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# Persistent opioid use after surgical treatment of paediatric fracture

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## Abstract

**Background:** The opioid epidemic is one of the most pressing public health crises in the USA. With fractures being amongst the most common reasons for a child to require surgical intervention and receive post-surgical pain management, characterisation of opioid prescription patterns and risk factors is critical. We hypothesised that the numbers of paediatric patients receiving opioids, or who developed persistent opioid use, are significant, and a number of risk factors for persistent opioid use could be identified.

**Methods:** We conducted a retrospective population-based cohort study. National claims data from the Truven Health Analytics® MarketScan database were used to (i) characterise opioid prescription patterns and (ii) describe the epidemiology and risk factors for single use and persistent use of opioids amongst paediatric patients who underwent surgical intervention for fracture treatment.

**Results:** Amongst 303 335 patients, 21.5% received at least one opioid prescription within 6 months after surgery, and 1671 (0.6%) developed persistent opioid use. Risk factors for persistent opioid use include older age; female sex; lower extremity trauma; surgeries involving the spine, rib cage, or head; closed fracture treatment; earlier surgery years; previous use of opioid; and higher comorbidity burden.

**Conclusions:** Amongst a cohort of paediatric patients who underwent surgical fracture treatment, 21.5% filled at least one opioid prescription, and 0.6% ($N$=1671) filled at least one more opioid prescription between 3 and 6 months after surgery. Understanding risk factors related to persistent opioid use can help clinicians devise strategies to counter the development of persistent opioid use for paediatric patients.

**Keywords:** fracture; opioid prescription; orthopaedic surgery; paediatrics; persistent opioid use; surgical reduction

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### Editor's key points

- Continued opioid use after surgery has been implicated in the 'opioid epidemic' in adults in the USA, but there is limited understanding of this in the paediatric population.
- This large-scale retrospective cohort study found around one-fifth of children received at least one postoperative opioid prescription, with 0.6% having ongoing use. A number of risk factors were identified that could be used to inform targeted management.
- Understanding this issue beyond the current data set, and on an international level, is important to define the problem and formulate a robust evidence-based response.
- It is important to ensure that children who might benefit from opioids receive them, but without contributing to longer-term harms.

It has been widely recognised that the opioid epidemic is one of the most pressing public health crises in the USA at present. Since 1999, opioid-related deaths have increased six-fold[1]; almost 50 000 opioid-related overdose deaths occurred in 2018 alone, with 32% of those involving prescription opioids.[2] This development has been significantly escalated, if not triggered, by problematic postoperative opioid prescription patterns.[3] Numerous studies have shown that patients who receive opioid prescriptions for post-surgical acute pain develop prolonged or persistent opioid use with concerning frequency, even if they were previously opioid naive.[4,5] Moreover, opioids dispensed liberally for post-surgical pain have an alarming tendency to be illicitly diverted or become a household hazard, facilitating recreational use, accidental, or even intentional overdoses by patients themselves or family members.[6] Although this interrelation is well defined in adults, there is a paucity of information for the paediatric population. With an annual occurrence rate of 9.47 per 1000 children (0–19 yr),[7] fractures are amongst the most common reasons for a child to require a surgical intervention, with possible treatment options ranging from immobilisation, reduction, and casting, to hardware implantation and osteosynthesis.

It has been attempted to establish protocols to mitigate the risk of inadequate opioid prescriptions for paediatric patients on nationwide, municipal, and institutional levels.[8] However, knowledge about current prescription patterns and modifiable risk factors for chronification of use is paramount to successfully implement such protocols. The purpose of this study was to (i) characterise opioid prescription patterns and (ii) describe the epidemiology and risk factors for the persistent use of opioids amongst paediatric patients who underwent surgical fracture treatment procedures using a nationwide database. We hypothesised that the numbers of paediatric patients receiving opioids, or developed persistent opioid use, are significant and that a number of risk factors for persistent opioid use could be identified.

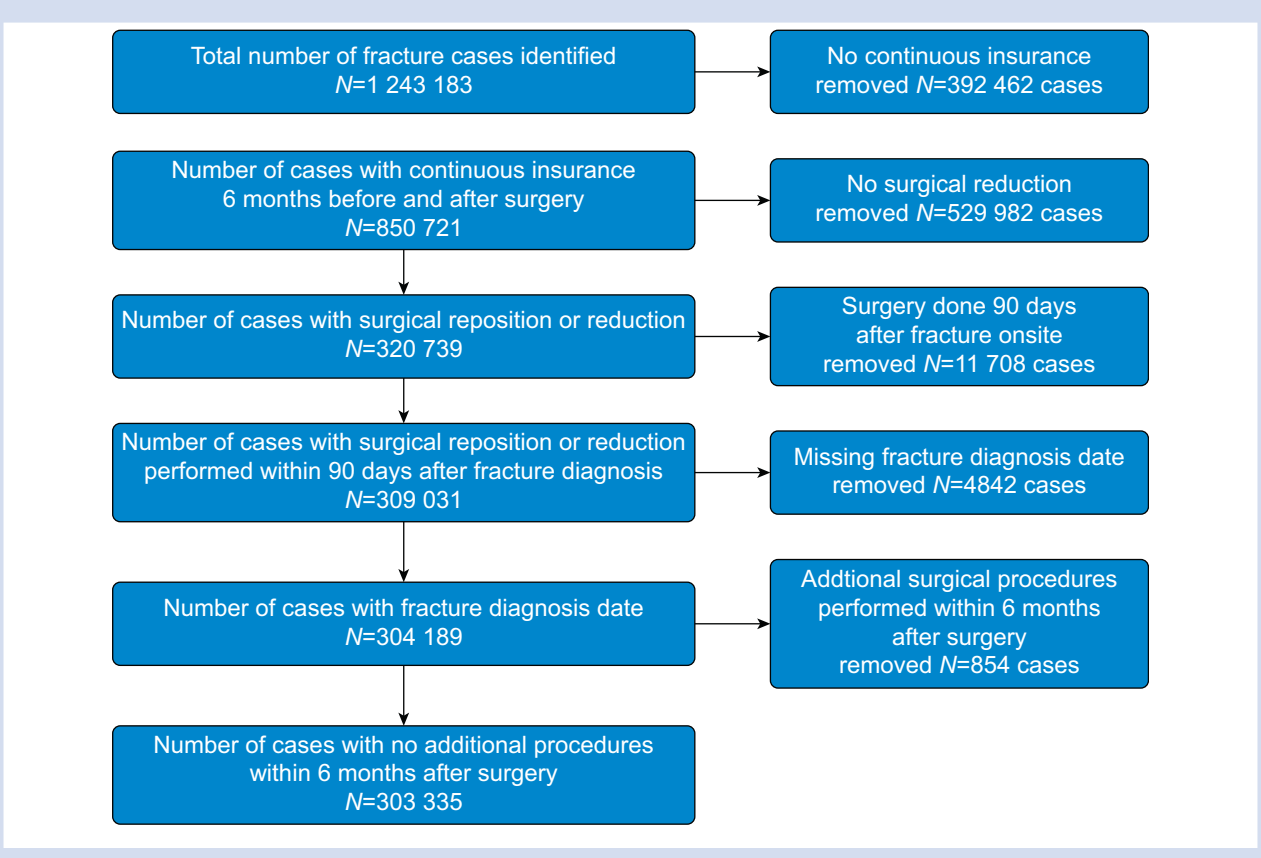


Fig 1. Strengthening the Reporting of Observational Studies in Epidemiology diagram.

Table 1 Patient characteristics by opioid prescription. ER, emergency room; IQR, inter-quartile range.

| | Opioid prescribed after surgery | No opioid prescribed after surgery | Overall | P-value |
|---|---|---|---|---|
| N (%) | 65 331 (21.5) | 238 004 (78.5) | 303 335 | |
| Age group (yr), n (%) | | | | <0.001 |
| 0–5 | 6071 (14.0) | 37 287 (86.0) | 43 358 (14.3) | |
| 6–12 | 19 228 (15.1) | 107 972 (84.9) | 127 200 (41.9) | |
| 13–18 | 27 697 (26.8) | 75 571 (73.2) | 103 268 (34.0) | |
| 19–21 | 12 335 (41.8) | 17 174 (58.2) | 29 509 (9.7) | |
| Sex, n (%) | | | | <0.001 |
| Male | 43 862 (23.1) | 146 309 (76.9) | 190 171 (62.7) | |
| Female | 21 469 (19.0) | 91 695 (81.0) | 113 164 (37.3) | |
| Year, n (%) | | | | <0.001 |
| 2013 | 22 850 (21.4) | 84 089 (78.6) | 106 939 (35.3) | |
| 2014 | 19 921 (19.1) | 84 651 (80.9) | 104 572 (34.5) | |
| 2015 | 10 574 (25.3) | 31 164 (74.1) | 41 738 (13.8) | |
| 2016 | 8053 (24.9) | 24 330 (75.1) | 32 383 (10.7) | |
| 2017 | 3933 (22.0) | 13 770 (77.8) | 17 703 (5.8) | |
| Preoperative opioid utilisation | | | | <0.001 |
| No opioid filled before surgery | 49 725 (18.8) | 214 218 (81.2) | 263 943 (87) | |
| Opioid filled only between fracture diagnosis and surgery | 8645 (37.6) | 14 326 (62.4) | 22 971 (7.6) | |
| Opioid filled before fracture diagnosis | 6961 (42.4) | 9460 (57.6) | 16 421 (5.4) | |
| Previous anxiolytics medication use, n (%) | | | | <0.001 |
| Yes | 2772 (42.8) | 3700 (57.2) | 6472 (2.1) | |
| No | 62 559 (21.1) | 234 304 (78.9) | 296 863 (97.9) | |
| Previous antidepressant medication use, n (%) | | | | <0.001 |
| Yes | 2836 (43.0) | 3757 (57.0) | 6593 (2.2) | |
| No | 62 495 (21.1) | 234 247 (78.9) | 296 742 (97.8) | |
| Deyo index, n (%) | | | | <0.001 |
| 0 | 56 415 (21.6) | 204 731 (78.4) | 261 146 (86.1) | |
| 1 | 8231 (20.8) | 31 378 (79.2) | 39 609 (13.0) | |
| 2 | 467 (25.8) | 1340 (74.2) | 1807 (0.6) | |
| 3+ | 218 (28.2) | 555 (71.8) | 773 (0.3) | |
| Obesity, n (%) | | | | 0.005 |
| Yes | 1575 (20.6) | 6073 (79.4) | 7648 (2.5) | |
| No | 63 756 (21.6) | 231 931 (78.4) | 295 687 (97.5) | |
| Type of procedure, n (%) | | | | <0.001 |
| Closed | 42 459 (16.1) | 221 241 (83.9) | 263 700 (86.9) | |
| Open | 22 872 (57.7) | 16 763 (42.3) | 39 635 (13.1) | |
| Place of procedure, n (%) | | | | <0.001 |
| Inpatient | 5189 (60.7) | 3363 (39.3) | 8552 (2.8) | |
| Outpatient | 29 058 (35.8) | 52 196 (64.2) | 81 254 (26.8) | |
| ER/urgent care | 11 382 (32.1) | 24 021 (67.9) | 35 403 (11.7) | |
| Physician's office | 11 731 (7.4) | 147 082 (92.6) | 158 813 (52.4) | |
| Other | 7971 (41.3) | 11 342 (58.7) | 19 313 (6.4) | |
| Time from fracture onsite to procedure (days), median [IQR] | 0 [0–3] | 0 [0–3] | 0 [0–3] | 0.018 |

## Methods

This study was approved by the Institutional Review Board at the Hospital for Special Surgery (IRB# 2017–0169). The requirement for written informed consent was waived given the de-identified nature of the data. We examined insurance claims data from all patients under the age of 21 yr who underwent surgical procedures after a fracture from 2013 to 2017 using Truven Health Analytics® MarketScan (copyright 2017; Truven Health Analytics, Inc., Ann Arbor, MI, USA), a claims database consisting of data from patients throughout the USA with employer-sponsored health insurance. The MarketScan database contains detailed longitudinal data, including information from both in- and outpatient visits in addition to pharmaceutical claims. This paper adheres to the applicable Consolidated Standards of Reporting Trials guidelines. Patients were included if they were diagnosed with a fracture and underwent surgical reduction or reposition. Cases were included if patients presented with fracture diagnosis and went through surgical interventions within 90 days of diagnosis. Cases were excluded if patients did not have continuous insurance coverage during the 6-month period before or after the procedure, or had a missing fracture diagnosis date, or underwent multiple procedures within 6 months after first surgery because of difficulty to know how long to follow-up. The final cohort included 303 335 patients (Fig 1). Diagnosis of fractures was identified using International Classification of Diseases (ICD)-9 and ICD-10 codes. Fracture treatment procedures were identified using ICD-9, ICD-10, and Current Procedural Terminology codes (see Supplementary Appendix 1).

Opioid prescriptions from pharmacy claims were identified by matching generic drug names with National Drug Codes, which detail specific drug doses and types. For each prescription, we converted the unit of the opioid component to

milligrams and calculated oral morphine equivalents (OMEs) by using published conversion standards.[9] Persistent opioid use was defined as one or more additional opioid prescription(s) filled between 90 and 180 days after the procedure.[10,11]

Patient characteristics data included age group (0–5, 6–12, 13–18, and 19–21 yr), sex, year of surgery, Charlson–Deyo[12] comorbidity index (categorised as 0, 1, 2, and 3+), obesity (yes/no), previous anxiolytic medication use (yes/no), previous antidepressant medication use (yes/no) (see Supplementary Appendix 2), and preoperative opioid utilisation 6 months before fracture diagnosis (no opioid filled before surgery, no opioid filled before fracture diagnosis but with opioid filled between fracture diagnosis and surgery, and opioid filled before diagnosis). Procedure-specific variables included the location of fracture (head, spine and rib, shoulder and clavicle, humerus and elbow, forearm and wrist, hand and finger, pelvis and hip, femur and knee, leg and ankle, and foot and toe), days from fracture diagnosis to procedure, open or closed procedure, and place of procedure performance (inpatient, outpatient, emergency room/urgent care, physician's office, and others).

### Statistical analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Continuous variables are summarised as medians with inter-quartile range (IQR). Categorical variables are summarised as counts and percentages. Continuous variables were analysed using the Kruskal–Wallis test and categorical variables were analysed using $\chi^2$ tests. A multivariable logistic regression model was created to identify risk factors for persistent opioid use by comparing persistent opioid use group with the group who filled at least one opioid prescription, but did not develop persistent opioid use. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported. All *P*-values reported were from two-tailed tests. A *P*-value <0.05 was used to determine significance of variables.

## Results

During the 5-yr study period from 2013 to 2017, a total of 303 335 patients under 21 yr old underwent surgical procedures for fracture treatment. As shown in Table 1, the majority of children were male (62.7%) and aged 6–12 yr old (41.9%). The most common type of procedure was a closed reduction (86.9%), which was usually performed at a physician's office (52.4%). In most cases, procedures were performed on the day of diagnosis (IQR [0–3] days). Paediatric patients undergoing fracture treatment were mostly healthy as evidenced by low comorbidity burden (with 99% of Deyo index 0 or 1), low obesity rate (2.5%), and high rates of no opioid filled 6 months before fracture (94.6%). The most common type of fracture involved the forearm and wrist (32.8%), followed by fractures of the hand and finger (22.4%) and leg and ankle (11.6%) (Table 2).

Of this cohort, 21.5% of patients (*N*=65 331) filled at least one opioid prescription within 6 months of surgery. Older paediatric patients were more likely to receive an opioid, with patients aged 19–21 (41.8%) being the most likely to receive opioid prescription (*P*<0.001). Male patients (*P*<0.001), patients with higher comorbidity burden (*P*<0.001), patients with previous opioid use (*P*<0.001), patients with previous use of anxiolytics (*P*<0.001) or antidepressants (*P*<0.001), the presence of obesity (*P*=0.005), those who underwent open procedures (*P*<0.001), those who experienced a longer waiting time from diagnosis to surgical procedure (*P*=0.018), or those who had procedures at non-physician office settings (*P*<0.001) were more likely to receive opioids. Fractures of the pelvis and hip (46.5%), femur and knee (38.8%), and spine and rib (36.1%) were the most common diagnosis associated with opioid prescription (Table 1).

Of all patients who filled at least one opioid prescription, 1671 (2.6%) developed persistent opioid use. Persistent opioid users refilled a median of four prescriptions (IQR [3–5]) with a median of 1110 OMEs (IQR [625–2363]) over the 6-month period after surgery, whereas non-persistent users usually just filled one prescription (IQR [1–1]) with a median of 270 OMEs (IQR [150–600]). The median days from surgery to last opioid refill was 137 days (IQR [113–160]) for persistent users, whereas for non-persistent users, this was the first day after surgery. The total OMEs prescribed at discharge did not differ between persistent users and non-persistent users (*P*=0.578). A total of 495 patients (0.8%) filled a combination of opioids (e.g. oxycodone and hydrocodone, and oxycodone and tramadol) at discharge. The most frequently prescribed opioids at discharge were hydrocodone (33.3%) and codeine (12.8%) (Table 3).

A multivariable logistic regression model was built to identify risk factors associated with paediatric patients who developed persistent opioid use after surgical procedures for fracture treatment (Fig 2). Controlling for other variables in the model, older patients were more likely to develop persistent

Table 2 Fracture location by opioid prescription.

| Fracture location, *n* (%) | Opioid prescribed after surgery | No opioid prescribed after surgery | Overall | *P*-value |
|---|---|---|---|---|
| N (%) | 65 331 (21.54) | 238 004 (78.46) | 303 335 | <0.001 |
| Head | 4741 (34.9) | 8861 (65.1) | 13 602 (4.5) | |
| Spine and rib | 118 (36.1) | 209 (63.9) | 327 (0.1) | |
| Shoulder and clavicle | 5785 (27.9) | 15 007 (72.1) | 20 792 (6.9) | |
| Humerus and elbow | 7918 (26.4) | 22 055 (73.6) | 29 973 (9.9) | |
| Forearm and wrist | 18 650 (18.7) | 80 897 (81.3) | 99 547 (32.8) | |
| Hand and finger | 12 379 (18.2) | 55 485 (81.8) | 67 864 (22.4) | |
| Pelvis and hip | 277 (46.5) | 319 (53.5) | 596 (0.2) | |
| Femur and knee | 2971 (38.8) | 4681 (61.2) | 7652 (2.5) | |
| Leg and ankle | 8813 (25.1) | 26 262 (74.9) | 35 075 (11.6) | |
| Foot and toe | 3679 (13.2) | 24 228 (86.8) | 27 907 (9.2) | |

Table 3 Opioid prescription pattern. IQR, inter-quartile range; OME, oral morphine equivalent.

| | Persistent user | Non-persistent user | Overall | P-value |
|---|---|---|---|---|
| N (%) | 1671 (2.6) | 63 660 (97.4) | 65 331 | |
| Total OME in 6 months, median [IQR] | 1110 [625–2363] | 270 [150–600] | 300 [150–675] | <0.001 |
| Number of prescriptions in 6 months, median [IQR] | 4 [3–5] | 1 [1–1] | 1 [1–1] | <0.001 |
| Days to last refill, median [IQR] | 137 [113–160] | 1 [0–8] | 1 [0–9] | <0.001 |
| Total OME prescribed at discharge, median [IQR] | 25 [0–60] | 25 [0–56] | 25 [0–56] | 0.578 |
| Opioid prescribed at discharge, *n* (%) | | | | |
| Combination | 53 (3.2) | 442 (0.7) | 495 (0.8) | |
| Hydrocodone | 500 (29.9) | 21 266 (33.4) | 21 766 (33.3) | |
| Oxycodone | 308 (18.4) | 7206 (11.3) | 7514 (11.5) | |
| Codeine | 75 (4.5) | 8318 (13.1) | 8393 (12.8) | |
| Tramadol | 24 (1.4) | 684 (1.1) | 708 (1.1) | |
| Others | 13 (0.8) | 140 (0.2) | 153 (0.2) | |
| No opioid prescribed at discharge | 698 (41.2) | 25 604 (40.2) | 26 302 (40.3) | |

opioid use, with 19–21 yr olds being the most likely to become persistent users (OR: 11.33; 95% CI: 7.16–17.92 compared with 0–5 yr olds). Female patients were more likely to develop persistent opioid use than male patients (OR: 1.2; 95% CI: 1.06–1.34). Patients who were treated in 2013 were found to be at higher risk for persistent opioid use compared with those treated in later years (2014–7). Compared with patients undergoing upper extremity procedures, patients who had lower extremity, spine, and rib and head procedures were more likely to develop persistent use of opioids, with pelvis and hip, femur and knee, and leg and ankle procedures being associated with the highest odds. Compared with those undergoing closed procedures, patients undergoing open procedures were less likely to develop persistent opioid use (OR: 0.77; 95% CI: 0.66–0.89). Patients with preoperative opioid use and patients with a higher comorbidity burden were more likely to develop persistent opioid use. The setting of the surgical procedure (inpatient, outpatient, emergency room/urgent care, physician's office, and others), time from fracture diagnosis to procedure, previous antidepressant and anti-anxiety medication use, or obesity did not alter the odds for persistent opioid use.

## Discussion

Ample evidence exists that excessively prescribed opioids to treat acute post-surgical pain are directly implicated with repeated use and later development of problematic use. Not least because of these realisations, guidelines for opioid use in children recommend that opioid prescriptions be reserved for severe conditions, for example, cancer, multisystem trauma, and serious chronic diseases.[13] Amongst our cohort of 303 335 patients aged 0–21 yr undergoing comparably simple surgical procedures for fracture treatment, more than one in five patients filled at least one opioid prescription after surgery. When comparing this rate to prior investigations with a nationally representative study by Groenewald and colleagues,[14] there were an average of 2.86% of children and adolescents receiving an opioid prescription each year from 1996 to 2012, thus rendering our findings concerning.

Persistent opioid use was found in 0.6% of paediatric patients, as defined by two or more prescriptions filled after discharge, an approach described and adopted in prior investigations.[15] The incidence of prolonged use was even higher (1.1%) amongst adolescents aged 13 and above. A retrospective cohort study by Harbaugh and colleagues[11] with commercial claims data from the Truven Health MarketScan research databases from 2010 to 2014 also focused on opioid prescription patterns amongst non-surgical and surgical paediatric patients. They reported persistent opioid use in 4.8% of surgical patients compared with 0.1% in the non-surgical group.[11] Our findings support that the ongoing opioid crisis does not exclude patients of younger age. However, our study also shows a reduction in persistent opioid use over the study period, which reflects an increasing effort of addressing of the risk of opioid abuse in the USA. Although there were only 21.5% paediatric patients with a filled opioid prescription, 0.6% patients led to at least one more prescription refill. Future investigations are indicated to understand the nature of such refills and potential intervention to minimising prolonged opioid exposure.

As demonstrated by Bot and colleagues[16] and Rosenbloom and colleagues,[17] opioid use after traumatic musculoskeletal injury is related to pain severity. Lower extremity fractures involving the pelvis, hip, femur, knee, leg, or ankle are known to be more painful and take longer time to full recovery. Consequently, a larger number of patients were prescribed opioids in this group (13.2–46.5%). Predicting children's pain level through the course of recovery presents a unique challenge, particularly as majority of patients in our cohort were treated in a physician's office (52.4%) or in an outpatient setting (26.8%), where access to follow-up pain management may be limited. Although physicians may worry that they are under-treating pain, O'Neill and Webb Thomas[18] and Rodgers and colleagues[19] showed that the majority of patients prescribed opioids after orthopaedic procedures did not require the full amount of prescribed opioids. Physicians need to be aware of this and strive to adjust the analgesic therapy intensity to the real rather than the expected pain level. Alternative strategies should be considered to reduce the need for postoperative opioid requirement, such as multimodal protocols, regional anaesthesia, psychological support, physical therapy, enhanced-recovery approaches, mindfulness exercises, and others.

Consistent with previous findings,[11,20–22] we found older age, female sex, and previous exposure to opioids as risk factors for persistent opioid use after paediatric fracture treatment. For adults, younger age, female sex, lower income,

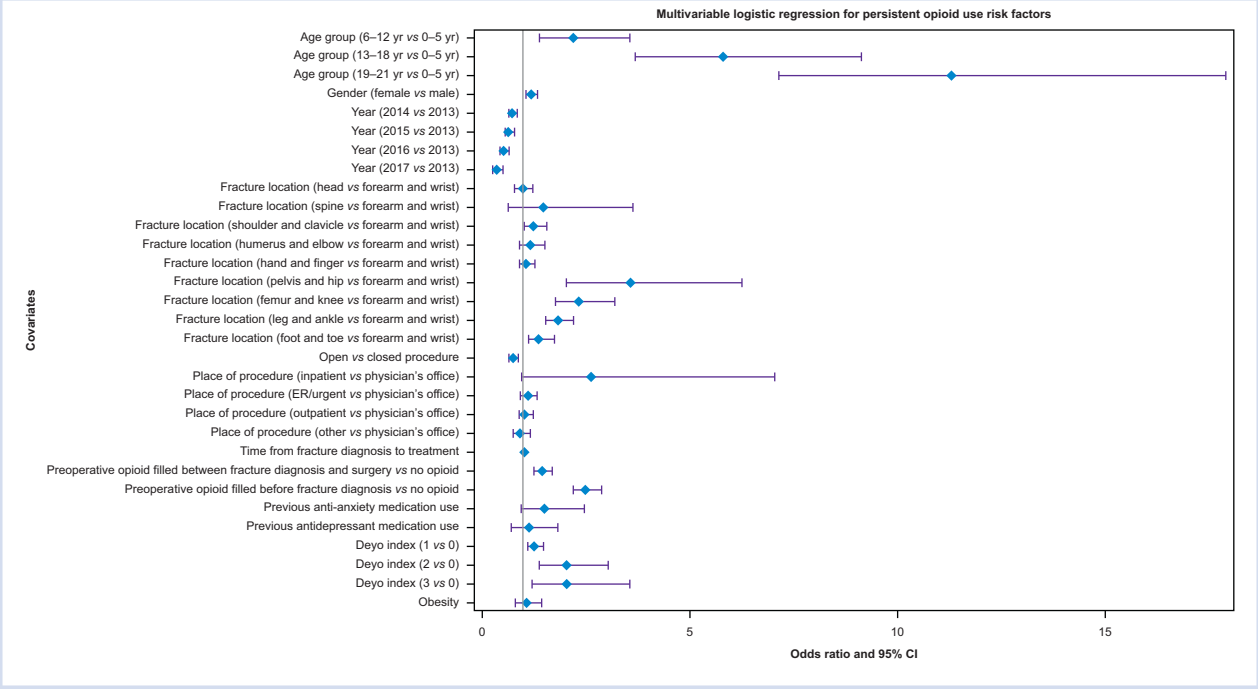


Fig 2. Multivariable logistic regression for persistent opioid use risk factors. CI, confidence interval; ER, emergency room.

higher comorbidity burden, mental health disorders, and tobacco dependence or abuse were associated with prolonged opioid use after fracture.[23,24] Compared with paediatric patients, adult patients report higher incidence of persistent opioid use after fracture, which may be related to higher comorbidities and substance abuse disorders amongst adults.

Evidence exists against the use of codeine and tramadol medicines in children because of their metabolism, leading to overdose and serious risk of respiratory depression and death.[25] In 2013, the Food and Drug Administration (FDA) restricted the use of codeine in children undergoing tonsillectomy or adenoidectomy.[26] In 2017, the FDA expanded the restriction to the use of codeine and tramadol medicines in children under 12 and some older children.[27] Codeine and tramadol were prescribed to 14% of children in our cohort during the study period from 2013 to 2017, with codeine being the second most frequently prescribed opioid at discharge. A future study is warranted to study the impact of the FDA restriction on prescription of codeine and tramadol in paediatric patients.

To our knowledge, this is the first study to examine opioid prescription patterns and persistent opioid use after surgical fracture treatment amongst paediatric patients using a large national database. Limitations include that the data set used for this investigation relies on billing codes of pharmacy dispensing, which raises the possibility of misclassification of prescribed medications. Only patients who had private insurance coverage were included in this study. A cohort containing patients with state or federal healthcare coverage may produce different results. Furthermore, opioid dispensing of pharmacy fills was used to approximate actual opioid consumption. It is likely that not all refilled opioid prescriptions were actually consumed by patients. However, the aim of this study was the characterisation of opioid prescription patterns rather than the actual consumption; access to prescribed opioids in households is a well-defined risk factor for illicit consumption, criminal mispurpose, and accidental intake.[28–30] Without proper disposal of excess opioids, children and other family members are put at risk. Around 11–38% of opioid misuse in young adults derives from a physician's prescription, including a patient's own leftover prescription.[6] Leftover opioids can easily be mistaken by other family members or get distributed amongst peers. This is a US healthcare database study, in which we included 19–21-yr-old patients.[31,32] However, other countries might have different definitions. Nonetheless, we believe these differences should not change our conclusion that continuous efforts should be made to address the risk of opioid abuse in the USA.

## Conclusions

In conclusion, amongst a large cohort of 303 335 paediatric patients who underwent surgical fracture treatment, 21.5% filled opioid prescriptions postoperatively and 0.6% (N=1671) filled at least one more opioid prescription over the course of 3–6 months after surgery. Understanding risk factors related to persistent opioid use may help clinicians to devise strategies to counter the development of persistent opioid use in children and adolescents.

## Authors' contributions

Study design/planning: all authors
Data analysis: HZ, LAW
Interpretation of results: all authors
Preparation of paper: HZ, HNL, LAW, KRD, JP, SGM
Review of paper: all authors

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Department of Anesthesiology, Critical Care & Pain Management, Hospital for Special Surgery.

## Declarations of interest

SGM is a director on the boards of the American Society of Regional Anesthesia and Pain Medicine and the Society of Anesthesia and Sleep Medicine; a one-time consultant for Sandoz, Inc. and Teikoku, and is currently on the medical advisory board of HATH; He has a pending US patent application for a Multicatheter Infusion System (US-2017-0361063); and is the owner of SGM Consulting, LLC and co-owner of FC Monmouth, LLC. None of the aforementioned relations influenced the conduct of the present study. All other authors declare no conflicts of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.12.044.

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