze hoofdstukken richten zich op het integreren van factoren die het maatschappelijk perspectief van deze patiënten beïnvloeden, in plaats van zich uitsluitend te concentreren op prothese-gerelateerde uitkomsten. Aanvullend onderzoek, gebaseerd op de resultaten uit de studies in dit proefschrift, is nodig om de resultaten te bevestigen en klinische praktijken te kunnen veranderen.



Appendices

List of publications

PhD portfolio

Dankwoord

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LIST OF PUBLICATIONS

Latijnhouwers, D., van Gils, J., Vliet Vlieland, T., van Steenberghe, L., Marang-van de Mheen, P., Cannegieter, S., Verdegaal, S., Nelissen, R., & Gademan, M. (2024). Multiple Joint Arthroplasty in Hip and Knee Osteoarthritis Patients: A National Longitudinal Cohort Study. *The Journal of arthroplasty*, S0883-5403(24)00532-1.

<https://doi.org/10.1016/j.arth.2024.05.060>

Latijnhouwers, D., Hoogendoorn, K., Nelissen, R., Putter, H., Vliet Vlieland, T., Gademan, M., & LOAS Study Group (2023). *Adherence to the Dutch recommendation for physical activity: prior to and after primary total hip and knee arthroplasty*. *Disability and rehabilitation*, 1–9.

<https://doi.org/10.1080/09638288.2023.2237409>

Latijnhouwers, D., Vlieland, T. P. M. V., Marijnissen, W. J., Damen, P. J., Nelissen, R. G. H. H., Gademan, M. G. J., & Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS) Group (2023). *Sex differences in perceived expectations of the outcome of total hip and knee arthroplasties and their fulfillment: an observational cohort study* *Rheumatology international*, 43(5), 911–922.

<https://doi.org/10.1007/s00296-022-05240-y>

Latijnhouwers, D., Pedersen, A., Kristiansen, E., Cannegieter, S., Schreurs, B. W., van den Hout, W., Nelissen, R., & Gademan, M. (2022). *No time to waste; the impact of the COVID-19 pandemic on hip, knee, and shoulder arthroplasty surgeries in the Netherlands and Denmark*. *Bone & joint open*, 3(12), 977–990.

<https://doi.org/10.1302/2633-1462.312.BJO-2022-0111.R1>

Latijnhouwers, D., Laas, N., Verdegaal, S., Nelissen, R., Vliet Vlieland, T., Kaptijn, H., Gademan, M., & Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS) Group (2022). *Activities and participation after primary total hip arthroplasty; posterolateral versus direct anterior approach in 860 patients*. *Acta orthopaedica*, 93, 613–622.

<https://doi.org/10.2340/17453674.2022.3149>

Groot, L., Latijnhouwers, D., Reijman, M., Verdegaal, S., Vliet Vlieland, T., Gademan, M., & Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS) Group (2022). *Recovery and the use of postoperative physical therapy after total hip or knee replacement*. BMC musculoskeletal disorders, 23(1), 666.

<https://doi.org/10.1186/s12891-022-05429-z>

Latijnhouwers, D., Martini, C., Nelissen, R., Verdegaal, S., Vliet Vlieland, T., Gademan, M., & Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS) Group (2022). *Acute pain after total hip and knee arthroplasty does not affect chronic pain during the first postoperative year: observational cohort study of 389 patients*. Rheumatology international, 42(4), 689–698.

<https://doi.org/10.1007/s00296-022-05094-4>

Loef, M., Gademan, M., Latijnhouwers, D., Kroon, H., Kaptijn, H., Marijnissen, W., Nelissen, R., Vliet Vlieland, T., Kloppenburg, M., & LOAS Study Group (2021). *Comparison of KOOS Scores of Middle-Aged Patients Undergoing Total Knee Arthroplasty to the General Dutch Population Using KOOS Percentile Curves: The LOAS Study*. The Journal of arthroplasty, 36(8), 2779–2787.e4.

<https://doi.org/10.1016/j.arth.2021.03.050>

Tolk, J., Janssen, R., Prinsen, C., Latijnhouwers, D., van der Steen, M., Bierma-Zeinstra, S., & Reijman, M. (2019). *The OARSI core set of performance-based measures for knee osteoarthritis is reliable but not valid and responsive*. Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA, 27(9), 2898–2909.

<https://doi.org/10.1007/s00167-017-4789-y>

PhD PORTFOLIO

Latijnhouwers D., Hoogendoorn, K., Nelissen, R., Marijnissen, W., Putter, H., Vliet Vlieland, T., Gademan, M. Adherence to the Dutch Recommendation for physical therapy; prior to and after primary total hip and knee arthroplasty.

Poster presentation at the EFORT Congress 2022

Latijnhouwers D., Pedersen, A., Kristiansen, D., Cannegieter, S., Schreurs, B., Poolman, R., van den Hout, W., Nelissen, R., Gademan, M. No time to waste; the impact of the COVID-pandemic on hip, knee and shoulder arthroplasty surgeries in The Netherlands and Denmark.

Oral presentation at the NOV Congress 2022

Latijnhouwers D., Martini, C., Nelissen, R., Verdegaal, S., Vliet Vlieland, T., Gademan, M., on behalf of the LOAS group. Acute postoperative pain after total hip and knee arthroplasty does not affect pain 1 year after surgery.

Poster presentation at the OARSI Congress 2021

Latijnhouwers D., Laas, N., Verdegaal, S., Nelissen, R., Vliet Vlieland, T., Kaptijn, H., Gademan, M., on behalf of the LOAS Group. Activities and participation after primary total hip arthroplasty; posterolateral vs direct anterior approach.

Poster presentation at the OARSI Congress 2021

Latijnhouwers D., Laas, N., Verdegaal, S., Nelissen, R., Vliet Vlieland, T., Kaptijn, H., Gademan, M., on behalf of the LOAS Group. Activities and participation after primary total hip arthroplasty; posterolateral vs direct anterior approach.

Poster presentation at the WEON Congress 2021

Latijnhouwers D., Laas, N., Verdegaal, S., Nelissen, R., Vliet Vlieland, T., Kaptijn, H., Gademan, M., on behalf of the LOAS Group. Activities and participation after primary total hip arthroplasty; posterolateral vs direct anterior approach.

Oral presentation at the EFORT Congress 2021

Latijnhouwers D., Martini, C., Nelissen, R., van der Linden-van der Zwaag, H., Verdegaal, S., Vliet Vlieland, T., Gademan, M., on behalf of het LOAS Study Group. Acute postoperative pain after total hip and knee arthroplasty does not affect pain 1-year after surgery.

Poster presentation at the EFORT Virtual Congress 2020

Latijnhouwers D., Martini, C., Nelissen, R., van der Linden-van der Zwaag, H., Verdegaal, S., Vliet Vlieland, T., Gademan, M., on behalf of het LOAS Study Group. Acute postoperative pain after total hip and knee arthroplasty does not affect pain 1-year after surgery.

Poster presentation at the EULAR E-Congress 2020

Latijnhouwers D., Tilbury, C., Leichtenberg, C., Kaptein, B., Koster, L., Verdegaal, S., Onstenk, R., van der Linden-van der Zwaag, H., Krips, R., Kaptijn, H., Vehmeijer, S., Marijnissen, W., Meesters, J., van Rooden, S., Brand, R., Nelissen, R., Gademan, M., Vliet Vlieland, T. Feasibility of collecting multiple patient-reported outcome measures alongside the Dutch Arthroplasty Register.

Oral presentation at the ISAR Congress 2019

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oneindige steun en relativerende vermogen en alle knuffels van Moos, had ik dit proefschrift niet af kunnen ronden. Je maakt mij een enorm gelukkig en vol persoon. Ik kijk uit naar alle avonturen die we, samen met Moos, gaan beleven!

CURRICULUM VITAE

Daisy Antonetta Jacoba Maria werd op 3 maart 1994 geboren in Helmond en is opgegroeid in Mierlo. Na het behalen van haar VWO diploma aan het Strabrecht College, te Geldrop in 2012, is ze gestart met haar studie Gezondheidswetenschappen aan de Universiteit van Maastricht, waarna ze in 2015 gestart is met de Master Human Movement Sciences, tevens aan de Universiteit van Maastricht. Na het behalen van haar Master diploma heeft ze in 2017 gedurende zes maanden gewerkt als Junior Onderzoeker bij Kliniek Viasana te Mill. Tijdens deze periode heeft zij onderzoek uitgevoerd naar de invloed van leefregels gedurende de herstelperiode na een heupprothese operatie op het luxatierisico van de betreffende heup.

Haar interesse voor orthopedisch onderzoek werd al vroeg gewekt, onder andere toen ze tijdens zowel haar stages als haar periode als Junior Onderzoeker onderzoek heeft gedaan naar heup en knie prothesiologie. Hier werd dan ook een passend vervolg aan gegevens toen zij in 2017 startte als promovenda bij de afdeling Orthopaedie van het Leids Universitair Medisch Centrum onder begeleiding van prof.dr R.G.H.H. Nelissen, prof.dr. T.P.M. Vliet Vlieland en dr. M.G.J. Gademan. Tot medio 2022 heeft zij als fulltime onderzoeker gewerkt binnen het Leids Universitair Medisch Centrum. In 2021 volgde zij ook daar haar opleiding tot Epidemioloog B op de afdeling Klinische Epidemiologie.

Momenteel werkt Daisy als Wetenschapscoördinator in het Amphia Ziekenhuis, te Breda. Waarbij ze zich bezighoudt met de strategische en beleidsmatige organisatie van wetenschappelijk onderzoek in het Amphia Ziekenhuis en tevens epidemiologische, methodologische en statistische input levert op onderzoek.

