Long-term opioid medication use before and after joint replacement surgery in New Zealand

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ABSTRACT

AIM: To describe the use of opioid analgesics over three years before and after total joint replacement surgery in New Zealand.

METHOD: We extracted information on all individuals undergoing publicly funded total hip or knee replacement surgery in New Zealand between June 2011 and December 2014, and linked data on opioid prescribing, from the Statistics New Zealand Integrated Data Infrastructure. We analysed monthly opioid use over the three years before and after surgery and the transition from pre-operative and/or immediate post-operative use to chronic post-operative use.

RESULTS: The prevalence of opioid use increased from 7% three years before surgery to 22% immediately prior to surgery, was common (75%) in the month following surgery and declined rapidly to 10–12% per month over the following years. Patients dispensed opioids prior to surgery or in the post-operative recovery period were at significantly higher risk of subsequent chronic opioid use.

CONCLUSION: Opioid analgesic prescribing was reduced following joint replacement surgery, although a substantial minority of patients remained long-term opioid users. Avoiding unnecessary pre-operative opioid use and limiting opioid use for post-operative pain management where appropriate could help to reduce the risk of potentially ineffective or harmful long-term opioid use in these patients.

Osteoarthritis (OA) is one of the most common chronic health conditions both in New Zealand and worldwide,[1,2] and the 13th leading cause of global disability.[2] Current treatment recommendations are for non-pharmacological, non-surgical interventions, including exercise therapy, weight management and patient education, as first-line treatments.[3,4] Medications such as non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular corticosteroids are recommended for patients not responding to first-line treatments,[3–5] and total joint replacement (TJR) surgery should be considered for patients with more severe hip or knee OA that is not relieved by non-surgical management.[4,5]

Opioid analgesics are not recommended for long-term pain management in OA, as there is limited evidence of benefit and substantial risk of harm.[6] Common side-effects include constipation, nausea, dizziness, drowsiness, vomiting and dry skin. Opioid use, especially in the elderly, is associated with increased risk of falls, fractures, drug-drug interactions, depression and death.[7,8] Long-term use is of limited effectiveness due to the development of tolerance and hyperalgesia.[9,10] Opioid misuse, abuse and addiction is a serious issue that has received substantial academic, clinical and media attention; a recent systematic review estimated that the prevalence of opioid use disorders was 8–12% and misuse 22–29%

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in patients being prescribed opioids for chronic non-cancer pain.[11] Despite this, opioid use to treat chronic non-cancer pain, including chronic OA pain, has been on the rise in recent decades around the world.[12,13]

Patients awaiting TJR are at particular risk of using opioids due to more severe joint pain.[14] Patients receiving opioids prior to surgery experience less pain relief following surgery, have higher risk of surgical complications and revision surgery, and are more likely to have persistent post-operative opioid use.[15–17] Use of opioid analgesics is common post-operatively; the considered use of oral opioids, as part of a multimodal regimen, is recommended by clinical practice guidelines for the management of acute post-operative pain,[18] although opioids used for acute pain management should be given at the lowest effective dose and ceased or tapered as soon as practicable.

Recent international studies have investigated the use of opioid analgesics over one year preceding and following TJR in Australia,[19] the US[20,21] and France,[22] with mixed results. Opioid use was common both before and after surgery in Australia and the US, with 34 percent and 49 percent of patients, respectively, continuing to use opioid medications beyond three months post-operatively; in France, only seven percent of patients used opioids after surgery. No studies to date have looked at longer-term opioid use after TJR beyond the first year, and no data have been reported for New Zealand.

The aim of this study is to describe the use of opioid analgesics over three years before and after TJR in the New Zealand population.

Methods

Study cohort

The study cohort includes individuals who had publicly funded knee or hip TJR surgery in New Zealand between June 2011 and Dec 2014. We excluded individuals who were not resident in New Zealand for at least three years before and after surgery (or who died within three years of surgery), to allow the identification of opioid medication use throughout the pre- and post-surgery periods. Individuals were also excluded if they had a second knee or hip replacement within six years, to avoid confounding post-surgery opioid use with that due to advanced OA in other joints. As these exclusions will be more likely to exclude those in poorer health, and may therefore underestimate the true use of opioid medications following surgery, we conducted sensitivity analyses by limiting the window of data availability to either two years or one year before and after surgery.

Data sources

All data were obtained from the Statistics New Zealand Integrated Data Infrastructure (IDI), a comprehensive, population-wide, individual-level linked database comprised of de-identified data from New Zealand government agencies, Statistics New Zealand surveys and non-government organisations. Within the IDI, information on TJR surgeries was collected from the New Zealand Ministry of Health's (MoH) publicly funded hospital discharges dataset, which contains diagnosis and procedure information for all publicly funded hospital events, and on opioid dispensing from the MoH pharmaceutical claims dataset, which contains data on all subsidised dispensing of prescription medications. Further demographic information on the patients was obtained from the personal details dataset maintained by Statistics New Zealand. The clinical codings used to identify the cohort are described in Table 1. Joint replacement surgeries were identified using the Australian Refined-Diagnosis Related Groups classification, versions 6.0–7.0. Opioid analgesics were identified from the PHARMAC Therapeutic Group Reference table, corresponding to ATC code N02A (Opioid Analgesics).

Opioid use measures

We calculated individuals' opioid medication use during each of the 36 30-day intervals (approx. three years) before and after the index procedure. For each interval, we calculated two measures of opioid use for each individual: 1) a binary variable indicating whether they filled any opioid prescription during the period and 2) a variable reflecting the quantity of opioids used during the period, measured in oral morphine equivalent daily dose (oMEDD), averaged over the 30-day period.[23–25] Where the period of prescription spanned more than one 30-day period, use per period was calculated by assuming a constant daily

Table 1: Codings used to identify TJR procedures and opioid medications.

Joint replacement surgery (AR-DRG code)	Opioid analgesics (Therapeutic Group)
I03A: Hip replacement W catastrophic CC	Nervous System > Analgesics > Opioid Analgesics (ATC code N02A)
I03B: Hip replacement W/O catastrophic CC	*Consisting of:*
	Codeine phosphate
I04A: Knee replacement W catastrophic or severe CC	Methadone hydrochloride
	Morphine hydrochloride
I04B: Knee replacement W/O catastrophic or severe CC	Morphine sulphate
	Paracetamol with codeine
	Pethidine hydrochloride
	Morphine tartrate
	Dihydrocodeine tartrate
	Fentanyl
	Oxycodone hydrochloride
	Tramadol hydrochloride
	Dextropropoxyphene[1]
	Dextropropoxyphene with paracetamol[1]

[1]Withdrawn from the New Zealand market in August 2010.

dosage throughout the period covered by the prescription. For example, for a one-week prescription spanning the last two days of one period and the first five days of the next, we assigned two-sevenths of the quantity to the first period, and five-sevenths to the second. For secondary analyses, opioid use was stratified into 'strong' opioids (morphine, oxycodone, fentanyl and pethidine) and 'mild' opioids (all others), and usage measures calculated separately for each class using the methods described above.

We categorised individuals' opioid use pre- and post-surgery as either 'None', 'Some' or 'Chronic'. 'Chronic' use pre-surgery was defined as a dispensing of opioid drugs in at least three consecutive 30-day periods during the 12 periods prior to surgery; 'Some' use was defined as having any opioid dispensing over the same 12 periods but not meeting the criterion for chronic use; and 'None' was defined as no opioid dispensing recorded over the 12 periods before surgery. The same definition was applied post-surgery to each of the first, second and third years following the date of surgery. For the first year post-surgery, we separated use into the first 90 days (ie, three 30-day periods), during which opioid prescriptions may be considered appropriate or recommended for acute pain management, and the remainder of the year (longer-term opioid use).

Cohort descriptive measures

Patients' ethnicity was sourced from the combined ethnicity indicator constructed by Statistics New Zealand. We classified ethnicity as European (including NZ European), Māori, Pacific and Asian, using the 'total response' measure recommended by Statistics New Zealand; this outcome allows individuals to indicate more than one ethnic affiliation, with all reported ethnicities included in the analysis (eg, an individual reporting both NZ European and Māori ethnicity would be included in both the European and Māori subgroups).

Comorbid health conditions were measured using the Elixhauser comorbidities index,[26,27] calculated using diagnosis codes recorded in hospital discharges during the pre-surgery period (up to and including the index procedure).

Statistical analysis

Baseline cohort statistics were described using mean (standard deviation) for continuous measures and count (percent) for categorical outcomes.

We plotted opioid use by month against time relative to surgery, from 36 months pre-surgery to 36 months post-surgery, to identify trajectories and patterns in pre- and post-operative opioid use. We tabulated and plotted longer-term post-operative opioid use status (none/some/chronic use in the first year following surgery and persistent chronic use over two and three years post-surgery), for the full cohort and stratified by pre-operative and acute post-operative opioid use.

The analyses were also conducted for sub-groups of the cohort stratified by surgery joint (knee/hip) and occurrence of surgical complications.

Sensitivity analyses

We compared the trajectories of opioid use for our primary cohort and for alternative cohorts defined by reducing the window of required data availability to one or two years before and after surgery. As individuals with poorer health are more likely to be excluded by data availability (due to increased risk of revision surgery or mortality), the latter samples are likely to be more representative of all TJR patients (at the cost of viewing a shorter period of data before and after surgery).

We also examined the sensitivity of our findings to alternative definitions of 'chronic' opioid use. We considered (1) a broader definition of chronic use, defined as opioid use in at least three months over the year, without requiring these months to be consecutive, and (2) a stricter definition of six consecutive months of opioid use over the year. The same analyses as described above were repeated for each of these alternative definitions.

Ethics

This study was approved by the University of Otago Human Research Ethics Committee (HD18/066). Access to the anonymised data used in this study was provided by Statistics New Zealand under the security and confidentiality provisions of the Statistics Act 1975. Careful consideration has been given to the privacy, security and confidentiality issues associated with using linked administrative data in the IDI; see the full disclaimer at the end of this article for further details.

Data sharing

The raw data underlying these analyses are not publicly available, due to the strict confidentiality and security provisions of the IDI. The summarised group-level data used to create the results reported in this paper are available on request from the authors.

Results

There were 35,148 publicly funded knee and hip replacement surgeries on 32,151 individuals over the study period. After excluding individuals with multiple joint replacement surgeries (n=3,156) and those who were not resident in New Zealand throughout the three-year window both before and after surgery (n=6,357) or who died within three years of surgery (n=3 387), 19,251 individuals (60%) were included in the analysis in this study.

The mean (SD) age of the cohort was 69 (11) years (Table 2). The majority of the patients were women (n=10,695, 56%), and of NZ/European ethnicity (n=16,926, 88%). Comorbidities were common, with 7,647 (40%) having at least one comorbid condition, and 2,088 (11%) having three or more. The majority of the surgeries in the sample were hip replacements (n=11,088, 58%), and 2,244 (12%) had surgical complications. In the year prior to surgery, 9,381 patients (49%) had no recorded opioid use, 6,396 (33%) had some use and 3,474 (18%) were chronic opioid users. Pre-operative opioid use was higher among women, patients having hip replacement surgery, and those with comorbid health conditions. The majority of prescriptions were for mild opioids, most commonly codeine, tramadol and codeine with paracetamol (Table 3).

There was a long period of steadily increasing opioid use prior to TJR, from 7% of the cohort being prescribed opioids in the first month (three years prior to surgery), to 11% 18 months before surgery, followed by a more rapid increase to 22% per month sustained over the three months immediately before surgery (Figure 1). Opioid use was common in the post-operative recovery period, with 14,475 (75%) individuals being dispensed opioids in the first month after

Table 2: Baseline characteristics of the study cohort.

Variable	All observations	Opioid use before surgery		
		None	Some	Chronic
Age at surgery, mean (SD)	69 (11)	70 (11)	69 (11)	68 (12)
Female	10695 (56)	4,950 (53)	3,651 (57)	2,094 (60)
Type of surgery				
Hip	11,088 (58)	5,091 (54)	3,624 (57)	2,373 (68)
Knee	8,163 (42)	4,290 (46)	2,772 (43)	1,101 (32)
Surgical complications				
Without catastrophic CC	17,007 (88)	8,229 (88)	5,694 (89)	3,084 (89)
With catastrophic CC	2,244 (12)	1,152 (12)	702 (11)	390 (11)
Ethnicity[1]				
European	16,926 (88)	8,256 (88)	5,565 (87)	3,105 (89)
Māori	1,959 (10)	894 (10)	675 (11)	390 (11)
Pacific	534 (3)	279 (3)	189 (3)	66 (2)
Asian	372 (2)	192 (2)	141 (2)	39 (1)
Number of Elixhauser comorbidities				
0	11,604 (60)	5,925 (63)	3,813 (60)	1,866 (54)
1–2	5,559 (29)	2,580 (28)	1,899 (30)	1,080 (31)
3+	2,088 (11)	876 (9)	684 (11)	528 (15)
Observations, n (% of total)	19,251 (100)	9,381 (49)	6,396 (33)	3,474 (18)

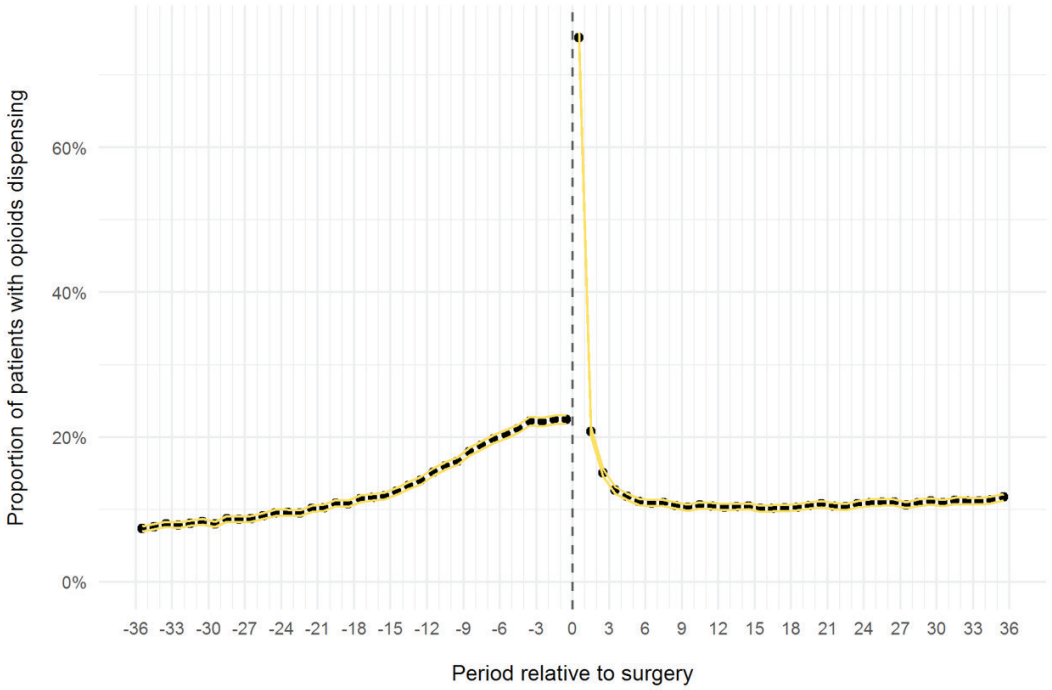
Values are count (percentage within group) unless otherwise stated.
[1]The sum of ethnicity category counts does not equal the total sample count, as individuals can identify with more than one, or none, of the given categories.

Table 3: Proportion of patients using opioid medications before and after joint replacement surgery, by medication type.

Medication	Before	After
Codeine	26.2%	16.3%
Tramadol	24.6%	17.2%
Codeine with Paracetamol	21.6%	12.0%
Morphine	5.3%	4.2%
Oxycodone	4.7%	4.9%
Fentanyl	0.7%	0.7%
Methadone	0.3%	0.3%
Pethidine	0.2%	0.1%

The periods 'Before' and 'After' refer to the 360 days before and after the date of surgery, respectively (excluding the 30-day period immediately after surgery).

Figure 1: Opioid use before and after joint replacement surgery.



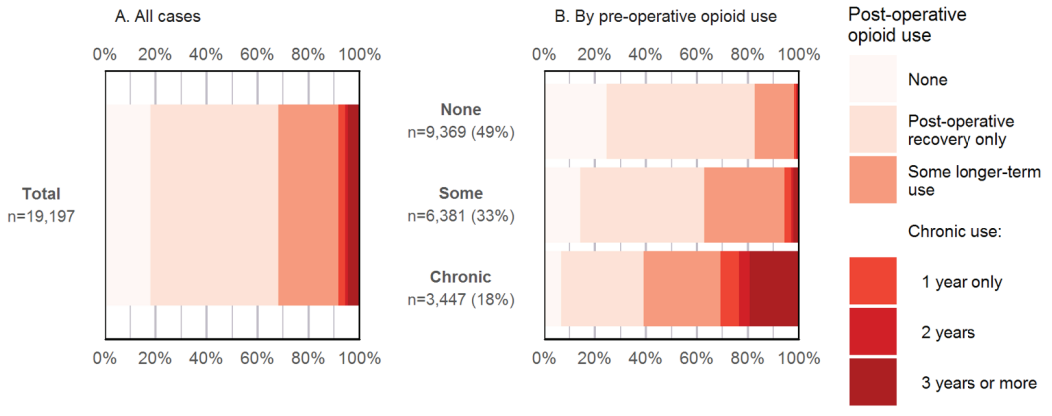
Periods refer to the 30-day (ie, approximately one-month) periods defined relative to the date of surgery for each individual.

surgery, but rapidly dropped to 13% by the fourth month and remained at a similar level throughout the remaining post-surgery period. A similar pattern was observed for the average daily quantity of opioids taken (Figure A1), and for both strong and mild opioids (Figure A2).

Over the year following surgery, 6,099 patients (32%) used opioid analgesics beyond the initial three-month post-operative recovery period (Figure 2). Of these, 1,587 (8% of the total) were classified as 'chronic' users in the first year following surgery, 1,077 (6%) remained chronic users over the first two years following surgery and 867 (5%) remained chronic users for at least three years after surgery.

Patients who were dispensed opioids prior to surgery were at much greater risk of long-term post-operative opioid use. Of the 9,369 patients who were not prescribed any opioid analgesics in the year prior to surgery, only 1,620 (17%) had any opioid use in the year after surgery (beyond the three-month

Figure 2: Long-term opioid use after joint replacement surgery.



Opioid use refers to a dispensing of any of the opioid medications listed in Table 1.

Figure 3: Long-term opioid use after joint replacement surgery, by use in post-operative recovery period.

Opioid use refers to a dispensing of any of the opioid medications listed in Table 1.
*Early post-operative use refers to the first three months following the date of surgery.

post-operative recovery period), and 174 (2%) were chronic users. These increased to 2,376 (37%) and 354 (6%) among the 6,381 patients with some (non-chronic) pre-operative opioid use, and 2,103 (61%) and 1,059 (31%) among the 3,447 patients with chronic pre-operative opioid use.

Patients prescribed opioids in the immediate post-operative recovery period were also at substantially increased risk of long-term opioid use (Figure 3). Of the 15,111 patients with an initial post-operative opioid prescription, 5,451 (36%) used opioids beyond the three-month recovery period and 1,554 (10%) were chronic opioid users in the year following surgery, compared to 648 (16%) and 33 (1%) among the 4,086 with no post-operative opioid prescription. This association remained strong even after adjusting for pre-operative opioid use: among the cohort with chronic opioid use in the year prior to surgery, only 87 (27%) of those without an early post-operative opioid prescription had any longer-term opioid use in the first year, and nine (3%) had chronic use, compared to 2,016 (64%) and 1,050 (34%), respectively, of those with an early post-operative opioid prescription.

Regardless of pre-surgery opioid use, patients receiving knee replacements (compared to hips) and those suffering surgical complications were more likely to use opioids post-surgery (Figures A3–A4).

Sensitivity analyses

Post-surgery opioid use was slightly higher in the larger cohorts provided by reducing the data window to one or two years before and after surgery, consistent with our hypothesis that requiring three years of complete data post-surgery would result in a small selection bias, although the differences were small and did not suggest any changes to our overall findings (Figures A5–A6). The estimated prevalence of chronic opioid use was, as expected, higher with the broader definition and lower with the stricter definition (Figures A7–A9). In both cases, the same patterns of use were seen as in the primary analysis: those who were opioid users before surgery and those prescribed opioids in the immediate post-surgery period were substantially more likely to be chronic opioid users in the period following surgery.

Discussion

This study has examined the use of opioid analgesics before and after total joint replacement surgery in the New Zealand population. These surgeries appear to be effective in reducing patients' joint pain and opioid use: most patients, including those who were using opioids in the year prior to surgery, had no or limited opioid use post-surgery. Use of strong opioids in particular was low, with five percent of

patients dispensed oxycodone, four percent dispensed morphine, and less than one percent dispensed fentanyl after the first month following surgery. Ongoing use of mild opioids was more common, however, with 37 percent of patients dispensed at least one mild opioid medication over the same period. Of particular concern is the subset of these patients with chronic use (many of whom continue to be chronic opioid users for several years thereafter).

Guidelines for osteoarthritis management recommend against use of opioids;[5,6] opioid prescribing guidelines recommend opioids to treat severe acute pain, at the lowest effective dosage, for the shortest possible time, and only when conservative non-pharmacological and non-opioid pharmacological treatments have proven ineffective.[28] In chronic pain, opioids should be used as a last resort, and should be re-evaluated frequently to ensure the benefits of treatment continue to outweigh the risk of harms.[28] Our finding that many patients continue to use opioids for more than three months after surgery (and many of those continue for several years) therefore suggests a high prevalence of potentially inappropriate prescribing. This issue deserves further attention to determine the extent to which this prescribing is clinically inappropriate and to identify ways to reduce the prevalence of inappropriate prescribing. In particular, reducing unnecessary opioid use before surgery and minimising the use of opioids for post-surgical recovery may help to reduce the risk of harm from potentially ineffective or harmful long-term opioid use after TJR. Further research should also investigate other factors that could be used to identify patients at high risk of long-term post-surgical opioid use to enable improved pain management strategies for these patients.

Limited international evidence is available on the prevalence of post-surgery opioid use in TJR patients. A recent study conducted in a cohort of Australian veterans reported very similar rates of opioid use following total knee replacement surgery (34% over the first year post-surgery, compared to 36% in the current study for those having knee replacement only).[19] Rates of opioid use after total knee replacement appear to be higher in the US, with a recent study reporting a prevalence of opioid use of 15–16% per month 6–12 months after surgery;[22] for comparison, rates of 11–12% were found in the corresponding cohort in our study.

As an observational cohort analysis of previously collected administrative data, this study does have some limitations. Data were only available on publicly funded surgeries, which account for approximately 70% of all TJR in New Zealand; our results may not be generalisable to patients having privately funded surgeries. Access to surgery in the public healthcare system is rationed, and there is a concern that prolonged delay in access may result in patients continuing to deteriorate while awaiting surgery; this hypothesis cannot be tested in the present study. However, our results do not seem to suggest this results in higher rates of opioid use prior to surgery: opioid use prevalence reached approximately 22% four months prior to surgery, and remained at that level throughout the remaining pre-surgery period (ie, the period when most patients are on the waiting list).

The indication for opioid prescribing was not available, so we cannot definitively state the extent to which prescribing was clinically justified; however, as opioids are generally recommended only as a last resort for short-term use in the treatment of acute pain,[28] and osteoarthritis guidelines recommend strongly against the use of opioids,[5] it is likely that much of this prescribing is medically unnecessary and has the potential to cause more harm than benefit for patients. Patients with a subsequent TJR within six years of the initial procedure were excluded, to avoid capturing post-surgery opioid use associated with end-stage OA in other joints. Lastly, only data on prescription opioids was available; weak opioids purchased over-the-counter without prescription, notably codeine with paracetamol, are therefore not captured in our results. International evidence suggests that initial use of prescription opioids can be a precursor to illegal use that would also not be captured in these data.[29,30] Future work will look at other outcomes, such as seeking addiction treatment, opioid-related fatalities and other healthcare use indicative of opioid use disorders.

Strengths of this study include the analysis, for the first time internationally, of opioid use in a comprehensive national

population cohort of TJR patients, and the long-term follow-up allowing the identification of prolonged chronic opioid use for many patients. This is also the first study in New Zealand to identify the prevalence of long-term opioid use following surgery, a crucial issue given the increasing worldwide concern with opioid use, misuse, addiction and related harms.

Conclusion

Rates of opioid analgesic dispensing among people with knee and hip pain were significantly reduced following TJR, and were similar to or lower than rates reported in Australia and the US. A substantial minority of patients, however, remained opioid users after surgery, many of whom continued long-term use for several years post-surgery. Identifying those patients at risk of long-term opioid use post-surgery, reducing unnecessary pre-operative opioid prescribing, and promoting non-opioid strategies for post-operative pain management where appropriate could help to reduce the risk of harm associated with long-term post-operative opioid use.

Appendix

Supplementary figures

Figure A1: Average daily opioid use before and after joint replacement surgery.

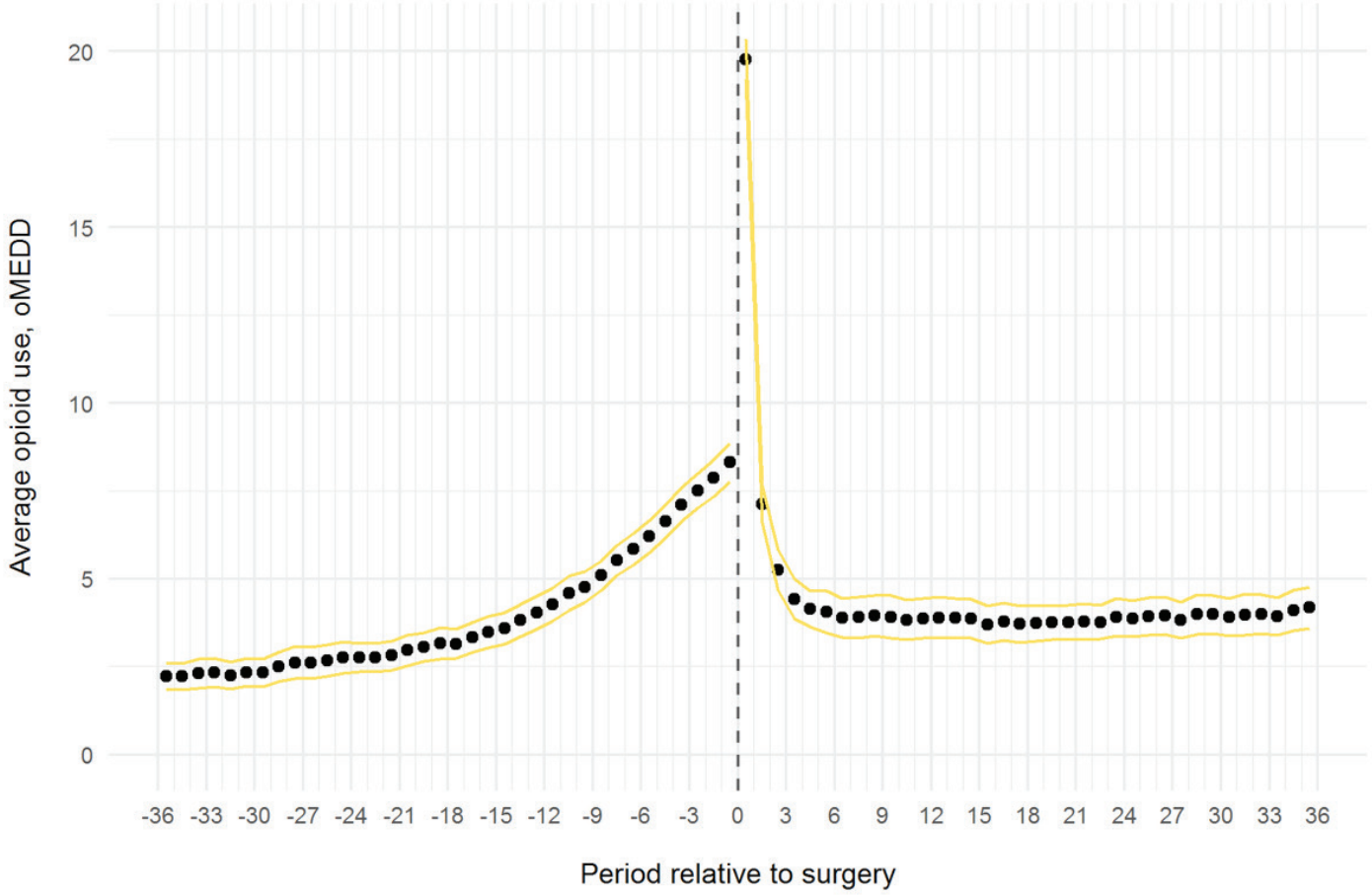


Figure A2: Opioid use before and after surgery, by opioid potency.

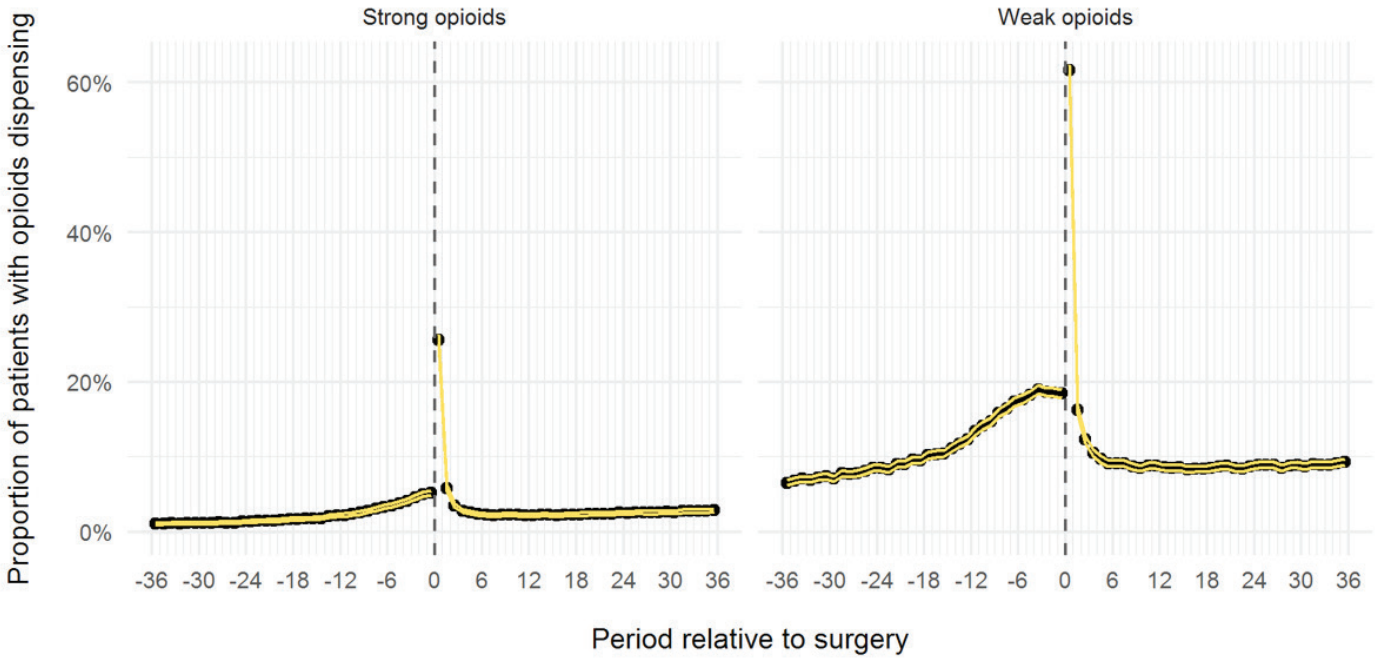


Figure A3: Long-term opioid use after joint replacement surgery, by joint.

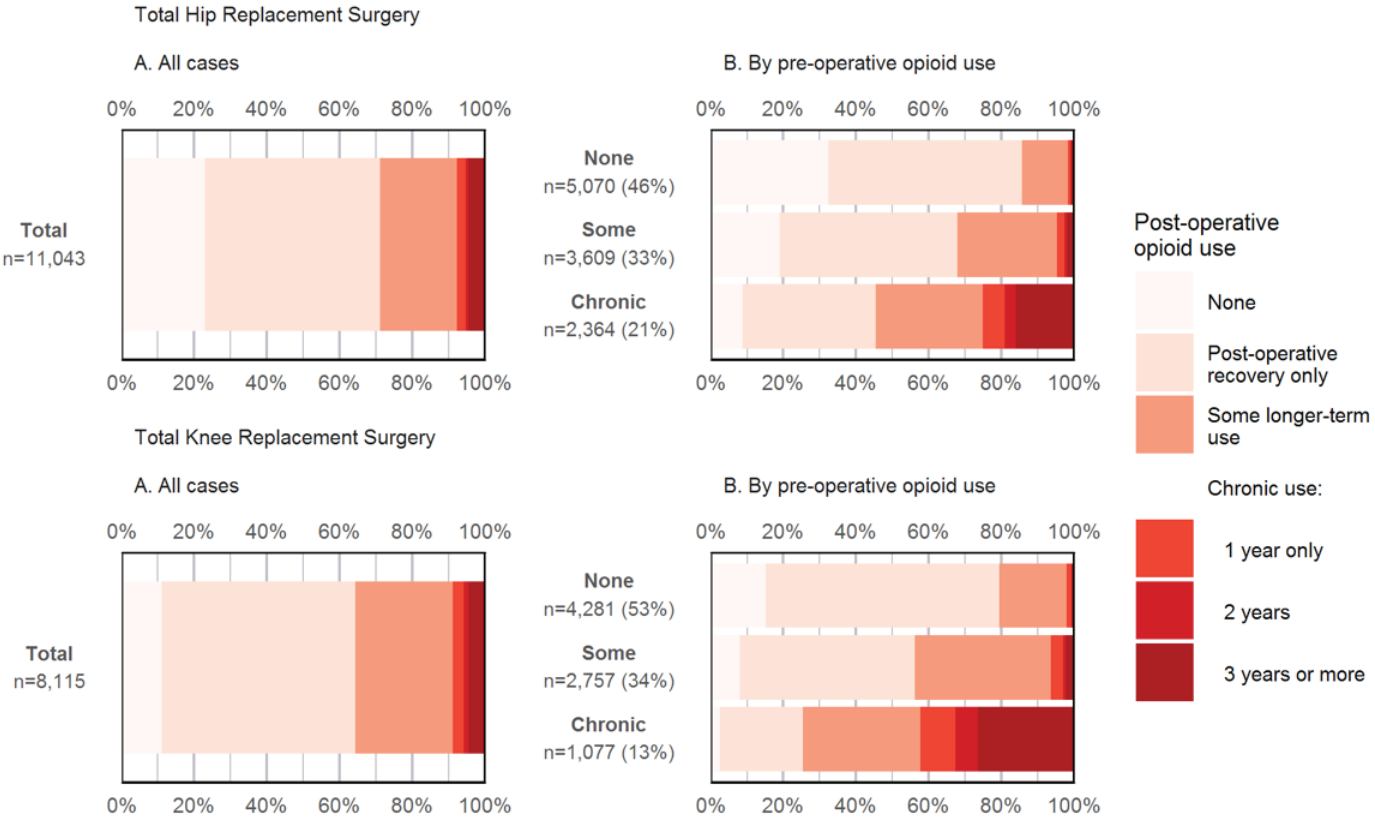


Figure A4: Long-term opioid use after joint replacement surgery, by surgical complications.

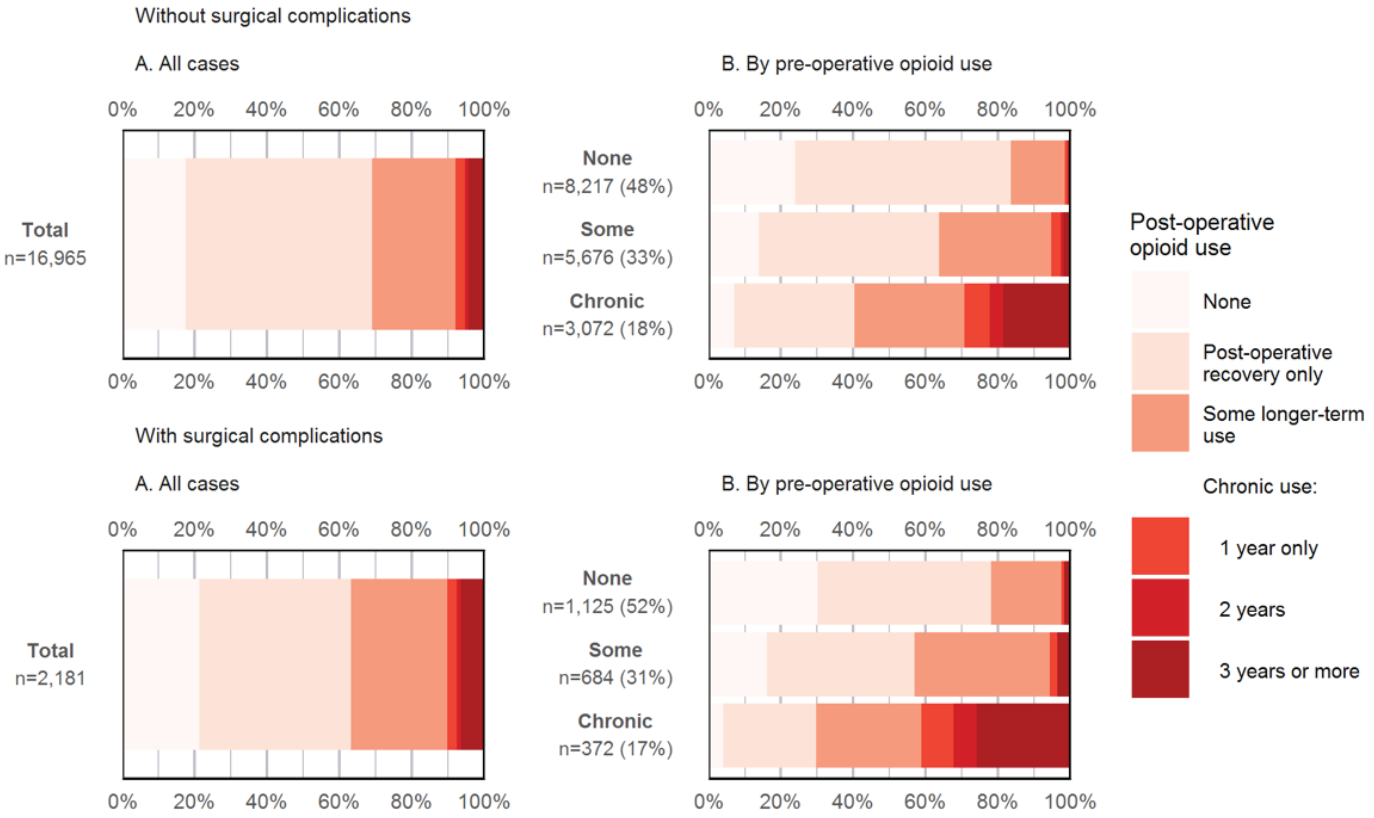


Figure A5: Opioid use before and after joint replacement surgery, three sample cohorts.

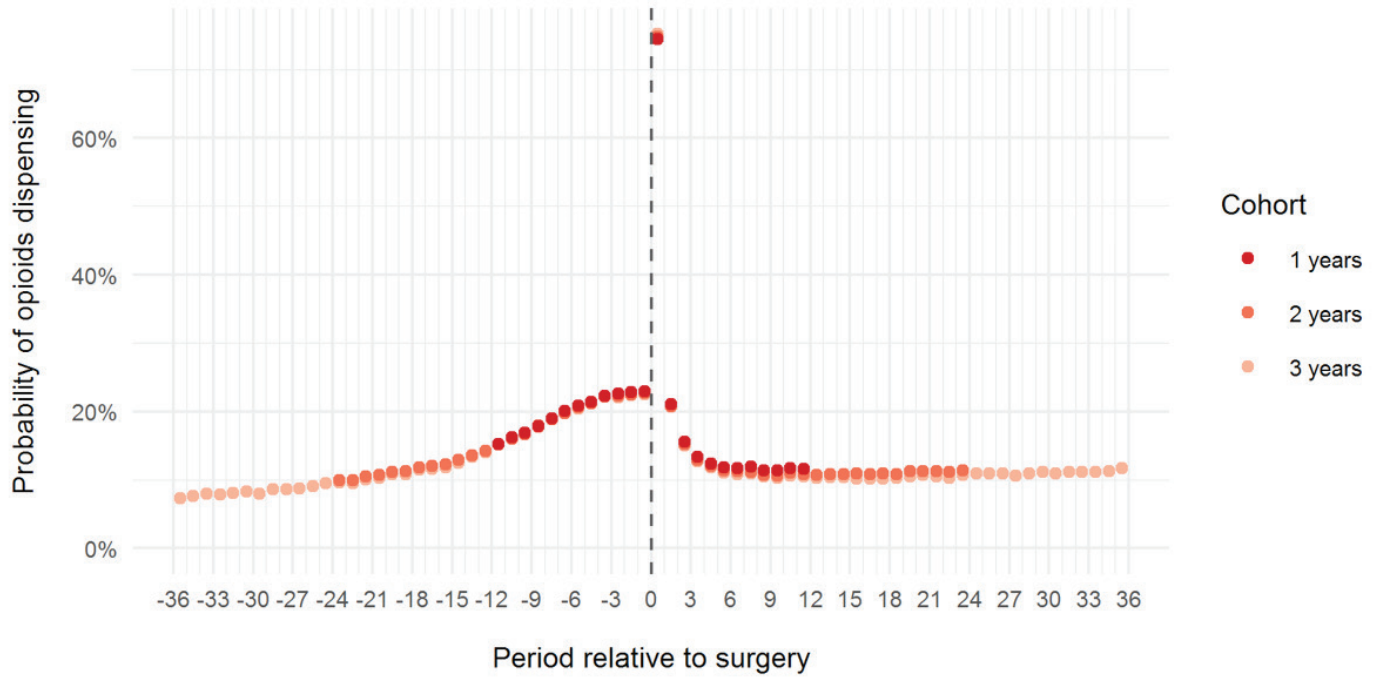


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Figure A6: Average daily opioid use before and after joint replacement surgery, three sample cohorts.

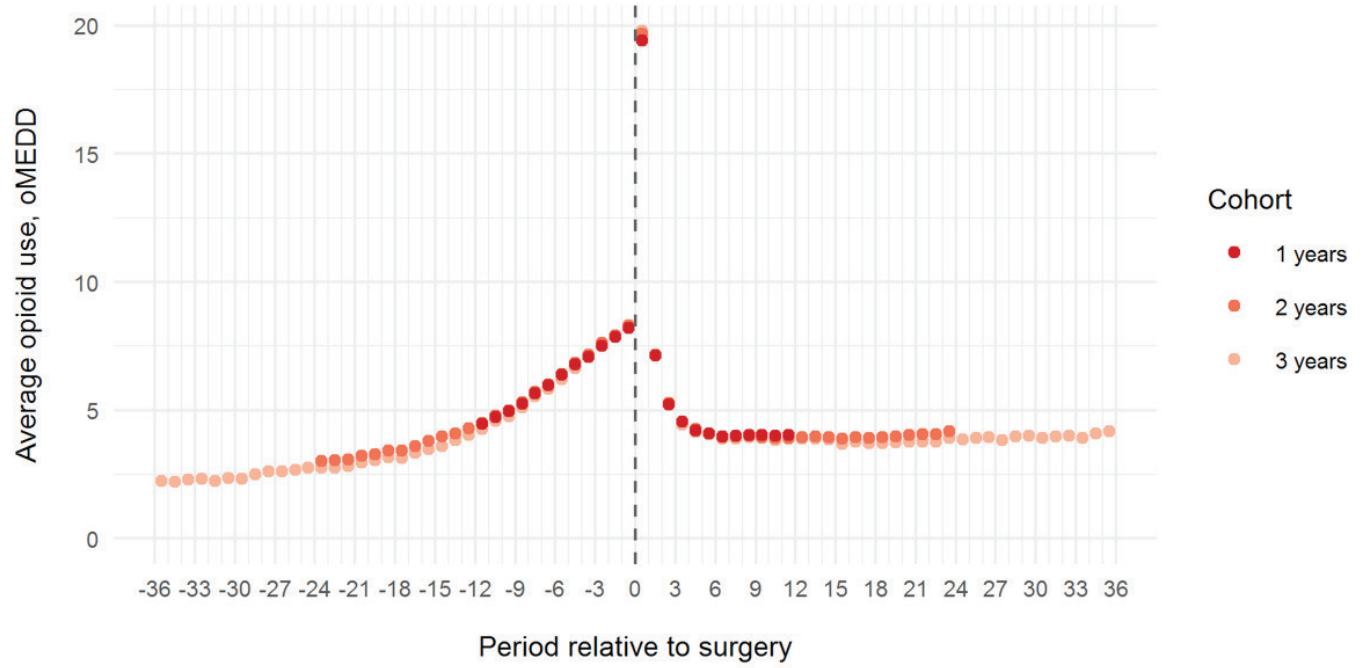
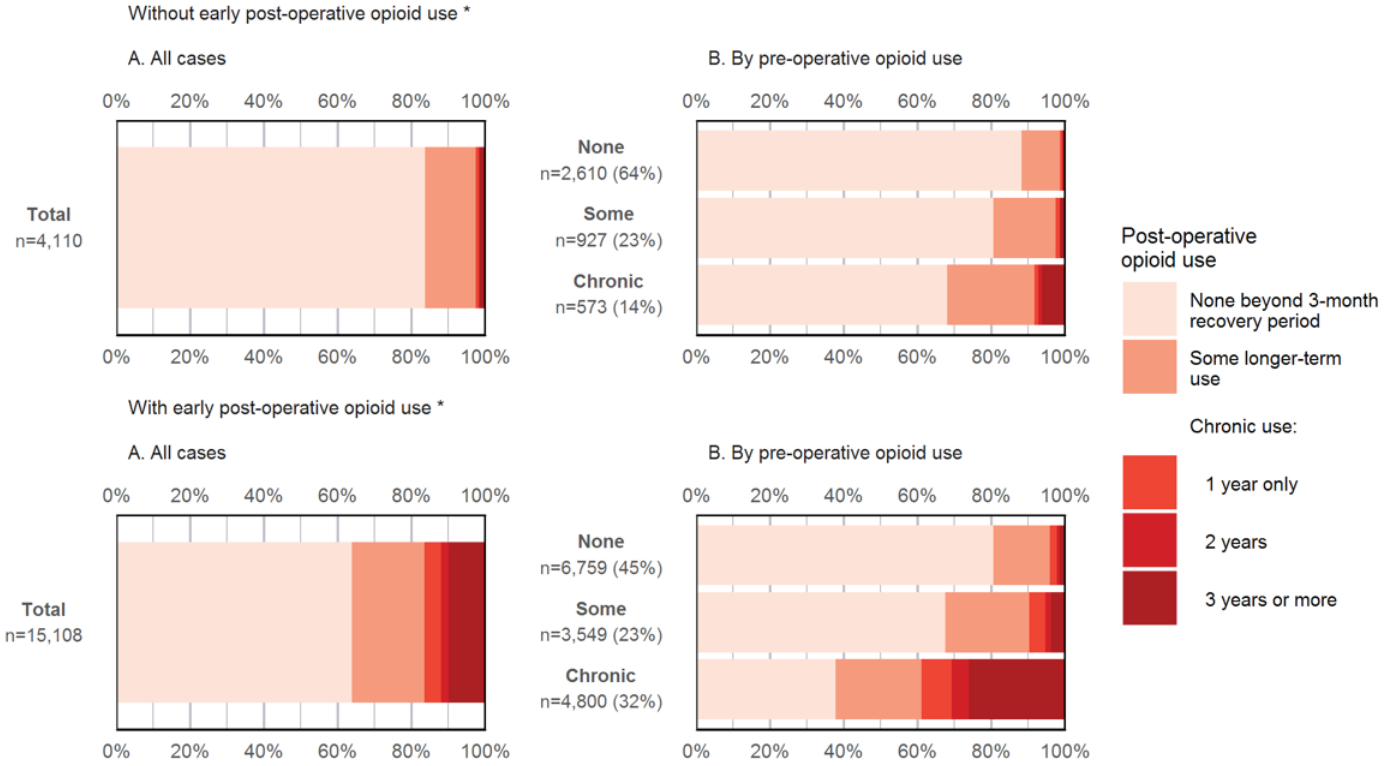


Figure A7: Long-term opioid use after joint replacement surgery, alternative definitions of 'chronic' use.

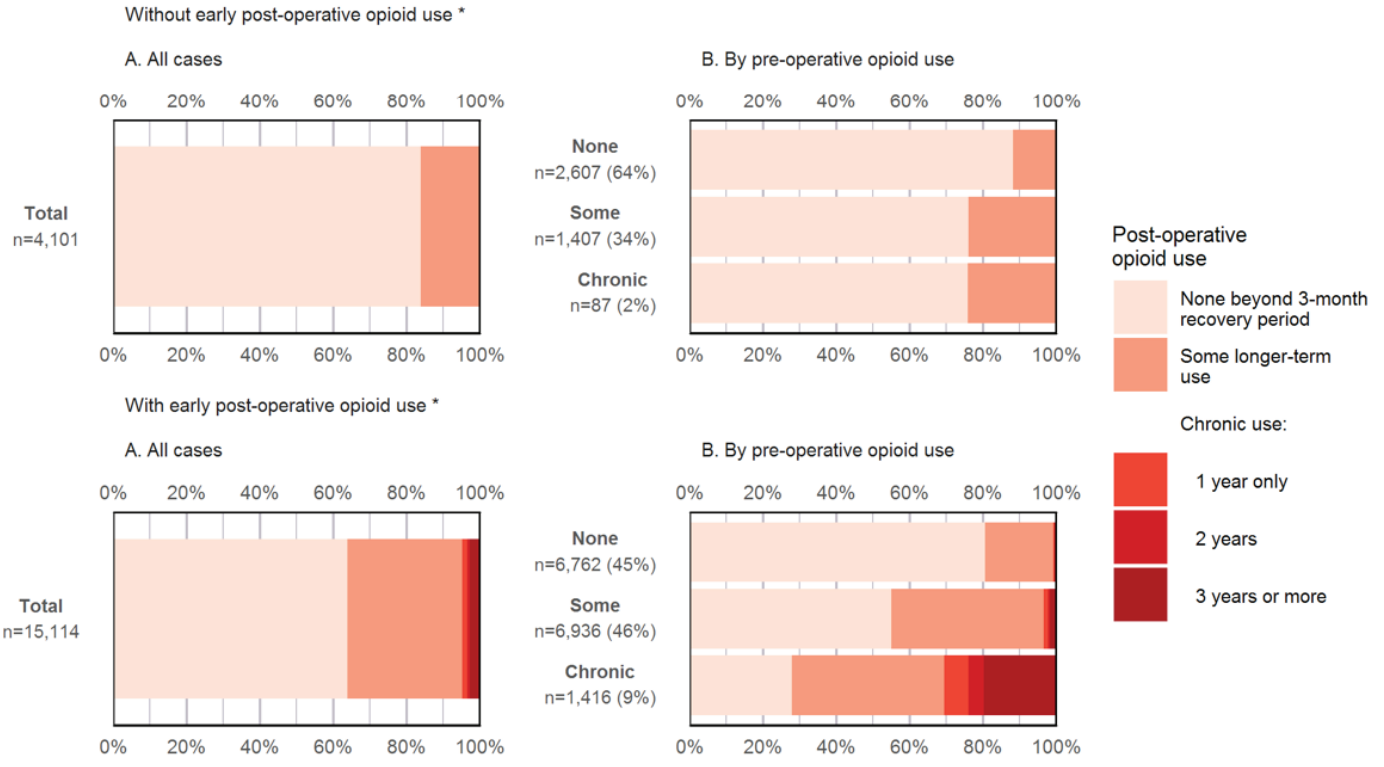
Narrow definition of 'chronic' opioid use: six consecutive months of recorded opioid use; Base case definition: three consecutive months; Broader definition: any three months of opioid use.

Figure A8: Long-term opioid use after joint replacement surgery, by use in post-operative recovery period, broader definition of chronic use.



*Early post-operative use refers to the first 3 months following the date of surgery.

Figure A9: Long-term opioid use after joint replacement surgery, by use in post-operative recovery period, narrower definition of chronic use.



*Early post-operative use refers to the first three months following the date of surgery.

Competing interests:
Dr Wilson and Dr Pryymachenko report grants from Otago Medical Research Foundation during the conduct of the study.

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The results in this paper are not official statistics. They have been created for research purposes from the Integrated Data Infrastructure (IDI), managed by Statistics New Zealand. The opinions, findings, recommendations, and conclusions expressed in this paper are those of the authors, not Statistics New Zealand. Access to the anonymised data used in this study was provided by Statistics NZ under the security and confidentiality provisions of the Statistics Act 1975. Only people authorised by the Statistics Act 1975 are allowed to see data about a particular person, household, business or organisation, and the results in this paper have been confidentialised to protect these groups from identification and to keep their data safe. Careful consideration has been given to the privacy, security and confidentiality issues associated with using administrative and survey data in the IDI. Further detail can be found in the Privacy impact assessment for the IDI available from www.stats.govt.nz
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