Pain or no pain, we will give you opioids: relationship between number of opioid pills prescribed and severity of pain after operation in US vs non-US patients

Moheb, M. el; Mokhtari, A.; Han, K.; Erp, I. van; Kongkaewpaisan, N.; Jia, Z.Y.; ... ; Int Patterns Opioid Prescribing

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Mohamad El Moheb, MD, Ava Mokhtari, MSc, Kelsey Han, MD, Inge van Erp, BSc, Napaporn Kongkaewpaisan, MD, Zhenyi Jia, MD, Gabriel Rodriguez, MD, Manasnun Kongwibulwut, MD, Haytham MA Kaafarani, MD, FACS, MPH; for the International Patterns of Opioid Prescribing Workgroup

BACKGROUND: Patients in the US receive disproportionally higher amounts of opioids after operations compared with their non-US counterparts. We aimed to assess the relationship between perceived pain severity after operation and the amount of opioid medications prescribed at discharge in US vs non-US patients.

METHODS: We conducted a post-hoc analysis of the International Patterns of Opioid Prescribing multicenter study. Patients 16 years and older who underwent appendectomy, cholecystectomy, or inguinal herniorrhaphy in 1 of 14 participating hospitals across 8 countries between October 2016 and March 2017 were included. In hospitals where pain severity was assessed using a 0 to 10 visual analog scale before hospital discharge, patients were stratified into the following groups, depending on the pain severity: none, mild (1 to 3), moderate (4 to 6), and severe (7 to 10). The number of opioid prescriptions, total number of pills, and oral morphine equivalents prescribed were calculated for each group and US and non-US patients were compared.

RESULTS: A total of 2,024 patients were included. Eighty-three percent of US patients without pain were prescribed opioids compared with 8.7% of non-US patients without pain ($p < 0.001$). The number of opioid prescriptions, number of pills, and oral morphine equivalents prescribed were similar across the 4 pain severity groups in US patients ($p > 0.05$). In contrast, the number of opioid prescriptions, number of opioid pills, and oral morphine equivalents prescribed among non-US patients were incrementally higher as the pain severity progressed from no pain to severe pain (all, $p < 0.05$).

CONCLUSIONS: US patients are prescribed opioids at high rates and doses regardless of pain severity. Additional efforts should be directed toward tailoring opioid prescriptions to patients' needs. (J Am Coll Surg 2020;231:639–648. © 2020 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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From the Department of Surgery, Massachusetts General Hospital, Boston, MA (El Mohab, Mokhtari, Han, van Erp, Kongkaewpaisan, Jia, Rodriquez, Kongwibulwut, Kaafarani), Division of Acute Care and Ambulatory Surgery, Siriraj Hospital, Mahidol University (Kongkaewpaisan), Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University (Kongwibulwut), Bangkok, Thailand, and Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, People's Republic of China (Jia).

Correspondence address: Haytham MA Kaafarani, MD, FACS, MPH, Division of Trauma, Emergency Surgery, and Surgical Critical Care, Massachusetts General Hospital, 165 Cambridge St, Suite 810, Boston, MA 02114. email: hkaafarani@mgh.harvard.edu

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The US is in the midst of an opioid epidemic that has already claimed the lives of hundreds of thousands of people. The number of deaths from drug overdose in 2016 alone was higher than the number of deaths from HIV at its peak in 1995, and higher than the number of deaths from motor vehicle crash at its peak in 1972.[1] Drug overdose is now the leading cause of accidental death in the US.[2] In addition to the elevated death toll, opioid use disorder is estimated to result in $78 billion of annual cost to the economy.[3]

The root of the epidemic can be traced back more than 2 decades ago when studies suggested that patients' pain was often underdiagnosed and undertreated, leading to increased hospitalizations, decreased quality of life, and loss of societal productivity.[4-7] In response, the Accreditation of Healthcare Organizations and the American Pain Society launched campaigns advocating for more aggressive pain management, mostly through the use of narcotics that pharmaceutical companies deceivingly promoted as near risk-free.[8,9] This led to a dramatic increase in opioid prescription rates, followed by an increase in opioid-related overdoses and deaths.[10] Surgeons prescribe a significant proportion of these opioids in the US, mainly to treat postoperative pain.[11] A recent multicenter international study found that 91% of patients in the US were prescribed opioids after common general surgery procedures, compared with only 5% of non-US patients undergoing the same type of operation.[12] The doses of opioids dispensed often exceed the amount needed for adequate pain control,[13] resulting in the unused opioid pills being diverted to and misused by the community.[14,15]

In recognition of this devastating public health crisis, institutional, regional, and national initiatives have been implemented and legislation passed to address the opioid epidemic in general and the opioid diversion problem specifically.[16] In 2017, CDC issued guidelines for primary care physicians treating chronic pain with opioids.[17] Surgeons, recognizing the need to change the opioid prescribing culture, have also issued specialty-specific guidelines for postoperative management of acute pain.[18,19] These guidelines emphasize the importance of dispensing opioid medications only when nonopioid alternatives fail to manage pain; however, there remains little evidence to indicate how postoperative pain affects physicians' decisions to prescribe more or less opioids at discharge. In this study, we sought to assess the relationship between perceived patient-reported postoperative pain and opioid prescription at discharge in the US vs other countries. We hypothesized that the quantity of opioids physicians prescribe in the US and outside the US is proportional to the level of pain reported by patients after operation.

METHODS

Study design

This is a post-hoc analysis of the International Patterns of Opioid Prescribing multicenter prospective cohort study. The International Patterns of Opioid Prescribing study compared postoperative opioid prescribing patterns after 3 common general surgery procedures in 14 hospitals across 8 countries.

Patient population

All patients 16 years or older who were admitted to the participating institutions between October 2016 and March 2017 for appendectomy, cholecystectomy, or inguinal hernia repair were included. The participating institutions included Massachusetts General Hospital (Boston, MA), Johns Hopkins University (Baltimore, MD), University of Arizona (Tucson, AZ), Hospital Departamental Villavicencio (Villavicencio, Colombia), Hospital Angeles del Pedregal (Mexico City, Mexico), Shanghai Tenth People's Hospital of Tongji University (Shanghai, China), Shanghai Sixth People's Hospital (Shanghai, China), Shanghai Chang Zheng Hospital (Shanghai, China), King Chulalongkorn Memorial Hospital (Bangkok, Thailand), Alrijne Hospital (Leiden, The Netherlands), Hospital Geral do Grajaú (São Paulo, Brazil), Siriraj Hospital (Bangkok. Thailand), Shanghai East Hospital of Tongji University (Shanghai, China), and the American University of Beirut Medical Center

(Beirut, Lebanon). Flexibility around the chosen study period was permitted, depending on the local hospital logistics (eg timing of adoption of electronic medical records) to optimize data accuracy. Open and laparoscopic as well as elective and emergent procedures were included.

Variables and outcomes analyzed

For each patient, pain severity was recorded on a 0 to 10 visual analog scale (10 being the most severe) at discharge. If the patient rated the pain as a range of values, the upper limit of the range was recorded. Patients were subsequently stratified into the following pain severity groups: none (0), mild (1 to 3), moderate (4 to 6), and severe (7 to 10). Patients with missing pain severity scores at discharge were excluded from the analysis. The medical records were systematically reviewed and the following information was extracted for each patient: demographic characteristics, perioperative variables (eg intraoperative adverse events, postoperative adverse events, and hospital length of stay), history of opioid intake within 3 months preoperatively, prescription of opioid medications at discharge including dose (in mg) and number of pills, prescription of nonopioid analgesics at discharge, and opioid prescription refills within 3 months of the operation. The total number of pills and oral morphine equivalents (OMEs) prescribed were calculated for each patient to facilitate comparisons between different opioid formulations. The primary outcomes were prescription (or not) of opioids and the amount of opioid prescribed (measured using number of pills and OMEs). Secondary outcomes included prescription refills and prescription of nonopioid analgesics.

Statistical analysis

Descriptive statistics were used to summarize the perioperative characteristics of the population. Categorical variables were summarized as proportions and continuous variables as mean (SD). Univariate analyses were performed to compare opioid prescriptions, OMEs, and number of opioid pills prescribed across pain severity groups using independent *t*-test or ANOVA for continuous variables, and Pearson chi-square or Fisher exact test for categorical variables, as appropriate. A comparison between US and non-US patients was conducted. Multivariable logistic and linear regression models were then built to evaluate the primary outcomes after adjusting for preoperative (age, sex, BMI, race, country, smoking status, prehospital opioid use, and procedure type), intraoperative (intraoperative adverse events and anesthesia type), and postoperative (ICU admission, return to operating room, hospital length of stay, and postoperative complications) variables that had $p < 0.2$ with the dependent variable on univariate analyses. For each pain severity group, the mean adjusted probability of opioid prescription and the mean adjusted OME and number of pills prescribed were estimated using the regression models along with the predictive margins command in STATA Software (Stata Corp).[20,21] This strategy provides a tangible and easily interpretable assessment of the influence of postoperative pain on the dependent variables, while controlling for different covariate distributions in the sample. Statistical significance was defined as a 2-sided $p < 0.05$. All statistical analysis was performed using STATA Software, version 15.1.

Missing data analysis

All of the variables were prospectively collected from patients' charts. A sensitivity analysis was performed excluding institutions with > 10% missing data for pain severity.

Ethical approval

The local IRB for each participating institution reviewed and approved this study. Individually negotiated data user agreements were signed between Massachusetts General Hospital and each participating site.

RESULTS

A total of 2,024 patients (43.2%) from 12 hospitals in 7 countries met eligibility criteria. The preoperative characteristics of the patient population are presented in Table 1. The mean (SD) age was 49.8 (18.0) years and 54% of patients were male. A total of 872 patients (43.1%) reported no pain, 774 (38.2%) reported mild pain, 246 (12.2%) reported moderate pain, and 132 (6.5%) reported severe pain. As pain severity increased from none to mild to moderate to severe, patients were more likely to be younger, have a history of opioid use before admission, undergo emergency procedures, have postoperative complications develop, have been admitted to the ICU, and have been readmitted to the hospital within 30 days of discharge (all, $p < 0.05$).

Table 2 summarizes patterns of pain management at discharge for all patients. The frequency of opioid prescription was higher in patients who experienced moderate to severe pain compared with those experiencing minimal to no pain (no pain: 12.2%, mild: 16.9%, moderate: 55.7%, severe: 50.0%; $p < 0.001$). The vast majority of patients were also prescribed nonopioid analgesics at discharge (no pain: 82.1%, mild: 89.5%, moderate: 86.6%, severe: 86.4%; $p < 0.001$). The calculated OMEs and total number of pills prescribed were also

Table 1. Demographic and Perioperative Characteristics

Characteristic	No pain (n = 872)	Mild pain (n = 774)	Moderate pain (n = 246)	Severe pain (n = 132)	p Value
Age, y, mean (SD)	51.4 (17.7)	50.1 (17.9)	47.4 (18.6)	42.7 (17.2)	< 0.001
Sex, female, n (%)	400 (46.1)	334 (43.3)	119 (48.6)	69 (52.3)	0.17
BMI group, n (%)					
Normal	706 (83.9)	573 (80.3)	164 (70.4)	89 (75.4)	< 0.001
Underweight	25 (3.0)	16 (2.2)	3 (1.3)	1 (0.8)	—
Obese	110 (13.1)	125 (17.5)	66 (28.3)	28 (23.7)	—
Race, n (%)					
White	140 (16.1)	505 (65.3)	140 (56.9)	39 (29.6)	< 0.001
Black or African American	7 (0.8)	16 (2.1)	23 (9.4)	7 (5.3)	—
Asian	418 (47.9)	199 (25.7)	21 (8.5)	2 (1.5)	—
Other	10 (1.2)	33 (4.3)	7 (2.9)	42 (31.8)	—
Unknown	297 (34.1)	21 (2.7)	55 (22.4)	42 (31.8)	—
Country, n (%)					
US	41 (4.7)	89 (11.5)	121 (49.2)	47 (35.6)	—
Non-US	831 (95.3)	685 (88.5)	125 (50.8)	85 (64.4)	< 0.001
Current smoker, n (%)	77 (9.0)	100 (13.6)	43 (17.7)	21 (15.9)	< 0.001
Prehospital opioid use, n (%)	17 (2.0)	39 (5.2)	27 (11.0)	19 (14.4)	< 0.001
Emergency procedure, n (%)	312 (38.1)	326 (42.2)	119 (48.4)	76 (57.6)	< 0.001
Anesthesia type, n (%)					
Neuraxial	183 (21.0)	99 (12.8)	20 (8.2)	25 (18.9)	< 0.001
General	687 (79.0)	674 (87.2)	225 (91.8)	107 (81.1)	—
Procedure, n (%)					
Open appendectomy	144 (16.5)	81 (10.5)	13 (5.3)	37 (28.0)	< 0.001
Lap appendectomy	80 (9.2)	186 (24.0)	67 (27.2)	27 (20.5)	—
Open cholecystectomy	1 (0.1)	1 (0.1)	2 (0.8)	4 (3.0)	—
Lap cholecystectomy	431 (49.4)	270 (34.9)	108 (43.9)	35 (26.5)	—
Open hernia repair	129 (14.8)	68 (8.8)	29 (11.8)	16 (12.1)	—
Lap hernia repair	87 (10.0)	168 (21.7)	27 (11.0)	13 (9.8)	—
Intraoperative adverse event, n (%)	21 (2.4)	34 (4.4)	34 (13.8)	18 (13.6)	< 0.001
Postoperative complication, n (%)	41 (4.7)	42 (5.5)	21 (8.5)	13 (9.8)	0.024
ICU admission, n (%)	5 (0.6)	5 (0.6)	3 (1.2)	3 (2.3)	0.17
Return to OR, n (%)	16 (1.8)	8 (1.0)	3 (1.2)	3 (2.3)	0.48
Hospital LOS, d, mean (SD)	3.6 (3.2)	2.5 (2.1)	2.5 (2.2)	3.8 (6.0)	< 0.001
30-d readmission, n (%)	9 (1.0)	12 (1.6)	18 (7.3)	14 (10.6)	< 0.001

Lap, laparoscopic; LOS, length of stay; OR, operating room.

higher with increasing pain severity (mean [SD] OME: none: 14.3 [52.1], mild: 28.0 [74.9], moderate: 103.7 [159.7], and severe: 91.7 [142.6]; $p < 0.001$; mean [SD] total number of pills: none: 2.2 [7.1], mild: 3.9 [9.9], moderate: 13.0 [16.1], and severe: 11.8 [16.8]; $p < 0.001$). Overall, the number of opioid prescription refills after discharge was higher among US patients compared with non-US patients (7.1% vs 0.1%; $p < 0.001$). In addition, the number of patients refilling their opioid prescription increased in a stepwise fashion with incrementally higher pain severity (none: 3 [2.8%], mild: 4 [3.1%], moderate: 7 [5.6%], and severe: 8 [16.7%]; $p < 0.002$). Table 3 summarizes the amount of opioids prescribed for each procedure and the corresponding pain severity at discharge in US and non-US patients.

When comparing US with non-US patients, 83% of US patients who reported no pain after operation were discharged on opioids compared with 8.7% of non-US patients ($p < 0.001$). Figure 1 shows that the opioid prescription rates were similar across all 4 pain groups in US patients (none: 34 [82.9%], mild: 82 [92.1%], moderate: 113 [93.4%], severe: 44 [93.6%]; $p = 0.19$), and they increased in a stepwise fashion with

Table 2. Discharge Pain Management

Patient type, analgesic prescribed	No pain	Mild pain	Moderate pain	Severe pain	p Value
All patients, n	872	774	246	132	—
Opioid, n (%)	106 (12.2)	131 (16.9)	137 (55.7)	66 (50.0)	< 0.001
Nonopioid, n (%)	716 (82.1)	693 (89.5)	213 (86.6)	114 (86.4)	< 0.001
Total OME, mg, mean (SD)	14.3 (52.1)	28.0 (74.9)	103.7 (159.2)	91.7 (142.6)	< 0.001
No. of pills, mean (SD)	2.2 (7.1)	3.9 (9.9)	13.0 (16.1)	11.8 (16.8)	< 0.001
Opioid prescription refill, n (%)	3 (2.8)	4 (3.1)	7 (5.6)	8 (16.7)	0.002
US patients, n	41	89	121	47	—
Opioid, n (%)	34 (82.9)	82 (92.1)	113 (93.4)	44 (93.6)	0.19
Nonopioid, n (%)	26 (63.4)	68 (76.4)	95 (78.5)	40 (85.1)	0.1
Total OME, mg, mean (SD)	150.9 (119.9)	166.9 (106.0)	194.8 (182.9)	223.8 (156.3)	0.075
No. of pills, mean (SD)	19.6 (15.7)	22.1 (14.0)	24.0 (16.1)	27.2 (18.3)	0.12
Opioid prescription refill, n (%)	3 (8.8)	3 (3.7)	7 (6.3)	8 (18.6)	0.025
Non-US patients, n	831	685	125	85	—
Opioid, n (%)	72 (8.7)	49 (7.2)	24 (19.2)	22 (25.9)	< 0.001
Nonopioid, n (%)	690 (83.0)	625 (91.2)	118 (94.4)	74 (87.1)	< 0.001
Total OME, mg mean (SD)	7.6 (34.5)	9.9 (45.4)	15.5 (41.9)	18.7 (56.4)	0.031
No. of pills, mean (SD)	1.4 (5.0)	1.5 (6.0)	2.4 (5.7)	3.2 (6.9)	0.01
Opioid prescription refill, n (%)	0 (0)	1 (2)	0 (0)	0 (0)	0.58

OME, oral morphine equivalent.

higher pain severity in non-US patients (none: 72 [8.7%], mild: 49 [7.2%], moderate: 24 [19.2%], severe 22 [25.9%]; $p < 0.001$). Despite an increasing trend in prescriptions of nonopioid analgesics, OME, and number of pills prescribed with more severe pain among US patients, statistical significance was not achieved ($p = 0.1$, $p = 0.075$, and $p = 0.12$, respectively). In contrast, the OMEs and number of pills prescribed among non-US patients were incrementally higher as pain severity progressed from no pain to severe pain. The vast majority of non-US patients were prescribed nonopioid analgesics at discharge (no pain: 83.0%, mild: 91.2%, moderate: 94.4%, severe: 87.1%; $p < 0.001$). Only 1 non-US patient refilled their opioid prescription compared with 7.0% of US patients. The rate of prescriptions refilled in the US increased with higher perceived postoperative pain.

The multivariable analyses showed similar trends; after adjusting for preoperative, intraoperative, and postoperative characteristics, there was no statistically significant difference in the frequency or amount of opioid prescribed after operation in US patients with different degrees of pain severity (Table 4). On average, 84% (95% CI, 71.8% to 95.3%) of patients without postoperative pain were prescribed opioids at discharge compared with 93% (95% CI, 85.4% to 100%) of patients with severe pain ($p > 0.05$). In contrast, a mean of 9% (95% CI, 6.3% to 10.6%) of non-US patients without postoperative were prescribed opioids at discharge compared with 46% (95% CI, 26.2% to 66.2%) of patients with severe pain ($p < 0.05$). In addition, the mean adjusted OME and number of pills increased from 156.1 (95% CI, 110.3 to 202) and 20.6 (95% CI, 15.7 to 25.4) in US patients without pain to 213.4 (95% CI, 169.9 to 256.8) and 27.1 (95% CI, 22.6 to 31.6) in patients with severe pain ($p > 0.05$). In non-US patients, the mean adjusted OME and number of pills increased from 9.8 (95% CI, 6.4 to 13.2) and 1.4 (95% CI, 0.9 to 1.8) in patients without pain to 26.8 (95% CI, 15.6 to 38) and 4.5 (95% CI, 3 to 6) in patients with severe pain ($p < 0.05$).

A sensitivity analysis excluding centers with > 10% missing data for pain severity was performed and showed similar results: 89% of US patients who did not experience postoperative pain were prescribed opioids at discharge, and there was no statistically significant difference in the rate or dose of opioid prescription across pain severity groups in US patients ($p > 0.05$). In contrast, non-US patients with worse pain severity were more likely to be prescribed opioids, and the mean OME and number of pills increased gradually with higher perceived postoperative pain (Table 5).

DISCUSSION

In this post-hoc analysis of the International Patterns of Opioid Prescribing multicenter international study, we have found that providers in the US prescribe high amounts of opioids after 3 of the most common surgical

Table 3. Comparison of Oral Morphine Equivalents Prescribed at Discharge for Each Surgical Procedure by Pain Severity

Patient type, procedure	Oral morphine equivalent					p Value
	No pain	Mild pain	Moderate pain	Severe pain	Total	
All patients, n	872	774	246	132	2,024	—
Procedure, mean (SD)						
Open appendectomy	4.3 (21.6)	9.6 (37.8)	7.7 (18.8)	2.7 (12.3)	3.2 (20.6)	0.45
Lap appendectomy	30.2 (101.4)	33.8 (82.2)	112 (130.7)	105.1 (147.8)	44.4 (94.2)	< 0.001
Open cholecystectomy	0 (0)	0 (0)	50 (70.7)	0 (0)	13.0 (91.5)	0.48
Lap cholecystectomy	14.1 (49.5)	38.8 (84.9)	129.6 (201.4)	196.9 (173.7)	37.0 (96.3)	<0.001
Open hernia repair	18 (38.2)	15.5 (41.7)	54.1 (69.2)	61.1 (104.7)	20.4 (51.4)	<0.001
Lap hernia repair	12.1 (49.3)	18.2 (70.4)	82.9 (109.8)	99.9 (117.7)	20.1 (66.6)	<0.001
US patients, n	41	89	121	47	298	—
Procedure, mean (SD)						
Open appendectomy	37.5 (53)	225 (0)	0 (0)	—	150 (38.7)	0.038
Lap appendectomy	160.2 (154.8)	182.3 (107.3)	195.8 (119.6)	235.9 (156.5)	179.2 (107.9)	0.52
Open cholecystectomy	0 (0)	0 (0)	100 (0)	—	265.3 (341.1)	—
Lap cholecystectomy	156.8 (108.2)	144.1 (85.5)	199.5 (227.1)	213.9 (175.6)	184.3 (144.5)	0.25
Open hernia repair	100 (86.6)	150 (0)	138.8 (73.7)	256.7 (92.9)	157.2 (86.0)	0.15
Lap hernia repair	200 (120.5)	206.9 (162)	215.8 (64.4)	232.5 (72.1)	210.3 (111.3)	0.98
Non-US patients, n	831	685	125	85	1,726	—
Procedure, mean (SD)						
Open appendectomy	3.9 (20.9)	4.1 (15.7)	7.7 (18.8)	2.7 (12.3)	1.9 (12.5)	0.87
Lap appendectomy	9.4 (72.4)	6.4 (32.9)	14.7 (51.5)	15.3 (19)	3.7 (30.0)	0.76
Open cholecystectomy	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	—
Lap cholecystectomy	6.4 (28.6)	17.7 (67.4)	15.5 (42.8)	128.6 (159.4)	5.2 (32.8)	< 0.001
Open hernia repair	16.1 (34.8)	13.5 (38.6)	21.8 (28.9)	16 (22.1)	10.2 (27.9)	0.82
Lap hernia repair	5.4 (29.1)	3.6 (22.6)	16.5 (49.5)	17.1 (19.5)	4.1 (22.4)	0.17

Lap, laparoscopic.

procedures, irrespective of the patient's reported pain severity before discharge. This comes in contrast to non-US providers, whose prescribing of opioids showed a clear relationship to the degree of patient-reported postoperative pain before discharge.

The difference in opioid prescribing practices after operation between the US and other countries has been documented recently. Lindenhovius and colleagues[22] found that 77% and 82% of US hospital patients undergoing hip and ankle fracture repair, respectively, were prescribed opioids after operation, compared with 0% and 6%, respectively, of their counterparts in a Dutch hospital. Similarly, Li and colleagues[23] compared patients undergoing head and neck surgery at a US hospital with those from a hospital in Hong Kong and found that 87% of patients in the US received opioids after operation vs < 1% of patients in Hong Kong. Kaafarani and colleagues[12] compared opioid prescriptions at discharge after 3 common general surgery procedures across 8 countries and found that 91% of patients in the US were prescribed opioids at discharge compared with only 5% of patients outside the US.

It is recommended that physicians avoid prescribing opioids to patients whose postsurgical pain is comfortably managed with nonopioid alternatives before discharge.[18] For example, several guidelines recommend prescribing ibuprofen after operation for all patients without a medical contraindication.[18] In our data, we found that providers in the US frequently prescribe opioid medications after operations even in the absence of any reported pain, contrary to current recommendations. In comparison, the vast majority of patients outside the US were prescribed nonopioid medications, with only a few receiving opioids. In fact, outpatient surgical pain management among non-US patients was more tailored to patients' needs, as there was a proportional increase in the quantity of opioids dispensed with higher levels of pain. In addition, opioid prescriptions among US surgeons exceeded the amount recommended by the Johns Hopkins Expert Panel Guidelines for laparoscopic cholecystectomy, laparoscopic hernia repair, and open hernia repair. In contrast, the amount prescribed by non-US surgeons was adequate for the same procedures.[18] Although the guidelines do not give recommendations for

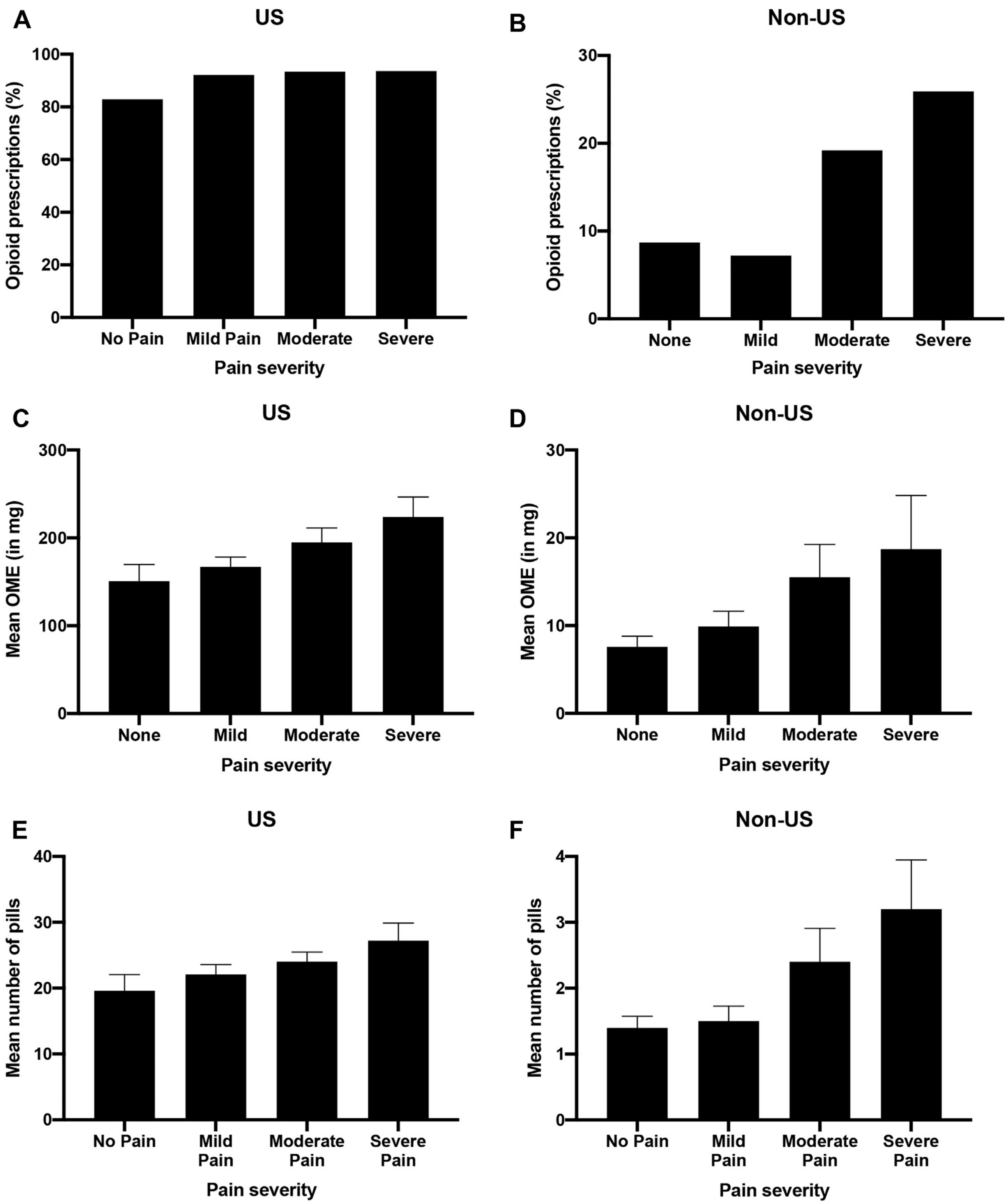

Figure 1. Comparison of discharge pain management between US and non-US patients. Error bars represent the SEM. (A) Proportion of US patients prescribed opioid at discharge across pain severity levels. (B) Proportion of non-US patients prescribed opioid at discharge across pain severity levels. (C) Mean oral morphine equivalents prescribed across pain severity levels in US patients. (D) Mean oral morphine equivalents prescribed across pain severity levels in non-US patients. (E) Mean number of pills prescribed across pain severity levels in US patients. (F) Mean number of pills prescribed across pain severity levels in non-US patients.

Table 4. Adjusted Discharge Pain Management by Pain Severity

Patient type, discharge pain management	No Pain	Mild pain	Moderate pain	Severe pain
All patients				
Opioid prescription, % (95% CI)	20.6 (18.4−22.8)	22.3 (19.7−24.9)	31.3 (25.4−37.1)	41.7 (30.7−52.8)
Total OME, mg, mean (95% CI)	33.0 (27.3−38.6)	35.2 (29.4−41.1)	49.1 (39.2−59)	63.7 (49.5−77.8)
No. of pills, mean (95% CI)	4.3 (3.6−4.9)	5.0 (4.3−5.7)	6.4 (5.3−7.5)	8.6 (6.9−10.2)
US patients				
Opioid prescription, % (95% CI)	83.5 (71.8−95.3)	88.4 (80.7−96.1)	91.7 (86.4−97.0)	92.9 (85.4−100)
Total OME, mg, mean (95% CI)	156.1 (110.3−202)	172.6 (141.3−203.9)	193 (166.4−219.5)	213.4 (169.9−256.8)
No. of pills, mean (95% CI)	20.6 (15.7−25.4)	21.9 (18.6−25.2)	23.9 (21−26.7)	27.1 (22.6−31.6)
Non-US patients				
Opioid prescription, % (95% CI)	8.5 (6.3−10.6)	10.2 (7.2−13.3)	21.5 (12.9−30.1)	46.2 (26.2−66.2)
OME, mg, mean (95% CI)	9.8 (6.4−13.2)	8.1 (4.4−11.9)	13.9 (6.1−21.8)	26.8 (15.6−38)
No. of pills, mean (95% CI)	1.4 (0.9−1.8)	1.6 (1.1−2.1)	2.5 (1.4−3.5)	4.5 (3−6)

OME, oral morphine equivalent.

appendectomy or open cholecystectomy, it is likely that US surgeons are prescribing in excess of what is needed to manage pain after open cholecystectomy and appendectomy. Interestingly, the number of opioid prescription refills was higher among US patients. This could suggest that US patients experience more pain after their discharge from the hospital compared with non-US patients.

Healthcare professionals might misjudge the pain intensity that patients experience. Although certain guidelines for the management of acute pain recommend prescribing strong analgesics for pain scores higher than 4,[24,25] most patients consider pain between 4 and 6 as tolerable.[26] Van Dijk and colleagues[27] specifically examined the relationship between patient reported pain (recorded on a 0 to 10 rating scale) after operation in the Netherlands and their own judgment for need for opioids. The authors found that 91% of patients did not want additional analgesics (median pain score 3 [interquartile range 1 to 5]), and only when pain score exceeded 8 did the majority express their need for additional opioids. Gan and colleagues[28] found that patients are even willing to have some degree of pain to avoid the adverse effects of narcotics. Physicians should adjust analgesic prescription not only according to the patient's reported pain but also to their response to nonopioids and desire to have or avoid opioids.

Strategies to reduce US physicians' overprescribing of opioids are needed to mitigate the wide variation in opioid prescription and the devastating toll of the epidemic.[29] A 2017 study by Bicket and colleagues[13] reported that the 67% to 92% of patients reported unused opioid pills after operation, with the overall proportion of unused tablets ranging from 42% to 71%. The large quantity of unused pills increases the risk of opioid misuse and diversion to the community at large. The US Food and Drug Administration has established recommendations about the proper disposal of unused pills

Table 5. Sensitivity Analysis Excluding Centers with Missing Data

Patient type, pain management	No pain	Mild pain	Moderate pain	Severe pain	p Value
All patients, n	798	655	155	36	—
Opioid, n (%)	88 (11.0)	101 (15.4)	73 (47.1)	30 (83.3)	< 0.001
Total OME, mg, mean (SD)	12.6 (50.1)	26.8 (76.1)	105.8 (180.3)	227.8 (177.3)	< 0.001
Number of pills, mean (SD)	2.2 (6.9)	3.7 (10.1)	13.3 (18.4)	27.4 (21.2)	< 0.001
US patients, n	18	60	65	26	—
Opioid, n (%)	16 (89)	54 (90)	59 (91)	26 (100)	0.42
Total OME, mg, mean (SD)	207.1 (136.9)	180.1 (119.0)	228.5 (220.7)	280.9 (161.3)	0.088
Number of pills, mean (SD)	27.6 (18.3)	24.1 (15.9)	28.4 (19.1)	34.2 (19.3)	0.12
Non-US patients, n	780	595	90	10	—
Opioid, n (%)	72 (9.2)	47 (7.9)	14 (15.6)	4 (40.0)	< 0.001
Total OME, mg, mean (SD)	8.1 (35.5)	11.3 (48.5)	17.2 (47.9)	90 (144.2)	< 0.001
Number of pills, mean (SD)	1.5 (5.1)	1.7 (6.4)	2.4 (6.1)	9.6 (14.8)	< 0.001

OME, oral morphine equivalent.

to mitigate the mishandling of narcotics; however, few patients are aware of these recommendations and even fewer dispose of their medications appropriately.[30-32] Efforts should focus on educating patients on the proper disposal methods and making them more convenient and accessible. The use of nonopioid alternatives for pain management should also be emphasized, as there is evidence showing that NSAIDs after operation can reduce the amount of opioids required and subsequently opioid-related adverse effects.[33] In addition, patient-level interventions that set expectations of tolerable pain rather than zero pain and provider-level interventions to raise awareness of standardized guidelines for postoperative pain management can significantly reduce the quantity of opioids prescribed without increasing refills.[34]

Our study has a few limitations. First, we did not measure patient satisfaction, and it is possible that patients were more satisfied with their pain management in the US. However, studies have shown that there is no association between the quantity of opioids dispensed after operation and patient satisfaction and pain scores.[15,35] Second, we did not collect data on medications received during hospitalization, and it is possible that pain severity was recorded when patients were on narcotics. Third, a number of patients had missing data for postoperative pain severity. Nevertheless, sensitivity analyses excluding centers with a high rate of missing data showed similar results—patients in the US are prescribed very large doses of opioids after operations irrespective of their pain level and pain management in patients outside the US is tailored to their needs.

CONCLUSIONS

Unlike their non-US counterparts, US providers prescribe high amounts of opioids after operations regardless of the patients' reported levels of pain severity. Additional efforts should be directed toward tailoring opioid prescriptions to patients' needs and perceived pain, and encouraging the use of nonopioid alternatives in the US.

APPENDIX

Members of the International Patterns of Opioid Prescribing Workgroup: Joseph V Sakran, MD, FACS, MPA, MPH, Division of Acute Care Surgery, Emergency General Surgery, The Johns Hopkins University, Baltimore, MD; Bellal Joseph, MD, FACS, Department of Surgery, College of Medicine, University of Arizona, Tucson, AZ; Camilo Ortega, MD, Hospital Departamental Villavicencio, Villavicencio, Colombia; Sonia Lopez Flores, MD, Bernardo J Gutierrez-Sougarret, MD, Department of Anesthesia, Hospital Angeles Pedregal, Mexico City, Mexico; Huanlong Qin, MD, Renyuan Gao, MD, Department of General Surgery, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai, People's Republic of China; Jun Yang, MD, Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, People's Republic of China; Zhiguo Wang, MD, Department of Colorectal Surgery, Changzheng Hospital, Navy Medical University, Shanghai, People's Republic of China; Zhiguang Gao, MD, Department of Emergency Surgery, Shanghai East Hospital of Tongji University, Shanghai, People's Republic of China; Supparerk Prichayudh, MD, Department of Surgery, King Chulalongkorn Memorial Hospital, Bangkok, Thailand; Gwendolyn van der Wilden, MD PhD: Department of Trauma Surgery, Leiden University Medical Center, Leiden, Netherlands; Napakadol Noppakunsomboom, MD, Division of Acute Care and Ambulatory Surgery, Siriraj Hospital, Mahidol University, Bangkok, Thailand; Ramzi Alami, MD, FACS, Department of Surgery, American University of Beirut, Beirut, Lebanon.

Author Contributions

Study conception and design: El Moheb, Mokhtari, Han, van Erp, Kongkaewpaisan, Jia, Rodriguez, Kongibulwut, Kaafarani, Sakran, Joseph, Ortega, Lopez Florez, Gutierrez-Sougarret, Qin, Yang, Gao, Wang, Gao, Prichayudh, van der Wilden, Noppakunsomboom, Alami

Acquisition of data: El Moheb, Mokhtari, Han, van Erp, Kongkaewpaisan, Jia, Rodriguez, Kongibulwut, Kaafarani, Sakran, Joseph, Ortega, Lopez Florez, Gutierrez-Sougarret, Qin, Yang, Gao, Wang, Gao, Prichayudh, van der Wilden, Noppakunsomboom, Alami

Analysis and interpretation of data: El Moheb, Mokhtari, van Erp, Kaafarani

Drafting of manuscript: El Moheb, Kaafarani

Critical revision: El Moheb, Mokhtari, Han, van Erp, Kongkaewpaisan, Jia, Rodriguez, Kongibulwut, Kaafarani, Sakran, Joseph, Ortega, Lopez Florez, Gutierrez-Sougarret, Qin, Yang, Gao, Wang, Gao, Prichayudh, van der Wilden, Noppakunsomboom, Alami

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Invited Commentary

Surgeons and the Opioid Crisis

Michael W Cripps, MD, MSCS, FACS
Dallas, TX

As surgeons, we are bound to our duty to cause no harm. In our well-meaning efforts to use opioids to assuage the