



Epidemiology and treatment of pain associated with osteoarthritis of the knee in Germany: A retrospective health claims data analysis

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ABSTRACT

Objective: Osteoarthritis of the knee (knee OA) is a serious joint disease leading to pain and reduced quality of life. Pharmacological treatments include anti-inflammatories, analgesics, intraarticular hyaluronic acid, and intra-articular corticosteroids while for severe knee OA, knee replacement is an option. This study examined the incidence, prevalence, patient characteristics, and uptake of medical and surgical treatments in knee OA patients in Germany.

Design: A non-interventional, retrospective health claims data analysis with anonymized data from the InGef database was performed. Patients ≥ 18 years were analyzed cross-sectionally for each year 2015–2020. Newly diagnosed patients in 2015 were also longitudinally analyzed until end of 2020.

Results: Annual knee OA prevalence increased from 7.07 % in 2015 to 7.39 % in 2020. Annual incidence proportions ranged from 1.71 % in 2015 to 1.46 % in 2020. Knee replacement was the most common surgery, with rising patient numbers (e.g., 7918 patients in 2015 and 8975 patients in 2019). Approximately 62 % of patients newly diagnosed in 2015 received prescription pharmacological pain treatment during follow-up. Most (96.95 %) received non-opioid analgesics, followed by weak opioids (8.14 %) and strong opioids (3.00 %) as first-line treatment (combinations possible). Knee surgery was performed in 16.6 % of patients during follow-up. Median time from first diagnosis until surgery was 346 days for any knee surgery and 564 days for knee replacement. **Conclusions:** The number of patients with knee OA in Germany is steadily rising, along with an increasing number of surgical interventions, especially knee replacement. Time until first surgery and knee replacement is relatively short, even for newly diagnosed patients.

1. Introduction

Osteoarthritis of the knee (knee OA) is a serious joint disease that causes pain and that may contribute to a reduced quality of life [1,2]. It is the most common form of arthritis and can manifest in two forms: idiopathic knee OA and knee OA due to trauma or mechanical misalignment [3]. The causes are multifactorial, yet still not fully understood [4]. Although knee OA usually progresses slowly, accelerated knee OA is also not uncommon [5].

Globally, the age-standardized prevalence of knee OA was estimated at 3.8 % in 2010 and, together with hip osteoarthritis, it was

ranked as the eleventh-highest contributor of global disability; In Western Europe, the age-standardized prevalence was 2.7 % in men and 4.5 % in women according to the 2010 global burden of disease study [6]. For Germany, self-reported data from a national health survey conducted in 2014/2015 revealed an overall OA (thus not restricted to knee OA) prevalence of 17.9 % in German adults, with a higher prevalence in females (21.8 %) compared to males (13.9 %) [7].

Next to female sex, the known risk factors for knee OA include older age, genetic predisposition, overweight and obesity, and previous injuries [1,4,7–9]. As knee OA is associated with older age, the number of

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patients with knee OA is expected to further increase in the future due to demographic change [3].

As there are currently no disease-modifying treatments for knee OA, treatment is focused on pain management and improvement of joint function [3,4]. Pharmacological treatments include the use of anti-inflammatories, analgesics, intraarticular hyaluronic acid, and intraarticular corticosteroids depending on geography [10]. A number of treatments, notably intraarticular injections of corticosteroids, hyaluronic acid, and platelet-rich plasma, are associated with minor adverse events for pain relief and may also delay surgical treatment [11]. For advanced, severe knee OA, partial or total knee replacement is a treatment option, with rising incidence and an estimated prevalence of 1.5 % or 4.7 million individuals in the US alone in 2010 [12].

While treatment options are well known, information on the share of these treatments amongst knee OA patients, as well as the timing and pattern of treatment, remains scarce.

The objectives of this study were to determine the yearly prevalence and incidence proportion of knee OA for the years 2015–2020 in Germany; to identify demographic and clinical characteristics of patients diagnosed with knee OA; and to identify the course of symptomatic treatment for patients newly diagnosed with knee OA in 2015 until end of 2020.

2. Methods

This study was based on anonymized claims data from the InGef (Institute for Applied Health Research Berlin GmbH) research database [13] spanning the years 2014–2020. The InGef database contains data from approximately 9 million persons insured in one of the ca. 60 statutory health insurances (SHI) contributing data to the InGef database. The data include information on demographics (quarter of birth and death (if applicable), sex, region of residence); inpatient care (e.g., diagnoses, surgeries and procedures, length of stay); outpatient services (e.g., diagnoses, treatments, physician specialty); dispensing of reimbursed drugs; dispensing of reimbursed remedies, devices, and aids; sick leave and sickness allowance; and costs from the SHI perspective. From the total InGef database, an age- and sex-representative sample of the German population is drawn, including approximately 4.8 million persons. This sample was used for this study. A more detailed description of the database and sampling strategy is provided elsewhere [13]. All patient-level and provider-level data in the InGef research database are anonymized to comply with German data protection regulations and German federal law. Hence, approval of an Ethics Committee was not required.

The study comprised two sub-studies (parts A and B): a cross-sectional study (part A), in which prevalence, incidence proportion, and patient characteristics were investigated for each study year; and a retrospective cohort study (part B), in which newly diagnosed patients identified in 2015 were followed up to the end of 2020 or until death, whichever came first. The years 2015–2020 were used for all analyses as study years, while the year 2014 only functioned as a diagnosis-free baseline year for calculating the incidence proportion in 2015. Table 1 summarizes the two study parts and their objectives.

Table 1
Overview of study modules.

Study module	Part A	Part B
Design	Cross-sectional	Longitudinal
Population	All knee OA patients and newly diagnosed knee-OA patients	Newly diagnosed knee OA patients from 2015
Study period	Full years 2015–2020, separately	From first diagnosis in 2015 until December 31, 2020 or date of death
Analysis objectives	Annual prevalence and incidence proportion, patient characteristics	Treatment patterns for medication and surgeries performed during follow-up

The study population comprised all patients with knee OA (identified by ICD-10-GM code M17). The diagnosis had to be present either as a primary or secondary inpatient diagnosis or as two verified outpatient diagnoses via this code in different quarters of the corresponding study year. Furthermore, all persons eligible for the study had to be at least 18 years old on 1 January of the corresponding study year and fully observable in the database in the corresponding study year or until death within the study year, as well as in the baseline year (the year prior to the study year). For the retrospective cohort study in part B, the patients newly diagnosed in 2015 additionally had to be fully observable until the end of 2020 or until their date of death, whichever came first.

Next to the diagnosis of knee OA, the following variables were compiled: age in groups 18–50, 51–65, and ≥66 years, sex (male/female), most common comorbidities (stratified by most common primary or secondary inpatient diagnoses and verified outpatient diagnoses), outpatient prescription of guideline-recommended treatment (by ATC code and categorized by WHO analgesic ladder), physiotherapy received, and in-hospital surgeries performed (arthroscopic knee surgery, knee replacement, as well as revision, change, and removal of knee replacement). The German guideline-recommended medications considered in this study are shown in Table 2.

Although part of the guideline-recommended treatment, intra-articular hyaluronic acid (ATC code M09AX01) was not considered in this study, as it is not reimbursed by German statutory health insurance and could thus not be detected in the data.

Furthermore, the specialty of the diagnosing physician who made the first diagnosis (if the first diagnosis was an outpatient diagnosis) was examined.

Prevalence and incidence proportions were calculated per 100,000 population with 95 % confidence intervals and projected to the total adult population of Germany based on age and sex. Continuous variables were displayed as summary statistics and discrete variables as frequency distributions. All analyses were conducted by InGef staff with the statistical program R, version 4.0.2.

3. Results

3.1. Study part A

Fig. 1 shows the annual prevalence and incidence proportion of knee OA for the years 2015–2020 projected to the total population of Germany by age and sex.

Table 2
Overview of guideline-recommended medications considered in the analysis.

ATC Code	Substance	WHO analgesic ladder category
M01A	Antiinflammatory and antirheumatic products, non-steroids	WHO I
M01B	Antiinflammatory/antirheumatic agents in combination	WHO I
M02A	Topical products for joint and muscular pain	WHO I
See appendix	Corticosteroid, intraarticular	WHO I
N02AA03	Hydromorphone	WHO III
N02AA05	Oxycodone	WHO III
N02AX06	Tapentadol	WHO III
N02AB03	Fentanyl	WHO III
N02AA58	Dihydrocodeine	WHO II
N02AA59	Codeine, combinations	WHO II
N02AX01	Tilidine	WHO II
N02AX02	Tramadol	WHO II
N02AX51	Tilidine/naloxone	WHO II
N02AJ	Opioids in combination with non-opioid analgesics	WHO II
N02AA55	Oxycodone/naloxone	WHO III
N02B	Other analgesics and antipyretics (metamizole included)	WHO I
N01BX04	Capsaicin (Qutenza)	WHO I
N01BB02	Lidocaine (Versatis)	WHO I

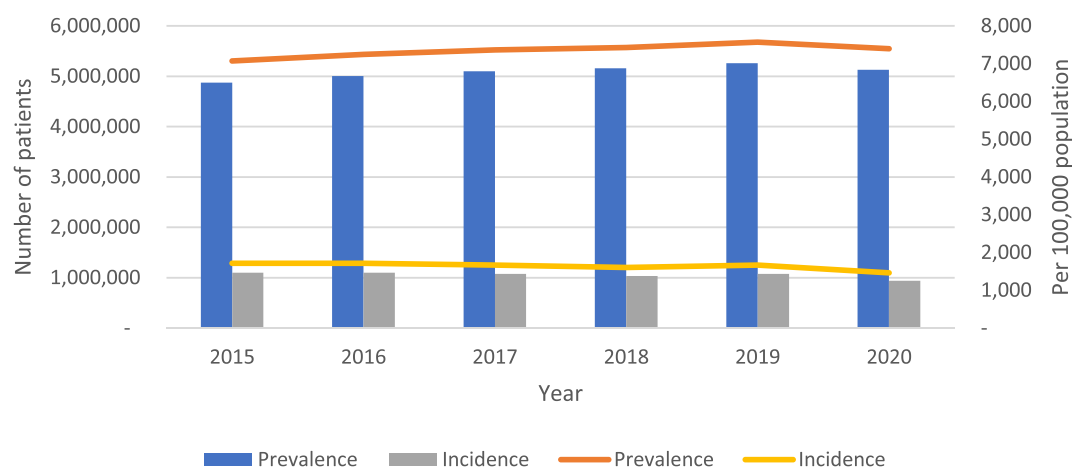


Fig. 1. Prevalence and incidence of knee OA, projected to the total population of Germany. The bar charts show the absolute numbers of patients, and the graphs represent the proportions per 100,000 population.

While the yearly incidence proportion remained quite stable, with an average of 1637 newly diagnosed patients per 100,000 population (range from 1.71 % of patients in 2015 to 1.46 % of patients in 2020), the prevalence grew slightly from 7.07 % in 2015 to 7.57 % in 2019 until a slight drop to 7.39 % was evident in 2020. Projected to the total German population, about 1 million patients were newly diagnosed with knee OA per year in Germany, contributing to a yearly total patient number of roughly 5 million people living with knee OA. The incidence proportion and prevalence were also stratified by age groups and sex (see appendix). Knee OA was more prevalent in female patients and in patients aged ≥ 66 years compared to males and younger age groups. The same distributions were also found for incidence proportions. In the age group 18–50 years, both the prevalence and incidence proportions were almost equally distributed among males and females.

Most patients were first diagnosed in the outpatient setting (93.40 % of all newly diagnosed patients). Orthopedists (49.88 %), followed by GPs (28.17 %) and internists (9.34 %) play a major role in making the first diagnosis of knee OA in the outpatient setting.

Comorbidities were investigated exploratively among prevalent and newly diagnosed patients in all study years. In both patient groups and throughout all study years, the most common comorbidities were quite similar: for example, for prevalent patients in 2020, most also had hypertension (73.73 % with an outpatient claim), while about half also had back pain (53.83 % with an outpatient claim). Other relevant comorbidities in prevalent patients diagnosed by physicians in an outpatient

setting were spondylosis (34.36 %), overweight and obesity (30.10 %), type 2 diabetes mellitus (27.75 %), unspecified pain (26.24 %), and depression (23.37 %). The most common main inpatient diagnoses were heart failure (1.59 %) and atrial fibrillation and flutter (1.05 %).

Throughout all the study years, around two thirds of prevalent patients were prescribed pain medications, of which the vast majority received WHO I agents. However, the proportion of patients with prescription medication declined slightly throughout all study years (66.05 % in 2015, 65.71 % in 2016, 64.99 % in 2017, 64.44 % in 2018, 64.48 % in 2019, and 63.18 % in 2020), while the proportion of patients with WHO I agents remained quite stable (93.54 % in 2015, 93.66 % in 2016, 93.63 % in 2017, 93.64 % in 2018, 93.96 % in 2019, and 93.75 % in 2020). The proportion of patients with WHO III agents was lowest, with a slight increase from 3.99 % in 2015 to 4.94 % in 2020 (4.19 % in 2016, 4.48 % in 2017, 4.59 % in 2018, and 4.57 % in 2019).

The proportion of patients in whom any knee surgery was performed decreased slightly from 5.38 % to 4.03 % during the considered study years (Fig. 2).

This was mostly due to a decrease in arthroscopic knee surgery, while the number of patients with knee replacement increased, except for 2020, presumably due to fewer elective surgeries because of COVID-19 (7918 patients (61.46 %) with knee replacement in 2015, 8539 patients (70.28 %) in 2016, 8845 patients (73.91 %) in 2017, 8669 patients (74.75 %) in 2018, 8975 patients (75.50 %) in 2019, and 7725 patients (76.45 %) in 2020). In all study years, between 6.20 % (in 2015) and

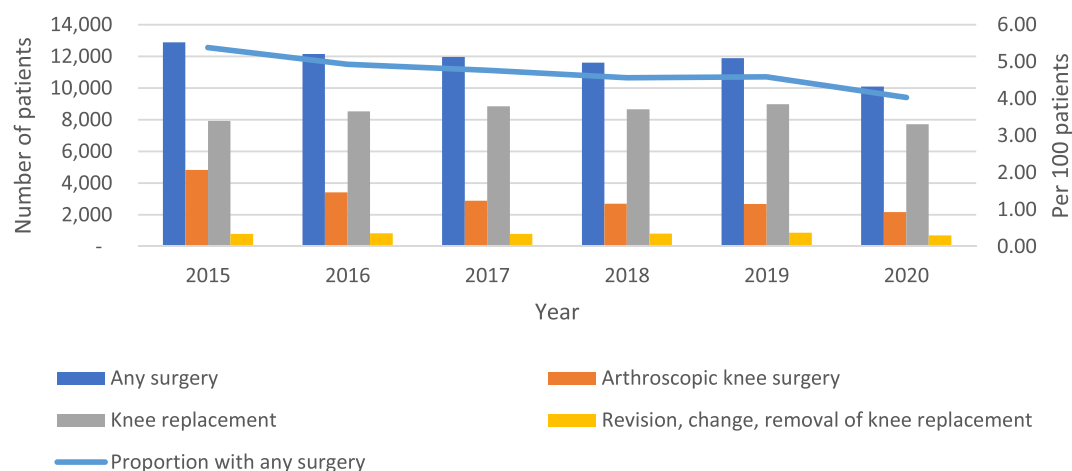


Fig. 2. Patients who underwent knee surgery. Numbers are displayed for the InGef research database. The bar charts show the absolute numbers of patients, and the graph displays the relative proportions as a percentage.

7.36 % (in 2019) received a revision, change, or removal of knee replacement.

3.2. Study part B

The longitudinal analysis included 50,184 eligible patients who were first diagnosed in 2015. Of these, 31,333 patients (62.44 %) received any of the guideline-recommended analgesic prescription medications during follow-up. As their first prescribed medication, most received WHO I (30,376 patients, 96.95 %), followed by WHO II (2551 patients, 8.14 %) and WHO III agents (941 patients, 3.00 %) (combinations between WHO categories possible). Regarding specific agents, most patients received NSAIDs (21,807 patients, 69.60 %) as their first medication, while other analgesics and antipyretics (metamizole included) were the second most common (8085 patients, 25.80 %). Opioids were not common as first medications, with tilidine/naloxone showing the highest proportion of all considered opioids (1350 patients, 4.31 %).

The proportion of patients who received physiotherapy during follow-up was assessed, which was 19.79 % (9933 patients).

The time from the first knee OA diagnosis to the first prescription of an analgesic was also analyzed and stratified by first medication: in the case of NSAIDs as first medication (21,807 patients), the median time until the first prescription was 39 days (IQR 4–101 days). For other analgesics and antipyretics (metamizole included, 8085 patients), the median time was 33 days (IQR 5–94 days). The shortest median times were found for oxycodone/naloxone (11 days, IQR 2–35 days, 239 patients) and topical products for joint and muscular pain (12 days, IQR 1–53 days, 73 patients). The longest median times were found for lidocaine (45 days, IQR 4–79 days, 29 patients) and opioids in combination with non-opioid analgesics (45 days, IQR 14–102 days, 238 patients).

Most patients who started with a pain medication according to WHO category I maintained therapy within this category during follow-up (17,173 patients, 56.59 % of all patients with WHO I medication as first medication), while less than 1 % switched to a WHO category II medication. Further switching patterns were also investigated and can be found in the appendix.

During follow-up, a total of 8318 patients out of 50,184 eligible patients first diagnosed in 2015 received any of the considered surgeries (16.58 %). Of these, most received knee replacement (5727 patients, 68.85 %), while arthroscopic knee surgery was performed in 3070 patients (36.91 %). Revision, change, and removal of knee replacement was performed in 543 patients (5.23 %). Time until the first surgery was also analyzed: those who received knee replacement had their surgery 564 days after their first diagnosis (median, IQR 204–1184 days, 5727 patients). The first arthroscopic knee surgery was performed a median of 157 days after the first diagnosis (IQR 54–595 days, 3070 patients), and revision, change, and removal of knee replacement after a median time of 812 days (IQR 351–1,367, 543 patients). Of the 8318 patients who underwent surgery, 6217 also received a medication before their first surgery (74.74 %). Those patients predominately received NSAIDs as their first prescription (5589 patients), followed by patients with other analgesics (3088 patients) and WHO II combinations (972 patients) as their first prescription.

4. Discussion

This study estimates that there are approximately 5 million adult knee OA patients in Germany, resulting in a prevalence of around 7 %. As population statistics on knee OA in Germany are scarce, no real comparison with recent data from Germany can be made. The lifetime prevalence of arthrosis in general is reported as 23.8 %, and it is known from previous studies that about half of all patients with self-reported arthrosis suffer from knee OA [14]. Compared to data from the Global Burden of Disease study [6], however, the prevalence of knee OA in Germany is higher. Both prevalence and incidence were relatively stable in all study years, with a slight decline in the incidence

in 2020 that may be associated with the COVID-19 pandemic and associated fewer hospital and physician visits. As this might also affect other results for 2020 for other outcomes such as knee surgery, these results should be treated with caution as the real number of cases might be underreported.

The distribution among males and females and across age groups was in line with previous findings [15] pointing to female sex and older age as risk factors. The higher prevalence among older people was also reflected in the most common comorbidities, such as hypertension or dorsalgia, but also overweight and obesity, a further well-known risk factor for OA. About one fourth of all patients were also diagnosed with pain and depression, which could be a secondary disease caused by knee OA and the associated pain. Regarding medical treatment, the vast majority of patients who received prescribed medications were treated with WHO I agents (around 93 %). This share was higher than in a previous study using the same database; however, that study focused on hip and knee OA instead of knee OA alone and data were collected earlier than in the present study (2011–2016) [15]. Another finding of study part A was the decline in knee surgery, particularly arthroscopic knee surgery. This could be explained by some changes in the reimbursement of arthroscopic knee surgery within statutory health insurance, whereby cover for certain procedures stopped in 2016.

A main focus of the study was the longitudinal analysis of newly diagnosed knee OA patients (study part B). In the course of the five-year follow-up, treatment patterns for medical and surgical interventions were identified. Approximately 60 % of all newly diagnosed patients received a prescription medication for the symptomatic treatment of their knee OA. This suggests that almost 40 % of patients receive no prescription pharmacological treatment that is covered by the German statutory health insurance. However, the OTC consumption cannot be covered by this study, and it should be noted that hyaluronic acid, which is often used in the early stages of knee OA, could not be covered in this analysis as it is not reimbursed by Germany statutory health insurance. Interestingly, of the 8318 patients who underwent surgery, 2101 (25.26 %) did not receive any prescription pharmacological treatment before their first surgery. Those patients who received a prescription medication mostly started treatment with NSAIDs or analgesics and antipyretics, while opioids were rarely prescribed as first line pharmacotherapy. Even during further follow-up, patients usually maintained monotherapy with either of the two classes of agents, while most switching patterns also did not include WHO category III medications. This could be due to the comparably short period of follow-up, presumably not covering the worsening progression of knee OA in many patients who may switch to opioids or intraarticular injections. However, the finding is in line with the low usage of opioids that was detected in the cross-sectional analysis as well. IA injections and opioids seem to play a minor role for the treatment of pain due to knee OA in Germany despite their inclusion within the German OA guidelines [16]. Furthermore, even in patients undergoing surgery, the distribution of treatments was similar, i.e., a low proportion of patients on opioids and IA injections.

Patients without medication during follow-up were either directly treated with surgical interventions, with conservative therapy options such as physiotherapy or equivalent, with over-the-counter medications not covered in the database, or not at all. As the majority of patients were first diagnosed in the outpatient setting, it can be assumed that some may only suffer from an early stage of knee OA, with no need for medical or surgical treatment that needs a prescription. Furthermore, dietary supplements are also recommended for knee OA treatment, but since they are usually over-the-counter medications, they could not be covered in the database. Physiotherapy is recommended in all stages of knee OA, but despite the recommendations, only around 20 % of newly diagnosed patients in 2015 received physiotherapy during follow-up. The proportion of patients with any kind of surgical interventions, however, was only slightly lower (16.58 %). Most of these patients received knee replacement instead of arthroscopic knee surgery, and the decline in the proportion of patients receiving arthroscopic knee surgery is in line with

recent recommendations, all the more so since certain kinds of arthroscopic surgeries are not reimbursed by the statutory health insurance anymore. Most of these patients (80.15 %) also received medication before knee replacement; however, the remaining 20 % (1137 patients) without prior prescribed medical treatment raise the question of what causes the rapid progression to knee replacement in Germany. It should be noted that only prior medical treatment before surgical intervention has been checked in the analysis, while other treatment options such as physiotherapy or even arthroscopic knee surgery may also have been conducted before knee replacement, as well as a change of lifestyle regarding nutrition and exercises. Nevertheless, the high proportion of patients progressing to a surgical intervention, primarily total knee replacement, without having received any prescription pharmacological treatment may indicate a lack of effective pharmacological treatment options or an ineffective use of pharmacological treatment. Surgery should be an option of last resort, and the results seem to indicate a discrepancy between clinical practice and guidelines. Further research should be conducted to investigate the characteristics of these patients, addressing the questions of whether there are any medical educational needs for the currently available treatments and whether there is an unmet need for patients due to missing options.

The patients who were first diagnosed in 2015 and followed up until the end of 2020 or until death were mostly diagnosed in the outpatient setting. Half of them were diagnosed by orthopedics and about one third by a GP. This is not an unusual distribution within the German healthcare system, as it is not GP-based and patients have the option to directly consult a specialist (in contrast to, e.g., the UK or Scandinavian countries). It can be speculated that direct consultation of a specialist could lead to an earlier decision to perform surgery.

The study has several strengths and limitations. One limitation is that the representativeness of the InGef research database can only be guaranteed regarding age and sex, although the InGef database also shows good overall accordance with the German population regarding morbidity, mortality, and drug use [13]. However, socioeconomic factors could not be covered, which may have an impact on disease distribution or underlying risk factors. The database also does not include any information on over-the-counter medications which are also relevant for knee OA therapy. A study from 2015 identified OTC analgesic use of 12 % in Germany [17]. In addition, medications given during a hospital stay cannot be captured with health claims data. Prescribed medications which are dispensed in a pharmacy were identified by their respective ATC code; however, the prescribed medications are not linked to a diagnosis code with which knee OA was identified. Hence, it was not possible to distinguish the use of pain medication between knee OA and other comorbidities. Another limitation is that the database does not include individual patient files to confirm the diagnoses of knee OA, which for data protection reasons is generally not feasible. However, the misclassification of some knee OA patients is possible, though rather unlikely due to the large sample size.

On the other hand, the study provides an updated overview of the prevalence, incidence, and treatment of knee OA pain, for which population-level data in Germany are scarce. Official statistics by the German national Public Health Institute (Robert Koch Institute) usually report patient numbers on OA in general, while the site of arthrosis is often only covered by self-reported data [7,14]. Moreover, the longitudinal part of the analysis gives first insights into the patient journey of newly diagnosed knee OA patients, revealing a potential undertreatment of patients in terms of medical treatment and physiotherapy, with, at the same time, high numbers of patients with surgical interventions, especially knee replacement.

5. Conclusion

The number of patients with knee OA in Germany is slightly increasing, along with the number of surgical interventions, especially knee replacement. While other treatment options, such as opioids, only

seem to play a minor role, the high proportion of knee replacements not only in the prevalent patient population, but also in newly diagnosed patients and, especially, in the newly diagnosed patients who have not received any prescribed pharmacological treatment, is surprising. Future studies should cover the underlying causes of rapid progression to surgery after the first diagnosis.

Author contribution

All authors contributed to the study concept and design. Material preparation and analysis were performed by DO and LB. The first draft of the manuscript was written by DO, all other authors revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Declaration of competing interest

HL is an employee of Grünenthal GmbH. SI is an employee of Grünenthal Ltd. DH is employed by WIG2 GmbH which received funding from Grünenthal GmbH. DO and LB are employed by InGef GmbH which acted as subcontractor and received funding from WIG2 GmbH for the execution of the study. JJ received a honoraria from Grünenthal GmbH for clinical input to interpretation of the data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ocarto.2023.100430>.

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