



Peri-Operative Pain Management, Education & De-escalation (POPPMED), a novel anaesthesiologist-led program, significantly reduces acute and long-term postoperative opioid requirements: a retrospective cohort study

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Abstract

Introduction: The opioid tolerant patient requiring surgery is highly likely to be discharged on high Oral Morphine Equivalent Daily Dosages (OMEDDs), with concomitant risk of increased morbidity and mortality.

Objectives: We proposed that a single anaesthesiologist-led POPPMED (Peri-Operative Pain Management, Education & De-escalation) service could reduce both short and long-term postoperative patient OMEDDs.

Methods: From April 2017, our anaesthesiologist-led POPPMED service, engaged 102 perioperative patients treated with >50mg preoperative OMEDDs. We utilized behavioural interventions; acute opioid reduction and/or rotation; and regional, multimodal and ketamine analgesia to achieve lowest possible hospital discharge and long term OMEDDs.

Results: Patients' preoperative OMEDDs were [median (IQR): 115mg (114mg)], and were representative of an older [age 62 (15) years], high-risk [89% ASA status 3 or 4] patient population. 46% of patients received an acute opioid rotation; 70% received ketamine infusions; and 44% regional analgesia. OMEDDs on discharge [-25mg (82mg), $p=0.003$] and at 6-12 months [-55mg (105mg), $p<0.0001$] were significantly reduced; 84% and 87% of patients achieved OMEDD reduction on discharge and at 6-12 months. Patients with >90mg preoperative OMEDDs achieved greater reductions [discharge: 71% of patients, -52 mg (118 mg) $p<0.0001$; 6-12 months: 90% of patients, -90mg (115mg), $p<0.0001$]. On comparison with a pre-POPPMED surgical cohort, Postoperative Day 1-3 11-point Numerical Rating Scale (NRS-11) area under the curve (AUC) measurements at rest and on movement were not significantly different (largest NRS-11:hours AUC difference [median(IQR)] 22 [13], $p=0.24$). Hospital length of stay was variably increased.

Conclusions: POPPMED achieved sustained OMEDD reductions safely in an older, high-risk opioid tolerant population, with analgesia comparable to a non-POPPMED cohort, and surgery specific effects on length of stay.

Keywords: Acute pain, Regional anaesthesia, Opioids, Chronic pain, Transitional Pain, Transitional pain service

1. Introduction

Increasing prescription-opioid-related morbidity and mortality is a well-recognized problem, with the situation in Australia following a similar trend to North America. Hospitalisations and deaths

related to opioid overuse, misuse, or overdose increased by 240% and 180%, respectively, with a corresponding 32-fold increase in yearly public health costs to \$271 million AUD within the past 2 decades.⁶ Unregulated postoperative analgesia outpatient prescriptions have been appropriately identified as a

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contributory factor, with The Royal Australian & New Zealand College of Anaesthesiologists responding accordingly with strong recommendations against routine prescription of sustained-release opioids for acute postoperative pain,²⁸ and the compulsory application of SafeScript (Department of Health & Human Services, Victoria, Australia) as a condition for outpatient opioid prescribing. Balanced against this is the need to ensure adequate analgesia for postoperative rehabilitation and recovery.

Patients receiving outpatient opioid therapy before surgery are a particularly high-risk population for elevated and sustained postoperative opioid prescription, at approximately 9 times the rate of those patients who are preoperatively opioid naive.²² Given the added burden of acute postoperative pain and reduced opioid analgesic efficacy, the perioperative period has historically been viewed as an inappropriate time for opioid reduction in the patient already receiving high-dose opioids.²³ However, the early observational experience with novel Transitional Pain Programs has demonstrated success in acute postoperative reduction in such patients' daily opioid requirements (oral morphine equivalent daily dosage [OMEDDs]).⁸

From 2017, we implemented a novel, single anaesthesiologist-led perioperative pain service (Peri OPERative Pain Management, Education, and De-escalation [POPPMED]). Our service focused on preoperative identification and engagement of opioid-tolerant patients requiring surgery with risk factors for perioperative opioid escalation. These patients were defined as those who had had an active background of one or more of preexisting opioid prescription; chronic pain; recreational drug use, or opioid replacement therapy. We made use of perioperative biological and nonbiological patient interventions (Fig. 1), while simultaneously closely coordinating the surgical, anaesthesia, acute pain, and allied health teams. We delivered a united, patient-specific

analgesia plan incorporating perioperative opioid rotation, ketamine infusion, and regional analgesia where suitable. We hypothesized that our service could achieve acute and long-term reduction in patient OMEDDs safely without significantly affecting early postoperative quality of analgesia and length of hospital stay.

2. Methods

As a retrospective cohort study, this study was not preregistered. Institutional review board approval was given by the Austin Health Human Research and Ethics Committee (approval #19/Austin/124).

The Austin Hospital POPPMED service (Fig. 2) was conceived by a single specialist anaesthesiologist and was envisioned as an anaesthesiologist-led service, using existing staff within our inpatient pain service (2 part-time clinical nurse consultants [CNCs]; one 3-month rotational anaesthesia registrar; and one anaesthesiologist rostered for one session [half a day] per weekday). This anaesthesiologist independently assessed all referred patients, formulated all patients' perioperative pain plans, either personally consulted with or coordinated through other inpatient pain staff to have each POPPMED inpatient seen on a daily basis postoperatively, and was primary contact for all pre- and postoperative POPPMED pain plan queries from nursing and surgical staff. All patients referred to POPPMED, regardless of preoperative OMEDDs or planned procedure type, had a perioperative pain plan formulated and delivered. A summary of the interventions offered by POPPMED are shown in Figure 1; the timeline over which interventions were delivered is shown in Figure 2. Owing to the highly variable time of referral to time of surgery, interventions were not always delivered both pre- and

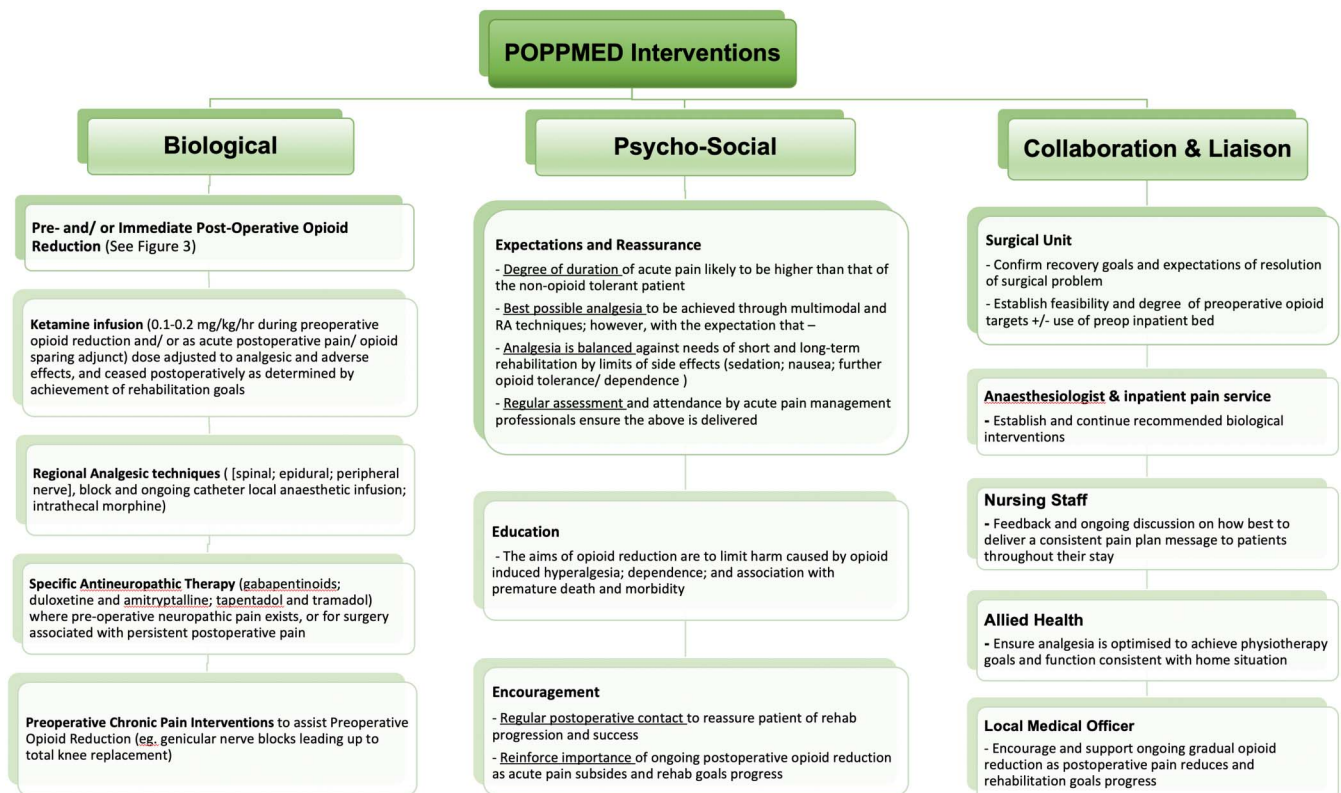


Figure 1. Perioperative pain management, education, and de-escalation interventions. POPPMED, perioperative pain management, education, and de-escalation; RA, regional analgesia.

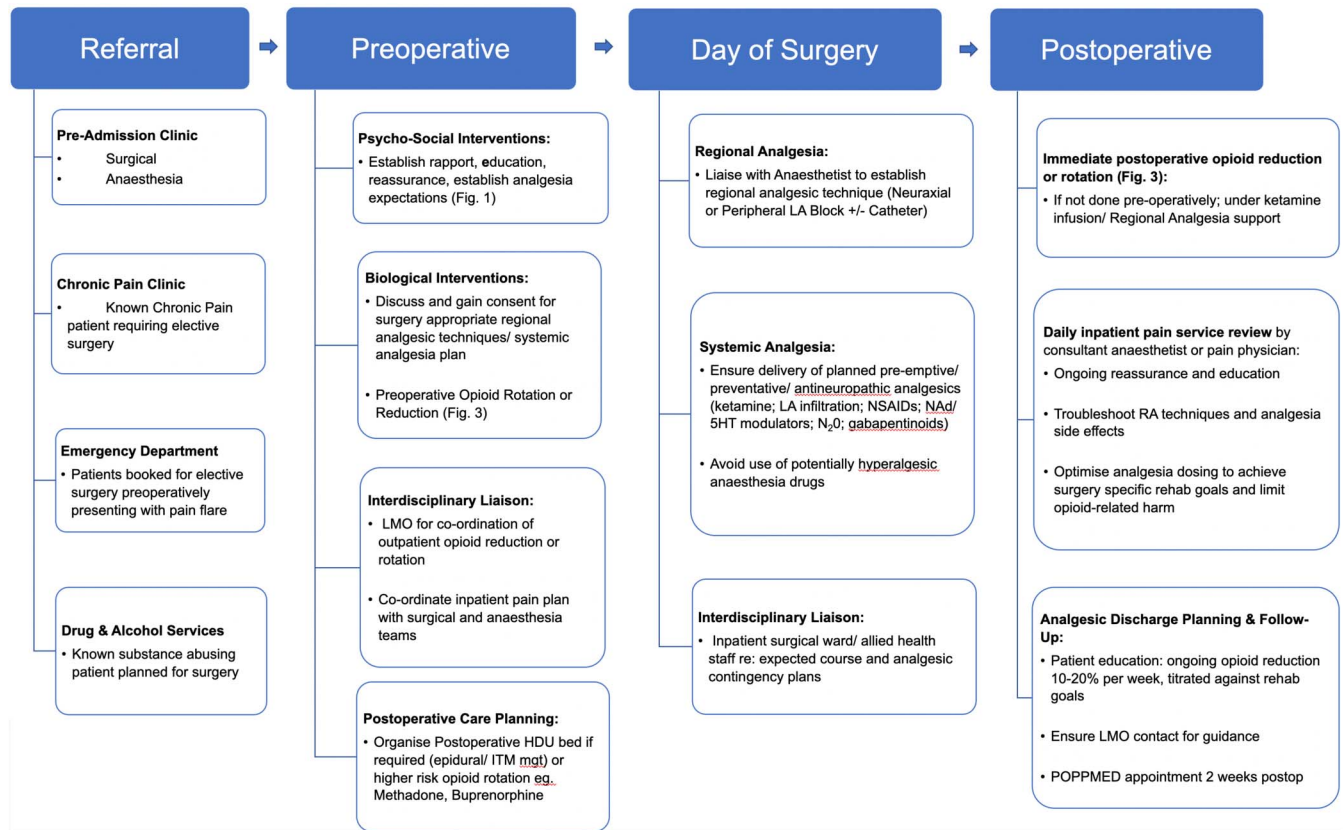


Figure 2. Perioperative pain management, education, and de-escalation management timeline. HDU, high dependency unit; ITM, intrathecal morphine; LA, local anaesthetic; LMO, local medical officer; NSAID, nonsteroidal anti-inflammatory drug; NAd, noradrenaline; 5HT, 5-Hydroxy-Tryptamine; N₂O, nitrous oxide; POPPMED, perioperative pain management, education, and deescalation.

postoperatively, and restriction to postoperative intervention alone was often encountered.

Patients were educated and engaged regarding expectations surrounding the services' primary means of OMEDD reduction (Figs. 1 and 3).

- (1) Expectations of best possible postoperative analgesia through the use of multimodal nonopioid systemic analgesia, ketamine infusions, or regional analgesia, where patient consent permitted.
- (2) Preoperative, or immediate postoperative opioid rotation, comprising
 - (a) An initial reduction of 50% OMEDDs based on approximate 50% incomplete opioid cross-tolerance and expected improvement in analgesic efficacy; and discharge target of a further 20% to 30% OMEDD reduction of fixed daily opioid with titration of additional opioid analgesia to rehabilitation goals or clinical features of opioid withdrawal.
 - (b) After discharge, ongoing reduction of daily postoperative OMEDDs titrated against markers of functional impairment, rather than pain rating scales alone.
- (3) OR, acute perioperative reduction of OMEDDs to attempt to minimise opioid tolerance in the face of potential persistent postoperative pain; to alleviate any component of opioid-induced hyperalgesia; and to reduce longer-term risk of morbidity and mortality associated with high discharge and postdischarge OMEDDs.

The principles of the POPPMED service were provision of biological interventions as well as psychosocial empowerment (Fig. 1). Interdisciplinary liaison was a key aspect of the service (Fig. 1) throughout patients' perioperative journey (Fig. 2). Pre- or immediate postoperative opioid rotation reduction was a

prominent systemic analgesic intervention used; engagement of the surgical unit was critical to enable potential inpatient preoperative opioid reduction or rotation if circumstances permitted (Fig. 3). The impact of continuity and regular psychosocial reinforcement of the goals of long-term OMEDD reduction with POPPMED patients could not be overemphasized; postoperative follow-up and local medical officer (LMO) liaison during the critical 2- to 6-week postoperative period enabled optimisation of the ongoing postoperative pain plan (Fig. 2). The patient-centred and context-specific nature of the service meant that the precise formula of interventions delivered were varied depending on the needs of the patient (Figs. 1–3).

The POPPMED anaesthesiologist adjusted each patient's pain plans after daily assessment, based on analgesic efficacy, presence of any clinical features of opioid withdrawal, and patient progress in postoperative recovery milestones (eg, First sit-out-of-bed and deep breath/cough efficacy after major abdominal surgery; first stand/assisted ambulation after lower limb orthopedic surgery). Postoperative opioid reduction was usually begun on the procedure-specific postoperative day where a non-opioid-tolerant patient would be expected to have an improvement in acute pain, with a view to ongoing reductions of 10% to 20% every 2 to 5 days.

Where possible, the POPPMED anaesthesiologist personally communicated reassurance and encouragement to patients on each postoperative day regarding their success in maintaining opioid reduction, achievement of postoperative rehabilitation goals, and the specific interventions being done to assist where analgesia was perceived by the patient as being inadequate. On day of discharge, the POPPMED anaesthesiologist discussed

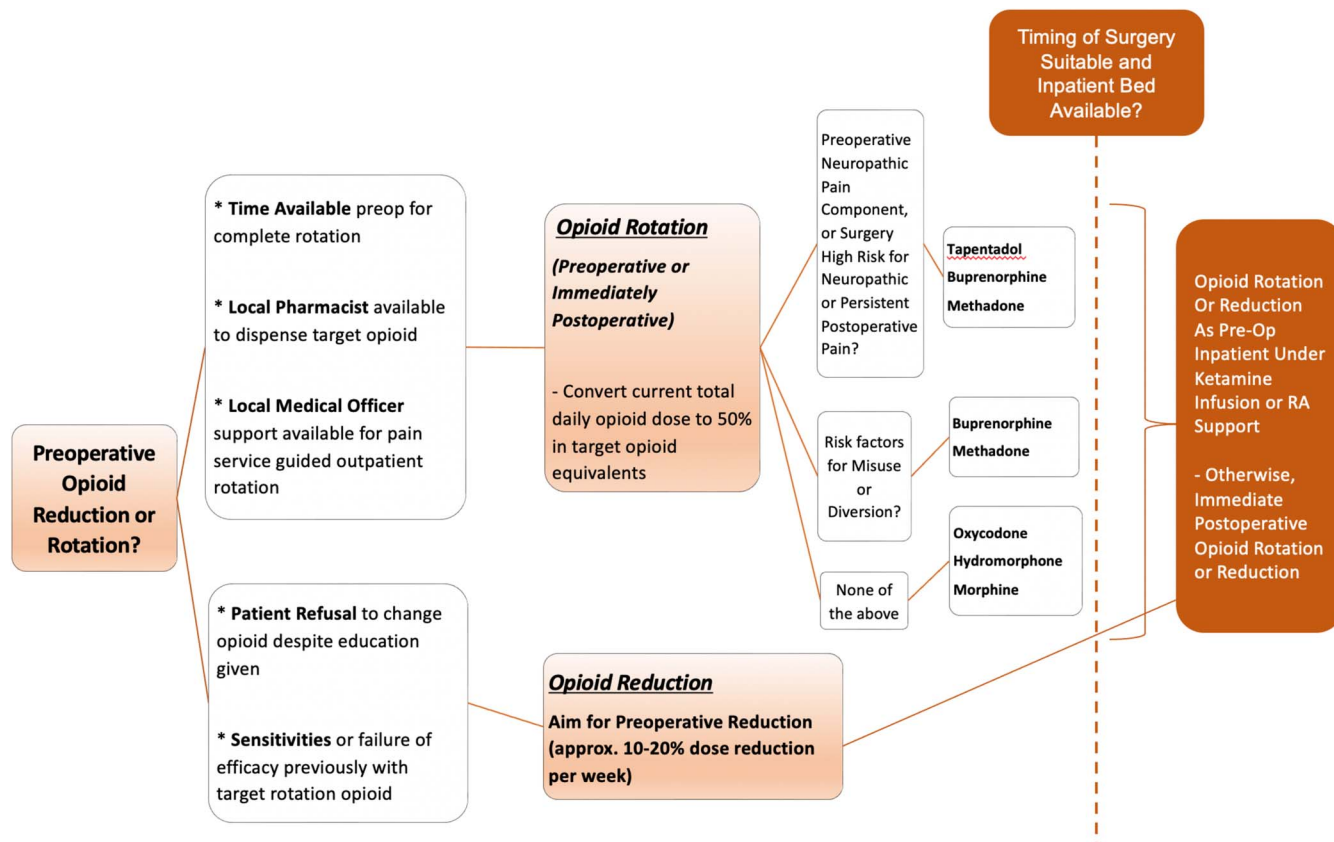


Figure 3. Perioperative pain management, education, and de-escalation opioid rotation or reduction management pathway. RA, regional analgesia.

with the patient and liaised directly with surgical junior medical staff to advise on the discharge opioid prescription plan and communicated this plan directly with the patient’s outpatient opioid prescriber.

The POPPMED STROBE (Strengthening Reporting of Observational Studies in Epidemiology) flow diagram is shown in Figure 4.

2.1. Data collection and stratification

Approval for collection of patient information was granted by Austin Health HREC (Approval# 19/Austin/124). We collected data from all patients referred to our POPPMED service from 2017 to 2019 who were treated with >50 OMEDDs preoperatively, a conservative estimate of the OMEDD use associated with opioid tolerance as per the Australian & New Zealand College of Anaesthetists Faculty of Pain Medicine (ANZCAFPM) official document on the use of opioid analgesics in patients with chronic noncancer pain.³ Patient demographic data, length of hospital stay, and discharge OMEDDs were obtained from hospital document and electronic records. Opioid doses were converted to OMEDDs via the ANZCA official conversion table.¹² Sustained opioid reduction was assessed by direct contact and discussion with each patient’s outpatient opioid prescriber between 6 and 12 months postoperatively and corroborated by information obtained via SafeScript, an online Victorian State Government initiative whereby any opioids prescribed and dispensed by any pharmacy in Victoria are recorded and identified by patient name, address, and date of birth. We separated analysis of efficacy of opioid reduction between

patients who were treated with 50 to 90 preoperative OMEDDs and those on 90 preoperative OMEDDs and higher, based on established data describing increased harm at these higher doses.²⁵ To establish the relative safety and efficacy of the opioid therapy used in POPPMED pain plains, we compared POPPMED patients’ postoperative day-1 to day-3 11-point Numerical Rating Scale (NRS-11:hours) area-under-the-curve (AUC) measurements at rest and on movement and modified McIntyre Sedation Score (appendix 1, available at <http://links.lww.com/PR9/A167>) AUC in a control cohort of non-POPPMED patients receiving similar proportions of surgery subtypes within the pre-POPPMED 15-month period. To establish the relative effect of the POPPMED program on postoperative length of stay, comparative length of stay data from this control cohort was also obtained. Patients were selected for this control cohort chronologically in reverse from the time of POPPMED initiation, until reaching a similar total number of non-POPPMED patients receiving equivalent proportions of subspecialty surgery was achieved. To further clarify the efficacy and safety of POPPMED interventions, the frequency of Respond Medical Emergency Team (MET) calls for altered conscious state, severe or uncontrolled pain, or low respiratory rate was compared in surgical patients 15 months after and before the initiation of POPPMED.

Comparative analgesia, sedation score, and MET data were collected through our hospital’s electronic nursing observations records (Cerner Millennium electronic medical records, Missouri, USA).

In order to account for the varying levels of acute postoperative pain between different surgical procedures, patients’ operations were classified arbitrarily into an ordinal scale (Table 1).

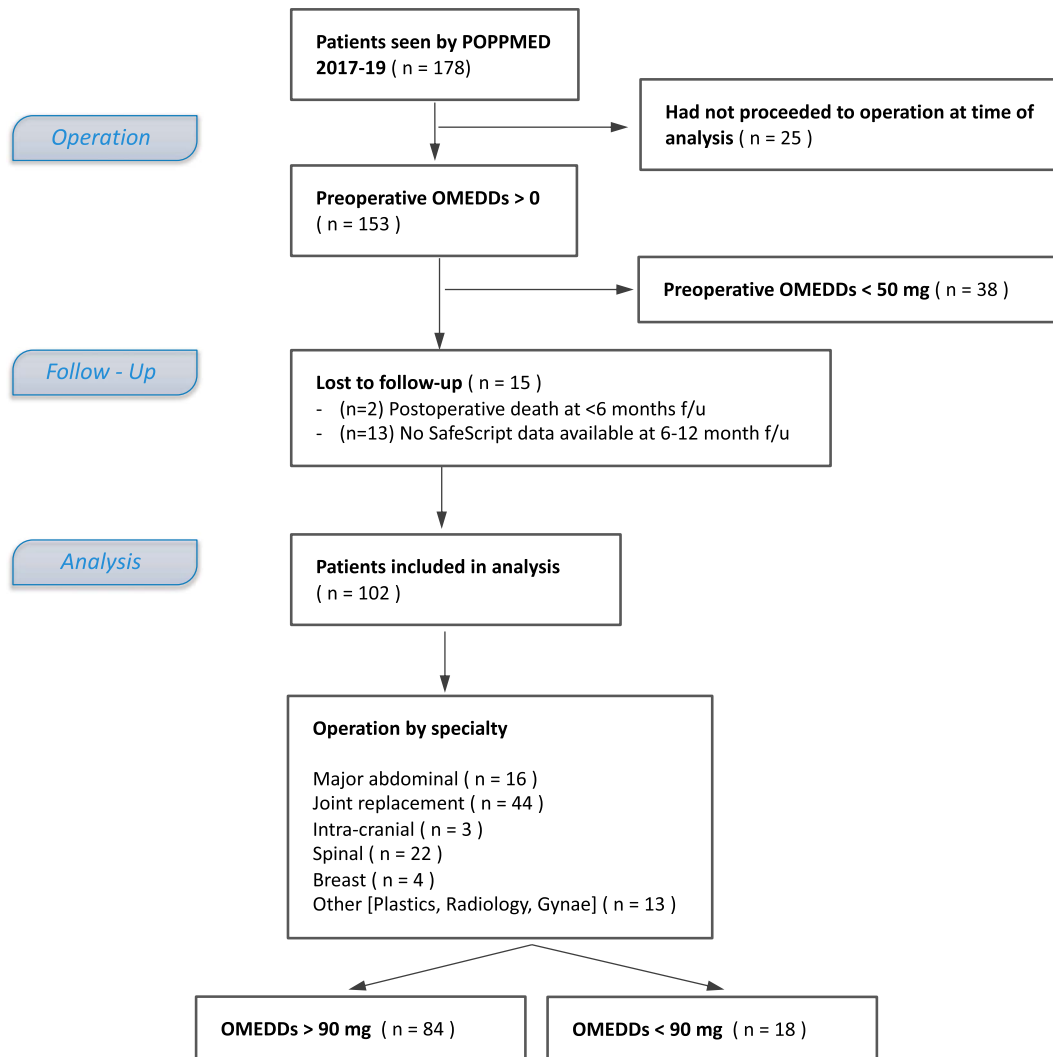


Figure 4. Perioperative pain management, education, and de-escalation STROBE diagram. OMEDDs, oral morphine equivalent daily dosages; POPPMED, perioperative pain management, education, and de-escalation; STROBE, strengthening reporting of observational studies in epidemiology; f/u, follow-up.

2.2. Statistical analysis

Oral morphine equivalent daily dosage, NRS-11 pain assessment, sedation score, and hospital length of stay data were deemed nonparametric by histogram and Kolmogorov–Smirnov normality testing, with corresponding descriptive metrics and inferential tests used. We used χ^2 tests for inferential comparisons of proportions. To examine the effect of individual interventions on hospital length of stay and degree of long-term OMEDD reduction, we used multivariate linear regression to assess the relative effect of regional analgesia, use of ketamine infusions, use of acute or preoperative opioid rotation, surgery type, and relationship of chronic pain source to surgery site. We did not perform inferential analyses comparing the length of stay to non-POPPMED patients due to small sample sizes within individual operation types.

3. Results

We present data from 102 patients in the first 2 years of our POPPMED anaesthesiologist-led service and comparative pain, sedation score, and MET call data from 94 non-POPPMED patients in the 15 months before POPPMED initiation, who received standard anaesthesia and postoperative analgesic care.

Surgical and demographic data are listed in **Table 1**; our primary outcome measures displayed in **Table 2** and **Figures 5 and 6**; and secondary outcome data listed in **Table 2** and Appendices 2–4 (available at <http://links.lww.com/PR9/A167>). There were no significant differences in demographic characteristics (age, sex, ASA, surgical subtype) between POPPMED and non-POPPMED cohorts. The majority of procedure types were major surgery requiring multiple days of length of stay (87%; 89 POPPMED patients). Approximately half of POPPMED patients either declined acute opioid rotation despite our recommendations or were deemed inappropriate. Ketamine infusions were delivered to the majority of POPPMED patients. No attempt was made perioperatively to reduce patient’s background opioid if their regular opioid was prescribed for substance abuse-related opioid replacement therapy (eg, suboxone, methadone), and hence, these patients were not included in the analysis of results. 3 POPPMED patients had cancer-related pain as the indication for preoperative opioid prescription.

For those POPPMED patients with >90 mg of preoperative OMEDDs, median reduction on discharge was 35% (–52 mg [118 mg]) and even greater up to 1 year later (60%; –90 mg [86 mg]), whereas in patients with <90 mg of preoperative OMEDDs, reduction was not achieved by discharge (+18 mg [46 mg])

Table 1
Patient and surgical characteristics.

Operation type	Frequency (#/%)	Surgical subtype	POPPMED (102 pts) #Pts	Non-POPPMED (94 pts) #Pts
<i>P</i> = 0.53				
Orthopedic	47 (46%)	Hip arthroplasty	21	18
		Knee arthroplasty	17	18
		Total shoulder replacement	4	7
		Arthroscopic shoulder intervention	6	4
Abdominal	21 (20%)	Open incision >7 cm	9	11
		Open incision <7 cm	7	6
		Laparoscopic	5	4
Spinal	20 (20%)	Cervico/Thoracic	5	2
		Lumbar	15	10
Cranial neurosurgery	3 (3%)		3	5
Breast	5 (5%)	Mastectomy	4	6
		Wide local excision and node biopsy	1	2
Other minor	6 (6%)		6	1
Demographics	POPPMED cohort Mean/SD or # (%)	Non-POPPMED cohort	<i>P</i>	
Age*	62 (15)	59 (13)	0.13	
ASA	2: 11 patients 3: 81 patients 4: 10 patients	2: 18 patients 3: 70 patients 4: 6 patients	0.2	
Sex	Male 36 (36%)	Male 45 (4%)	0.06	
POPPMED cohort	No. (%)			
Operative pain site vs chronic pain site	41 patients had their chronic pain site distinct from surgical site (41%)			
Surgery type & postoperative pain severity—ordinal category				
1	Breast wide local excision; endoscopy; peripheral vascular angiography/angioplasty; superficial surgery	9 (9%)		
2	Internal fixation distal long bones; single-level spinal surgery; laparoscopic abdominal surgery; mastectomy	14 (13%)		
3	Total hip replacement; total shoulder replacement; multi-level spinal surgery; open abdominal surgery incision <7 cm	65 (64%)		
4	Total knee arthroplasty; open abdominal surgery incision >7 cm	14 (12%)		

* Values are median (IQR).

ASA, American Society of Anesthesiologists risk score; IQR, inter-quartile range; POPPMED, perioperative pain management, education, and de-escalation.

P = 0.17). Reduction in the longer term was marked however (50% [22 mg], **Table 2**). These OMEDD reductions were achieved despite no significant differences in postoperative day-1 to day-3 NRS-11 AUC pain assessments at rest and on movement between pre-POPPMED and post-POPPMED cohorts (**Table 2**). Pre-POPPMED cohort OMEDDs on discharge were significantly less than the POPPMED cohort, with no significant difference in sedation score:hours AUC.

The difference in frequency of postoperative MET call emergency responses for severe/uncontrolled pain or altered conscious state between the 15-month period of our POPPMED service case series and the same period prior was also not statistically significant; MET call responses for low respiratory rate

in fact decreased over the POPPMED period (Appendix 2, available at <http://links.lww.com/PR9/A167>).

The 13 patients in whom long-term follow-up failed were assumed to be secondary to the patient moving interstate or that the patients' usual prescriber had been informed of this or had lost contact with the patient. It was possible that some of these patients may have remained in Victoria and had ceased the use of any opioid whatsoever, but this was not assumed in the results. Missing data were not imputed. Length of stay appeared most significantly increased for POPPMED patients who received total hip replacement, mastectomy, and spinal surgery but not so in other surgical subtypes (Appendix 2, available at <http://links.lww.com/PR9/A167>).

On multivariate linear regression analysis, pain severity of surgery type; background chronic pain site relation to surgery; preoperative and discharge OMEDDs; use of ketamine infusion, regional analgesia, or acute opioid rotation use; and the type of rotation opioid had no statistically significant effect on POPPMED patient length of stay (Appendix 3, available at <http://links.lww.com/PR9/A167>). When adjusted for the above covariates, only increased preoperative OMEDDs had a statistically significant effect on greater 6- to 12-month OMEDD reduction (unstandardized beta coefficient 1.1 increase in OMEDD reduction for every 1 mg of preoperative OMEDD, *P* = 0.01) (Appendix 4, available at <http://links.lww.com/PR9/A167>).

4. Discussion

The morbidity and adverse health economic effects associated with chronic high OMEDD use in Australia (defined by ANZCA as ≥ 50 mg¹²) are well-recognized. In Victoria, Australia alone, opioid-related hospital admissions increased 6.8% per year between 2006 and 2014.⁵ The lack of effect of regulatory interventions (removal of codeine; tamper-resistant opioid formulations) has given rise to the call for targeted, multidisciplinary pain management strategies focused on containing excessive use of opioid analgesia.¹⁹

The perioperative period has historically been viewed as an inappropriate time to reduce patient's baseline OMEDDs; common practice was to increase patient's opioids by at least 20% for acute pain and target a reduction back to baseline OMEDDs within the following week.²¹ Despite the seemingly difficult task of reducing both inpatient discharge and longer-term OMEDDs in opioid-tolerant patients after surgery, dedicated multidisciplinary teams in North America have successfully achieved these goals.⁸ The Toronto General Hospital Transitional Pain Service (TGHTPS) is an outpatient preoperative, immediate inpatient postoperative, and outpatient postoperative program with funding for pain physiotherapists, pain psychologists, 5 dedicated anaesthesiology pain specialists, and 3 clinical pain nurse consultants. Our novel POPPMED program has demonstrated efficacy in achieving similar, if not greater, long-term OMEDD reductions (60% in POPPMED patients with >90 mg of preoperative OMEDDs vs 44% at the TGHTPS in opioid-tolerant patients) in the Australian context with the addition of a single anaesthesiologist to our hospital's existing inpatient pain staffing. Inpatient pain psychology is not funded in Australia; traditionally, pain psychology has formed a critical arm of chronic pain management and was pivotal in the success of the TGHTPS through their utilization of the "accept and commit" approach⁹ to opioid reduction. However, without formal psychology training, our POPPMED anaesthesiologist instead achieved a similar sense of engagement, empowerment, and ownership with patient's regulation of their analgesics (**Fig. 1**).

Table 2

Oral morphine equivalent daily dosages outcomes and comparative analgesic outcomes.

POPPMED cohort	All POPPMED patients (102 patients)	50–90 OMEDD POPPMED patients [18 patients (18%)]	>90 OMEDD POPPMED patients [84 patients (82%)]
Preoperative OMEDDs†	115 mg (114 mg)	62 mg (18 mg)	150 mg (126 mg)
Discharge OMEDDs	90 mg (60 mg)	79 mg (58 mg)	98 mg (60 mg)
<i>P</i> (vs Preop OMEDDs)	<0.0001	0.17	<0.0001
OMEDDs at 6–12 mo	60 mg (70 mg)	25 mg (49 mg)	60 mg (57 mg)
<i>P</i> (vs Preop OMEDDs)	<0.0001	0.02	<0.0001
Perioperative ketamine infusion used at 0.1–0.2 mg/kg/h		69 patients (67%)	
Regional analgesic technique used‡		45 patients (44%)	
Acute opioid rotation used	32 patients (31%)	Rotation opioid	Patients (no. [%])
		Tapentadol	12 (38%)
		Hydromorphone	8 (25%)
		Methadone	5 (16%)
		Buprenorphine	3 (9%)
		Morphine	2 (6%)
		Oxycodone	1 (3%)

Comparative postoperative day-1 to day-3 outcomes (POPPMED vs non-POPPMED cohort)

	POPPMED (102 patients)	Non-POPPMED (94 patients)	<i>P</i>
NRS-11:hours AUC on movement	105 (136)	92 (121)	0.56
NRS-11:hours AUC at rest	87 (89)	65 (102)	0.24
Sedation score:hours AUC	2 (11)	2 (6)	0.13
Discharge OMEDDs	90 mg (60 mg)	22 mg (27 mg)	<0.0001

† Values are median (IQR).

‡ Including epidural catheter infusion, single shot peripheral nerve or plexus block or catheter, and intrathecal morphine, but not including single shot spinal anaesthesia.

AUC, area under the curve; NRS, numerical rating scale; OMEDD, oral morphine equivalent daily dosage; POPPMED, perioperative pain management, education, and de-escalation.

The much greater impact of POPPMED on long-term opioid reduction in patients on higher preoperative OMEDDs was an unexpected result in our analysis. Our multivariate analysis

confirms that there are no single interventions that individually are responsible for this effect (Appendix 4, available at <http://links.lww.com/PR9/A167>); rather, those patients with preoperative OMEDDs 50 to 90 mg appear to have a smaller proportional

<90 Pre-op OMEDDs: Discharge and 6-12 months Opioid

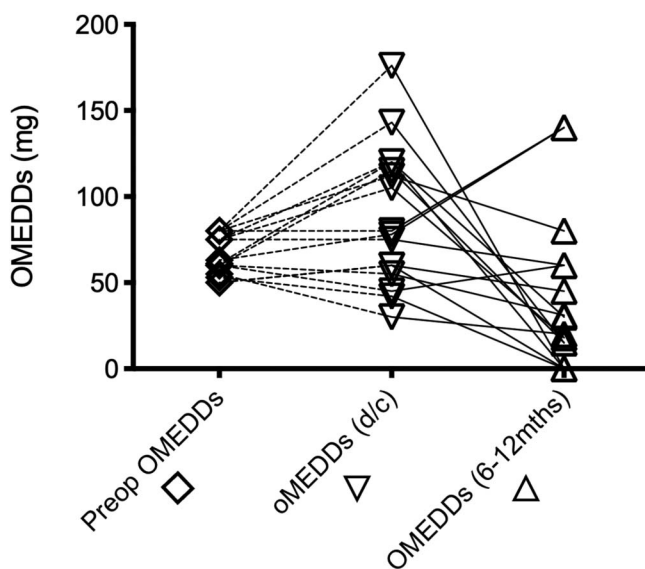


Figure 5. Patients treated with 50 to 90 mg of preoperative oral morphine equivalent daily dosages: preoperative, hospital discharge, and 6- to 12-month postoperative oral morphine equivalent daily dosages. Each individual data point represents a single patient’s opioid dose at the specified perioperative stage. OMEDDs, oral morphine equivalent daily dosages.

>90 Pre-op OMEDDs: Discharge and 6-12 months Opioid

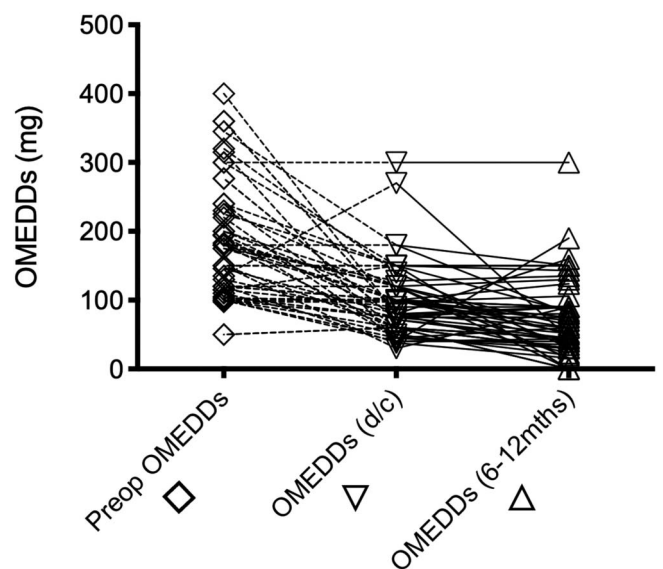


Figure 6. Patients treated with >90 mg of preoperative oral morphine equivalent daily dosages: preoperative, hospital discharge, and 6- to 12-month postoperative oral morphine equivalent daily dosages. Each individual data point represents a single patient’s opioid dose at the specified perioperative stage. OMEDDs, oral morphine equivalent daily dosages.

reduction to make when faced with their surgery and its associated postoperative analgesic requirements. Nevertheless, the remarkable gains made in those with higher preoperative OMEDDs reinforces the utility of POPPMED and similar programs for targeting patients at higher risk of long-term opioid-related harm.^{11,17} Moreover, this was achieved without significant differences in postoperative day-1 to day-3 NRS-11:hours AUC pain assessments at rest and on movement when compared with a similar surgical cohort of non-POPPMED patients. We predicted some impact on the length of stay (LOS) because of the time taken to establish an opioid weaning trajectory and ensure adequate recovery for POPPMED patients. Within the limitations of the small numbers within surgical subtypes, the largest delay in LOS was a median difference of 4 days after total hip replacement and spinal surgery, whereas other major surgery (abdominal, cranial neurosurgery, total knee arthroplasty) was unaffected. This disparate result suggests that the POPPMED approach per se does not consistently impair attainment of rehabilitation goals and discharge; however, this result must be interpreted with caution because we could not select for similar opioid-tolerant patients in the pre-POPPMED period.

Opioid rotation is commonly used in chronic and cancer pain settings.¹⁵ Its structured use in our POPPMED program for the purpose of analgesic efficacy and perioperative OMEDD reduction is a more novel application in the acute perioperative scenario. Its proposed efficacy is based on the concept of tolerance to the analgesic effects of a chronically administered opioid, whereupon incomplete cross-tolerance to a structurally different opioid improves the analgesic response for a given equi-analgesic dose of that opioid.²⁶ As variability of cross-tolerance has been implicated in narcosis during opioid rotation²⁹ we aggressively underestimated opioid equivalence, ensured adequate breakthrough opioid to account for any error, and closely assessed patients for features of withdrawal or narcosis. With the exception of responses for low respiratory rate (which was in fact improved over the POPPMED service time period) our MET Response findings confirm that frequency of postoperative MET Call activation for altered conscious state or severe/uncontrolled pain was not statistically significantly different from the same time period prior, suggesting that our application of acute opioid rotation did not incur significant under- or over-prescription of opioid analgesia. This result is more meaningful when considering the older, higher-risk sample in our study.

Our choice of destination opioid when rotating was guided by prior patient experience with other opioids; presence of suspected neuropathic pain component (favouring the selection of buprenorphine¹⁴; methadone²; or tapentadol¹³); and clinical assessment of psychological patient traits that may predispose to longer-term escalation in self-administered doses with opioids known to have a high affinity for reward centre stimulation.¹⁸ In this circumstance we endeavoured to avoid selection of oxycodone¹⁶ and morphine.²⁷ Practical considerations (difficulty sourcing patients' local pharmacies or general practitioners able to, or familiar with, prescription of outpatient opioids such as buprenorphine or methadone) were also evaluated. The majority of rotated patients' "destination" opioid was tapentadol or hydromorphone, chiefly due to the suspicion of neuropathic pain or practical considerations.

With its analgesic efficacy in opioid-tolerant patients,⁴ we used ketamine infusions in more than half of all POPPMED patients, with no identified cases of side effect-related MET Emergency Response calls. Ketamine's preventative analgesic effects have an established perioperative role, reducing opioid requirements and related side effects,¹⁰ and reducing acute⁷ and chronic

postoperative pain.²⁰ We reserved the use of ketamine analgesia for procedures predicted to cause at least moderate postoperative pain or to provide transitional analgesia for periprocedural opioid reduction. Regional analgesia also enhances perioperative analgesia while reducing opioid requirements^{1,24,30} and was also frequently employed, with almost half of POPPMED patients received epidural, peripheral nerve, or intrathecal morphine analgesia.

Our study is limited by various factors. Inferences drawn from the data presented in our study are chiefly limited by its retrospective nonrandomised nature, lack of a control arm with respect to our long-term OMEDD outcome measures, and small sample size. Although our multivariate analysis revealed that the degree of long-term OMEDD reduction was not affected by whether surgery impacted the source of chronic pain, this is not a surrogate for a control arm and may be underpowered (subject to type 2 error) given the sample size. While we have demonstrated similar early postoperative analgesia in our POPPMED cohort compared with non-POPPMED patients, we have not reported long-term postoperative pain assessments. Although the majority of POPPMED patients were primarily managed by a single anaesthesiologist, we could not guarantee that the level of patient rapport or engagement was identical with other POPPMED team members. We placed importance on the use of an arbitrary postoperative pain category dependent on procedure type, in an effort to stratify for known very painful procedures (eg, total knee arthroplasty) against known mildly painful procedures (eg, simple mastectomy) and their effects on outcomes; however, this scale is lacking in validation. Our study cohort is heterogeneous, with small numbers of patients with a mixture of prescribed preoperative opioid use, and cancer-related pain. Due to these small subgroup sizes, we did not perform additional subgroup analyses to quantify the effects of these confounders. Selection of patients for our non-POPPMED cohort was performed in chronological reverse order by surgical subspecialty before the initiation of POPPMED, so cannot strictly be considered an absolute control group. Finally, our use of SafeScript data and corroboration with patients' general practitioners to measure long-term OMEDDs cannot account for opioid obtained outside of prescribed channels.

5. Conclusions

A single, anaesthesiologist-led, perioperative pain service, using ketamine, regional, and acute opioid rotation analgesia in selected cases, can achieve long-term OMEDD reductions safely and with equivalent quality in postoperative analgesia in opioid-tolerant patients receiving surgery in an Australian tertiary health care institution. This effect is most pronounced in patients treated with higher preoperative OMEDDs and had surgery-specific and variable effects on the length of stay. No single intervention from the service has a statistically significant effect alone, confirming that multiple biological interventions together with nonexpert application of basic psychological support in the form of patient education, reassurance, and engagement can achieve sustained postoperative OMEDD reduction.

Disclosures

The authors declare that the manuscript is a transparent and accurate report of the research undertaken, and that there are no conflicts of interest to disclose.

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This study was not preregistered. No financial or material support was supplied outside of routine clinical practice. The authors have

elected not to provide access to our data set based on privacy concerns of potentially sensitive re-identifiable patient data.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PR9/A167>.

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References

- [1] Andreae MH, Andreae DA. Regional anaesthesia to prevent chronic pain after surgery: a cochrane systematic review and meta-analysis. *Br J Anaesth* 2013;111:711–20.
- [2] Anghelescu DL, Faughnan LG, Hankins GM, Ward DA, Oakes LL. Methadone use in children and young adults at a cancer center: a retrospective study. *J Opioid Manag* 2011;7:353–61.
- [3] ANZCA. PS01(PM)-statement-regarding-the-use-of-opioid-analgesics-in-patients-with-chronic-non-cancer-pain.pdf. FPMANZCA Prof Doc 2020. Available: [https://www.anzca.edu.au/getattachment/7d7d2619-6736-4d8e-876e-6f9b2b45c435/PS01\(PM\)-Statement-regarding-the-use-of-opioid-analgesics-in-patients-with-chronic-non-cancer-pain](https://www.anzca.edu.au/getattachment/7d7d2619-6736-4d8e-876e-6f9b2b45c435/PS01(PM)-Statement-regarding-the-use-of-opioid-analgesics-in-patients-with-chronic-non-cancer-pain). Accessed August 28, 2021.
- [4] Barreveld AM, Correll DJ, Liu X, Max B, McGowan JA, Shovel L, Wasan AD, Nedeljkovic SS. Ketamine decreases postoperative pain scores in patients taking opioids for chronic pain: results of a prospective, randomized, double-blind study. *Pain Med* 2013;14:925–34.
- [5] Berecki-Gisolf J, Hassani-Mahmoodei B, Clapperton A, McClure R. Prescription opioid dispensing and prescription opioid poisoning: population data from Victoria, Australia 2006 to 2013. *Aust N Z J Public Health* 2017;41:85–91.
- [6] Blanch B, Pearson S-A, Haber PS. An overview of the patterns of prescription opioid use, costs and related harms in Australia. *Br J Clin Pharmacol* 2014;78:1159–66.
- [7] Brinck EC, Tiippana E, Heesen M, Bell RF, Straube S, Moore RA, Kontinen V. Perioperative intravenous ketamine for acute postoperative pain in adults. *Cochrane Database Syst Rev* 2018;12:CD012033.
- [8] Clarke H, Azargive S, Montbriand J, Nicholls J, Sutherland A, Valeeva L, Boullis S, McMillan K, Ladak SSJ, Ladha K, Katznelson R, McRae K, Tamir D, Lyn S, Huang A, Weinrib A, Katz J. Opioid weaning and pain management in postsurgical patients at the Toronto general hospital transitional pain service. *Can J Pain* 2018;2:236–47.
- [9] Dindo L, Zimmerman MB, Hadlandsmyth K, StMarie B, Embree J, Marchman J, Tripp-Reimer T, Rakel B. Acceptance and commitment therapy for prevention of chronic postsurgical pain and opioid use in at-risk veterans: a pilot randomized controlled study. *J Pain* 2018;19:1211–21.
- [10] Ding X, Jin S, Niu X, Wang T, Zhao X, Ren H, Tong Y, Li Q. Morphine with adjuvant ketamine versus higher dose of morphine alone for acute pain: a meta-analysis. *Int J Clin Exp Med* 2014;7:2504–10.
- [11] Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, Weisner CM, Silverberg MJ, Campbell CI, Psaty BM, Von Korff M. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med* 2010;152:85–92.
- [12] Faculty of Pain Medicine, Australian & New Zealand College of Anaesthetists. Opioid dose equivalence—calculation of oral morphine equivalent daily dose (oMEDD). *Prof Doc* 2015; PM01 (Appx 2). Available: <https://fpm.anzca.edu.au/documents/opioid-dose-equivalence.pdf>. Accessed July 30, 2019.
- [13] Freo U, Romualdi P, Kress HG. Tapentadol for neuropathic pain: a review of clinical studies. *J Pain Res* 2019;12:1537–51.
- [14] Hans G. Buprenorphine—a review of its role in neuropathic pain. *J Opioid Manag* 2007;3:195–206.
- [15] Huxtable CA, Roberts LJ, Somogyi AA, Macintyre PE. Acute pain management in opioid-tolerant patients: a growing challenge. *Anaesth Intensive Care* 2011;39:804–23.
- [16] Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. Monitoring the future national survey results on drug use, 1975–2009: Volume II, College students and adults ages 19–50 (NIH Publication No. 10-7585). Bethesda, MD: National Institute on Drug Abuse, 2010. Available at: <https://files.eric.ed.gov/fulltext/ED514367.pdf>. Accessed August 14, 2020.
- [17] Kidner CL, Mayer TG, Gatchel RJ. Higher opioid doses predict poorer functional outcome in patients with chronic disabling occupational musculoskeletal disorders. *J Bone Joint Surg Am* 2009;91:919–27.
- [18] Kosten TR, George TP. The neurobiology of opioid dependence: implications for treatment. *Sci Pract Perspect* 2002;1:13–20.
- [19] Larance B, Degenhardt L, Peacock A, Gisev N, Mattick R, Colledge S, Campbell G. Pharmaceutical opioid use and harm in Australia: the need for proactive and preventative responses. *Drug Alcohol Rev* 2018;37: S203–5.
- [20] McNicol ED, Schumann R, Haroutounian S. A systematic review and meta-analysis of ketamine for the prevention of persistent post-surgical pain. *Acta Anaesthesiol Scand* 2014;58:1199–213.
- [21] Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology* 2004;101:212–27.
- [22] Mudumbai SC, Oliva EM, Lewis ET, Trafton J, Posner D, Mariano ER, Stafford RS, Wagner T, Clark JD. Time-to-cessation of postoperative opioids: a population-level analysis of the veterans affairs health care system. *Pain Med* 2016;17:1732–43.
- [23] Richebé P, Beaulieu P. Perioperative pain management in the patient treated with opioids: continuing professional development. *Can J Anesth* 2009;56:969–81.
- [24] Richman JM, Liu SS, Courpas G, Wong R, Rowlingson AJ, McGready J, Cohen SR, Wu CL. Does continuous peripheral nerve block provide superior pain control to opioids? A meta-analysis. *Anesth Analg* 2006; 102:248–57.
- [25] Risks of prescribing high dose opioids—for health professionals. Victorian Department of Health, Australia: safer use of opioids; 2016; NPS MedicineWise. Available at: <https://www.health.vic.gov.au/sites/default/files/migrated/files/collections/policies-and-guidelines/safe-opioid-use/risks-of-prescribing-high-dose-opioids—for-health-professionals.pdf>. Accessed August 30, 2020.
- [26] Simpson GK, Jackson M. Perioperative management of opioid-tolerant patients. *BJA Educ* 2017;17:124–8.
- [27] Stafford J, Burns L. National drug and alcohol research centre (Australia), Illicit drug reporting system (Australia). Australian drug trends 2014: findings from the Illicit drug reporting system (IDRS). University of New South Wales, Sydney, Australia: National Drug and Alcohol Research Centre, 2015.
- [28] Statement on the use of slow-release opioid preparations in the treatment of acute pain. ANZCA; 2018. Available at: <https://www.anzca.edu.au/getattachment/243f608f-8ea9-4a8c-bb86-eb19dc26a04f/ANZCA-Bulletin-March-2018>. Accessed June 21st, 2020.
- [29] Webster LR, Fine PG. Review and critique of opioid rotation practices and associated risks of toxicity. *Pain Med* 2012;13:562–70.
- [30] Werawatganon T, Charuluxanun S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. *Cochrane Database Syst Rev* 2005; CD004088.