Published in final edited form as:

Anesth Analg. 2020 October ; 131(4): 1237–1248. doi:10.1213/ANE.0000000000004823.

Incidence of and Factors Associated with Prolonged and Persistent Postoperative Opioid Use in Children 0 to 18 Years of Age

Andrew Ward, M.S.,

Department of Electrical Engineering, Stanford University, Stanford, CA, United States

Elizabeth De Souza, Ph.D.,

Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, United States

Daniel Miller, Ph.D.,

Department of Electrical Engineering, Stanford University, Stanford, CA, United States

Ellen Wang, M.D.,

Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, United States

Eric C. Sun, M.D., Ph.D.,

Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine and Department of Health Research and Policy, Stanford, CA, United States

Nicholas Bambos, Ph.D.,

Department of Electrical Engineering and Department of Management Science & Engineering, Stanford University, Stanford, CA, United States

Thomas Anthony Anderson, Ph.D., M.D.

Corresponding Author: Thomas Anthony Anderson, Ph.D., M.D., Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, 300 Pasteur Drive, MC5640, Stanford, CA, United States, 650-725-5742, tanders0@stanford.edu.

Contribution

Andrew Ward: This author helped with research conceptualization and design, data analysis, data interpretation, writing and final approval of the manuscript.

Elizabeth De Souza: This author helped with research conceptualization and design, data analysis, data interpretation, writing and final approval of the manuscript.

Daniel Miller: This author helped with research conceptualization and design, data analysis, and final approval of the manuscript.

Ellen Wang: This author helped with research conceptualization and design, writing and final approval of the manuscript.

Eric C. Sun: This author helped with research conceptualization and design, writing and final approval of the manuscript.

Nicholas Bambos: This author helped with research conceptualization and design, writing and final approval of the manuscript.

Thomas Anthony Anderson: This author helped with research conceptualization and design, data analysis, data interpretation, writing and final approval of the manuscript.

Conflicts of Interest

Dr. Sun acknowledges consulting fees unrelated to this work from Egalet, Inc, and the Mission Lisa Foundations. The remaining authors declare no competing interests.

Clinical trial number and registry URL

Not applicable.

Prior Presentations: This work was presented as poster presentations at the International Anesthesia Research Society and Association of University Anesthesiologists meetings in Montreal, Canada (May 2019).

Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, United States

Abstract

Background—Long-term opioid use has negative healthcare consequences. Opioid-naïve adults are at risk for prolonged and persistent opioid use after surgery. While these outcomes have been examined in some adolescent and teenage populations little is known about the risk of prolonged and persistent postoperative opioid use after common surgeries compared to children who do not undergo surgery, and factors associated with these issues among pediatric surgical patients of all ages.

Methods—Using a national administrative claims database, we identified 175,878 surgical visits by opioid-naïve children aged 18 who underwent 1 of the 20 most common surgeries from each of four age groups between December 31, 2002 and December 30, 2017, and who filled a perioperative opioid prescription 30 days before to 14 days after surgery. Prolonged opioid use after surgery (filling 1 opioid prescription 90–180 days after surgery) was compared to a reference sample of 1,354,909 nonsurgical patients randomly assigned a false “surgery” date. Multivariable logistic regression models were used to estimate the association of surgical procedures and 22 other variables of interest with prolonged opioid use and persistent postoperative opioid use (filling 60 days’ supply of opioids 90–365 days after surgery) for each age group.

Results—Prolonged opioid use after surgery occurred in 0.77%, 0.76%, 1.0%, and 3.8% of surgical patients ages 0–<2, 2–<6, 6–<12, and 12–18 respectively. It was significantly more common in surgical patients than nonsurgical patients (ages 0–<2: odds ratio [OR] 4.6, 95% confidence interval [CI] 3.7–5.6; ages 2–<6: OR 2.5, 95% CI 2.1–2.8; ages 6–<12: OR 2.1, 95% CI 1.9–2.4; ages 12–18: OR 1.8, 95% CI 1.7–1.9). In the multivariable models for ages 0–<12, few surgical procedures and none of the other variables of interest were associated with prolonged opioid use. In the models for ages 12–18, ten surgical procedures and five other variables of interest were associated with prolonged opioid use. Persistent postoperative opioid use occurred in <0.1% of patients in all age groups.

Conclusions—Some patient characteristics and surgeries are positively and negatively associated with prolonged opioid use in opioid-naïve children of all ages, but persistent opioid use is rare. Specific pediatric subpopulations (e.g., older patients with a history of mood/personality disorder or chronic pain) may be at markedly higher risk.

Introduction

Opioid misuse has reached epidemic proportions in the U.S. In 2017, 4.2% of the population over 12 years of age misused opioids, 46,700 Americans died of an opioid overdose, and 17,029 of those deaths were from prescription opioids.^{1,2} Exposure to opioids occurs via both legitimate and illegitimate routes, including prescriptions from healthcare providers, a subset of which are prescribed for perioperative pain management. Children who have not taken opioids previously are often introduced to them just before, during, or after surgery, and this increases the risk of prolonged opioid use after surgery (POUS, here defined as 1 opioid prescription filled in the 90–180 days after surgery) and persistent postoperative

opioid use (PPOU, here defined as ≥ 60 days of opioid prescriptions filled in the 90–365 days after surgery).^{3,4} One hundred million adult and pediatric outpatient and inpatient medical procedures occur in the United States each year.^{5,6} While there is significant attention on the implications of chronic opioid use and abuse among adults, less research has investigated these issues in children. A recent study found that almost 9% of 12th graders misused opioids in the prior 12-month period.⁷ Alarming, the pediatric mortality rate from prescription and illicit opioid poisonings increased almost 300% between 1999 and 2016.⁸

Increased rates of opioid prescription fills, and presumably use, after surgery is a well-recognized and described problem in adult surgical populations; up to 13% of adults will continue to use opioids after surgery.^{9–11} Long-term opioid use is associated with a host of negative consequences, including death and disability.^{12,13} While nearly six million medical procedures take place in children in the United States annually,^{5,6,14} the risk of POUS and PPOU in this vulnerable population have not been as well-defined. Previous studies assessed the risks of POUS and PPOU in children who underwent subsets of dental or surgical procedures and found it to be as high as 15%.^{3,4,15} Harbaugh et al., investigated the incidence of ≥ 1 opioid prescription fill in the 90–180 days after surgery in opioid-naïve patients 13–21 years of age who underwent 1 of 13 surgeries.⁴ They found an incidence of 4.8% with the highest risk after cholecystectomy and colectomy and independent risk factors of older age, female, substance use disorder, chronic pain, and preoperative opioid prescription fill. Another study of patients 8–25 years of age who underwent cleft palate surgery found an incidence of prolonged opioid use after surgery of 4.4% with higher risk associated with distractor placement, gastrointestinal comorbidity, and increasing age.³ However, POUS, PPOU, and chronic opioid use after surgery are variably defined in much of the adult and pediatric literature. Some previous studies have defined PPOU as ≥ 1 opioid prescription filled in the 90–180 days after surgery,^{3,4,9} yet others have defined this as POUS,¹⁰ and still others have defined chronic opioid use as ≥ 10 opioid prescriptions filled or >120 days' supply in the 90–365 days after surgery.¹¹ Kent et al., reviewed this topic in detail and created a consensus statement that included a definition of PPOU (≥ 60 days of opioid prescriptions filled in the 90–365 days after surgery).¹⁶

Although understudied in all ages, especially younger children, long-term opioid use by children also has significant negative consequences.¹⁷ Information linking opioid prescribing to pediatric patients and subsequent opioid use issues is lacking.¹⁸ While information on risk factors for POUS and PPOU are available in adult populations,¹⁶ it is not apparent which children are at increased risk for POUS and PPOU across all ages and a wide range of surgeries or what strategies should be utilized perioperatively to decrease this risk.^{3,4}

POUS and PPOU have previously been defined within the literature on this topic using opioid prescription fills as a surrogate for use.¹⁶ Our primary and secondary hypotheses were that rates of POUS (≥ 1 opioid prescription filled in the 90–180 days after surgery) and PPOU (as ≥ 60 days of opioid prescriptions filled in the 90–365 days after surgery) among opioid-naïve children who underwent one of the 20 most common surgeries in each of four age groups, would be elevated compared to controls who did not undergo surgery. Our primary aim was to estimate the percentage of surgical and non-surgical patients with POUS

and PPOU. Our secondary aims were to investigate the factors associated with increased and decreased odds of POUS in surgical patients from each age group, including age, sex, race, year of surgery, history of chronic pain, mood/personality disorders, substance use disorders, cancer, and other comorbidities as identified by the pediatric complex chronic conditions (CCC) classification system.

Methods

This study used the Optum Clinformatics™ Data Mart Database (OptumInsight, Eden Prairie, MN), a de-identified database from a national insurance provider. The database contains medical and pharmacy claims from December 31, 2002 to December 30, 2017. The medical claims data contain information including international classification of diseases (ICD) codes (ninth and tenth revisions), current procedural terminology (CPT) codes, pharmacy prescription fills, and dates of service for inpatient and outpatient encounters. Due to the de-identified nature of the dataset, the Stanford University Institutional Review Board determined that this research does not involve human subjects as defined in 45 CFR 46.102(f) or 21 CFR 50.3(g) and waived the need for approval and written informed consent from de-identified database subjects.

Study sample

Patients 0–18 years of age who underwent one of the 20 most common surgery types within each of four age groups (0–<2 years, 2–<6 years, 6–<12 years, and 12–18 years) between December 31, 2002 and December 30, 2017 were included. (Supplementary Table 1) These age groups were chosen based on physiologic similarities and differences between children of different ages as suggested by the World Health Organization and the National Institute of Child Health and Human Development.^{19,20} The top 20 surgeries for each age group were determined by CPT code frequencies in the database.

To be eligible, patients were required to be opioid-naïve, defined as not having filled an opioid prescription in the 90 days prior to surgery,¹⁶ and had to have filled a perioperative opioid prescription, defined as an opioid prescription filled from 30 days before surgery to 14 days after surgery.^{3,4,21} Opioid prescriptions included were identified by American Hospital Formulary Service Class 280808, 280812 28080800, or 28081200 (opiate agonists and partial agonists, excluding opiates used only in cough suppressants). To improve data quality and reduce inaccuracies, patients were additionally required to have a general anesthesia CPT code recorded within one calendar day of their surgical CPT code. (Supplementary Table 1) Patients aged 2–18 years of age were eligible if they had been enrolled for at least one year prior to surgery and remained enrolled for at least one year following surgery. This ensured we could estimate opioid-naïve status at time of surgery, identify comorbidities, and assess POUS and PPOU. Patients aged 0–<2 years of age were only required to be enrolled for at least one year following surgery, since they might be aged under one year at the time of surgery.

Additionally, to ensure patients were not exposed to opioids due to additional surgeries, we excluded patients who had a general anesthesia claim either in the 3–365 days prior to their

surgery date or in the 3–365 days following their surgery date. Patients whose surgery date fell within a hospital stay that exceeded 30 days were also excluded.

Reference Sample

To estimate the baseline incidence of opioid use, we defined a reference sample for this study by taking a random 25% sample of patients in each age group. These patients acted as an ‘unexposed’ control group, with which we could compare surgical patient variables and provide data on incidence of opioid use in patients not undergoing surgery. For each patient in the control group, a fictitious surgery date was randomly selected.^{4,9} Similar to surgical patients, control patients aged 2–18 years at the time of their fictitious surgery date were required to be enrolled for at least one year prior to and at least one year following their fictitious surgery date. Patients aged 0–<2 years were not required to have a year of enrollment prior to surgery. Eligible patients were required to be opioid-naïve, defined as not having filled an opioid prescription in the 90 days prior to their fictitious surgery date. To ensure patients were not exposed to opioids due to additional surgeries, we excluded patients who had a general anesthesia claim either in the one year prior to their fictitious surgery date or in the one year following their fictitious surgery date.

Outcome measure

The primary outcome was POUS, defined as having filled ≥ 1 opioid prescription in the 90–180 days after surgery among opioid-naïve patients who filled a perioperative opioid prescription.²¹ The secondary outcome was PPOU, defined as having filled ≥ 60 days’ supply of opioids in the 90–365 days after surgery among opioid-naïve patients who filled a perioperative opioid prescription.¹⁶ We estimated the percentage of patients with POUS and PPOU, and investigated patient and surgery characteristics positively and negatively associated with POUS and PPOU.

Other variables of interest

The following covariates and potential confounders of the relationship between surgery and POUS were identified based on the adult and pediatric literature and included in our logistic regression models for all age groups: age, sex, race, year of surgery, cancer, chronic pain, mood/personality disorders (for age 6–<12 and 12–18), substance use disorders (for age 6–<12 and 12–18), and pediatric complex chronic conditions (CCC) classification system.^{4,9,22} A history of chronic pain, cancer, substance use disorders, and mood or personality disorders was estimated by searching for at least one mention of any of the ICD codes listed in Supplementary Table 2 in the year prior to surgery. Since chronic pain may not always be identified as chronic pain in medical claims, we also identified ICD codes which represented acute pain. If a patient had the same acute pain ICD code reported on two medical claims that were >3 months apart, that patient was classified as having chronic pain.

Statistical methods

Analysis was carried out in R and Python 3.6. Patient demographics and characteristics were reported as frequency counts, and differences between the surgical and nonsurgical patient cohorts were assessed with *t* tests or chi-square tests. Overall

significance of race was determined by the likelihood ratio test. The analysis was stratified by age because of the inherent differences in the age groups.

Two separate logistic regression models were fit for each age group, and Bonferroni corrections were used to adjust for multiple testing and maintain a family-wise error rate of 0.05. The first model was fit on both surgical and nonsurgical patients to estimate the association between surgical procedures and POUS, controlling for other variables described above. Bonferroni corrections adjusted the significance criterion for the number of distinct procedures compared to the reference sample without adjustment for controlling for confounding variables, thus for each age group $P < 0.05/(\text{number of different surgical procedures})$ was considered statistically significant.²³ Different denominators applied because different numbers of surgeries were included in each model, reflecting the fact that some surgeries did not have any associated cases of POUS.

The second logistic regression model was fit only on surgical patients to estimate the association between other variables of interest and POUS, controlling for surgical procedures. Bonferroni corrections adjusted for the number of variables (not levels of variables), thus $P < 0.05/(\text{number of variables of interest in the model})$ was considered statistically significant.²³ The different denominators applied because different numbers of variables of interest were included in each model, reflecting the fact that some variables did not have any associated cases of POUS.

Assuming an incidence of POUS of 2% in the nonsurgical population,²⁴ in order to detect an OR of 1.5⁴ for surgery (corresponding to an incidence of POUS of approximately 3%) with 90% power and 5% significance level, a sample size of 21,639 is required.²⁴

Results

The top 20 surgeries accounted for 82.4% of all surgeries in the 0–<2 age group, 81.7% of all surgeries in the 2–<6 age group, 67.4% of all surgeries in the 6–<12 age group, and 43.7% of all surgeries in the 12–18 age group. From the youngest to oldest age group respectively, the percentages of surgical patients who were excluded from the study because they did not fill a perioperative opioid prescription were 85.7%, 54.8%, 36.6%, and 17.1%. There were 23,820 surgeries, 14,722 patient visits, and 14,684 unique patients aged 0–<2; 56,057 surgeries, 42,857 patient visits, and 42,467 unique patients aged 2–<6; 55,045 surgeries, 47,920 patient visits, and 47,545 patients aged 6–<12, and 88,464 surgeries, 70,379 patient visits, and 68,692 patients aged 12–18 included in the study (Figure 1). In the nonsurgical control group, there were 271,326 patients, 217,674 patients, 394,200 patients, and 471,709 patients in the 0–<2, 2–<6, 6–<12, and 12–18 age groups, respectively, and each patient had one false surgical visit date assigned to them. The sample size in each age group exceeds the minimum required by our power analysis. Patient characteristics of the surgical and nonsurgical groups, along with the incidences of POUS and PPOU, are shown in Table 1.

Supplementary Table 3 shows the 20 most common surgeries for each age group, and the number of patients who met inclusion criteria and had each of the surgeries. While patients

with a different surgical visit within 1 year of their top 20 surgery were excluded, some patients had multiple top 20 surgeries more than 1 year apart or within the same surgical visit. (Supplementary Tables 4 and 5) The percentage of patients with POUS and the ranges across the most common 20 surgeries with 10 cases of POUS were 1) ages 0–<2: 0.77% versus 0.17% of nonsurgical patients (odds ratio [OR] 4.5, 95% CI 3.7–5.6), ranging from 0.49% to 1.4% across individual surgeries; 2) ages 2–<6: 0.76% versus 0.31% of nonsurgical patients (OR 2.5, 95% CI 2.1–2.8), ranging from 0.74% to 1.0% across individual surgeries; 3) ages 6–<12: 1.0% versus 0.47% of nonsurgical patients (OR 2.1, 95% CI 1.9–2.4), ranging from 0.74% to 1.3% across individual surgeries; 4) ages 12–18: 3.8% versus 2.1% of nonsurgical patients (OR 1.8, 95% CI 1.7–1.9), ranging from 2.1% to 6.0% across individual surgeries. We do not report exact percentages for surgeries which had fewer than 10 cases of POUS due to patient privacy considerations. (Figure 2) Multivariable logistic regression model results for associations between individual surgeries and POUS by age group are shown in Table 2. Multivariable logistic regression model results in surgical patients for prolonged opioid use after surgery by age group are shown in Table 3.

For ages 0–<2 years, myringotomy was associated with increased rates of POUS. For ages 2–<6 years, adenoidectomy, tonsillectomy, and tonsillectomy/adenoidectomy were positively associated with POUS, and among surgical patients, year of surgery was negatively associated with POUS. For ages 6–<12 years, laparoscopic appendectomy, tonsillectomy, tonsillectomy/adenoidectomy, and tympanoplasty with tympanomeatal flap were positively associated with POUS, and among surgical patients, year of surgery was negatively associated with POUS.

For ages 12–18 years, closed treatment of nose fracture, knee arthroscopic chondroplasty, knee arthroscopic partial synovectomy, laparoscopic appendectomy, removal of deep fixation device, septoplasty, shoulder arthroscopic capsulorrhaphy, tonsillectomy, and tonsillectomy/adenoidectomy were positively associated with POUS, and removal of completely impacted tooth was negatively associated with POUS. Among surgical patients, age, history of mood/personality disorder, and history of chronic pain were positively associated with POUS, while male gender, Asian race, and year of surgery were negatively associated with POUS.

For ages 0–<2, 2–<6, and 6–<12, there were fewer than 10 patients with PPOU, so we are unable to report exact statistics. Across all three younger age groups, PPOU occurred in fewer than 10 of 105,499 (<0.009%) surgical patients and 11 of 883,200 (0.001%) nonsurgical patients. For ages 12–18, PPOU occurred in 37 (0.053%) surgical patients and 107 (0.023%) nonsurgical patients (OR 2.2, 95% CI 1.5–3.3). The number of patients with PPOU was too low in all age groups to build adjusted regression models.

Discussion

In this study, we investigated prolonged and persistent opioid use after surgery in opioid-naïve patients aged 0–18 years. Approximately 1% of 0–<2, 2–<6, and 6–<12-year-olds filled one or more opioid prescription 90–180 days after surgery, while approximately 4% of 12–18-year-olds did. In the nonsurgical control groups, POUS occurred in <1% of patients

among 0–<2, 2–<6, and 6–<12-year-olds, and approximately 2% in 12–18-year-olds. The percentage of patients with PPOU was low (<0.1%) across all age groups (but highest in the 12–18-year age group, 0.053%). While perioperative opioid prescription rates are higher in each successive age group, it is difficult to draw conclusions given that different surgeries are included in each age group.

In the multivariable logistic regression models, increasing age within 12–18-year-olds was positively associated with POUS, which was consistent with the increased incidence of POUS in this age group compared to the younger age groups. The number of surgeries and other variables associated with POUS was greater in the older age groups: 9 (45%) surgeries had positive associations and 1 (5%) had a negative association, and six of the 21 other variables considered (29%) were associated with POUS in patients 12–18 years of age. This may reflect the larger number of patients in the older age groups, and hence increased power, or may reflect a real increase in variables associated with POUS. The negative association of POUS with calendar year may be a result of increased awareness of opioid risks and the overall decline in opioid prescriptions from 2013–2018, as reported by the American Medical Association 2019 Opioid Task Force.^{3,4,25}

Among prior publications in older children and adult populations, there is heterogeneity and overlap in the definitions of prolonged opioid use after surgery and persistent postoperative opioid use, making direct comparison of results difficult. However, the percentage of patients with POUS in the adolescent age group here is similar to that found in multiple adult and adolescent studies.^{3,4,9} Given the small amount of prior information available on this topic in patients from 0–18 years of age, we chose to assess POUS in the 20 most frequent surgeries for each of four age groups. Consistent with multiple prior adult studies, mood/personality disorders and chronic pain were associated with POUS.^{4,10,11,15,26} Findings in the 12–18 year age group that POUS is associated with age, chronic pain, and sex are similar to those in the study by Harbaugh et al.⁴ The finding that Asian race/ethnicity is associated with decreased POUS in 12–18-year-olds is consistent with a study of 16–25-year-olds who filled dental prescriptions.¹⁵ The findings here of decreased odds of POUS associated with a removal of completely impacted tooth are surprising and unexplained, and may warrant further investigation.

These findings have multiple important clinical implications. This study suggests that there are age-specific variables associated with POUS. Here, adolescents and teenagers were found to have a higher risk of POUS than younger patients. Prior studies have revealed that adolescents and teenagers are a particularly vulnerable population for high risk behaviors, including substance abuse.^{27,28} Thus, understanding more fully the factors associated with prolonged and persistent opioid use in this population should be a priority. If these findings are validated in additional patient cohorts, predictive risk factors could be used to monitor and minimize prolonged opioid use after surgery in this population.²⁹ Consistent with prior work,³⁰ this study also revealed that >2% of children 12–18 years of age who did not have surgery filled 1 opioid prescription within a 3 month time period. This finding should be further investigated to better understand non-perioperative pediatric opioid prescribing practices.

While a PPOU definition of 60 days of opioid prescriptions filled in the 90–365 days after surgery has been suggested as a consensus measure of concerning postoperative opioid use based on the adult literature,¹⁶ little is known about the true level of opioid use at which clinically meaningful negative consequences exist. PPOU is a sufficiently rare outcome in pediatric patients (a reassuring finding) that we could not fit models to investigate factors associated with it. Since little is known about what level of opioid use is actually associated with clinically important negative consequences in different populations, especially pediatric patients, we investigated POUS and factors associated with it. Given the limited literature on longer-term postoperative opioid use in pediatric patients, we feel this was an important starting point for future studies.

Recent pediatric studies investigating the amount of opioid prescribed and used postoperatively have found that many pills go unused,^{31,32} but clinicians have begun to assess the optimal amount and duration of postoperative opioid prescription.³³ Not surprisingly, patients who receive an opioid prescription within seven days after surgery are more likely to become long-term opioid users,³⁴ and prescription duration is a predictor of opioid use and misuse after surgery.³⁵ However, utilization of the perioperative surgical home and acute pain service to identify high-risk patients and a transitional pain service to manage such patients may decrease the risk of long-term opioid use.³⁶ Unfortunately, currently there is not enough data available to recommend strategies for the prevention of long-term opioid use after surgery.³⁷ While the use of multi-modal analgesia and patient education can reduce postoperative pain and the need for opioids, this may not translate to POUS or PPOU reduction as patients who receive regional anesthesia perioperatively are no less likely to use opioids long-term after surgery.^{38,39}

This study was limited to privately insured children and therefore may not be generalizable to all pediatric populations; however, more than 50% of children in the United States have private health insurance coverage.⁴⁰ The outcome was measured by pharmacy fills, which is an objective measure necessarily used here and in many other similar studies, but which may not accurately reflect consumption. In the absence of large-scale data about whether the medications were actually taken by the child, this is the best measure available. There were, however, limitations inherent to the data. Some surgeries were much more common than others, so their analysis had greater power. The nonsurgical control populations differed in a number of ways from the surgical groups, but the regression models have controlled for many potential confounding variables, including cancer. However, we cannot account for unknown or unmeasured confounders. Observed associations may reflect patient genetics, unmeasured or unknown comorbidities, or underlying conditions, and these associations do not imply causation. Some patients had additional surgeries at the same time as one of the top 20 explored here; combinations of surgeries may influence associations with POUS in complex ways not examined here.

Conclusions

These results suggest that opioid-naïve children of all ages undergoing common surgeries are at increased risk of POUS. Some variables associated with POUS may be age-specific, but the adolescent age group had the highest rates of perioperative opioid prescriptions,

POUS, and PPOU. Future research should examine these and additional factors across a greater number of surgeries and pediatric populations. There is a need to develop methods to decrease the risk of prolonged opioid use after pediatric surgery as well as to investigate and define the level of opioid use that results in negative outcomes for children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Data for this project were accessed using the Stanford Center for Population Health Sciences (PHS) Data Core. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Funding Disclosures

The PHS Data Core is supported by a National Institutes of Health National Center for Advancing Translational Science Clinical and Translational Science Award (UL1 TR001085) and from Internal Stanford funding. A. Ward is supported by the Department of Defense through the National Defense Science & Engineering Graduate Fellowship Program. Dr. Sun acknowledges support from the National Institute on Drug Abuse (K08DA042314). All additional support was provided from institutional and/or departmental sources.

Glossary

POUS	prolonged opioid use after surgery
PPOU	persistent postoperative opioid use
ICD	international classification of diseases
CPT	current procedural terminology
CCC	complex chronic conditions
CI	confidence interval
OR	odds ratio
aOR	adjusted odds ratio
LOS	length of stay
N	number
NA	not applicable

References:

1. Bose J, Hedden SL, Lipari RN, Park-Lee E. Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. In: Administration SAaMHS, ed. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, 5600 Fishers Lane, Room 15-E09D, Rockville, MD 20857; 2018.

2. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths – United States, 2013–2017. In: Prevention CfDCA, ed. Vol 67. Morbidity and Mortality Weekly Report: Centers for Disease Control and Prevention; 2019:1419–1427.
3. Bennett KG, Harbaugh CM, Hu HM, et al. Persistent Opioid Use Among Children, Adolescents, and Young Adults After Common Cleft Operations. *J Craniofac Surg*. 2018;29(7):1697–1701. [PubMed: 30059422]
4. Harbaugh CM, Lee JS, Hu HM, et al. Persistent Opioid Use Among Pediatric Patients After Surgery. *Pediatrics*. 2018;141(1).
5. Hall MJ, Schwartzman A, Zhang J, Liu X. Ambulatory Surgery Data From Hospitals and Ambulatory Surgery Centers: United States, 2010. *Natl Health Stat Report*. 2017(102):1–15.
6. Committee SS. NQF-Endorsed Measures for Surgical Procedures, 2015–2017. In: Services HaH, ed. 1030 15th St NW, Suite 800 Washington, DC 20005: National Quality Forum; 2017.
7. Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. Monitoring the future, national survey results on drug use: 1975–2014: overview, key findings on adolescent drug use. Ann Arbor, MI: Institute for Social Research, University of Michigan; 2015.
8. Gaither JR, Shabanova V, Leventhal JM. US National Trends in Pediatric Deaths From Prescription and Illicit Opioids, 1999–2016. *JAMA Netw Open*. 2018;1(8):e186558. [PubMed: 30646334]
9. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surg*. 2017;152(6):e170504. [PubMed: 28403427]
10. Johnson SP, Chung KC, Zhong L, et al. Risk of Prolonged Opioid Use Among Opioid-Naive Patients Following Common Hand Surgery Procedures. *J Hand Surg Am*. 2016;41(10):947–957 e943. [PubMed: 27692801]
11. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period. *JAMA Intern Med*. 2016;176(9):1286–1293. [PubMed: 27400458]
12. Baldini A, Von Korff M, Lin EH. A Review of Potential Adverse Effects of Long-Term Opioid Therapy: A Practitioner's Guide. *Prim Care Companion CNS Disord*. 2012;14(3).
13. Brown RT, Zuelsdorff M, Fleming M. Adverse effects and cognitive function among primary care patients taking opioids for chronic nonmalignant pain. *J Opioid Manag*. 2006;2(3):137–146. [PubMed: 17319447]
14. National Center for Health Statistics (U.S.). National Hospital Discharge Survey: 2010 Table, Procedures by Selected Patient Characteristics - Number by Procedure Category and Age. In. DHHS publication. Hyattsville, Md: U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention; 2010:v.
15. Schroeder AR, Dehghan M, Newman TB, Bentley JP, Park KT. Association of Opioid Prescriptions From Dental Clinicians for US Adolescents and Young Adults With Subsequent Opioid Use and Abuse. *JAMA Intern Med*. 2019;179(2):145–152. [PubMed: 30508022]
16. Kent ML, Hurley RW, Oderda GM, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative-4 Joint Consensus Statement on Persistent Postoperative Opioid Use: Definition, Incidence, Risk Factors, and Health Care System Initiatives. *Anesth Analg*. 2019;129(2):543–552. [PubMed: 30897590]
17. Jain G, Mahendra V, Singhal S, et al. Long-term neuropsychological effects of opioid use in children: a descriptive literature review. *Pain Physician*. 2014;17(2):109–118. [PubMed: 24658471]
18. Groenewald CB. Opioid-prescribing Patterns for Pediatric Patients in the United States. *Clin J Pain*. 2019;35(6):515–520. [PubMed: 30985396]
19. Knoppert DRM, Benavides S, Totton J, Hoff D, Moffett F, Norris K, Vaillancourt R, Aucoin R, Worthington M. Paediatric Age Categories to be Used in Differentiating Between Listing on a Model Essential Medicines List for Children World Health Organization; 4 20, 2007 2007.
20. Williams K, Thomson D, Seto I, et al. Standard 6: age groups for pediatric trials. *Pediatrics*. 2012;129 Suppl 3:S153–160. [PubMed: 22661762]
21. Gil JA, Gunaseelan V, DeFroda SF, Brummett CM, Bedi A, Waljee JF. Risk of Prolonged Opioid Use Among Opioid-Naive Patients After Common Shoulder Arthroscopy Procedures. *Am J Sports Med*. 2019;47(5):1043–1050. [PubMed: 30735622]

22. Feudtner C, Feinstein JA, Zhong W, Hall M, Dai D. Pediatric complex chronic conditions classification system version 2: updated for ICD-10 and complex medical technology dependence and transplantation. *BMC Pediatr*. 2014;14:199. [PubMed: 25102958]
23. Benjamini YKA, Yekutieli D. Adaptive linear step-up procedures that control the false discovery rate. *Biometrika*. 2006;93(3):17.
24. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41(4):1149–1160. [PubMed: 19897823]
25. Opioid Task Force 2019 Progress Report. American Medical Association;2019.
26. Kim SC, Choudhry N, Franklin JM, et al. Patterns and predictors of persistent opioid use following hip or knee arthroplasty. *Osteoarthritis Cartilage*. 2017;25(9):1399–1406. [PubMed: 28433815]
27. Luciana M, Bjork JM, Nagel BJ, et al. Adolescent neurocognitive development and impacts of substance use: Overview of the adolescent brain cognitive development (ABCD) baseline neurocognition battery. *Dev Cogn Neurosci*. 2018;32:67–79. [PubMed: 29525452]
28. Nock NL, Minnes S, Alberts JL. Neurobiology of substance use in adolescents and potential therapeutic effects of exercise for prevention and treatment of substance use disorders. *Birth Defects Res*. 2017;109(20):1711–1729. [PubMed: 29251846]
29. Karhade AV, Ogink PT, Thio Q, et al. Machine learning for prediction of sustained opioid prescription after anterior cervical discectomy and fusion. *Spine J*. 2019.
30. Gagne JJ, He M, Bateman BT. Trends in Opioid Prescription in Children and Adolescents in a Commercially Insured Population in the United States, 2004–2017. *JAMA Pediatr*. 2018.
31. Hunsberger JB, Hsu A, Yaster M, et al. Physicians Prescribe More Opioid Than Needed to Treat Pain in Children After Outpatient Urological Procedures: An Observational Cohort Study. *Anesth Analg*. 2019.
32. Monitto CL, Hsu A, Gao S, et al. Opioid Prescribing for the Treatment of Acute Pain in Children on Hospital Discharge. *Anesth Analg*. 2017;125(6):2113–2122. [PubMed: 29189368]
33. Scully RE, Schoenfeld AJ, Jiang W, et al. Defining Optimal Length of Opioid Pain Medication Prescription After Common Surgical Procedures. *JAMA Surg*. 2018;153(1):37–43. [PubMed: 28973092]
34. Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term analgesic use after low-risk surgery: a retrospective cohort study. *Arch Intern Med*. 2012;172(5):425–430. [PubMed: 22412106]
35. Brat GA, Agniel D, Beam A, et al. Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study. *BMJ*. 2018;360:j5790. [PubMed: 29343479]
36. Vetter TR, Kain ZN. Role of the Perioperative Surgical Home in Optimizing the Perioperative Use of Opioids. *Anesth Analg*. 2017;125(5):1653–1657. [PubMed: 28742770]
37. Wu CL, King AB, Geiger TM, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Perioperative Opioid Minimization in Opioid-Naive Patients. *Anesth Analg*. 2019;129(2):567–577. [PubMed: 31082966]
38. Egbert LD, Battit GE, Welch CE, Bartlett MK. Reduction of Postoperative Pain by Encouragement and Instruction of Patients. A Study of Doctor-Patient Rapport. *N Engl J Med*. 1964;270:825–827. [PubMed: 14108087]
39. Sun EC, Bateman BT, Memtsoudis SG, Neuman MD, Mariano ER, Baker LC. Lack of Association Between the Use of Nerve Blockade and the Risk of Postoperative Chronic Opioid Use Among Patients Undergoing Total Knee Arthroplasty: Evidence From the MarketScan Database. *Anesth Analg*. 2017;125(3):999–1007. [PubMed: 28430692]
40. Cohen RA MM, Zammitti EP. Health insurance coverage: Early release of estimates from the National Health Interview Survey, January–March 2018. In: Statistics NCfH, ed: Centers for Disease Control and Prevention; 2018:36.

Key Points**Question:**

What are the incidences of, and factors associated with, prolonged opioid use after surgery and persistent postoperative opioid use in children?

Findings:

Some patient characteristics and surgeries are positively and negatively associated with prolonged opioid use in opioid-naïve children of all ages, but persistent opioid use is rare.

Meaning:

Specific pediatric subpopulations may be at markedly higher risk for prolonged opioid use after surgery.

Figure 1.

Flow diagram showing the number of patients included in this study before and after application of the inclusion and exclusion criteria

*Patients aged 0 to <2 were not required to have one year of eligibility before surgery
0 to <2 – 0 to <2 years of age; 2 to <6 – 2 to <6 years of age; 6 to <12 – 6 to <12 years of age; 12 to 18 – 12 to 18 years of age; LOS – length of stay

Figure 2. Total incidences of prolonged opioid use among opioid-naïve surgical and nonsurgical pediatric patients and the range across the most common 20 surgeries per age group
POUS – prolonged opioid use after surgery

Table 1.

Cohort summary characteristics and univariate analyses results by age group

	Age 0 to <2			Age 2 to <6			Age 6 to <12			Age 12 to 18		
	surgical N (%)	control N (%)	p value	surgical N (%)	control N (%)	p value	surgical N (%)	control N (%)	p value	surgical N (%)	control N (%)	p value
male gender	12381 (84)	134574 (50)	<.00 1	25457 (59)	107751 (50)	<.00 1	25710 (54)	199434 (51)	<.00 1	34955 (50)	244747 (52)	<.00 1
age in years, mean (SD)	0.59 (0.5)	0.19 (0.61)	<.00 1	3.66 (1.1)	3.65 (1.1)	0.09	8.04 (1.7)	8.53 (1.7)	<.00 1	15.82 (1.8)	15.0 (2.0)	<.00 1
year of surgery, mean (SD)	2008.77 (3.6)	2009.5 (4.3)	<.00 1	2009.24 (3.3)	2009.47 (4.1)	<.00 1	2009.58 (3.4)	2009.07 (4.1)	<.00 1	2009.98 (3.5)	2008.73 (4.0)	<.00 1
race: Asian	523 (3.6)	19850 (7.3)	<.00 1	1212 (2.8)	14501 (6.7)	<.00 1	1259 (2.6)	19303 (4.9)	<.00 1	1218 (1.7)	16936 (3.6)	<.00 1
race: Black	1074 (7.3)	17757 (6.5)		2789 (6.5)	15271 (7.0)		2690 (5.6)	29679 (7.5)		3677 (5.2)	37514 (8.0)	
race: Hispanic	1053 (7.2)	31812 (12)		3463 (8.1)	25614 (12)		3859 (8.1)	45299 (11)		4433 (6.3)	50677 (11)	
race: Unknown	1448 (9.8)	35136 (13)		5348 (12)	31791 (15)		7458 (16)	68404 (17)		12827 (18)	103710 (22)	
race: White	10624 (72)	166771 (61)		30045 (70)	130497 (60)		32654 (68)	231515 (59)		48224 (69)	262872 (56)	
mood/ personality disorder	<10 (<0.068)	82 (0.03)	0.64	200 (0.47)	550 (0.25)	<.00 1	1259 (2.6)	6377 (1.6)	<.00 1	4675 (6.6)	17738 (3.8)	<.00 1
substance use disorder	<10 (<0.068)	26 (0.0096)	0.46	12 (0.028)	35 (0.016)	0.14	13 (0.027)	69 (0.018)	0.2	1201 (1.7)	4383 (0.93)	<.00 1
chronic pain	22 (0.15)	76 (0.028)	<.00 1	185 (0.43)	275 (0.13)	<.00 1	475 (0.99)	1276 (0.32)	<.00 1	4921 (7.0)	3588 (0.76)	<.00 1
cancer	21 (0.14)	132 (0.049)	<.00 1	59 (0.14)	111 (0.051)	<.00 1	75 (0.16)	277 (0.07)	<.00 1	160 (0.23)	575 (0.12)	<.00 1
congenital/ genetic defect CCC	334 (2.3)	2104 (0.78)	<.00 1	429 (1.0)	584 (0.27)	<.00 1	502 (1.0)	2024 (0.51)	<.00 1	1681 (2.4)	7212 (1.5)	<.00 1
cardiovascular CCC	332 (2.3)	2726 (1.0)	<.00 1	489 (1.1)	991 (0.46)	<.00 1	574 (1.2)	1918 (0.49)	<.00 1	1226 (1.7)	3771 (0.8)	<.00 1
gastrointestinal CCC	54 (0.37)	301 (0.11)	<.00 1	99 (0.23)	107 (0.049)	<.00 1	76 (0.16)	181 (0.046)	<.00 1	205 (0.29)	521 (0.11)	<.00 1
hematologic/ immunologic CCC	118 (0.8)	704 (0.26)	<.00 1	338 (0.79)	493 (0.23)	<.00 1	288 (0.6)	636 (0.16)	<.00 1	339 (0.48)	839 (0.18)	<.00 1
malignancy CCC	86 (0.58)	505 (0.19)	<.00 1	233 (0.54)	563 (0.26)	<.00 1	473 (0.99)	2127 (0.54)	<.00 1	1860 (2.6)	6113 (1.3)	<.00 1
metabolic CCC	418 (2.8)	4437 (1.6)	<.00 1	2019 (4.7)	5000 (2.3)	<.00 1	2375 (5.0)	7891 (2.0)	<.00 1	3105 (4.4)	10879 (2.3)	<.00 1
premature/ neonatal CCC	173 (1.2)	1666 (0.61)	<.00 1	70 (0.16)	94 (0.043)	<.00 1	16 (0.033)	41 (0.01)	<.00 1	10 (0.014)	31 (0.0066)	0.05
neurologic/ neuromuscular CCC	145 (0.98)	855 (0.32)	<.00 1	288 (0.67)	548 (0.25)	<.00 1	354 (0.74)	1209 (0.31)	<.00 1	479 (0.68)	1561 (0.33)	<.00 1
renal/urologic CCC	266 (1.8)	1034 (0.38)	<.00 1	257 (0.6)	303 (0.14)	<.00 1	118 (0.25)	320 (0.081)	<.00 1	124 (0.18)	371 (0.079)	<.00 1

	Age 0 to <2			Age 2 to <6			Age 6 to <12			Age 12 to 18		
	surgical N (%)	control N (%)	<i>p</i> value	surgical N (%)	control N (%)	<i>p</i> value	surgical N (%)	control N (%)	<i>p</i> value	surgical N (%)	control N (%)	<i>p</i> value
respiratory CCC	371 (2.5)	2518 (0.93)	<.00 1	1287 (3.0)	3754 (1.7)	<.00 1	1348 (2.8)	5450 (1.4)	<.00 1	2895 (4.1)	7818 (1.7)	<.00 1
technology dependence CCC	61 (0.41)	273 (0.1)	<.00 1	95 (0.22)	108 (0.05)	<.00 1	72 (0.15)	154 (0.039)	<.00 1	300 (0.43)	300 (0.064)	<.00 1
transplantation CCC	<10 (<0.068)	<10 (<0.01)	0.81	11 (0.026)	14 (0.0064)	<.00 1	13 (0.027)	58 (0.015)	0.07	48 (0.068)	137 (0.029)	<.00 1
POUS	113 (0.77)	461 (0.17)	<.00 1	324 (0.76)	672 (0.31)	<.00 1	484 (1.0)	1864 (0.47)	<.00 1	2689 (3.8)	10070 (2.1)	<.00 1
PPOU	<10 (<0.068)	<10 (<0.01)	0.51	<10 (<0.023)	<10 (<0.01)	0.26	<10 (<0.021)	<10 (<0.01)	0.47	37 (0.053)	107 (0.023)	<.00 1
Total patient visits	14,722	271,326		42,857	217,674		47,920	394,200		70,379	471,709	

P values determined by *t* test for age and year of surgery, and by chi-square test for all other variables. Chi-square test p-value for race is for five categories of race, and group surgical or control.

N – number; SD – standard deviation; CCC – complex chronic conditions; POUS – prolonged opioid use after surgery; PPOU – persistent postoperative opioid use

Table 2.

Multivariable logistic regression model results for associations between individual surgeries and POUS by age group

	Age 0 to <2		Age 2 to <6		Age 6 to <12		Age 12 to 18	
	aOR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value
Adenoidectomy, 12+ years							1.3 (0.96–1.8)	0.088
Adenoidectomy, <12 years	1.4 (0.82–2.5)	0.210	2.1 (1.5–3)	<.001 *	1.5 (1–2.2)	0.032		
Appendectomy					1.1 (0.41–2.9)	0.860		
Chordee surgical correction	1.1 (0.37–3)	0.930						
Chordee surgical correction, plastic surgery	0.27 (0.036–2)	0.190						
Circumcision	1.8 (1–3.1)	0.045	1.8 (0.79–4.1)	0.160	1.7 (0.87–3.5)	0.120		
Closed treatment of distal radius/ulna fracture					1.7 (1–2.8)	0.032		
Closed treatment of nose fracture							1.6 (1.2–2)	<.001 *
Closed treatment of radius/ulna shaft fracture			1.4 (0.34–5.6)	0.650	1.6 (0.85–2.9)	0.150		
Dental surgery			2.8 (1.3–6.3)	0.012	2.3 (1.1–4.8)	0.030	0.86 (0.62–1.2)	0.360
Hypospadias repair, stage 1, distal	0.57 (0.079–4.2)	0.590						
Hypospadias repair, stage 1, distal, with glanuloplasty	1 (0.3–3.4)	0.990						
Inguinal hernia repair, 5+ years			0.51 (0.071–3.7)	0.500	1.9 (1.1–3.2)	0.021	1.5 (1.1–1.9)	0.003
Inguinal hernia repair, 6month–5years	1.3 (0.52–3.1)	0.600	1.8 (0.9–3.8)	0.094				
Knee arthroscopy, anterior cruciate repair							1 (0.91–1.2)	0.580
Knee arthroscopy, chondroplasty							1.6 (1.3–1.9)	<.001 *
Knee arthroscopy, meniscectomy							1.2 (1–1.3)	0.042
Knee arthroscopy, meniscus repair							0.97 (0.77–1.2)	0.790
Knee arthroscopy, partial synovectomy							2.0 (1.6–2.3)	<.001 *
Laparoscopic appendectomy					2.7 (1.9–3.8)	<.001 *	1.9 (1.7–2.2)	<.001 *
Lysis of post-circumcision adhesions	0.44 (0.059–3.2)	0.410						
Myringoplasty			2 (0.63–6.4)	0.240	2.7 (1.2–6.3)	0.021		
Myringotomy	3.7 (2.3–6.1)	<.001 *	1 (0.76–1.3)	0.960	1.4 (0.97–1.9)	0.079	1.5 (0.98–2.3)	0.065

	Age 0 to <2		Age 2 to <6		Age 6 to <12		Age 12 to 18	
	aOR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value
Myringotomy and aspiration	3.4 (0.8–14)	0.097	1.4 (0.65–3)	0.400				
Orchiopexy, inguinal approach	0.91 (0.31–2.7)	0.870	0.34 (0.046–2.5)	0.290	0.42 (0.15–1.2)	0.098		
Percutaneous fixation of humerus supracondylar fracture			0.5 (0.13–2)	0.330	0.94 (0.45–2)	0.880		
Reconstruction of tongue fold	1.3 (0.17–9.3)	0.810						
Removal completely impacted tooth							0.74 (0.64–0.85)	<.001 *
Removal of deep fixation device							1.8 (1.4–2.3)	<.001 *
Removal of impacted tooth, soft tissue							0.97 (0.72–1.3)	0.840
Removal partially impacted tooth							0.79 (0.64–0.97)	0.025
Repair of incomplete circumcision	2.7 (1.4–5.2)	0.004	0.95 (0.23–3.9)	0.940				
Septoplasty							1.4 (1.1–1.7)	0.001 *
Shoulder arthroscopy, capsulorrhaphy							1.5 (1.3–1.8)	<.001 *
Skin tissue rearrangement head/face/hand, <10 cm ²	1.8 (0.66–4.6)	0.260						
Strabismus surgery, horizontal muscle			4.5 (1.1–18)	0.035	1.8 (0.25–13)	0.570		
Tonsillectomy, 12+ years							1.7 (1.5–1.9)	<.001 *
Tonsillectomy, <12 years			2.2 (1.4–3.5)	<.001 *	1.8 (1.3–2.5)	<.001 *		
Tonsillectomy/adenoidectomy, 12+ years							1.7 (1.5–1.9)	<.001 *
Tonsillectomy/adenoidectomy, <12 years	1.9 (0.97–3.6)	0.062	2.5 (2.1–2.9)	<.001 *	2.3 (2–2.6)	<.001 *		
Trigger finger release			0.9 (0.13–6.4)	0.920				
Turbinate reduction, bone					1.5 (0.89–2.6)	0.130	1.1 (0.88–1.3)	0.430
Turbinate reduction, mucosal					1.2 (0.54–2.5)	0.710		
Tympanoplasty			0.72 (0.22–2.3)	0.570	0.99 (0.31–3.2)	0.990		
Tympanoplasty w/ tympanomeatal flap					2.4 (1.4–4.1)	0.002 *		
Umbilical hernia repair, 5+ years					0.9 (0.29–2.8)	0.860		
Umbilical hernia repair, <5 years			0.44 (0.061–3.1)	0.410				
Urethral meatal revision			0.82 (0.11–6.2)	0.850				

Both surgical and nonsurgical patients were used to fit the logistic regression models. Models included the top 20 surgical procedures, age, sex, race, year of surgery, and history in the year prior to surgery of: cancer, chronic pain, mood/personality disorders (for age 6–<12 and 12–18), substance use disorders (for age 6–<12 and 12–18) and pediatric complex chronic conditions (CCC).

* Surgery had a significant association with POUS. After using the Bonferroni correction, $P < 0.05/(\text{number of different surgical procedures})$ was considered statistically significant, thus P values less than 0.0033, 0.0026, 0.0025, and 0.0025 were considered significant for ages 0 to <2, 2 to <6, 6 to <12, and 12 to 18 respectively. The different denominators apply because some surgeries did not have any associated cases of POUS and therefore were not included in the model.

aOR – adjusted odds ratio (for each named surgery, compared to other patients in the model for that age group who did not have that surgery, ie the reference sample, and surgical patients undergoing other surgeries, controlling for the fact that some patients underwent more than one named surgery within a procedure); CI – confidence interval

Table 3.

Multivariable logistic regression model results in surgical patients for prolonged opioid use after surgery by age group

	Age 0 to <2		Age 2 to <6		Age 6 to <12		Age 12 to 18	
	aOR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value
male gender	1.4 (0.84–2.2)	0.220	0.98 (0.79–1.2)	0.890	0.86 (0.72–1)	0.110	0.82 (0.75–0.89)	<.001 *
age in years	0.8 (0.53–1.2)	0.290	1.1 (1–1.2)	0.056	1.1 (1.0–1.1)	0.028	1.2 (1.1–1.2)	<.001 *
year of surgery	0.94 (0.89–0.99)	0.031	0.92 (0.89–0.95)	<.001 *	0.93 (0.90–0.95)	<.001 *	0.95 (0.94–0.96)	<.001 *
race: White	1 [Reference]	0.279 [†]	1 [Reference]	0.188 [†]	1 [Reference]	0.592 [†]	1 [Reference]	<0.001 ^{†*}
race: Asian	0.96 (0.30–3.1)	0.950	0.24 (0.06–0.97)	0.046	0.33 (0.12–0.90)	0.029	0.51 (0.34–0.77)	0.001 *
race: Black	0.98 (0.49–2.0)	0.960	1.5 (1.0–2.2)	0.030	1.2 (0.84–1.7)	0.320	0.86 (0.71–1.0)	0.110
race: Hispanic	1.0 (0.50–2.2)	0.910	0.94 (0.62–1.4)	0.790	0.81 (0.56–1.2)	0.250	0.79 (0.66–0.94)	0.007
race: Unknown	0.76 (0.38–1.5)	0.430	1.0 (0.75–1.4)	0.800	1.0 (0.78–1.3)	1.000	1.0 (0.92–1.1)	0.770
mood/personality disorder					1.1 (0.63–1.9)	0.770	1.4 (1.2–1.6)	<.001 *
substance use disorder							1.3 (1.0–1.7)	0.023
chronic pain			0.76 (0.11–5.4)	0.780	1.2 (0.53–2.7)	0.670	1.4 (1.2–1.6)	<.001 *
cancer			2.3 (0.32–17)	0.400	2.4 (0.57–10)	0.230	0.98 (0.46–2.1)	0.970
congenital/genetic defect CCC	1.2 (0.36–3.9)	0.790	1.7 (0.7–4.3)	0.240	0.68 (0.25–1.9)	0.450	1.1 (0.88–1.4)	0.350
cardiovascular CCC	0.37 (0.051–2.8)	0.330	0.24 (0.033–1.7)	0.160	1.0 (0.45–2.3)	0.950	1.3 (1.0–1.7)	0.041
gastrointestinal CCC			2.9 (0.67–12)	0.150	2.2 (0.53–9.2)	0.280	1.2 (0.66–2.3)	0.500
hematologic/immunologic CCC			1.1 (0.36–3.6)	0.830	1.3 (0.46–3.4)	0.650	1.7 (1.1–2.6)	0.011
metabolic CCC	0.7 (0.21–2.3)	0.560	0.63 (0.31–1.3)	0.190	1.7 (1.2–2.5)	0.004	1.1 (0.95–1.3)	0.170
premature/neonatal CCC	1.1 (0.14–8)	0.950	2 (0.27–15)	0.490				
neurologic/neuromuscular CCC	2.2 (0.5–9.2)	0.300	0.36 (0.048–2.7)	0.320	1.7 (0.73–3.8)	0.230	0.95 (0.60–1.5)	0.840
renal/urologic CCC	0.69 (0.095–5)	0.720			1.8 (0.43–7.5)	0.420	1 (0.42–2.6)	0.940
respiratory CCC	2.1 (0.9–5.1)	0.086	1.2 (0.64–2.4)	0.530	1.3 (0.78–2.0)	0.360	1.3 (1.1–1.5)	0.004
technology dependence CCC							1.2 (0.7–2.0)	0.550
transplantation CCC							1 (0.24–4.4)	0.970

Only surgical patients were used to fit the models. The models adjusted for type of surgery.

* Risk factor had a significant association with POUS. After using the Bonferroni correction, $P < 0.05/(\text{number of variables of interest in the model})$ was considered statistically significant, thus P values less than 0.0036, 0.0029, 0.0026, and 0.0024 were considered significant for ages 0 to <2, 2 to <6, 6 to <12, and 12 to 18, respectively. The different denominators apply because some variables did not have any associated cases of POUS.

[†] Overall significance of race was determined by the likelihood ratio test.

aOR – adjusted odds ratio; CI – confidence interval; CCC – complex chronic conditions; NA – not applicable

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript