Observational study

Edward Ho*, Matthew Doherty, Robert Thomas, John Attia, Christopher Oldmeadow and Matthew Clapham

Prescription of opioids to post-operative orthopaedic patients at time of discharge from hospital: a prospective observational study

https://doi.org/10.1515/sjpain-2017-0149
Received October 16, 2017; revised January 18, 2018; accepted January 30, 2018; previously published online February 23, 2018

Abstract

Background and aims: Excessive opioid prescribing can lead to adverse consequences including stockpiling, misuse, dependency, diversion and mortality. Increased prescriptions to post-operative inpatients as part of their discharge planning may be a significant contributor. Primary aims included comparing the amount of opioids prescribed, consumed, left unused and their relationship with pain and functionality.
Methods: A total of 132 consecutive patients who underwent elective orthopaedic surgery were prospectively audited. Daily oral morphine equivalent (DME) of opioids prescribed was compared with opioids consumed and amount left unused 7–10 days after discharge. For analysis, patients were split into three groups: total knee replacement (TKR), hand surgery (Hands), and miscellaneous (Misc).
Results: The mean dose of opioid prescribed per patient was 108.5 mg DME. TKR consumed 33–35% more opioids than Misc ($p = 0.0283$) and Hands ($p = 0.0975$). Age was a significant independent factor for opioid consumption in the 50th and 75th percentiles of Hands ($p \leq 0.05$). An average of 36 mg DME per patient was left unused with Hands having the highest median DME (37 mg) unused. In the total cohort, 26% of patients were discharged with more DME than their last 24 h as an inpatient and had at least 50% of their tablets left unused at follow-up.
Conclusions: Over-prescription of opioids occurs at discharge which can increase the risk of harm. New intervention is needed to optimise prescribing practises.
Implications: Changes to prescribing habits and workplace culture are required to minimise unnecessary opioid prescribing but will be challenging to implement. A multilayered approach of electronic prescribing, opioid stewardship and targeted educational awareness programmes is recommended.

Keywords: morphine; opioids; orthopaedic; over prescribing; patient discharge.

1 Introduction

Global opioid use has been sharply increasing and a similar trend has been described in Australia. With a reported 15-fold increase in opioid dispensing between 1992 and 2012 [1] Australia is the third highest consumer of oxycodone per capita in the world [2, 3]. In parallel, opioid misuse is rising, with a shift from illicit to prescription drugs [4]. A contributing factor may be hospital prescriptions with almost 50% of patients being discharged from hospital with opioids following major elective surgery [5–9]. In Australia, almost 2.5 million hospitalisations involve surgery every year [10] and in orthopaedic surgery, opioid analgesia on discharge is the standard of practise for the majority of patients [5, 6, 11–14]. While opioids are an effective form of post-operative analgesia, harms from increased opioid prescribing are well documented in the literature including: adverse drug effects, stockpiling, diversion and opioid

***Corresponding author: Edward Ho,** Department of Anaesthesia, John Hunter Hospital, Lookout Rd, New Lambton Heights, NSW, 2305, Australia, Phone: (+61) 4921 3000, E-mail: Edward.ho@health.nsw.gov.au
Matthew Doherty: John Hunter Hospital, Lookout Rd, New Lambton Heights, NSW, 2305, Australia
Robert Thomas: Department of Anaesthesia, John Hunter Hospital, Lookout Rd, New Lambton Heights, NSW, 2305, Australia
John Attia: John Hunter Hospital, Lookout Rd, New Lambton Heights, NSW, 2305, Australia; Hunter Medical Research Institute, New Lambton Heights, NSW, 2305, Australia; and University of Newcastle, Callaghan NSW, 2308, Australia
Christopher Oldmeadow and Matthew Clapham: Hunter Medical Research Institute, New Lambton Heights, NSW, 2305, Australia

dependence [9]. 6.8% of patients who had a total knee arthroplasty were still consuming opioids at 2 and 5 years after their first prescription [14]. Oxycodone is increasingly diverted in Australia [15] with some studies reporting that up to 50% of oxycodone related mortality is associated with use from a diverted source [3]. 62–92% of patients report that opioids prescribed to them for analgesia postoperatively were not always required [16]. We hypothesise that prescribed opioids at hospital discharge may be excessive and investigated this in an Australian orthopaedic population of a tertiary hospital. Primary outcomes included the amount of opioids prescribed, consumed, left unused and their relationship with pain and functionality.

2 Materials and methods

A prospective audit of opioid prescriptions to orthopaedic patients was conducted in a tertiary level hospital from August 2015 to January 2016. Consecutive orthopaedic patients who had elective procedures on hands and long bones distal to the shoulder and hip joints were enrolled into the study. Patients were 18 years or older and excluded if there was a history of regular opioid use greater than 6 months, chronic pain, established chronic renal disease, cardiac failure or peptic ulcer disease.

Baseline demographic data and analgesia ordered on the ward post-operatively and on discharge were obtained from electronic medical records and pharmacy records. This included drug type, dose and frequency, morphine equivalent as an inpatient in the 24 h preceding discharge and daily oral morphine equivalent (DME) on discharge. Prescribers were blinded from the study. Opioid conversions were calculated according to the opioid calculator published by the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists [17]. At 7–10 days post-discharge, each patient was followed up via a standardised phone interview to determine the number of opioid tablets remaining, pain scores and functionality scores. If patients did not answer their phone the first time, two more attempts were made before excluding them from the study.

Statistical analysis was completed using SAS software v9.4 [18], Stat v13.0 [19] and R [20]. Multivariate linear regression and quantile regression was used to assess the predictive ability of the surgery type on the amount of opioids prescribed and consumed. The relationship between opioid use and pain, and correlation between pain and function was assessed with an ANOVA model and Kendall's Tau-b coefficient, respectively. Ethics approval was granted by the hospital's Human Research Ethics Committee (AU201508-02).

3 Results

There were 337 relevant orthopaedic cases screened of which 200 were excluded from final analysis due to exclusion criteria ($n=57$), no discharge prescription for analgesia or uncollected dispensed drugs ($n=65$) and unavailability for phone interview ($n=83$) (Fig. 1). Of the 220 patients who were followed up by phone, 137 were successfully contacted and completed our phone interview, representing a response rate of 62%. On follow-up, five patients disclosed they had not collected their hospital prescriptions and therefore had missing data for opioid use and prescribing, leaving 132 patients with complete follow-up. All 137 participants had pain and function scores.

The mean age was 54 years (range 18–90). Gender was equally distributed (female = 68, male = 69). Patients underwent a range of orthopaedic surgeries and for statistical analysis were categorised into three groups: total knee replacement (TKR, $n=38$), Hand surgery (Hands, $n=38$) and Miscellaneous (Misc, $n=56$, including foot arthrodesis [2], arthroscopy [10], tendon repair [8], limb

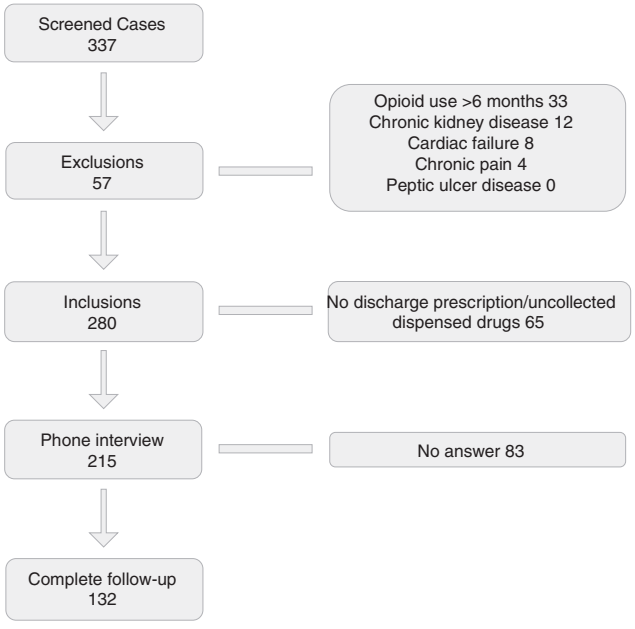

Fig. 1: Patient recruitment.

Table 1: Comparing opioid use and prescriptions between surgical groups.

		TKR ($n=38$)	Misc ($n=56$)	Hands ($n=38$)	Total ($n=132$)
Opioid Consumed in DME (mg)	Mean (SD)	98.8 (70.5)	70.9 (73.5)	46.8 (47.2)	72.0 (68.5)
	Median (min, max)	78.8 (0.0, 300.0)	46.8 (0.0, 300.0)	48.6 (0.0, 150.0)	54.0 (0.0, 300.0)
Opioid Prescribed in DME (mg)	Mean (SD)	143.7 (63.8)	101.6 (69.3)	83.4 (47.6)	108.5 (66.1)
	Median (min, max)	150.0 (37.5, 300.0)	54.0 (45.0, 300.0)	54.0 (54.0, 210.0)	75.0 (37.5, 300.0)
Opioid unused DME (mg)	Mean (SD)	48 (62)	28 (34)	37 (39)	36 (45)
	Median (min, max)	30 (0, 300)	27 (0, 150)	38 (0, 150)	27 (0, 300)

DME = Daily Oral Morphine Equivalent; mg = milligrammes; SD = standard deviation; TKR = total knee replacement; Misc = Miscellaneous surgery; Hands = Hand surgery.

open reduction internal fixation (ORIF) [12], knee ligament reconstruction [9] and debridement [15]).

The mean dose of total opioid prescribed per patient at hospital discharge was 108.5 mg DME (Table 1). Between surgical groups, quantile regression showed that TKR was prescribed the highest median dose of opioids at 150 mg DME. This was 96 mg DME greater than Misc and Hands ($p<0.0001$, $p<0.0001$) (Fig. 2). Oxycodone was the most commonly prescribed opioid on discharge (48%), mostly for TKR patients. Paracetamol/codeine combinations were also common prescription choices (42%), particularly in the Misc (51%) and Hands group (47%).

Trends in opioid consumption similarly favoured the TKR group. Multivariate linear regression with robust standard error estimates demonstrated that TKR had a higher mean consumption of opioids at 108 mg DME, compared to Misc (63.3 mg DME) and Hands groups (48.6 mg DME), respectively ($p=0.0077$, $p<0.0001$) (Fig. 3).

At 7–10 days post-discharge, the mean amount of unused opioids per patient was 36 mg DME. Between surgical groups, Hands had the highest median DME of unused opioids (38 mg) compared to TKR (30 mg) and Misc (27 mg) (Table 1). In Hands, these mostly consisted of 500/30 mg paracetamol/codeine (69%) and 5 mg oxycodone tablets (31%). Twenty-six percent of patients (35/137, TKR = 4, Misc = 15, Hands = 16) were discharged with more DME than their last 24 h as an inpatient and also had at least 50% of their opioid tablets left unused. Thirteen (10%) of these patients did not require any opioids in their last 24 h of hospital stay yet were still prescribed these on discharge.

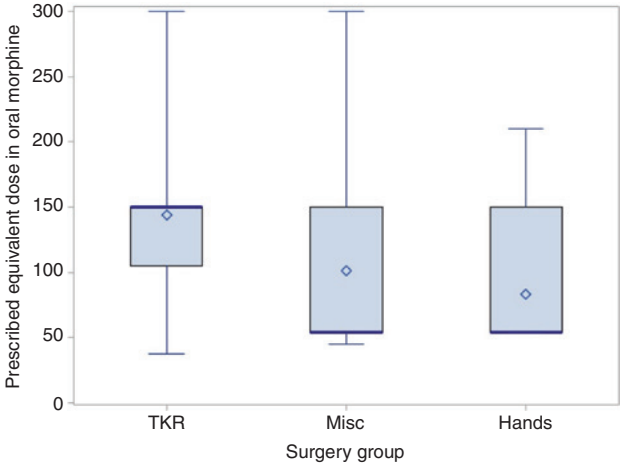

Fig. 2: Comparing the distribution of prescribed opioid doses (milligrammes) on discharge between surgical groups shown in box plot. ◊ = Mean; Bold line = Median.

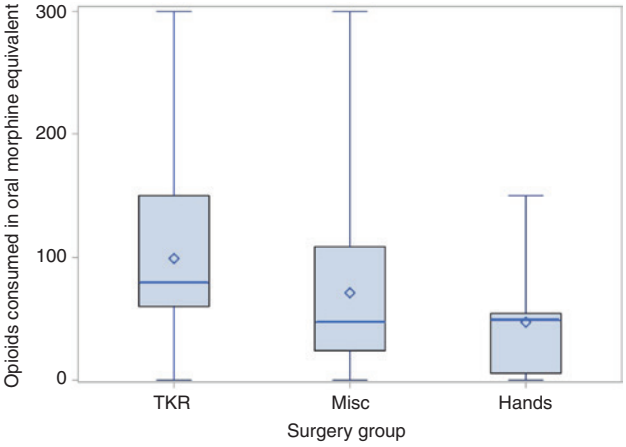

Fig. 3: Comparing the distribution of consumed opioid doses (milligrammes) on discharge between surgical groups shown in box plot. ◊ = Mean; Bold line = Median.

The adjusted R^2 was 0.079 indicating that age, gender, surgery type and pain only explained 8% of this wide variation. The majority of opioids prescribed ranged from 50 to 150 mg DME but the actual proportion of this consumed was very variable, ranging from 0 to 100% (Fig. 4). Between groups, quantile regression showed that the median proportion of consumed opioids in TKR was 35% and 33% more than Misc and Hands group, respectively ($p=0.0283$, $p=0.0975$) 7–10 days post-discharge (Table 2).

Age (median = 57, range 21–90) as an independent variable was the only statistically significant factor in

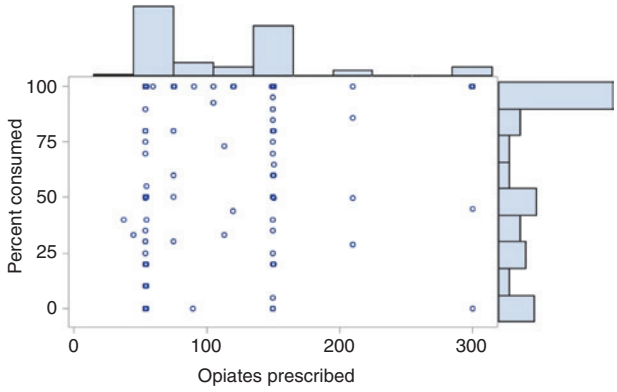

Fig. 4: Percentage of opioids consumed against amount prescribed in oral DME (milligrammes).

Table 2: Difference in percentage of opioids consumed compared to TKR group.

Surgical group	Opioid consumed % (95% CI)	Standard error	*T*-value	*p*-Value
Hands	−0.33 (−0.72, 0.06)	0.196	−1.67	0.0975
Misc	−0.35 (−0.66, −0.04)	0.157	−2.22	0.0283
TKR	Reference	–	–	–

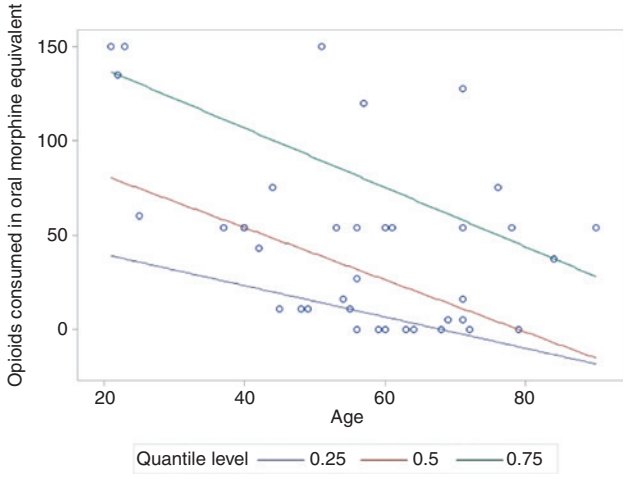

Fig. 5: Opioids consumed (milligrammes) according to age – Hand Surgery.

determining the DME consumption in Hands for patients in the 50th and 75th percentile ($p \leq 0.05$) (Fig. 5). There was a trend of lower opioid consumption with older age in majority of the cohort except for TKR patients in the 75th percentile. However, this was not statistically significant and the TKR group overall was comparatively older (median age = 68, range 52–84).

The majority of patients rated their pain as 1 = mild (45%) and 2 = moderate (38%) and functional limitation as mild (61%) (Tables 3 and 4). Seventy-two percent of the patients with nil to moderate pain also reported nil to mild functional limitation at time of follow-up. Correlation between pain and function was weakly positive with a Kendall's Tau-b correlation coefficient of 0.29 (95% CI 0.14–0.44) ($p = 0.0001$).

4 Discussion

In our study, patients with TKR had the highest median prescription (150 mg DME) and consumption of opioids (78.8 mg DME) but it was hand surgery patients who had the most DME left unused (38 mg). Almost half of our patients (67/137) were prescribed more DME on discharge than their last 24 h as an inpatient. The majority of these patients (52%, $n = 35$, TKR [4]; Misc [15]; Hands [16]) had at least 50% of their opioid tablets left unused. This suggests that opioids may be over-prescribed in Misc and Hands compared to TKR. In a hand surgery study 63% of tablets from filled prescriptions were unused over 1 month and 92% of the patients reported adequate pain management [21]. This is comparable to our study, as the median pain score for the total cohort, Misc and Hands was 1 (mild) while TKR was 2 (moderate).

In a systematic review of 810 patients, over two-thirds of patients had unused prescription opioids after surgery, including thoracic, orthopaedic and obstetric procedures. Adequate pain control accounted for 71–83% of these cases [16]. We did not survey reasons for leftover opioids but with 72% of patients reporting nil to moderate pain which correlated with nil to mild functional limitation, adequate analgesic relief was likely to be the main reason for ceasing opioid use. Older age, male gender and anxiety are also known to be predictors of opioid use [14], highlighting the complexity of pain physiology. Our study showed only a weakly positive correlation between higher perceived pain and worse functional scores.

Unused opioids inadvertently leads to a reservoir of tablets that can contribute to harmful nonmedical use. Diverted opioids from numerous sources have been linked to significant morbidity and mortality [9, 22–24], not uncommonly from friends or family members who have legitimate prescriptions [25].

In a study of 212 patients who underwent a dermatologic operation 53% intended to keep the surplus of their opioid prescription [26]. The risk of dependency is reinforced in a Canadian study of over 27,000 patients who

Table 3: Comparing age and verbal reports of pain and function between surgical groups.

		TKR ($n=42$)	Misc ($n=56$)	Hands ($n=39$)	Total ($n=137$)[a]
Age	Mean (SD)	67 (8)	42 (18)	57 (18)	54 (19)
	Median (min, max)	68 (52, 84)	39 (18, 77)	57 (21, 90)	57 (18, 90)
Pain rating	Median (min, max)	2 (1, 3)	1 (0, 3)	1 (0, 2)	1 (0, 3)
Functional limitation (*n*)	No limitation	1	10	10	21
	Mild limitation	33	31	19	83
	Severe limitation	8	15	10	33

SD = standard deviation; Pain rating 0 = no pain; 1 = mild pain; 2 = moderate pain; 3 = severe pain; TKR = total knee replacement; Misc = Miscellaneous surgery; Hands = Hand surgery. [a]Includes the five patients (4 TKR, 1 Hands) who had missing data for opioid use and prescriptions on discharge.

Table 4: Relationship of pain score with functional limitation.

Self-reported pain	Self-reported functional limitation		
	Nil	Mild	Severe
0 (nil)	10	4	0
1 (mild)	9	37	17
2 (moderate)	2	37	12
3 (severe)	0	5	4

$n=137$.

had low-risk surgery such as cataract surgery and laparoscopic cholecystectomy. The authors found that patients who were prescribed opioids within 7 days of discharge were 44% more likely to become long-term prescription opioid users within 1 year compared with those who had none [6].

Our study found age was a significant independent variable for opioid consumption in at least 50% of hand surgery patients. This potentially has useful clinical applications in predicting the optimal maximum DME for these patients postoperatively. Due to multiple comorbidities and frailty, older patients are more susceptible to adverse effects of opioids at equivalent doses, such as falls, cardiotoxicity, hepatotoxicity and cognitive impairment [27]. A nomogram style prescribing tool to guide a prescriber with initial dosing could improve titration and safety.

Oxycodone is the most commonly prescribed opioid for postoperative pain. Oxycodone prescriptions have increased by 152% between 2002 and 2008 and seems out of proportion to population growth [3, 9]. There is growing evidence in the milieu of increased oxycodone use that over-prescribing of opioids at time of hospital discharge is a contributing factor with subsequent stockpiling, diversion and abuse. Our study strongly suggests this with 48% of patients prescribed oxycodone and 50% (69/137) prescribed only opioids without other co-analgesia at discharge. In this subgroup, only three patients did not receive oxycodone.

There are limitations to our study. The sample size was modest due to the losses to follow-up with a relatively large proportion of uncollected prescriptions and unanswered phone calls. In future studies, an alternative strategy could be a direct face-to-face survey at the outpatient orthopaedic clinics as part of standard postoperative care. Our patients were only located at a single institution and results are only reflective of the orthopaedic population. Recall bias is an inherent limitation because all follow-up data regarding consumption, pain and function scores was self-reported by patients and not validated. We attempted to reduce confounding factors of opioid consumption such as chronic opioid use, dependency and relative contraindications for opioids with our exclusion criteria.

5 Conclusions

Our prospective audit of orthopaedic patient opioid prescriptions and consumption with data expressed in DME is the first of its kind in Australia. Our results suggest that hospital discharge prescriptions after surgery can be a contributor to excess opioid use and stockpiling in the community. This poses greater risk of unintended long term use, dependency and diversion. A multi-layered approach of electronic prescribing, opioid stewardship and targeted educational awareness programmes to prescribers is recommended.

6 Implications

The challenge in minimising the amount of opioid prescribed is heavily reliant on changing the behaviour and

culture in the workplace. Providing only education and raising awareness of the problem to prescribers is unlikely to have a long lasting effect. In a quality improvement project of a hand surgery department, a palm-size opioid prescribing card led to an overall reduction in the number of opioid tablets prescribed for post-operative pain and continued for 9 months after intervention [28]. An effective modern strategy would be the addition of electronic prescribing which can alert the prescriber of potentially excessive prescriptions when compared to the patient's opioid consumption for the previous 24 h prior to discharge. This can be integrated with a traffic light system according to the strength and potency of different opioid drugs.

Authors' statements

Research funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest: None.

Informed consent: Consent for collecting data from hospital patient medical records was not required as information was de-identified. As part of our follow-up protocol informed consent was obtained from study participants at the time of the telephone interview.

Ethical approval: The study was granted ethics approval by the Hunter New England Human Research Ethics Committee (HREC) (AU201508-02). Apart from registration with the hospital HREC, the study protocol has not been registered elsewhere.

References

[1] Blanch B, Pearson S, Haber P. An overview of the patterns of prescription opioid use, costs and related harms in Australia. Br J Clin Pharmacol 2014;78:1159–66.

[2] Atluri S, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and misuse of opioid analgesics from 2004 to 2011. Pain Physician 2014;17:E119–28.

[3] Roxburgh A, Bruno R, Larance B, Burns L. Prescription of opioid analgesics and related harms in Australia. Med J Aust 2011;195:280–4.

[4] Nielsen S, Bruno R, Degenhardt L, Stoove MA, Fischer JA, Carruthers SJ, Lintzeris N. The sources of pharmaceuticals for problematic users of benzodiazepines and prescription opioids. Med J Aust 2013;199:696–9.

[5] Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. Br Med J 2014;348:g1251.

[6] Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term analgesic use after low-risk surgery: a retrospective cohort study. Arch Intern Med 2012;172:425–30.

[7] Choo CY, Ong CYY, Chan SY. Oxycodone – an audit of its prescription in a local hospital. Ann Acad Med Singapore 2009;38:947–51.

[8] Denison Davies E, Schneider F, Childs S, Hucker T, Krikos D, Peh J, McGowan C, Stone P, Cashman J. A prevalence study of errors in opioid prescribing in a large teaching hospital. Int J Clin Pract 2011;65:923–9.

[9] Macintyre PE, Huxtablet CA, Flint SLP, Dobbin MDH. Costs and consequences: a review of discharge opioid prescribing for ongoing management of acute pain. Anaesth Intensive Care 2014;42:558–74.

[10] AIHW. 2014. Australian hospital statistics 2012–13. Health services series no. 54. Cat. no. HSE 145. Canberra: AIHW.

[11] Carroll I, Barelka P, Wang CK, Wang BM, Gillespie MJ, McCue R, Younger JW, Trafton J, Humphreys K, Goodman SB, Dirbas F, Whyte RI, Donington JS, Cannon WB, Mackey SC. A pilot cohort study of the determinants of longitudinal opioid use after surgery. AnesthAnalg 2012;115:694–702.

[12] de Beer JdV, Winemaker MJ, Donnelly GAE, Miceli PC, Reiz JL, Harsanyi Z, Payne LW, Darke AC. Efficacy and safety of controlled-release oxycodone and standard therapies for postoperative pain after knee or hip replacement. Can J Surg 2005;48:277–83.

[13] Roberts M, Brodribb W, Mitchell G. Reducing the pain: a systematic review of postdischarge analgesia following elective orthopedic surgery. Pain Med 2011;13:711–27.

[14] Singh JA, Lewallen DG. Predictors of use of pain medications for persistent knee pain after primary Total Knee Arthroplasty: a cohort study using an institutional joint registry. Arthritis Res Ther 2012;14:R248.

[15] Leong M, Murnion B, Haber PS. Examination of opioid prescribing in Australia from 1992 to 2007. Intern Med J 2009;39:676–81.

[16] Bicket MC, Long JJ, Pronovost PJ, Alexander G, Wu CL. Prescription opioid analgesics commonly unused after surgery: a systematic review. JAMA Surg 2017;152:1066–71.

[17] Opioid Dose Equivalence. Calculation of oral Morphine Equivalent Daily Dose (oMEDD). Melbourne, Australia: Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists; 2014; Available from: http://fpm.anzca.edu.au/documents/opioid-dose-equivalence.pdf.

[18] SAS v9.4. SAS Institute Inc., Cary, NC, USA.

[19] StataCorp. Stata Statiscal Software: Release 13.0. College Station, TX: StataCorp LP; 2013.

[20] R Core Team. R: a language and environment for statistical computing. R Foundation for Statisical Computing, Vienna, Austria. 2017.

[21] Rodgers J, Cunningham K, Fitzgerald K, Finnerty E. Opioid consumption following outpatient upper extremity surgery. J Hand Surg – Am Vol 2012;37:645–50.

[22] Okie S. A flood of opioids, a rising tide of deaths. Erratum appears in N Engl J Med 2011;364:290. N Engl J Med 2010;363:1981–5.

[23] Duncan B. A rising tide. Of Substance 2012;10:4.

[24] Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, Green JL. Trends in opioid analgesic abuse and mortality in the United States. N Engl J Med 2015;372:241–8.

[25] Manchikanti L, Helm S 2nd, Fellows B, Janata JW, Pampati V, Grider JS, Boswell MV. Opioid epidemic in the United States. Pain Physician 2012;15(Suppl. 3):ES9–38.
[26] Harris K, Curtis J, Larsen B, Calder S, Duffy K, Bowen G, Hadley M, Tristani-Firouzi P. Opioid pain medication use after dermatologic surgery. JAMA Dermatol 2013;149:317.
[27] Rubin R. Analysis reveals large increase in hospitalizations in recent years among older patients prescribed opioids. J Am Med Assoc 2014;312:1621–3.
[28] Stanek JJ, Renslow MA, Kalliainen LK. The effect of an educational program on opioid prescription patterns in hand surgery: a quality improvement program. J Hand Surg 2015;40:341–6.