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Impact of opioid-free analgesia on pain severity and patient satisfaction after discharge from surgery: multispecialty, prospective cohort study in 25 countries

TASMAN Collaborative*

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A full list of PubMed-citable authors of the TASMAN Collaborative with corresponding roles is available in the *supplementary material*.

Abstract

Background: Balancing opioid stewardship and the need for adequate analgesia following discharge after surgery is challenging. This study aimed to compare the outcomes for patients discharged with opioid *versus* opioid-free analgesia after common surgical procedures.

Methods: This international, multicentre, prospective cohort study collected data from patients undergoing common acute and elective general surgical, urological, gynaecological, and orthopaedic procedures. The primary outcomes were patient-reported time in severe pain measured on a numerical analogue scale from 0 to 100% and patient-reported satisfaction with pain relief during the first week following discharge. Data were collected by in-hospital chart review and patient telephone interview 1 week after discharge.

Results: The study recruited 4273 patients from 144 centres in 25 countries; 1311 patients (30.7%) were prescribed opioid analgesia at discharge. Patients reported being in severe pain for 10 (i.q.r. 1–30)% of the first week after discharge and rated satisfaction with analgesia as 90 (i.q.r. 80–100) of 100. After adjustment for confounders, opioid analgesia on discharge was independently associated with increased pain severity (risk ratio 1.52, 95% c.i. 1.31 to 1.76; $P < 0.001$) and re-presentation to healthcare providers owing to side-effects of medication (OR 2.38, 95% c.i. 1.36 to 4.17; $P = 0.004$), but not with satisfaction with analgesia (β coefficient 0.92, 95% c.i. −1.52 to 3.36; $P = 0.468$) compared with opioid-free analgesia. Although opioid prescribing varied greatly between high-income and low- and middle-income countries, patient-reported outcomes did not.

Conclusion: Opioid analgesia prescription on surgical discharge is associated with a higher risk of re-presentation owing to side-effects of medication and increased patient-reported pain, but not with changes in patient-reported satisfaction. Opioid-free discharge analgesia should be adopted routinely.

Introduction

Postoperative pain is common, complex, and often severe, affecting up to 80% of patients[1]. It is frequently managed using opioid analgesia, which, although potent, incurs the risk of significant adverse events. There are ongoing concerns regarding the inappropriate, excessive, and unsafe prescription of opioid analgesia after surgery[2,3]. Such practices are associated with worse patient outcomes, greater healthcare demands, and the 'opioid epidemic'[4,5].

Surgeons are high prescribers of opioids, accounting for approximately 10% of all prescriptions[6]. The overprescription of opioids in the postoperative phase likely stems from healthcare providers' desire to reduce patient discomfort, and concerns regarding poor patient satisfaction[7,8]. Unused postoperative opioids represent an important contributor to opioid diversion in the community[9]. Despite the perception that opioids aid pain management in this setting, multiple studies have indicated that opioid-sparing protocols after surgery are not associated patient satisfaction, provided that pain is controlled adequately using non-opioid analgesia, and patient expectations are managed appropriately[7,10].

A recent meta-analysis by Fiore *et al.*[11] reported that opioid prescription at discharge after elective procedures did not improve pain control, but was associated with increased harm. This review was limited to minor and moderate procedures such as dental procedures or cholecystectomies, but demonstrated that the default stance to prescribe opioids at surgical discharge may be a practice steeped in culture rather than evidence. Given the variation in prescribing practices between countries, centres, and individual clinicians[12], international, multispecialty data are required to understand the relationship between opioid prescription and patient-reported pain and satisfaction outcomes, particularly after emergency and major procedures.

This study aimed to describe patient-reported outcomes of patient pain, satisfaction, and quality of life after common surgical procedures, and to investigate the effect of opioid prescription on patient-reported postdischarge outcomes and the risk of re-presentation owing to inadequate analgesia or adverse effects.

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Methods

Study design

The OPERAS (Opioid PrEscRiptions and Usage After Surgery) study was an international multicentre collaborative study developed by the Trials and Audit in Surgery by Medical Students in Australia and New Zealand (TASMAN) Collaborative, an Australasian student- and trainee-led collaborative network. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12621001451897p) and the protocol (*Appendix S1*) has been published elsewhere[13]. The collaborative research model has been used by other studies internationally and described previously[14,15]. Study requirements and approvals were achieved according to country-specific regulations before recruitment of participants began. This analysis was conducted in line with the STROBE reporting guidelines for observational studies[16]. Patients or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Ethical approval

Ethical approval was obtained at each participating site in line with local protocols and verified by the central steering committee. The protocol was approved by the Hunter New England Human Research Ethics Committee (2021/ETH11508) in Australia as the lead site.

Eligibility criteria

Adult patients aged 18 years or above who underwent an eligible general surgical (cholecystectomy, appendicectomy, inguinal hernia repair, colonic resection, fundoplication or sleeve gastrectomy), orthopaedic (total or reverse shoulder arthroplasty, rotator cuff or labral repair, anterior cruciate ligament repair, or hip or knee arthroplasty), gynaecological (hysterectomy, oophorectomy, or salpingectomy and oophorectomy), or urological (prostatectomy, cystectomy or nephrectomy) operation during the data collection phases were approached for inclusion[13]. Elective and emergency operations were included. Patients who fulfilled any of the following criteria were excluded: currently on medication-assisted treatment of opioid dependence; discharged to another healthcare setting (for example rehabilitation service); multivisceral resection; and returned to the operating room during index admission. Eligible patients were identified through inspection of surgical operating lists. All participants provided written informed consent before inclusion and each centre obtained ethical approval before data collection.

Data collection

Data were collected prospectively during six separate 2-week intervals between April and September 2022, from inpatient hospital records and by a follow-up telephone call 7 days after discharge. The follow-up interview was conducted using a prespecified protocol and script (*Appendix S2*) to ensure standardization.

Data were collected on patient demographics (age, sex, smoking status, BMI, ASA physical status grade), co-morbidities, diagnosis and procedure-specific details (indication, surgical approach, and urgency), opioid use in the 24 h before discharge from hospital, postoperative complications, and preoperative regular opioid and non-opioid analgesic use. Regular analgesic use was defined as a minimum of once-weekly use in the 3 months immediately before surgery. Minimally invasive surgery was defined as arthroscopic, laparoscopic or robotic surgery. Open surgery was defined as planned open surgery, and laparoscopic/robotic operations that were converted to open procedures. Data were also collected on opioid and non-opioid medication prescriptions at discharge.

To enable comparison between opioids of different potencies, all data on opioid doses were converted to oral morphine equivalents (OMEs). Further details on how OMEs were calculated are provided in *Appendix S3*.

Outcomes

The primary outcome was the amount of time spent in severe pain in the first 7 days after discharge measured on a numerical analogue scale from 0 to 100%. Secondary outcomes included patient-reported satisfaction with the quality of analgesia received on a scale of 0 to 100, patient-reported quality of life measured by the EQ-5D-5L™ tool (EuroQol Group, Rotterdam, the Netherlands) 7 days after discharge, number of presentations to healthcare professionals owing to inadequate analgesia, and number of presentations to healthcare because of side-effects of analgesia including nausea, vomiting, drowsiness, itching, dizziness or constipation. Outcome measures related to the prescription and consumption of analgesics are reported elsewhere[17].

The EQ-5D-5L™ tool is used to measure patient quality of life in five domains, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The tool also includes an EQ-VAS score, which rates a patient's self-reported health from 0 (worst possible) to 100 (best possible)[18]. Re-presentation to healthcare was defined as any visit to primary care, emergency department, surgeon's office, or readmission to hospital for inadequately treated pain or side-effects of analgesic medication between discharge and 7 days after discharge.

Statistical analysis

Statistical analyses were completed in R 4.0.3 for statistical computing (R Core Team, Vienna, Austria). Descriptive statistics were used to compare demographic and in-hospital differences between patients discharged on opioid and opioid-free analgesia using χ^2 tests for categorical variables and Kruskal–Wallis tests for continuous variables.

Propensity score matching was used to minimize the selection bias of participants prescribed opioid and opioid-free analgesia on discharge using the *MatchIt* package[19]. The propensity score was defined as the probability that a patient would receive opioid analgesia adjusted for age, sex, ASA grade, BMI, presence of chronic kidney disease and liver disease, smoking status, preoperative opioid and non-opioid analgesia use, surgical procedure, duration of operation, indication for surgery, postoperative complications, duration of hospital stay, concomitant discharge prescription of paracetamol and non-steroidal anti-inflammatory drugs, and OMEs consumed in the 24 h before discharge. Full matching was used to allow multiple patients from each group to be matched together (if appropriate) and weighted for balancing, avoiding inappropriate discarding of data that can occur with nearest-neighbour matching[20]. Balance between groups was assessed before and after matching using the standardized mean difference, with an absolute value of less than 0.1 as an indication of a well balanced variable.

Multiple imputation by chained equations was used to impute values for patients with missing data using the *mice* package[21]. Visual inspection of variables with missing data stratified by presence of opioid analgesia at discharge was completed to

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ensure that variables were missing at random. Ten imputed data sets were created, with propensity score matching subsequently performed on each using the *MatchThem* package[22]. The pooled results of models are presented.

Mixed-effects models, using centre and country as random effects, were fitted for primary and secondary outcomes. Logistic regression models were built for binary outcomes, and negative binomial regression or generalized linear regression models for continuous outcomes. Co-variate selection was guided by clinical plausibility and previous literature[23], and relevant preoperative, intraoperative, and postoperative variables were included as fixed effects. Residual, Q-Q plots, and variance inflation factors were interrogated to assess model assumptions.

Subgroup analysis

Procedures were stratified into abdominal procedures (including general, gynaecological, and urological operations) and orthopaedic procedures. Sensitivity analyses were undertaken for these subgroups. Prescribing practices and patient-reported outcomes were compared between different regions of the world, and between high-income countries (HICs) and low- and middle-income countries (LMICs) as defined by the Organisation for Economic Co-operation and Development (OECD)[24].

Results

Data from 4273 patients from 114 hospitals in 25 countries were collected over the study interval, (*Fig. 1*). The majority of patients included were from Australia (813), Egypt (594), Aotearoa New Zealand (560), Libya (372), and Turkey (296) (*Table S1*). Patient demographics and co-morbidities stratified by opioid analgesia prescription on discharge are presented in *Table 1* and *Table S2*. The median age of the cohort was 50 years, and 53.1% were women. Of those included, 3056 (71.5%) underwent general surgical procedures, 591 (13.8%) orthopaedic procedures, 393 (9.2%) gynaecological procedures, and 233 (5.5%) urological procedures (*Table 1*).

A total of 1311 patients (30.7%) were prescribed opioid analgesia at discharge. For those prescribed any opioid on discharge, the median quantity was 100 (i.q.r. 60–200) OMEs. At 7 days, the median quantity consumed was only 40 (7.5–100) OMEs ($P < 0.001$). Complete data on the proportion of prescribed opioids that were consumed by 7 days are available elsewhere[17]. Of note, 197 patients who received a prescription for opioids at discharge (15.0%) did not consume any opioid analgesia in the 24 h before discharge. A total of 2596 patients (60.8%) recalled receiving education about pain management before discharge.

Propensity score matching produced well matched cohorts, demonstrated by the plot of standardized mean differences of included variables (*Fig. S1* and *Table S3*.).

Postdischarge patient-reported outcomes

The reported time spent in severe pain after discharge, stratified by procedure, is displayed in *Fig. 2a*. After propensity score matching and adjustment for confounding factors in mixed-effects negative binomial regression, patients prescribed opioids spent more time in severe pain after discharge (risk ratio 1.52, 95% c.i. 1.31 to 1.76; $P < 0.001$) (*Tables 3* and *S4*).

Despite the differences in pain severity, there was no difference in patient-reported satisfaction with pain treatment on univariable analysis (median satisfaction rating 90 of 100 in both opioid and no-opioid groups; $P = 0.157$) (*Table 2*), or after propensity score matching and adjustment for confounding factors in mixed-effects linear regression (β coefficient 0.92, 95% c.i. −1.52 to 3.36; $P = 0.468$) (*Tables 3* and *S5*).

There was no dose-dependent relationship between the quantity of opioids prescribed on discharge and pain severity or patient-reported satisfaction in both unadjusted (*Fig. S2*) and adjusted analyses (*Fig. 3*).

Quality of life and re-presentation to healthcare

Before risk adjustment, patients prescribed opioids reported poorer quality of life at 7 days after discharge compared with those not prescribed opiates when measured by a composite EQ-5D-5L™ score (median 80.9 *versus* 87.9; $P < 0.001$) and EQ-VAS score (75 *versus* 82; $P < 0.001$). This association persisted after adjustment in mixed-effects linear regression and with propensity score matching; quality of life was poorer as measured by both EQ-5D-5L™ score (β coefficient −2.27; $P = 0.005$) (*Tables 3* and *S6*) and EQ-VAS score (β coefficient −2.82; $P = 0.002$) (*Tables 3* and *S7*). Opioid prescription at discharge did not increase the likelihood of patients seeking additional healthcare for pain relief (OR 1.01, 95% c.i. 0.70 to 1.46; $P = 0.948$) (*Tables 3* and *S8*), but increased the risk of presentation to

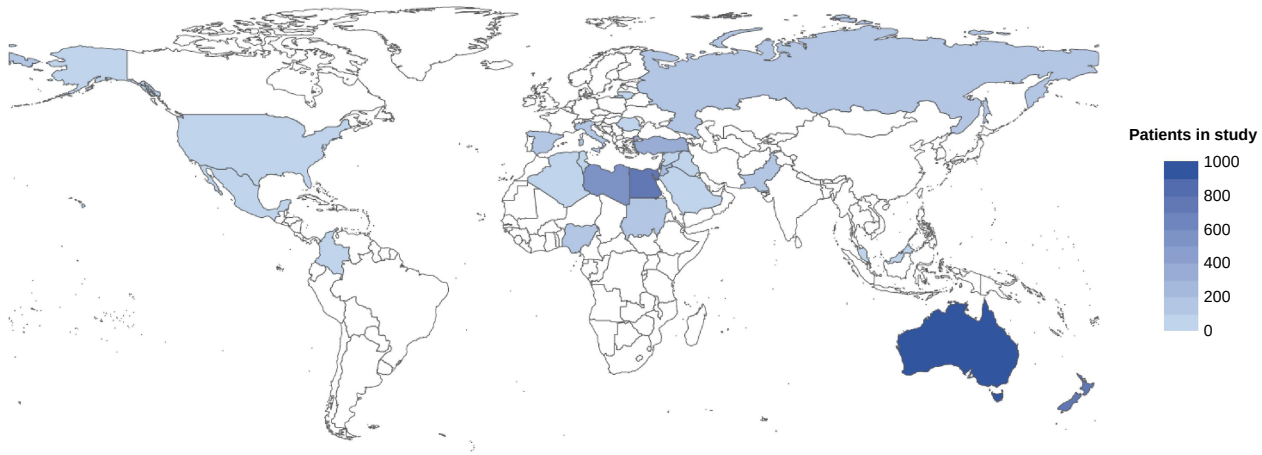


Fig. 1 Patients contributed to the OPERAS study by country
Full details are available in *Table S1*.

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Table 1 Patient characteristics

	No opioids (*n* = 2962)	Opioids (*n* = 1311)	Total (*n* = 4273)	*P**
Age (years), median (i.q.r.)	48 (33–64)	52 (37–66)	50 (34–64)	< 0.001†
Sex				0.033
Female	1579 (53.3)	692 (52.8)	2271 (53.1)	
Male	1383 (46.7)	616 (47.0)	1999 (46.8)	
Other	0 (0)	3 (0.2)	3 (0.1)	
ASA fitness grade				< 0.001
I	1377 (46.5)	386 (29.4)	1763 (41.3)	
II–III	1559 (52.6)	907 (69.2)	2466 (57.7)	
IV—V	24 (0.8)	15 (1.1)	39 (0.9)	
Missing	2 (0.1)	3 (0.2)	5 (0.1)	
BMI (kg/m^2)				< 0.001
Normal (18.5–24.9)	835 (28.2)	327 (24.9)	1162 (27.2)	
Overweight (25.0–29.9)	1078 (36.4)	385 (29.4)	1463 (34.2)	
Obese (30.0-39.9)	603 (20.4)	333 (25.4)	936 (21.9)	
Severely obese (>40.0)	111 (3.7)	94 (7.2)	205 (4.8)	
Underweight (< 18.5)	56 (1.9)	13 (1.0)	69 (1.6)	
Missing	279 (9.4)	159 (12.1)	438 (10.3)	
Smoking status				< 0.001
Never smoked	1841 (62.2)	723 (55.1)	2564 (60.0)	
Current smoker	550 (18.6)	182 (13.9)	732 (17.1)	
Ex-smoker	355 (12.0)	307 (23.4)	662 (15.5)	
Missing	216 (7.3)	99 (7.6)	315 (7.4)	
Procedure				< 0.001
Appendicectomy	522 (17.6)	241 (18.4)	763 (17.9)	
Cholecystectomy	880 (29.7)	346 (26.4)	1226 (28.7)	
Colorectal resection	271 (9.1)	122 (9.3)	393 (9.2)	
Inguinal hernia repair	440 (14.9)	136 (10.4)	576 (13.5)	
Nissen fundoplication	23 (0.8)	5 (0.4)	28 (0.7)	
Sleeve gastrectomy	49 (1.7)	21 (1.6)	70 (1.6)	
ACL repair	57 (1.9)	21 (1.6)	78 (1.8)	
Knee arthroplasty	110 (3.7)	147 (11.2)	257 (6.0)	
Hip arthroplasty	110 (3.7)	91 (6.9)	201 (4.7)	
Rotator cuff repair	11 (0.4)	11 (0.8)	22 (0.5)	
Shoulder arthroplasty	9 (0.3)	11 (0.8)	20 (0.5)	
Shoulder labral repair	12 (0.4)	1 (0.1)	13 (0.3)	
Cystectomy	28 (0.9)	4 (0.3)	32 (0.7)	
Nephrectomy	62 (2.1)	38 (2.9)	100 (2.3)	
Prostatectomy	66 (2.2)	35 (2.7)	101 (2.4)	
Hysterectomy	228 (7.7)	59 (4.5)	287 (6.7)	
Oophorectomy and salpingectomy	28 (0.9)	13 (1.0)	41 (1.0)	
Oophorectomy only	21 (0.7)	3 (0.2)	24 (0.6)	
Salpingectomy only	35 (1.2)	6 (0.5)	41 (1.0)	
Surgical approach				< 0.001
MIS	1487 (50.2)	814 (62.1)	2301 (53.8)	
Open	1474 (49.8)	496 (37.8)	1970 (46.1)	
Missing	1 (0.0)	1 (0.1)	2 (0.0)	
Indication				0.630
Benign disease	2601 (87.8)	1144 (87.3)	3745 (87.6)	
Malignancy	360 (12.2)	167 (12.7)	527 (12.3)	
Missing	1 (0.0)	0 (0)	1 (0.0)	
Urgency				< 0.001
Elective	2098 (70.8)	818 (62.4)	2916 (68.2)	
Emergency	863 (29.1)	493 (37.6)	1356 (31.7)	
Missing	1 (0.0)	0 (0)	1 (0.0)	
Duration of surgery (min), median (i.q.r.)	80 (55–120)	98 (66–135)	87 (60–120)	< 0.001†
Opioid use before surgery				< 0.001
No	2909 (98.2)	1180 (90.0)	4089 (95.7)	
Yes	53 (1.8)	131 (10.0)	184 (4.3)	
Non-opioid analgesia use before surgery				< 0.001
No	2396 (80.9)	933 (71.2)	3329 (77.9)	
Yes	566 (19.1)	378 (28.8)	944 (22.1)	
Clavien–Dindo grade of complication				< 0.001
None	2450 (82.7)	1025 (78.2)	3475 (81.3)	
I–II	487 (16.4)	265 (20.2)	752 (17.6)	
III–IV	21 (0.7)	20 (1.5)	41 (1.0)	
Missing	4 (0.1)	1 (0.1)	5 (0.1)	
Duration of hospital stay (days), median (i.q.r.)	2 (1–3)	2 (1–3)	2 (1–3)	0.698†
OMEs consumed 24 h before discharge, median (i.q.r.)	0.0 (0.0–30.0)	35.0 (10.0–67.8)	9.0 (0.0–40.0)	< 0.001†

Values are *n* (%) unless otherwise indicated. ACL, anterior cruciate ligament; MIS, minimally invasive surgery; OME, oral morphine equivalent. *χ^2 test, except †Kruskal–Wallis test.

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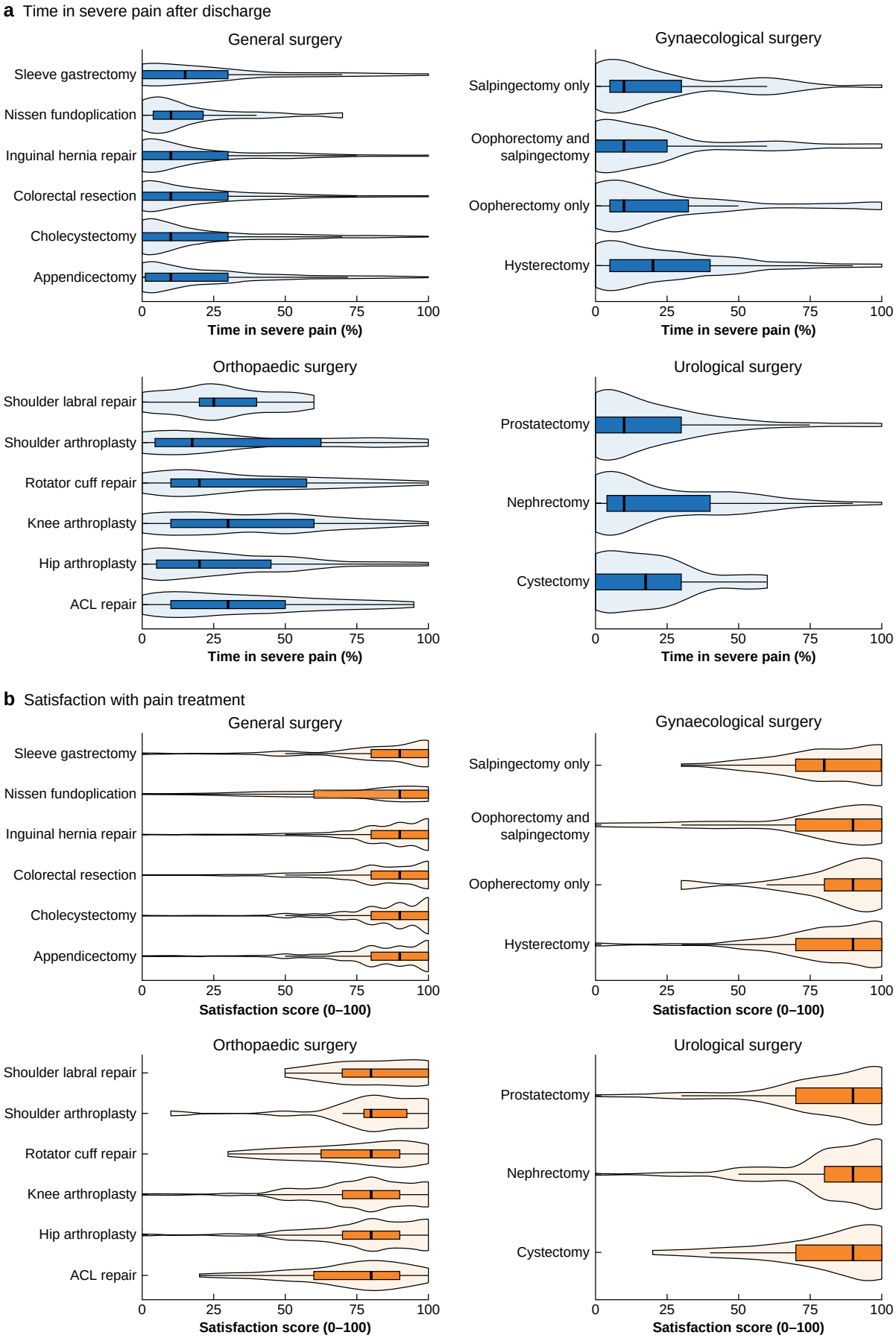


Fig. 2 Pain severity after discharge and satisfaction with pain treatment, stratified by procedure

a Time in severe pain after discharge and **b** satisfaction with pain treatment. Violin and box plots show range, i.q.r., and median values. ACL, anterior cruciate ligament.

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Table 2 Patient outcomes after discharge from hospital

	No opioids (n = 2962)	Opioids (n = 1311)	Total (n = 4273)	P*
Time in severe pain in week after discharge (%), median (i.q.r.)	10 (0–30)	20 (5–40)	10 (1–30)	< 0.001†
Satisfaction with pain treatment (0–100), median (i.q.r.)	90 (80–100)	90 (80–100)	90 (80–100)	0.157†
Satisfaction with amount of analgesia provided				< 0.001
Too little	622 (21.0)	229 (17.5)	851 (19.9)	
Just right	2226 (75.2)	887 (67.7)	3113 (72.9)	
Too much	110 (3.7)	194 (14.8)	304 (7.1)	
Missing	4 (0.1)	1 (0.1)	5 (0.1)	
EQ-5D-5L™ composite score (0–100), median (i.q.r.)	87.9 (76.1–95.0)	80.9 (69.1–89.2)	85.9 (73.8–93.7)	< 0.001†
EQ-VAS score (0–100), median (i.q.r.)	82 (70–90)	75 (60–85)	80 (70–90)	< 0.001†
Postdischarge medical presentation for pain				< 0.001
No	2701 (91.2)	1121 (85.5)	3822 (89.4)	
Yes	261 (8.8)	190 (14.5)	451 (10.6)	
Postdischarge medical presentation for side-effects of medication				
No	2851 (96.3)	1220 (93.1)	4071 (95.3)	< 0.001
Yes	111 (3.7)	91 (6.9)	202 (4.7)	

Values are n (%) unless otherwise indicated. * χ test, except †Kruskal-Wallis test.

Table 3 Multivariable analysis of the effect of opioids on outcomes

	Group	Univariable analysis (complete case)		Hierarchical regression analysis (multiple imputation)		Propensity-score matched and regression analysis (multiple imputation)	
		Effect size	P	Effect size	P	Effect size	P
Mixed-effects negative binomial regression*							
Time in severe pain in week after discharge (%)*	No opioids on discharge	Reference		Reference		Reference	
	Opioids on discharge	1.28 (1.15, 1.41)	< 0.001	1.51 (1.34, 1.71)	< 0.001	1.52 (1.31, 1.76)	< 0.001
Mixed-effects linear regression†							
Satisfaction with pain treatment (0–100)†	No opioids on discharge	Reference		Reference		Reference	
	Opioids on discharge	0.08 (−0.21, 0.37)	0.586	0.84 (−0.82, 2.51)	0.322	0.92 (−1.52, 3.36)	0.468
EQ-5D-5L™ (composite score, 0–100)†	No opioids on discharge	Reference		Reference		Reference	
	Opioids on discharge	−17.38 (−23.15, −11.61)	< 0.001	−1.48 (−2.99, 0.02)	0.054	−2.27 (−3.82, −0.72)	0.005
EQ-VAS score (0–100)†	No opioids on discharge	Reference		Reference		Reference	
	Opioids on discharge	−4.24 (−5.09, −3.40)	< 0.001	−1.64 (−3.37, 0.09)	0.064	−2.82 (−4.51, −1.14)	0.002
Mixed-effects logistic regression‡							
Postdischarge medical presentation for pain‡	No opioids on discharge	Reference		Reference		Reference	
	Opioids on discharge	1.73 (1.37, 2.17)	< 0.001	1.32 (0.97, 1.80)	0.080	1.01 (0.70, 1.46)	0.948
Postdischarge medical presentation for medication side-effects‡	No opioids on discharge	Reference		Reference		Reference	
	Opioids on discharge	1.83 (1.31, 2.55)	< 0.001	2.92 (1.84, 4.63)	< 0.001	2.38 (1.36, 4.17)	0.004

Values in parentheses are 95% confidence intervals. Effect sizes are shown as *risk ratios, †β coefficients, and ‡ORs.

healthcare owing to side-effects of medication (OR 2.38, 1.36 to 4.17; $P = 0.004$) (*Tables 3* and *S9*).

Excess and insufficient analgesia prescription

Overall, 14.8% of patients prescribed opioid analgesia felt that they were prescribed too much pain relief medication, compared with 3.7% of those prescribed only non-opioid analgesia. Conversely, 17.5% of patients prescribed opioids felt they were prescribed too little pain relief medication, compared with 21.0% of those prescribed no opioids ($P < 0.001$) (*Table 2*).

Factors associated with reporting receiving too little pain relief on multivariable analysis included female sex (OR 1.25, 95% c.i. 1.03 to 1.51; $P < 0.001$), preoperative regular use of opioid analgesia (OR 1.94, 1.32 to 2.82; $P < 0.001$), ASA grade IV–V (OR 2.66, 1.27 to 5.54, *versus* ASA I), postoperative complications (OR 1.41, 1.13 to 1.76, for Clavien–Dindo grade I–II *versus* no complications; $P < 0.003$), and specific orthopaedic or urological procedures (*Table S10*).

Patients who underwent orthopaedic procedures reported severe pain more frequently in the 7 days after discharge than those who had abdominal procedures (median 30 (i.q.r. 10–50) and 10 (0–30)% respectively; $P < 0.001$) (*Fig. 2a*), and reported a lower level of satisfaction with pain relief after discharge (median 80 (i.q.r. 70–90) *versus* 90 (80–100) of 100; $P < 0.001$) (*Fig. 2b*). Orthopaedic patients reported lower quality-of-life scores after discharge than those who had abdominal procedures

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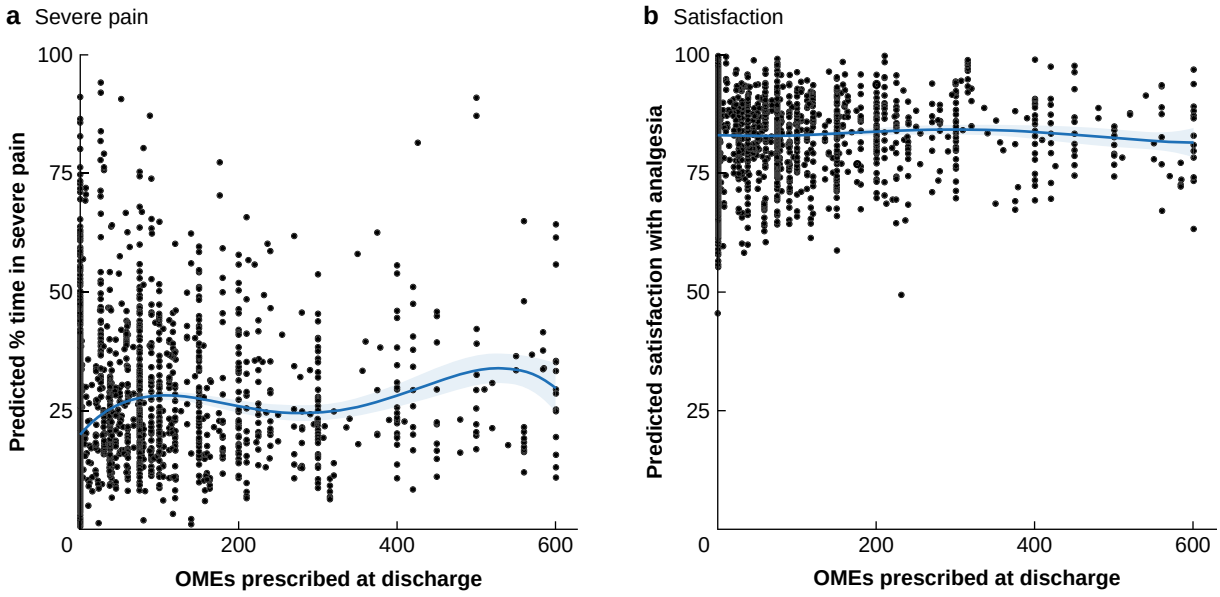


Fig. 3 Relationship between quantity of oral morphine equivalents prescribed at discharge and modelled time in severe pain and modelled patient satisfaction with pain treatment

a Modelled time in severe pain and **b** modelled patient satisfaction with pain treatment adjusted for patient demographics, co-morbidity, operation type, duration and indication, preoperative opioid and non-opioid analgesia, postoperative complications, and oral morphine equivalent (OME) requirements 24 h before discharge. Each individual dot represents an individual patient. The solid lines and shaded areas represent the polynomial regression lines and 95% confidence intervals respectively.

(median EQ-VAS score 70 (i.q.r. 60–80) *versus* 80 (70–90) of 100; $P < 0.001$), and were more likely to seek further analgesia (18.3 *versus* 9.3%; $P < 0.001$), and re-present to healthcare owing to side-effects of analgesia (9.1 *versus* 4.0%; $P < 0.001$).

Geographical variation

The 1923 patients from HICs as defined by the OECD were prescribed more opioids on average than the 2350 patients from LMICs (median 37.5 (0–112.5) and 0 (0–0) OMEs respectively; $P < 0.001$). Patients from HICs had nine times higher odds of receiving opioids on surgical discharge than those from LMICs after adjusting for case mix, patient co-morbidity, postoperative complications, and analgesic needs after propensity score matching (adjusted OR 9.10, 95% c.i. 7.70 to 11.10) (*Table S11*). Similar results were found without propensity score matching (adjusted OR 10.0, 8.30 to 12.50).

Although there was a statistically significant difference, there were no clinically significant differences in time spent in severe pain (median 10 (i.q.r. 0–30)% in first week in HICs *versus* 10 (3–30)% in LMICs; $P < 0.001$) or patient satisfaction between HICs and LMICs (median 90 (80–100) and 85 (70–100) respectively; $P < 0.001$).

Geographical differences in patients and outcomes between Asia Pacific, North America, Central and Latin America, Middle East and North Africa, Europe and Central Asia, Sub-Saharan Africa, and South Asia are presented in full in *Tables S12 and S13*.

Discussion

This multinational prospective cohort study demonstrated that prescription of opioids at hospital discharge after common surgical procedures was not associated with improved treatment satisfaction compared with opioid-free analgesia. Furthermore, increasing opioid prescription quantities was not associated with changes in pain severity or patient satisfaction. Opioid prescription was associated with increased presentation for management of pain medication side-effects, without an associated reduction in presentations for further pain management. This study expands on previous work limited to mostly minor elective day-case procedures[11,25–27], by including acute operations, major visceral resections, and major orthopaedic procedures. The present study provides prospective, international data to inform discharge analgesia prescription after common surgical procedures, and highlights that opioid-free analgesia at discharge can be the default rather than the exception.

It is becoming increasingly apparent across a range of surgical procedures that most patients do not benefit from opioid pain relief at discharge, with only a small targeted set of patients requiring opioid prescriptions on discharge[11,25,28]. In this study, female sex, opioid use before surgery and on discharge, lower limb orthopaedic surgery, elective procedures, and mild postoperative complications (Clavien Dindo grades I–II) were associated with increased time spent in severe pain, consistent with findings reported in other reviews. Clinician concern surrounding patient dissatisfaction after discharge and healthcare reutilization owing to uncontrolled pain is a major driver of opioid overprescription[7,29], but this was not shown in the present cohort and others[23,30]. Similar studies conducted in general surgical procedures[7,10], breast procedures[26,27], major abdominal and urological procedures[11,28], gynaecological procedures[31], as well as orthopaedic sports operations[32] have shown that decreasing opioid prescriptions or opioid-free analgesia following discharge does not decrease patient satisfaction scores after surgery. On the contrary, healthcare utilization for patients experiencing side-effects of medication was increased for those with opioid analgesia compared with those receiving opioid-free analgesia, a finding that replicates previous studies[11]. The present study therefore reinforces previous findings that increasing opioid prescription on discharge is not independently associated with pain severity,

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and indicates that clinicians should not prescribe opioids as a panacea for postoperative pain.

Marked global variation in opioid prescribing was demonstrated in this cohort. Similar geographical differences have been demonstrated in other studies, with the USA and Canada typically seeing significantly higher quantities of opioids being prescribed for the same procedures compared with other countries including Sweden, China, Lebanon, Brazil, Mexico and the Netherlands[33,34]. This study extends the findings of previous studies and demonstrates that, at follow-up 7 days after discharge, there is no clinically meaningful difference in reported pain levels when the patient cohort is stratified by geography. Current geographical variations in opioid prescribing likely reflect entrenched medicocultural practices rather than evidence-based pain management.

Patient outcomes differ across different surgical procedures, with patients who undergo orthopaedic procedures experiencing greater postoperative pain and lower satisfaction than those having abdominal procedures. Given that many patients undergoing arthroplasty are regular users of opioids in the preoperative phase, those in this situation are at a higher risk of uncontrolled postoperative pain and chronic opioid use after surgery[35]. However, regardless of procedure, a multimodal approach to pain management is required, with preoperative assessment for high-risk pain characteristics, appropriate modulation of patient expectations, multimodal analgesia, and pain treatment planning on discharge[36]. Preoperative counselling on pain management and opioid use may reduce patient-reported pain scores, increase the likelihood of patients using non-pharmacological therapies, and increase levels of function at 6 months after operation[37].

For this study, it was possible to collect prospective international patient-reported data across a range of surgical specialties with high rates of follow-up. Nevertheless, there are several limitations. After extensive co-variate adjustment, matching, and subgroup analysis, this study showed results consistent with randomized data[11]. However, observational data are not a substitute for randomized data for deducing causal relationships, and the results need to be interpreted with this in mind. Furthermore, although extensive physical co-morbidity data were collected, it was not possible to adjust for co-existing anxiety, depression or pain catastrophizing, which are other factors associated with pain severity[23]. At follow-up, patient-reported outcomes may be prone to recall bias, but this was minimized by the relatively short duration of follow-up. Although a 7-day follow-up may be considered a short time frame for outcomes assessment, this was selected as clinical care standards recommend limiting the duration of usual discharge opioid prescriptions to less than 7 days[38,39]. Lastly, cultural differences in pain perception and reporting may confound patient recall of outcomes[40]. This potential risk to the results was mitigated by factoring in centre and country-level effects into mutivariable models.

The present results suggest that opioid prescribing at surgical discharge is not associated with reduced patient satisfaction, but with an increased risk of presentation to healthcare owing to the side-effects of pain medication. Increasing the quantity of prescribed opioid was not associated with changes in patient-reported pain. Further studies should focus on developing prescribing guidelines for high-risk patients, including those with preoperative opioid needs, and for specific procedures associated with high analgesia requirements.

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Author contributions

A full list of PubMed-citable authors of the TASMAN Collaborative with corresponding roles is available in the supplementary material.

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

References

1. Gan TJ, Habib AS, Miller TE, White W, Apfelbaum JL. Incidence, patient satisfaction, and perceptions of post-surgical pain: results from a US national survey. *Curr Med Res Opin* 2014;**30**:149–160
2. Macintyre PE, Quinlan J, Levy N, Lobo DN. Current issues in the use of opioids for the management of postoperative pain: a review. *JAMA Surg* 2022;**157**:158–166
3. The Lancet Public Health. Opioid overdose crisis: time for a radical rethink. *Lancet Public Health* 2022;**7**:e195
4. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *J Pain Res* 2017;**10**:2287–2298
5. Oderda GM, Said Q, Evans RS, Stoddard GJ, Lloyd J, Jackson K *et al.* Opioid-related adverse drug events in surgical hospitalizations: impact on costs and length of stay. *Ann Pharmacother* 2007;**41**:400–406
6. Levy B, Paulozzi L, Mack KA, Jones CM. Trends in opioid analgesic-prescribing rates by specialty, U.S., 2007–2012. *Am J Prev Med* 2015;**49**:409–413
7. Louie CE, Kelly JL, Barth RJ Jr. Association of decreased postsurgical opioid prescribing with patients' satisfaction with surgeons. *JAMA Surg* 2019;**154**:1049–1054
8. Dineen KK, DuBois JM. Between a rock and a hard place: can physicians prescribe opioids to treat pain adequately while avoiding legal sanction? *Am J Law Med* 2016;**42**:7–52
9. Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription opioid analgesics commonly unused after surgery: a systematic review. *JAMA Surg* 2017;**152**:1066–1071
10. Fry BT, Howard RA, Gunaseelan V, Lee JS, Waljee JF, Englesbe MJ *et al.* Association of postoperative opioid prescription size and patient satisfaction. *Ann Surg* 2022;**276**:e1064–e1069
11. Fioire JF Jr, El-Kefraoui C, Chay MA, Nguyen-Powanda P, Do U, Olleik G *et al.* Opioid *versus* opioid-free analgesia after surgical discharge: a systematic review and meta-analysis of randomised trials. *Lancet* 2022;**399**:2280–2293
12. Schieber LZ, Guy GP Jr, Seth P, Young R, Mattson CL, Mikosz CA *et al.* Trends and patterns of geographic variation in opioid prescribing practices by state, United States, 2006–2017. *JAMA Netw Open* 2019;**2**:e190665
13. TASMAN Collaborative Project Management Group. Opioid PrEscRiptions and usage after surgery (OPERAS): protocol for a prospective multicentre observational cohort study of opioid use after surgery. *BMJ Open* 2022;**12**:e063577

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14. Bhangu A, Kolias AG, Pinkney T, Hall NJ, Fitzgerald JE. Surgical research collaboratives in the UK. *Lancet* 2013;**382**:1091–1092
15. Hunter SPARTAN Collaborative, QUEST Collaborative, STARC Collaborative, STORCC Collaborative, STRATA Collaborative, STRIVE WA Collaborative *et al.* Trainee- and student-led research networks: promoting research skills and competency through collaboration. *ANZ J Surg* 2020;**90**:2177–2179
16. 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. *Ann Intern Med* 2007;**147**:573–577
17. TASMAN Collaborative; Varghese C. Patterns of opioid use after surgical discharge: a multicentre, prospective cohort study in 25 countries. *bioRxiv* 2023. https://www.medrxiv.org/content/10.1101/2023.09.30.23296378v1.abstract (accessed 3 October 2023)
18. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D *et al.* Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;**20**:1727–1736
19. Ho D, Imai K, King G, Stuart EA. Matchit: nonparametric preprocessing for parametric causal inference. *J Stat Softw* 2011;**42**:1–28
20. Stuart EA, Green KM. Using full matching to estimate causal effects in nonexperimental studies: examining the relationship between adolescent marijuana use and adult outcomes. *Dev Psychol* 2008;**44**:395–406
21. van Buuren S, Groothuis-Oudshoorn K. Mice: multivariate imputation by chained equationsi R. *J Stat Softw* 2011;**45**:1–67
22. Pishgar F, Greifer N, Leyrat C, Stuart E. MatchThem:: matching and weighting after multiple imputation. *The R Journal* 2021;13:292–305
23. Yang MMH, Hartley RL, Leung AA, Ronksley PE, Jetté N, Casha S *et al.* Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. *BMJ Open* 2019;**9**:e025091
24. OECD. *OECD Income (IDD) and Wealth (WDD) Distribution Databases*. https://www.oecd.org/social/income-distribution-database.htm (accessed 15 April 2023)
25. Davies B, Brummett CM. Anchoring to zero exposure: opioid-free minimally invasive surgery. *Ann Surg* 2020;**271**:37–38
26. Kang R, Read JT, Glaser AC, Barth RJ Jr. Eliminating opioids from breast conserving surgery: perioperative pain management pathway. *J Am Coll Surg* 2020;**230**:975–982
27. Moo TA, Pawloski KR, Sevilimedu V, Charyn J, Simon BA, Sclafani LM *et al.* Changing the default: a prospective study of reducing discharge opioid prescription after lumpectomy and sentinel node biopsy. *Ann Surg Oncol* 2020;**27**:4637–4642
28. Mian BM, Singh Z, Carnes K, Lorenz L, Feustel P, Kaufman RP Jr *et al.* Implementation and assessment of no opioid prescription strategy at discharge after major urologic cancer surgery. *JAMA Surg* 2023;**158**:378–385
29. Boretsky K, Mason K. In the arms of morpheus without morphia; mitigating the United States opioid epidemic by decreasing the surgical use of opioids. *J Clin Med Res* 2021;**10**:1472
30. van Boekel RLM, Bronkhorst EM, Vloet L, Steegers MAM, Vissers KCP. Identification of preoperative predictors for acute postsurgical pain and for pain at 3 months after surgery: a prospective observational study. *Sci Rep* 2021;**11**:16459
31. Glaser GE, Kalogera E, Kumar A, Yi J, Destephano C, Ubl D *et al.* Outcomes and patient perspectives following implementation of tiered opioid prescription guidelines in gynecologic surgery. *Gynecol Oncol* 2020;**157**:476–481
32. Moutzouros V, Jildeh TR, Khalil LS, Schwartz K, Hasan L, Matar RN *et al.* A multimodal protocol to diminish pain following common orthopedic sports procedures: can we eliminate postoperative opioids? *Arthroscopy* 2020;**36**:2249–2257
33. Kaafarani HMA, Han K, El Moheb M, Kongkaewpaisan N, Jia Z, El Hechi MW *et al.* Opioids after surgery in the United States *versus* the rest of the world: the international patterns of opioid prescribing (iPOP) multicenter study. *Ann Surg* 2020;**272**:879–886
34. Ladha KS, Neuman MD, Broms G, Bethell J, Bateman BT, Wijeysundera DN *et al.* Opioid prescribing after surgery in the United States, Canada, and Sweden. *JAMA Netw Open* 2019;**2**:e1910734
35. Kuck K, Naik BI, Domino KB, Posner KL, Saager L, Stuart AR *et al.* Prolonged opioid use and pain outcome and associated factors after surgery under general anesthesia: a prospective cohort association multicenter study. *Anesthesiology* 2023;**138**:462–476
36. Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T *et al.* Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;**17**:131–157
37. Rucinski K, Cook JL. Effects of preoperative opioid education on postoperative opioid use and pain management in orthopaedics: a systematic review. *J Orthop* 2020;**20**:154–159
38. Australian Commission on Safety and Quality in Health Care. *Opioid Analgesic Stewardship in Acute Pain—Clinical Care Standard—Acute Care Edition.* https://www.safetyandquality.gov.au/sites/default/files/2022-04/opioid-analgesic-stewardship-in-acute-pain-clinical-care-standard.pdf (accessed 1 February 2023)
39. Schug SA, Palmer GM, Scott DA, Alcock M, Halliwell R Mott JF. *Acute Pain Management Scientific Evidence*. Melbourne, Australia: Australian and New Zealand College of Anaesthetists, 2020
40. Chan EY, Blyth FM, Cheow SL, Fransen M. Postoperative pain following hospital discharge after knee replacement surgery: a patient survey. *Pain Manag* 2013;**3**:177–188

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