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Introduction

Total Hip Replacement (THR) and Total Knee Replacement (TKR) are effective surgical interventions, which alleviate pain and improve Health-Related Quality of Life (HRQoL) in patients with hip or knee joint degeneration.[1] National joint replacement registries show good long-term results regarding the probability of revision surgery, which is lower than 10% at 10 years follow-up, both for THR and TKR.[2, 3] Compared to non-operative treatment, both THR and TKR have been shown to be cost-effective interventions.[4–7]

Epidemiology  Annually, 25,000 THR and 20,000 TKR are performed in the Netherlands.[8] These numbers are projected to rise substantially, due to demographical changes, the rising incidence of overweight and obesity, improved long-term outcomes of joint replacements, more active lifestyle of the elderly and the increasing number of orthopaedic surgeons.[9] The annual numbers of THR and TKR performed are expected to increase to approximately 50,000 and 60,000 in 2030.[9]

In the Netherlands, the majority (80%) of THR are performed for osteoarthritis (OA).[8] Less frequent indications for joint replacement include a displaced femoral neck fracture, osteonecrosis, secondary posttraumatic OA, rheumatoid arthritis, OA due to Legg-Calvé-Perthes disease and the treatment of a neoplasm.[8] The mean age at joint replacement is 70 years, two-thirds of the patients are females.[8] The majority (96%) of TKR are also performed for OA.[8] Less frequent indications for joint replacement include rheumatoid arthritis, secondary posttraumatic OA, osteonecrosis and the treatment of a
neoplasm. The mean age at joint replacement is 68 years, two-thirds of the patients are females.

**Implants** Currently, a wide variety of Total Hip Implants is available to orthopaedic surgeons worldwide. The probability of revision surgery varies considerably between different implants. In order to prevent unnecessary harm and limit secondary health care costs, it is imperative to choose an implant with a low probability of revision surgery, when performing primary THR.

**Patient and Surgeon Factors** Although joint replacements are highly effective in improving HRQoL and joint specific functioning at the group level, this is not the case for each individual patient. Persistent pain is reported in 9% of THR patients and 20% of TKR patients at long term follow-up. Additionally, up to 30% of patients are dissatisfied with the results after surgery.

The therapeutic options for patients with an unfavourable outcome after THR or TKR are limited. The outcome of revision surgery performed without a specific mechanical or physiological indication is highly unpredictable. Predicting which patient groups are at increased risk of an unfavourable outcome after joint replacement may provide additional insights in the mechanisms involved and offer the possibility of intervention in order to optimise the outcome. At the very least, it allows patients to be well informed of their specific risks and expected gains before surgery.

In this thesis, we have investigated the role of two potential predictors, which are inexpensive to measure and easily available in clinical practice. Firstly, we studied whether the patients’ Socio-Economic Position was associated with the improvement in Health-Related Quality of Life and patient satisfaction after THR and TKR. Secondly, we studied whether the preoperative radiographic severity of OA was associated with the improvement in Health-Related Quality of Life and patient satisfaction after THR and TKR.

**Research Methodology**

**Competing Risks:** The probability of revision surgery at a specific point in time (given
that revision surgery has not occurred up to that point in time) is of special interest. The Kaplan-Meier estimator is often used to estimate this probability.[22] This method assumes independence of the time to event and the censoring distribution. In the presence of competing events, this assumption is violated.

**Clinimetrics:** Health-Related Quality of Life can be studied at multiple levels. Minimal Clinically Important Differences (MCIDs), Clinically Important Differences (CID) and Patient Acceptable Symptom States (PASS) are closely related concepts, which could provide more insight into the patients outcome at the individual level. MCIDs are defined as the *minimal* improvement in a specific outcome measure, which is perceived by patients as beneficial or harmful. The CID constitutes a larger, more clinically relevant improvement. In PASS, the focus is shifted from the improvement to the actual outcome achieved.

**Questionnaire Mode Preference:** Electronic forms of data collection have gained interest in recent years.[23] Expected advantages include more complete data capturing, immediate availability of results and less costs in administrating and entering data.[23, 24] However, electronic questionnaires might induce selection bias, as some patients could be less inclined to participate in a study which exclusively uses electronic questionnaires.

**The Paprika Study** In order to study predictors of clinical outcome in THR and TKR, we set up the Paprika Study: “Patients Prospectively Recruited in Knee and Hip Arthroplasty” (CCMO-Nr: NL29018.058.09; MEC-Nr: P09.189; Netherlands Trial Register: NTR2190). Patients who previously participated in the Trigger Study or the TOMaat Study, both multicenter randomised controlled trials, were eligible for inclusion in the Paprika Study. The Trigger Study compared the effect of a restrictive blood transfusion policy compared to standard care on the red blood cell transfusion rate after THR and TKR.[25, 26] The TOMaat Study compared the effect of different blood management modalities on the red blood cell transfusion rate during and after THR and TKR (Netherlands Trial Register: NTR303). Patients who were willing to participate in the Paprika Study, were sent a questionnaire and a saliva DNA collection kit.
In this thesis, we focussed on the improvement in Health-Related Quality of Life after primary THR and TKR. Therefore, only patients who previously participated in the TOMaat Study were available for analyses, as Health-Related Quality of Life was not measured before joint replacement in the Trigger Study. A comprehensive overview of the study population of each paper, in which data from the Paprika Study was used, is presented in figure 1.1 on the facing page.

**Thesis Overview** In chapter 2 (p. 9), we have systematically searched and appraised the literature to compare the probability of revision surgery at 10 years follow-up for each THI to the National Institute for Clinical Excellence (NICE) benchmarks. Based on this systematic review of the literature, we can recommend a number of THI for primary THR, which outperform NICE benchmarks.

Using data from the Paprika Study, we investigated whether the patients Socio-Economic Position affects the improvement in HRQoL and satisfaction with the surgical results in chapter 3 (p. 37). In chapter 4 (p. 55), we investigated whether the preoperative radiographic severity of OA affects the improvement in HRQoL and satisfaction with the surgical results, using data from the Paprika Study.

In chapter 5 (p. 71), we assessed how much bias is introduced by the Kaplan-Meier estimator in a long-term cohort study.

In chapter 6 (p. 81), we performed a systematic review to find studies reporting MCIDs in HRQoL after primary or revision THR and TKR. In chapter 7 (p. 93), we determined CID in HRQoL after primary THR and TKR, using data from the Paprika Study. In chapter 8 (p. 105), we determined PASS in joint specific functioning scores after primary THR and TKR, using data from the Paprika Study.

In chapter 9 (p. 119), we assessed which questionnaire mode THR and TKR patients preferred in the Paprika Study.
2257 patients underwent primary hip or knee replacement

- 172 patients died or underwent revision surgery
- 2085 patients alive without further surgery

114 patients had incomplete data at baseline

1971 patients eligible for inclusion in Paprika study

- 703 patients refused participation
- 1268 patients agreed to participate

- 186 patients did not return questionnaire
- 1082 patients returned questionnaire

- 96 patients has missing preoperative Quality of Life data

986 patients with complete preoperative Quality of Life data

131 patients had secondary osteoarthritis
132 patients had missing radiographs

Study population of Chapter 3: 668 patients

Study population of Chapter 4: 723 patients

318 patients had missing data on highest completed level of schooling

Study population of Chapter 7: 970 patients

17 patients had missing data on external criteria

Study population of Chapter 8: 917 patients

69 patients had missing data on Oxford hip or knee score

Study population of Chapter 9: 952 patients

34 patients had missing data on questionnaire preference

Figure 1.1: Flow-chart of Paprika Study. Study population of Chapter 3, 4, and 7 – 9.