Prevalence and predictors of persistent post-surgical opioid use: a prospective observational cohort study

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Summary

Post-surgical opioid prescribing intended for the short-term management of acute pain may lead to long-term opioid use. This study was undertaken to determine the prevalence of persistent post-surgical opioid use and patient-related factors associated with post-surgical opioid use. One thousand and thirteen opioid-naïve patients awaiting elective surgery in a tertiary private hospital in Sydney were enrolled. Preoperatively, patients completed a questionnaire comprising potential predictors of persistent post-surgical opioid use. Patients underwent surgery with routine perioperative care, and were followed up at 90 to 120 days after surgery to determine opioid use. Factors associated with opioid use were assessed with logistic regression. We had an overall response rate of 95.8% (n=970) of patients, of whom 10.5% (n=102) continued to use opioids at >90 days after surgery. On surgical subtype analysis, the prevalence of persistent opioid use was 23.6% after spinal surgery, and 13.7% after orthopaedic surgery. Four factors were independently associated with persistent post-surgical opioid use in a multivariate model: having orthopaedic (odds ratio [OR] 4.6, 95% confidence interval [CI] 2.0 to 10.8, *P* <0.001) or spinal surgery (OR 4.0, 95% CI 1.7 to 9.2, *P* <0.001), anxiety (OR 2.1, 95% CI 1.1 to 4.1, *P*=0.03), attending pre-admission clinic (OR 3.7, 95% CI 1.6 to 8.6, *P*=0.002), and higher self-reported pain score at >90 days after surgery (*P* <0.001). More than 10% of opioid-naïve patients undergoing elective surgery experience persistent post-surgical opioid use. Identification of factors associated with persistent post-surgical opioid use may allow development of a risk stratification tool to predict those at highest risk.

Key Words: opioid, opioid analgesics, analgesics, persistent opioid use, opioid cessation, prevalence, risk factors, surgery, orthopaedic surgery, spinal surgery, post-surgical, Australia

There are growing concerns that surgery is a risk factor for long-term opioid use[1]. Existing studies suggest that post-surgical opioid prescribing intended for the short-term management of acute pain may result in unintended long-term opioid use for a small but meaningful number of patients, with post-surgical opioid use continuing in some patients for years after surgery[2].

Opioids have proven efficacy for the management of acute post-surgical pain, but can cause significant harm when used long-term for non-cancer pain. Acute post-surgical pain is followed by persistent pain in 10% to 50% of individuals after common operations[3]. It is possible that there is a link between persistent post-surgical pain and persistent post-surgical opioid use, however the nature of this link remains largely unstudied.

Studies in the United States and Canada report persistent post-surgical opioid use in 0.1% to 8.2% of opioid-naïve patients after a variety of minimally invasive, invasive, and orthopaedic procedures[1,4-10]. Persistent opioid use is highest after spinal surgery, and has been reported in up to 80% of this group of patients[11,12].

Preoperative risk stratification tools may be of use in identifying surgical patients at risk of persistent opioid use. Validated tools are widely used to identify patients at high risk of opioid misuse in the chronic pain setting[13], but currently there is no optimal method to predict patients at risk of persistent opioid use after surgery. As stated by Macintyre et al, risk stratification should become standard practice for patients being prescribed opioids for acute post-surgical pain[2].

Existing studies have found that a wide range of patient characteristics and psychiatric comorbidities are associated with persistent opioid use in a post-surgical setting. Persistent post-surgical opioid use has been found to have a significant association with age greater than 50 years[1], body mass index >30 kg/m^2 [8], surgical subtype[1,6], low socioeconomic status[6], preoperative psychiatric conditions[14], including anxiety[9] and depression[1,5,8,10,14], specific medical comorbidities (diabetes, heart failure, lung disease)[6], preoperative use of opioids[5,7], benzodiazepines[1] or antidepressants[1], preoperative alcohol or drug abuse[1], high levels of preoperative pain[7], preoperative pain catastrophising[7], and longer duration of postoperative pain[5]. Risk factors vary between existing studies and settings. Data from Australian hospitals are limited.

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Objectives

Our primary study objective was to determine the prevalence of persistent post-surgical opioid use in opioid-naïve patients, defined in our study as the taking of opioids greater than 90 days after surgery. Our secondary objective was to identify patient-related factors that are independently associated with persistent post-surgical opioid use.

Materials and methods

Ethics review and trial registration

This study was registered with ClinicalTrials.gov (Registration number: NCT02571400), and had ethics approval from the St Vincent's Hospital Human Research Ethics Committee (HREC), reference number 15/198, and the University of Notre Dame Australia HREC, reference number 015133S.

Study design and setting

We conducted a prospective, observational cohort study at St Vincent's Private Hospital, Sydney, from October 2015 to September 2016. Patients were recruited from October 2015 to June 2016, then followed up via phone call or email from January to September 2016.

Participants

A convenience sample of opioid-naïve adults (aged ≥18 years) scheduled to undergo surgery at St Vincent's Private Hospital were enrolled. Patients were excluded from the study if they were using opioids on a daily basis. Participants were recruited via the pre-admission clinic or day surgery unit. The referral process detailing which patients attend pre-admission clinic versus the day surgery unit is complex and dependent on multiple patient, surgical, anaesthetic, and hospital factors. Patients having surgery relating to malignancy, minimally invasive surgery (e.g. bronchoscopy, colonoscopy), multiple surgical procedures or surgery completed under local anaesthetic were excluded. All other surgical procedures were included. Patients who were unable to complete study questionnaires due to psychological illness, medical condition or significant language barrier were also excluded.

Data sources and measurement/procedures

Patients meeting inclusion criteria were approached by nursing staff in the surgical pre-admission clinic or day surgery unit and asked to participate. Written, informed consent was obtained prior to study enrolment. Prior to their scheduled surgery, patients completed a 20-item questionnaire comprising potential predictors of persistent opioid use (preoperative variables). Patients underwent surgery with routine pre- and postoperative care. Patients were followed up between 90 and 120 days after surgery via email or phone call to determine ongoing opioid use, type of opioid used, opioid dose per day, reason for opioid use, and current self-reported pain score (postoperative variables).

Preoperative variables

Recorded variables included age, surgical type, attendance at the pre-admission clinic or day surgery unit, and any history of prescription opioid use or substance use for management of anxiety. Anxiety was assessed using the two-item Generalised Anxiety Disorder Questionnaire (GAD-2)[15]. Depression was assessed using the two-item Patient Health Questionnaire (PHQ-2)[16]. The five-item Screener and Opioid Assessment for Patients with Pain (SOAPP-R version 1.0-SF)[17,18] was used to measure risk of developing problematic opioid use. Patients were asked to assign a self-perceived risk of addiction to analgesics on a four-point Likert scale (not at all, unlikely, somewhat likely, very likely)[5]. The short versions of these validated tools were used so that if they were found to be independently associated with persistent opioid use they could be incorporated more easily into a screening tool. Average sleep per night over the previous four weeks was recorded as less than two, two to four, four to six, or greater than six hours. Self-perceived general health[19] was assessed using a five-point Likert scale (poor, fair, good, very good, excellent). Venn diagrams were used to assess connectedness to family, friends and community on a seven-point scale.

Postoperative variables

Persistent post-surgical opioid use was defined as prescription or over-the-counter opioid use greater than 90 days after surgery and information regarding opioid type and dose was also collected. Patients using opioids for reasons unrelated to their surgery were classified as not having persistent post-surgical opioid use. Pain score was recorded using the Numeric Rating Scale (score 0 to 10)[20] with the participant self-reporting their average pain over the previous 24 hours, specifically relating to their surgery. Patients were asked to specify their main reason for opioid use (to improve pain, to relieve depression or anxiety, to improve sleep, to allow exercise, other). We were unable to collect data regarding opioid use during the intraoperative and acute postoperative period, and did not collect data regarding source of opioid prescription at follow-up.

Bias

To control for measurement bias, research nurses were trained and used a standardised protocol to recruit patients. The initial questionnaire was standardised, and completed in writing by the participant. Follow-up questionnaires were completed using a standardised telephone or email script. Where possible, we incorporated validated screening tools into our questionnaires. We aimed to collect all follow-up data at 90 days after surgery, but allowed an extra 30 days to capture patients who were initially non-responders in order to minimise loss to follow-up. Information regarding

Table 1

Characteristics of study cohort

	Total Cohort		Ceased opioids		Persistent opioid use		*P*-value
Age, years							0.03
Median, IQR	61 (46–69)		60 (45–69)		64 (53–70)		
Range	18–88		18–88		24–86		
Sex, n (%)							0.7
Male	461	(47.5%)	411	(47.4%)	50	(49%)	
Female	509	(52.5%)	457	(52.6%)	52	(51%)	
TOTAL	970	(100%)	868	(100%)	102	(100%)	
Surgical subtype, n (%)							<0.001
Cardiothoracic	26	(2.7%)	25	(2.9%)	1	(1%)	
ENT	71	(7.3%)	70	(8.1%)	1	(1%)	
Gastrointestinal	106	(10.9%)	100	(11.6%)	6	(5.9%)	
Gynaecology	81	(8.4%)	81	(9.4%)	0	(0%)	
Head and neck	5	(0.5%)	5	(0.6%)	0	(0%)	
Spinal	178	(18.4%)	136	(15.7%)	42	(41.1%)	
Neurosurgery	14	(1.4%)	14	(1.6%)	0	(0%)	
Plastic	29	(3%)	29	(3%)	0	(0%)	
Urology	71	(7.3%)	70	(8.1%)	1	(1%)	
Vascular	17	(1.8%)	17	(2%)	0	(0%)	
Orthopaedic	364	(37.5%)	314	(36.2%)	50	(49%)	
Ophthalmology	1	(0.1%)	1	(0.1%)	0	(0%)	
Unknown	7	(0.7%)	6	(0.7%)	1	(1%)	
TOTAL	970	(100%)	100	(100%)	102	(100%)	

ENT, ear nose and throat; IQR, interquartile range.

current opioid use and pain scores was collected regardless of timepoint, so as to eliminate recall bias.

Study size

Power calculations were based on the minimum detectable odds ratio for characteristics potentially associated with the study outcome, using the prevalence of anxiety in the general Australian population of 14% as an example[21]. Based on previous studies[1,4-10], we assumed that 10% of our study cohort would continue to use opioids greater than 90 days after surgery, and the prevalence of anxiety would be higher in those who continued to use opioids than those who did not. With a total proposed sample of 1,000 participants, we would have 80% power to detect an odds ratio of 2.1 at a two-sided significance level of 5%.

Statistical methods

Study participant characteristics were summarised for the entire cohort, and by whether or not the patients continued to take opioids at greater than 90 days after surgery. Comparisons between study groups were made with a Wilcoxon test for continuous variables, and a chi-square or Fisher's exact test as appropriate for categorical variables. We calculated the overall prevalence of persistent post-surgical opioid use, and the prevalence according to surgical discipline. Pain medication usage was summarised for all subjects with persistent opioid use.

Multiple logistic regression was used to assess independent relationships between persistent opioid use and patient characteristics. Multivariate models were developed adjusting for characteristics that were significant in univariate analysis at a level of $P < 0.1$. The linearity of age against the logit function was assessed, and since this assumption was not met, age was modelled as quartiles. The odds ratio (OR) and 95% confidence interval (CI) for the second and third quartiles were very similar, and these quartiles were collapsed. For categorical covariates, cells with zero counts were collapsed against the adjacent categories so that an OR could be calculated. Two surgical subtypes showed increased odds for persistent opioid use, and other surgical subtypes were combined as a reference group.

Statistical analyses were performed using Stata, version 14.2 (Statacorp, College Station, TX, USA). We assigned statistical significance as $P < 0.05$.

Table 2

Opioid use at greater than 90 days post-surgery

Drug		n (%)
Paracetamol/codeine *500 mg/30 mg*	Alone	28 (27.4%)
	PLUS oxycodone IR	2 (1.9%)
	PLUS tramadol	1 (1%)
Oxycodone IR *Variable dose*	Alone	18 (17.7%)
	PLUS tramadol	3 (2.9%)
	PLUS oxycodone/naloxone	2 (1.9%)
	PLUS buprenorphine	1 (1%)
	PLUS oxycodone ER	1 (1%)
	PLUS morphine	1 (1%)
Tramadol *Variable dose*	Alone	17 (16.7%)
	PLUS oxycodone/naloxone	2 (1.9%)
	PLUS oxycodone ER	1 (1%)
Oxycodone/naloxone *Variable dose*	Alone	12 (11.8%)
Ibuprofen/codeine *200 mg/12.8 mg*	Alone	4 (3.9%)
Fentanyl *Variable dose*	Alone	1 (1%)
	PLUS physeptone	1 (1%)
Paracetamol/codeine *500 mg/8 mg*	Alone	1 (1%)
Morphine *Dose not specified*	Alone	1 (1%)
Oxycodone ER *10 mg*	Alone	1 (1%)
Tapentadol *50 mg*	Alone	1 (1%)
Did not specify		3 (2.9%)
TOTAL		102 (100%)

IR, immediate release; ER, extended release.

Results

Participants

One thousand and thirteen participants were enrolled; 28 patients (2.8%) were lost to follow-up, five patients declined to participate in follow-up (0.5%), and ten patients (1%) experienced significant medical complications or had multiple surgical procedures during the study period. The overall response rate was therefore 95.8%.

There were minimal missing data. We had a poor response for the Venn diagrams assessing connectedness to friends, family and community. Study nurses reported patients found this difficult to complete and the tool was therefore removed from study analyses.

Table 3

Self-reported main reason for opioid use

Reason for opioid use	n	(%)
Improve pain	82	(80.4%)
Improve sleep	6	(5.9%)
Facilitate exercise	1	(1%)
Improve pain, depression + anxiety	1	(1%)
Improve pain + sleep	1	(1%)
Other, not specified	11	(10.7%)
TOTAL	102	(100%)

Participant characteristics/descriptive data

Of our final patient cohort (n=970, Table 1), 52.5% were male. Median age was 61 years (interquartile range [IQR] 46 to 69 years), with an age range of 18 to 88 years. There were 12 surgical subtypes represented.

Primary outcome

Ten-and-a-half percent (n=102) of patients continued to use opioids at greater than 90 days after surgery. Of these patients, 51% were female and the median age was 64 years (range 24 to 86 years), 49% (n=50) had orthopaedic surgery, 41.1% (n=42) had spinal surgery, and 5.9% (n=6) had gastrointestinal surgery (Table 1).

Of the opioid medications used (Table 2), combination paracetamol/codeine was the most common (28.4%), followed by oxycodone (17.7%), tramadol (16.7%), and combination oxycodone/naloxone (11.8%). Five patients (5%) specified use of over-the-counter opioid preparations. Four patients (4%) did not specify which opioid medication they used.

Incomplete daily opioid dosage data were collected as many patients did not specify the dosage or frequency of the opioid medication used. We obtained complete data regarding daily opioid dosage for thirty-eight patients (36%) who continued to use opioids and these were converted to a daily oral morphine equivalent dose (mg): the range was 2 to 130 mg daily (median 15 mg, mean 30.6 mg).

The majority of patients using opioids at greater than 90 days after surgery reported using them for pain relief (80.4%, Table 3) but 5.9% reported use to improve sleep, and 1% reported use to facilitate exercise or to manage their depression/anxiety.

Secondary outcomes

In univariate analysis (Table 4), several factors showed a statistically significant association with persistent opioid use. These included spinal surgery, orthopaedic surgery, attending pre-admission clinic, history of prescription opioid use, positive GAD-2 score (anxiety), less sleep per night, fair or poor self-perceived health and higher self-reported pain

score at follow-up. No significant association was found with age, positive PHQ-2 score (depression), positive SOAPP-R-SF score (problematic opioid use) or self-perceived susceptibility to addiction.

After adjusting for age, SOAPP-R-SF score, average sleep per night, and self-perceived health status in a multivariate model, four factors were independently associated with persistent post-surgical opioid use in a multivariate model. These were undergoing orthopaedic surgery (OR 4.6, 95% CI 2.0 to 10.8) or spinal surgery (OR 4.0, 95% CI 1.7 to 9.2) versus other surgery (*P* <0.001), attending pre-admission clinic versus the day surgery unit (OR 3.7, 95% CI 1.6 to 8.6, *P* <0.001), positive GAD-2 score (OR 2.1, 95% CI 1.1 to 4.1, *P* <0.001), and higher self-reported pain scores at follow-up (*P* <0.001). Compared to patients with pain scores of <1, those with pain scores of 2–3 had increased odds of 5.8 (95% CI 2.9 to 11.9), those with pain scores of 4–5 had increased odds of 16.2 (95% CI 7.9 to 33.4), and those with pain scores of 6 to 10 had increased odds of 21.2 (95% CI 10.1 to 44.6).

Table 4

Predictors of persistent opioid use, univariate and multivariate analysis

Characteristic	Univariate		Multivariate	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age, years		0.06		0.65
18–45	1 (ref)		1 (ref)	
46–68	1.5 (0.8–2.6)		1.0 (0.5–2.0)	
69–88	2.1 (1.1–3.8)		1.1 (0.5–2.5)	
Surgical type		<0.001		<0.001
Other	1 (ref)		1 (ref)	
Spinal	12.5 (6.1–25.6)		4.0 (1.7–9.2)	
Orthopaedic	6.8 (3.4–12.6)		4.6 (2.0–10.8)	
Pre-admission clinic versus day surgery unit		0.001		0.002
Day surgery unit	1 (ref)		1 (ref)	
Pre-admission clinic	2.9 (1.5–5.6)		3.7 (1.6–8.6)	
History of prescription opioid use		<0.001		0.11
No	1 (ref)		1 (ref)	
Yes	3.1 (1.7–5.7)		1.8 (0.9–3.6)	
History of substance use to manage anxiety		0.15		
No	1 (ref)			
Yes	1.4 (0.9–2.1)			
GAD-2 score (anxiety)		<0.001		0.03
≤2	1 (ref)		1 (ref)	
≥3 (positive score)	2.9 (1.7–4.9)		2.1 (1.1–4.1)	
PHQ-2 score (depression)		0.2		
≤2	1 (ref)			
≥3 (positive score)	1.7 (0.8–3.7)			
SOAPP-R-SF score (problematic opioid use)		0.08		0.54
≤3	1 (ref)		1 (ref)	
≥4	1.7 (0.9–3.2)		1.3 (0.6–2.8)	
Self-perceived susceptibility to addiction		0.35		
Not at all	1 (ref)			
Unlikely	1.4 (0.9–2.3)			
Somewhat likely or very likely	0.7 (0.1–5.4)			
Average sleep per night		0.01		0.47
>6 hours	1 (ref)		1 (ref)	
4–6 hours	1.5 (1.0–2.3)		1.0 (0.6–1.7)	
<4 hours	2.9 (1.4–5.8)		1.6 (0.7–3.9)	
Self-perceived health		0.004		0.33
Good, Very Good, Excellent	1 (ref)		1 (ref)	
Fair or poor	2.3 (1.3–4.0)		1.4 (0.7–2.9)	
Pain scores at follow-up		<0.001		<0.001
0–1	1 (ref)		1 (ref)	
2–3	8.2 (4.2–16.1)		5.8 (2.9–11.9)	
4–5	23.3 (12.0–45.5)		16.2 (7.9–33.4)	
6–10	32.7 (16.5–64.9)		21.2 (10.1–44.6)	

OR, odds ratio; GAD-2, generalised anxiety disorder; PHQ-2, patient health questionnaire; SOAPP-R-SF, Screener and Opioid Assessment for Patients with Pain-Revised; CI, confidence interval; ref, reference.

Discussion

Major findings

In this privately insured, metropolitan population, 10.5% of opioid-naïve adults continued to use opioid analgesics longer than 90 days after surgery. This prevalence is higher than a number of studies in the United States and Canada that reported persistent opioid use in 0.1% to 8.2% of opioid-naïve patients after a variety of surgical procedures[1,4-10].

High-risk surgical subtypes included spinal and orthopaedic surgery, with persistent opioid use seen in 23.6% of patients undergoing spinal surgery, and 13.7% of patients undergoing orthopaedic surgery. Additionally, higher self-reported pain scores at follow-up, anxiety, and attending pre-admission clinic were independently associated with persistent post-surgical opioid use in this population.

Transition from acute to chronic use of opioids

Opioids are an essential part of the management of acute post-surgical pain[6,22], but can cause significant harm when used longer-term for chronic non-cancer pain[23]. Opioids should therefore ideally be ceased for most patients early in the post-surgical period, but this may be difficult if self-reported pain scores remain high, or if there is coexisting psychological distress or behavioural disorders. Current recommendations for post-surgical care advise opioid tapering as pain resolves, which most patients are able to do with minimal instruction from their surgeon or general practitioner[24]. If a patient continues to take opioids beyond the expected healing time of the surgery, a medical review is warranted to assess the reason for continued opioid use.

The majority of patients using opioids at greater than 90 days post-surgery reported pain as the main self-reported reason for use. Patients with persistent post-surgical

opioid use may be experiencing an emerging chronic pain state, or may have pre-existing pain that has not changed following surgery. Some patients may develop post-surgical neuropathic pain, or experience primary surgical failure which is particularly relevant when examining orthopaedic and spinal surgery, often performed to alleviate pain associated with musculoskeletal pathology. Some patients may have an ongoing nociceptive or inflammatory source of pain, whilst others may experience chronic post-surgical pain, a persistent pain state that is apparent at least two months after an operation, and cannot be explained by other sources[25]. Chronic post-surgical pain has been reported in 10% to 50% of patients after a variety of surgical procedures[3,25-28]. It is worth noting that there may be some overlap between the risk factors for chronic post-surgical pain and risk factors for persistent post-surgical opioid use[3,25,28], but the link between chronic post-surgical pain and post-surgical opioid use remains unknown.

Anxiety was independently associated with persistent opioid use in our study cohort. This is comparable to the findings of Singh and Lewallen who reported a strong association between anxiety and persistent opioid use after total knee replacement[9]. Depression was not found to be associated with persistent opioid use, which is counter to evidence found in multiple existing studies[5,9,10,24]. There is growing evidence that some patients may have non-pain drivers of opioid use, such as psychological distress, or psychiatric comorbidities. A large study conducted by Quinn et al in the United States found that psychiatric and behavioural conditions were associated with use of prescription opioids, and these patients were more likely to transition to long-term opioid use[14].

Attending the pre-admission clinic, compared with attending the day surgery unit, was associated with increased odds of persistent post-surgical opioid use. This finding is confounded by factors including surgical type, patient group, and the clinical association between pre-admission clinic, complex surgical procedures, and patients with multiple medical comorbidities. Nevertheless, this might be clinically important, as the pre-admission clinic provides an opportunity to target patients for opioid risk stratification and provide interventions aimed at reducing post-surgical opioid use. Existing literature suggests pre-admission clinic interventions can reduce postoperative complications, and facilitate patient recovery[29].

Clinical implications

Patients at high risk of persistent post-surgical opioid use should not be deprived of treatment with opioids for severe acute pain, but should be followed more closely after hospital discharge. Additionally, high-risk patients should be targeted for pre- and postoperative interventions which may reduce the risk of long-term opioid use.

Study strengths and limitations

This study has sound methodology, large numbers, and small loss to follow-up. However, we did not collect data regarding socioeconomic status, education level, pre-existing pain scores, use of non-opioid medications, or coexisting medical and psychiatric diagnoses. This is due, in part, to the paucity of studies linking these factors to persistent post-surgical opioid use at the time of study planning. We did collect data regarding the dose and frequency of opioid use at greater than 90 days after surgery but these data were incomplete. Additionally, we were unable to gather data regarding intraoperative and acute postoperative use of opioids. Our study was undertaken in a single setting in a private hospital in metropolitan Sydney, so our findings may not be applicable to non-metropolitan settings, or settings where the majority of patients do not have private health insurance.

Conclusion

The prevalence of persistent post-surgical opioid use in opioid-naïve patients was 10.5% in our Australian metropolitan setting. On surgical subtype analysis, the prevalence of opioid use was 23.6% after spinal surgery, and 13.7% after orthopaedic surgery. Other factors independently associated with persistent post-surgical opioid use included preoperative anxiety, higher pain scores at follow-up, and attending the pre-admission clinic. These study findings may be helpful in the future development of a preoperative risk stratification tool which might allow clinicians to provide clinical interventions aimed at reducing the risk of long-term opioid use and its associated harm in high-risk patients.

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