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Pain

PAIN

Out-of-hospital opioid prescriptions after knee and hip arthroplasty: prescribers and the first prescribed opioid

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Abstract

Background: We determined the first prescribed opioid and the prescribers of opioids after knee and hip arthroplasty (KA/HA) between 2013 and 2018 in the Netherlands. We also evaluated whether the first prescribed opioid dose was associated with the total dispensed dose and long-term opioid use in the first postoperative year.
Methods: The Dutch Foundation for Pharmaceutical Statistics was linked to the Dutch Arthroplasty Register. Stratified for KA/HA, the first out-of-hospital opioid within 30 days of operation was quantified as median morphine milligram equivalent (MME). Opioid prescribers were orthopaedic surgeons, general practitioners, rheumatologists, anaesthesiologists, and other physicians. Long-term use was defined as ≥1 opioid prescription for >90 postoperative days. We used linear and logistic regression analyses adjusted for confounders.
Results: Seventy percent of 46 106 KAs and 51% of the 42 893 HAs were prescribed ≥1 opioid. Oxycodone increased as first prescribed opioid (from 44% to 85%) whereas tramadol decreased (64–11%), but their dosage remained stable (stronger opioids were preferred by prescribers). An increase in the first prescription of 1% MME resulted in a 0.43%/0.37% increase in total MME (KA/HA, respectively). A 100 MME increase in dose of the first dispensed opioid had a small effect on long-term use (prevalence: 25% KA, 20% HA) (odds ratio=1.02/1.01 for KA/HA, respectively). Orthopaedic surgeons increasingly prescribed the first prescription between 2013 and 2018 (44–69%). General practitioners mostly prescribed consecutive prescriptions (>50%).
Conclusion: Oxycodone increased as first out-of-hospital prescription between 2013 and 2018. The dose of the first prescribed opioid was associated with the total dose and a small increased risk of prolonged use. First prescriptions were mostly written by orthopaedic surgeons and consecutive prescriptions by general practitioners.

Keywords: dosage; hip arthroplasty; knee arthroplasty; opioid prescription; pharmacoepidemiology; prescribers

Editor's key points

- Opioids are often prescribed after knee and hip arthroplasty.
- This retrospective analysis of Dutch data between 2013 and 2018 investigated the dose of the first opioid prescribed, its relation to the total prescribed dose and prolonged opioid prescription, and the prescribers of opioids in the first year after arthroplasty.
- Results show a shift from tramadol to oxycodone, oxycodone being more often prescribed as a first opioid prescribed, but dosages remained stable between 2013 and 2018. The dose of the first prescribed

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opioid was associated with the total prescribed dose and a small increased risk of prolonged use.
- Orthopaedic surgeons increasingly prescribed the first opioids while consecutive prescriptions came mainly from general practitioners.

Opioids are often prescribed after knee/hip arthroplasty (KA/HA) surgery. It is reported to be 90% in the USA,[1] but in Europe high prevalence has also been reported with 75% after HA and 89% after KA in the Netherlands.[2] Postoperative opioid prescription induces a risk for long-term opioid use, which has been reported to occur in 25–40% of arthroplasty patients in the USA[3,4] and 15–16% in Denmark and Sweden.[5,6] Prolonged opioid use[7] and use of high opioid dosages (>50 morphine milligram equivalent [MME] per day)[8] have been shown to increase the risk of addiction, overdose, and death. With regard to outcomes after arthroplasty surgery, it is linked to an increased revision risk.[9]

Taking these risks into account, it is necessary to reduce the use of opioids, even though they are effective analgesics.[10] A possible target is the first postoperative prescription after arthroplasty surgery. Recently it was shown that a higher first prescribed opioid dose was associated with a higher risk of prolonged opioid use,[11] and that by lowering the first prescription dose the opioid refill rates and total MME could be lowered.[12] However, studies from European countries, which differ substantially from their counterparts in the USA (e.g. health coverage), are lacking. In addition, these studies were performed in small populations, and national population-based cohort studies are necessary to ensure representativity.

Another target for future preventive interventions are the prescribers of opioids. In the Netherlands, in the general population, between 75% of primary prescriptions and 90% of repeat prescriptions come from general practitioners (GPs).[13] In the USA, it has been reported that orthopaedic surgeons prescribed 47% of opioid prescriptions in the first 90 days after KA/HA; this rate decreased to 14% a year postoperatively.[14] Again, numbers from European countries are lacking.

To gain more insight in opioid prescription practices and to identify possible intervention targets, we investigated, among osteoarthritis (OA) patients undergoing KA and HA, (1) the first prescribed opioid and its dose after arthroplasty surgery over time between 2013 and 2018, (2) whether the dose of the first out-of-hospital prescription was associated with the total dose of opioids prescribed in the first postoperative year and with prolonged opioid use, and (3) the prescribers of opioids after arthroplasty surgery over time between 2013 and 2018.

Methods

We performed a longitudinal cohort study in which we linked two national databases, the Dutch Arthroplasty Register (LROI) and the Dutch Foundation for Pharmaceutical Statistics (SFK).

Data sources

The LROI covers all hospitals performing arthroplasties in the Netherlands. The data completeness of primary KA and HA is >98%.[15] The LROI provided information on individual arthroplasties, with patient and prosthesis characteristics. Pharmaceutical dispensing data were obtained from the SFK, which contains dispensing data from >95% of the community pharmacies, including outpatient pharmacies within hospitals.[16] Opioid dispensing data were derived 1 yr before and 1 yr after arthroplasty, including Anatomic–Therapeutic–Chemical (ATC) codes from the WHO, the dose, the number dispensed, and information regarding the prescriber.

Data linkage

The linkage between LROI and SFK datasets was performed on a combination of year of birth, sex, four-digit postcode, and surgery date together with the dispensing date of low-molecular-weight heparin prescribed around the surgery date (4 days before–10 days after) as a proxy for surgery date which was unavailable in the SFK.

Ethics and confidentiality

Approval by an ethics committee was waived by the Medical Ethics Committee Leiden–Den Haag–Delft (reference number: G19.018). Data from both LROI and SFK were pseudonymised before they were received.

Study population

All primary KA and HA surgeries for OA between 2013 and 2018 were included, except patellofemoral KA. Exclusion criteria were: <18 yr old, arthroplasties with administrative errors (e.g. wrongly retrieved survival time). Moreover, only arthroplasties that could be linked to a community pharmacy were included to be able to follow them over time. Hence, if an arthroplasty was solely linked to outpatient pharmacies and not to a community pharmacy before 2017, it would not be possible to trace the arthroplasty to the patients' local community pharmacy. After 2017, an overarching identifier was added.

Measures

Demographics

The following patient characteristics were available: age (years), sex, BMI, current smoking status (yes/no), American Society of Anesthesiologists (ASA) physical status, and Charnley score. ASA physical status ranged from ASA 1 (healthy)–ASA 4 (severe systemic disease, constant threat to life). The Charnley score categorises the degree of OA ranging from A (one joint affected) to C (multiple joints affected or a chronic disease that limits quality of life). Socioeconomic status (SES) was based on individual four-digit postcodes from SFK. SES originated from the 2014–16 measurements of the Netherlands Institute for Social Research, based on income, education, and occupation. SES scores were based on the quintile z-scores: very low ($\leq$−1.5), below average (−1.49 to −0.5), average (−0.49 to 0.49), above average (0.5–1.49), and very high ($\geq$1.5).

Arthroplasty

The following prosthesis-related information was derived: joint (knee/hip), type of prosthesis (total, resurfacing, hemi, unicondylar), fixation (cemented, uncemented, hybrid).

Opioid prescriptions

Opioids were classified according to ATC-5 classification. Postoperative opioid use was defined as ≥1 dispensed opioid prescription. Opioid users were defined as prevalent (≥1 opioid prescription 1 yr before surgery) or opioid naive (no opioid prescription 1 yr before surgery). For preoperative opioid users, we also assessed the quarter in which they received their last opioid (last opioid prescription in the 12–10/9–7/6–4/3–1 preoperative months). The first prescribed out of hospital opioid was defined as the first prescription within 30 days after arthroplasty. When two or more different opioids were prescribed at the same time, all were counted. Prolonged opioid use was defined as ≥1 prescription after 90 days postoperatively.

Opioid exposure was assessed in MME hereafter to be called 'opioid dose'. MMEs were calculated using the ATC classification by adding the dosages of the opioid prescription and multiplying this dose by a MME conversion factor.[17] For example, 1 mg oxycodone equals 1.5 MME, whereas 1 mg tramadol equals 0.1 MME. We defined the total dose of prescribed opioids as the total prescribed MMEs within the first year after surgery minus the MME of the first prescription. The total preoperative opioid use was defined as the total prescribed MME in the last preoperative year before surgery.

Other medication

All other medication was classified according to ATC-5 classification. Preoperative exposure to these medication types was defined as ≥1 prescription in the 6 months before surgery. The other medication was classified as benzodiazepines, tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and other antidepressants, pregabalin and gabapentin, and antiepileptics.

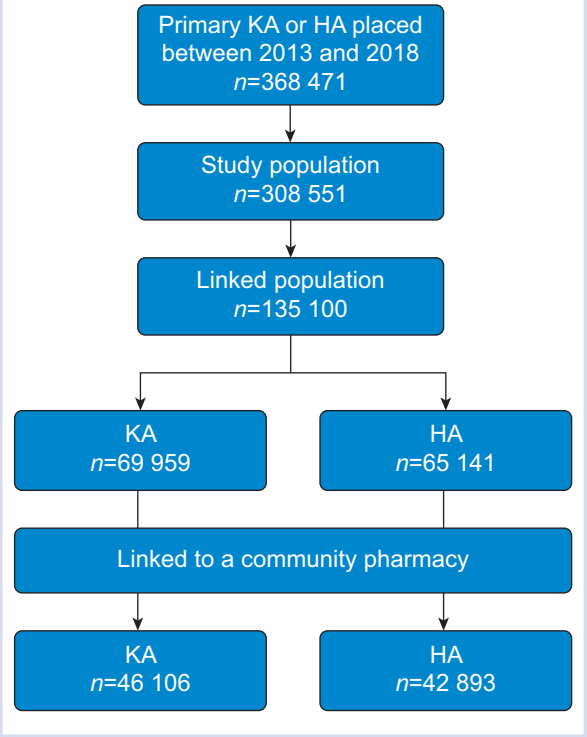

Fig 1. Flowchart showing patient selection. KA, knee arthroplasty; HA, hip arthroplasty.

Prescribers of opioids after arthroplasty surgery

Opioid prescriptions were categorised into prescription categories to assess the prescribers: 1st prescription, 2nd, 3rd, 4th, 5th, 6–10th, and 11–20th. For each opioid prescription category, the number and proportion of prescriptions prescribed by an orthopaedic surgeon, GP, rheumatologist, anaesthesiologist, or other healthcare professional were calculated and also the number of arthroplasties per year.

Data analysis

All analyses were stratified for KA and HA. The population characteristics were described using descriptive statistics. Continuous outcomes were shown as mean with standard deviation (SD) and categorical outcomes as a proportion per category.

Descriptive statistics were used to assess the first prescribed opioid in the first 30 days postoperatively for each year between 2013 and 2018. Median MMEs and their interquartile ranges were calculated for the five most frequent prescribed first opioids after arthroplasty. All other opioids were clustered in the other category.

To assess the association between the dose of the first opioid prescription and the total dose dispensed in the first postoperative year, we used a linear regression model adjusted for: preoperative opioid use[18–20] (MME in the preoperative year and the last preoperative quarter in which an opioid was prescribed), age,[19,21,22] sex,[19,21] BMI,[3,23] ASA classification,[24,25] and other medication use at least once in the 6 months before arthroplasty surgery (TCAs, SSRIs and other antidepressants, pregabalin and gabapentin, benzodiazepines, and other antiepileptics).

All crude and adjusted coefficients were calculated with 95% confidence intervals (CIs). To assess whether the MME of the first opioid prescription was associated with prolonged opioid use after 90 days, we used a logistic regression model adjusted for the same confounders as in the linear regression model. For the independent variable, MME, increments per 100 were used. As some of these confounders were not available in the LROI before 2014, we performed a complete case analysis. Furthermore, only the index procedures were used, meaning that consecutive KA or HA procedures within an individual were excluded. All assumptions were checked. If in the linear model the linearity assumption was violated, $\log_{10}$ transformations were performed.

Sensitivity analysis

To assess the impact of excluding the arthroplasties that were solely linked to outpatient pharmacy prescriptions, we also calculated the proportion for the prescribed opioids and the dose of the first prescription in this subgroup.

All data cleaning and analyses were performed in R 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Population

We linked 135 100 primary hip and knee arthroplasties for OA (69 959 KA, 65 141 HA), of which 88 999 primary arthroplasties

Table 1 Population characteristics stratified for primary knee and hip arthroplasties for osteoarthrosis.

	Knee (*n*=46 106)	Hip (*n*=42 893)
Characteristics		
Age (yr), mean (range)	67.10 (27–97)	68.46 (18–98)
Sex, female (%)	27 318 (59.3)	26 272 (61.3)
Missing (%)	– (–)	– (–)
BMI[a] (%)		
Underweight (≤18.5)	60 (0.1)	244 (0.6)
Normal weight (18.5–25)	7052 (16.1)	12 418 (30.7)
Overweight (25–30)	18 162 (41.6)	17 677 (43.7)
Obesity (30–40)	16 922 (38.7)	9675 (23.9)
Morbid obesity (>40)	1486 (3.4)	457 (1.1)
Missing (%)	2424 (5.3)	2422 (5.6)
ASA physical status (%)		
1	7082 (15.4)	8084 (18.9)
2	31 427 (68.3)	28 174 (65.8)
3–4	7490 (16.3)	6548 (15.3)
Missing (%)	107 (0.2)	87 (0.2)
SES (%)		
Very low	6155 (13.4)	4847 (11.3)
Below average	8956 (19.5)	7843 (18.4)
Average	17 460 (38.1)	16 276 (38.1)
Above average	11 208 (24.5)	11 341 (26.6)
Very high	2060 (4.5)	2383 (5.6)
Missing (%)	267 (0.2)	203 (0.5)
Smoking,[a] Yes (%)	4104 (9.9)	4506 (11.7)
Missing (%)	4618 (10.0)	4393 (10.2)
Charnley classification[a] (%)		
A	17 849 (43.8)	17 301 (45.6)
B1	14 030 (34.4)	11 459 (30.2)
B2	7830 (19.2)	8225 (21.7)
C	932 (2.3)	802 (2.1)
Not applicable	114 (0.3)	120 (0.3)
Missing (%)	5351 (11.6)	4986 (11.6)
Year of operation		
2013	4643 (10.1)	4495 (10.5)
2014	8000 (17.4)	7586 (17.7)
2015	8387 (18.2)	7868 (18.3)
2016	7881 (17.1)	7488 (17.5)
2017	8430 (18.3)	7818 (18.2)
2018	8765 (19.0)	7638 (17.8)
Prosthesis-related		
Type of prosthesis (%)		
Total prosthesis	40 983 (88.9)	42 688 (99.5)
Hemi-	–	186 (0.4)
Unicondylar	5113 (11.1)	–
Resurfacing	–	4 (0.0)
Other	9 (0.0)	5 (0.0)
Missing (%)	1 (0.0)	10 (0.0)
Fixation (%)		
Cemented	40 575 (87.9)	9495 (22.2)
Uncemented	4 278 (9.3)	29 530 (68.9)
Hybrid	1 185 (2.8)	3811 (8.9)
Missing (%)	68 (0.1%)	–57 (0.1%)
Opioid use before surgery		
Prevalent users, Yes (%)	12 062 (26.2)	11 640 (27.1)
Missing (%)	– (–)	– (–)

[a] Available since 2014. Charnley Classification: A, one joint affected with osteoarthrosis; B1, two joints affected (both hips/both knees); B2, contralateral joint with prothesis; C, multiple joints affected with osteoarthrosis or a chronic disease impairing quality of life (in walking). *n*, number of arthroplasties; SD, standard deviation, ASA, American Society of Anesthesiologists; SES, socioeconomic status.

Table 2 Annual distribution of different opioids as a first prescription after primary knee and hip arthroplasty and the median amount of morphine milligram equivalent dispensed and interquartile range.

Operation year	*n*	Oxycodone		Tramadol		Morphine		Fentanyl		Buprenorphine		Other	
		%	MME	%	MME	%	MME	%	MME	%	MME	%[a]	MME
KA													
2013	2360	43.7	300 (150–450)	52.0	150 (100–150)	0.7	300 (140–900)	0.7	1296 (520–4032)	0.5	378 (221–1008)	2.4	98 (45–180)
2014	4303	58.1	285 (150–450)	37.6	150 (75–150)	1.6	225 (100–310)	0.7	968 (762–1800)	0.4	252 (126–504)	1.6	113 (80–180)
2015	5485	62.9	240 (150–435)	32.6	113 (60–150)	2.7	216 (140–300)	0.6	882 (432–1800)	0.4	189 (74–473)	0.8	90 (49–171)
2016	5663	73.0	263 (150–435)	22.6	150 (75–150)	2.9	200 (159–300)	0.6	864 (360–1800)	0.4	504 (189–630)	0.5	158 (80–360)
2017	6763	80.9	300 (180–450)	15.9	150 (75–150)	2.2	180 (60–400)	0.4	864 (432–1800)	0.4	236 (70–357)	0.2	90 (60–135)
2018	7607	85.3	270 (150–420)	10.7	150 (100–150)	3.1	20 (20–380)	0.4	832 (324–1662)	0.4	195 (91–504)	0.1	270 (135–880)
HA													
2013	1341	30.2	225 (150–540)	63.6	150 (100–150)	1.5	100 (63–200)	0.7	1800 (1132–4275)	0.8	504 (252–882)	3.2	90 (62–135)
2014	2675	49.3	225 (150–450)	44.7	105 (75–150)	1.3	250 (85–300)	1.7	900 (432–1800)	1.0	252 (126–898)	2.0	90 (45–180)
2015	3500	68.6	210 (113–300)	26.8	100 (70–150)	2.2	216 (198–300)	0.9	990 (410–1800)	0.5	252 (166–504)	1.0	113 (90–270)
2016	3936	75.6	225 (150–338)	19.4	100 (70–150)	3.0	216 (155–300)	1.0	1181 (801–3540)	0.4	378 (189–1008)	0.6	180 (90–304)
2017	4947	82.0	225 (150–360)	13.5	100 (75–150)	2.4	100 (29–400)	1.1	900 (540–1332)	0.5	266 (205–504)	0.5	135 (45–275)
2018	5459	83.6	225 (150–300)	11.3	75 (75–150)	3.9	20 (20–400)	0.6	900 (432–1650)	0.5	252 (60–504)	0.2	120 (60–180)

[a] Combination of: codeine with paracetamol, tapentadol, piritramide, pethidine, pentazocine, nicomorphine, hydromorphone. HA, hip arthroplasty; KA, knee arthroplasty; *n*, number of arthroplasties with an opioid prescription; %, percentage of first opioid prescriptions with specific opioid.

(46 106 KAs and 42 893 HAs) could be linked to dispensing data from at least one community pharmacy (Fig 1).

The population characteristics are shown in Table 1. The mean age for KA was 67 yr (range, 27–97 yr) and that for HA was 68 yr (range, 18–98 yr). About 60% of the arthroplasties were performed in women. Preoperative opioid prescriptions were prevalent in 26% of KAs and 27% of HAs.

First prescribed opioid type and its dose

Opioids were prescribed after 32 181 KAs (69.8%) (Table 2). As a first postoperative prescription, oxycodone increased from 44% in 2013, to 85% in 2018, whereas tramadol decreased from 52% to 11%. Morphine increased from 0.7% to 3%, whereas buprenorphine and fentanyl stayed at a similar rate. Opioids were prescribed after 21 858 (51.0%) HAs. As a first prescription, oxycodone and morphine increased, whereas tramadol decreased, similar to the KAs (Table 2).

In both KA and HA, the median dose of the first prescription of oxycodone, tramadol, and fentanyl exposure remained stable over time. In MMEs, the opioid dose was twice as high when the first prescription was oxycodone compared with tramadol. Fentanyl had the highest initial MME dose (Table 2).

Association between dose of the first opioid prescription and total MME

In 24 385 index KAs with postoperative opioid use, we found that the dose of the first opioid prescription was positively associated with the total dose in the first postoperative year; 1% increase in MME of the first opioid prescription after KA resulted in 0.43% increase in the total MME (Table 3). For instance, a change in the first prescription from tramadol (median MME, 150) to oxycodone (median MME, 300) for a prevalent user (with a preoperative opioid prescription) which is a 100% increase of MME, would result in a 34% increase in total MME in the first year. In 16 691 HAs we found similar results, in which a 1% increase in MME of the first opioids resulted in 0.37% increase in the total MME (Table 3). An example of the effect for a fictional person can be found in Table 4.

Association between the dose of the first opioid prescription and prolonged opioid use

Prolonged use was found in 6136 index KAs (25.2%). We found a small positive association between an increase in MME of the first opioid prescription and the odds of having an opioid prescription after 90 days postoperatively (odds ratio [OR]= 1.02; CI, 1.01–1.03) (Table 3). A MME increase of 100 in the first prescribed opioid would result in 2% increase in odds of having an opioid prescription after 90 days.

Prolonged use was found in 3422 index HAs (20.5%). Here, we also found a small positive association between the MME of the first opioid prescription and the odds of having an opioid prescription after 90 days (OR=1.01; CI, 1.00–1.03) (Table 3). A MME increase of 100 in the first prescribed opioid would result in 1% increase in odds of having an opioid prescription after 90 days.

Prescribers of opioids after arthroplasty

Most first opioid dispenses were prescribed by an orthopaedic surgeon. This percentage increased from 44% in 2013 until 69% in 2018 for KA. After HA these proportions increased from 33% in 2013 to 66% in 2018 (Fig 2). From the second prescription onwards, GPs prescribed most opioids for both KA and HA. The proportion of second prescriptions prescribed by an orthopaedic surgeon increased from 14% in 2013 to 27% in 2018 for KAs and from 10% in 2013 to 22% in 2018 for HAs. Subsequently, the proportion of second prescriptions by a GP decreased between 2013 and 2018. The number of first prescriptions by anaesthesiologists seemed to increase over time from roughly 1% of prescriptions in 2013 to 3% in 2018 (Supplementary Table S1 [KAs]; Supplementary Table S2 [HAs]).

Sensitivity analysis

In the subgroup of arthroplasties that could solely be linked to outpatient pharmacy prescriptions, the results were similar to the ones here described above (results not shown).

Discussion

Between 2013 and 2018, oxycodone increased as a first prescription whereas tramadol decreased in both KA and HA. For

Table 3 Associations between MME of the first prescription and total MME and risk of opioid prescription after 90 days.

Log linear association between MME of the first prescription and total MME		
	Total MME Log_{10} (beta [95% CI])	**Total MME Log_{10} (beta[a] [95% CI])**
Log_{10} MME 1st prescription (KA)	0.68 (0.63–0.73)	0.43 (0.38–0.48)
Log_{10} MME 1st prescription (HA)	0.72 (0.66–0.77)	0.37 (0.32–0.43)
Logistic association between MME of the first prescription and risk of opioid prescription after 90 days		
	Prescription after 90 days Odds ratio (95% CI)	**Prescription after 90 days Odds ratio[a] (95% CI)**
MME 1st prescription (KA)/100	1.08 (1.07–1.09)	1.02 (1.01–1.03)
MME 1st prescription (HA)/100	1.09 (1.08–1.11)	1.01 (1.00–1.03)

[a] Adjusted for: age, sex, BMI, comorbidities, the last preoperative quarter in which opioids are used, preoperative MME, medication use (benzodiazepines, tricyclic antidepressants, gabapentin, other antiepileptics, selective serotonin reuptake inhibitors and other antidepressants). CI, confidence interval; HA, hip arthroplasty; KA, knee arthroplasty; MME, morphine milligram equivalent.

Table 4 Predicted total morphine milligram equivalent for a fictional patient. Predicted outcome for a female patient, age 67 yr, BMI 25 kg m^{-2}, ASA physical status 2, with no preoperative opioid use or with preoperative opioid use. In the case of preoperative opioid use we used the median MME of preoperative use, namely 666.8 MME in hip arthroplasty and 450 MME in knee arthroplasty. MME, morphine milligram equivalent.

First prescription MME	Knee arthroplasty		First prescription MME	Hip arthroplasty	
	Preoperative opioid user	No preoperative opioid use		Preoperative opioid user	No preoperative opioid use
75	139.2	9.0	75	47.5	3.2
150	187.2	12.1	112.5	55.3	3.8
225	222.6	14.4	187.5	66.9	4.5
375	276.9	17.9	300	79.7	5.4
570	331.2	21.4	465	93.9	6.4

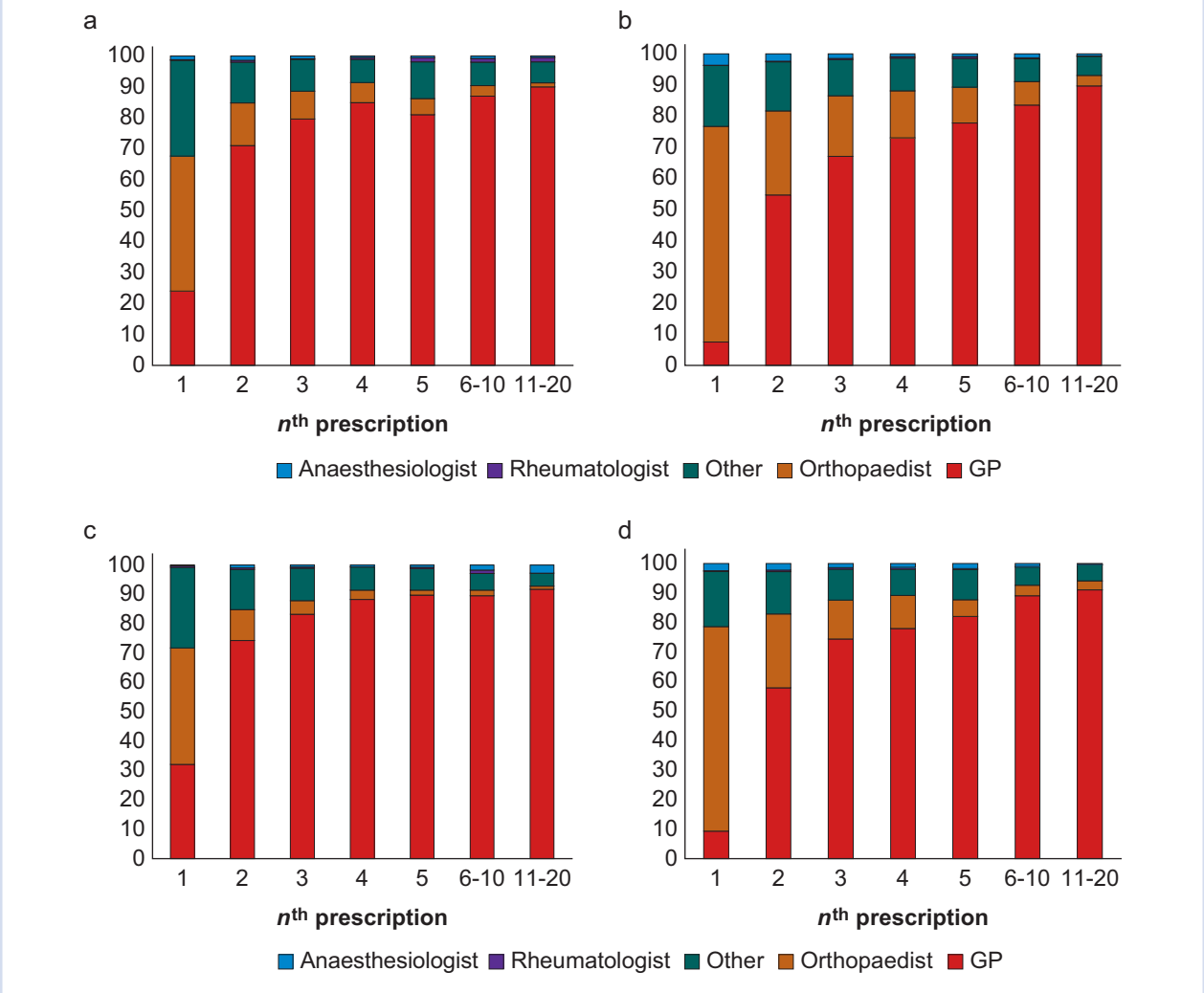

Fig 2. Distribution of prescribers over the different number of prescriptions after knee and hip arthroplasty in 2013 and 2018. GP, general practitioner.

each respective opioid, there was no change in first prescription dose, but the amount prescribed remained the same. A higher first prescribed opioid dose was associated with an increase in the total prescribed dose in the first year after both KA and HA, and a higher dose was also associated with a small increase in the risk of opioid prescriptions after 90 days. Furthermore, we found that orthopaedic surgeons became more often the prescriber of the first opioid after arthroplasty between 2013 and 2018. For consecutive prescriptions, the proportion of prescriptions by orthopaedic surgeons decreased. As from the second prescription onwards, GPs were the largest prescriber group for both KA and HA.

The shift from tramadol to oxycodone as observed in our study is as expected, and could be the reflection of the reintroduction of oxycodone in postoperative guidelines since 2013.[26] However, a shift from tramadol to oxycodone might also be explained by greater pain relief from oxycodone combined with fewer side-effects such as nausea and dizziness than with tramadol. Given these possible advantages, and although oxycodone is a more potent opioid with more possible side-effects, oxycodone might be preferred by the clinician. Furthermore, a decrease in hospitalisation days is an effect of enhanced recovery after surgery protocols.[27] These are part of the postoperative knee and hip arthroplasty guidelines, and could lead to a higher chance of postoperative pain at hospital discharge, thus necessitating more potent pain management (with oxycodone). This highlights the balancing act necessary between effective pain management on the one hand, and the negative side-effects of prescribing an opioid with a higher MME on the other hand.

No other observed change in prescribing practice other than the shift from tramadol to oxycodone occurred. Per respective opioid, the amount prescribed on the first prescription remained the same. The median MME found after both KA and HA was similar to what was found in a recent study in other surgical postoperative prescriptions in the USA, Canada, and Sweden.[28] For example the median MME in the first 6 days after meniscectomy in Sweden was similar to what we found after KA/HA (210 (inter-quartile range [IQR], 210–315).[28] Furthermore, the number of dosages (expressed in defined daily dosages) for the first prescription also did not change.

The shift from tramadol to oxycodone as a first prescription could lead to several unintended effects. As demonstrated in this study, a change from tramadol to oxycodone as a first prescription (which results in a doubling of MME) was associated with an increase in total MME in the postoperative year, which is in line with the article by Ruddell and colleagues.[11] We also found that higher MME of the first prescribed opioid was associated with a small increased risk of having an opioid prescription after 90 days postoperatively. Earlier orthopaedic research showed similar results among total HA patients in the USA between 2013 and 2016.[29] In addition, a Canadian study in which multiple surgical procedures were compared found that an initial daily dose ranging from >20 to 200 MME, compared with 0–20 MME, had an increased risk of long-term use (OR=1.13–1.15).[30] This does suggest that some evidence exists that a higher dose of the first prescribed opioid is associated with long-term use within the arthroplasty population. In addition, it is known that roughly 9% of postoperative HA and 20% of postoperative KA patients report unfavourable postoperative pain outcomes between 3 months and 5 yr after arthroplasty surgery.[31] This suggests that a part of the patients with prolonged opioid prescriptions might be taking them to subdue chronic postoperative pain. Another factor to take into account is the addictive nature of opioids. However, the reason for prolonged opioid use cannot be distilled from the available medication data. A recent study aimed at showing the risk of opioid overdose showed that the MME of the prescription in the first 6 postoperative months was not associated with the risk of overdose and that patient factors may be more important.[32] If patient characteristics are indeed more important than the first prescribed dose, this could explain why the relationship we found between the first prescribed opioid and the risk of prescription after 3 months was attenuated after adjustment for confounding. Further research is necessary to fully understand this.

In addition, the aforementioned study by Delaney and colleagues[29] also emphasised that the focus of research and possible interventions should be on the opioid prescriber. Determining the prescribers of long-term opioid prescriptions is important to understand where changes can be made in opioid prescribing in both practice and prescriber education.[33] We found that the orthopaedic surgeon was the main prescriber of the first prescribed opioid prescriptions in our data. Also, the first prescription came more often from an orthopaedic surgeon, suggesting that the orthopaedic surgeon is becoming more involved with postoperative pain treatment. The other medical specialists (rheumatologist and anaesthesiologist) were less often prescribers of out-of-hospital opioids. Within the Netherlands, in-hospital, the anaesthesiologist is involved in pain treatment, and an acute pain team/acute pain service is present in most hospitals to provide adequate pain management in the first postoperative hours. During stays in the wards and upon discharge, prescriptions are the responsibility of the doctors in the hospital ward. Moreover, consecutive prescriptions were often prescribed by a GP, as was also found in the USA among total KA/HA patients.[14] Information on opioid prescribers after KA/HA is limited and could therefore not be compared with that in other European countries. Furthermore, GPs appear to continue the opioid prescription after the first opioid prescription, and could be targeted to prevent prolonged opioid prescriptions. As a first prescriber, the orthopaedic surgeon could be a possible target to change their practice towards less opioid prescriptions after discharge from the hospital.

A major strength of our study is that we were able to use MME, allowing a detailed evaluation of opioid prescriptions. We were thereby able to analyse the association between the first prescribed opioid and total prescriptions and the relationship with prolonged use. For that purpose, we adjusted for a large number of confounders. Furthermore, we used two national datasets, leading to national coverage. However, several limitations should be considered. First, with prescription registers, such as the SFK, there is no certainty that prescribed drugs were ingested. Also, opioids could have been prescribed for other reasons, which were not recorded in the database. In addition, we did not have information on the pharmacy, as such we could not assess how many pharmacies delivered opioids to a single patient, which could have served as a proxy to detect opioid addiction.[32] Limitations related to the data linkage are published elsewhere.[2]

In conclusion, there was a shift in the first prescribed opioid from tramadol to oxycodone, whereas no change in the MME of the first prescription was observed regardless of the opioid type. An increase in the MME of the first opioid prescription was associated with an increase in the total MME of prescribed opioids in the first postoperative year, and it was associated

with a small increased risk of an opioid prescription after 90 days. Furthermore, the prescribers of the first opioid was most often an orthopaedic surgeon, whereas consecutive prescriptions came from GPs; a shift was seen where there was an increase seen in the proportion of second prescriptions prescribed by an orthopaedic surgeon.

Authors' contributions

Writing of the manuscript: HvB, MG.
Conceptualisation and funding acquisition: RN, AD, MG.
Data curation for the LROI data: LvS.
Formal analyses and visualisation: HvB.
Methodology: HvB, RN, FR, MB, EvD, MG.
Supervision: RN, MG.
All authors interpreted the data and contributed to the final manuscript.

Declarations of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.12.024.

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