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Predictors of patient-reported pain and functional outcomes over 10 years after primary total knee replacement: a prospective cohort study

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ABSTRACT

BACKGROUND: This study aimed to identify preoperative predictors of patient-reported outcomes after total knee replacement (TKR) and to investigate their association with the outcomes over time.

METHODS: We used data from 2,080 patients from the Knee Arthroplasty Trial (KAT) who received primary TKR in the UK between July 1999 and January 2003. The primary outcome measure was the Oxford Knee Score (OKS) collected annually over 10 years after TKR. Preoperative predictors included a range of patient characteristics and clinical conditions. Mixed-effects linear regression model analysis of repeated measurements was used to identify predictors of OKS overall score, pain and function subscale scores over 10 years, separately.

RESULTS: Worse preoperative OKS score, worse mental well-being, BMI>35 kg/m², living in the most deprived areas, higher American Society of Anaesthesiologists grade, presence of comorbidities, and history of previous knee surgery were associated with worse OKS overall score over 10 years after surgery. The same predictors were identified for pain and function subscale scores, and for both long-term (10 years) and short-/mid-term outcomes (1 and 5 years). However, fitted models explained more variations in function and shorter-term outcomes than in pain and longer-term outcomes, respectively.

CONCLUSION: The same predictors were identified for pain and functional outcomes over both short-to-medium term and long term after TKR. Within the factors identified, functional and shorter-term outcomes were more predictable than pain and longer-term outcomes, respectively. Regardless of their preoperative characteristics, on average, patients achieved substantial improvement in pain over time, though improvement for function was less prominent.
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Total knee replacement (TKR) is a commonly performed and effective surgical intervention to relieve pain and restore function in severely damaged knee joints. As the burden of knee arthritis keeps increasing, the number of TKRs performed is reported to be increasing every year [1]. However, variation in postoperative outcomes has been observed among patients, with up to 20% of patients dissatisfied with their outcomes [2]. It is important, therefore, for both clinicians and patients to understand the prognosis of surgery on an individual basis so as to decide whether or not to undergo TKR and whether it is necessary to enhance treatment protocols. In recent years, patient-reported outcome measures (PROMs) have been widely used to assess clinical outcomes from patients’ perspective, which is believed to better reflect patients’ health status and quality-of-life [3-5].

A range of potential predictors of PROMs after TKR have been identified within the literature, including preoperative level of pain and function [6-15], age [6-8, 12, 13, 16-20], sex [6, 8, 9, 13, 16, 19, 21], Body Mass Index (BMI) [13, 15, 18, 20], comorbidities [6-9, 12-15, 20, 22], preoperative mental health [9, 10, 12, 18, 20, 22], and surgeon volume [22]. Most of these studies had a follow-up less than 5 years after TKR. Very few studies examined the effect of predictors over time [23]. Several studies suggested that predictors of pain were not necessarily the same as function [11, 13, 18, 19, 22, 24, 25]. It should be noted, however, that these studies distinguished pain and function based on the wording of questions without formal statistical validation.

Using data from the Knee Arthroplasty Trial (KAT) [26, 27] which included patients receiving TKRs in the UK, this study aimed to: 1) identify pre-operative predictors of PROMs as measured by the Oxford Knee Score (OKS) over 10 years after primary TKR, with pain and function analysed separately; and 2) investigate their effect over short-to-medium term outcomes.

**MATERIAL AND METHODS**

The study used data from the Knee Arthroplasty Trial (KAT), a pragmatic, multi-centre, randomised controlled trial [26, 27] (International Standard Randomized Trial No. ISRCTN45837371). From July 1999 to January 2003, 2,352 patients across 34 centres in the UK were randomly allocated to primary knee replacement with metal-backed tibial component or not; patellar resurfacing or not; mobile bearing or not; or, TKR or uni-compartmental replacement.
Outcome variables

The primary outcome measure was the Oxford Knee Score (OKS) [28] completed by patients at baseline (preoperative), at one year after operation, and annually thereafter by postal questionnaire. The OKS is a validated questionnaire specifically developed to assess patient's pain and function status after knee replacement. It comprises 12 questions, each with five responses on a Likert scale. Each question is scored from 0 (most severe pain or most limited function) to 4 (no pain or no function limitation). An OKS overall score is created by summing the scores for each question, ranging from 0 (the worst outcome) to 48 (the best outcome) [29]. OKS pain and function subscale scores were calculated according to Harris et al. [30]: the function subscale score was obtained by summing the scores for OKS questions #2, 3, 7, 11, 12 (ranging from 0 to 20); and the pain subscale score by summing scores for the other 7 questions (ranging from 0 to 28). Higher subscale scores indicate better function or less pain. Patients were censored for follow-up if they died or received revision surgery within 10 years after the primary TKR.

Predictor variables

Patient characteristics including age at operation (<60, 60-70, 70-80, or 80+ years), sex, marital status [married or living alone], and BMI (<25, 25-30, 30-35, or 35+ kg/m²) were collected by local research nurses using patient entry questionnaires and routine medical database [27]. The Index of Multiple Deprivation (IMD) 2004 was used as a measure of social deprivation [31]. Residential postcodes of patients at randomisation were linked to the Lower Layer Super Output Areas (LSOA). A higher score indicates higher rate of deprivation in that area. IMD 2004 was analysed using quintiles in this study.

Preoperative mental well-being was assessed using the 12-Item Short Form Health Survey Mental Component Summary (SF-12 MCS) [32], with higher score indicating better mental well-being. In the analysis, SF-12 MCS score was categorized into two groups: <50 and 50+. This was based on the sample distribution in this study (the mean of preoperative SF-12 MCS was 49.9) and also on previous studies [33].

Preoperative clinical conditions included diagnosis of arthritis [osteoarthritis (OA) or rheumatoid arthritis (RA)], joints affected (one knee, both knees, or general), presence of comorbidities, history of previous surgery, and the American Society of Anaesthesiologists (ASA) grade. ASA grading system is a standard assessment of the patient’s general physical health prior to surgery [34]. In the KAT study, the range of ASA
grade is from 1 (fit and healthy) to 4 (symptomatic with severe restriction on daily activities). Grade 3 and 4 were collapsed into one group to ensure a sufficient number of patients.

Statistical methods

STATA 13.0 (Statacorp, USA) was used for all statistical analyses. Complete case analysis can be biased [35]. Moreover, missing data in several variables often leads to a substantial loss of observations, reducing the power and precision of estimates. Multiple imputation (MI) has been proposed to overcome this problem [36]. In this study, Multiple Imputation by Chained Equations (MICE) procedures in Stata were used [37]. We included all predictor variables as described above and the outcome variable in each imputation process. For each analysis (at 1 year, over 5 years and over 10 years), a total of 200 imputed datasets were created separately. The statistically significance level was set at 0.05.

Predictors of OKS overall score, pain and function subscale scores over time

To identify predictors of continuous outcomes over 10 years, multi-level mixed-effects linear regression with an unstructured variance-covariance matrix was conducted to take into account of clustering on the same patient. For each predictor variable as described above, a univariable model adjusting for preoperative OKS was performed. Variables with p<0.20 in the univariable models were included in the multivariable model. Age at operation, sex, preoperative OKS, and year of follow-up were included as a priori predictors. Fractional polynomial regression modelling was used to explore evidence of non-linear relationships for continuous variables. An interaction term was fitted between the predictor variable and year of follow-up to see if the effect of predictors depended on time. The same process was repeated for OKS overall score, pain and function subscale scores respectively. To better understand the effect of predictor variables over medium and short term outcomes, we repeated the above process for OKS outcomes over 5 years and at 1 year after TKR.

Changes in OKS overall score, pain and function subscale scores over 10-year time, stratified by identified predictors

For analyses over 10 years, after the final model was built, the outcome was expanded to include both baseline OKS (year 0) and follow-up OKS (year 1 through to year 10) and an interaction term was fitted between predictors that have been identified as statistically significant and year of follow-up. Average marginal effects
were obtained to show the adjusted mean OKS over time across categories of important predictors. The same process was repeated for OKS overall score, OKS pain and function subscale scores respectively.

RESULTS

Description of the study sample

One hundred patients were excluded from this study because they received uni-compartmental knee replacement, withdrew from the trial before surgery, or died before the first follow-up of the trial. Out of the remaining 2,252 patients receiving TKR, 75.8% of patients completed the OKS at 1 year and 41.6% responded at 10 years after TKR [254 (11.3%) patients died within 10 years and 101 (4.5%) patients received revision surgery during follow-up]. Patients were included for analysis if they completed the preoperative and at least one postoperative OKS questionnaire during follow-up, which included 1,980 (87.9%) for analyses over 10 years, 1,967 (87.3%) over 5 years, and 1,636 (72.6%) at 1 year (Figure 1). A comparison of the patients who were included and excluded from analysis over 10 years is described in Table A.1. Patients included tended to be younger, had better preoperative OKS, better mental well-being and lower ASA grading system. They were also more likely to have a history of previous knee surgery or present with comorbidities.

The mean preoperative OKS overall score was 18.2±7.5 (mean ± SD), with a pain subscale score of 9.5±4.6 and function subscale score of 8.5±3.5. Histograms of the absolute difference between year 10 and preoperative OKS scores (Figure A.1) suggested that whereas a small number of patients received no improvement or got worse at 10 years after TKR, the majority achieved improvement in OKS overall score, as well as pain and function subscale scores.

Predictors of OKS scores over time after TKR

A number of variables were identified as statistically significant predictors of postoperative OKS scores over 10 years after TKR (Tables 1-3, last column). Better baseline scores were associated with better postoperative scores over 10 years, while worse mental well-being (SF-12 MCS<50), BMI>35 kg/m², living in more deprived areas, higher ASA grade, presence of comorbidities, and history of previous knee surgery were associated with worse outcomes. A statistically significant interaction was found between age at the time of operation and sex (Figure A.2). For women, patients aged younger than 60 or older than 80 at the time of operation presented worse outcomes over 10 years; while for men, only those younger than 60 showed
statistically significantly worse outcomes. For patients younger than 60, women had better outcome while for those older than 80, men did better. There was also strong evidence that all OKS scores decreased over time, with an average annual decrease of 0.3 points for overall scores, and 0.2 points for both pain and function subscale scores. Predictors and their direction of effect were the same for both pain and functional outcomes, whereas difference was observed in the $R^2$ statistic. The final model of OKS overall score explained 14.5% of variability in outcome, whereas the model for function explained 20.7% and pain only 10.1%. No significant interaction was found between predictors and year of follow-up. For outcomes over 5 years and at 1 year, the same predictors were identified but the fitted models explained slightly more of the variability in each outcome measure (Tables 1-3, first column for outcomes at 1 year and second column for outcomes over 5 years).

**Changes in OKS scores over time, stratified by important predictors**

Figures 2-4 describe the change in outcomes over time stratified by predictors identified. The graphs highlighted again that the effect of predictors on pain and functional outcomes remained almost unchanged over time. They also demonstrated that despite the small size of difference in the attained postoperative outcomes among patients with different preoperative characteristics, on average, these patients achieved substantial improvement in pain from preoperative level regardless of which group they belong to. For functional outcomes, on average, the improvement was less prominent especially for patients whose preoperative function score was among the highest quintile.

**DISCUSSION**

**Main findings**

Using a large prospective cohort of patients receiving primary TKR in the UK, we identified a number of statistically significant predictors of patient-reported pain and functional outcomes as measured by the OKS over 10 years after operation. Worse preoperative OKS scores, worse mental well-being (SF-12 MCS <50), BMI >35 kg/m$^2$, living in the most deprived areas, higher ASA grade, presence of comorbidities, and history of previous knee surgery were associated with worse postoperative outcome. A statistically significant interaction was found between sex and age at time of operation. Predictors and their direction of effect were the same for both pain and functional outcomes, and for both short and midterm results. Within the predictors
identified, functional outcome was more predictable than pain, and shorter-term outcomes more predictable than longer-term outcomes. There was a slight yet statistically significant decrease in postoperative OKS scores over time.

What is already known?

In line with previous studies, we found that worse baseline scores, living the most deprived areas, history of previous knee surgery, presence of comorbidities, and worse mental well-being were associated with worse short-term and long-term OKS scores. The association between age and postoperative PROMs is inconclusive in the literature, with some indicating no relationship [7], while others showing that older age is related with poorer outcomes [11-13, 19, 38]. Most previous studies analysed age by fitting a linear relationship with the outcome. In this study, non-linear relationship was evident and the effect varied by sex. For patients younger than 60, women had better outcome while for those older than 80, men did better. Possible explanation might be that daily activities are more physically demanding for younger male patients; while older female patients might suffer more disabling conditions or experience more pain.

Several studies suggested that predictors of pain were not necessarily the same as function [11, 13, 18, 19, 22, 24, 25]. One of them used OKS as the outcome measure [11]. In that study, the authors extracted pain and function subscale scores based on face validity (i.e. the wording of questions) and looked at outcomes 6 months after TKR. In this study, we extracted subscale scores according to Harris et al. [30] who distinguished pain and function scores using formal factor analysis. Different from what they have found, the same predictors were identified for both pain and function outcomes in this study.

Fitted models explained more variability in functional outcome than in pain over 10 years (20.7% vs. 10.1%). It is possible that unmeasured predictors might explain a greater proportion of pain variability such as expectations of surgery. Some suggested that greater expectation of surgical outcome independently predicted greater pain relief but not for function [39]. Several studies also demonstrated that pain catastrophizing scale, the extent of a patient's negative or exaggerated orientation to pain, was a strong predictor of pain outcome after TKR [24, 40]. It is also possible that the way information is measured on predictors is not detailed enough to capture the variability in their relation to pain. Previous studies suggested some patients might experience chronic pain after TKR despite the lack of noxious stimuli, which might be due to a dysfunction of...
pain modulation in the central nervous system, known as central sensitisation [41]. The proportion of outcome variability explained by fitted models also decreased over time, which might be due to that some other unknown or unmeasured factors start to play an increasing role in the variability of outcomes. Although our results showed statistically significant difference in attained postoperative OKS relating to preoperative patient and clinical characteristics, the size of effect for all identified variables is small. Moreover, regardless of their preoperative characteristics, on average, patients still achieved substantial improvement in pain and benefited from surgery over a long term. Improvement in function was less prominent, especially for patients with the highest quintile of preoperative function subscale scores. This might be explained by a ceiling effect or that TKR is less effective in restoring function compared to relieving pain.

**What this study adds?**

Within this study, we have identified a number of preoperative predictors of attained postoperative PROMs over a long-term after TKR. Predictors were the same for both pain and functional outcomes, and for both short-to-mid-term and long-term results. Within the variables collected, functional outcome was more predictable than pain and shorter-term outcomes more predictable than longer-term outcomes. Changes in outcomes over time revealed that regardless of their preoperative characteristics, on average, patients benefited from TKR and improved substantially in pain over 10 years, though the improvement was less prominent in functional outcomes.

**Strengths and limitations**

The strengths of this project include: 1) relatively large cohort. A total of 1,980 patients were included in the multivariable analysis over 10 years; 2) long-term follow-up. Repeated measurements of OKS were examined over 10 years after TKR.; 3) the inclusion of a wide range of predictor variables. This made it possible to identify predictor variables more comprehensively and to minimize residual confounding; 4) pain and functional outcome analysed separately. This is important to inform patients of their specific outcomes that can be expected. Limitations include that other potential predictor variables suggested by previous studies, for example, patient expectations [39] and surgeon volume [22], were not measured in this project. The medical conditions of the involved knee joint were not examined either. Response bias is also possible as those included for analysis
tended to be younger and healthier. Patients who were recruited in the KAT study might also have different characteristics from those declining to participate or not eligible and thus limit the generalizability of this study. However, the sample of patients included for analysis (mean age of 70 years with 56.4% females) is similar to all patients treated by the NHS in 2005-6 (mean age of 70 years with 57.7% females) [42], suggesting that our sample is fairly representative of the general population in the UK.

**CONCLUSIONS**

The same predictors were identified for pain and functional outcomes over both short-to-medium-term and long-term after primary TKR. Functional outcome and shorter-term outcomes were more predictable than pain and longer-term outcomes, respectively. Regardless of their preoperative characteristics, on average, patients still benefited from surgery and improved substantially in pain, though the improvement in function was less prominent.
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## APPENDIX A. SUPPLEMENTARY DATA

### Table A.1. Descriptive statistics and comparison of those who were included, and not, into the analysis

| Variables                        | Categories |Missing | Overall (N=2252) | Inclusion into analysis | Excluded (n=272) | p-value |
|----------------------------------|------------|--------|------------------|-------------------------|------------------|---------|
|                                  |            |        | (Mean, SD)       | Included (n=1980)       |                  |         |
| Pre-op overall OKS (mean, SD)    |            | 121 (5.4%) | 18.0 (7.5)       | 18.2 (7.5)              | 15.2 (7.3)       | <0.001  |
| Post-op overall OKS (Median, IQR)| 1 year     | 544 (24.2%) | 36 (28, 42)      | 36 (28, 42)             | 34 (25, 42)      | 0.35    |
|                                  | 2 year     | 683 (30.3%) | 38 (28, 43)      | 38 (28, 43)             | 38 (28, 42)      | 0.78    |
|                                  | 3 year     | 603 (26.8%) | 37 (28, 43)      | 37 (28, 43)             | 38 (30, 44)      | 0.48    |
|                                  | 4 year     | 608 (27.0%) | 37 (27, 43)      | 36 (27, 43)             | 39 (29, 44)      | 0.23    |
|                                  | 5 year     | 690 (30.6%) | 37 (28, 43)      | 37 (28, 43)             | 39 (28, 44)      | 0.30    |
|                                  | 6 year     | 838 (37.2%) | 37 (28, 43)      | 37 (28, 43)             | 39 (31, 43)      | 0.34    |
|                                  | 7 year     | 912 (40.5%) | 37 (27, 43)      | 37 (27, 43)             | 37 (30, 42)      | 0.77    |
|                                  | 8 year     | 989 (43.9%) | 37 (27, 43)      | 36 (27, 43)             | 37 (28, 41)      | 0.78    |
|                                  | 9 year     | 1105 (49.1%) | 36 (27, 43)     | 36 (27, 43)             | 36 (29, 42)      | 0.53    |
|                                  | 10 year    | 1316 (58.4%) | 36 (26, 43)     | 36 (26, 43)             | 35 (27, 42)      | 0.68    |

### Patient characteristics

| Sex, n/| | | | | | |
|-------| | | | | | |
| Female| 0 | 1271(56.4%) | 1116(56.4%) | 155(57.0%) | 0.85 |
| Male  | 781(43.6%) | 864(43.6%) | 117(43.0%) | | |

| Marital status, n/ | | | | | | |
|-------------------| | | | | | |
| Married | 38 (1.7%) | 1458(65.8%) | 1305(66.3%) | 153(62.5%) | 0.23 |
| Alone  | 756(34.2%) | 664(33.7%) | 92(38.5%) | | |

| Age, years (mean, SD) | | | | | | |
|----------------------| | | | | | |
| 0 | 71 (8) | 70 (8) | 72 (9) | 0.004 |

| BMI, kg/m² | | | | | | |
|------------| | | | | | |
| <25 | 366(17.1%) | 327(17.1%) | 39(17.0%) | 0.98 |
| 25-30 | 878(40.9%) | 781(40.8%) | 97(42.2%) | |
| 30-35 | 597(27.8%) | 534(27.9%) | 63(27.4%) | |
| 35+ | 305(14.2%) | 274(14.3%) | 31(13.5%) | |

| IMD 2004 quintiles | | | | | | |
|-------------------| | | | | | |
| 819 (36.4%) | 210(14.6%) | 179(14.4%) | 31(16.6%) | 0.53 |
| 1st (most deprived) | 255(17.8%) | 227(18.2%) | 28(15.0%) | |
| 2nd | 343(23.9%) | 304(24.4%) | 39(20.9%) | |
| 3rd | 349(24.4%) | 299(24.0%) | 50(26.7%) | |
| 4th | 276(19.3%) | 237(19.0%) | 39(20.9%) | |
| 5th (most affluent) | 305(14.2%) | 274(14.3%) | 31(13.5%) | |

### Preoperative mental well-being

| Pre-op SF-12 MCS | | | | | | |
|------------------| | | | | | |
| 148 (6.6%) | 1024(48.7%) | 916(47.8%) | 108(57.5%) | 0.01 |
| 1080(51.3%) | 1000(52.2%) | 80(42.5%) | |

### Preoperative clinical conditions

| Diagnosis, n/ | | | | | | |
|---------------| | | | | | |
| OA | 42 (1.9%) | 2102(95.1%) | 1871(95.2%) | 231(94.7%) | 0.74 |
| RA | 108(4.9%) | 95(4.8%) | 13(5.3%) | |

| Joint affected, n/ | | | | | | |
|--------------------| | | | | | |
| One knee | 42 (1.9%) | 569(25.8%) | 515(26.2%) | 54(22.1%) | 0.18 |
| Both knees | 874(39.5%) | 765(38.9%) | 109(44.7%) | |
| General | 767(34.7%) | 686(34.9%) | 81(33.2%) | |

| ASA Grade, n/ | | | | | | |
|---------------| | | | | | |
| Grade 1 | 111 (4.9%) | 366(17.1%) | 332(17.5%) | 34(14.1%) | 0.002 |
| Grade 2 | 1320(61.7%) | 1185(62.4%) | 135(56.0%) | |
| Grade 3-4 | 455(21.3%) | 383(20.2%) | 72(39.9%) | |

| Previous knee surgery, n/ | | | | | | |
|---------------------------| | | | | | |
| No | 42 (1.9%) | 1420(64.3%) | 1246(63.4%) | 174(71.3%) | 0.02 |
| Yes | 790(36.7%) | 720(36.6%) | 70(28.7%) | |
Table A.1. Continued

| Previous contralateral TKR, n/% | 42 (1.9%) |
|---------------------------------|----------|
| No                              | 1916(86.7%) | 1705(86.7%) | 211(86.5%) | 0.91 |
| Yes                             | 294(13.3%)  | 261(13.3%)  | 33(13.5%)  |      |

| Co-morbidities, n/%             | 49 (1.9%) |
|---------------------------------|----------|
| No                              | 1882(85.4%) | 1688(86.0%) | 194(81.2%) | 0.05 |
| Yes                             | 321(14.6%)  | 276(14.0%)  | 45(18.8%)  |      |

OKS, Oxford knee score; BMI, Body mass index; Pre-op, preoperative; Post-op, postoperative; SF-12 PCS, 12-item Short-Form Health Survey Physical Component Summary; SF-12 MCS, 12-item Short-Form Health Survey Mental Component Summary; IMD, Index of Multiple deprivation; IQR: interquartile range; OA, Osteoarthritis; RA, Rheumatology Arthritis; ASA, American Society of Anaesthesiologists; TKR, Total knee replacement.

The t-tests were used for continuous variables and $\chi^2$ tests for categorical variables; * t-test based on log transformation of IMD 2004.
Figure A.1. Distribution of absolute differences in OKS overall, pain and function subscale scores between baseline and 10-year follow-up after primary total knee replacement.

Figure A.2. Marginal effect (95% CI) of age groups on post-operative OKS scores divided by sex and controlling for preoperative variables retained into the final regression model.
Figure 1

Enrolment

n=2,252 primary TKR patients

Exclusion

n=121 patients did not complete the preoperative OKS questionnaire
and/or 

n=172 patients did not complete any postoperative OKS questionnaires

n=2,080 patients included in analysis

Analysis

n=1,980 patients over 10 years
n=1,967 patients over 5 years
n=1,636 patients at 1 year

# 21 patients did not complete neither the pre-operative OKS questionnaire nor any postoperative OKS questionnaires.

TKR: Total Knee Replacement; OKS: Oxford Knee Score
Figure 3

Patient characteristics

Overall Oxford Knee Score vs. Year

Sex
- Female
- Male

Age at Operation
- <60
- 60-70
- 70-80
- 80+

Index of Multiple Deprivation 2004 Quintiles
- Baseline BMI
- <25
- 25-30
- 30-35
- >35
- Quintile 1-Most deprived
- Quintile 2
- Quintile 3
- Quintile 4
- Quintile 5-Least deprived
Figure 4
Preoperative health status

Overall Oxford Knee Score vs. Year for different factors:
- Preoperative SF-12 Mental Component Summary score
- ASA Grade
- History of previous knee surgery
- Presence of other pre-operative conditions affecting mobility
FIGURE LEGENDS

**Figure 1.** A flow diagram of patients included and excluded for each analysis

**Figure 2.** Distribution of absolute differences in OKS overall, pain and function subscale scores between baseline and 10-year follow-up after primary total knee replacement.

**Figure 3.** Change in OKS overall score over 10 years after primary TKR, stratified by preoperative patient characteristics and controlled for variables retained into the final regression model. The best possible score for OKS overall, pain and function subscale score is 48, 28, and 20, respectively.

**Figure 4.** Change in OKS overall score over 10 years after primary TKR, stratified by preoperative health status and controlled for variables retained into the final regression model. The best possible score for OKS overall, pain and function subscale score is 48, 28, and 20, respectively.
# Table 1. Multivariable analysis of OKS overall score at 1 year, over 5 and 10 years after TKR

| Variables                  | Categories          | At 1 year (n=1636) | over 5 years (n=1967) | over 10 years (n=1980) |
|----------------------------|---------------------|--------------------|-----------------------|------------------------|
|                            |                     | Multivariable$^a$  | Multivariable$^a$    | Multivariable$^a$     |
|                            |                     | coefficient (95%CI)| coefficient (95%CI)  | coefficient (95%CI)  |
|                            |                     | $R^2= 18.76\%$    | $R^2= 15.62\%$      | $R^2= 14.51\%$      |
| Patient characteristics    |                     |                    |                      |                        |
| Sex                       | Female              | 0                  | 0                    | 0                      |
|                           | Male                | 0.44(-1.05, 1.92)  | 0.33(-0.96, 1.61)    | 0.31(-0.96, 1.58)    |
| Age at operation (years)  | <60                 | -0.86(-3.18, 1.46) | -2.09(-3.89, -0.30) *| -1.96(-3.73, -0.20) *|
|                           | 60-70               | 0                  | 0                    | 0                      |
|                           | 70-80               | 0.74(-0.59, 2.08)  | 0.07(-1.11, 1.25)    | -0.28(-1.45, 0.88)   |
|                           | 80+                 | -2.75(-4.98, -0.51) *| -2.92(-4.73, -1.10)**| -3.23(-5.03, -1.42) ***|
| Sex/#Age at operation$^b$ | male/#age<60        | -4.29(-7.80, -0.78) *| -1.90(-4.63, 0.83)   | -1.94(-4.64, 0.76)   |
|                           | male/#age(60-70)    | -0.53(-2.48, 1.41) | -0.10(-1.83, 1.62)   | -0.15(-1.86, 1.55)   |
|                           | male/#age(80+)      | 2.74(-0.36, 5.84)† | 3.57(0.90, 6.23) **   | 3.42(0.76, 6.08) *   |
| Marital status            | Married             | 0                  | 0                    | 0                      |
|                           | Living alone        | -0.48(-1.48, 0.52) | -0.65(-1.52, 0.21) †| -0.72(-1.59, 0.15) † |
| BMI (kg/m2)               | <25                 | 0                  | 0                    | 0                      |
|                           | 25-30               | -0.33(-1.55, 0.90) | -0.36(-1.45, 0.73)   | -0.36(-1.40, 0.69)   |
|                           | 30-35               | -1.84(-3.23, -0.46) **| -0.95(-2.11, 0.21) †| -0.92(-2.06, 0.21) † |
|                           | >35                 | -1.97(-3.62, -0.32) *| -1.67(-3.07, -0.27) *| -1.79(-3.12, -0.46) **|
| IMD 2004 quintiles        | 1st (most deprived) | 0                  | 0                    | 0                      |
|                           | 2                   | 1.22(-0.82, 3.25)  | 0.39(-0.53, 1.32)    | 0.39(-0.28, 1.05)    |
|                           | 3                   | 2.38(0.47, 4.29) * | 1.08(0.19, 1.98) *   | 0.82(0.21, 1.43) **  |
|                           | 4                   | 2.70(0.86, 4.53) **| 1.07(0.17, 1.97) *   | 0.96(0.35, 1.58) **  |
|                           | 5th (most affluent)  | 1.97(0.04, 3.91)   | 1.08(0.15, 2.02) *   | 0.94(0.26, 1.61) **  |
| Preoperative patient-reported health status | Pre-op OKS overall score | 0.35(0.29, 0.42) *** | 0.39(0.34, 0.45) *** | 0.41(0.35, 0.46) *** |
|                            | Pre-op SF-12 MCS    | 1.65(-0.70, 2.61) ** | 1.77(0.96, 2.57) *** | 1.61(0.81, 2.40) *** |
| Preoperative clinical conditions | ASA Grade          | Fit and healthy    | 0                    | 0                      |
|                            |                     | Asymptomatic       | -1.04(-2.25, 0.17) †| -0.81(-1.83, 0.21) †| -0.66(-1.60, 0.28)   |
|                            |                     | Symptomatic        | -2.69(-4.25, -1.13) **| -2.19(-3.43, -0.95) **| -1.91(-3.07, -0.75) **|
|                            | Previous knee surgery | No                | 0                    | 0                      |
|                            |                      | Yes                | -1.78(-2.72, -0.84)***| -1.24(-2.07, -0.42) **| -1.17(-1.98, -0.36) **|
|                            | Comorbidities       | No                 | 0                    | 0                      |
|                            |                      | Yes                | -3.00(-4.35, -1.65)***| -2.37(-3.50, -1.24) ***| -2.24(-3.36, -1.12) ***|
|                            | Year of follow-up   |                    |                      | -0.16(-0.25, -0.06) ** | -0.33(-0.38, -0.27) ***|

OKS: Oxford Knee Score; IMD: Index of multiple deprivation; BMI: Body mass index; ASA: American Society of Anaesthesiologists. Coefficient: the regression coefficient represents the difference in outcome compared with the reference group. A positive value indicates that the group has better post-operative pain/function.

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$^a$ In the multivariable models, all variables are mutually adjusted and an interaction term between age and sex was included;

$^b$ Interaction between sex and age at operation

***.$<0.001$; **.$<0.01$; *.$.<0.05$; †.$<0.20$
Table 2. Multivariable analysis of OKS pain subscale score at 1 year, over 5 and 10 years after TKR

| Variables                          | Categories                | at 1 year (n=1636) | over 5 years (n=1967) | over 10 years (n=1980) |
|-----------------------------------|---------------------------|---------------------|-----------------------|------------------------|
|                                   |                           | Multivariable       | Multivariable         | Multivariable          |
|                                   |                           | coefficient (95%CI) | coefficient (95%CI)  | coefficient (95%CI)    |
|                                   |                           | R²= 14.85%          | R²= 10.89%            | R²= 10.10%             |
| **Patient characteristics**       |                           |                     |                       |                        |
| Sex                               | Female                    | 0                   | 0                     | 0                      |
|                                   | Male                      | -0.29(-1.23, 0.65)  | -0.23(-1.03, 0.57)    | -0.22(-1.01, 0.56)     |
| Age at operation (years)          | <60                       | -0.78(-2.29, 0.73)  | -1.53(-2.65, -0.40)** | -1.52(-2.63, -0.42)** |
|                                   | 60-70                     | 0                   | 0                     | 0                      |
|                                   | 70-80                     | 0.54(-0.31, 1.39)   | 0.27(-0.47, 1.01)     | 0.11(-0.62, 0.83)      |
|                                   | 80+                       | -1.50(-2.94, -0.07)* | -1.61(-2.75, -0.48)** | -1.74(-2.86, -0.61)** |
| Sex#Age at operationb             | male#age<60               | -2.38(-4.67, -0.09)* | -1.06(-2.77, 0.64)    | -1.10(-2.78, 0.58)     |
|                                   | male#age(60-70)           | -0.21(-1.45, 1.03)  | -0.11(-1.19, 0.96)    | -0.22(-1.28, 0.84)     |
|                                   | male#age(80+)             | 1.92(-0.04, 3.88)†  | 2.44(0.77, 4.11)**    | 2.30(0.64, 3.96)**     |
| Marital status                    | Married                   | 0                   | 0                     | 0                      |
|                                   | Living alone              | -0.38(-1.01, 0.25)  | -0.43(-0.97, 0.11)†   | -0.46(-1.00, 0.07)†    |
| BMI (kg/m2)                       | <25                       | 0                   | 0                     | 0                      |
|                                   | 25-30                     | -0.33(-1.10, 0.44)  | -0.28(-0.96, 0.40)    | -0.27(-0.92, 0.39)     |
|                                   | 30-35                     | -1.28(-2.17, -0.39)** | -0.63(-1.35, 0.09)†   | -0.60(-1.29, 0.08)†    |
|                                   | >35                       | -1.25(-2.31, -0.19)* | -1.00(-1.86, -0.14)*  | -1.11(-1.93, -0.28)** |
| IMD 2004 quintiles               | 1st (most deprived)       | 0                   | 0                     | 0                      |
|                                   | 2                         | 0.75(-0.54, 2.04)   | 0.26(-0.35, 0.86)     | 0.25(-0.20, 0.70)      |
|                                   | 3                         | 1.49(0.30, 2.69)*   | 0.74(0.14, 1.35)*     | 0.55(0.13, 0.97)*      |
|                                   | 4                         | 1.60(0.43, 2.77)**  | 0.71(0.11, 1.31)*     | 0.63(0.21, 1.05)**     |
|                                   | 5th (most affluent)       | 1.18(-0.06, 2.42)†  | 0.72(0.11, 1.34)*     | 0.62(0.17, 1.06)**     |
| **Preoperative patient-reported health status** | | | | |
| Pre-op OKS pain score             | <50                       | 0.29(0.22, 0.36)*** | 0.30(0.24, 0.35)***   | 0.31(0.26, 0.37)***    |
|                                   | >50+                      | 1.11(0.51, 1.72)*** | 1.26(0.76, 1.76)***   | 1.16(0.68, 1.65)***    |
| **Preoperative clinical conditions**|                           |                     |                       |                        |
| ASA Grade                         | Fit and healthy           | 0                   | 0                     | 0                      |
|                                   | Asymptomatic              | -0.56(-1.33, 0.21)† | -0.41(-1.05, 0.23)    | -0.35(-0.94, 0.25)     |
|                                   | Symptomatic               | -1.60(-2.60, -0.60)** | -1.33(-2.11, -0.55)** | -1.17(-1.90, -0.44)** |
| Previous knee surgery             | No                        | 0                   | 0                     | 0                      |
|                                   | Yes                       | -1.20(-1.79, -0.59)*** | -0.81(-1.33, -0.30)** | -0.75(-1.25, -0.25)** |
| Comorbidities                     | No                        | 0                   | 0                     | 0                      |
|                                   | Yes                       | -1.73(-2.61, -0.85)*** | -1.34(-2.04, -0.63)** | -1.29(-1.99, -0.60)** |
| Year of follow-up                 |                           | -0.04(-0.10, 0.03)  | -0.15(-0.19, -0.12)***|

OKS: Oxford Knee Score; IMD: Index of multiple deprivation; BMI: Body mass index; ASA: American Society of Anaesthesiologists. Coefficient: the regression coefficient represents the difference in outcome compared with the reference group. A positive value indicates that the group has better post-operative pain/function.

*a In the multivariable models, all variables are mutually adjusted and an interaction term between age and sex was included;  
*b Interaction between sex and age at operation

***<0.001; **<0.01; *<0.05; †<0.20
### Table 3. Multivariable analysis of OKS function subscale score at 1 year, over 5 and 10 years after TKR

| Variables                        | Categories                      | at 1 year (n=1636) | over 5 years (n=1967) | over 10 years (n=1980) |
|----------------------------------|---------------------------------|--------------------|----------------------|-----------------------|
|                                  |                                 | R²= 23.76%         | R²= 22.30%           | R²= 20.72%            |
| Patient characteristics          |                                 |                    |                      |                       |
| Sex                              | Female                          | 0                  | 0                    | 0                     |
|                                  | Male                            | 0.66(0.04, 1.28)*   | 0.49(-0.05, 1.03)†    | 0.49(-0.05, 1.02)†    |
| Age at operation (years)         | <60                             | -0.13(-1.07, 0.80) | -0.65(-1.40, 0.09)†   | -0.53(-1.26, 0.21)    |
|                                  | 60-70                           | 0                  | 0                    | 0                     |
|                                  | 70-80                           | 0.24(-0.33, 0.81)   | -0.16(-0.66, 0.33)    | -0.35(-0.84, 0.13)    |
|                                  | 80+                             | -1.20(-2.13, -0.27)* | -1.24(-2.00, -0.49)** | -1.42(-2.18, -0.67)*** |
| Sex*Age at operation             | male*age<60                     | -1.84(-3.24, -0.44)* | -0.74(-1.88, 0.39)    | -0.76(-1.89, 0.36)    |
|                                  | male*age(60-70)                 | -0.29(-1.11, 0.52)  | 0.07(-0.64, 0.79)     | 0.11(-0.60, 0.82)     |
|                                  | male*age(80+)                   | 0.91(-0.42, 2.24)   | 1.22(0.11, 2.33)*     | 1.20(0.09, 2.30)*     |
| Marital status                   | Married                         | 0                  | 0                    | 0                     |
|                                  | Living alone                    | -0.11(-0.53, 0.31)  | -0.23(-0.59, 0.14)    | -0.26(-0.63, 0.10)    |
| BMI (kg/m2)                      | <25                             | 0                  | 0                    | 0                     |
|                                  | 25-30                           | 0.02(-0.51, 0.55)   | -0.08(-0.54, 0.38)    | -0.09(-0.54, 0.36)    |
|                                  | 30-35                           | -0.55(-1.14, 0.04)† | -0.32(-0.82, 0.17)    | -0.34(-0.84, 0.16)    |
|                                  | >35                             | -0.75(-1.44, -0.06)* | -0.73(-1.32, 0.14)*   | -0.75(-1.33, -0.17)*  |
| IMD 2004 quintiles              | 1st (most deprived)            | 0                  | 0                    | 0                     |
|                                  | 2                               | 0.50(-0.34, 1.33)   | 0.16(-0.22, 0.54)     | 0.15(-0.13, 0.44)     |
|                                  | 3                               | 0.92(0.02, 1.72)*   | 0.40(0.04, 0.77)*     | 0.31(0.05, 0.57)*     |
|                                  | 4                               | 1.13(0.37, 1.89)**  | 0.42(0.04, 0.79)*     | 0.38(0.12, 0.64)**    |
|                                  | 5th (most affluent)             | 0.84(0.05, 1.62)*   | 0.42(0.04, 0.80)*     | 0.36(0.08, 0.64)*     |
| Preoperative patient-reported health status | | | | |
| Pre-op OKS function score        | 0.40(0.34, 0.47)***             | 0.46(0.41, 0.51)*** | 0.47(0.42, 0.52)***   |
| Pre-op SF-12 MCS                 | <50                             | 0                  | 0                    | 0                     |
|                                  | 50+                             | 0.57(0.17, 0.97)**  | 0.59(0.25, 0.93)**    | 0.54(0.20, 0.88)**    |
| Preoperative clinical conditions |                                 |                    |                      |                       |
| ASA Grade                        | Fit and healthy                 | 0                  | 0                    | 0                     |
|                                  | Asymptomatic                    | -0.46(-0.97, 0.05)† | -0.39(-0.82, 0.03)†   | -0.32(-0.72, 0.08)†   |
|                                  | Symptomatic                     | -1.05(-1.70, -0.40)** | -0.87(-1.39, -0.35)** | -0.77(-1.27, -0.28)*** |
| Previous knee surgery            | No                              | 0                  | 0                    | 0                     |
|                                  | Yes                             | -0.58(-0.97, -0.19)** | -0.43(-0.77, -0.08)* | -0.42(-0.76, -0.08)*  |
| Comorbidities                    | No                              | 0                  | 0                    | 0                     |
|                                  | Yes                             | -1.24(-1.77, -0.70)*** | -1.03(-1.50, -0.57)*** | -0.96(-1.43, -0.50)*** |
| Year of follow-up                |                                 | -0.11(-0.15, -0.07)*** | -0.17(-0.20, -0.15)*** |                       |

OKS: Oxford Knee Score; IMD: Index of multiple deprivation; BMI: Body mass index; ASA: American Society of Anaesthesiologists. Coefficient: the regression coefficient represents the difference in outcome compared with the reference group. A positive value indicates that the group has better post-operative pain/function.

* In the multivariable models, all variables are mutually adjusted and an interaction term between age and sex was included;

b Interaction between sex and age at operation

***<0.001; **<0.01; *<0.05; †<0.20
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