

Prescription Opioid Analgesics Commonly Unused After Surgery

A Systematic Review

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IMPORTANCE Prescription opioid analgesics play an important role in the treatment of postoperative pain; however, unused opioids may be diverted for nonmedical use and contribute to opioid-related injuries and deaths.

OBJECTIVE To quantify how commonly postoperative prescription opioids are unused, why they remain unused, and what practices are followed regarding their storage and disposal.

EVIDENCE REVIEW MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials were searched from database inception to October 18, 2016, for studies describing opioid oversupply for adults after a surgical procedure. The primary outcome—opioid oversupply—was defined as the number of patients with either filled but unused opioid prescriptions or unfilled opioid prescriptions. Two reviewers independently screened studies for inclusion, extracted data, and assessed the study quality.

FINDINGS Six eligible studies reported on a total of 810 unique patients (range, 30-250 patients) who underwent 7 different types of surgical procedures. Across the 6 studies, 67% to 92% of patients reported unused opioids. Of all the opioid tablets obtained by surgical patients, 42% to 71% went unused. Most patients stopped or used no opioids owing to adequate pain control, and 16% to 29% of patients reported opioid-induced adverse effects. In 2 studies examining storage safety, 73% to 77% of patients reported that their prescription opioids were not stored in locked containers. All studies reported low rates of anticipated or actual disposal, but no study reported US Food and Drug Administration–recommended disposal methods in more than 9% of patients.

CONCLUSIONS AND RELEVANCE Postoperative prescription opioids often go unused, unlocked, and undisposed, suggesting an important reservoir of opioids contributing to nonmedical use of these products, which could cause injuries or even deaths.

JAMA Surg. 2017;152(11):1066-1071. doi:10.1001/jamasurg.2017.0831
Published online August 2, 2017.

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Opioid analgesics play an important role as a safe and effective method for pain relief when used appropriately. Despite this role, the benefits of opioids in treating pain have to be balanced with their risks, including tolerance, dependence, and respiratory depression. *Nonmedical use* of opioids, defined as taking medication for a purpose other than as prescribed, often leads to more serious harms, such as abuse, addiction, or life-threatening overdose. To address the opioid epidemic, efforts have largely focused on opioid prescribing among those with chronic non-cancer pain.¹ In contrast, the risks for and evidence of patients with acute pain following surgery are less well characterized.²

Surgery often serves as the inaugural event for many patients to obtain a prescription for opioids, fill it at the pharmacy, and take opioid medications on a frequent basis. Prescriptions may go

unfilled for several reasons, including adequate pain control after surgery. When prescriptions are filled, opioid-naïve patients may inadvertently transition into long-term opioid users.^{3,4} Low-risk surgical procedures give rise to most opioid-naïve patients receiving and filling prescriptions for oxycodone, hydrocodone, or another opioid.⁵ Patients may fill the prescription but not use all of the medication, leading to a reservoir of pills that can potentially contribute to the nonmedical use of opioids.

Given the lack of data-driven approaches to opioid prescribing after surgery, we conducted a systematic review to examine the prevalence of unused prescription opioids among home-going adults following inpatient or outpatient surgery. We defined our primary outcome—*opioid oversupply*—as the number of patients who either elected to not fill an opioid prescription or filled the

opioid prescription but did not use the medication following surgery. We also examined the volume of unused opioids, reasons for not taking the medication, and storage and disposal practices.

Methods

Data Sources and Search

We adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines, including protocol registration with PROSPERO on June 9, 2016.⁶ We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials without language restriction from database inception to July 20, 2016, and updated our search on October 18, 2016. For studies fulfilling the inclusion criteria, we used Web of Science to search citation lists and cite studies from database inception to July 20, 2016. We created a search strategy using a controlled vocabulary of known studies meeting the inclusion criteria and focused on specific terms associated with the concepts of adults (population), opioids (intervention), surgery or procedure (intervention), and medication use and prescription (outcome; eMethods in the [Supplement](#)).

Inclusion Criteria and Outcome Definition

We included cross-sectional and cohort studies and randomized clinical trials of adult surgical patients who were prescribed an oral opioid medication by a medical professional at the time of postsurgical discharge. We included both inpatient and outpatient procedures and did not apply any restrictions regarding surgery type. We required studies to report on *unused opioid medication*, defined as unfilled prescriptions or unused tablets. We excluded retrospective studies, those that described nonsurgical or pediatric (age <18 years) patients, and those that did not report the outcome of unused opioids.

We calculated the percentage of patients who had an oversupply of a prescription opioid as the sum of patients not filling opioid prescriptions and patients filling opioid prescriptions but reporting unused opioids. For the denominator, we used the number of patients provided an opioid prescription after surgery. Secondary outcomes included the number of opioid tablets (or volume of solution) unused by the patient, morphine equivalents of prescription opioid medication unused by the patient, reasons for not using or stopping opioid therapy, and opioid storage and disposal characteristics.

Two reviewers (M.C.B. and J.J.L.) independently assessed 2419 nonduplicate studies, with 2324 studies failing title and abstract screening. Of the 95 studies retrieved and assessed by the 2 reviewers, 6 (6%) fulfilled the inclusion criteria (κ statistic = 0.78) (eFigure in the [Supplement](#)).

Data Extraction and Quality Assessment

Two of us (M.C.B. and J.J.L.) independently extracted relevant study characteristics using a data extraction template. Data included study design, setting, patient population, type of surgery, opioid prescription characteristics, unused opioid tablets, reasons for stopping or not using opioid therapy, and opioid storage and disposal characteristics. Storage characteristics included the location and use of a lock to secure opioids according to the guidelines of the US Food and Drug Administration and the Centers for Disease Control and Prevention.^{1,7} For disposal, Food and Drug Administration-

Key Points

Question How commonly are prescription opioid analgesics unused among adult patients after a surgical procedure?

Findings In this review of 6 studies involving 810 unique patients who underwent orthopedic, thoracic, obstetric, and general surgical procedures, 67% to 92% of patients reported unused opioids. Rates of safe storage and/or disposal of unused prescription opioids were low.

Meaning Unused opioids prescribed for patients after surgery are an important reservoir of opioids available for nonmedical use and could cause injuries or even deaths.

recommended methods included returning the medication to the pharmacy or a drug take-back program or flushing the medication down the sink or toilet. Two reviewers (M.C.B. and J.J.L.) assessed the quality of studies and the potential bias using the Newcastle-Ottawa Scale⁸ adapted for observational studies or the Cochrane Risk of Bias Tool⁹ for clinical trials. Disagreements between the reviewers regarding data extraction and quality assessment ratings were resolved by discussion and consensus.

Data Synthesis

We aggregated extracted data by type of surgery, reporting on study characteristics, opioid use, reasons for opioid therapy cessation, and opioid storage and disposal characteristics. We qualitatively summarized outcomes across surgery type because of differences in patient populations, which precluded quantitative data pooling.

Results

After full-text review, 6 studies met our prespecified inclusion criteria, with all studies describing populations in the United States ([Table 1](#) and eTable 1 in the [Supplement](#)).¹⁰⁻¹⁵ Among the prospective studies considered for this review, 1 study was identified as having duplicate reports^{14,16} and 3 were excluded¹⁷⁻¹⁹ for inability to distinguish surgical from nonsurgical reports of unused opioid medications.

Six eligible studies prospectively evaluated the oversupply of opioids after 7 types of surgery, including obstetric, thoracic, orthopedic, and urologic. Practice settings described surgeons employed by 4 institutions and 1 private practice between January 1, 2011, and December 31, 2016. Studies primarily evaluated outpatient procedures ($n = 4$), with fewer reports of inpatient ($n = 2$) or mixed ($n = 1$) procedures. In all, 810 unique patients received at least 1 opioid prescription after surgery. Patient samples ranged in size from 30 for cesarean delivery to 250 for orthopedic surgery. Follow-up most commonly ranged in duration from 1 to 5 weeks after surgery.

All 6 studies were rated as having intermediate quality. Reporting of baseline characteristics important for comparability, such as preprocedural use of opioid medications, varied among the studies: 3 studies excluded patients because of preprocedural opioid use (within 7 or 30 days),^{13,15,16} 1 study assessed and reported preprocedural use via self-report,¹⁰ and 2 studies neither excluded such patients nor recorded this characteristic.^{11,12}

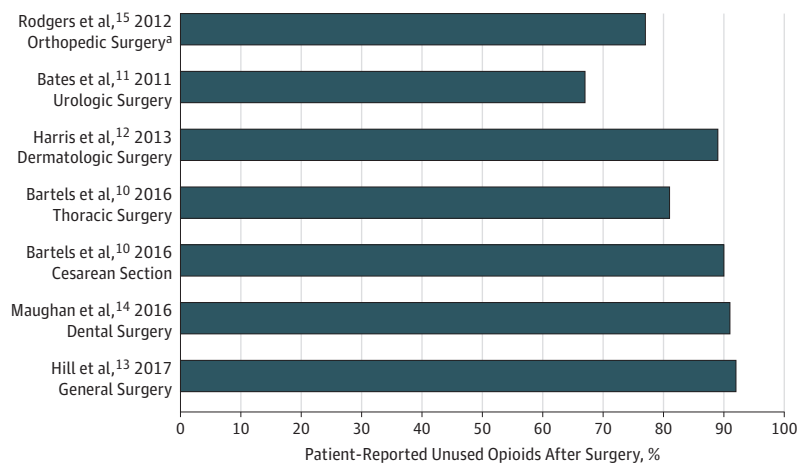
Table 1. Characteristics of Studies Assessing Unused Opioids After Surgery

Source	Study Design	Study Setting	Procedure Type	Study Population	All Patients, No.	Female, No. (%)	Study Length, Mean (SD), d
Bartels et al, ¹⁰ 2016 ^a	Cross-section	University of Colorado	Cesarean delivery	Inpatient	30	30 (100)	30 (12)
Bartels et al, ¹⁰ 2016 ^a	Cross-section	University of Colorado	Thoracic surgery	Inpatient	31	16 (52)	32 (14)
Bates et al, ¹¹ 2011	Cross-section	University of Utah	Urologic surgery	Mixed	226	NR	NR (14 to 28)
Harris et al, ¹² 2013	Prospective cohort	University of Utah	Dermatologic surgery	Outpatient	72	20 (28)	NR (3 to 4)
Hill et al, ¹³ 2017	Cross-section	Dartmouth Medical Center	General surgery	Outpatient	127	NR	NR (NR to 180)
Maughan et al, ¹⁴ 2016	RCT	University of Pennsylvania	Dental surgery	Outpatient	74	NR	21 (NR)
Rodgers et al, ¹⁵ 2012	Cross-section	Iowa private practice	Orthopedic surgery	Outpatient	250	167 (67)	11 (7 to 14)

Abbreviations: NR, data not reported; RCT, randomized clinical trial.

^a Bartels et al report on 2 distinct surgical populations—cesarean delivery and thoracic surgery.

Figure. Prevalence of Unused Opioids Prescribed After Surgery



^a Percentage of patients reporting use of 15 tablets or fewer.

Table 2. Utilization in Studies Assessing Unused Opioids After Surgery

Source	Patients Reporting, No. (%)			Unused Opioid Tablets	
	Any Unused Opioid	Unfilled Opioid Prescription	Filled Prescription Without Opioid Use	No. Unused/Used (%)	Mean (SD) ^a
Bartels et al, ¹⁰ 2016 ^b	27/30 (90)	4/30 (13)	2/30 (7)	NR	NR
Bartels et al, ¹⁰ 2016 ^b	25/31 (81)	0/31 (0)	3/31 (10)	NR	NR
Bates et al, ¹¹ 2011	NR (67)	13/226 (6)	NR	NR (42)	NR
Harris et al, ¹² 2013	64/72 (89)	15/72 (21)	10/72 (14)	NR (68)	5 (4)
Hill et al, ¹³ 2017	117/127 (92)	NR	NR	2527/3545 (71)	20 (NR)
Maughan et al, ¹⁴ 2016	67/74 (91)	2/74 (3)	NR	1102/2051 (54)	15 (NR)
Rodgers et al, ¹⁵ 2012	193/250 (77) ^c	NR	NR	4639/NR	19 (NR)

Abbreviation: NR, data not reported.

^a Mean unused opioid tablets per patient.

^b Bartels et al report on 2 distinct surgical populations—cesarean delivery and thoracic surgery.

^c Percentage of patients reporting use of 15 tablets or fewer.

Opioid Oversupply

The prevalence of unused opioids after surgery was high for all 7 procedures examined, with 67% to 92% of patients reporting unused opioids (Figure). Table 2 highlights the primary outcome and associated secondary outcomes. Patients reported large amounts of unused opioids following both outpatient surgery (77%-92%) and inpatient surgery (67%-90%). In 5 of the 7 surgical settings examined, more than 80% of patients reported unused opioids. Three studies examined patient reports of filling

a prescription but no opioid use and patient reports of not filling the opioid prescription, and 2 studies examined only the latter outcome. A small number of patients either did not fill their opioid prescription (0%-21%) or filled the prescription but did not take any opioids (7%-14%). A significant number of opioid tablets went unused after surgery, ranging from 42% to 71% of pills dispensed.

Reasons for not consuming opioid medications were reported for 3 types of procedures (eTable 2 in the Supplement). Most patients

Table 3. Storage and Disposal Characteristics for Unused Opioids After Surgery

Study	Patients Reporting, No. (%)					
	Storage		Unlocked Storage	Disposal		
	Locked or Unlocked Location			Performed or Planned	FDA-Recommended Method Used	No Disposal Instructions
Bartels et al, ¹⁰ 2016 ^a	6/23 (26)	Cupboard/wardrobe	17/22 (77)	1/23 (4)	1/23 (4)	NR
	16/23 (70)	Medicine cabinet/other box				
Bartels et al, ¹⁰ 2016 ^a	5/24 (21)	Cupboard/wardrobe	16/22 (73)	2/24 (8)	1/24 (4)	NR
	13/24 (54)	Medicine cabinet/other box				
Bates et al, ¹¹ 2011	NR	NR	NR	15/164 (9)	5/164 (3)	213/231 (92)
Harris et al, ¹² 2013	NR	NR	NR	9/49 (18)	2/49 (4)	NR
Hill et al, ¹³ 2017	NR	NR	NR	NR (26)	NR (9)	NR
Maughan et al, ¹⁴ 2016	NR	NR	NR	8/27 (30) ^b	NR	NR

Abbreviation: FDA, Food and Drug Administration; NR, data or descriptive text not reported.

^b Based on control group.

^a Bartels et al report on 2 distinct surgical populations—cesarean delivery and thoracic surgery.

(71%- 83%) described not taking opioids because of adequate pain control, and fewer patients (16%-29%) reported concern for adverse effects induced by opioids. Only 1 study examined patients' concern about addiction: 8% of patients who underwent thoracic surgery avoided opioids for this reason.¹⁰

Storage and Disposal

Patients' storage of prescription opioids was characterized for 2 types of surgery, focusing on cesarean delivery and thoracic surgery (Table 3). Most patients stored opioids in a medicine cabinet or another box (54% to 70%), and some used a cupboard or wardrobe (21% to 26%). Notably, a high percentage (73% to 77%) of patients stored opioids in unlocked locations. Five studies examined patients' opioid disposal practices: few patients (4% to 30%) planned to or actually disposed of their unused prescription opioids, and even fewer patients (4% to 9%) considered or used a disposal method recommended by the Food and Drug Administration.

Discussion

In this systematic review, more than two-thirds of patients reported unused prescription opioids following surgery. These findings were consistent across several studies of general, orthopedic, thoracic, and obstetric inpatient and outpatient surgeries. Of the 5 studies examining storage and disposal practices, 3 of 4 patients reported failing to store opioids in a locked location, and planned or actual safe disposal of opioids rarely occurred. These findings are important because of the magnitude of injuries and deaths attributable to the nonmedical use of prescription opioids in the United States, and oversupply of these products contributes to this epidemic.

Several factors likely contribute to how commonly patients report unused opioid medications. Health care professionals may not be aware of how commonly opioids go unused,² and heterogeneous patient populations and procedure types complicate the development of evidence-based prescribing guidelines in these settings. However, some patient-reported outcomes and psychological

profiles may inform pain intensity and subsequent analgesic use after surgery. For example, Thomazeau et al²⁰ correlated postoperative pain for total knee arthroplasty with preoperative pain at rest, anxiety levels, and symptoms of neuropathic pain. In another example, Carvalho et al²¹ associated pain scores and analgesic use for women after cesarean delivery with psychological questionnaires and simple patient-reported ratings.

We recommend a data-driven approach to prescribing opioids after surgery. An inappropriate response to the problem of unused opioids would be to pursue a reflexive one-size-fits-all tactic that indiscriminately curtails opioid prescribing after invasive procedures given the critical consequences of pain undertreatment, the possibility of inducing drug-seeking behavior, and the important role that opioid medications serve in controlling postoperative pain.^{2,22} As health care professionals encounter new regulations, such as prescription drug monitoring programs in most states and electronic prescribing requirements in New York,²³ the evidence associated with these interventions continues to evolve.²⁴ At a national level, guidelines emphasize the importance of nonopioid analgesics, such as acetaminophen, nonsteroidal anti-inflammatory drugs, and gabapentoids, as well as nonpharmacologic approaches, such as exercise, cold, and heat.^{2,25}

In addition, we found that opioids were seldom stored and disposed of correctly. Safe storage practices mitigate risks for other household members, such as adolescents at risk of misusing medication accessible in the house.^{26,27} The failure to properly dispose of opioids highlights the role of stockpiling as an important contributor to their nonmedical use. Stockpiling is common given the time and energy involved in properly disposing medicine. Patients may perceive a future utility for keeping opioids besides saving money: pain medication will relieve acute pain should it return in the future. Medication take-back programs help to address the oversupply of tablets sitting around the house.²⁸ Pharmacies and health systems facilitate the capture of an enormous amount of drug products during US Drug Enforcement Agency-sanctioned take-back days, community-based collection events,²⁹ and coordinated programs, such as National Prescription Drug Drop-off Day in Canada.³⁰ However, these events secure only a small fraction of

opioids available for nonmedical use and remain in rudimentary stages of implementation.²⁹ Pharmacies appear as one possible solution but assume unwanted costs and liabilities in taking back scheduled medications. Few commercial solutions (eg, disposal bags) exist, relegating patients to flushing opioids down the sink or toilet, which may reduce individual risk at the expense of the environment.

The combination of unused opioids, poor storage practices, and lack of disposal sets the stage for the diversion of opioids for nonmedical use. Based on the 2015 National Survey on Drug Use and Health, an estimated 3.8 million Americans engage in the nonmedical use of opioids every month.³¹ More than half of people (54%) who misused an opioid medication in 2014 obtained opioids from a friend or relative.³² Most of these pills were either given for free, bought, or taken without asking. The second largest source of misused opioids (36%) was a prescription from 1 or more physicians and other clinicians.³² Because more than 90% of opioids originate from medical practitioners, family, or friends, the oversupply of opioids in health care environments that appear otherwise innocuous deserves additional scrutiny.

Limitations

Despite the importance of our findings, our review had several limitations. First, the studies we examined were of intermediate rather than high methodological quality, and the questionnaires completed by patients varied in form, structure, phrasing, and timing across the studies. Many studies also failed to ascertain a history of opioid use among respondents and did not describe essential fea-

tures for cross-sectional and cohort studies, such as nonrespondents and missing data. Evidence gaps also exist for surgical subspecialties as well as for individual surgical operations aside from the 7 types reported here. Second, we were not able to estimate leftover morphine equivalents for these patients because this information was not reported in any of the studies examined or to examine more granular data regarding unused opioid pill counts to determine a consistent, clinically relevant definition of unused opioids. Data on additional surgical subspecialties would enhance the generalizability of these findings, which largely agree with most estimates of nonsurgical opioid prescribing in acute, chronic, or both types of pain. For example, Porucznik et al¹⁸ showed similarly high rates of leftover pills among adults prescribed opioids. Regarding storage, Reddy et al¹⁹ showed similar rates of unlocked medication in cancer patients prescribed opioids. Finally, heterogeneity across the studies precluded any quantitative pooling of the results.

Conclusions

Most patients who underwent surgery in these studies had unused prescription opioids, and safe storage and disposal of unused medications rarely occurred. Increased efforts are needed to develop and disseminate best practices to reduce the oversupply of opioids after surgery, especially given how commonly opioid analgesics prescribed by clinicians are diverted for nonmedical use and may contribute to opioid-associated injuries and deaths.

ARTICLE INFORMATION

Accepted for Publication: March 4, 2017.

Published Online: August 2, 2017.
doi:10.1001/jamasurg.2017.0831

Author Contributions: Dr Bicket had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Bicket, Pronovost, Wu.
Acquisition, analysis, or interpretation of data: Bicket, Long, Alexander.

Drafting of the manuscript: Bicket, Long, Wu.
Critical revision of the manuscript for important intellectual content: Bicket, Pronovost, Alexander.
Statistical analysis: Bicket.

Administrative, technical, or material support: Bicket.

Study supervision: Bicket, Pronovost, Alexander, Wu.

Conflict of Interest Disclosures: Dr Alexander reported being chair of the US Food and Drug Administration's Peripheral and Central Nervous System Advisory Committee and serving as a paid consultant to PainNavigator, a mobile startup to improve patients' pain management; as a paid consultant to QuintilesIMS; and on a scientific advisory board of QuintilesIMS Health. This arrangement has been reviewed and approved by The Johns Hopkins University according to its conflict-of-interest policies. No other disclosures were reported.

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