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Naloxone co-prescriptions for surgery patients prescribed opioids: A retrospective cohort study

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Abstract

Background: Surgeon-prescribed opioids contribute to 11% of prescription drug overdoses in the United States (US). With prescription opioids involved in 24% of all opioid-related overdose deaths in 2020, the US Centers for Disease Control and Prevention (CDC) recommends naloxone co-prescribing to patients at high-risk of overdose and death as a harm reduction strategy. We sought to 1) examine naloxone co-prescribing rates to surgical patients (using common post-surgical prescribing amounts) and those with potential risk factors for opioid-related overdoses or adverse events, and 2) identify the factors associated with patients receiving naloxone co-prescriptions.

Methods: We conducted a single-institution, retrospective study using the electronic medical records of all patients undergoing surgery at an academic institution between August 2020 and May 2021. We included post-surgical adults prescribed opioids that were sent to a pharmacy in our health system. The primary outcome was the percentage of co-prescribed naloxone in patients prescribed opioids.

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Declarations of interest

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

CRediT authorship contribution statement

Lyen C. Huang: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Supervision, Writing – review & editing. **Henry Nibley:** Conceptualization, Funding acquisition, Investigation, Writing – original draft, Writing – review & editing. **Melissa Cheng:** Conceptualization, Investigation, Writing – review & editing. **Josh Bleicher:** Data curation, Formal analysis, Validation, Writing – review & editing. **Hyunkyu Ko:** Data curation, Formal analysis, Writing – review & editing. **Jordan E. Johnson:** Resources, Project administration, Writing – review & editing. **Marta L. McCrum:** Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Results: The overall naloxone co-prescription rate was low (1.7%). Only 14.6% of patients prescribed ≥350 morphine milligram equivalents (MME, equivalent to 46.7 oxycodone 5 mg tablets) and 8.6% of patients using illicit drugs were co-prescribed naloxone. On multivariable analysis, patients who were prescribed >350 MME, used illicit drugs or tobacco, underwent an elective or emergent general surgery procedure, self-identified as Hispanic, or had ASA scores of 2-4 were more likely to receive a naloxone co-prescription.

Conclusions: Naloxone co-prescribing after surgery remains low, even for high-risk patients. Harm reduction strategies such as naloxone, safe storage, and disposal of leftover opioids could reduce surgeons' iatrogenic contributions to the worsening US opioid crisis.

Keywords

Opioids; Naloxone; Harm reduction; Surgery; Patient safety; Overdose

1. Introduction

Opioid prescribing by surgeons directly and indirectly contributes to the ongoing opioid crisis in the United States (US). While much of the focus in the crisis has been on illicit opioids, prescription opioids were involved in 24% of the 68,630 opioid-related overdose deaths in 2020 [1]. Approximately 64 million operations are performed each year in the US and while prescribing after surgery has decreased recently, 56–70% of these patients will still be prescribed opioids [2-6]. Surgeon-prescribed opioids were involved in 11% of prescription opioid drug overdoses [7]. In addition, prescription opioids are often the first exposure to opioids for many and can lead to future heroin and other illicit drug use [8,9].

Naloxone co-prescribing has been widely promoted as a harm reduction strategy to reduce opioid-related overdoses. Naloxone rapidly reverses the effects of opioids and is the primary treatment for an opioid-related overdose. In 2018, then Surgeon General Jerome Adams issued an advisory on the importance of prescribing naloxone for patients "taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, [or] individuals using illicit opioids" [10]. In 2022, the US Centers for Disease Control and Prevention (CDC) reported that only 1 naloxone prescription is dispensed for every 70 high-dose opioid prescriptions and rural counties are nearly 3 times more likely to be ranked as low-dispensing for naloxone than metropolitan counties [11]. While specific guidelines were not been released for surgeons, CDC guidelines suggest naloxone co-prescribing for patients who use ≥50 morphine milligram equivalents (MME) per day (the equivalent of 6.67 tablets of oxycodone 5 mg) and/or have a history of illicit drug use or substance use disorder at increased risk [12,13]. Several states such as Vermont and Virginia mandated naloxone for patients taking high-doses of opioids leading to higher rates of co-prescribing [14,15]. However, naloxone co-prescribing rates range from 0.46%-4.37% in a variety of national studies [14-17].

Despite the ubiquity of opioid prescribing after surgery, few studies examining naloxone co-prescribing upon discharge after surgery. For surgeons, naloxone co-prescribing could potentially reduce the risks of opioid-related harms to their patients. Patients who received a naloxone co-prescription along with opioids for chronic pain had 63% fewer emergency

department visits for opioid-related adverse events than those who did not receive naloxone [18]. Naloxone co-prescribing also appears to raise patient awareness of opioid-related harms leading to a decrease in opioid overdoses even when the naloxone prescription is not filled [19].

The CDC guidelines recommend a 50 MME per day threshold which is appropriate for patients using who use the same quantities of opioids each day for chronic pain. However, surgery patients use opioids after surgery as needed which can result in variable day-to-day consumption (at times exceeding 50 MME) [20]. Also, patients often use opioids to treat ailments other than pain (e.g., insomnia) [21]. For example, a patient prescribed "1-2 tablets oxycodone 5 mg q4h prn pain, quantity #20 for 5 days" would have a prescription that does not exceed the 50 MME/day CDC guideline. Yet they might follow the instructions and take 12 tablets in a single day (90 MME). Thus, larger opioid prescriptions can put patients at risk even if the daily MME quantity and duration would not cross the CDC threshold. These risks also extend to families and friends. Few patients store opioids securely [22-24] contributing to a three-fold increase in child poisonings and deaths from 1999 and 2016 [25]. One-third of patients shared their prescriptions, which can lead to misuse or illicit drug use by others [26-28].

Thus, we conducted a single-institution, retrospective study with the goals of 1) examining naloxone co-prescribing rates to surgical patients using several MME thresholds representing common opioid prescriptions, and 2) identifying the patient- and surgery-level factors associated with patients receiving naloxone co-prescriptions.

2. Methods

2.1. Study setting, participants, and design

We conducted a single-institution, retrospective cohort study using the electronic medical records of all patients undergoing surgery at a single academic institution between August 2020 and May 2021. We included adults (age ≥18) who underwent a cardiothoracic, general surgery, otolaryngology, plastic, transplant, urology, or vascular surgery and were prescribed opioids at discharge. We excluded trauma patients due to the heterogenous nature of their injuries and variable prescribing by different services. We excluded patients who were not discharged home (5.9% of all post-surgical discharges). For patients who had more than one discharge opioid prescription during the study period, we assessed for naloxone prescriptions associated with patient's first opioid prescription. The study was approved by the Institutional Review Board at the University of Utah and was conducted in compliance with STROBE guidelines [29].

Our primary outcome of interest was the percentage of patients co-prescribed naloxone and opioids after surgery. We categorized patients by discharge opioid prescriptions into six categories: 0 MME (patients not receiving any opioids at discharge), 1-75 MME (representing a prescription of up to ten tablets of oxycodone 5 mg), 76-150 MME, 151-200 MME, 201-350 MME, and >350 MME. We based these prescriptions on prior studies by our groups and others reflecting common discharge prescriptions [20,21,30]. Our secondary

outcomes were to examine the association between opioid prescription quantities as well as demographic, clinical, and surgical characteristics, and naloxone co-prescription.

2.2. Data collection, cleaning, and statistical analyses

The data in this study was extracted using Structured Query Language (SQL) from our electronic data warehouse which is updated daily with data from our commercial electronic medical record (EMR) system (Epic Systems Corporation, Verona, Wisconsin). We used the predefined fields and categories for patient demographics (age, gender, race, ethnicity, home zip code), current medical and social history (cardiac and respiratory co-morbidities, illicit drug, tobacco, or alcohol use) the pre-operative anesthesia record (American Society of Anesthesiology [ASA] score), the surgical case record (case urgency, outpatient or inpatient classification, attending surgeon, specialty), and pharmacy data (discharge medications including opioids). We used the patient's home zip code and the Federal Office of Rural Health Policy Data Files to categorize patients as rural or urban [31]. A systematic review by the CDC found that there was no conclusive evidence about demographic or clinical risk factors associated with overdoses [13]. But the review and prior literature suggest that older adults; rurality; patients with a history of overdoses or illicit drug use, alcohol use, and patients with cardiac and respiratory co-morbidities are at increased risk of opioid-related overdoses and adverse events [12,13,32]. The data from patient demographics, current medical history, and social history are generally completed (and updated) by patients prior to their hospital visits via a secure patient portal. Clinic staff and providers can further update these records. The total discharge dosages of all discharge opioid medications were converted into morphine milligram equivalents (MME) [33].

Categorical variables were summarized as counts and percentages and analyzed using chi-squared tests. In cases where the normal conditions of a chi-squared test were not met, we calculated p-values via Monte-Carlo simulation. We used pairwise deletion to remove patients missing data in any of these categories [34]. Continuous variables were summarized by median and interquartile range (IQR) and analyzed by stratifying data into discrete groups.

To assess the factors associated with naloxone co-prescribing, we conducted a multivariable analysis using a logistic regression model, accounting for potential clustering by surgeon. We included all variables in the adjusted model (rather than using a selection process) as our goal was identifying the relevant factors rather than creating a predictive model. We calculated standard errors at the surgeon level to account for autocorrelation between surgeons within the same specialty. Odds ratios (OR) and 95% confidence intervals (95% CI), and p-values were reported for each of the variables examined. Results were considered statistically significant when two-tailed p-values were <0.05. To address potential unobserved confounding, we ran a separate random effects model but saw minimal differences. The analysis was performed using Stata Version MP/17.0 (Stata Corp, College Station, TX, USA).

3. Results

At our institution, 10,414 unique patients underwent surgery during the study period. Overall, 6,492 (62.3%) patients were prescribed opioids at discharge after surgery while 3,922 (37.7%) patients were not prescribed opioids. The median patient age was 51 (IQR 37–65). Patient-level demographics and clinical characteristics are shown in Table 1. Patient gender was evenly distributed between males and females. Patients most commonly identified as Caucasian/White (86.1%), other (8.5%), or Black or African American (1.5%). Hispanics constituted 10.3% of the study population. Most patients lived in non-rural settings (74.2%). A small percentage of patients reported illicit drug use (7.7%) and active tobacco use (8.1%) while more than a third actively used alcohol (35.3%). For those prescribed opioids, the median opioid dosage prescribed at discharge was 75.0 MME (IQR 45.0–150.0). Overall, 3,716 (35.7%) of patients were prescribed 1-75 MME, 1,888 (18.1%) were prescribed 76-150 MME, 260 (2.5%) were prescribed 151-200 MME, 470 (4.5%) were prescribed 201-350 MME), and 158 (1.5%) were prescribed >350 MME. The overall naloxone co-prescription rate for patients receiving an opioid prescription was 1.7%.

The characteristics of the surgeries performed are shown in Table 2. Overall, 9,159 (88.0%) of patients underwent elective procedures. Most operations were done outpatient (n=7,580, 72.8%). The highest volume specialties were general surgery (n=3,522, 33.8%), urology (n=2,177, 20.9%), and otolaryngology (n=1,988, 19.1%).

We conducted a univariable analysis examining the association between previously identified risk factors for opioid-related overdoses and adverse events with naloxone co-prescribing (Table 3). The naloxone co-prescription rate ranged from 0.6% (for patients who were prescribed 1-75 MME) to 14.6% (for patients prescribed >350 MME). Patients with cardiac (but not respiratory) co-morbidities, illicit drug use, active tobacco use, or those who underwent emergent or inpatient surgery had higher rates of naloxone co-prescriptions. We used a multivariable logistic regression to identify the factors associated with naloxone co-prescribing (Table 4). We controlled for age, gender, race, home rurality, and cardiac and respiratory co-morbidities. Patients prescribed >350 MME (odds ratio [OR] 4.7, 95% confidence interval [CI] 1.68-13.0); using illicit drugs (OR 3.51, 95% CI 1.94-6.34) or tobacco (OR 1.87, 95% CI 1.02-3.43); patients who underwent a general surgery procedure (OR 2.90, 95% CI 1.01-8.30) or an emergent surgery (OR 8.25, 95% CI 2.55-26.62); patient self-identifying as Hispanic (OR 2.57, 95% CI 1.24-5.35); or patients with ASA scores of 2 (OR 4.55, 95 CI 1.11-18.68), 3 (OR 12.77, 95% CI 2.98-54.80), or 4 (OR 9.51, 95% CI 1.84-49.12) were more likely to receive a naloxone co-prescription. Patients prescribed 1-75 MME (OR 0.22, 95% CI 0.13-0.39); patients who underwent a plastics (OR 0.49, 95% CI 0.26-0.93) or vascular (OR 0.05, 95% CI 0.007-0.36); or who were active alcohol users (OR 0.50, 95% CI 0.30-0.82) were less likely to receive a co-prescription.

4. Discussion

In this study, we examined the rate of naloxone co-prescribing to patients prescribed opioids after surgery. We found that the overall naloxone co-prescription rate was low among all patients who received opioids (1.7%) but generally increased with higher MME

discharge prescriptions. Patients at higher risk of overdoses did have higher rates of naloxone co-prescribing. Among the patients who were prescribed ≥350 MME, 14.6% were co-prescribed naloxone. Only 8.6% of patients using illicit drugs and discharged with opioids received a naloxone co-prescription. Prescribers appeared to be most concerned about those patients undergoing emergent surgery but even then, only 14.1% were co-prescribed naloxone. On multivariable analysis, patients prescribed >350 MME, using illicit drugs or tobacco, undergoing a general surgery or emergent procedure, self-identifying as Hispanic, or ASA scores of 2-4 were factors associated with an increased likelihood of naloxone co-prescription.

Our overall low rates of naloxone co-prescribing are consistent with the 0.46%-4.37% reported in national pharmacy claims studies [14-17]. A variety of strategies have been proposed to increase co-prescribing rates outside of surgery. Mandatory prescribing laws passed in Vermont and Virginia in 2016 led to 1,515% and 2,650% increases in naloxone prescriptions in the subsequent year, respectively, though most high-risk patients still did not receive naloxone [14]. Other states such as Arizona, California, Ohio, Rhode Island, and Washington have followed suit [35]. At the health system-level, a clinical decision support alert increased the rate from 0.28% to 4.51% at one academic medical center [36]. Physician, nurse, and pharmacist education combined with electronic alerts similarly increased naloxone prescriptions at another academic center [37].

The literature is limited on the patient-level factors associated with naloxone co-prescribing [13]. Naloxone co-prescribing may be less likely to occur for rural patients than for their urban counterparts [16]. A study by Ong et al found that naloxone prescriptions were slightly more likely to be dispensed to female patients [38,39]. The only demographic factor we found associated with naloxone co-prescribing was Hispanic ethnicity. A recent report by the Substance Abuse and Mental Health Services Administration suggests that the rate of prescription opioid misuse among patients who identify as Hispanic/Latino is the same as the national population rate (4%) and the opioid-related overdose death rates is lower compared to non-Hispanic Whites, Blacks, and American Indian/Alaska Natives. However, the death rate from prescription and synthetic non-prescription opioids in the Hispanic population increased between 2014-2017 by 122% and 617%, respectively. Whether increased naloxone co-prescribing to patients of Hispanic ethnicity by our providers is a result of the rapid increase of overdoses in this population or represents potential bias cannot be determined from this study.

One challenge not addressed by our study is the rate of naloxone filling by patients. Prior studies suggest that only 20-42% of patients prescribed naloxone fill their prescriptions [40-43]. Patient concerns about cost have been identified as a barrier to naloxone acceptance, and co-prescribing naloxone to every patient that receives opioids would be unnecessary and expensive [44]. Prescription fill rates increase in patients who have witnessed an opioid overdose or experienced a personal opioid reversal with naloxone, but these are likely to be uncommon among many patients undergoing elective surgery. Pharmacists may also be uncomfortable providing naloxone to patients, citing a lack of training in the use of over the counter naloxone and, less often, concern that dispensing naloxone will increase the likelihood of opioid overdose [45]. Also, naloxone is variably

covered by different payers and while there are no-cost options, patients and pharmacies are not always aware of these options. Our state does have a standing order allowing pharmacists to dispense naloxone (without a prior prescription), to anyone at increased risk of experiencing an overdose, but most of these efforts are focused on those using non-prescription synthetic opioids (e.g., fentanyl) [46].

Our study has several limitations. First, our data reflects the naloxone co-prescribing practices of a single academic institution and may not reflect those of other institutions or populations. Second, we examined de novo naloxone co-prescribing rates so a small percentage of patients may have already had naloxone at home, leading to an underestimation of the reach of naloxone in our population. Third, we examined naloxone co-prescription rates, but not naloxone pickup rates. Available evidence suggests pharmacy pickup rates are lower than naloxone prescription rates, so the number of patients with readily available naloxone is likely much lower than the number of patients who were prescribed naloxone. Finally, our data is limited by what is contained in the EMR. Patients are prompted through a secure patient portal to review and update their medical history and medications but there is likely under-reporting for fields such as illicit drug use. Prescribed medications such as opioids from other systems may also not be accessible in our system and may explain why some patients not prescribed opioids at discharge received naloxone prescriptions.

5. Conclusion

To date, surgeons have focused primarily on reducing the amount of opioids they prescribe after surgery. However, further reducing the iatrogenic harms of prescription opioids will require a broader strategy of opioid stewardship that encompasses patient and provider education and expectation-setting, promoting safe and appropriate disposal of leftover opioids, and harm reduction through safe storage initiatives and naloxone co-prescriptions. Offering naloxone may reduce overdose rates even when it is not utilized and, as part of a broader public health effort, increasing naloxone co-prescription would likely reduce overdose death rates in the general population, especially among high-risk individuals and communities. Whether these strategies should be applied broadly to all patients or through interventions targeting those at high-risk will require further research and testing.

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References

[1]. U.S. Overdose Deaths In 2021 Increased Half as Much as in 2020 - But Are Still Up 15% 2022. https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm (accessed May 18, 2022).

[2]. Hall MJ, Schwartzman A, Zhang J, Liu X. Ambulatory surgery data from hospitals and ambulatory surgery centers: United States. Natl Health Stat Rep 2010;2017:1–15.

[3]. McDermott KW, Freeman WJ, Elixhauser A. Overview of operating room procedures during inpatient stays in U.S. hospitals, 2014. Agency for healthcare research and quality (US). 2017.

[4]. Brat GA, Agniel D, Beam A, Yorkgitis B, Bicket M, Homer M, et al. Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study. BMJ 2018;360:j5790. 10.1136/bmj.j5790. [PubMed: 29343479]

[5]. Wunsch H, Wijeysundera DN, Passarella MA, Neuman MD. Opioids Prescribed After Low-Risk Surgical Procedures in the United States, 2004-2012. JAMA 2016;315:1654–7. 10.1001/jama.2016.0130. [PubMed: 26978756]

[6]. Vu JV, Howard RA, Gunaseelan V, Brummett CM, Waljee JF, Englesbe MJ. Statewide implementation of postoperative opioid prescribing guidelines. N Engl J Med 2019;381:680–2. 10.1056/NEJMc1905045. [PubMed: 31412184]

[7]. Lev R, Lee O, Petro S, Lucas J, Castillo EM, Vilke GM, et al. Who is prescribing controlled medications to patients who die of prescription drug abuse? Am J Emerg Med 2016;34:30–5. 10.1016/j.ajem.2015.09.003. [PubMed: 26476578]

[8]. Cicero TJ, Ellis MS, Kasper ZA. Increased use of heroin as an initiating opioid of abuse. Addict Behav 2017;74:63–6. 10.1016/j.addbeh.2017.05.030. [PubMed: 28582659]

[9]. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. N Engl J Med 2016;374:154–63. 10.1056/NEJMra1508490. [PubMed: 26760086]

[10]. Office of the Surgeon General. U.S. Surgeon General's Advisory on Naloxone and Opioid Overdose. US Surg Gen Advis Naloxone Opioid Overdose HHSgov 2018. https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-naloxone/index.html (accessed November 16, 2022).

[11]. CDC - National Center for Injury Prevention and Control. Naloxone. Naloxone Opioids CDC 2022. https://www.cdc.gov/opioids/naloxone/index.html (accessed November 16, 2022).

[12]. When to offer naloxone to patients. Centeres Disease Control Prevention 2022.

[13]. Dowell D, Ragan K, Jones C, Baldwin G, Chou R. CDC clinical practice guideline for prescribing opioids for pain. MMWR Recomm Rep 2022;71:1–95.

[14]. Jones CM, Compton W, Vythilingam M, Giroir B. Naloxone Co-prescribing to PATIENTS RECEIVING PRESCRIPTION OPIOIDS IN THE MEDICARE PArt D Program, United States, 2016-2017. JAMA 2019;322:1–3. 10.1001/jama.2019.7988.

[15]. Sohn M, Talbert JC, Huang Z, Lofwall MR, Freeman PR. Association of naloxone coprescription laws with naloxone prescription dispensing in the United States. JAMA Netw Open 2019;2:e196215. 10.1001/jamanetworkopen.2019.6215. [PubMed: 31225895]

[16]. Stein BD, Smart R, Jones CM, Sheng F, Powell D, Sorbero M. Individual and community factors associated with naloxone co-prescribing among long-term opioid patients: a retrospective analysis. J Gen Intern Med 2021;36:2952–7. 10.1007/s11606-020-06577-5. [PubMed: 33598891]

[17]. Dunphy C, Zhang K, Guy GP, Jones CM. Naloxone dispensing among the commercially insured population in the United States from 2015 to 2018. Prev Med 2021;153:106820. 10.1016/j.ypmed.2021.106820. [PubMed: 34599923]

[18]. Coffin PO, Behar E, Rowe C, Santos G-M, Coffa D, Bald M, et al. Non-randomized intervention study of naloxone co-prescription for primary care patients on long-term opioid therapy for pain. Ann Intern Med 2016;165:245–52. 10.7326/M15-2771. [PubMed: 27366987]

[19]. Abuse NI on D. Naloxone DrugFacts. Natl Inst Drug Abuse 2022. https://nida.nih.gov/publications/drugfacts/naloxone (accessed May 22, 2022).

[20]. Bleicher J, Fender Z, Johnson JE, Cain BT, Phan K, Powers D, et al. Use of post-discharge opioid consumption patterns as a tool for evaluating opioid prescribing guidelines. Am J Surg 2021. 10.1016/j.amjsurg.2021.12.020.S0002961021007480.

[21]. Hill MV, McMahon ML, Stucke RS, Barth RJ. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. Ann Surg 2017;265:709–14. 10.1097/SLA.0000000000001993. [PubMed: 27631771]

[22]. McDonald EM, Kennedy-Hendricks A, McGinty EE, Shields WC, Barry CL,Gielen AC. Safe storage of opioid pain relievers among adults living in households with children. Pediatrics 2017;139:e20162161. 10.1542/peds.2016-2161. [PubMed: 28219969]

[23]. Broman MJ, Ellis JD, Victor GA, Kollin R, Pasman E, Lister JJ, et al. Predictors of safe prescription opioid storage and participation in drug take-back events: results from a statewide survey. J Community Health 2021;46:1000–7. 10.1007/s10900-021-00983-4. [PubMed: 33797682]

[24]. Bartels K, Mayes LM, Dingmann C, Bullard KJ, Hopfer CJ, Binswanger IA. Opioid use and storage patterns by patients after hospital discharge following surgery. PLoS One 2016;ll:e0147972. 10.1371/journal.pone.0147972.

[25]. Gaither JR, Shabanova V, Leventhal JM. US national trends in pediatric deaths from prescription and illicit opioids, 1999-2016. JAMA Netw Open 2018;1:e186558. 10.1001/jamanetworkopen.2018.6558. [PubMed: 30646334]

[26]. Kennedy-Hendricks A, Gielen A, McDonald E, McGinty EE, Shields W, Barry CL. Medication sharing, storage, and disposal practices for opioid medications among US adults. JAMA Intern Med 2016;176:1027. 10.1001/jamainternmed.2016.2543. [PubMed: 27295629]

[27]. Lewis ET, Cucciare MA, Trafton JA. What do patients do with unused opioid medications? Clin J Pain 2014;30:654–62. 10.1097/01.ajp.0000435447.96642.f4. [PubMed: 24281287]

[28]. Varady NH, Chen AF, Niu R, Chung M, Freccero DM, Smith EL. Association between surgical opioid prescriptions and opioid initiation by opioid-naïve spouses. Ann Surg 2021. 10.1097/SLA.0000000000005350. Publish Ahead of Print.

[29]. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Bull World Health Organ 2007;85:867–72. 10.2471/blt.07.045120. [PubMed: 18038077]

[30]. Robinson KA, Thiels CA, Stokes S, Duncan S, Feranil M, Fleishman A, et al. Comparing clinician consensus recommendations to patient-reported opioid use across multiple hospital systems. Ann Surg 2022;275:e361–5. 10.1097/SLA.0000000000003986. [PubMed: 32590547]

[31]. Federal Office of Rural Health Policy (FORHP) Data Files | HRSA n.d. https://www.hrsa.gov/rural-health/about-us/what-is-rural/data-files (accessed May 19, 2022).

[32]. Herzig SJ, Stefan MS, Pekow PS, Shieh M-S, Soares W, Raghunathan K, et al. Risk factors for severe opioid-related adverse events in a national cohort of medical hospitalizations. J Gen Intern Med 2020;35:538–45. 10.1007/s11606-019-05490-w. [PubMed: 31728892]

[33]. MDCalc Morphine Milligram Equivalents (MME) Calculator n.d. https://www.mdcalc.com/calc/10170/morphine-milligram-equivalents-mme-calculator (accessed June 1, 2022).

[34]. Newman DA. Missing data: five practical guidelines. Organ Resarch Methods 2014;17:372–411.

[35]. Ostrov Barbara Feder. More states say doctors must offer overdose reversal drug along with opioids. Kais Health News 2019.

[36]. Nelson SD, McCoy AB, Rector H, Teare AJ, Barrett TW, Sigworth EA, et al. Assessment of a naloxone coprescribing alert for patients at risk of opioid overdose: a quality improvement project. Anesth Analg 2022;135:26–34. 10.1213/ANE.0000000000005976. [PubMed: 35343932]

[37]. Devries J, Rafie S, Polston G. Implementing an overdose education and naloxone distribution program in a health system. J Am Pharm Assoc 2017;57:S154–60. 10.1016/j.japh.2017.01.002.

[38]. Ong AR, Lee S, Bonar EE. Understanding disparities in access to naloxone among people who inject drugs in Southeast Michigan using respondent driven sampling. Drug Alcohol Depend 2020;206:107743. 10.1016/j.drugalcdep.2019.107743. [PubMed: 31801107]

[39]. Jones CM, Lurie PG, Compton WM. Increase in naloxone prescriptions dispensed in US retail pharmacies since 2013. Am J Public Health 2016;106:689–90. 10.2105/AJPH.2016.303062. [PubMed: 26890174]

[40]. Cariveau D, Fay AE, Baker D, Fagan EB, Wilson CG. Evaluation of a pharmacist-led naloxone coprescribing program in primary care. J Am Pharm Assoc JAPhA 2019;59:867–71. 10.1016/j.japh.2019.07.012.

[41]. Siff JE, Margolius D, Papp J, Boulanger B, Watts B. A healthcare system-level intervention to increase naloxone availability for patients with opioid prescriptions. Am J Addict 2021;30:179–82. 10.1111/ajad.13136. [PubMed: 33378097]

[42]. Whittington R, Whittington K, Whittington J, Porter J, Zimmermann K, Case H, et al. One-on-one care management and procurement of Naloxone for ambulatory use. J Public Health Oxf Engl 2018;40:858–62. 10.1093/pubmed/fdy029.

[43]. Pietrusza LM, Puskar KR, Ren D, Mitchell AM. Evaluation of an opiate overdose educational intervention and naloxone prescribing program in homeless adults who use opiates. J Addict Nurs 2018;29:188–95. 10.1097/JAN.0000000000000235. [PubMed: 30180005]

[44]. Mueller SR, Koester S, Glanz JM, Gardner EM, Binswanger IA. Attitudes toward naloxone prescribing in clinical settings: a qualitative study of patients prescribed high dose opioids for chronic non-cancer pain. J Gen Intern Med 2017;32:277–83. 10.1007/s11606-016-3895-8. [PubMed: 27798775]

[45]. Thornton JD, Lyvers E, Scott VGG, Dwibedi N. Pharmacists' readiness to provide naloxone in community pharmacies in West Virginia. J Am Pharm Assoc JAPhA 2017;57:S12–8. 10.1016/j.japh.2016.12.070. e4.

[46]. Utah Department of Health & Human Services. Naloxone Distribution is Saving Lives. Naloxone Distrib Sav Lives Utah Dep Health n.d. https://health.utah.gov/featured-news/naloxone-distribution-is-saving-lives (accessed November 16, 2022).

Table 1

Demographic and clinical characteristics of the patients undergoing surgery during the study period (August 2020 to May 2021), by discharge opioid prescription categories.

Demographic and clinical characteristics	Total	Discharge opioid prescription category						p-value
		0 MME	1-75 MME	76-150 MME	151-200 MME	201-350 MME	>350 MME	
Overall N= (row %)	10,414 (100%)	3,922 (37.7%)	3,716 (35.7%)	1,888 (18.1%)	260 (2.5%)	470 (4.5%)	158 (1.5%)	
Co-prescribed naloxone								<0.001
Yes	196 (1.9%)	86(2.2%)	22 (0.6%)	38 (2.0%)	3(1.1%)	24(5.1%)	23 (14.6%)	
No	10,218 (98.1%)	3,836 (97.8%)	3,694 (99.4%)	1,850 (98.0%)	257 (98.9%)	446 (94.9%)	135 (85.4%)	
Age (years)								<0.001
18-30	1,580 (15.2%)	498 (12.7%)	606 (16.3%)	310 (16.4%)	58 (22.3%)	81 (17.2%)	27 (17.1%)	
31-40	1,698 (16.3%)	551 (14.1%)	647 (17.4%)	338 (17.9%)	48 (18.5%)	84 (17.9%)	30 (19.0%)	
41-50	1,845 (17.7%)	612 (15.6%)	665 (17.9%)	364 (19.3%)	57 (21.9%)	111 (23.6%)	36 (22.8%)	
51-60	1,825 (17.5%)	690 (17.6%)	605 (16.3%)	352 (18.6%)	50 (19.2%)	86 (18.3%)	42 (26.6%)	
61-70	1,969 (18.9%)	838 (21.4%)	652 (17.6%)	356 (18.9%)	31 (11.9%)	78 (16.6%)	14 (8.9%)	
71-80	1,207 (11.6%)	582 (14.8%)	426 (11.5%)	148 (7.8%)	15 (5.8%)	28 (6.0%)	8 (5.0%)	
>80	290 (2.8%)	151(3.8%)	115 (3.0%)	20 (1.1%)	1(0.4%)	2(0.4%)	1 (0.6%)	
Gender								<0.001
Female	5,144 (49.40%)	1,877 (47.9%)	1,750 (47.09%)	1,040 (55.1%)	193 (74.2%)	211 (44.9%)	73 (46.2%)	
Male	5,265 (50.55%)	2,041 (52.0%)	1,965 (52.88%)	848 (44.9%)	67 (25.8%)	259 (55.1%)	85 (53.8%)	
Non-Binary	5 (0.05%)	4(0.1%)	1(0.03%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Race								0.08
American Indian/Alaska Native	135 (1.3%)	66 (1.7%)	34 (0.9%)	23 (1.2%)	4 (1.6%)	7(1.5%)	1 (0.6%)	
Asian	157 (1.5%)	63(1.6%)	61 (1.7%)	22 (1.2%)	4 (1.6%)	7(1.5%)	0(0%)	
Black or African American	157 (1.5%)	58(1.5%)	45 (1.2%)	36 (1.9%)	2 (0.7%)	11 (2.4%)	5 (3.2%)	
Caucasian/White	8,853 (86.1%)	3,324 (85.8%)	3,154 (85.9%)	1,612 (86.5%)	223 (87.1%)	399 (86.2%)	141 (91.6%)	
Native Hawaiian/Pacific Island	104 (1.0%)	41(1.1%)	41 (1.1%)	15 (0.8%)	1 (0.4%)	6(1.3%)	0(0%)	
Other	876 (8.5%)	320 (8.3%)	338 (9.2%)	156 (8.4%)	22 (8.6%)	33 (7.1%)	7 (4.6%)	
Ethnicity								0.45
Hispanic/Latino	1,054 (10.3%)	379 (9.8%)	380 (10.4%)	192 (10.3%)	26 (10.3%)	60 (13.0%)	17 (11.0%)	

Demographic and clinical characteristics	Total	Discharge opioid prescription category						p-value
		0 MME	1-75 MME	76-150 MME	151-200 MME	201-350 MME	>350 MME	
Non-Hispanic/Latino	9,159 (89.7%)	3,470 (90.2%)	3,260 (89.6%)	1,664 (89.7%)	227 (89.7%)	401 (87.0%)	137 (89.0%)	
Home rurality								<0.001
Rural	2,685 (25.8%)	1,088 (27.7%)	863 (23.2%)	472 (25.0%)	61 (23.5%)	142 (30.3%)	59(37.3%)	
Non-rural	7,727 (74.2%)	2,833 (72.3%)	2,853 (76.8%)	1,416 (75.0%)	199 (76.5%)	327 (69.7%)	99 (62.7%)	
ASA Score								<0.001
1	1,054 (10.12%)	307 (7.8%)	466 (12.5%)	201 (10.7%)	38 (14.6%)	35 (7.4%)	7 (4.4%)	
2	4,582 (44.00%)	1,511 (38.5%)	1,901 (51.2%)	882 (46.7%)	133 (51.2%)	126 (26.8%)	29 (18.4%)	
3	4,065 (39.03%)	1,700 (43.4%)	1,253 (33.7%)	725 (38.4%)	76 (29.2%)	213 (45.3%)	98 (62.0%)	
4	689 (6.62%)	393 (10.0%)	93 (2.5%)	78 (4.1%)	13 (5.0%)	91 (19.4%)	21 (13.3%)	
5	24 (0.23%)	11 (0.3%)	3 (0.1%)	2 (0.1%)	0 (0%)	5 (1.1%)	3 (1.9%)	
Cardiac co-morbidity								<0.001
Yes	779 (7.5%)	442 (11.3%)	121 (3.3%)	97 (5.1%)	7 (2.7%)	87 (18.5%)	25 (15.8%)	
No	9,635 (92.5%)	3,480 (88.7%)	3,595 (96.7%)	1,791 (94.9%)	253 (97.3%)	383 (81.5%)	133 (84.2%)	
Respiratory co-morbidity								<0.001
Yes	772 (7.4%)	289 (7.4%)	294 (7.9%)	97 (5.1%)	14 (5.4%)	66 (14.0%)	12 (7.6%)	
No	9,642 (92.6%)	3,633 (92.6%)	3,422 (92.1%)	1,791 (94.9%)	246 (94.6%)	404 (86.0%)	146 (92.4%)	
Illicit drug use								0.006
Yes	726 (7.7%)	261 (7.4%)	244 (7.1%)	147 (8.7%)	24 (10.1%)	31 (8.0%)	19 (15.3%)	
No/Never	8,669 (92.3%)	3,263 (92.6%)	3,186 (92.9%)	1,547 (91.3%)	214 (89.9%)	354 (92.0%)	105 (84.7%)	
Active tobacco use								0.042
Yes	784 (8.1%)	287 (7.9%)	270 (7.7%)	153 (8.8%)	17 (6.9%)	37 (9.2%)	20 (14.9%)	
No/Never	8,852 (91.9%)	3,330 (92.1%)	3,233 (92.3%)	1,583 (91.2%)	228 (93.1%)	364 (90.8%)	114 (85.1%)	
Active alcohol use								<0.001
Yes	3,380 (35.3%)	1,169 (32.6%)	1,299 (37.2%)	665 (38.6%)	103 (42.4%)	113 (29.0%)	31 (25.2%)	
No/Never	6,181 (64.7%)	2,420 (67.4%)	2,194 (62.8%)	1,059 (61.4%)	140 (57.6%)	276 (71.0%)	92 (74.8%)	

Column percentages are shown unless otherwise indicated. MME=Morphine milligram equivalent; ASA=American Society of Anesthesiology.

Table 2

Characteristics of the surgeries performed during the study period (August 2020 to May 2021), by discharge opioid prescription categories.

Surgery characteristics		Discharge opioid prescription category						
	Total	0 MME	1-75 MME	76-150 MME	151-200 MME	201-350 MME	>350 MME	p-value
Surgery urgency								<0.001
Elective	9,159 (88.0%)	3,429 (87.5%)	3,347 (90.1%)	1,660 (88.1%)	239 (91.9%)	367 (78.1%)	117 (74.1%)	
Urgent	1,172 (11.3%)	468 (11.9%)	355 (9.5%)	195 (10.4%)	20 (7.7%)	94 (20.0%)	40 (25.3%)	
Emergent	78 (0.7%)	24 (0.6%)	14 (0.4%)	29 (1.5%)	1 (0.4%)	9 (1.9%)	1 (0.6%)	
Surgery classification								<0.001
Outpatient	7,580 (72.8%)	2,825 (72.0%)	3,213 (86.5%)	1,196 (63.4%)	178 (68.5%)	150 (31.9%)	18 (11.4%)	
Inpatient	2,834 (27.2%)	1,097 (28.0%)	503 (13.5%)	692 (36.6%)	82 (31.5%)	320 (68.1%)	140 (88.6%)	
Specialty								<0.001
Burn	108(1.0%)	45(1.1%)	14(0.4%)	11(0.6%)	4(1.5%)	15(3.2%)	19(12.0%)	
Cardiothoracic	545(5.2%)	164(4.2%)	69(1.8%)	112(5.9%)	15(5.7%)	141(30.0%)	44(27.9%)	
General Surgery	3,522(33.8%)	860(21.9%)	1,698(45.7%)	756(40.0%)	48(18.4%)	118(25.1%)	42(26.6%)	
Otolaryngology	1,988(19.1%)	1,087(27.7%)	610(16.4%)	190(10.1%)	21(8.1%)	66(14.0%)	14(8.9%)	
Plastics	1,153(11.1%)	291(7.4%)	170(4.6%)	482(25.5%)	149(57.3%)	53(11.3%)	8(5.0%)	
Transplant	297(2.9%)	148(3.8%)	22(0.6%)	47(2.5%)	10(3.9%)	48(10.2%)	22(13.9%)	
Urology	2,177(20.9%)	861(22.0%)	1,036(27.9%)	255(13.5%)	10(3.9%)	12(2.6%)	3(1.9%)	
Vascular	624(6.0%)	466(11.9%)	97(2.6%)	35(1.9%)	3(1.2%)	17(3.6%)	6(3.8%)	

Column percentages are shown unless otherwise indicated. MME=Morphine milligram equivalent; ASA=American Society of Anesthesiology.

Table 3

Univariable analysis of opioid-related overdose/adverse event risk factors and their association with naloxone co-prescribing.

	Naloxone co-prescribed N= (%)	Naloxone not co-prescribed N= (%)	p-value
Overall (N=, row %)	196 (1.9%)	10,218 (98.1%)	
Opioid total prescription			<0.001
0 MME	86 (2.2%)	3,836 (97.8%)	
1-75 MME	22 (0.6%)	3,694 (99.4%)	
76-150 MME	38 (2.0%)	1,850 (98.0%)	
151-200 MME	3 (1.2%)	257 (98.9%)	
201-350 MME	24 (5.1%)	446 (94.9%)	
>350 MME	23 (14.6%)	135 (85.4%)	
ASA Score			<0.001
1	3 (0.3%)	1,051 (99.7%)	
2	48 (1.0%)	4,534 (99.0%)	
3	132 (3.2%)	3,933 (96.8%)	
4	13 (1.9%)	676 (98.1%)	
5	0 (0%)	24 (100%)	
Cardiac co-morbidity			0.01
Yes	24 (3.1%)	755 (96.9%)	
No	172 (1.8%)	9,463 (98.2%)	
Respiratory co-morbidity			0.897
Yes	15 (1.9%)	757 (98.1%)	
No	181 (1.9%)	9,461 (98.1%)	<0.001
Illicit drug use			
Yes	54 (7.4%)	672 (92.6%)	
No/Never	126 (1.4%)	8.543 (98.6%)	
Active tobacco use			<0.001
Yes	35 (4.5%)	749 (95.5%)	
No/Never	149 (1.7%)	8,703 (98.3%)	
Active alcohol use			<0.001
Yes	39 (1.2%)	3,341 (98.9%)	
No/Never	144 (2.3%)	6,037 (97.7%)	
Surgery urgency			<0.001
Elective	164 (1.8%)	8,995 (98.2%)	
Urgent	21 (1.8%)	1,151 (98.2%)	
Emergent	11 (14.1%)	67 (85.9%)	
Surgery classification			<0.001
Outpatient	118 (1.6%)	7,462 (98.4%)	
Inpatient	78 (2.7%)	2,756 (97.3%)	
Specialty			<0.001
Burn	15 (13.9%)	93 (86.1%)	

	Naloxone co-prescribed N= (%)	Naloxone not co-prescribed N= (%)	p-value
Cardiothoracic	10 (1.8%)	535 (98.2%)	
General Surgery	88 (2.7%)	3,434 (97.3%)	
Otolaryngology	30 (1.5%)	1,958 (98.5%)	
Plastics	19 (1.7%)	1,134 (98.3%)	
Transplant	2 (0.7%)	295 (99.3%)	
Urology	29 (1.3%)	2,148 (98.7%)	
Vascular	3 (0.5%)	621 (99.5%)	

Row percentages are reported here to allow for comparison of the primary study outcome. MME=Morphine milligram equivalent; ASA=American Society of Anesthesiology.

Table 4

Multivariable logistic regression of the patient-level (demographic and clinical) and surgery-level characteristics associated with naloxone co-prescription.

Patient and surgery-level characteristics	OR (95% CI)	P-value
Prescribed opioid dosage		
0 MME (Reference)	-	
1-75 MME	0.22 (0.13-0.39)	<0.001
76-150 MME	0.72 (0.44-1.18)	0.19
151-200 MME	0.45 (0.10-1.98)	0.29
201-350 MME	1.64 (0.86-3.12)	0.13
>350 MME	4.7 (1.68-13.00)	0.003
Illicit drug use		
Yes	3.51 (1.94-6.34)	<0.001
Ethnicity		
Hispanic/Latino	2.57 (1.24-5.35)	0.011
Specialty		
General Surgery (Reference)	2.90 (1.01-8.30)	0.047
Burn	2.34 (0.84-6.49)	0.10
Cardiothoracic	0.35 (0.12-1.06)	0.062
Otolaryngology	0.65 (0.31-1.37)	0.26
Plastics	0.49 (0.26-0.93)	0.03
Transplant	0.21 (0.03-1.45)	0.11
Urology	0.56 (0.30-1.05)	0.07
Vascular	0.05 (0.007-0.36)	0.003
ASA score[†]		
1 (Reference)	-	
2	4.55 (1.11-18.68)	0.04
3	12.77 (2.98-54.80)	0.001
4	9.51 (1.84-49.12)	0.007
5	-	-
Active tobacco use		
Yes	1.87 (1.02-3.43)	0.04
Active alcohol use		
Yes	0.50 (0.30-0.82)	0.007
Surgery Urgency		
Elective (Reference)	-	
Urgent	0.92 (0.51-1.69)	0.80
Emergent	8.25 (2.55-26.62)	<0.001

MME=Morphine milligram equivalent; OR=Odds ratio, 95% CI= 5% confidence interval. Included in the model but not shown (as none were statistically significant predictors) are age, gender, race, home rurality, and cardiac and respiratory co-morbidities. The model is also adjusted for clustering by individual surgeons. †: There was little variation in this variable to estimate the effect on receiving naloxone co-prescriptions for ASA=5.