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Tackling the opioid epidemic: Reducing opioid prescribing while maintaining patient satisfaction with pain management after outpatient surgery



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ABSTRACT

Introduction: Results of a quality improvement (QI) project to standardize our opioid prescribing practices following five common outpatient general surgery procedures are presented.

Methods: Opioid prescribing habits were reviewed from June to December 2017. QI measures were implemented. We prospectively collected data on opioid prescribing habits and patients' pain management ratings from September 2018 to February 2019.

Results: Following implementation, combination pills were less prescribed. More patients were prescribed adjuncts pre- (66% vs. 3%; $p < 0.01$) and post-operatively (85% vs. 50%; $p < 0.01$). One-third of pills were prescribed (1363 vs. 4185), with only 520 consumed. Average OME prescribed decreased from 179 to 127 mg ($p < 0.001$). At follow-up, 52 patients (54%) reported taking 11 pills (1–20) post-operatively for five days. Pain management was rated as good/excellent (88.6%) or fair (9.3%).

Conclusions: Using a pragmatic multimodal approach, decreasing opioid prescriptions at discharge allows for adequate pain management.

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Introduction

Opioids have become a pillar in the treatment of pain and are heavily relied upon by healthcare professionals. In 2016, prescription opioid overdoses resulted in about 20,000 deaths in America.¹ From 1999 to 2017, the number of opioid-related deaths increased six fold.² This number continues to increase, challenging our healthcare system on how best to treat our patients' pain both effectively and safely. Surgeons are at the forefront as prescribers of opioid medication for post-surgical pain. Prior studies suggest that 21–29% of post-surgical patients will misuse their medication. Additionally, of that population, 6–10%, will become new persistent users.^{3,4} Given the high risk of opioid misuse, our habits as prescribers must be evaluated to transition to safer, less addictive options.

Prescriber education is one of many ways to impact on the current opioid crisis as, through education, we can alter prescribing habits. Because prescribing habits are formed early during training, it is crucial to target trainees early.⁵ Even within the same

department, provider prescribing habits of opioids dramatically differ for the same operation and are often based on the individual physician's experience.⁶ Not only do providers' prescribing habits vary in term of the number of pills prescribed to each patient, but opioids are often overprescribed.⁷ Without education in safe disposal techniques, these excess pills remain available for inappropriate use.

With the paradigm shifting away from primarily opioids and toward safer, less addictive medications, practitioners must develop new pain management protocols. As a result, a large body of research now focuses on assessing the effectiveness of appropriate adjuncts to help achieve a satisfactory pain level with patients post operatively. Gabapentin has attracted the attention for its potential to reduce postoperative pain, in combination with opioid medications if taken pre-operatively and continued through the acute post-operative course.⁸ While some meta-analysis studies provided mixed results,^{9,10} others suggested that preoperative gabapentin significantly reduces postoperative opioid consumption.¹¹ The use of anti-inflammatory medications such as acetaminophen and ibuprofen also impact on pain, resulting in decreased pain requiring less opioid medication.¹²

At the beginning of our study, the University of Iowa Acute Care

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Surgery Division had no guidelines or protocols in place for post-operative analgesia, thus opioid prescribing was left to the provider's discretion. A quality improvement (QI) project was designed to assess whether the amount of opioids prescribed could be decreased without affecting our patients' overall satisfaction regarding pain management following our five most common elective, outpatient procedures: laparoscopic cholecystectomy, laparoscopic inguinal hernia repair, laparoscopic umbilical hernia repair, open umbilical hernia repair, and open inguinal hernia repair.

To this end, we retrospectively studied the prescribing habits following those five elective outpatient procedures performed by surgeons in the Acute Care Surgery Division. Based on this information, we instituted a QI project with three goals: 1) to improve surgeon and patient knowledge of the risks of opioid use, 2) to maintain patient satisfaction with post-operative pain management of adequate pain control, and 3) to decrease the total number of pills prescribed and total amount of narcotics (OME) following these procedures. We hypothesized that, with education and collaboration of the surgeons, clinic nurses, advanced practice providers, and residents, optimization of non-opioid adjuncts, and development of both preoperative and postoperative order sets, we could decrease the number of opioids prescribed and consumed while maintaining patients' satisfaction regarding pain management.

Methods

Ethical statement

This QI protocol was deemed exempt from review by the University of Iowa Hospitals and Clinics institutional review board. This quality improvement project follows the SQUIRE 2.0 guidelines for quality improvement studies.

Patient population

All patients who underwent one of the following elective outpatient procedures: laparoscopic cholecystectomy, laparoscopic inguinal hernia repair, laparoscopic umbilical hernia repair, open umbilical hernia repair, and laparoscopic inguinal hernia repair were included in this study.

Retrospective data collection

All patients who underwent one of the abovementioned elective outpatient procedures from June through December 2017 were included. We collected information regarding the frequency and type of pre-operative adjuncts used (acetaminophen, gabapentin, and NSAIDs), the frequency of use of local anesthetic and/or transversus abdominis plane (TAP) blocks, the quantity of opioid prescribed at discharge, and the frequency and type of post-operative adjuncts prescribed (acetaminophen and NSAIDs). We also queried electronic medical records for the number of phone calls generated regarding pain, the number of refills that were provided, and the amount of opioid prescribed to those patients who called with concerns regarding their pain control and those who received refills.

Quality improvement project

Data retrospectively collected (as described above) were used to initiate a QI project in the general surgery clinic with three goals: 1) to improve patient/provider education, 2) to decrease the number of opioids prescribed, and 3) to maintain our patients' overall

satisfaction regarding pain control.

Following retrospective data collection, we took a collaborative and multifaceted approach to address the issue. We worked with our hospital's Office of Patient Experience to create a new handout that is now included in the preoperative packet and discussed with the patient during their preoperative visit. This handout informs our patients of the risks associated with opioid use. We discussed our current prescribing practices as well as many published guidelines at an Acute Care Surgery Division meeting in the presence of the faculty surgeons and advanced practice providers who staff this clinic. A consensus was achieved by all providers as to which opioids would be included on the order set. As part of our education initiative, the residents on the emergency general surgery service are educated during their rotation on the risks of opioid use and optimal ways to improve our prescribing habits, while appropriately treating our patients' acute pain.

Additionally, we created new pre-operative and post-operative order sets for these procedures for ease and compliance. The hernia order set includes an automatic order for a Transversus Abdominis Plane (TAP) block. Gabapentin, acetaminophen, and Celecoxib vs. Toradol are on the order set, available to be checked as appropriate for each patient. The post-operative order set includes a box to prescribe scheduled acetaminophen and ibuprofen for five days. Three opioids are listed to choose from with a prefilled quantity of 20 pills: oxycodone 5 mg, Tramadol 50 mg, and Dilaudid 2 mg.

Our follow up clinic notes now include a prompt in the EMR template to ensure that all patients are being asked the following questions regarding their pain control: "How do you consider your post-operative pain management?" (Excellent, good, fair, poor), "How many days did you take your opioid medication?", "How many pills did you take?", and "What adjuncts did you use post operatively to help with pain control?"

Prospective data collection

After implementation of this project, we prospectively collected data on patients who underwent the same five abovementioned operations from September 2018 through February 2019. Data collected from medical records were the same as those collected retrospectively. Additionally, we collected the patients' post-operative pain satisfaction rating which was reported during their follow up clinic visit.

Statistical analysis

Descriptive statistics were obtained for both the pre-implementation and post-implementation data. Pre- and post-implementation data were compared using Chi-square, Mann-Whitney, and Wilcoxon tests as appropriate using SPSS 25 (Chicago, IL, USA). Graphs were prepared using GraphPrism (San Diego, CA, USA). Additionally, post-implementation discharge opioid prescribed were compared to reported use of opioids. Patients' rating of pain management is reported. Linear regression analysis was used to assess the effect of variations in the type of surgery performed pre and post implementation and being on opioids prior to surgery on OME prescribed at discharge.

Results

Retrospective review of opioid prescribing habits

One hundred thirty-three patients were included in the pre-intervention group. The characteristics of these patients are presented in [Table 1](#). Mean age was 51, ranging from 18 to 87; 61% were

Table 1
Patient characteristics and pain management information.

		Pre-implementation n = 133	Post-implementation n = 107	P-value
Age (mean ± SD)		51.2 ± 18.5	47.6 ± 14	0.1
Gender (%)	Male	61	75	0.023
Surgery type (n)	Laparoscopic cholecystectomy	61	27	0.001
	Open umbilical hernia	11	23	0.003
	Laparoscopic unilateral inguinal hernia	16	28	0.005
	Laparoscopic bilateral inguinal hernia	5	5	0.725
	Open unilateral inguinal hernia	40	29	0.613
	Open bilateral inguinal hernia	1	2	0.439
Home opioid [n (%)]		18 (13.5)	7 (6.5)	0.091
preop adjunct [n (%)]		4 (3)	71 (66.4)	<0.001
Block or local prior to surgery [n (%)]	block	6 (4.5)	6 (5.6)	0.14
	local	124 (93.2)	93 (86.9)	
	none	3 (2.3)	8 (7.5)	
	total	130 (97.7)	99 (92.5)	
Prescribed OME, mg (mean ± SD)		178.9 ± 80.3	126.7 ± 41.1	<0.001
Prescribed Adjunct at discharge [n (%)]		50 (37.4)	85 (79.4)	<0.001
First adjunct (n)	acetaminophen	32	74	
	ibuprofen	14	10	
	naproxen	4	1	
	total	50	85	
Second adjunct (n)	acetaminophen	0	9	
	ibuprofen	13	49	
	naproxen	0	1	
	total	13	59	
Phone call for pain [n (%)]		17 (12.8)	6 (5.6)	0.06
Refill [n (%)]		6 (4.5)	2 (1.9)	0.22

male. The total median oral morphine equivalent (OME) prescribed was 150 mg, ranging from 37.5 to 525 mg OME. Seventeen patients (12.8%) called regarding pain management post-discharge. Six patients (4.5%) asked for refills and their original prescription ranged from 50 to 200 mg OME. The total number of pills prescribed ranged from three to 60; the median number of pills prescribed was 30 and the total number of pills prescribed from June to December 2017 was 4185. Of these patients, only 50 (37.6%) were prescribed a postoperative adjunct of acetaminophen or ibuprofen. Only 13 (9.8%) were prescribed more than one adjunct post-operatively. Only four patients (3%) received a pre-operative adjunct (acetaminophen, NSAID, or gabapentin).

Post-implementation

Post-intervention data were prospectively collected. A total of 107 patients were included. As shown in Table 1, the mean age was 48, ranging from 21 to 85. There was a significant difference in the type of surgery performed pre and post implementation. There was a significant reduction in the combination pills prescribed at discharge. As shown in Fig. 1, the number of combination pills prescribed significantly decreased after implementation. Prior to implementation, Lortab was the most frequently prescribed (37.6% pre vs. 5.6% post-implementation, $p < 0.001$), while oxycodone was the most frequently prescribed opioid post-implementation (9.8% pre vs. 54.2% post-implementation, $p < 0.001$). Prior to implementation, only four patients (3%) were prescribed a pre-operative adjunct (acetaminophen, Celebrex, or gabapentin); following implementation, 71 (66.4%) were given one ($p < 0.01$). There was no difference in the number of patients who received local anesthetic and/or a TAP block (97.7% vs. 92.5%, $p = 0.14$). While muscle relaxant could be considered as an adjunct for pain control, none of our patients was prescribed one as this is not part of our usual practice.

Prior to implementation, all patients were discharged with opioid prescriptions, while, following implementation, 32 patients (30%) were not prescribed opioids at discharge. The total quantity of opioid pills prescribed significantly decreased from 4185 prior to

intervention to 1363 following implementation. Interestingly, based on patients' report, only 520 pills were used following implementation (Fig. 2a). Additionally, the average number of pills prescribed per patient was also significantly lower post-implementation (Fig. 2b). The lower number of pills prescribed post-implementation also reflected a significantly lower OME prescribed per patient post-implementation (Table 1 and Fig. 2c). Linear regression showed that implementation of changes in our prescription habits is associated with a significant decrease in OME prescribed at discharge ($B = -53.3$ mg OME [-33.1 to -73.5]; $p < 0.001$). Although the type of surgery performed differed significantly pre and post-implementation (Table 1), this was not associated with a significant decrease in OME prescribed at discharge ($B = -1.4$ [-5.6 to 2.8]; $p = 0.511$). Similar results were observed when assessing the impact of being on opioids prior to admission ($B = 25.1$ [-4.9 to 55.0]; $p = 0.101$).

Ninety-six patients (90%) presented for their follow up clinic visit. Only 52 (54%) patients who returned to clinic reported taking an opioid post-operatively. Those 52 reported taking on average 11 pills (1–20), representing 81 mg OME (4–150 mg) for five days. As shown in Fig. 2b and c, the reported amount of opioid use was significantly lower than what the patients were prescribed at discharge. More patients were prescribed a post-operative adjunct (acetaminophen or ibuprofen) following implementation than prior (85 vs. 50%, $p < 0.01$).

Regarding pain satisfaction, seventeen patients (12.8%) called with concerns regarding their pain control and six (4.5%) received an opioid prescription refill prior to intervention. Following implementation, there were only six phone calls (5.6%) and only two patients (1.9%) received an opioid prescription refill. Patients' satisfaction ratings regarding their pain management are summarized in Fig. 3. Overall, 88.6% of patients rated their pain management as excellent or good, 9.3% as fair, and 2.1% as poor. As mentioned, 32 patients (30%) did not receive an opioid at discharge. One of these patients was using an opioid pre-operatively and one patient called with concerns for pain but was not prescribed an opioid in response. Eighteen of these patients were prescribed an adjunct at discharge. Twenty-seven of these patients followed up in

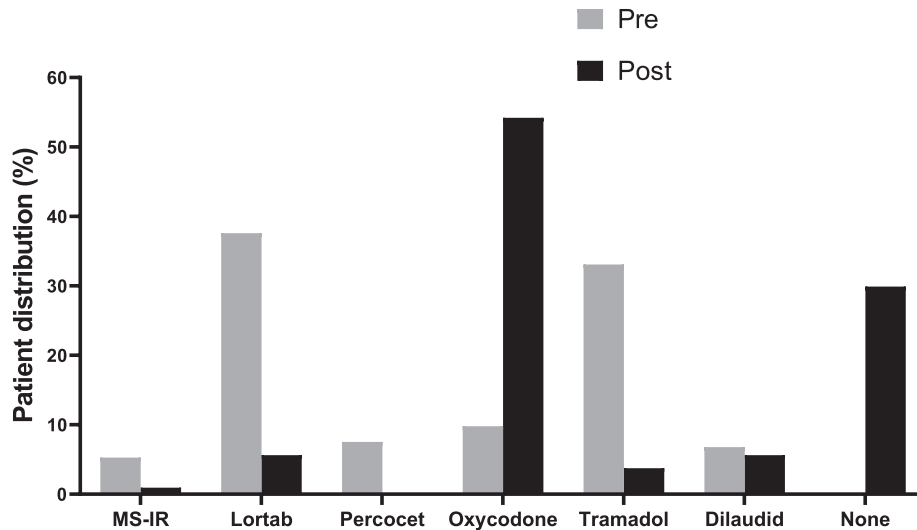


Fig. 1. Distribution of patients prescribed combination pills and/or opioids at discharge pre and post-implementation. Chi-square test showed a significant difference between the groups $p < 0.001$.

clinic and 26 of them described their pain control as good, one described it as fair.

Discussion

Since the 1990's, the number of opioids prescribed has been alarmingly high in the United States, peaking in 2010 and remaining the highest in the world. Simultaneously, the number of complications, including addiction and death, related to opioids has risen and continues to rise.¹³ While surgeons do not prescribe the majority of opioids, they do commonly prescribe them to opioid naïve patients; one in sixteen of whom become long term users following surgery.³ There has been an increased focus on responsible opioid prescribing throughout the country. This study provides a roadmap and demonstrates a collaborative and pragmatic approach that can be implemented for the most common general surgery cases to decrease opioid prescriptions while controlling patients' post-operative pain. While significantly decreasing the number of pills prescribed as well as the OME per patient, we found that opioids are still over prescribed relative to actual patient consumption, and there is still room for improvement.

Part of our approach included patient education. Patients were informed of the plan regarding their pain management during their initial preoperative visit and risks associated with opioid use were described to them in a handout that was reviewed with them by the nursing staff. A recent study on patients undergoing total knee arthroplasty shows that, by engaging with patients regarding their pain management preoperatively, opioid use is decreased postoperatively.¹⁴

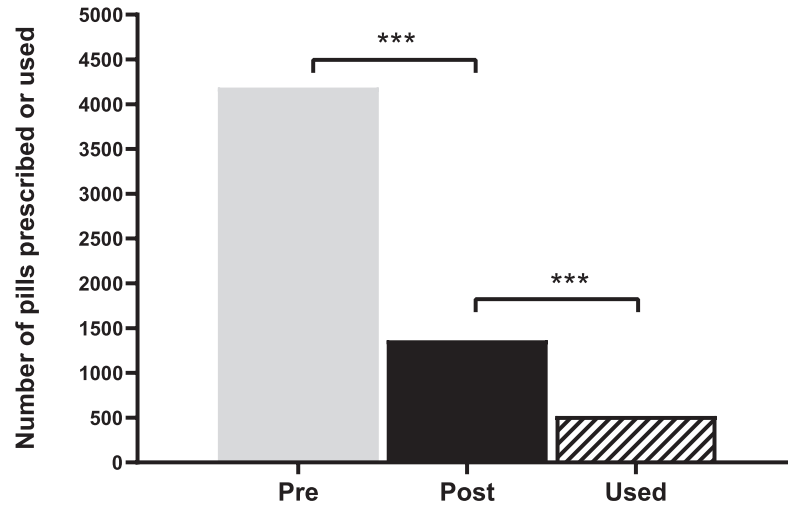
Another key part of our success was securing the engagement of our surgical team. Louie et al. recently showed that educating surgeons on the risk of opioids did not impact on clinician satisfaction ratings.¹⁵ The core faculty surgeons who staff the acute care surgery clinic met to create a consensus after review of the Division's current practice, published papers, and guidelines. An order set was created that all members agreed upon to increase compliance of use. Our advance practice providers were educated and modified the follow up notes to ensure appropriate tracking of patient reported use and satisfaction. Our clinic nurses were educated on the importance of preoperative pain management education and, along with the surgeon, spend time discussing

predicted pain and pain management post operatively, risks of opioid use following surgery, and safe disposal habits. Additionally, there is limited education on opioid prescribing recommendations in medical school and during residency.⁵ We aimed to counter that by educating our residents during their rotation on the emergency general surgery service. A recent study showed that the number of opioids prescribed decreased by half by simply providing education to surgeons.¹⁶ As important, this decrease in opioid prescribing did not increase the number of refills prescribed. These findings were confirmed in our study.

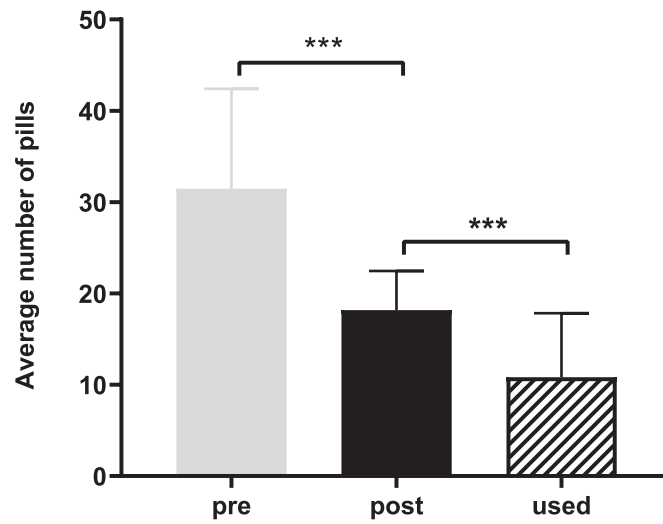
Consistent with previously reported studies,^{17–19} we first showed that, prior to our intervention, a significant variability was observed in prescribing patterns of opioids following common elective outpatient procedures within our own institution. Some surgeons prescribed combination pills, some preferred the single agents. The number of pills prescribed varied significantly and did not appear to correlate with patient calls about concerns regarding their pain control or who received refills. To decrease the variability, we created pre- and post-operative order sets to use for the most commonly performed procedures. Consistent with previous data showing that simply changing the default quantity of pills in an order set can be successful,²⁰ we decreased the median number of opioid pills prescribed from 30 to 20 by having a pre-filled form on the post-operative order set. Furthermore, the use of preoperative and postoperative adjuncts, like acetaminophen, gabapentin, and/or ibuprofen significantly increased. Most importantly, we noted fewer phone calls from patients with concerns regarding their pain control and a decrease in the number of requests for refills.

Our study presents some limitations. First, this was conducted in a single institution and its sample size is small. Because we used a multimodal approach as part of this QI project, involving patient and provider education and the creation of an order set for ease and compliance, we do not specifically know which of the initiatives resulted in the significant decrease in opioid prescribing. Secondly, while we did perform more cholecystectomies in the pre-implementation group and more laparoscopic inguinal hernias and open umbilical hernias in the post procedure group, we do not believe this alone accounts for the decrease in opioid prescribing as shown by our multivariate analysis and pain satisfaction post-operatively. Prior to implementation, it is possible that patients

a.



b.



c.

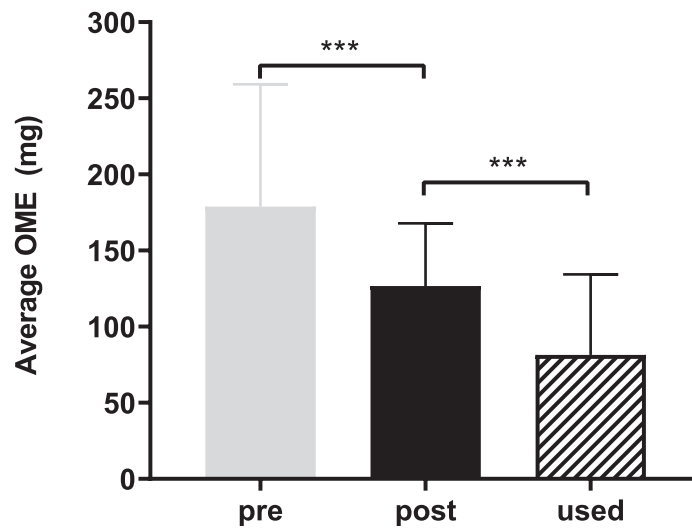


Fig. 2. Change in opioid prescription. a) Overall number of opioid pills prescribed pre- and post-implementation and number of opioid pills used as reported by patients during their follow up visit. b) Average number of pills prescribed pre- and post-implementation and average number of opioid pills used as reported by patients during their follow up visit. c) Average oral morphine equivalent (OME) pre- and post-implementation and average OME used as reported by patients during their follow up visit. *** = $p < 0.001$.

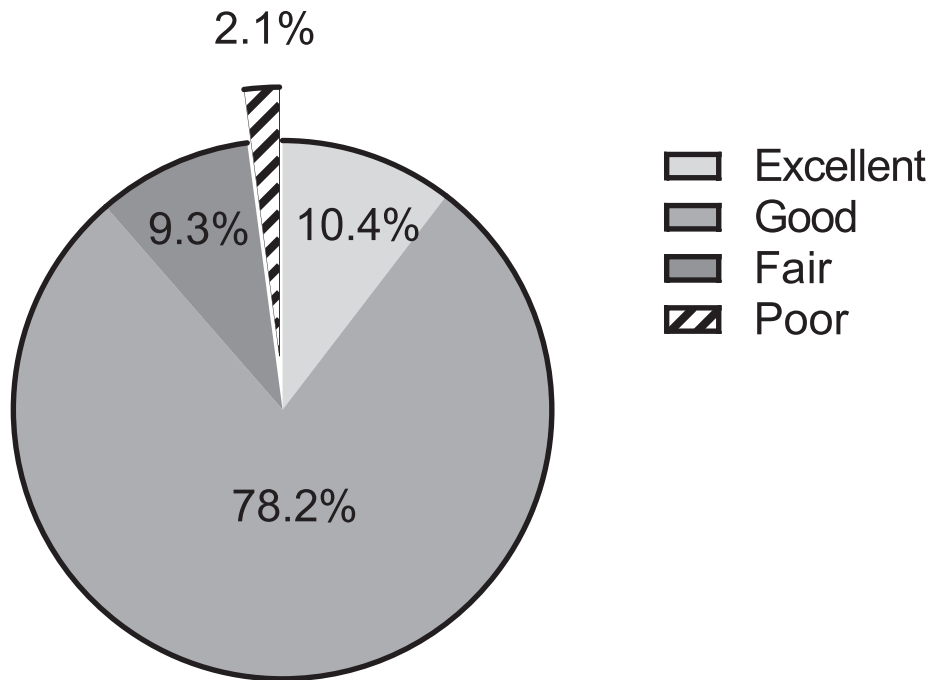


Fig. 3. Patient satisfaction ratings regarding pain management.

were taking over the counter, non opioid adjuncts. While we report a significant increase in non-opioid analgesics that were prescribed, the actual use may not be as significant. Additionally, pain management satisfaction was not recorded in the initial patient cohort; thus, patients' satisfaction may have decreased, though certainly not to an unacceptable level based on the results presented in this study. Finally, our data is limited to that collected in our clinic. While the Iowa Prescription Monitoring Program does allow physicians to assess whether patients are being prescribed opioids by other providers, we are not allowed to use this information for research purposes. Thus, patients may have been prescribed opioids by clinicians other than those in our group; however, we were unable to capture this information.

Conclusions

This study describes a successful, collaborative and pragmatic approach to a quality improvement initiative aimed at standardizing our approach to peri-operative pain control for outpatient general surgery procedures. We collected data on current practice and identified key areas of improvement. Starting by engaging the healthcare team and patients in post-operative pain management education and expectations, creating standardized order sets to facilitate the use of pre- and post-operative adjuncts, and decreasing the number of opioids prescribed following the five most common elective outpatient procedures, we demonstrated a significant decrease in the number of opioids prescribed and used without affecting patients' overall satisfaction regarding pain management. Our data contributes to the growing literature supporting a comprehensive approach to decreasing the amounts of opioid pills prescribed following surgery. Further studies are warranted to evaluate the ability to implement a comprehensive approach on the inpatient setting and to identify patients' specific factors that affect opioid use following surgery.

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Declaration of competing interest

The authors have no conflict of interest to declare.

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References

1. Asam. *Opioid Addiction 2016 Facts & Figures*; 2019. <https://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf>.
2. CDC, National Center for Health Statistics. Wide-ranging Online Data for Epidemiologic Research (WONDER). Atlanta, G <http://wonder.cdc.gov>. 2017.
3. 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.
4. Vowles KE, McEntee ML, Julnes PS, et al. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *Pain.* 2015;156(4):569–576.
5. Chiu AS, Healy JM, DeWane MP, et al. Trainees as agents of change in the opioid epidemic: optimizing the opioid prescription practices of surgical residents. *J Surg Educ.* 2018;75(1):65–71.
6. Linnaus ME, Sheaffer WW, Ali-Mucheru MN, et al. The opioid crisis and surgeons: national survey of prescribing patterns and the influence of motivators, experience, and gender. *Am J Surg.* 2019;217(6):1116–1120.

7. Tan WH, Yu J, Feaman S, et al. Opioid medication use in the surgical patient: an assessment of prescribing patterns and use. *J Am Coll Surg.* 2018;227(2): 203–211.
8. Crisologo PA, Monson EK, Atway SA. Gabapentin as an adjunct to standard postoperative pain management protocol in lower extremity surgery. *J Foot Ankle Surg.* 2018;57(4):781–784.
9. Fabritius ML, Geisler A, Petersen PL, et al. Gabapentin for post-operative pain management - a systematic review with meta-analyses and trial sequential analyses. *Acta Anaesthesiol Scand.* 2016;60(9):1188–1208.
10. Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. *Br J Anaesth.* 2011;106(4):454–462.
11. Arumugam S, Lau CS, Chamberlain RS. Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis. *J Pain Res.* 2016;9:631–640.
12. Gupta A, Abubaker H, Demas E, Ahrendtsen L. A randomized trial comparing the safety and efficacy of intravenous ibuprofen versus ibuprofen and acetaminophen in knee or hip arthroplasty. *Pain Physician.* 2016;19(6):349–356.
13. CDC. Annual Surveillance Report of Drug-Related Risks and Outcomes - United States. Surveillance Special Report. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Published August 31, 2018. Accessed [September 4, 2019] <https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf> 2018.
14. Yajnik M, Hill JN, Hunter OO, et al. Patient education and engagement in postoperative pain management decreases opioid use following knee replacement surgery. *Patient Educ Counsel.* 2019;102(2):383–387.
15. Louie CE, Kelly JL, Barth Jr RJ. Association of decreased postsurgical opioid prescribing with patients' satisfaction with surgeons. *JAMA Surg.* 2019. <https://doi.org/10.1001/jamasurg.2019.2875>.
16. Chiu AS, Ahle SL, Freedman-Weiss MR, et al. The impact of a curriculum on postoperative opioid prescribing for novice surgical trainees. *Am J Surg.* 2019;217(2):228–232.
17. Eid AI, DePesa C, Nordestgaard AT, et al. Variation of opioid prescribing patterns among patients undergoing similar surgery on the same acute care surgery service of the same institution: time for standardization? *Surgery.* 2018;164(5):926–930.
18. Hill MV, McMahon ML, Stucke RS, Barth Jr RJ. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg.* 2017;265(4):709–714.
19. Nooromid MJ, Blay Jr E, Holl JL, et al. Discharge prescription patterns of opioid and nonopioid analgesics after common surgical procedures. *Pain Rep.* 2018;3(1):e637.
20. Chiu AS, Jean RA, Hoag JR, et al. Association of lowering default pill counts in electronic medical record systems with postoperative opioid prescribing. *JAMA Surg.* 2018;153(11):1012–1019.