

# Primary care consultations and pain medicine prescriptions: a comparison between patients with and without chronic pain after total knee replacement

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## Research Article

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# Abstract

## Background

Approximately 20% of patients experience chronic pain after total knee replacement (TKR). The impact of chronic pain after TKR on primary care services in the UK is currently unknown. The aim of this study was to compare primary care consultations and pain medicine prescriptions between patients with and without chronic pain after TKR.

## Methods

Data from 5,055 patients who received TKR between 2009-2016 with anonymised linked data from the Clinical Practice Research Datalink Gold (CPRD) and English Hospital Episode Statistics (HES) Patient Reported Outcome Measures (PROMs) programme were analysed. The exposure time was from 10 years pre-operative to eight years post-operative. Patients with a score  $\leq 14$  on the Oxford Knee Score pain component scale at 6 months post-operative were classified as having chronic pain after TKR. Primary care consultations and prescribed pain medicines were quantified, and costs calculated based on national cost data.

## Results

721 patients (14%) had chronic pain after TKR. The prevalence and costs of primary care consultations and pain medicine prescriptions per year were consistently higher for patients with chronic pain after TKR compared with those without chronic pain after TKR; these differences were observed both before and after surgery. There was a substantial and sustained increase in the cost of opioid prescriptions after surgery for patients with chronic pain after TKR, peaking at seven years post-operative.

## Conclusions

Increased primary care consultations and pain medicine prescriptions associated with chronic pain after TKR represent a considerable financial cost to primary care services. Evaluation of interventions to reduce the risk of developing this pain condition and improve the early management of pain after TKR are needed to improve outcomes for patients and reduce costs to healthcare services.

## Background

Osteoarthritis is the most common musculoskeletal condition worldwide and is the leading cause of disability in the UK, with one third of people aged  $\geq 45$  year old having sought treatment for their osteoarthritis [1]. It is also associated with substantial healthcare and societal costs [2]. The National Institute for Health and Care Excellence (NICE) Clinical Guideline for osteoarthritis [3] recommends patients are provided with information and individualised self-management strategies are discussed. Core treatments include exercise, weight loss (if appropriate), use of appropriate aids and devices, pain medications (paracetamol and non-steroidal anti-inflammatory drugs as first line treatment for pain) and

intra-articular corticosteroid injections. If these treatments are not effective at controlling pain, then patients can be referred to secondary care for consideration for joint replacement.

TKR is one of the most common elective operations; it has been estimated that nearly five million people were living with a TKR in the USA in 2010 [4]. In the UK National Health Service (NHS), over 100,000 operations are performed annually [5, 6]. Due to changes in population demographics and obesity, the rate of TKR has been predicted to increase [7]. The principal aim of surgery is to improve function and provide relief from chronic knee pain [5]. For many patients, TKR is successful at providing pain relief, however approximately 20% of patients experience chronic post-surgical pain, defined as pain that occurs or increases in intensity at three months or longer after surgery [8]. Chronic pain after TKR is associated with reduced quality of life and functional limitations [9], and people are often disappointed with their outcome, struggle to make sense of their pain and may not seek help [10, 11].

In the UK, management of chronic pain after TKR is provided within primary and secondary care services. Primary care services provide the first point of contact in the healthcare system and are free at the point of delivery and receipt. Research indicates that 32% of healthcare costs in the second year after TKR are primary care costs [12]. However, the impact of chronic pain after TKR on primary care services has not yet been explored. The aim of this study was to compare primary care consultations and prescribed pain medicines between patients with and without chronic pain after TKR by analysing routine NHS healthcare data.

## Methods

### Study design

This was a retrospective observational study using anonymised linked data from the Clinical Practice Research Datalink Gold (CPRD), English Hospital Episode Statistics (HES) Patient Reported Outcome Measures programme (PROMs), HES Admitted Patient Care, HES outpatient, Office for National Statistics (ONS) mortality data and Index of Multiple Deprivation 2015. All methods were performed in accordance with the relevant guidelines and regulations and reporting of the findings adhere to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines.

### Data sources

The CPRD dataset contained anonymised information on >14 million patients registered at 714 UK general practices. Data include computerised records of all consultation and prescription events in primary care and comprehensive demographic information. CPRD provides access to HES-PROMs data held under the CPRD Data Linkage Scheme. HES holds information on patients admitted to NHS hospitals in England, including diagnostic International Classification of Diseases (ICD) codes providing information about a patient's condition and OPCS Classification of Interventions and Procedures version 4 procedural codes for surgery. Since April 2009, HES provides PROMs data on patients undergoing knee

replacement in English NHS hospitals, including a preoperative and 6 month post-operative quality of life questionnaire (EQ-5D) and joint-specific PROM (Oxford Knee Score; OKS).

## Sample

Our linked CPRD-HES-PROMs dataset included all NHS patients with a CPRD record for a primary TKR between 2009 (when PROMs data collection began) and 2016 (when the data were extracted). Analysis was limited to patients with linked HES records who completed a 6-month post-operative OKS. A data science tool was used to perform automated data engineering, data mining and advanced curation on CPRD and HES data cuts. The tool received raw data as input and provided as output selected and structured information ready for analysis.

## Definition of chronic pain after TKR

The OKS is a validated 12-item joint-specific questionnaire that assesses knee pain and function in patients undergoing TKR[13]. A 7-item OKS pain component score (OKS-PS) [14] can be derived from the OKS, with scores ranging from 0-28 (worst to best). Research has found that individuals with a score of  $\leq 14$  on the OKS-PS have pain that is likely to negatively impact on their health-related quality of life [15]. For the analyses, patients were classified based on their 6-month post-operative OKS-PS as either having chronic pain after TKR (score of 0-14) or not having chronic pain after TKR (score of 15-28).

## Primary care consultations

A primary care consultation was defined as any direct health-related encounter with a primary care healthcare professional. Given the large number of staff roles (additional file 1), these were grouped into General Practitioners (GPs), nurses, and other. Consultation types classed as direct health-related encounters were included (detailed criteria in additional file 1). Reason for consultation is not recorded in CPRD, therefore all direct health-related consultations were included in the analyses. Costs for the primary care consultations were calculated based on mean national unit cost of consultation with respective healthcare staff as reported in the Personal Social Services Research Unit.

## Prescribed pain medicines

Included medicines were those identified using a list developed with expert clinicians based on their views about which medications would be prescribed to patients with pain related to their knee. Pain medicines were grouped into paracetamol (acetaminophen), antidepressants, non-steroidal anti-inflammatories (NSAIDs), and opioids (additional file 1). To calculate costs, we searched the British National Formulary website for each medication (e.g. <https://bnf.nice.org.uk/medicinal-forms/paracetamol.html>) and extracted unit cost based on strength and number of units. Based on the unit cost and quantity prescribed as reported in CPRD records, the total cost of each pain medicine prescription was calculated.

## Analyses

Exposure time was defined as the period valid CPRD data were collected for patients before and after TKR; this varied from patient to patient because of different start and end dates linked to surgery data

collection; quality of data; and patient registration, change, or death. Death was calculated using CPRD GOLD and ONS linked data using a published algorithm[16]. Reporting is by year before and after surgery as long as the patient was active during that 12-month period. Sensitivity analyses were conducted adjusting for exposure time, such that values over partial years were inflated as an estimate of a full-year resource use or cost. Analyses were conducted over the period between 10 years before and eight years after TKR; after that the sample of active patients dropped below 500 and the number of patients with chronic pain was deemed too low (additional file 1).

Descriptive analyses were undertaken to report patients' demographic and clinical characteristics. Primary care consultations and pain medicine prescriptions were calculated for patients with and without chronic pain after TKR. Resource use was calculated as the mean number of primary care consultations per patient per year for any cause and associated costs were calculated as the mean cost per patient per year. Pain medicine prescription costs were calculated as mean cost per patient per year. Some specific medicinal forms were excluded because formulation was not costed or because the quantity was not available. In all such cases, the number of prescriptions excluded as a percentage of the total is reported. Analyses were conducted using R.

## Results

### Patients

A total of 5,055 patients were included in the analyses. Of these, 721 (14.3%) had a score of  $\leq 14$  on their 6-month post-operative OKS-PS and were classified as having chronic pain after TKR. Patient demographics and clinical characteristics are displayed in Table 1. Patients had a mean age at surgery of 69 (standard deviation 9) and 56% were female. Mean BMI was 31 (standard deviation 5), 6% of patients were current smokers, 91% had a Charlson Comorbidity score of 0 in the past year and 10% were in the lowest quintile of the IMD deprivation score. The mean exposure time was four years (standard deviation 3).

Table 1  
Demographic and clinical characteristics of the sample population

	<b>Total (n=5,055)</b>	<b>Chronic pain patients (n=721)</b>	<b>Non-chronic pain patients (n=4334)</b>
Age: mean (SD)	69 (9)	67 (10)	69 (9)
Female: n (%)	2849 (56%)	420 (58%)	2429 (56%)
BMI: mean (SD)	31 (5)	32 (6)	30 (5)
Exposure time (years)	4 (3)	4 (3)	4 (3)
Current smoker: n (%)	302 (6%)	97 (14%)	205 (5%)
Current drinker: n (%)	2528 (79%)	331 (72%)	2197 (80%)
Charlson Comorbidity: n (%) (5 years prior)	3570 (71%)	472 (65%)	3098 (71%)
None	423 (8%)	61 (8%)	362 (8%)
1	614 (12%)	99 (14%)	515 (12%)
2	448 (9%)	89 (12%)	359 (8%)
3+			
Charlson Comorbidity: n (%) (1 year prior)	4619 (91%)	644 (89%)	3975 (92%)
None	209 (4%)	34 (5%)	175 (4%)
1	186 (4%)	33 (5%)	153 (4%)
2	41 (1%)	10 (1%)	31 (1%)
3+			

Missing data: BMI = 898 missing; current smoker=413 missing; current drinker=1882 missing; IMD deprivation score=6 missing

	Total (n=5,055)	Chronic pain patients (n=721)	Non-chronic pain patients (n=4334)
IMD deprivation score: n (%) (quintiles; least to most deprived)	1233 (24%)	119 (17%)	1114 (26%)
1	1313 (26%)	162 (22%)	1151 (27%)
2	1136 (22%)	168 (23%)	968 (22%)
3	844 (17%)	140 (19%)	704 (16%)
4	523 (10%)	131 (18%)	392 (9%)
5			
Missing data: BMI = 898 missing; current smoker=413 missing; current drinker=1882 missing; IMD deprivation score=6 missing			

## Primary care consultations

The mean number of primary care consultations for patients with and without chronic pain after TKR from the 10 years before surgery to eight years after surgery is displayed in Figure 1. The mean number of primary care consultations per patient was highest in the year immediately before and immediately after TKR; this pattern was observed for patients with and without chronic pain after TKR. The mean number of primary care consultations per year was consistently higher in patients with chronic pain compared to those without chronic pain after TKR; this pattern was consistent across consultations with different types of healthcare professionals (additional file 1).

The mean primary care consultation costs per year for patients with and without chronic pain after TKR, overall and by healthcare professional category, are provided in Table 2. In the 10 years prior to TKR, patients who would go on to develop chronic pain after TKR cost on average £39-£72 more per year in primary care consultations than patients who did not develop chronic pain after TKR. Post-operatively, this excess cost between patients with and without chronic pain was generally higher, ranging from £66 to £107 on average per year. The main driver of the cost differences in primary care consultations between patients with and without chronic pain were the higher use of GP appointments by patients with chronic pain.

Table 2  
Costs of primary care consultations by year for patients with and without chronic pain

Year	With chronic pain				Without chronic pain			
	GPs	Nurses	Other	Total	GPs	Nurses	Other	Total
-10	£190	£27	£12	£229	£139	£23	£11	£172
-9	£183	£31	£15	£229	£143	£25	£15	£183
-8	£185	£30	£22	£237	£149	£29	£17	£195
-7	£191	£35	£21	£247	£154	£32	£22	£207
-6	£204	£38	£30	£271	£158	£33	£27	£218
-5	£217	£38	£44	£300	£162	£34	£32	£228
-4	£225	£41	£48	£314	£171	£34	£36	£241
-3	£231	£43	£48	£323	£181	£37	£41	£260
-2	£251	£45	£54	£350	£200	£39	£49	£287
-1	£290	£51	£67	£408	£240	£43	£58	£341
1	£316	£55	£73	£445	£228	£50	£68	£347
2	£261	£55	£66	£381	£190	£41	£56	£286
3	£256	£51	£61	£367	£183	£40	£47	£270
4	£247	£55	£65	£367	£174	£40	£46	£260
5	£232	£50	£53	£335	£178	£42	£50	£269
6	£220	£48	£56	£323	£171	£36	£48	£255
7	£243	£40	£64	£347	£171	£35	£43	£249
8	£251	£41	£50	£341	£167	£37	£45	£248

## Prescribed pain medicines

Yearly costs for paracetamol, antidepressants, NSAIDs and opioids for patients with and without chronic pain are summarised in Figure 2 (further results are provided in additional file 1). Prescription costs for patients with chronic pain were consistently higher than those without chronic pain after TKR, the costs were higher both before and after TKR, with stronger pain medication driving greater percentages of total prescription costs leading up to surgery. Pain medicine prescription costs generally increased as patients reached surgery, and then they dropped only to increase again, slightly for patients without chronic pain but a larger increase for those with chronic pain after TKR.



Of particular note, whilst the cost of opioid prescriptions decreased only slightly after TKR and remained relatively stable after that for patients without chronic pain, for those with chronic pain it increased, peaking at seven years post-operative. The proportion of patients receiving a prescription for opioids increased for both groups as they approached surgery (34% and 20% the year prior to TKR for patients with and without chronic pain, respectively), peaking the year after (52% and 32%). After that, the proportion of patients receiving a prescription for opioids averaged values similar to those observed the year before surgery.

## Discussion

Our analysis of English routine NHS healthcare data indicated that primary care consultations and prescribed pain medicines were consistently higher for patients with chronic pain after TKR compared to patients without chronic pain. These differences were evident during the entire observational period of our analyses, persisting from 10 years pre-operative until eight years post-operative. There was a considerable difference in the prescription of opioids in the period after surgery, with a steep increase in costs for patients with chronic pain after TKR which peaked at seven years post-operative.

People living with chronic musculoskeletal pain make high use of healthcare and receive a large number of prescriptions for pain medicines [17, 18]. Our study is the first to quantify the impact of chronic pain after TKR on English primary care services. Chronic pain after TKR poses a considerable cost to primary care, given the high prevalence and long-term nature of this kind of pain. The consistently higher rate of primary care consultations and pain medicine prescriptions in the 10-year pre-operative period by patients who developed chronic pain after TKR highlights an increased healthcare utilisation even before their surgery. It was not possible to determine causes for these differences within our study, however risk factors for chronic post-surgical pain include multimorbidity, multi-site pain and mental health conditions [19], which could potentially contribute to increased use of healthcare services.

The cost of opioid prescriptions increased substantially after surgery for patients with chronic pain after TKR and remained high over the eight-year post-operative observational period. This suggests that opioids are prescribed for long-term management of chronic pain after TKR. However, opioids are no longer indicated for chronic pain [20], with clear evidence that they provide minimal relief of chronic pain symptoms, including pain due to osteoarthritis, and are associated with considerable harm [21]. Our data from 2009-2016 shows a recent historical trend of high opioid prescription costs within primary care for patients with chronic pain after TKR. Further research is needed to evaluate current prescription patterns in light of recent national guidance advising against opioid prescription for patients living with chronic pain.

Our analyses used CPRD data, which contains detailed patient-level and prescription-level data on a large sample of patients from across England. However, limitations of our analyses should be acknowledged when interpreting the results. The data in CPRD are based on a subset of GP practices, and our analysis was restricted to those patients with linked HES records that completed a 6-month post-operative OKS,

which may have limited the generalisability of the findings. The data only contain GP prescriptions and not pharmacy dispensations, and therefore it was not possible to confirm the quantity of medications that were bought. We also did not capture the costs to patients of purchasing their own pain medication, and this is an area which may warrant further research. We defined chronic pain status at six months post-operative, a time point at which pain outcomes generally plateau after TKR [22], however there can be within-person variability in longer-term outcomes [23] and we were unable to account for fluctuations in post-operative pain status.

In conclusion, our study demonstrated that increased primary care consultations and pain medicine prescriptions associated with chronic pain after TKR represent a considerable financial cost to primary care services in England and that patients with chronic pain after TKR are prescribed more opioid medications than those without chronic pain. Evaluation of interventions to reduce the risk of developing this pain condition and improve the early management of pain after TKR are needed to improve outcomes for patients and reduce costs to healthcare services.

## **Abbreviations**

TKR: Total knee replacement

CPRD: Clinical Practice Research Datalink Gold

HES: Hospital Episode Statistics

PROMs: Patient Reported Outcome Measures

NICE: National Institute for Health and Care Excellence

NHS: National Health Service

ONS: Office for National Statistics

STROBE: STrengthening the Reporting of OBservational studies in Epidemiology

ICD: International Classification of Diseases

OKS-PS: Oxford Knee Score pain component score

GPs: General Practitioners

NSAIDs: non-steroidal anti-inflammatories

## **Declarations**

## **Ethics approval and consent to participate**

The research was conducted in accordance with the Declaration of Helsinki. Ethical approval for the study was obtained from a National Research Ethics Committee (REC) and has been approved by the Independent Scientific Advisory Committee (ISAC) for Medicines and Healthcare products Regulatory Agency (MHRA) Database Research with protocol number 11\_050AMnA2RA2. This work uses anonymised healthcare routinely collected data securely shared by GP practices across the UK and provided by Clinical Practice Research Datalink (CPRD). CPRD is a government organisation that obtain annual regulatory permission to supply anonymised data to researchers for approved public health studies and ensure that the supplied data are used to benefit public health and improve patient care. CPRD only receives and supplies anonymised patient data and complies with robust ethics, governance and security regulatory frameworks. The patient health data that CPRD holds have been processed in accordance with the Information Commissioner's Office (ICO) Anonymisation Code of Practice. Individual patients have the right to opt out of their data being collected by CPRD for research.

## Consent for publication

Not applicable

## Availability of data and materials

The datasets analysed during the current study cannot be shared publicly because restrictions apply to the availability of these data, which were used under licence for the current study. CPRD Gold and HES-PROMS linked data are available through data applications to the Independent Scientific Advisory Committee for MHRA database research.

## Competing interests

AJ reports grants from NIHR during the conduct of the study; personal fees from Freshfields Bruckhaus Derringer, personal fees from Anthera Pharmaceuticals Ltd, outside the submitted work; RGH reports grants from NIHR during the conduct of the study; RPV reports research funding from UK-NIHR, Kyowa Kirin Services, International Osteoporosis Foundation, and lecture fees and/or consulting honoraria from Amgen, UCB, Kyowa Kirin Services, and Mereo Biopharma, all outside of the scope of this study; VW reports grants from NIHR during the conduct of the study. All other authors declare no conflicts of interest.

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## Authors' contributions

RPV, NH, AJ, RGH and VW were involved in the conception and design of the study. RPV, SK and AD analysed the data. RPV and VW drafted the article and all authors revised it critically for important intellectual content.

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# Figures

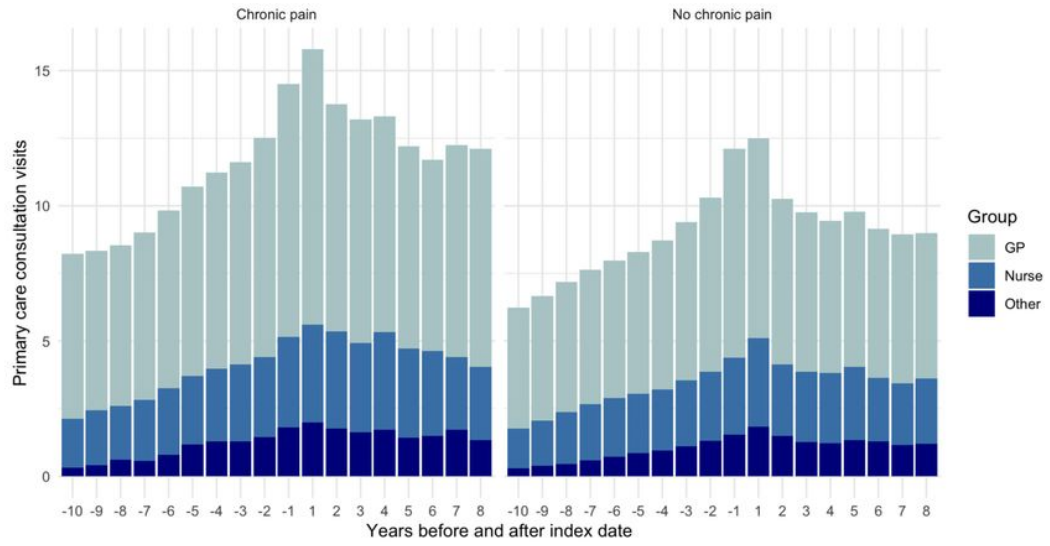
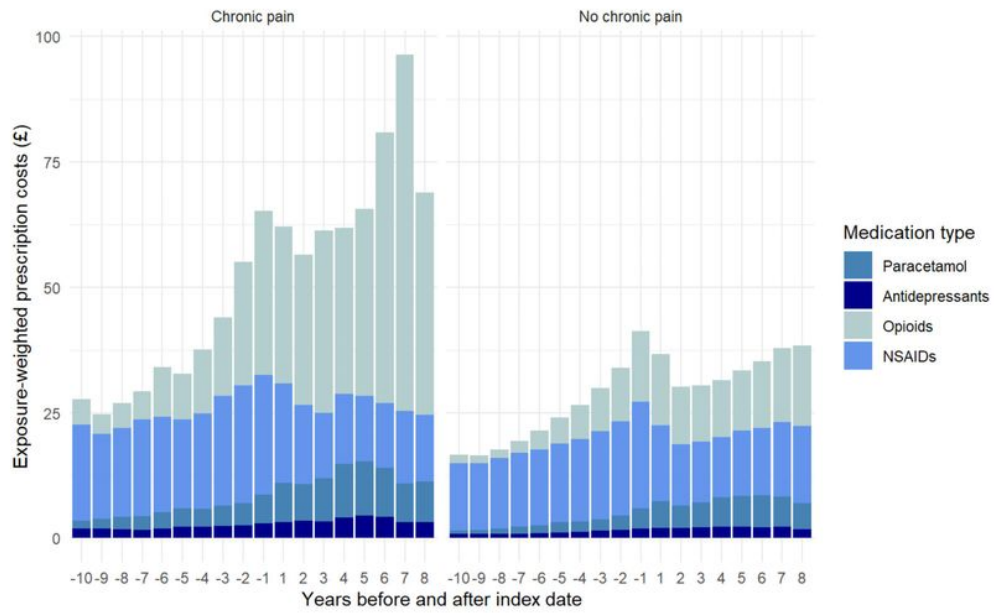


Figure 1

Mean number of consultations by healthcare professional for patients with and without chronic pain



**Figure 2**

Mean cost of pain medicine prescriptions by year for patients with and without chronic pain

## Supplementary Files

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