

Online Supplemental File 1

Supplementary Technical Appendix

The definition and the selection of study population

We selected patients with a recorded consultation for hip pain/osteoarthritis or knee pain/osteoarthritis pain between 1 January 1992 and 31 December 2015 and who had complete registration and no recorded hip pain/osteoarthritis or knee pain/osteoarthritis consultations in the 3 years before their index consultation (the first consultation for hip or knee pain/osteoarthritis recorded in the study period, reflecting a first or new episode). The entry date for each patient was the date of index consultation.

Consultations for hip pain/osteoarthritis and knee pain/osteoarthritis were defined using morbidity (“Read”) codes for diagnosed osteoarthritis and hip or knee pain codes likely to represent osteoarthritis previously determined by six academic general practitioners with an interest in musculoskeletal conditions [22]. Read codes are used to record morbidity in UK primary care and the codes used are available from www.keele.ac.uk/mrr.

Defining primary total hip and knee replacement

We used the earliest recorded date of the outcome after the index consultation. To reduce the potential for reverse causality (e.g. the act of referring for joint replacement led to recording of osteoarthritis), we excluded patients with hip or knee replacements within 2 years of the index consultation (initial descriptive (Kaplan-Meier) analysis identified a much higher risk of TKR / THR in the first 2 years that is likely to be attributable to reverse causality), and those whose records were censored (died, de-registration with practice, or last upload of computerised data) during this 2-year period. Among patients with both hip and knee replacements, their hip replacements were defined as outcomes in the hip model and knee replacements were defined as outcomes in the knee model.

Systematic review and source of conventional risk factors

Briefly, we searched Medline, Embase, Allied and Complementary, Cumulative Index to Nursing and Allied Health Literature and Web of Science™ core collection up to December 2014 for all studies investigating risk factors for THR and TKR. 35 studies were undertaken in 22 unique datasets from 12 different countries. Of the 35 studies identified, 16 rated as high quality were used in the best evidence synthesis, in which there were 21 possible predictors for TKR and 28 possible predictors for THR identified and include in the comprehensive list.

35 conventional predictors used across QResearches were also extracted and included in the comprehensive list.

ReWAS study

96,450 and 165,413 incident THR and TKR cases between 1992 - 2015 were identified from the CPRD using 3-year run-in period. An age-, gender- and practice-matched control with ≥ 1 consultations in the past 3 years was selected for each case using risk-set sampling [1]. For ReWAS, firstly, we identified all third-level Read codes and third-level sections within the British National Formulary (BNF) which had been recorded in $\geq 1\%$ of cases in the 3 years prior to date of total joint replacement as potential prognostic factors ($n=6,109$ and 325 respectively); secondly, we used conditional logistic regression to estimate their association with outcome, with 'hits' defined as those factors with a population attributable risk (PAR) $\geq 1\%$ or $\leq -1\%$ (**S3 Fig upper panel: 3rd level read codes for TKR and S4 Fig upper panel: 3rd level read code for THR; S5 Fig upper panel: BNF sections for TKR and S6 Fig upper panel: BNF section for THR**) and with significant Bonferroni-corrected P-values (**S3 Fig lower panel: 3rd level read codes for TKR and S4 Fig lower panel: 3rd level read code for THR; S5 Fig lower panel: BNF sections for TKR and S6 Fig lower panel: BNF section for THR**). Finally, we repeated the ReWAS method in a case-control study with 874 incident knee/hip replacement cases and 4,370 matched controls, derived from a regional dataset - Consultations in Primary Care Archive (CiPCA). We identified 36 'hits', i.e. potential prognostic factors recorded in $\geq 1\%$ of cases, and having PAR $\geq 1\%$ / $\leq -1\%$ and P-value $< 1.539 \times 10^{-4}$ (32 for THR; 33 for TKR (29 associated with both outcomes)).

Definition of predictors

Comorbidities (i.e. anxiety or depression), process of care, and prescription predictors identified from REWAS were defined based on their corresponding code at the 3rd level of Read codes hierarchy or BNF section. Potential predictors identified from the systematic review and the QResearch algorithms were defined using code lists used in previous Centre studies developed through consensus of expert GP and EHR researchers, or if these did not exist, by modifying code lists used in external studies and / or consensus of 7 GP and EHR researchers.

Smoking status was defined as non-smoker, ex-smoker, light smoker (1-9 cigarettes/day), moderate smoker (10-19 cigarettes/day), and heavy smoker (≥ 20 cigarettes/day); drinking status was defined as non-drinker, ex-drinker, light drinker (1-2 unit/day), moderate drinker (3-6 unit/day) and heavy drinker (≥ 7 unit/day); physical activity status was defined as no physical activity (General practice physical activity questionnaire physical activity index: inactive), taking light physical activity (General practice physical activity questionnaire physical activity index: moderately inactive), taking moderate physical activity (General practice physical activity

questionnaire physical activity index: moderately active) and taking heavy physical activity (General practice physical activity questionnaire physical activity index: active).

Statistical analysis for model derivation

For the 45 categorical candidate predictors in the THR derivation cohort and 53 categorical candidate predictors in the TKR derivation cohort, we first fitted a full multivariable Fine-Gray subdistribution hazard model, accounting for the competing risk of death (including all candidate predictors) to calculate the adjusted hazard ratio for receiving a THR/TKR. Candidate predictors with population attributable risk (PAR) >1% (or <-1%) were taken forward to the next stage of model development in which multivariable Fine-Gray models were fitted to the remaining categorical predictors, and the 6 continuous predictors. A multivariable fractional polynomial approach was used, in which fractional polynomial terms were considered to flexibly model the 6 continuous predictors while at the same time using backward elimination ($p > 0.1$ based on log likelihood) to exclude seemingly unimportant predictors from the model.

Model performance evaluation

We assessed the performance of each model in terms of both discrimination and calibration. Discrimination measures the model's ability to distinguish between individuals that will and will not have a THR/TKR, and was measured using Harrell's C-statistic (0.50 represents no discrimination, 1.00 perfect discrimination) [30]. Calibration measures the agreement between the observed risks and the model's predicted risks, and was evaluated using the calibration slope (a value of 1.00 is ideal) [30-32] over the 10-years of follow-up. Calibration plots were also produced, in which patients were classified into 10 risk groups based on their predicted probability of the outcome.

Internal-external cross-validation (IECV) approach

Using this approach, a single cycle of IECV involves separating the data into a development cohort and validation cohort, with 12 of the 13 geographical regions forming the development cohort and reserving the other region for validation. The model development strategy (PAR elimination + backward elimination) was applied to the development cohort and the derived model was then validated in the reserved validation cohort. This process was repeated multiple times, each time reserving a different region for validation, therefore there were 13 cycles and each geographical region was used once for validation (see table below).

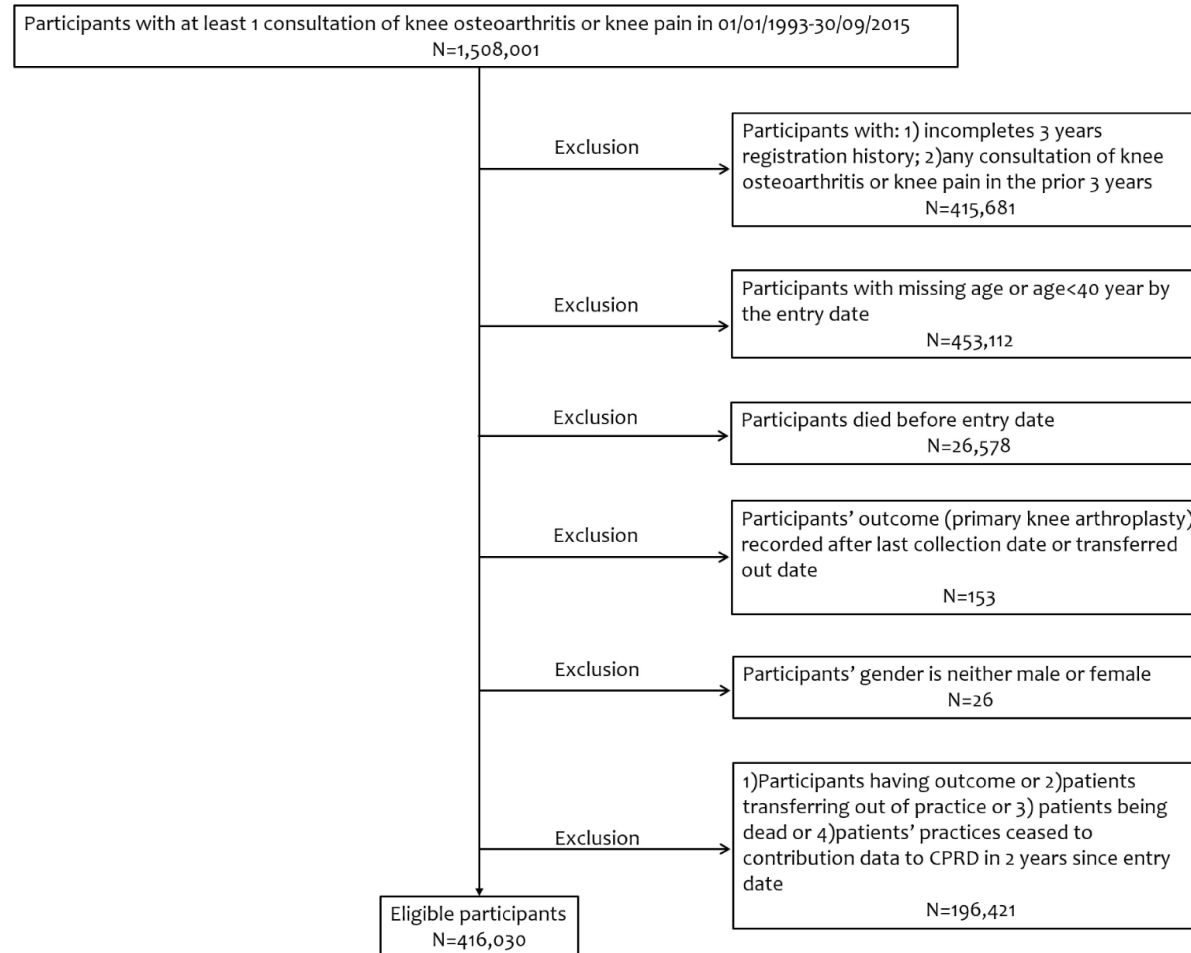
Cycle of IECV	Development cohort	Validation cohort
1	Regions 2-13	Region 1
2	Regions 1, 3-13	Region 2
3	Regions 1, 2, 4-13	Region 3
...
13	Regions 1-12	Region 13

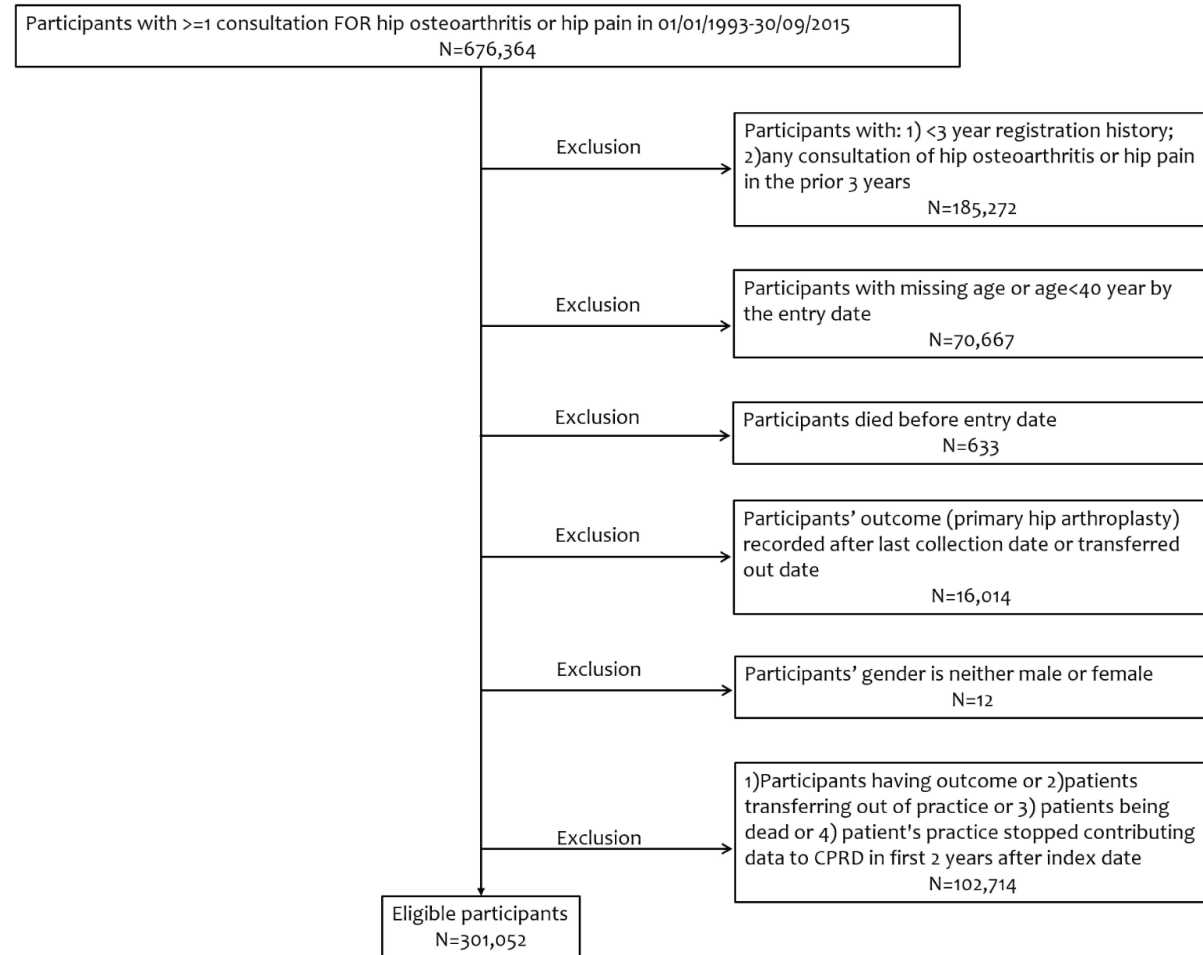
Internal validation aims to assess the reproducibility of the model, i.e. evaluates the modelling process. External validation aims to assess the generalisability of the model (to different regions in this case). Therefore the IECV process can be used to give more realistic estimates of model performance (than apparent performance) and also reveal how the developed models are likely to perform in new data, independent to that used for model development.

Performance statistics were also summarised across regions using a random-effects meta-analysis, reporting the average performance statistic with 95% confidence interval (derived using the Hartung-Knapp-Sidik-Jonkman variance correction) and 95% prediction interval.

Handling of missing data

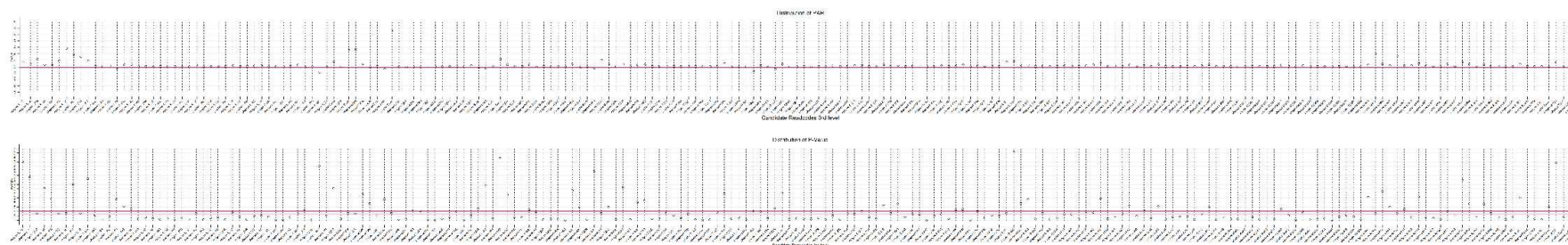
Our derivation cohorts had missing information on body mass index (5.39% for THR cohort and 5.26% for TKR cohort). For missing values in the categorical variables (ethnicity, smoking status, drinking status, mental health disorder, and joint specific osteoarthritis), a ‘not recorded’ category was introduced and combined with the reference category for each variable. We used multiple imputation within each derivation cohort (THR and TKR cohorts) prior to model development and validation. Multiple imputation using chained equations (MICE) was applied, and the imputation model included all candidate predictors and outcome. We created 5 imputed datasets, and final model estimates were obtained by combining estimates across all imputed datasets using Rubin’s rules [36]. In the validation, performance statistics were also combined across imputations using Rubin’s rules. However, calibration plots were produced for each imputed dataset and presented for one imputed dataset if representative of what was seen in the other imputations.

Supplementary figure S1. Workflow chart of the selection of participants for total knee replacement model

Supplementary figure S2. Workflow chart of the selection of participants for total hip replacement model

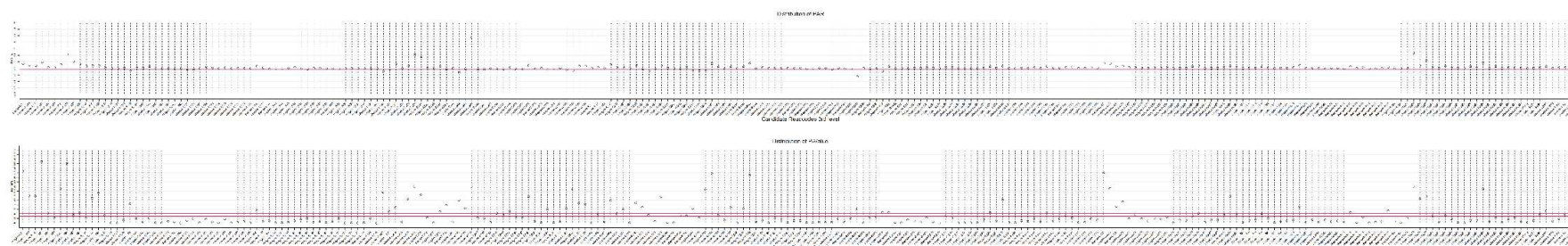
Supplementary figure S3. Population attributable risk for association between each third level Read code and total knee replacement: findings from population based case-control study

High-resolution figure could be found at: <https://doi.org/10.6084/m9.figshare.5249041.v1>



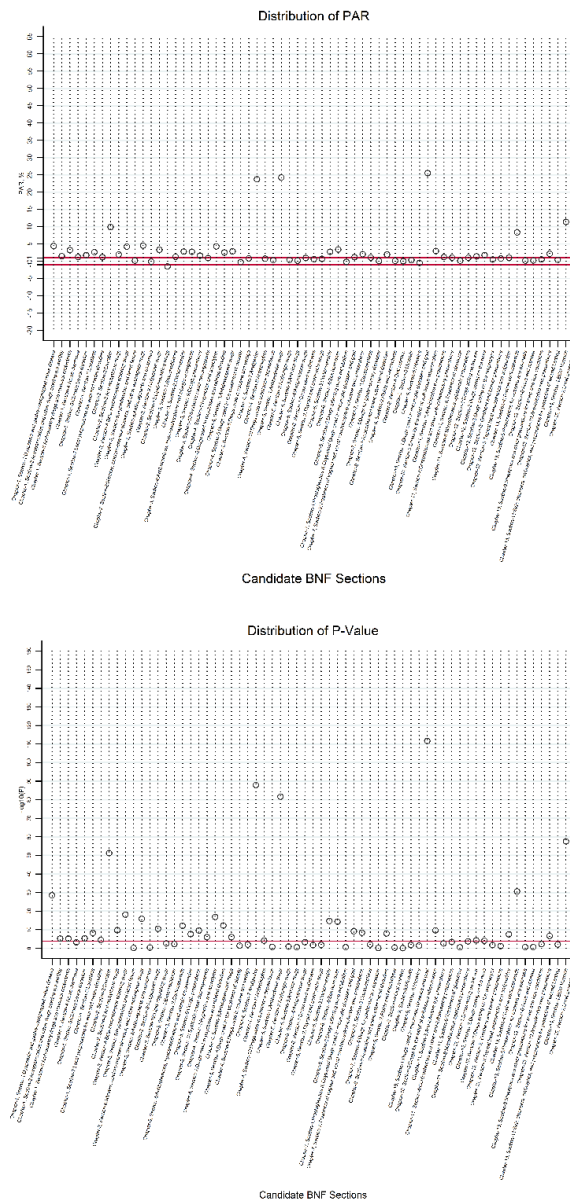
Supplementary figure S4. Population attributable risk for association between each third level Read code and total hip replacement: findings from population based case-control study

High-resolution figure could be found at: <https://doi.org/10.6084/m9.figshare.5249047.v1>



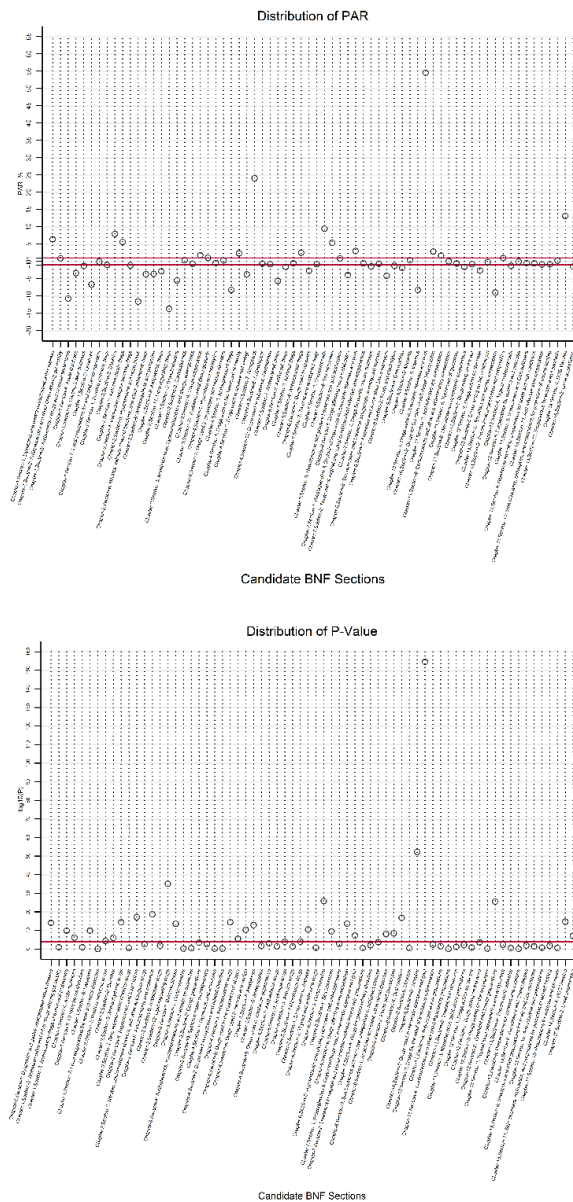
Supplementary figure S5. Population attributable risk for association between each BNF section and total knee replacement: findings from population based case-control study

High-resolution figure could be found at: <https://doi.org/10.6084/m9.figshare.5249059.v1>

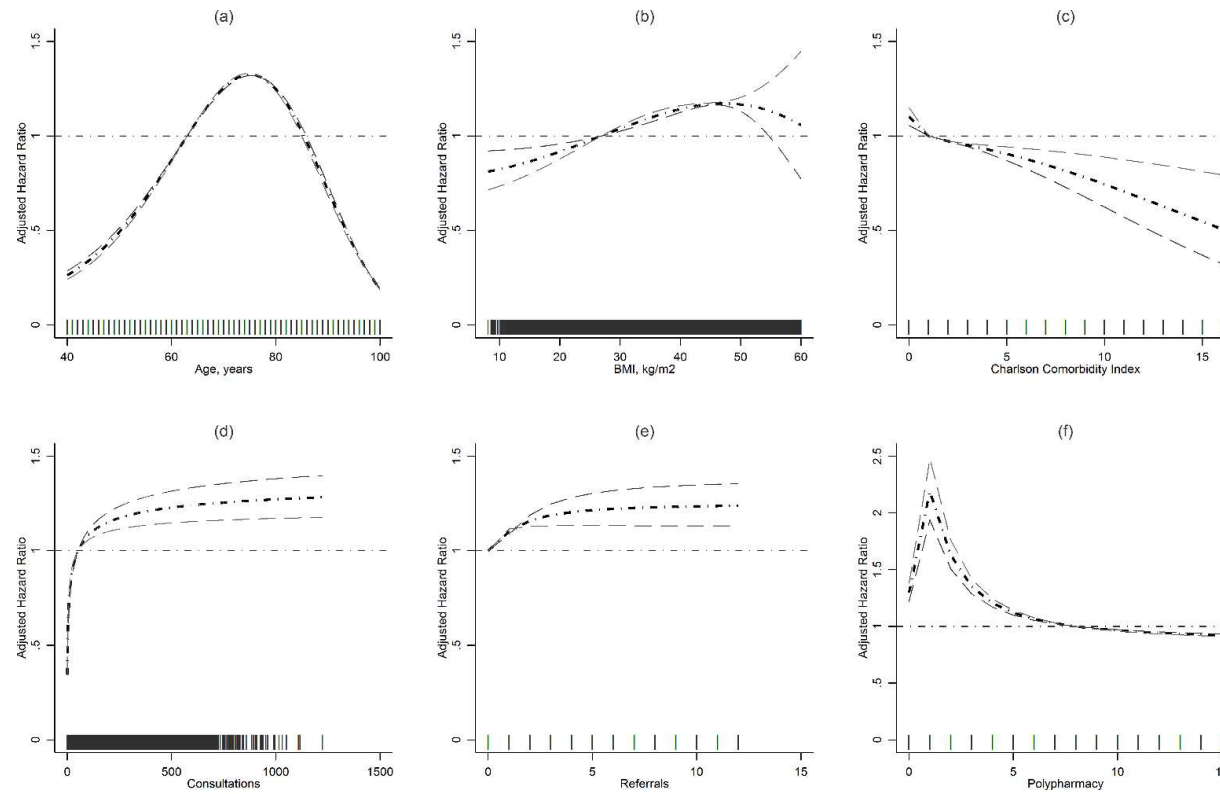


Supplementary figure S6. Population attributable risk for association between each BNF section and total hip replacement: findings from population based case-control study

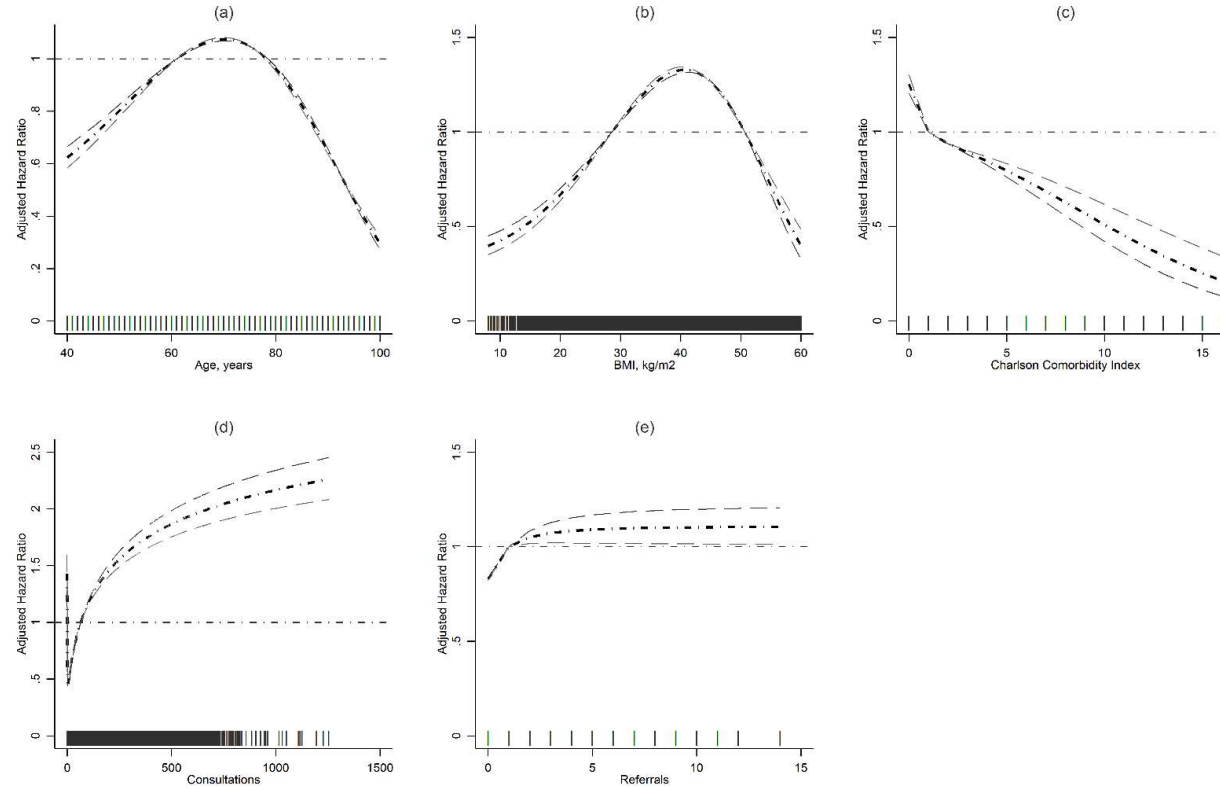
High-resolution figure could be found at: <https://doi.org/10.6084/m9.figshare.5249068.v1>



Supplementary Figure S7. Adjusted subdistribution hazard ratios for primary total hip replacement by age, body mass index, Charlson comorbidity index, consultation counts, referrals, and polypharmacy (BNF chapters) in THR derivation cohort

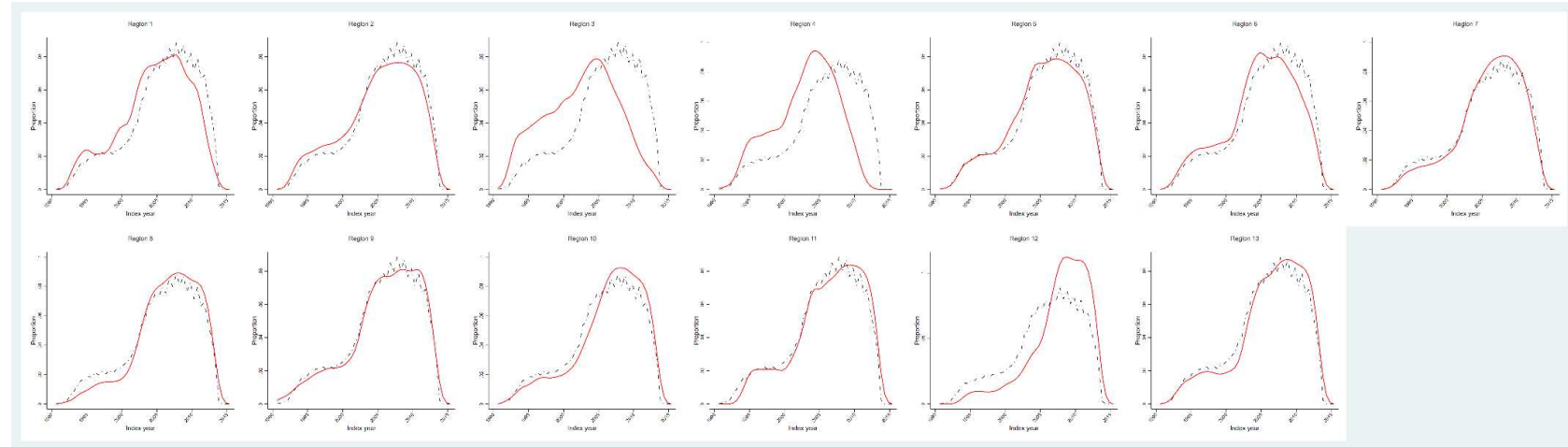


Supplementary Figure S8. Adjusted subdistribution hazard ratios for primary total knee replacement by age, body mass index, Charlson comorbidity index, consultation counts, referrals in TKR derivation cohort



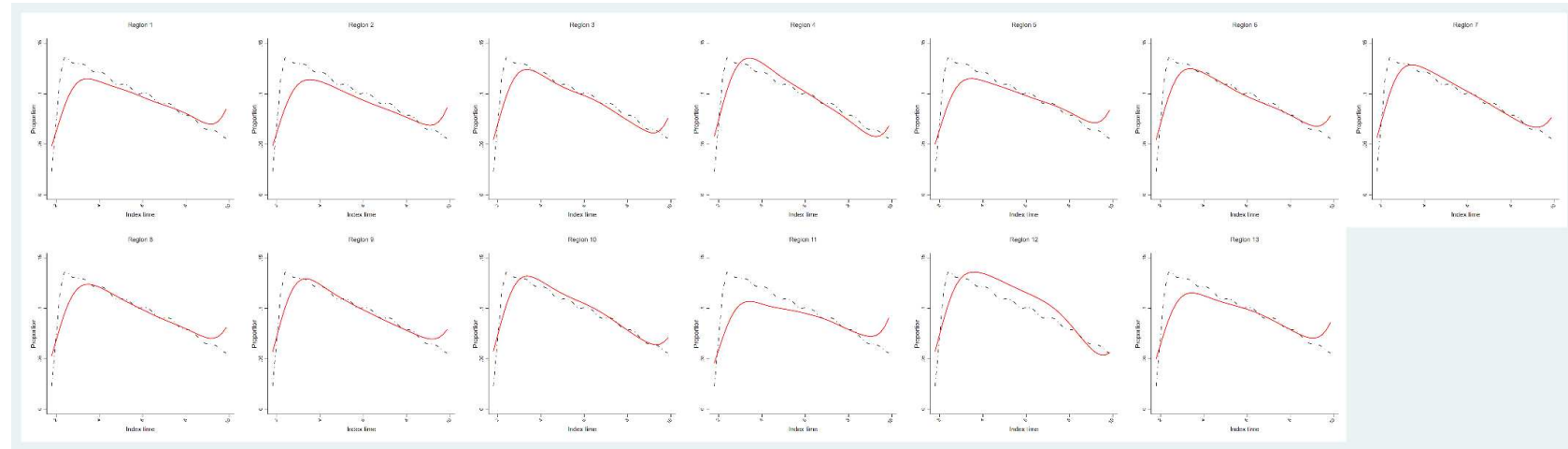
Supplementary Figure S9. Distribution of entry year by regions in TKR cohort

Dash-line indicates the distribution in the whole TKR cohort; the solid line indicates the distribution in the regional cohort.

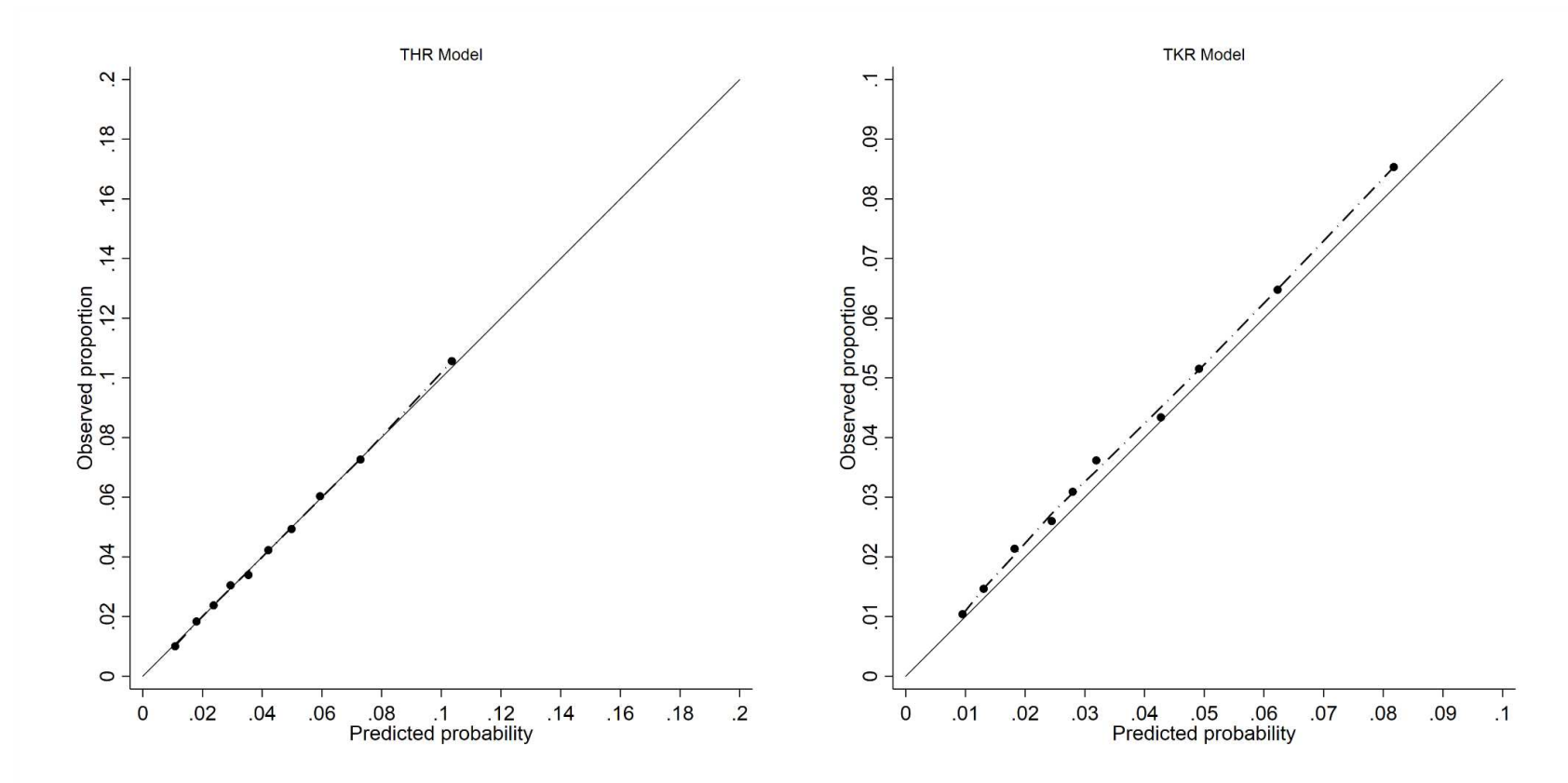


Supplementary Figure S10. Distribution of follow-up time by regions in TKR cohort

Dash-line indicates the distribution in the whole TKR cohort; the solid line indicates the distribution in the regional cohort.



Supplementary Figure S11. Sensitivity analysis: apply risk algorithms in the sample incorporating patients with early (within 2 years since entry date) outcomes The calibration plot in each validation cohort was presented for one imputed dataset, but comparable to the calibration plots in the other imputations (**Left** for THR and in **Right** for TKR).



Supplementary Table S1. Source of predictors and the selection of predictors

QResearch	Systematic Review	Supplemented or emphasized by 1st round review	ReWAS study	Risk factor / potential predictor	Exclusion Votes	THR/TKR	Feasibility check and action notes
●	●			Age	1	Both	included (inc)
●	●			Gender	1	Both	inc
●			●	Ethnicity	1	Both	inc
		●		Region or trust	1	Both	inc
●		●		Deprivation (townsend score or SEIFA score)	1	Both	Not available (N/A)
●				Family history of outcome (knee or hip arthroplasty)	2	Both	N/A
			●	Family history	2	Both	The 2 were combined to one indicator and restricted to the 2 read codes for FH Arthritis and FH Osteoarthritis
			●	Family history yes	3	Both	
●	●		●	Smoking Status	0	Both	inc
●			●	Drinking Status	0	Both	inc
			●	Physical activity	0	Both	inc
			●	Diet consultation	2	Both	inc
			●	Health education consultation	4	Both	Drop
		●		Charlson comorbidity index	0	Both	inc
		●		Number of consultations	0	Both	inc
		●		Number of referrals	1	Both	inc
●			●	Cardiovascular disease	1	Both	Use the subgroup of cardiovascular diseases as below rather than the general definition
●				Atrial fibrillation	3	Both	inc
●				Congestive cardiac failure	2	Both	inc

•				Valvular heart disease	3	Both	inc
•				Varicose veins	4	Both	drop
•				Venous thromboembolism	3	Both	inc
•			•	Treated hypertension	3	Both	inc
			•	Diagnosis of respiratory diseases	4	Knee	Drop
•			•	Asthma	3	Knee	inc
•				COPD	3	Knee	inc
•				Chronic liver disease	3	Both	inc
•				Type 1 diabetes	3	Both	Combining type 1 diabetes and type 2 diabetes to diabetes mellitus
•				Type 2 diabetes	2	Both	
•				Malabsorption	3	Both	inc
•				Inflammatory bowel diseases	2	Both	inc
•				Dementia	3	Both	inc
		•		Other chronic neurological disease - e.g. multiple sclerosis, cerebral palsy, cerebrovascular disease	3	Both	Use multiple sclerosis, cerebral palsy and cerebrovascular disease as separate indicators
		•	•	Mental problem: anxiety / depression	3	Both	inc
•			•	Rheumatoid arthritis	0	Knee	inc
•				Systemic lupus erythematosus	2	Both	inc
•				Falls	0	Both	inc
			•	History of musculoskeletal disorders	0	Both	used the detailed definition as below
•		•		Previous Fracture/injury	0	Both	combining joint-specific fracture/injury and sprain as one indicator
	•	•	•	Previous Knee Injury	0	Both	

		●		Osteoporosis/osteopenia/osteoporotic fracture history	1	Both	inc
		●		Referred (groin) pain	1	Both	N/A
		●		Widespread pain / multiple consultations for different pain conditions	1	Both	N/A
		●		Pain and positioning of pain in detecting hip osteoarthritis and its severity	1	Both	N/A
		●		O/E- Knee effusion	1	Both	inc
●				Previous bleed	3	Both	inc
				O/E - diabetic foot	3	Hip	inc
	●		●	Height	1	Both	Using the BMI below as indicator rather than this two separate measurements
	●		●	Weight	0	Both	
●	●		●	BMI	0	Both	inc
		●		Rheumatoid factor	2	Both	inc
		●		Scoliosis / kyphosis	1	Both	inc
		●		Developmental Dysplasia of the hip (DDH)	0	Both	inc
		●		Chondrocalcinosis	1	Both	inc
			●	Osteoarthritis and allied disorders	0	Both	inc, with joint specification
			●	Arthropathy	0	Both	Drop due to the feasibility in the EHR
			●	Non-specific osteoarthritis	1	Both	inc
			●	Low back pain	1	Both	inc
			●	Pain Consultation	1	Both	drop, the first joint pain consultation is the entry criteria
		●		Polypharmacy	1	Both	inc
●		●	●	Knee joint injection	0	Knee	inc
		●		Previous knee arthroscopy	0	Knee	inc
		●		Previous ACL reconstruction	0	Knee	inc

•				Phenytoin	3	Both	inc
			•	Physiotherapy or remedial therapy	2	Both	inc
•			•	Corticosteroids	2	knee	inc
•			•	Antidepressant drugs	3	Both	inc
•		•	•	Opioid Analgesics	2	Both	inc
•			•	Sex hormones	3	Both	inc
			•	Prostaglandins & Oxytocics	3	Both	inc
		•		Biphosphonates / Anti-osteoporosis drugs	2	Both	inc
•		•	•	NSAIDS or COX-2	2	Both	inc
			•	Topical NSAIDS or other topical creams	2	Both	inc
			•	Glucocosteroids	2	Both	inc

Supplementary Table S2. Multivariable adjusted hazard ratios (full model) and population attributable risk between each candidate predictor and total hip replacement in derivation cohort

	HR	95% CI of HR		EXPO	PAR	95% CI of PAR		Exclusion by PAR*
Gender (male as reference)	1.02	0.98	1.07	0.64	1.53%	-1.03%	4.05%	3
Ethnicity (Whited as reference)								
Not Recorded	1.00	0.96	1.03	0.68	-0.29%	-2.79%	2.18%	1
Other ethnicity group	0.37	0.28	0.49	0.01	-0.76%	-0.87%	-0.62%	1
Family history of arthritis / osteoarthritis (no history as reference)	1.11	0.91	1.35	0.01	0.07%	-0.06%	0.21%	2
Smoking status (not-recorded/non-smoker/Ex-smoker as reference)								
Light smoker	0.65	0.55	0.76	0.02	-0.81%	-1.04%	-0.54%	1
Moderate/Heavy smoker	0.76	0.71	0.81	0.12	-2.84%	-3.45%	-2.20%	3
Drinking status (not-recorded/non-drinker as reference)								
Ex-drinker	1.01	0.91	1.12	0.04	0.04%	-0.32%	0.43%	2
Light drinker	1.21	1.16	1.27	0.70	12.94%	10.07%	15.75%	3
Moderate drinker	1.39	1.21	1.60	0.01	0.54%	0.29%	0.82%	2
Heavy drinker	1.08	0.85	1.38	0.01	0.05%	-0.10%	0.25%	2
Physical Activity (not-recorded/no physical activity as reference)								
Taking light physical activity	1.02	0.96	1.09	0.09	0.21%	-0.36%	0.80%	2
Taking moderate physical activity	1.09	1.01	1.17	0.06	0.53%	0.08%	1.00%	2
Taking heavy physical activity	1.38	1.14	1.66	0.01	0.25%	0.09%	0.43%	2
Having diet consultation (no as reference)	1.01	0.97	1.05	0.37	0.35%	-1.00%	1.71%	2
Chronic Liver Disease (no as reference)	0.99	0.88	1.12	0.02	-0.01%	-0.27%	0.28%	1
Diabetes Mellitus (no as reference)	0.84	0.79	0.89	0.14	-2.31%	-3.06%	-1.53%	3
Malabsorption (no as reference)	0.82	0.62	1.08	0.00	-0.09%	-0.19%	0.04%	1
Inflammatory Bowel Disease (no as reference)	0.95	0.88	1.03	0.06	-0.27%	-0.70%	0.18%	1
Dementia (no as reference)	0.34	0.18	0.63	0.00	-0.28%	-0.35%	-0.16%	1
Cerebral Palsy (no as reference)	1.68	0.80	3.53	0.00	0.03%	-0.01%	0.13%	2

Multiple Sclerosis (no as reference)	0.75	0.51	1.11	0.00	-0.08%	-0.15%	0.04%	1
Cerebrovascular Disease (no as reference)	0.85	0.76	0.95	0.04	-0.60%	-0.94%	-0.22%	1
Mental Problem (no as reference)								
Anxiety	0.85	0.80	0.90	0.13	-1.92%	-2.57%	-1.23%	3
Depression	0.85	0.80	0.90	0.16	-2.48%	-3.32%	-1.60%	3
Systemic Lupus erythematosus (no as reference)	0.79	0.51	1.23	0.00	-0.05%	-0.11%	0.05%	1
Falls (no as reference)	0.89	0.84	0.96	0.10	-1.06%	-1.64%	-0.45%	3
Fracture, sprain, injury (no as reference)	1.83	1.67	2.02	0.02	1.93%	1.56%	2.34%	3
Osteoporosis (no as reference)	0.88	0.79	0.98	0.04	-0.52%	-0.92%	-0.07%	1
Diabetic foot	1.02	0.91	1.13	0.05	0.07%	-0.42%	0.61%	2
Bleed (no as reference)	0.95	0.90	1.00	0.15	-0.71%	-1.44%	0.05%	1
Scoliosis/kyphosis (no as reference)	0.92	0.75	1.14	0.01	-0.06%	-0.20%	0.11%	1
Development Dysplasia of the Hip (no as reference)	5.35	2.96	9.67	0.00	0.10%	0.04%	0.19%	2
Chondrocalcinosis (no as reference)	0.90	0.64	1.27	0.00	-0.03%	-0.09%	0.07%	1
Osteoarthritis and allied disorders (no as reference)								
Knee OA	1.17	0.74	1.86	0.00	0.02%	-0.02%	0.08%	2
Hand OA	0.36	0.32	0.42	0.03	-2.14%	-2.30%	-1.95%	3
Generalised OA	0.54	0.47	0.61	0.03	-1.21%	-1.38%	-1.01%	3
other joint OA	0.43	0.39	0.48	0.04	-2.39%	-2.59%	-2.17%	3
Non-specific OA (no as reference)	0.48	0.46	0.50	0.41	-27.20%	-28.55%	-25.89%	3
Low back pain (no as reference)	0.99	0.96	1.03	0.50	-0.39%	-2.22%	1.45%	1
Hypertension (no as reference)	1.00	0.96	1.04	0.34	0.01%	-1.30%	1.34%	2
Artrial Fibrillation (no as reference)	1.00	0.90	1.11	0.03	-0.01%	-0.34%	0.35%	1
Congestive Cardiac Failure (no as reference)	0.68	0.57	0.80	0.02	-0.69%	-0.92%	-0.42%	1
Venous Thromboembolism (no as reference)	1.02	0.91	1.13	0.03	0.05%	-0.23%	0.35%	2
Valvular Heart Disease (no as reference)	0.99	0.96	1.03	0.50	-0.39%	-2.22%	1.45%	1
Phenytoin (no as reference)	0.95	0.66	1.37	0.00	-0.01%	-0.09%	0.10%	1
Physiotherapy (no as reference)	1.07	1.01	1.14	0.09	0.65%	0.10%	1.23%	2
Glucocosteroids (no as reference)	0.96	0.90	1.01	0.11	-0.47%	-1.05%	0.15%	1

Antidepressant (no as reference)	0.96	0.92	1.01	0.36	-1.30%	-2.95%	0.37%	3
Analgesics (no as reference)								
Weak combination opioids	0.93	0.89	0.96	0.64	-5.02%	-7.64%	-2.43%	3
Moderate combination opioids	1.00	0.85	1.19	0.01	0.01%	-0.16%	0.20%	2
Strong / very strong combination opioids	1.07	0.88	1.30	0.01	0.07%	-0.12%	0.30%	2
Hormone treatment (no as reference)	0.95	0.91	1.00	0.27	-1.25%	-2.44%	-0.03%	3
Bisphosphonates (no as reference)	1.18	1.06	1.30	0.05	0.88%	0.31%	1.51%	2
Topical NSAIDs (no as reference)								
NSAIDS	0.73	0.70	0.77	0.23	-6.41%	-7.28%	-5.51%	3
OTHER	0.71	0.59	0.85	0.01	-0.35%	-0.50%	-0.18%	1
Drugs for rheumatoid disease and gout (no as reference)								
NSAIDS	1.02	0.98	1.06	0.61	1.32%	-1.10%	3.73%	3
COX2	1.06	0.99	1.14	0.07	0.41%	-0.07%	0.92%	2
Prostaglandins & Oxytocics (no as reference)	0.92	0.83	1.01	0.03	-0.28%	-0.58%	0.04%	1
Rheumatoid factor test (no as reference)	1.03	0.76	1.37	0.00	0.01%	-0.07%	0.11%	2

tag=1, PAR in (-1,0); tag=2, PAR in (0, 1); tag=3, PAR<=-1 or PAR>=1; predictors labelled as tag3 (or at least one level labelled as tag3 for categorical predictors) and not excluded by backward elimination remained in the final model.

Supplementary Table S3. Multivariable adjusted hazard ratios (full model) and population attributable risk between each candidate predictor and total knee replacement in derivation cohort

	HR	95% CI of HR		EXPO	PAR	95% CI of PAR		Exclusion by PAR*
Gender (male as reference)	0.87	0.84	0.90	0.5734	-8.23%	-10.44%	-6.02%	3
Ethnicity (Whited as reference)								
Not Recorded	1.03	0.99	1.06	0.6828	1.72%	-0.51%	3.92%	3
Other ethnicity group	0.88	0.76	1.03	0.0144	-0.17%	-0.35%	0.04%	1
Family history of arthritis / osteoarthritis (no history as reference)								
FH of Arthritis/Osteoarthritis	0.84	0.69	1.03	0.0051	-0.08%	-0.16%	0.01%	1
Smoking status (not-recorded/non-smoker/Ex-smoker as reference)								
Light smoker	0.77	0.65	0.91	0.0204	-0.48%	-0.72%	-0.19%	1
Moderate/Heavy smoker	0.75	0.71	0.80	0.1163	-2.98%	-3.51%	-2.43%	3
Drinking status (not-recorded/non-drinker as reference)								
Ex-drinker	0.93	0.84	1.02	0.0335	-0.25%	-0.53%	0.05%	1
Light drinker	1.12	1.07	1.16	0.7078	7.73%	4.96%	10.45%	3
Moderate drinker	1.31	1.17	1.47	0.0157	0.49%	0.26%	0.74%	2
Heavy drinker	1.01	0.84	1.21	0.0076	0.01%	-0.12%	0.16%	2
Physical Activity (not-recorded/no physical activity as reference)								
Taking light physical activity	1.06	1.01	1.11	0.1079	0.66%	0.14%	1.19%	2
Taking moderate physical activity	1.12	1.06	1.18	0.0713	0.82%	0.41%	1.26%	2
Taking heavy physical activity	1.34	1.15	1.55	0.0078	0.26%	0.12%	0.43%	2
Having diet consultation (no as reference)	1.01	0.97	1.04	0.1884	0.10%	-0.49%	0.71%	2
Asthma (no as reference)	1.08	1.01	1.14	0.1426	1.07%	0.17%	2.00%	3
COPD (no as reference)	0.72	0.66	0.78	0.0483	-1.38%	-1.65%	-1.09%	3
Chronic Liver Disease (no as reference)	0.93	0.86	1.02	0.026	-0.17%	-0.37%	0.04%	1
Diabetes Mellitus (no as reference)	0.79	0.74	0.84	0.1306	-2.85%	-3.55%	-2.10%	3
Malabsorption (no as reference)	0.86	0.70	1.06	0.005	-0.07%	-0.15%	0.03%	1
Inflammatory Bowel Disease (no as reference)	0.92	0.87	0.97	0.0642	-0.52%	-0.85%	-0.17%	1
Dementia (no as reference)	0.78	0.62	0.98	0.0066	-0.14%	-0.25%	-0.01%	1
Cerebral Palsy (no as reference)	0.72	0.32	1.61	0.0005	-0.01%	-0.03%	0.03%	1
Multiple Sclerosis (no as reference)	1.01	0.77	1.32	0.0031	0.00%	-0.07%	0.10%	2
Cerebrovascular Disease (no as reference)	0.89	0.82	0.98	0.0388	-0.42%	-0.72%	-0.08%	1
Mental Problem (no as reference)								
Anxiety	0.78	0.74	0.82	0.135	-3.09%	-3.63%	-2.53%	3

Depression	0.85	0.82	0.90	0.0866	-1.28%	-1.63%	-0.91%	3
Rheumatoid arthritis (no as reference)	1.22	1.12	1.32	0.0245	0.53%	0.30%	0.78%	2
Systemic Lupus erythematosus (no as reference)	0.89	0.64	1.25	0.0866	-0.92%	-3.23%	2.15%	1
Falls (no as reference)	0.96	0.92	1.00	0.1198	-0.50%	-1.01%	0.03%	1
Fracture, sprain, injury (no as reference)								
knee fracture/knee sprain/knee injury	1.30	1.25	1.37	0.0568	1.70%	1.38%	2.04%	3
Osteoporosis (no as reference)	0.95	0.87	1.03	0.0468	-0.25%	-0.62%	0.15%	1
Knee effusion (no as reference)	1.11	1.02	1.20	0.015	0.16%	0.03%	0.30%	2
Bleed (no as reference)	0.96	0.92	0.99	0.1696	-0.76%	-1.39%	-0.11%	1
Scoliosis/kyphosis (no as reference)	0.92	0.77	1.09	0.0079	-0.07%	-0.18%	0.07%	1
Development Dysplasia of the Hip (no as reference)	0.62	0.16	2.49	0.0002	-0.01%	-0.02%	0.03%	1
Chondrocalcinosis (no as reference)	1.24	1.05	1.46	0.0038	0.09%	0.02%	0.17%	2
Osteoarthritis and allied disorders (no as reference)								
Hip OA	0.59	0.55	0.63	0.064	-2.72%	-2.99%	-2.44%	3
Hand OA	0.61	0.56	0.68	0.0299	-1.17%	-1.34%	-0.98%	3
Generalised OA	0.74	0.68	0.81	0.0258	-0.67%	-0.84%	-0.49%	1
other joint OA	0.75	0.69	0.81	0.0364	-0.92%	-1.13%	-0.69%	1
Non-specific OA (no as reference)	1.17	1.12	1.22	0.3536	5.62%	4.04%	7.16%	3
Low back pain (no as reference)	0.88	0.85	0.91	0.5257	-6.81%	-8.59%	-5.03%	3
Hypertension (no as reference)	0.95	0.92	0.99	0.3589	-1.71%	-2.92%	-0.48%	3
Atrial Fibrillation (no as reference)	0.86	0.79	0.93	0.0397	-0.57%	-0.83%	-0.28%	1
Congestive Cardiac Failure (no as reference)	0.77	0.68	0.88	0.0232	-0.54%	-0.76%	-0.29%	1
Venous Thromboembolism (no as reference)	1.06	0.99	1.14	0.0294	0.19%	-0.03%	0.42%	2
Valvular Heart Disease (no as reference)	0.88	0.78	1.00	0.0164	-0.19%	-0.35%	-0.01%	1
Joint Injection (no as reference)	1.65	1.59	1.72	0.102	6.24%	5.68%	6.81%	3
Knee Arthroscopy (no as reference)	14.23	13.70	14.78	0.02	20.92%	20.26%	21.60%	3
ACL Reconstruction (no as reference)	1.23	0.98	1.54	0.001	0.02%	0.00%	0.05%	2
Phenytoin (no as reference)	0.90	0.68	1.18	0.003	-0.03%	-0.10%	0.05%	1
Physiotherapy (no as reference)	1.00	0.96	1.05	0.0999	0.02%	-0.41%	0.46%	2
Corticosteroids (no as reference)	0.99	0.94	1.05	0.1493	-0.09%	-0.93%	0.78%	1
Glucocosteroids (no as reference)	1.08	1.04	1.12	0.1241	0.98%	0.48%	1.51%	2
Antidepressant (no as reference)	0.95	0.92	0.99	0.3843	-1.91%	-3.35%	-0.46%	3
Analgesics (no as reference)								
Weak combination opioids	1.35	1.29	1.41	0.6452	18.44%	15.74%	21.09%	3
Moderate combination opioids	1.39	1.23	1.56	0.0116	0.44%	0.27%	0.64%	2
Strong / very strong combination opioids	1.64	1.49	1.80	0.0153	0.96%	0.74%	1.21%	2
Hormone treatment (no as reference)	1.01	0.97	1.05	0.258	0.14%	-0.87%	1.18%	2
Bisphosphonates (no as reference)	1.03	0.96	1.11	0.058	0.18%	-0.26%	0.64%	2

Topical NSAIDS (no as reference)									
NSAIDS	0.93	0.90	0.96	0.2709	-1.90%	-2.82%	-0.96%	3	
OTHER	1.17	1.08	1.28	0.0178	0.31%	0.14%	0.49%	2	
Drugs for rheumatoid disease and gout (no as reference)									
NSAIDS	1.40	1.34	1.47	0.6462	20.74%	17.98%	23.43%	3	
COX2	1.26	1.17	1.35	0.0643	1.64%	1.10%	2.20%	3	
Prostaglandins & Oxytocics (no as reference)	0.93	0.87	1.00	0.0381	-0.26%	-0.50%	-0.01%	1	
Rheumatoid factor test (no as reference)	0.76	0.58	1.00	0.0027	-0.06%	-0.11%	0.00%	1	

tag=1, PAR in (-1,0); tag=2, PAR in (0, 1); tag=3, PAR<=-1 or PAR>=1; predictors labelled as tag3 (or at least one level labelled as tag3 for categorical predictors) and not excluded by backward elimination remained in the final model.

Supplementary Table S4. Sensitivity analysis: discrimination and calibration slope by applying risk algorithms in the sample incorporating patients with early (within 2 years since entry date) outcomes

	C-statistics (95% CI)	Calibration slope (95% CI)
THR cohort	0.72 (0.72 to 0.73)	0.99 (0.92 to 1.06)
TKR cohort	0.77 (0.75 to 0.78)	1.05 (1.02 to 1.08)

Supplementary Table S5. Sensitivity analysis: model coefficients by applying final predictors in the sample incorporating patients with early (within 2 years since entry date) outcomes

Predictor	Subdistribution Hazard Ratio (95 CI)	Beta Coefficient
Final Model for primary total hip replacement		
Gender: Women Vs Men	1.00 (0.96, 1.04)	0.002176
Smoking status		
Non-smoker/not recorded/Ex-smoker	reference	
Light smoker	0.64 (0.54, 0.76)	-0.44662
Moderate / Heavy smoker	0.75 (0.71, 0.80)	-0.28342

Drinking status		
Non-drinker/not recorded	reference	
Ex-drinker	1.01 (0.91, 1.11)	0.008539
Light drinker	1.18 (1.14, 1.23)	0.167596
Moderate drinker	1.36 (1.18, 1.55)	0.304063
Heavy drinker	1.06 (0.85, 1.34)	0.062208
Diabetes Mellitus: yes vs no	0.86 (0.81, 0.90)	-0.15431
Mental disorders: yes vs no		
No /Not recorded	reference	
Anxiety	0.85 (0.80, 0.90)	-0.16286
Depression	0.85 (0.81, 0.89)	-0.16449
Falls	0.85 (0.81, 0.91)	-0.15729
Previous hip injury: yes vs no	1.54 (1.41, 1.69)	0.432443
Recorded diagnosis of joint-specific osteoarthritis		
No/not recorded	reference	
Knee OA	1.02 (0.65, 1.58)	0.01519
Hand OA	0.21 (0.18, 0.23)	-1.58291
Generalised OA	0.29 (0.25, 0.33)	-1.24289
Other joint OA	0.23 (0.20, 0.26)	-1.47375
Recorded diagnosis of non-specific Osteoarthritis: yes vs no	0.27 (0.26, 0.28)	-1.31222
Analgesics		
No prescription	reference	
Weak combination opioids	0.93 (0.89, 0.97)	-0.07207
Moderate combination opioids	1.00 (0.86, 1.17)	0.002591
Strong / very strong combination opioids	1.06 (0.88, 1.28)	0.056439
Antidepressant: yes vs no	0.96 (0.92, 1.01)	-0.03609
Topical NSAIDS		
No prescription	reference	
NSAIDS	0.77 (0.73, 0.80)	-0.26674

Other	0.78 (0.66, 0.92)	-0.24756
NSAIDS/COX2		
No prescription	reference	
NSAIDS	1.06 (1.02, 1.09)	0.056441
COX2	1.18 (1.11, 1.25)	0.164300
Hormone treatment: yes vs no	0.96 (0.92, 1.00)	-0.03914
(Age/10) ³	-	0.056923
(Age/10) ³ *ln(Age/10)	-	-0.02491
(BMI/10) ²	-	0.137869
(BMI/10) ³	-	-0.02498
((Charlson Comorbidity Index+1)/10) ⁻²	-	0.00158
((Charlson Comorbidity Index+1)/10) ²	-	-1.31862
((Number of referrals+1)/10) ⁻²	-	-0.01552
((Number of referrals+1)/10) ⁻² *ln((Number of referrals+1)/10)	-	-0.00546
((Number of consultations+1)/1000) ^{-0.5}	-	-0.17164
((Number of consultations+1)/1000) ^{-0.5} *ln((Number of consultations+1)/1000)	-	-0.0174
((Number of BNF chapters+1)/10) ⁻²	-	0.110529
((Number of BNF chapters+1)/10) ⁻² *ln((Number of BNF chapters+1)/10)	-	0.046406
Final Model for primary total knee replacement		
Gender: Women Vs Men	0.87 (0.85, 0.89)	-0.139496
Ethnicity		
White	reference	-
Other ethnicity group	0.90 (0.88, 0.93)	-0.100227
Not recorded	1.04 (0.95, 1.12)	0.034938
Smoking status		
Non-smoker/not recorded/Ex-smoker	reference	-
Light smoker	0.75 (0.70, 0.80)	-0.292253
Moderate / Heavy smoker	0.75 (0.72, 0.77)	-0.294128

Drinking status		
Non-drinker/not recorded	reference	-
Ex-drinker	1.13 (1.10, 1.17)	0.122508
Light drinker	1.21 (1.110, 1.32)	0.190747
Moderate drinker/Heavy drinker	1.34 (1.190, 1.51)	0.293720
Asthma, yes vs no	1.07 (1.020, 1.12)	0.064279
COPD, yes vs no	0.71 (0.680, 0.74)	-0.340306
Diabetes mellitus: yes vs no	0.88 (0.840, 0.92)	-0.128850
Mental disorders: yes vs no		
Anxiety	0.76 (0.740, 0.78)	-0.270620
Depression	0.85 (0.830, 0.87)	-0.162216
Previous knee injury: yes vs no	1.29 (1.240, 1.34)	0.254646
Recorded diagnosis of joint-specific osteoarthritis		
No/not recorded	reference	-
Hip OA	0.59 (0.580, 0.61)	-0.521571
Hand OA	0.61 (0.590, 0.64)	-0.493812
Generalised OA/	0.76 (0.730, 0.8)	-0.274384
Other joint OA	0.74 (0.710, 0.77)	-0.301054
Recorded diagnosis of non-specific Osteoarthritis: yes vs no	1.17 (1.150, 1.19)	0.158083
Low back pain: yes vs no	0.87 (0.850, 0.89)	-0.138259
Hypertension: yes vs no	0.96 (0.940, 0.98)	-0.040532
Joint Injection: yes vs no	1.66 (1.590, 1.73)	0.507833
Knee Arthroscopy: yes vs no	14.47 (10.580, 19.8)	2.672140
Antidepressant: yes vs no	0.95 (0.930, 0.97)	-0.051037
Analgesics		
No prescription	reference	-
Weak combination opioids	1.34 (1.30, 1.38)	0.292199
Moderate combination opioids	1.37 (1.240, 1.52)	0.317573
Strong / very strong combination opioids	1.59 (1.450, 1.75)	0.464372

Topical NSAIDS		
No prescription	reference	-
NSAIDS	0.94 (0.920, 0.96)	-0.065295
Other	1.18 (1.10, 1.26)	0.162558
NSAIDS/COX2		
No prescription	reference	-
NSAIDS	1.42 (1.370, 1.47)	0.350504
COX2	1.27 (1.210, 1.34)	0.240079
(Age/10) ³	-	0.029616
(Age/10) ³ *ln(Age/10)	-	-0.132653
(BMI/10) ²	-	0.281292
(BMI/10) ³	-	-0.047230
((Charlson Comorbidity Index+1)/10) ⁻²	-	0.002391
((Charlson Comorbidity Index+1)/10) ²	-	-1.440470
((Number of referrals+1)/10) ⁻²	-	-0.010520
((Number of referrals+1)/10) ⁻² *ln((Number of referrals+1)/10)	-	-0.002960
((Number of consultations+1)/1000) ^{-0.5}	-	-0.541070
((Number of consultations+1)/1000) ^{-0.5} *ln((Number of consultations+1)/1000)	-	-0.073452

Supplementary Table S6. Clinical examples for total hip replacement model

Predictor	Clinical Examples	
	Patient A	Patient B
ClF ₀ (t=10 years)	6.8%	6.8%
Age, year	70	60
Gender	Male	Female
Smoking status	Non-smoker	Non-smoker
Drinking status	Light drinker	Light drinker

Diabetes Mellitus	No	No
Mental disorders	No	No
Falls	No	No
Previous hip injury	Yes	No
Recorded diagnosis of joint-specific osteoarthritis	No	No
Recorded diagnosis of non-specific osteoarthritis	No	No
Analgesics	No	Weak combination opioids
Topical NSAIDs	No	No
NSAIDs/COX2	NSAIDs	NSAIDs
Hormone treatment	No	Yes
Body mass index, kg/m ²	24.8	35.1
Charlson Comorbidity Index	2	1
Number of referrals	2	0
Number of consultations	20	35
Number of BNF chapters	1	7
10-year risk of THR	79.7%	62.4%
	High risk	High risk

Supplementary Table S7. Clinical examples for total knee replacement model

Predictor	Clinical Examples	
	Patient A	Patient B
CIF ₀ (t=10 years)	7.5%	7.5%
Age, years	58	70
Gender	Male	Female
Ethnicity	Not Recorded	White
Smoking status	Non-smoker	Non-smoker
Drinking status	Non-drinker	Non-drinker
Asthma	No	No
COPD	No	No
Diabetes Mellitus	No	No
Mental disorders	No	No
Previous knee injury	No	No
Recorded diagnosis of joint-specific osteoarthritis	No	No
Recorded diagnosis of non-specific osteoarthritis	Yes	No

Low back pain	Yes	No
Hypertension	No	No
Joint Injection	No	No
Knee Arthroscopy	Yes	No
Antidepressant	No	No
Analgesics	No	Weak combination opioids
Topical NSAIDs	No	No
NSAIDs/COX2	No	NSAIDs
Body mass index, kg/m ²	26.0	42.0
Charlson Comorbidity Index	0	0
Number of referrals	2	1
Number of consultations	26	30
10-year risk of TKR	87.0%	31.7%
	High risk	Low risk