Opioid prescribing patterns after arthroplasty of the knee and hip: a Dutch nationwide cohort study from 2013 to 2018

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Background and purpose — Numbers on opioid prescriptions over time in arthroplasty patients are currently lacking. Therefore we determined the annual opioid prescribing rate in patients who received a hip/knee arthroplasty (HA/KA) between 2013 and 2018.

Patients and methods — The Dutch Foundation for Pharmaceutical Statistics, which provides national coverage of medication prescriptions, was linked to the Dutch Arthroplasty Register, which provides arthroplasty procedures. The opioid prescription rates were expressed as the number of defined daily dosages (DDD) and morphine milligram equivalent (MME) per person year (PY) and stratified for primary and revision arthroplasty. Amongst subgroups for age (< 75; ≥ 75 years) and sex for primary osteoarthritis arthroplasties, prescription rates stratified for opioid type (weak/strong) and prevalent preoperative opioid prescriptions (yes/no) were assessed.

Results — 48,051 primary KAs and 53,964 HAs were included, and 3,540 revision KAs and 4,118 HAs. In 2013, after primary KA 58% were dispensed ≥ 1 opioid within the first year; this increased to 89% in 2018. For primary HA these numbers increased from 38% to 75%. In KAs the prescription rates increased from 13.1 DDD/PY to 14.4 DDD/PY, mainly due to oxycodone prescriptions (2.9 DDD/PY to 7.3 DDD/PY), while tramadol decreased (7.3 DDD/PY to 4.6 DDD/PY). The number of MME/PY also increased (888 MME/PY to 1224 MME/PY). Similar changes were observed for HA and revision arthroplasties. Irrespective of joint, prescription of opioid medication increased over time, with highest levels in groups with preoperative opioid prescriptions while weak opioid prescriptions decreased.

Interpretation — In the Netherlands, between 2013 and 2018 postoperative opioid prescriptions after KA and HA increased, mainly due to increased oxycodone prescriptions with highest levels after surgeries with preoperative prescriptions.

Worldwide, approximately 70% of drug-induced deaths can be linked to opioids (1). While opioid use is lower in Europe than in the Unioted States, it also increased during the last decade (2-6). In the Netherlands between 2013 and 2017 an increase in opioid prescriptions was observed from 4.9% to 6.0% (3) and has plateaued since (7).

Compared with the general population, arthroplasty patients are more exposed to opioid medication, as opioids are frequently prescribed before and after arthroplasty (8). Furthermore, arthroplasty patients may continue to require pain medication as 9–20% perceive persistent pain after surgery (9).

Numbers on opioid prescriptions over time in Europe in arthroplasty patients are currently lacking. In the United States, prolonged opioid usage rates were between 25% and 40% in postoperative arthroplasty patients (10,11). Insight into prescription rates over time is needed as the lifetime risk for hip arthroplasty (HA) is estimated at 8–16%, and for knee arthroplasty (KA) 6–23% in Western countries (12,13). The consequences of opioid use may therefore be substantial and could have a major impact on healthcare systems and patients' lives.

To create awareness on opioid use we assessed the opioid prescription rates in Dutch HA and KA patients 1 year after surgery between 2013 and 2018. Moreover, we assessed these rates in high-risk subgroups, such as previous opioid users, the elderly, women, and patients with lower physical status (3). We conducted the subgroup analysis in osteoarthritis (OA) patients as this is the primary indication for KA/HA and also the group with likely preoperative pain.

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Patients and methods

Data sources

This study was based on 2 national databases. Data on HA and KA surgeries and most patient demographics was obtained from the Dutch Arthroplasty Register (LROI). The LROI covers all hospitals performing arthroplasties in the Netherlands. The completeness of total HA and KA (primary and revision), calculated using the hospital information system in which all operations performed in the Netherlands are registered, has been stable at > 95% since 2016 (14).

Pharmaceutical dispensing data was obtained from the Dutch Foundation for Pharmaceutical Statistics (SFK), which contains out-of-hospital prescriptions from > 95% of community pharmacies, including outpatient pharmacies. Individual-level opioid dispensing data was derived 1 year before and 1 year after arthroplasty, including Anatomic-Therapeutic-Chemical (ATC5) codes, dose, and number dispensed.

Datasets from Statistics Netherlands (CBS) were used to validate our results: opioid reimbursement data and hospital admission data. The CBS, specifically the hospital data (completeness > 97% since 2014) provides information on all operations in the Netherlands with the exception of operations performed in private hospitals. The dispensing of medication in CBS is provided on ATC4 level, which is limited to the chemical subgroup.

Data linkage

The deterministic linkage between LROI and SFK datasets was performed on a combination of birthyear, sex, 4-digit postcode, and surgery date together with the start of thromboprophylaxis prescribed around the surgery date (4 days before, 10 days after) as a proxy for surgery date (unavailable in the SFK). If an arthroplasty, registered in the LROI, matched with a patient, based on sex, birthyear, and 4-digit postcode in the SFK, also had thromboprophylaxis medication in the time-period around the surgical date of the arthroplasty, this patient was linked. Data linkage was performed by the SFK. All data were pseudonymized before they were received.

Study population

All primary and revision KA/HA surgeries between 2013 and 2018 were included, except patellofemoral KA. Revision surgery was defined as any change (insertion, replacement, or removal) of ≥ 1 components of the prosthesis. Exclusion criteria were: < 18 years, arthroplasties with administrative errors (survival wrongfully retrieved from medical record), or > 4,000 DDDs opioids prescribed.

Measures

Demographics

The following patient demographics were included: age, sex, BMI, current smoking status (yes/no), joint (knee/hip), OA as surgery indication (yes/no), ASA, and Charnley score. Socioeconomic status (SES) was based on individual 4-digit postcodes from SFK. SES originated from the 2014 and 2016 measurements of the Netherlands Institute for Social Research, based on income, education, and occupation of the Dutch inhabitants and was received from the SFK. SES scores were based on quintiles: very low (≤ –1.5), below average (–1.49 to –0.5), average (–0.49 to 0.49), above average (0.5 to 1.49), and very high (≥ 1.5).

Arthroplasty

The following prosthesis-related information was derived: procedure type (primary/revision), prosthesis type (total, resurfacing, hemi/unicondylar), fixation (cemented, uncemented, hybrid), and revision type (total, partial, removal, other).

Opioid usage

Opioid use before and after arthroplasty was defined as ≥ 1 dispensed opioid prescription at a Dutch pharmacy, either 1 year before or after surgery. The annual opioid prescription rate was expressed as defined daily doses (DDDs), and morphine milligram equivalent (MME) per person years (PYs) for the first year after arthroplasty. PYs were calculated for all arthroplasties performed per calendar year. PYs were counted for each arthroplasty until one year follow-up, or censored at death. DDDs were defined as the supplied dose divided by the average maintenance dose according to the WHO Collaborating Centre for Drug Statistics Methodology. MMEs were calculated by calculating the dosages of each opioid prescription multiplied by an MME conversion factor. If no MME/DDD existed for a certain opioid, it was not counted (DDD for codeine–paracetamol combination non-existent). All arthroplasties were stratified into opioid prevalent (≥ 1 opioid prescription 1 year before surgery) and opioid naive (no opioid prescription 1 year before surgery) arthroplasties. Codeine and tramadol were considered as weak opioids, all other opioids as strong. For primary arthroplasties, the number of prescriptions were categorized: 1 prescription, 2, 3, 4, 5, 6–10, 11–20, 21–50, and ≥ 50 prescriptions. As such, we could assess whether the number of prescriptions dispensed per surgery or the pills/DDDs/MMEs per prescription changed. Multiple prescriptions on the same date were counted as 1.

Data analysis

All analyses were stratified for KA and HA. Characteristics of the LROI population and the linked arthroplasties were compared to assess representativeness. For continuous variables the standardized mean differences (SMD) were calculated; SMD > 0.1 was considered a meaningful difference (15).

Descriptive statistics were used to assess yearly opioid prescriptions after all arthroplasties annually from 2013 to 2018. The proportion of patients with ≥ 1 opioid prescription after surgery was calculated. Opioid prescription rates of the 5 most

frequent prescribed opioids were expressed as DDD/PY and MME/PY for both primary and revision arthroplasties. The 95% confidence intervals (CI) were calculated.

For each category regarding the number of prescriptions per surgery we calculated the following per calendar year: the number and percentage of arthroplasties, the percentage of opioid prescriptions, the median number of pills prescribed (interquartile range), and the DDDs/PY and MME/PY.

The opioid prescription rates were shown in subgroups: men/women, age (< 75 years/≥ 75 years (based on the average age in this population and the expected age of death)), and ASA classification (ASA I/ASA II/ASA III–IV). Weak and strong opioids, and prevalent and opioid naive arthroplasties were shown separately.

A sensitivity analysis was performed on primary index arthroplasties. When a patient received > 1 arthroplasty, only the first arthroplasty was included. Within this group, the yearly opioid prescription rates were shown separately for the 5 most frequently prescribed opioids.

Our study results were validated by assessing the proportion of opioid users in the year of surgery within the CBS (Appendix, see Supplementary data).

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

Ethics, funding, data sharing, and potential conflicts of interest

Approval by an ethics committee was waived by the Medical Ethics Committee Leiden–Den Haag–Delft (reference number: G19.018). This work was funded by the van Rens Foundation (Project number:VRF2019-002). Data cannot be shared publicly because of confidentiality. Data is available from the SFK and LROI Institutional

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Results

Population

368,471 primary arthroplasties were performed between 2013 and 2018, and 31,606 revisions. Arthroplasties that could not be linked on patient postcode, or on low-molecular weight heparin, or only on hospital pharmacy prescriptions, were excluded. Our study population included 48,051 primary KAs, 53,964 primary HAs, 3,540 revision KAs and 4,118 HAs (Figure 1). This population was somewhat younger (mean (SD): 68 (10) versus 71 (10) years), more often had OA as indication (88% versus 82%), and was somewhat healthier, indicated by the ASA classification, than unlinked arthroplasties (Tables 1–2, see Supplementary data).

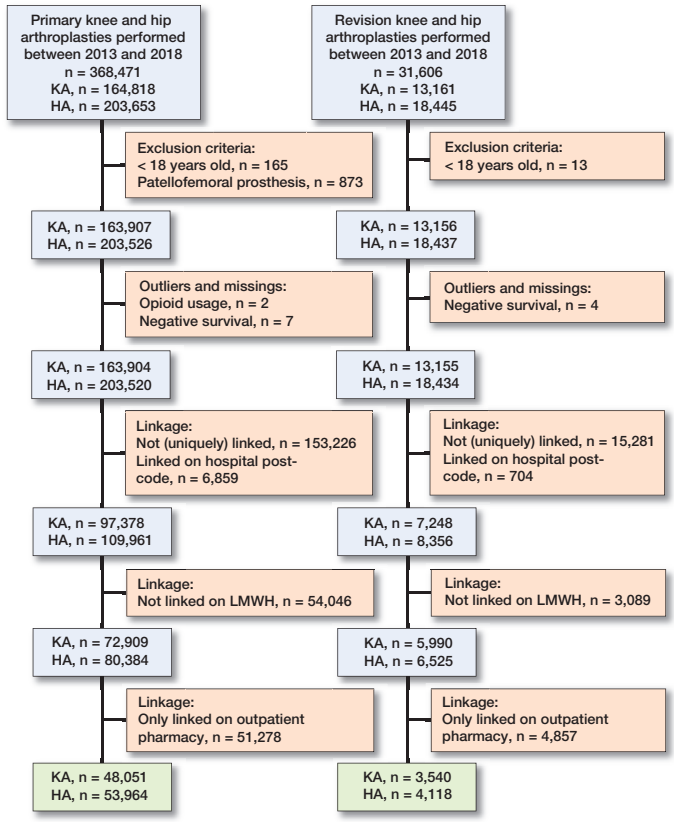

Figure 1. Flowchart showing data selection. KA = knee arthroplasty; HA = hip arthroplasty.

Table 3 shows the population characteristics for arthroplasties with a known indication for surgery. Arthroplasties with unknown or missing indication (n = 246 hips; n = 228 knees) were not shown. The mean age for KA for OA was 67 (9.1) versus 62 (12) in KAs for another indication. HAs for OA were performed at a mean age of 69 (9.8), versus 70 (15) in HAs for other indications. About 60% of arthroplasties were performed in women. In the OA group, 26% of arthroplasties had prevalent opioid prescriptions; this was 30% amongst other indications. Most arthroplasties were total arthroplasties.

The mean age for revision KA was 66 (9.6) and for HA it was 70 (11). Some 60% of the revision arthroplasties were performed in women. For revision KA almost 50% were a total revision; for revision HA this was 20% (Table 4, see Supplementary data).

Opioid prescriptions over time

In primary KA, the proportion of patients with ≥ 1 opioid prescription increased from 58% (CI 57–59%) in 2013 to 89% (CI 88–90%) in 2018. In primary HA this proportion increased from 38% (CI 37–40%) to 75% (CI 74–76%). The 5 most often prescribed opioids were oxycodone, tramadol, morphine, fentanyl, and buprenorphine. All other opioids were: codeine, tapentadol, hydromorphone, pethidine, piritramide, pentazocine, and nicomorphine. In primary KA opioid pre-

Table 3. Population characteristics stratified for primary hip and knee arthroplasties and diagnosis (osteoarthritis vs. non-osteoarthritis). Values are count (%) unless otherwise specified

	Knee		Hip	
	Osteo-arthritis n = 46,109	Other indication n = 1,714	Osteo-arthritis n = 42,891	Other indication n = 10,827
Demographics				
Age, mean (SD)	67 (9.1)	62 (12)	69 (9.8)	70 (15)
missing	0 (0)	0 (0)	0 (0)	0 (0)
Female sex	27,321 (59)	1,044 (61)	26,270 (61)	6,756 (62)
missing	0 (0)	0 (0)	0 (0)	0 (0)
BMI [a]				
≤ 18.5	60 (0.1)	21 (1.3)	244 (0.6)	416 (4.3)
18.5–25	7,052 (16)	424 (26)	12,418 (31)	4,647 (48)
25–30	18,166 (42)	642 (40)	17,673 (44)	3,358 (34)
30–40	16,921 (39)	480 (30)	9,677 (24)	1,295 (13)
> 40	1,486 (3.4)	44 (2.7)	457 (1.1)	51 (0.5)
missing	2,424 (5.3)	103 (6.0)	2,422 (5.6)	1,060 (9.8)
ASA class				
I	7,082 (15)	249 (15)	8,084 (19)	1,418 (13)
II	31,430 (68)	1,116 (65)	28,172 (66)	5,438 (50)
III–IV	7,490 (16)	347 (20)	6,548 (15)	3,933 (37)
missing	107 (0.2)	2 (0.1)	87 (0.2)	38 (0.4)
Socioeconomic status				
very low	6,156 (13)	263 (15)	4,845 (11)	1,545 (14)
below average	8,957 (20)	318 (19)	7,843 (18)	2,325 (22)
average	17,460 (38)	635 (37)	16,274 (38)	4,054 (38)
above average	11,209 (25)	416 (24)	11,343 (27)	2,388 (22)
very high	2,060 (4.5)	78 (4.6)	2,383 (5.6)	460 (4.3)
missing	267 (0.6)	4 (0.2)	203 (0.5)	55 (0.5)
Smoking [a]	4,104 (9.9)	257 (17)	4,504 (12)	1,491 (16)
missing	4,618 (10)	188 (11)	4,393 (10)	1,244 (12)
Charnley classification [a]				
A	17,848 (44)	682 (45)	17,300 (46)	4,023 (41)
B1	14,029 (34)	355 (23)	11,459 (30)	879 (9.0)
B2	7,832 (19)	153 (10)	8,224 (22)	701 (7.2)
C	933 (2.3)	119 (7.8)	802 (2.1)	246 (2.5)
not applicable	114 (0.3)	218 (14)	120 (0.3)	3,912 (40)
missing	5,353 (12)	187 (11)	4,986 (12)	1,066 (9.8)
Prosthesis-related				
Type of prosthesis				
total prosthesis	40,987 (89)	1,626 (95)	42,686 (100)	6,368 (59)
hemi/unicondylar	5,112 (11)	80 (4.7)	186 (0.4)	4,433 (41)
resurfacing	–	–	4 (0.0)	–
other	9 (0.0)	8 (0.5)	5 (0.0)	18 (0.2)
missing	1 (0)	0 (0)	10 (0)	8 (0.1)
Fixation				
cemented	40,579 (88)	1,540 (90)	9,492 (22)	5,230 (48)
uncemented	4,277 (9.3)	107 (6.2)	29,531 (69)	4,680 (43)
hybrid	1,185 (2.6)	65 (3.8)	3,811 (8.9)	900 (8.4)
missing	68 (0.1)	2 (0.1)	57 (0.1)	17 (0.2)
Opioid use before surgery				
prevalent users	12,064 (26)	574 (34)	11,639 (27)	3,254 (30)
missing	0 (0)	0 (0)	0 (0)	0 (0)

[a] available since 2014
Charnley classification: A = 1 joint affected with osteoarthrosis; B1= 2 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).

scription rates increased from 13.1 DDDs/PY (CI 11.1–15.0) to 14.4 DDDs/PY (CI 12.9–15.9) between 2013 and 2018. Oxycodone increased from 2.9 DDDs/PY (CI 2.0–3.8) to 7.3 DDDs/PY (CI 6.2–8.4) between 2013 and 2018, while prescription of tramadol decreased from 7.3 DDDs/PY (CI 5.9–8.7) to 4.6 DDDs/PY (CI 3.8–5.5). All other opioids remained relatively stable (Figure 2). When opioid prescription was expressed as MME/PY similar patterns were found (Figure 2).

In primary HA similar patterns were found. Opioid prescription rates increased from 9.1 DDDs/PY (CI 7.5–10.6) to 11.6 DDDs/PY (CI 10.3–12.9) between 2013 and 2018. Oxycodone increased from 2.2 DDDs/PY (CI 1.5–3.0) in 2013, to 4.8 DDDs/PY (CI 4.0–5.7) in 2018, and fentanyl increased from 1.5 DDDs/PY (CI 0.9–2.2) to 3.1 DDDs/PY (CI 2.4–3.7). Tramadol decreased from 4.7 DDDs/PY (CI 3.6–5.8) in 2013, to 2.9 DDDs/PY (CI 2.2–3.5) in 2018; all other opioids remained relatively stable. When opioid prescription was expressed as MME/PY similar patterns were found.

In the revision arthroplasty population similar changes were found, albeit at higher opioid prescription rates and with slightly different increase patterns than in their respective primary counterparts (Figures 3–4, see Supplementary data).

Opioids per prescription dispensing category

After KA the percentage of opioid prescriptions within each prescription dispensing category remained the same. However, in parallel with the higher proportion of opioid users, the number of arthroplasty surgeries with prolonged opioid prescriptions increased (Table 5). Intermittent years are shown in Table 6 (see Supplementary data).

After HA, more often 1 or 2 prescriptions were dispensed. Comparing 2018 with 2013, the higher prescription categories were stable, or decreased slightly (Table 7). In both KA and HA DDDs/PY decreased between 2013 and 2018, while MME increased in most categories. This implies a decrease in the number of dosages prescribed, but an increase in the opioid potency. Intermittent years are shown in Table 8 (see Supplementary data).

Furthermore, despite an increasing number of prescriptions, the median number of pills remained similar. However, the MME/PY increased more progressively between the 3rd and the 4th prescription compared with the earlier prescriptions. This was present in both KA and HA and suggests a difference between early postoperative and long-term users.

Opioid use over time in subgroups

Figure 5 shows the prescribed opioids over time amongst primary KA for OA in distinct subgroups for age, sex, and ASA classification. In most subgroups, strong opioid prescription

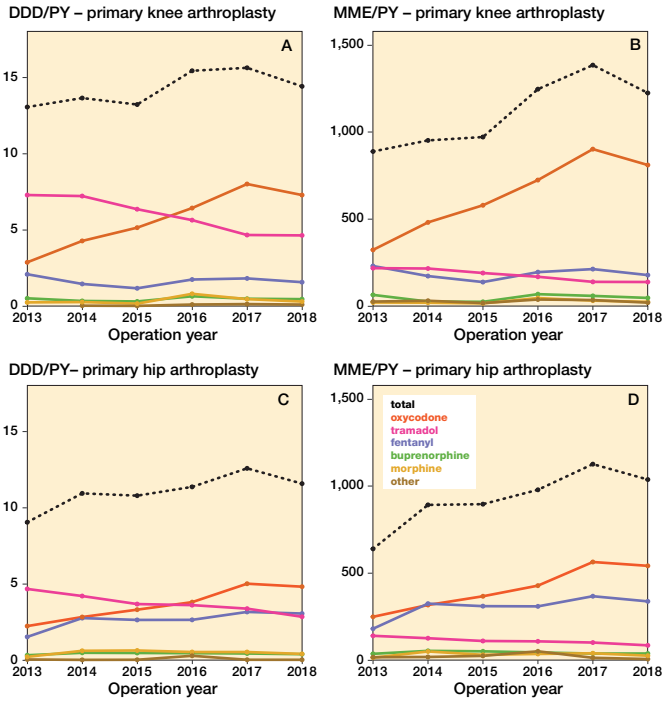

Figure 2. Opioid prescriptions over time in different opioid types in defined daily dosages and morphine milligram equivalent amongst primary knee and hip arthroplasties per person year. DDD = defined daily dosage, MME = morphine milligram equivalent, PY = person year. DDDs for codeine–paracetamol combination were non-existent.

increased, with the exception of the prevalent opioid male arthroplasty group. Weak opioids decreased in all subgroups. The ASA III–VI groups received more opioids in both DDD/PY and MME/PY. The prevalent opioid group had a higher overall prescription rates than the naive group (e.g., mean MME/PY prevalent opioid group < 75 years (strong opioids) over time: 2,339 MME/PY (CI 2,320–2,357); mean MME/PY opioid naive opioid group < 75 years (strong opioids) over time 447 MME/PY (CI 442–453)). The opioid prescription rates in the total KA OA populations are shown in Figure 6 (see Supplementary data).

In primary HA for OA similar patterns can be observed. In most subgroups, strong opioids increased, except for the subgroup of prevalent opioid group ≥ 75 years old, which remained stable (Figure 7). The highest opioid exposure was found amongst the prevalent opioid group (e.g., mean MME/PY prevalent opioid group < 75 years (strong opioids) over time: 1,740 MME/PY (CI 1,723–1,758); mean MME/PY opioid naive group < 75 years (strong opioids) over time 191 MME/PY (CI 187–194)). Weak opioid exposure decreased in all subgroups. The opioid prescription rates in the total HA OA populations are shown in Figure 6 (see Supplementary data).

Sensitivity analysis

The sensitivity analysis yielded similar results to our main analysis (Tables 9–10 and Figure 8, see Supplementary data).

Table 5. Opioid prescriptions per prescription dispensing category after primary knee arthroplasty

Opioid prescription category	Operation year	n	Yearly arthro-plasties (%)	Yearly arthroplasties with opioid prescription (%)	Median prescription moment (Q1–Q3)	Median supply (Q1–Q3)	DDDs/PY	MME/PY
1 prescription	2013	1,346	28	47	4 (3–8)	21 (15–30)	3.9	228
	2018	3,907	43	48	2 (1–2)	20 (11–30)	2.8	269
2 prescriptions	2013	541	11	19	20 (12–16)	30 (15–30)	8.4	468
	2018	1,564	17	19	13 (7–34)	20 (12–30)	6.0	544
3 prescriptions	2013	261	5.3	9.2	38 (22–17)	30 (20–30)	16	894
	2018	776	8.6	9.6	27 (15–79)	20 (14–30)	10	888
4 prescriptions	2013	184	3.8	6.5	67 (35–168)	30 (20–42)	28	1,461
	2018	506	5.6	6.3	44 (24–122)	20 (14–30)	17	1,378
5 prescriptions	2013	116	2.4	4.1	88 (49–180)	30 (20–56)	35	1,620
	2018	318	3.5	3.9	66 (35–162)	28 (15–30)	26	2,030
6–10 prescriptions	2013	243	5.0	8.5	141 (85–236)	30 (20–60)	61	3,779
	2018	632	7.0	7.8	124 (63–224)	30 (15–40)	50	3,690
11–20 prescriptions	2013	122	2.5	4.3	220 (138–290)	30 (21–60)	125	9,245
	2018	286	3.2	3.5	213 (135–288)	30 (16–60)	113	9,749
21–50 prescriptions	2013	23	0.5	0.8	231 (172–296)	30 (14–60)	361	37,047
	2018	71	0.8	0.9	270 (204–317)	30 (14–45)	243	22,913
> 50 prescriptions	2013	11	0.2	0.4	316 (270–346)	15 (7–30)	224	18,027
	2018	12	0.1	0.1	315 (269–347)	20 (14–30)	337	35,540

Median supply in number of pills supplied per prescription category per prescription; Yearly arthroplasties (%): among arthroplasties within an operation year, percentage of arthroplasties within a certain prescription category; Yearly arthroplasties with opioid prescription: among patients with postoperative opioids the percentage of arthroplasties within a certain prescription dispensing category; Q1–Q3 = 1st to 3rd quartile; DDD = Defined Daily Dosage, MME = Morphine Milligram Equivalent.

Table 7. Opioid prescriptions per prescription dispensing category after primary hip arthroplasty

Opioid prescription category	Operation year	n	Yearly arthro-plasties (%)	Yearly arthroplasties with opioid prescription (%)	Median prescription moment (Q1–Q3)	Median supply (Q1–Q3)	DDDs/PY	MME/PY
1 prescription	2013	1,168	21	56	3 (3–18)	22 (15–30)	4.0	201
	2018	4,583	47	63	1 (1–3)	18 (10–28)	2.4	229
2 prescriptions	2013	327	5.9	16	44 (15–156)	30 (20–39)	11	553
	2018	1,186	12	16	19 (8–105)	20 (10–30)	5.9	508
3 prescriptions	2013	172	3.1	8.2	94 (31–193)	30 (20–30)	17	879
	2018	446	4.6	6.1	50 (20–146)	20 (10–30)	11	931
4 prescriptions	2013	87	1.6	4.1	94 (49–223)	30 (15–60)	35	1,834
	2018	279	2.9	3.8	50 (34–187)	20 (14–30)	19	1,427
5 prescriptions	2013	70	1.3	3.3	148 (70–240)	30 (20–60)	48	2,285
	2018	133	1.4	1.8	109 (48–205)	24 (13–40)	37	2,468
6–10 prescriptions	2013	160	2.9	7.6	187 (97–268)	30 (20–60)	78	5,144
	2018	356	3.7	4.9	154 (82–245)	30 (14–36)	56	4,408
11–20 prescriptions	2013	77	1.4	3.7	217 (134–286)	30 (10–60)	146	12,133
	2018	204	2.1	2.8	208 (138–290)	30 (12–60)	151	14,078
21–50 prescriptions	2013	37	0.7	1.8	273 (216–320)	21 (14–30)	233	23,162
	2018	83	0.9	1.1	267 (202–315)	30 (14–60)	300	28,272
> 50 prescriptions	2013	4	0.1	0.2	350 (339–358)	14 (7–28)	377	34,445
	2018	13	0.1	0.2	275 (189–337)	14 (6–21)	386	45,342

For footnotes: see Table 2.

Discussion

We found that from 2013 to 2018 opioid prescription rates after both primary and revision surgery increased in the first year after arthroplasty. The increase was present for strong opioids, was highest in the prevalent opioid group, and was independent of operated joint. Additionally, after KA, the number of prescriptions did not change. However, it did change after HA. The number of dosages decreased, while the potency of the prescribed opioids increased in most prescription categories.

The increase in opioid prescriptions is consistent with previous literature concerning the general population (2-6). Amongst the arthroplasty population the results are heterogeneous. In the United States, postoperative prevalence ranged between 60% and 90% (10,11,16,17). In Europe, little has been published on this prevalence in recent studies. A Finnish study found 26% of HA and 40% of KA with ≥ 1 mild opioid, and 1.5% of HA and 3.3% of KA with ≥ 1 strong opioid in the first postoperative year between 2002 and 2013 (18). The difference in found prevalence might be due to the earlier timeframe and possible legislative differences. To our knowledge, only one recent study assessed the prevalence over time, and found a less steep increase in opioid prescriptions (17). However, these results apply to the US population and with variable results in postoperative prevalence might not be comparable to our population. Furthermore, recently, preoperative opioid use was linked to continued postoperative use (19), which would also lead to higher MME and DDD as was found in our study. It would therefore be important that future research focuses on the preoperative opioid prescriptions over time, to assess changes before arthroplasty.

The increase in opioid prescriptions could be explained by several factors. First, enhanced recovery after arthroplasty surgery, where patients sometimes are discharged on the day of surgery (20), which implies immediate postoperative pain control. For that matter several measures (e.g., multimodal analgesia, wound care) have been altered to reduce length of stay. Second is the focus on adequate postoperative pain relief during the first 72 hours after surgery (21). Since 2009, this has been an important benchmark for hospital quality of care in the Netherlands, which may encourage postoperative opioid prescribing. Furthermore, oxycodone was reintroduced in postoperative guidelines in 2013 (22), possibly explaining the increase seen in our study.

With increased opioid prescriptions, more people are exposed to opioid medication. Hence more people are at risk of prolonged opioid use with consequently possible adverse events (23). We observed that, with increasing postoperative opioid prescriptions, the number of arthroplasties with multiple prescriptions also increased over time. Additionally, the largest increase in opioid prescriptions was found in the prevalent opioid group, which has been linked to less pain relief after arthroplasty (24). This subsequently leads to unfavorable outcomes after surgery, which again poses an extra risk for prolonged postoperative use; thus a vicious circle of pain and increased opioid medication is created. While more arthroplasty patients were dispensed opioid medication, we found that in each prescription category the DDD decreased. However, the potency increased, exemplified by the shift from tramadol to oxycodone. Oxycodone is a stronger opioid, which might lead to more chronic users (25). We believe that orthopedic surgeons, as first prescribers, and general practi-

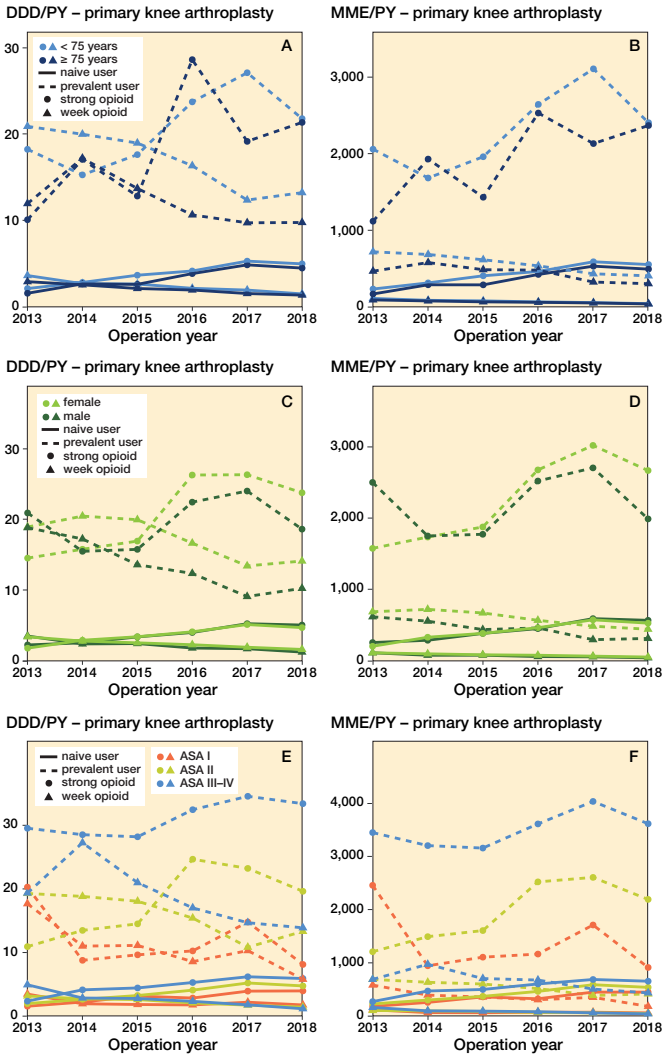

Figure 5. Opioid prescriptions in primary knee arthroplasties with an osteoarthritis indication stratified for opioid strength, age, user type, sex, and ASA classification. In MMEs codeine–paracetamol combination and tramadol were considered weak opioids, in DDDs tramadol was considered a weak opioid as DDDs for codeine–paracetamol combination were non-existent. For abreviations, see Figure 2.

Figure 7. Opioid prescriptions in primary hip arthroplasties with an osteoarthritis indication stratified for opioid strength, age, user type, sex, and ASA classification. For symbols, see Figure 3 and for abbreviations, see Figure 2.

tioners, should be cautious in their opioid prescribing. Known preoperative opioid users should be closely monitored and, if possible, helped in opioid weaning.

A major strength of our study is that national databases were used with arthroplasty coverage and out-of-hospital pharmaceutical prescriptions. Furthermore, we were able to compare MMEs and DDDs, allowing a precise evaluation of opioid prescriptions. Some limitations should also be considered. First, the SFK is a prescription register, so a dispensed drug may not have been consumed. Furthermore, it holds no information on prescriptions during hospitalization, thereby underestimating the postoperative opioid prescription prevalence. Also, because the reason for the prescription was unavailable, opioids could have been prescribed for indications other than arthroplasty. However, we aimed to describe the opioid usage irrespective of its cause. Related to our linkage, opioid prescriptions were linked to arthroplasties, instead of persons, resulting in double-counted prescriptions if a second surgery occurred within one year of the index surgery. However, the sensitivity analysis in which only the index arthroplasty was included yielded similar results, leaving us to conclude this effect was trivial. Additionally, the datasets were not linked on a unique identifier, but on a combination of identifiers. As such, it remains a probability linkage. Furthermore, only patients who used LMWH as thromboprophylaxis in the period 3 days before and 10 days after arthroplasty were included. As such, the patients using DOACs as antithrombotic treatment for their arthroplasty instead of LMWH were not included. This could have led to bias as patients who chronically use DOACs have an indication for effective anticoagulation that could be associated with

opioid use. We were able to link 28% of primary and 24% of revision surgeries. This could have influenced generalizability to the arthroplasty population as a whole. Our linked population appeared to be somewhat younger and healthier, possibly due to the unavailability of pharmaceutical data for nursing home residents. However, our results were externally validated and showed relatively similar results.

In conclusion, the proportion of KA and HA patients with ≥ 1 postoperative opioid prescription increased between 2013 and 2018 in the Netherlands, with the highest increase in prescription rates in arthroplasties with a preoperative opioid prescription. The increase was mainly due to a shift toward oxycodone. Future research should assess the possible effects of this increase as well as preoperative opioid prescriptions to ensure the best quality of care for arthroplasty patients.

HvB and MG wrote the original draft. Conceptualization and funding acquisition was performed by RN, WL, AD, and MG. LvS provided data curation for the LROI data.. Formal analyses and visualization were performed by HvB. Methodology was done by HvB, RN, FR, MB, EvD and MG. Supervision was done by RN and MG. All authors interpreted the data and contributed to the final manuscript.

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Supplementary data

Table 1. The primary arthroplasty study population compared to not linked population. Values are count (%) unless otherwise specified

	Not linked n = 265,409	Study population n = 102,015	SMD [a]
Knee arthroplasty	115,853 (44)	48,051 (47)	
Female sex	176,038 (66)	61,696 (61)	
Age, mean (SD)	70.2 (10)	67.9 (10.4)	0.22
BMI [b]			
missing	35,236 (13)	6,135 (6.0)	
≤ 18.5	2,494 (1.1)	744 (0.8)	
18.5–25	65,098 (28)	24,607 (26)	
25–30	93,347 (41)	39,999 (42)	
30–40	64,177 (28)	28,486 (30)	
> 40	5,057 (2.2)	2,044 (2.1)	
Smokers [b]	22,084 (10)	10,392 (11)	
missing	44,858 (17)	10,634 (10)	
Osteoarthritis	219,544 (84)	89,000 (88)	
missing	2,723 (1.0)	474 (0.5)	
Charnley classification [b]			
missing	47,901 (18)	11,919 (12)	
A	92,763 (43)	39,921 (44)	
B1	60,970 (28)	26,765 (30)	
B2	41,345 (19)	16,937 (19)	
C	6,291 (2.9)	2,107 (2.3)	
not applicable	16,139 (7.4)	4,366 (4.8)	
ASA classification			
missing	2,134 (0.8)	345 (0.3)	
I	39,651 (15)	16,900 (17)	
II	166,896 (63)	66,406 (65)	
III–IV	56,728 (22)	18,364 (18)	

[a] Standardized Mean Difference between the study population and non-linked population.
Charnley A = One joint affected with osteoarthrosis; B1= 2 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).
[b] available since 2014.

Table 2. The revision arthroplasty study population compared to not linked population. Values are count (%) unless otherwise specified

	Not linked n = 23,935	Study population n = 7,658	SMD [a]
Knee arthroplasty	9,616 (40.2)	3,540 (46.2)	
Female sex	15,637 (65.3)	4,625 (60.4)	
Age, mean (SD)	70.9 (11)	68.1 (11)	0.26
BMI [b]			
missing	3,525 (15)	526 (6.9)	
≤ 18.5	236 (1.2)	71 (1.0)	
18.5–25	5,709 (28)	1,780 (25)	
25–30	7,987 (39)	2,953 (41)	
30–40	5,932 (29)	2,170 (30)	
> 40	546 (2.7)	158 (2.2)	
Smokers [b]	1,937 (9.8)	878 (13)	
missing	4,216 (18)	809 (11)	
Charnley classification [b]			
missing	5,197 (22)	1,150 (15)	
A	8,808 (47)	3,155 (49)	
B1	2,764 (15)	1,026 (16)	
B2	4,715 (25)	1,623 (25)	
C	1,169 (6.2)	341 (5.2)	
not applicable	1 282 (6.8)	363 (5.6)	
Type of revision			
missing	249 (1.0)	17 (0.2)	
total revision	7,632 (32)	2,495 (33)	
partial revision	15,954 (67)	5,134 (67)	
other	100 (0.4)	12 (0.2)	
ASA classification			
missing	693 (2.9)	126 (1.6)	
I	2,449 (11)	877 (12)	
II	13,962 (69)	4,863 (65)	
III–IV	6,831 (29)	1,792 (24)	

For Footnotes, see Table 1.

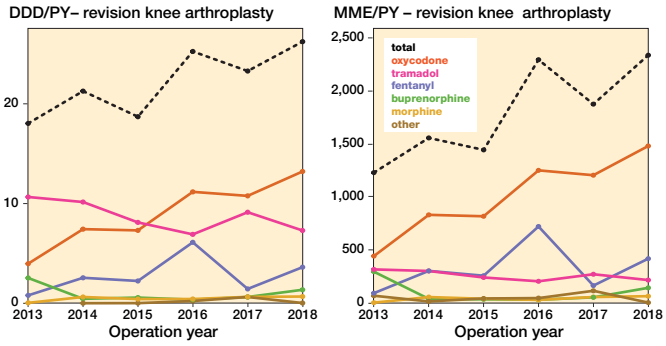


Figure 3. Opioid prescriptions over time in different opioid types in daily defined dosages (DDD) and morphine milligram equivalent (MME) amongst revision knee arthroplasty per person year (PY). DDDs for codeine-paracetamol combination were non-existent.

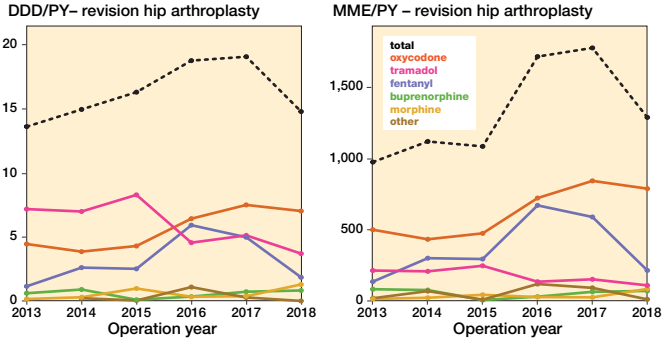


Figure 4. Opioid prescriptions over time in different opioid types in daily defined dosages (DDD) and morphine milligram equivalent (MME) amongst revision hip arthroplasty per person year (PY). DDDs for codeine-paracetamol combination were non-existent.

Table 4. Population characteristics for hip and knees revision arthroplasties. Values are count (%) unless otherwise specified

	Knee n = 3,540	Hip n = 4,118
Demographics		
Age, mean (SD)	66 (9.6)	70 (11)
missing	0 (0)	0 (0)
Female sex	2,177 (62)	2,448 (59)
missing	0 (0)	0 (0)
BMI [b]		
≤ 18.5	5 (0.2)	66 (1.7)
18.5–25	504 (15)	1,276 (33)
25–30	1,306 (40)	1,647 (43)
30–40	1,361 (41)	809 (21)
> 40	118 (3.6)	40 (1.0)
missing	246 (6.9)	280 (6.8)
ASA score		
I	417 (12)	460 (13)
II	2,334 (67)	2,529 (2.4)
III–IV	728 (21)	1,046 (26)
missing		
Socioeconomic status		
very low	540 (15)	486 (12)
below average	709 (20)	853 (21)
average	1,309 (37)	1,570 (38)
above average	821 (23)	1,009 (25)
very high	148 (4.2)	185 (4.5)
missing	13 (0.4)	15 (0.4)
Smoking [b]	403 (13)	475 (13)
missing	340 (9.6)	469 (11)
Charnley classification [b]		
A	1,560 (52)	1,595 (46)
B1	566 (19)	460 (13)
B2	590 (20)	1,033 (30)
C	155 (5.1)	186 (5.3)
not applicable	160 (5.3)	203 (5.8)
missing	509 (14)	641 (16)
Prosthesis-related		
Type of revision		
total revision	1,670 (47)	825 (20)
partial revision	1,745 (50)	3,276 (80)
other	–	12 (0.3)
removal	113 (3.2)	NA
missing	12 (0.3)	5 (0.1)
Fixation		
cemented	2,890 (82)	1,835 (45)
uncemented	455 (13)	1,836 (45)
hybrid	76 (2.2)	428 (10.4)
not applicable		95 (2.7)
missing	24 (0.7)	19 (0.5)
Opioid use before surgery		
prevalent users	1,386 (39)	1,449 (35)
missing	0 (0)	0 (0)

For Footnotes, see Table 1.

Table 6. Opioid prescriptions per prescription dispensing category after primary knee arthroplasty

Opioid prescription category Operation year	n	Yearly arthro-plasties (%)	Yearly arthroplasties with opioid prescription (%)	Median prescription moment (Q1–Q3)	Median supply (Q1–Q3)	DDDs/PY	MME/PY
1 prescription							
2013	1,346	28	47	4 (3–8)	21 (15–30)	3.9	228
2014	2,355	28	46	4 (2–8)	20 (14–30)	3.7	254
2015	3,019	34	49	3 (2–5)	20 (10–30)	3.2	242
2016	2,989	37	48	2 (1–4)	20 (10–30)	3.1	254
2017	3,396	39	46	2 (1–3)	20 (12–30)	3.2	300
2018	3,907	43	48	2 (1–2)	20 (11–30)	2.8	269
2 prescriptions							
2013	541	11	19	20 (12–60)	30 (15–30)	8.4	468
2014	976	12	19	19 (11–60)	22 (15–30)	8.3	567
2015	1,149	13	19	16 (9–52)	20 (14–30)	7.3	508
2016	1,158	14	18	15 (9–45)	20 (14–30)	7.2	567
2017	1,400	16	19	14 (8–45)	20 (14–30)	7.1	617
2018	1,564	17	19	13 (7–34)	20 (12–30)	6.0	544
3 prescriptions							
2013	261	5.3	9.2	38 (22–117)	30 (20–30)	16	894
2014	496	5.9	9.7	40 (21–111)	30 (16–30)	15	916
2015	593	6.8	9.6	34 (18–99)	20 (14–30)	12	858
2016	603	7.4	9.6	30 (17–93)	20 (14–30)	12	905
2017	739	8.4	10	28 (15–87)	20 (14–30)	11	973
2018	776	8.6	9.6	27 (15–79)	20 (14–30)	10	888
4 prescriptions							
2013	184	3.8	6.5	67 (35–168)	30 (20–42)	28	1,461
2014	310	3.7	6.1	69 (34–158)	30 (20–42)	31	1,521
2015	344	3.9	5.5	55 (28–143)	30 (15–30)	22	1,325
2016	357	4.4	5.7	52 (27–144)	25 (14–30)	22	1,622
2017	444	5.1	6.1	49 (26–140)	25 (15–30)	18	1,465
2018	506	5.6	6.3	44 (24–122)	20 (14–30)	17	1,378
5 prescriptions							
2013	116	2.4	4.1	88 (49–180)	30 (20–56)	35	1,620
2014	231	2.8	4.5	98 (46–194)	30 (20–42)	33.	2,010
2015	241	2.8	3.9	76 (38–175)	30 (15–42)	29	1,750
2016	266	3.3	4.2	77 (39–174)	28 (15–32)	42	3,398
2017	299	3.4	4.1	74 (36–182)	28 (15–30)	29	2,316
2018	318	3.5	3.9	66 (35 -162)	28 (15–30)	26	2,030
6–10 prescriptions							
2013	243	5.0	8.5	141 (85–236)	30 (20–60)	61	3,779
2014	463	5.5	9.0	158 (85–251)	30 (20–60)	64	4,069
2015	546	6.2	8.8	139 (72–240)	30 (20–60)	50	3,286
2016	547	6.7	8.7	140 (73–231)	30 (15–42)	49	3,712
2017	643	7.4	8.8	130 (67–222)	30 (15–40)	48	3,616
2018	632	7.0	7.8	124 (63–224)	30 (15–40)	50	3,690
11–20 prescriptions							
2013	122	2.5	4.3	220 (138–290)	30 (21–60)	125	9,245
2014	223	2.7	4.4	216 (140–293)	30 (20–60)	127	10,379
2015	229	2.6	3.7	218 (138–291)	30 (20–60)	127	10,100
2016	266	3.3	4.2	223 (139–296)	30 (20–60)	117	9,847
2017	318	3.6	4.3	213 (140–291)	30 (20–60)	112	10,546
2018	286	3.2	3.5	213 (135–288)	30 (16–60)	113	9,749
21–50 prescriptions							
2013	23	0.5	0.8	231 (172–296)	30 (14–60)	361	37,047
2014	54	0.7	1.1	260 (202–310)	28 (14–42)	195	16,379
2015	74	0.8	1.2	266 (207–315)	30 (15–50)	219	19,676
2016	80	1.0	1.3	259 (197–310)	30 (14–56)	263	22,629
2017	69	0.8	0.9	273 (220–317)	30 (20–60)	307	29,574
2018	71	0.8	0.9	270 (204–317)	30 (14–45)	243	22,912
> 50 prescriptions							
2013	11	0.2	0.4	316 (270–346)	15 (7–30)	224	18,027
2014	15	0.2	0.3	332 (300–351)	21 (14–21)	283	23,359
2015	12	0.1	0.2	342 (323–353)	21 (14–28)	271	20,375
2016	13	0.2	0.2	344 (330–355)	14 (14–28)	269	23,421
2017	11	0.1	0.2	346 (329–357)	14 (7–18)	314	42,654
2018	12	0.1	0.1	315 (269–347)	20 (14–30)	337	35,540

Median supply in number of pills supplied per prescription category per prescription; Yearly arthroplasties (%): among arthroplasties within an operation year, percentage of arthroplasties within a certain prescription category; Yearly arthroplasties with opioid prescription: among patients with postoperative opioids the percentage of arthroplasties within a certain prescription dispensing category; Q1–Q3 = 1st to 3rd quartile; DDD = Defined Daily Dosage, MME = Morphine Milligram Equivalent.

Table 8. Opioid prescriptions per prescription dispensing category after primary hip arthroplasty

Opioid prescription category Operation year	n	Yearly arthro-plasties (%)	Yearly arthroplasties with opioid prescription (%)	Median prescription moment (Q1–Q3)	Median supply (Q1–Q3)	DDDs/PY	MME/PY
1 prescription							
2013	1,168	21	56	3 (3–18)	22 (15–30)	4.0	201
2014	2,297	25	57	2 (2–10)	20 (14–30)	3.6	236
2015	3,027	31	59	2 (2–6)	20 (10–30)	2.8	219
2016	3,421	36	60	1 (1–5)	20 (10–30)	2.9	251
2017	4,023	41	59	1 (1–4)	20 (10–30)	2.7	255
2018	4,583	47	63	1 (1–3)	18 (10–28)	2.4	229
2 prescriptions							
2013	327	5.9	16	44 (15–156)	30 (20–39)	11	553
2014	629	6.7	16	36 (14–139)	28 (15–30)	9.2	580
2015	785	7.9	15	29 (11–124)	20 (12–30)	7.8	525
2016	878	9.2	15	26 (10–129)	20 (12–30)	6.9	557
2017	1,104	11	16	20 (9–110)	20 (12–30)	6.4	551
2018	1,186	12	16	19 (8–105)	20 (10–30)	5.9	508
3 prescriptions							
2013	172	3.1	8.2	94 (31–193)	30 (20–30)	17	879
2014	304	3.2	7.5	76 (29–188)	30 (14–30)	19	1,274
2015	376	3.8	7.3	66 (24–161)	20 (14–30)	15	954
2016	349	3.6	6.1	58 (23–170)	20 (14–30)	14	1,048
2017	457	4.6	6.8	55 (20–157)	20 (13–30)	13	985
2018	446	4.6	6.1	50 (20–146)	20 (10–30)	11	931
4 prescriptions							
2013	87	1.6	4.1	94 (49–223)	30 (15–60)	35	1,834
2014	170	1.8	4.2	76 (49–204)	30 (14–60)	31	1,998
2015	190	1.9	3.7	66 (39–190)	30 (14–42)	23	1,522
2016	234	2.4	4.1	58 (39–201)	21 (14–30)	27	1,849
2017	273	2.8	4.0	55 (37–196)	25 (12–30)	23	1,803
2018	279	2.9	3.8	50 (34–187)	20 (14–30)	19	1,427
5 prescriptions							
2013	70	1.3	3.3	148 (70–240)	30 (20–60)	48	2,285
2014	112	1.2	2.8	133 (69–227)	30 (10–42)	42	3,810
2015	133	1.3	2.6	124 (56–216)	30 (14–40)	37	2,184
2016	155	1.6	2.7	123 (60–222)	30 (15–42)	33	2,044
2017	168	1.7	2.5	116 (54–208)	27 (14–30)	34	2,140
2018	133	1.4	1.8	109 (48–205)	24 (13–40)	37	2,468
6–10 prescriptions							
2013	160	2.9	7.6	187 (97–268)	30 (20–60)	78	5,144
2014	312	3.3	7.7	178 (97–258)	30 (15–60)	66	5,083
2015	314	3.2	6.1	167 (93–248)	30 (15–60)	63	4,729
2016	354	3.7	6.2	174 (96–261)	30 (15–60)	70	5,575
2017	413	4.2	6.1	174 (93–252)	30 (14–60)	66	5,267
2018	356	3.7	4.9	154 (82–245)	30 (14–36)	56	4,408
11–20 prescriptions							
2013	77	1.4	3.7	217 (134–286)	30 (10–60)	146	12,133
2014	155	1.7	3.8	218 (130–293)	30 (10–60)	200	17,734
2015	212	2.1	4.2	228 (137–297)	30 (10–60)	150	13,834
2016	222	2.3	3.9	222 (134–303)	30 (10–60)	141	13,424
2017	233	2.3	3.4	228 (143–295)	30 (10–60)	144	13,601
2018	204	2.1	2.8	208 (138–290)	30 (12–60)	151	14,078
21–50 prescriptions							
2013	37	0.7	1.8	273 (216–320)	21 (14–30)	233	23,162
2014	59	0.6	1.5	253 (194–310)	20 (7–45)	266	24,097
2015	75	0.8	1.5	258 (194–310)	15 (10–30)	328	31,523
2016	72	0.8	1.3	259 (195–310)	28 (14–30)	262	25,704
2017	92	0.9	1.4	271 (209–317)	28 (14–56)	262	26,102
2018	83	0.9	1.1	267 (202–315)	30 (14–60)	300	28,272
> 50 prescriptions							
2013	4	0.1	0.2	350 (339–358)	14 (7–28)	377	34,445
2014	19	0.2	0.5	336 (304–353)	14 (14–21)	343	35,915
2015	13	0.1	0.3	259 (117–328)	14 (6–21)	244	20,073
2016	15	0.2	0.3	341 (325–353)	14 (10–21)	212	15,216
2017	16	0.2	0.2	343 (322–354)	14 (14–21)	377	39,093
2018	13	0.1	0.2	275 (189–337)	14 (6–21)	386	45,342

For Footnotes, see Table 6.

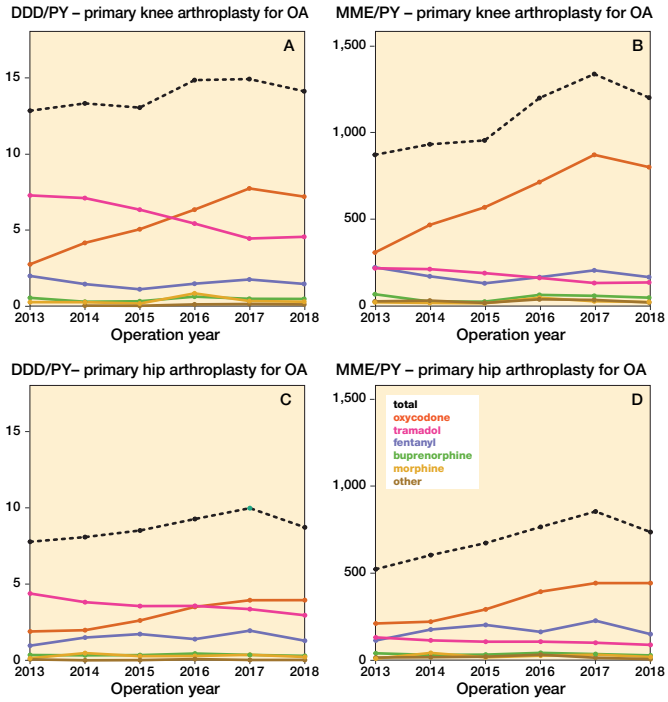


Figure 6. Opioid prescriptions over time in different opioid types in daily defined dosages (DDD) and morphine milligram equivalent (MME) amongst osteoarthritis patients in both knee and hip arthroplasties per person year (PY). DDDs for codeine-paracetamol combination were non-existent.

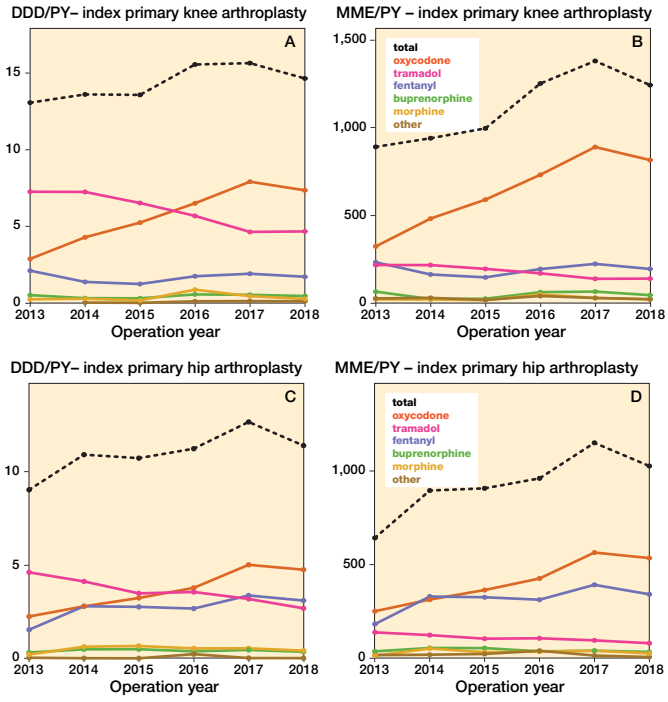


Figure 8. Opioid prescriptions over time in different opioid types in daily defined dosages (DDD) and morphine milligram equivalent (MME) amongst index primary knee and hip arthroplasties per person year (PY). DDDs for codeine-paracetamol combination were non-existent.

Table 9. Index primary knee arthroplasties after which an opioid is prescribed

Operation year	Number of arthroplasties	Opioids after arthroplasty, n (%)
2013	4,834	2,808 (58)
2014	7,900	4,842 (61)
2015	8,000	5,698 (71)
2016	7,390	5,666 (77)
2017	7,784	6,525 (84)
2018	7,987	7,114 (89)

Table 10. Index primary hip arthroplasties after which an opioid is prescribed

Operation year	Number of arthroplasties	Opioids after arthroplasty, n (%)
2013	5,451	2,082 (38)
2014	8,972	3,886 (43)
2015	9,255	4,803 (52)
2016	8,818	5,257 (60)
2017	9,028	6,197 (69)
2018	8,709	6,529 (75)

Appendix

Validation in Statistics Netherlands

The linkage between the LROI and the SFK was validated by comparing our results with results from similar analyses performed on data from Statistics Netherlands. Primary knee and hip arthroplasties were selected from the Dutch Hospital Data [1] in which procedures performed in all Dutch hospitals are registered with the exception of independent treatment centers. Independent treatment centers were part of the hospitals in the LROI-SFK dataset. The selected codes, used for registration of hip and knee arthroplasties, are shown in Table 1. The opioid reimbursement data from the Health Care Insurance Board [2] were used to assess the opioid prescriptions (ATC-code N02A) in the year of arthroplasty surgery. The primary knee and hip arthroplasties were selected and linked to the medication data. Opioid use before and after arthroplasty was defined as at least one dispensed opioid prescription, at a Dutch pharmacy, either before or after the arthroplasty surgery.

Table 2 and 3 show the proportion of arthroplasties with at least one opioid prescription in the year of surgery in the CBS and the proportion of arthroplasties with at least one opioid prescription in the year of surgery in the LROI-SFK dataset. In hip arthroplasties the differences between these proportions were small with the exception of 2018 in which a difference of 11.3% was found, in knee arthroplasties the differences ranged from 1.7% to 4.3%. In both datasets the proportion of patients with at least one opioid prescription increased with similar rates between 2013 and 2018 indicated by the parallel lines in Figures 1 and 2.

1. **Dutch Hospital Data. National Basic Registration of Hospital Care** [in Dutch]. [cited 2021 February 22]; Available from: https://www.dhd.nl/producten-diensten/LBZ/Paginas/Dataverzameling-LBZ.aspx.
2. **Statistics Netherlands.** Structure and instructions for medication data on ATC-4 classification [in Dutch]. [cited 2021 February 23]; Available from: https://www.cbs.nl/nl-nl/onze-diensten/maatwerk-en-microdata/microdata-zelf-onderzoek-doen/microdatabestanden/medicijntabgeneesmiddelen-op-atc-code--4--.

Appendix Table 1. Proceeding codes for primary knee and hip arthroplasty

CBV	CBV [a]	CvV	ZA
38567	338663L	5814	38567
38663	338663M	58145	38663
190306	338663N	581450	190305
190314	338663P	581451	190306
190377	338663Q	581452	190314
190378	338663R	581453	190375
190379	338663T	581454	190376
338567	338669	58149	190377
338567B	338669A	5815	190378
338567C	338669B	58150	190379
338567D	688660	5816	338561
338567E	688660A	58160	338562
338567F	688660B	58161	338563G
338567G	688660C	58162	338563L
338567H	688661	58168	338565
338567J	688662	58169	338566Q
338567K	038565	58556	338567
338567L	338566	58558	338567C
338567R	338566A		338567D
338567W	338566B		338567E
338568	338566D		338567F
338568A	338566E		338567G
338568B	338566L		338567H
338568C	338566R		338567J
338568D	688660D		338567K
338568E	685320		338567L
338568F	685321		338567R
338568I	685322		338567W
338568J	685324		338568
338568K	685325		338568A
338568L	338567B		338568B
338568M	338566S		338568J
338568N	338566T		338568K
338568P	338566U		338568L
338568R	338566W		338568P
338568W	338566X		338568R
338569J	338567M		338568W
338569K	338567N		338662C
338640F	338662J		338662E
338640G	338662W		338662F
338640H	338662X		338662G
338662C			338662H
338662D			338662T
338662E			338662U
338662F			338663C
338662G			338663L
338662H			338663M
338662T			338663N
338662U			338663R
338663C			338669

CBV = systematic list with which all medical, paramedical and nursing procedures can be recorded;
CvV = systematic list with which all medical, paramedical and nursing procedures can be recorded;
ZA = Care activity provided by medical, paramedical and nursing staff
[a] continuation of first CBV row

Appendix Table 2. The difference between the number of primary hip arthroplasty procedures with an opioid prescription in the year of surgery

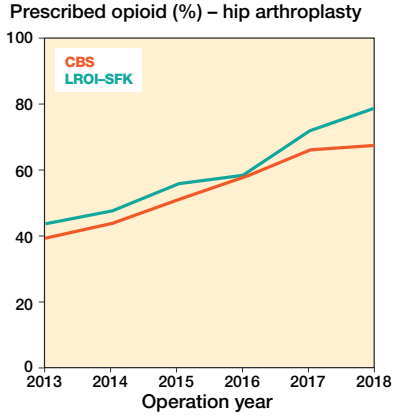
Operation year	Operations CBS	Opioids prescribed (%)	Operations SFK-LROI	Opioids prescribed (%)	Δ PPD (%)
2013	18,945	7,537 (39.8)	5,513	2,401 (43.6)	3.8
2014	27,301	11,764 (43.9)	9,354	4,454 (47.6)	3.7
2015	29,108	14,838 (51.0)	9,903	5,522 (55.8)	4.8
2016	30,278	17,531 (57.9)	9,580	5,591 (58.4)	0.5
2017	30,935	20,445 (66.1)	9,926	7,125 (71.8)	5.7
2018	33,647	22,720 (67.5)	9,688	7,633 (78.8)	11.3

Opioids prescribed: primary hip arthroplasties that had an opioid prescription in the same year as their operation.
Δ PPD: percent point difference in SFK-LROI compared with CBS.

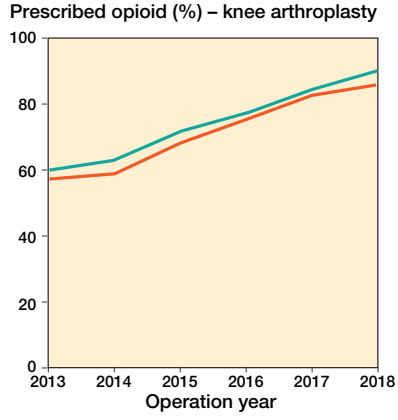
Appendix Table 3. The difference between the number of primary knee arthroplasty procedures with an opioid prescription in the year of surgery

Operation year	Operations CBS	Opioids prescribed (%)	Operations SFK-LROI	Opioids prescribed (%)	Δ PPD (%)
2013	18,945	7,537 (39.8)	5,513	2,401 (43.6)	3.8
2013	12,338	7,097 (57.3)	4,897	2,938 (60.0)	2.7
2014	20,614	12,135 (58.9)	8,372	5,272 (63.0)	4.1
2015	21 930	14,940 (68.1)	8,767	6,294 (71.8)	3.7
2016	22,501	16,940 (75.3)	8,196	6,336 (77.3)	2.0
2017	23,591	19,510 (82.7)	8,746	7,397 (84.4)	1.7
2018	24,239	20,832 (85.9)	9,073	8,187 (90.2)	4.3

Footnote: see Appendix Table 2.



Appendix Figure 1. Annual percentage of prescribed opioids according to the prescriptions in the year of hip arthroplasty over different years.



Appendix Figure 2. Annual percentage of prescribed opioids according to the prescriptions in the year of primary knee arthroplasty over different years.