Use of non-surgical treatments on the journey to knee replacement in patients with knee osteoarthritis: a 10-year population-based case-control study

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ORIGINAL RESEARCH

Use of non-surgical treatments on the journey to knee replacement in patients with knee osteoarthritis: a 10-year population-based case–control study

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ABSTRACT

Aim To investigate temporal trends in primary care visits, physiotherapy visits, dispensed non-steroidal anti-inflammatory drugs (NSAIDs) and opioids in knee osteoarthritis (OA) patients who have and have not undergone knee replacement.

Methods We analysed 5665 OA patients from the Skåne Healthcare Register, Sweden, who underwent knee replacement between 2015 and 2019. Controls were OA patients without knee replacement, matched 1:1 by sex, age, time and healthcare level of initial OA diagnosis, and assigned a pseudo-index date corresponding to their case's knee replacement date. Annual prevalence and prevalence ratio of primary care and physiotherapy visits, dispensed NSAIDs and opioids (all for any cause) in the 10 years before knee replacement were estimated using Poisson regression.

Results The annual prevalence of all-cause primary care visits, physiotherapy visits and opioid use was similar between cases and controls until 3 years before the index date when it started to increase among the cases. The year before the index date, the prevalence ratio (cases vs controls) for physiotherapy use was 1.8 (95% CI 1.7, 1.8), while for opioid use 1.6 (1.5, 1.7). NSAID use was consistently higher among cases, even 10 years before the index date when the prevalence ratio versus controls was 1.3 (1.2, 1.3), increasing to 1.8 (1.7, 1.9) in the year preceding the index date.

Conclusions Management of OA patients who have and have not undergone knee replacement appears largely similar except for higher use of NSAIDs in knee replacement cases. Symptomatic treatments start to increase a few years before the surgery in knee replacement cases.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Knee replacement for osteoarthritis (OA) is a common surgical procedure worldwide.
⇒ First-line interventions preceding knee replacement are underused in favour of pharmacological pain management with non-steroidal anti-inflammatory drugs (NSAIDs) or even opioids—which are not recommended for the management of OA pain.

WHAT THIS STUDY ADDS

⇒ This is the first study to investigate the pattern and timing of OA management in patients receiving knee replacement in comparison to patients with OA who have and have not undergone the surgery over 10 years.
⇒ The initial management of patients who progress to knee replacement is similar to those who do not progress to surgery within the same timeframe. Differences emerge in the last 2–3 years before surgery, with a higher prevalence of all analysed treatments among knee replacement cases.
⇒ The uptake and timing of physiotherapy fall short of guidelines, with only a small percentage of patients receiving the recommended number of sessions.
⇒ NSAID dispensation is consistently higher among knee replacement cases, however, part of this difference can be explained by the higher prevalence of cardiovascular conditions among the controls.
⇒ Opioid use is highly prevalent in both cases and controls, with a peak in prevalence at the time of diagnosis, raising concerns about the appropriateness of care.
⇒ Overall, treatment prevalence peaks at the time of diagnosis and in the year preceding knee replacement, suggesting a reactive approach to OA care.

INTRODUCTION

More than 600 million people are estimated to suffer from knee osteoarthritis (OA) worldwide.[1] With no disease-modifying treatment available, international guidelines recommend a holistic approach that starts with exercise, education, and weight loss and progresses to pharmacological and surgical treatments.[2–5] According to these guidelines, joint replacement should be offered only to patients who have already received other interventions, but still experience a high level of symptoms and reduced quality of life. Nevertheless, the timing and frequency

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study highlights the need for improved adherence to guidelines regarding physiotherapy and exercise as first-line interventions for knee OA.
⇒ The findings suggest that the observed treatment patterns may be driven by factors other than symptom severity, such as patients' preferences or clinicians' practices.
⇒ The prevalence of NSAID use among knee replacement cases indicates the need for alternative pain management strategies for OA.
⇒ The study raises questions about the appropriateness of care and the lack of disease-modifying treatments for knee OA, which may influence future research, practice and policy decisions in the field.
⇒ The high prevalence of opioid dispensation already at diagnosis—in light of the opioids epidemic and recommendations against their use to treat OA pain—underlines the importance of monitoring the prescription of these medications.

of non-surgical care preceding a knee replacement are poorly described: it is unclear how often and when OA patients visit a physician or physiotherapist (PT), or how often they are prescribed non-steroidal anti-inflammatory drugs (NSAIDs) and opioids.

Evidence suggests that patients undergoing knee replacement often do not receive the recommended treatments while they may receive low-value care.[6–8] First-line interventions, which include exercise and education, with physiotherapy involvement, are often underused in favour of pharmacological options such as NSAIDs and opioids, despite the latter no longer featuring in most OA management guidelines.[5 6 9] Moreover, randomised control trials as well as observational evidence have suggested that first-line interventions have the potential to delay the need for knee replacement, a surgery expected to become economically unsustainable in the upcoming decades.[10–14]

Mapping the management of knee OA preceding knee replacement can thus provide valuable information to identify gaps and guide implementation strategies. Current evidence describing the pathway to knee replacement is limited by small studies with cross-sectional designs, studies focusing on a single therapy such as analgesics, or relying on self-reported data.[6 9 15 16] These limitations fail to capture the complexity of knee OA care. Most importantly, no study has compared the management of patients who progress to knee replacement to those with knee OA who do not receive the surgery within the same time frame after diagnosis. Using knee OA controls will allow us to understand at which time point and for which treatments the management potentially diverges.

Thus, we aimed to investigate the temporal trends of primary care and PT visits, as well as dispensed NSAIDs and opioids, in patients with knee OA who have and have not undergone knee replacement.

PATIENTS AND METHODS

Study design and data source

This was a population-based, case–control study. We used four registers comprising the entire population of Skåne, the southernmost region in Sweden with approximately 1.4 million inhabitants (13% of the total Swedish population as December of 2020).[17] The Skåne region, one of Sweden's most densely populated regions, encompasses both urban and rural areas. All levels of care are present in the region, and the demographic and socioeconomic structure is similar to that of the whole of Sweden.[17] From the Swedish Population Register, we retrieved data on age, sex, residential address and deaths, while individual-level data on income, education, marital status and country of birth were retrieved from the Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA by Swedish acronym). From the Skåne Healthcare Register (SHR) we extracted information about visits (to physicians or PTs) and diagnoses provided at healthcare visits to a physician. The SHR does not record contact with private healthcare providers or care delivered in elderly homes. Finally, from the Swedish Prescribed Drug Register, we extracted information on all NSAIDs and opioids prescribed and dispensed at a pharmacy or healthcare institution in the country. Data from the four registers were linked using patients' pseudo-anonymised personal unique identification number, which is assigned to all residents in Sweden by the Swedish Tax Agency.

We reported the study according to the REporting of studies Conducted using Observational Routinely-collected health Data guidelines.[18] There was no patient or public involvement in this study.

Case definition

International Classification of Diseases 10th Revision (ICD-10) M17 code and surgical codes (KVÅ codes in Swedish) were used to identify cases aged 45 years and over who underwent primary knee replacement between 1 July 2015 and 31 December 2019 (code lists available in online supplemental file 1). To be eligible for inclusion, subjects had to be registered in the healthcare database for a minimum of 10 years before their knee replacement (ie, index date) and had no knee replacement recorded between 1998 and 1 July 2015 (online supplemental file 2).

Control definition

One control for each case was randomly selected among patients with knee OA (ascertained with ICD-10 codes). Controls were matched by sex, age at first knee OA diagnosis (±1 year), quarter of the year of first knee OA diagnosis and healthcare level of first knee OA diagnosis (primary care vs specialist care). Controls were assigned the same index date as their 1:1 matched case. Controls could not have received a knee joint replacement up to their assigned index date. We selected controls using

incidence density sampling, resulting in controls having equivalent at-risk time compared with matched cases.[19]

'Exposure' definition: prior all-cause and OA-specific healthcare

We retrieved data on all exposure events during the 10 years preceding the index date. Main exposures were: (i) primary care visit (binary, yes/no); (ii) PT visit (binary, yes/no); (iii) NSAID dispensation (binary, yes/no); (iv) opioid dispensation (binary, yes/no); all for any cause (ie, not only for OA). We retained any primary care visits, except for the first visit where the diagnosis of knee OA was registered for the first time (used for matching). For PT and primary care, we considered only physical visits (not letters or telephone contacts, etc). PT visits were identified using the code for the profession 'physiotherapist' among visits within outpatient care. We used Anatomical Therapeutic Chemical codes to identify NSAID and opioid dispensations (online supplemental file 3). For opioids, we also calculated the Milligrams of Morphine Equivalent (MME) based on the dispensed dose recorded in the Swedish Prescribed Drug Register.[20 21] In a secondary analysis, we used primary care visits for knee OA as exposure. We considered a primary care visit to be for knee OA when an ICD-10 code of M17 was registered during the visit.

Healthcare in Sweden

Sweden has publicly funded healthcare with a high-cost protection scheme where there is a ceiling for out-of-pocket payments for healthcare visits and medications. This means that after reaching this ceiling threshold within a period of 12 months any additional care is free of charge.[22] Treatments for knee OA—including surgery, prescribed analgesics and physiotherapy—are included in this scheme. For drug dispensation, the ceiling threshold for a patient's co-payments over 12 months (starting from the first purchase) is SEK 2400 (at the date of data extraction, equivalent to ≈€220) after which any dispensation within 12 months is free of charge. Similarly, the annual ceiling threshold for doctor and physiotherapy visits (ie, both count towards the same threshold) can reach up to SEK 1300 (≈€120).[23]

Statistical analysis

Contingency tables were generated for both populations to describe the frequency of exposures in cases and controls. Besides the participants' demographic, we reported the presence of common comorbidities (cardiovascular diseases (CVDs), cancer and diabetes) to describe the study sample. Comorbidities were defined by the presence of ICD-10 codes in patients' health records throughout the 10-year study period and were not considered pure confounders (they could occur both before and after the exposures of interest). Codes for comorbidities had been previously developed and used in prior studies.[15] Yearly prevalence and prevalence ratio (PR) (with 95% CIs) of having at least one recorded treatment modality: primary care visit for any cause, physiotherapy visit, dispensed NSAIDs and dispensed opioids, in each of the 10 years preceding knee replacement were estimated using Poisson regression models adjusted for matching factors with robust SEs and were presented descriptively as a percentage of the total sample. Visits to a primary care physician for knee OA were included apart from the first visit (used for matching). Some cases and controls could have their first visit with knee OA registered before the 10-year exposure period, and thus their OA visits from the whole 10-year period were eligible for inclusion.

We conducted a series of secondary analyses to better understand the pattern of care. In this analysis, we created new exposures: primary care visits for OA, 10 consecutive PT visits, 180+ NSAIDs DDD/year and MME for opioids. Primary care visits for OA were those visits with an OA code indicated as the main reason for the visit. We categorised PT visits into 10 consecutive visits (defined as visits happening within 30 days of each other and attributed to the year of the first visit) to capture participation in a rehabilitation intervention. Ten visits were chosen as we considered them to be equivalent to 'good attendance' on a rehabilitative intervention given the Swedish Board of Health and Welfare (Socialstyrelsen) recommendation of 12 exercise sessions for people with OA.[2] For NSAIDs, we selected 180 or more DDD per year (equivalent to a DDD every other day for a year) to represent frequent NSAID use. In the secondary analyses, we presented: the median and IQR per year (all the treatments), prevalence and PR (only for the dose/frequency categorisation), stratified prevalence by year of knee OA diagnosis (all treatments) and PR (cases vs controls) stratified by the presence of CVD comorbidities and OA in other joints (only for NSAIDs). The latter were adjusted by age, sex, level of first diagnosis (specialist vs primary care) and year of first knee OA diagnosis as stratification may disrupt the balance in covariates achieved by matching.

RESULTS

We identified 5714 eligible individuals with knee replacement in the study period and included 5665 for whom we could identify a matched control knee OA patient (table 1). Ten years before the index date, the prevalence of treatments was similar between patients undergoing knee replacement (cases) and patients not having had a knee replacement at the index date (controls). The prevalence of treatments remained largely stable over the study period but began to diverge 3 years before the surgery. NSAIDs were an exception as dispensations were more prevalent in cases already 10 years before the index date. Nonetheless, the pattern of NSAIDs dispensation resembled the pattern of the other treatments showing a rise in prevalence among cases in the 3 years preceding the index date. At the index date, the prevalence of PT visits and NSAIDs was 80% higher among cases (PT visits PR (95% CI): 1.8 (1.7, 1.8); NSAIDs: 1.8 (1.7, 1.9)), while the prevalence of opioids was 60% higher among cases

Table 1 Basic demographic data and number of surgeries in cases and controls

Variables	Cases (n=5665)	Controls (n=5665)
Age, mean (SD)	69.0 (8.9)	69.0 (8.9)
≥65 years, n (%)	3878 (68.5%)	3878 (68.5%)
Females, n (%)	3198 (56.4%)	3198 (56.4%)
Healthcare level of OA diagnosis		
Primary care	2548 (45.0%)	2548 (45.0%)
Specialist care	3117 (55.0%)	3117 (55.0%)
Year of knee replacement, n (%)		
2015†	543 (9.6%)	–
2016	1246 (22.0%)	–
2017	1275 (22.5%)	–
2018	1257 (22.2%)	–
2019	1344 (23.7%)	–
Years between diagnosis and surgery, n (%)		
1	1420 (25%)	1420 (25%)
2	643 (11%)	643 (11%)
3	464 (8%)	464 (8%)
4	379 (7%)	379 (7%)
5	312 (6%)	312 (6%)
6	294 (5%)	294 (5%)
7	278 (5%)	278 (5%)
8	258 (5%)	258 (5%)
9	232 (4%)	232 (4%)
10	214 (4%)	214 (4%)
10+	1171 (21%)	1171 (21%)
Comorbidities, n (%)		
Cancer	1091 (19%)	1173 (21%)
Cardiovascular	1175 (21%)	1408 (25%)
Diabetes	781 (14%)	931 (16%)
Depression	901 (16%)	906 (16%)
Other OA	2504 (44%)	2023 (36%)
Back pain	1934 (34%)	1993 (35%)
Other MSK conditions	4907 (87%)	4939 (87%)

*Controls were matched by sex, age at first knee OA diagnosis (±1 year), quarter of the year of first knee OA diagnosis and healthcare level of first knee OA diagnosis (primary care vs specialist care).
†In year 2015 inclusions starts at 1 July.
MSK, musculoskeletal; OA, osteoarthritis.

(1.6 (1.5, 1.7)) (figures 1 and 2; online supplemental files 4,5). At the index date, nearly the totality of cases (99.6%) and controls (99.5%) had received at least one primary care visit (cumulative prevalence), more cases had received at least one PT visit (95.3% vs 86.8%), one NSAID dispensation (85.5% vs 77.0%) or one opioid dispensation (68.8% vs 61.6).

The secondary analyses showed results mostly consistent with the main analysis (online supplemental files 6–23). Median and IQR showed large overlaps in the number of PT visits and dispensations (either NSAIDs or opioids) per patient received by cases and controls. Consecutive PT visits (10+) and frequent NSAID use (180+ DDD/year) showed a similar pattern to the main analysis, however, the PR for these exposures was higher than the PR for PT visits and opioid dispensations obtained from the main analysis. Analysis by year of diagnosis showed a double-peak pattern for all the treatments: one peak in the year of diagnosis for both cases and controls and one at the index date for cases only. Finally, the PR of NSAID use between cases and controls was higher throughout the study period in people without cardiovascular comorbidities and higher during the 2 years before the index date in people with OA in other joints, but the estimates largely overlapped.

DISCUSSION

Knee replacement for OA is one of the most common surgical procedures performed worldwide.[24] Our study

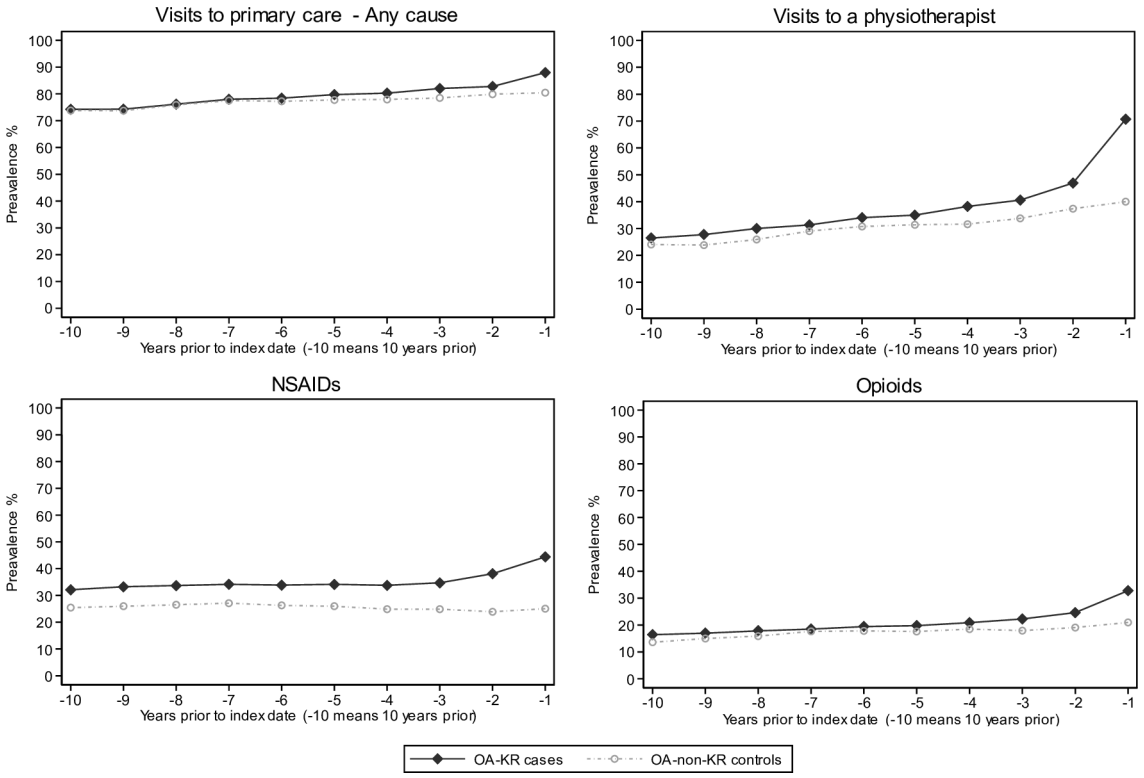

Figure 1 Prevalence of patients receiving at least once one of the different osteoarthritis (OA) treatments in the 10 years preceding knee replacement (KR; for cases) and index date (for controls). CIs are not reported in the figure as they were so narrow to be hidden by the marker of the prevalence. CIs for the figure can be found in online supplemental file 4.

using healthcare register data shows that the initial management of patients who progress to knee replacement is similar to that of those who do not progress to surgery within the same timeframe. Differences in management can, however, be seen in the last 2–3 years before the surgery, where the prevalence of all the

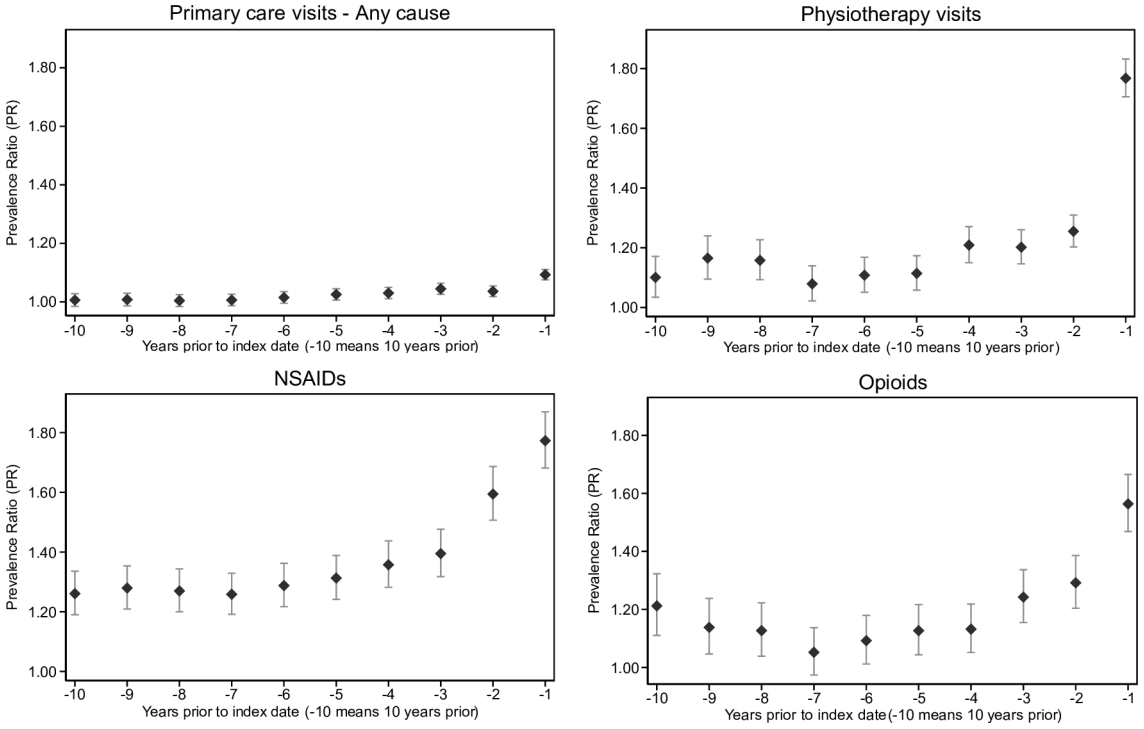

Figure 2 Prevalence ratio and CIs of patients receiving at least once one of different osteoarthritis treatments in the 10 years preceding knee replacement (for cases) and index date (for controls). NSAIDs, non-steroidal anti-inflammatory drugs.

analysed outcomes is higher among cases. Nonetheless, a similar pattern in the provided treatment raises questions on whether symptom severity or other factors, such as a person's wish to undergo surgery, are the drivers of care.

Primary care visits for any cause were similarly distributed between cases and controls, suggesting that the propensity to visit a healthcare provider is unlikely to explain the pattern of findings. The larger prevalence of visits in the years immediately before the knee replacement for the cases was largely due to visits for OA, which could be expected (online supplemental file 7). Existing evidence systematically reports the underusage of physiotherapy and exercise among people undergoing knee replacement for OA.[6 25–27] Our data shows what could be considered a good uptake of PT, with roughly 60% of the participants visiting a PT in the year of diagnosis, while 95% of the cases and 87% of the controls had received at least one PT visit before the index date (online supplemental file 9). Indeed, a single consultation with a PT does not conform to both Swedish and international clinical guidelines, which recommend a regimen of 12 exercise sessions as the primary intervention for OA.[2 4]

In our sample, only 20%–30% of both cases and controls underwent 10 consecutive visits during the year of the first registered OA. At the index date, only 50% of all the cases had undergone 10 or more consecutive PT visits at least once, just 10% more than the controls. Considering that the Swedish National Board of Health and Welfare has recommended PT and physical activity as the first-line intervention for OA since 2012 and that PT in Sweden is tax-financed, we would have expected to observe more people undergoing multiple consecutive sessions of PT.[28] Several factors could explain the observed trends. PTs, despite knowing the guideline recommendations, can be hesitant to prescribe exercise to people with more severe pain.[29] Considering the poor uptake of PT at diagnosis, the peak in prevalence preceding knee replacement can be interpreted as a way to comply with referral pathways, which in the Skåne region requires the attempt of PT care before knee replacement for all patients who are able to exercise. However, PT is part of the core treatments for OA and such a pattern of care—where exercise appears to be a tick-box treatment before proceeding to knee replacement—can be viewed as inappropriate care. Patient's perception of the intervention can contribute to this pattern as exercise is often perceived as a stepping stone towards surgery.[30] Finally, the availability of PT within the region may vary and may for some be a barrier, particularly for attending multiple visits.

Dispensation of NSAIDs was the only intervention consistently more prevalent among cases. NSAIDs are the most used intervention to treat OA pain despite being recommended only for short periods and at the lowest possible dose.[3] The higher prevalence of NSAIDs among cases may suggest that people progressing to knee replacement have overall more severe and rapidly progressing symptoms than controls. This trend is visible when analysing the prevalence (including cumulative prevalence) of subjects with frequent NSAID use which is higher than in controls at any time point and grows steadily over time, with new patients becoming users every year. Our secondary analysis suggests that this tendency cannot be explained by the higher prevalence of OA in other joints among cases and cardiovascular comorbidities among controls (which constitute a potential contraindication to the use of NSAIDs). Nonetheless, even in the stratified analysis, the pattern of NSAID dispensation is similar; the prevalence of NSAIDs increases among cases in the last 3 years before the index date.

Opioids are strong and widely used analgesics, mainly advised for acute conditions and postsurgical management of pain but are not recommended for chronic conditions like OA. The relatively high prevalence in our data highlights once again the lack of alternatives for knee OA pain management. In a previous study, we showed that people with knee OA had a substantially higher prevalence of opioid use than OA-free controls.[15] Here, when comparing knee OA patients who have and have not received a knee replacement (in the same timeframe), the use of opioids is largely similar until 3 years before surgery. Interestingly, we observed a peak in the prevalence of opioid prescription already at the year of diagnosis when nearly 30% of both cases and controls dispensed an opioid prescription—a similar prevalence to the one observed in cases the year before knee replacement (online supplemental file 13). This trend brings to question whether the pattern of opioid dispensations can be considered as evidence of ingrained low-value care, especially given the lack of effectiveness in treating OA pain, the safety concerns associated with opioid use, and the scale and timing of use which cannot be considered a 'last resort' use.

All in all, our results raise questions about whether the observed trends in the treatments are driven by symptoms or by the clinicians' and patients' preferences as the prevalence of all the treatments peaks at the time of initial diagnosis—for both cases and controls—and again for cases only in the last 3 years preceding surgery. A patient's willingness to seek care and treatments for joint symptoms is a complex phenomenon—only in part driven by pain severity—and may partially explain the observed patterns.[12 13 31–33] Previous studies have suggested that a wish to undergo surgery is a stronger predictor for knee replacement than pain and walking difficulties and may even influence postsurgical satisfaction.[34 35]

Finally, the peak in treatments among cases before knee replacement may be interpreted as the clinician's attempt to manage symptoms while awaiting surgery. However, the median waiting time in 2023 for a knee replacement in the Skåne region was 135 days with only 22% of the patients having to wait more than 1 year. Thus, we believe that treatment provided to patients on a waiting list could not completely explain the rise in prevalence starting already 3 years before surgery—especially considering that waiting

time for knee replacement in the region has historically been shorter.[36]

Some limitations should be acknowledged. To determine the first registered knee OA diagnosis, we considered only physician diagnosis. This may not coincide with knee OA incidence, and thus the matched cases and controls may be at different stages of the disease, despite having first registered knee OA diagnosis at the same age, calendar time and healthcare level (specialist vs primary care). Further, we included PT visits, NSAID and opioid use for any cause, as the reason for using these treatments could not be extrapolated from the available data. Thus, comparisons between cases and controls are valid under the assumption that the use of these treatments due to other conditions would be comparable in the two groups. A similar prevalence of comorbidities may support this assumption. The two exceptions, CVD and OA of other joints cannot explain the observed patterns, as evaluated in our sensitivity analysis. Of all physical visits within public care, 6% had no diagnostic code assigned. Further, 19% of all primary care visits happened within private providers that at the time did not register diagnoses. Thus, we may have underestimated the proportion of persons consulting primary care for knee OA. Given the matching of cases to controls also on the time of first knee OA diagnosis and level of care, case–control comparisons should still be valid. Finally, this is a descriptive study, and the estimates should not be interpreted as indicating any causal associations, but rather as describing patterns of care in persons with knee OA. Since 2014, also PTs can register diagnostic codes in Sweden. This implies that a person may have been diagnosed by a PT before consulting a physician. Nonetheless, considering our study timeline, this should affect only a minority of patients.

Conclusions

Our study using healthcare register data on knee OA patients shows that the initial post-diagnostic management of patients who have progressed to knee replacement is largely similar to those who have not, with the exception of NSAID dispensation, which was consistently higher among cases. We also observed differences emerging in the last 2–3 years prior to surgery, with a higher prevalence of all analysed treatments among knee replacement cases. PT uptake and timing fall short of guidelines and opioid dispensations are highly prevalent already at diagnosis, potentially reflecting low-value care. The observed trends raise questions about the driver of care and appropriateness of management potentially reflecting the concerning lack of disease-modifying treatments for knee OA.

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Contributors All the authors conceived the research question and contributed to the design of the study. AT and ME were involved in data retrieval. AD and AT performed the statistical analyses. All authors contributed to the interpretation of the results and writing and editing of the manuscript. All authors approved the final draft.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The use of Swedish register data was approved by the Lund University Ethics Committee (Dnr 2011e432 with amendment Dnr 2014_276 and Dnr 2018_233).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data can be accessed upon request to Skåne region (https://www.skane.se/en/).

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