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# Six-year trends in postoperative prescribing and use of multimodal analgesics following total hip and knee arthroplasty: A single-site observational study of pain management

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## Abstract

**Background:** Guidelines for acute postoperative pain management recommend administering analgesics in multimodal combination to facilitate synergistic benefit, reduce opioid requirements and decrease side-effects. However, limited observational research has examined the extent to which multimodal analgesics are prescribed and administered postoperatively following joint replacement.

**Methods:** In this longitudinal study, we used three-point prevalence surveys to observe the 6-year trends in prescribing and use of multimodal analgesics on the orthopaedic wards of a single Australian private hospital. We collected baseline postoperative data from total hip and knee arthroplasty patients in May/June 2010 (Time 1, $n = 86$), and follow-up data at 1 year (Time 2, $n = 199$) and 5 years (Time 3, $n = 188$). During the follow-up, data on prescribing practices were presented to anaesthetists.

**Results:** We found a statistically significant increase in the prescribing ($p < 0.001$) and use ($p < 0.001$) of multimodal analgesics over time. The use of multimodal analgesics was associated with lower rest pain ($p = 0.027$) and clinically significant reduction in interference with activities ($p < 0.001$) and sleep ($p < 0.001$). However, dynamic pain was high and rescue opioids were likely under-administered at all time points. Furthermore, while patients reported high levels of side-effects, use of adjuvant medications was low.

**Conclusions:** We observed significant practice change in inpatient analgesic prescribing in favour of multimodal analgesia, in keeping with contemporary recommendations. Surveys, however, appeared to identify a clinical gap in the bedside assessment and management of breakthrough pain and medication side-effects, requiring additional targeted interventions.

**Significance:** Evaluation of 6-year trends in a large Australian metropolitan private hospital indicated substantial growth in postoperative multimodal analgesic prescribing. In the context of growing global awareness concerning multimodal analgesia, findings suggested diffusion of best-evidence prescribing into clinical practice. Findings indicated the effects of postoperative multimodal analgesia in real-world

  

conditions outside of experimental trials. Postoperative multimodal analgesia in the clinical setting was only associated with a modest reduction in rest pain, but substantially reduced interference from pain on activities and sleep.

## 1 | INTRODUCTION

Joint replacements are commonly performed, and rank among the most painful operative procedures (Ip, Abrishami, Peng, Wong, & Chung, 2009). Well-established control of acute postoperative pain is associated with early mobilization, improved joint rehabilitation (Buvanendran et al., 2003) and lower likelihood of developing chronic pain (Kehlet, Jensen, & Woolf, 2006). However, research indicates high levels of uncontrolled acute postoperative pain are common sequelae of joint replacement surgery (Lindberg et al., 2013; Lorentzen, Hermansen, & Botti, 2012; Wylde, Rooker, Halliday, & Blom, 2011), suggesting that the quality of pharmacological pain management is suboptimal.

Current clinical practice guidelines recommend the administration of multimodal analgesics following joint replacement, to manage pain with synergistic medication combinations targeting distinct mechanisms of action (e.g. Chou et al., 2016; PROSPECT Working Group, 2019). Effective multimodal analgesia is associated with improved mobilization and patient satisfaction, reduced postoperative pain, opioid consumption and side effects (Elia, Lysakowski, & Tramèr, 2005; Gan et al., 2004; Lamplot, Wagner, & Manning, 2014; McDaid et al., 2010; Ong, Seymour, Lirk, & Merry, 2010; Rømsing, Møiniche, Mathiesen, & Dahl, 2005). In addition to intraoperative regional analgesia and anaesthesia (PROSPECT Working Group, 2019), optimal postoperative pain management following total hip (THA) and knee (TKA) arthroplasty includes paracetamol (Schug, Palmer, Scott, Halliwell, & Tinca, 2015), a cox-2 inhibitor or conventional nonsteroidal anti-inflammatory drug (NSAID) unless contraindicated (PROSPECT Working Group, 2019; Thomazeau et al., 2016), a slow-release opioid (e.g. de Beer et al., 2005) and a rescue opioid titrated for dynamic pain (PROSPECT Working Group, 2019). The use of gabapentinoids as adjuvant analgesics and antiemetics are also indicated to support opioid-sparing (e.g. Axelby & Kurmis, 2020; Buvanendran & Kroin, 2007; Chou et al., 2016) and manage nausea and vomiting (Gan et al., 2014).

Despite the high volume of trials involving multimodal analgesics, limited observational research has examined the extent to which arthroplasty patients are typically prescribed and receive them. However, published reports suggest their suboptimal postoperative use in this patient population, in several distinct domains. First, findings suggest that standard prescribing often fails to support the administration of multimodal analgesics. Research indicates unnecessary variation in analgesic prescribing (Beverly, Kaye, & Urman, 2017) and low use of fixed schedule prescriptions (Cohen et al., 2008; Eid & Bucknall, 2008). This increases the complexity of nurses' decision making about patients' pain relief requirements. Second, descriptive studies commonly indicate systematic underuse of analgesic medications, whereby surgical patients (Dihle, Helseth, Kongsgaard, Paul, & Miaskowski, 2006; Lorentzen et al., 2012; Watt-Watson, Stevens, Garfinkel, Streiner, & Gallop, 2001), are typically administered <50% of prescribed analgesics. Finally, a recent survey of THA and TKA cases within the United States (US; $N = 145{,}288$) found that less than one-in-ten patients received a perioperative multimodal regimen, suggesting persisting low use of multimodal analgesics despite increasing international focus.

This study reports the 6-year evolution of multimodal analgesic prescribing and administration for acute postoperative pain in THA and TKA patients at one private-sector site in Victoria, Australia. We explored trends in the quality of pharmacological pain management using three-point prevalence surveys undertaken between 2010 and 2016. This research aimed to: (a) observe trends in the quality of multimodal analgesic prescribing and administration; (b) investigate associations between use of multimodal analgesics and patients' postoperative pain experience and (c) examine opioid-induced side effects and the prescription and administration of adjuvants.

## 2 | METHOD

### 2.1 | Design

Australian hospital statistics indicate that the majority of total joint replacements within Australia – 64% of all hip replacement surgeries and 70% of all knee replacement surgeries – are undertaken within the private healthcare sector (Australian Institute of Health and Welfare, 2017). This 6-year observational trend study investigated the pharmacological management of postoperative pain on three orthopaedic wards of a large metropolitan private, tertiary referral hospital in Victoria, Australia. This hospital conducts a high volume of joint arthroplasty, including over 2,200 hip and knee replacement surgeries annually. Point prevalence surveys of consecutive patients were undertaken in 2010 (Time 1), and 1 year (Time 2, 2011/2012) and 5 years (Time 3, 2015/2016) later. Study data were collected from May to June 2010, between November 2011 and April 2012, and between December 2015 and May 2016. Surveys were sequential, with survey

days selected purposively to capture all surgeon-anaesthetist dyads.

Between Time 1 and Time 2, a multimodal pain management algorithm to aid prescribing, was developed at our research centre from a review of best-evidence (Botti et al., 2014). Prescribing data from the Time 1 survey and the pain management algorithm were presented by the last author to anaesthetists at hospital grand rounds and clinical symposia, and to relevant hospital Clinical Institute chairs. The data helped inform the establishment of a hospital-wide acute pain service in September 2015.

## 2.2 | Participants

Participants were a point prevalence sample of all THA and TKA patients aged 18 years or older in postoperative recovery on the orthopaedic wards (see Figure 1). A total of 587 patients were recruited into cross-sectional surveys conducted at Time 1, 2 and 3. Information on analgesics were not available for one patient at Time 1, and two patients were unable to be interviewed about their pain: Time 1 ($n = 1$); Time 2 ($n = 1$). To ensure that study data uniformly reflected postoperative care during a preceding 24-hr period, patients interviewed on postoperative Day 0 were excluded from analyses ($n = 89$). In addition, due to their small number, and because such patients were likely to have issues prolonging their length of stay, participants surveyed beyond postoperative Day 5 were removed from analyses ($n = 47$). The final sample comprised 473 patients: 2010 ($n = 86$); 2011/2012 ($n = 199$); and 2015/2016 ($n = 188$). Study data were derived from 471 patient interviews and 472 medication charts.

## 2.3 | Measures

We measured patients' postoperative pain experience with the American Pain Society Patient Outcome Questionnaire (APS-POQ; American Pain Society Quality of Care Committee, 1995). As the revised questionnaire (APS-POQ-R; Gordon et al., 2010) became available by Time 2, this was administered at Time 2 and 3. For consistency, only pain intensity, pain interference and side effects data were analysed for this study.

### 2.3.1 | American Pain Society Patient Outcome Questionnaire

The APS-POQ is a 19-item measure of the quality of pain care delivered to hospital inpatients during the past 24-hr. The instrument measures four domains: (a) pain intensity; (b) pain interference; (c) satisfaction with pain treatment; and (d) beliefs about pain and pain treatment (American Pain Society Quality of Care Committee, 1995; McNeill, Sherwood, Starck, & Thompson, 1998). Pain intensity items measure current pain (pain at rest), worst pain (denoting pain associated with movement) and average pain on a 0–10 Numerical Rating Scale (NRS) anchored by 0, '*no pain*' and 10, '*worst pain possible*'. Pain interference items measure interference with general activity, mood, walking ability, relations with other people, sleep and coughing and deep breathing exercises on a 0–10 NRS anchored by 0, '*does not interfere*' and 10, '*completely interferes*'. Findings within the empirical literature support the utility (Hjermstad et al., 2011), reliability and validity (Williamson & Hoggart, 2005) of the 0–10 NRS for pain measurement. Psychometric testing of the APS-POQ revealed strong levels of internal consistency of pain intensity and pain interference items (McNeill et al., 1998).

### 2.3.2 | Revised American Pain Society Patient Outcome Questionnaire

Gordon et al. (2010) detail the construction and initial psychometric validation of the APS-POQ-R. A key addition to

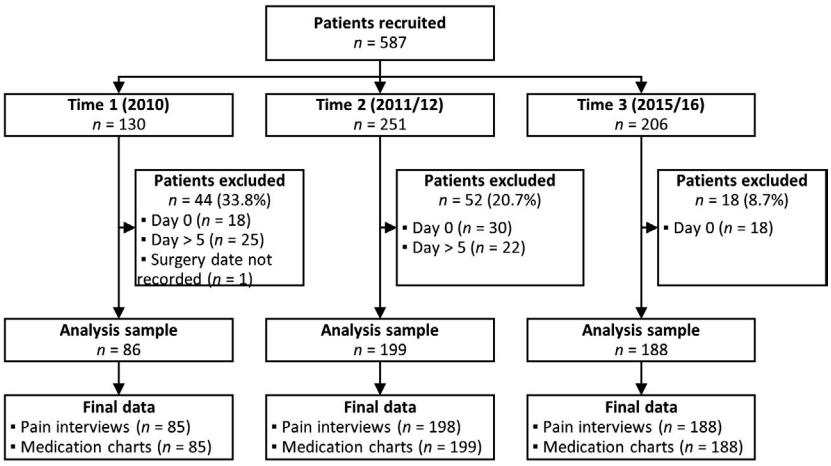


**FIGURE 1** Survey recruitment and data collection outcomes: Patients on study wards at Time 1, 2 and 3

the revised instrument was the inclusion of measures of medication-induced side effects (drowsiness, dizziness, itching, nausea). Pain severity and pain interference items measure least and worst pain, and interference with activities in and out of bed, falling asleep and staying asleep, respectively, on a 0–10 NRS.

Initial psychometric testing with a sample of US medical-surgical patients ($n = 299$) identified five constructs with good overall internal consistency ($\alpha = 0.86$). Subsequent validation of the APS-POQ-R with Australian surgical patients identified good construct validity but questionable internal consistency ($\alpha = 0.67$; Botti et al., 2015). Differences in internal consistency between studies likely reflected variation in the period being recalled in the Australian (range: Day 0–7), compared to the US (Day 0, first-24 hr) validation. Present analyses were restricted to postoperative Days 1–5 and where possible, differences in postoperative day were controlled for statistically.

The APS-POQ-R was designed to measure pain during the first-24 hr following surgery. However, to be consistent with the original APS-POQ, participants of this study rated the period 24-hr prior to interview. This modified period has been reported in past research (Botti et al., 2015; Zoëga, Ward, & Gunnarsdottir, 2014) and likely reduces cognitive bias associated with retrospective pain recall over long periods (Broderick et al., 2008).

## 2.4 | Analyses

We performed data summaries and statistical analyses in SPSS Statistics 25 (IBM). Characteristics of survey samples were compared with chi-square tests of Independence, Fisher's exact test and one-way ANOVA. We examined standardized residuals ($z_{res}$) to determine the importance of individual cells. Cells with $z_{res}$ values exceeding ±1.96 were considered statistically significant.

Trend data were independent cross sections and were analysed with statistical analyses suitable for independent observations. The distribution of postoperative interview day significantly differed between surveys ($\chi^2 = 10.278$, $p = 0.006$). Consequently, continuous data were compared with two-way ANCOVA (surgical group × time), controlling for postoperative interview day. If data failed to support two-way ANCOVA due to heteroscedasticity (Levene's test, $p < 0.05$), one-way ANCOVA, or two/one-way ANOVA was performed. Main effects were adjusted with the Sidak correction. Post hoc tests were performed using the Sidak $t$ test. Non-parametric comparisons were performed using the Kruskal–Wallis $H$ test, with the Mann–Whitney $U$ test as a post hoc test. Associations with dichotomous variables were analysed with binary logistic regression.

We considered current pain at rest (APS-POQ) and least pain (APS-POQ-R) intensity variables to measure *rest pain*, and worst pain intensity to measure *dynamic pain*. To facilitate combined analyses of APS-POQ and APS-POQ-R pain interference data, we created two composite variables (*worst activity interference, worst sleep interference*). *Worst activity interference* was the highest interference rating related to physical activity: general activity, walking ability (APS-POQ); activities in bed, activities out of bed (APS-POQ-R). *Worst sleep interference* was the highest interference rating related to sleep: sleep (APS-POQ); falling asleep, staying asleep (APS-POQ-R). We calculated the morphine equivalent dosage of standard opioid medications using formulas provided by the Australian and New Zealand College of Anaesthetists Faculty of Pain Medicine (Faculty of Pain Medicine – Australian & New Zealand College of Anaesthetists, 2017). The morphine equivalent dosage of methadone was calculated using a formula provided by the Centers for Disease Control and Prevention (Centers for Disease Control & Prevention, 2017).

Some pain and analgesic outcome data were missing due to patient non-response and incomplete documentation on medication charts. The proportion of missing values were low (range: 0.2%–4.2%), and determined to be Missing Completely at Random (MCAR), Little's MCAR test, $p = 1.0$. Consequently, missing data were handled using pairwise deletion.

## 2.5 | Ethics

Ethical approval was obtained from the institutional review board of the Deakin University Human Research Ethics Committee and the affiliated hospital. Informed consent was obtained from each participant.

# 3 | RESULTS

## 3.1 | Patient characteristics

Characteristics of the three survey samples are presented in Table 1. Patients were primarily aged 65 years or over ($n = 288$, 60.9%), were overweight (body mass index [BMI] ≥ 25; $n = 162$, 34.2%) or obese (BMI ≥ 30; $n = 195$, 41.2%), spoke English at home and presented with osteoarthritis. Patient age ($F(2, 472) = 0.938$, $p = 0.392$) and BMI ($F(2, 409) = 0.156$, $p = 0.855$, log 10 transformed) did not significantly differ between samples. There were no significant associations between survey year and distributions of gender ($\chi^2 = 1.632$, $p = 0.442$), surgical procedure ($\chi^2 = 1.737$, $p = 0.42$), rates of English speaking at home ($\chi^2 = 2.214$, $p = 0.331$) and rheumatoid arthritis ($\chi^2 = 4.742$, $p = 0.093$). Although two patients required an interpreter at

**TABLE 1** Characteristics of survey samples

| Participant characteristics | Time 1 ($n = 86$) | Time 2 ($n = 199$) | Time 3 ($n = 188$) | Total ($n = 473$) | $p$ |
|---|---|---|---|---|---|
| Age (*M*, *SD*) | 67.5 (10.4) | 65.7 (10.3) | 65.7 (11.3) | 66 (10.7) | ns[b] |
| Gender (*n*, %) | | | | | |
| Male | 36 (41.9) | 89 (44.7) | 93 (49.5) | 218 (46.1) | ns[c] |
| Female | 50 (58.1) | 110 (55.3) | 95 (50.5) | 255 (53.9) | |
| BMI (*M*, *SD*) | 29.9 (5.1) | 30.8 (6.7) | 30.9 (6.9) | 30.8 (6.7) | ns[b,d] |
| Surgery (*n*, %) | | | | | |
| THA | 42 (48.8) | 101 (50.8) | 83 (44.1) | 226 (47.8) | ns[c] |
| TKA | 44 (51.2) | 98 (49.2) | 105 (55.9) | 247 (52.2) | |
| English spoken at home (*n*, %) | 74 (89.2) | 177 (88.9) | 175 (93.1) | 426 (90.6) | ns[c] |
| Interpreter required (*n*, %) | 2 (2.4) | 0 (0) | 0 (0) | 2 (0.4) | 0.031[e] |
| Indicators for joint replacement (*n*, %)[a] | | | | | |
| Osteoarthritis | 73 (94.8) | 193 (97.5) | 187 (99.5) | 453 (97.8) | 0.039[e] |
| Rheumatoid arthritis | 4 (5.2) | 15 (7.5) | 5 (2.7) | 24 (5.1) | ns[c] |
| Fracture, acute injury | 4 (5.2) | 10 (5.1) | 2 (1.1) | 16 (3.5) | ns[c] |
| Postoperative interview day (*Mdn*, *IQR*) | 2 (2) | 3 (3) | 2 (2) | 2 (3) | 0.006[f] |

Abbreviations: BMI, body mass index; ns, not significant; THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a]$n = 463$.

[b]$p$-value, one-way ANOVA.

[c]$p$-value, chi-square test of Independence.

[d]log 10 transformed, univariate outliers removed.

[e]$p$-value, Fisher's exact test.

[f]$p$-value, Kruskal–Wallis test.

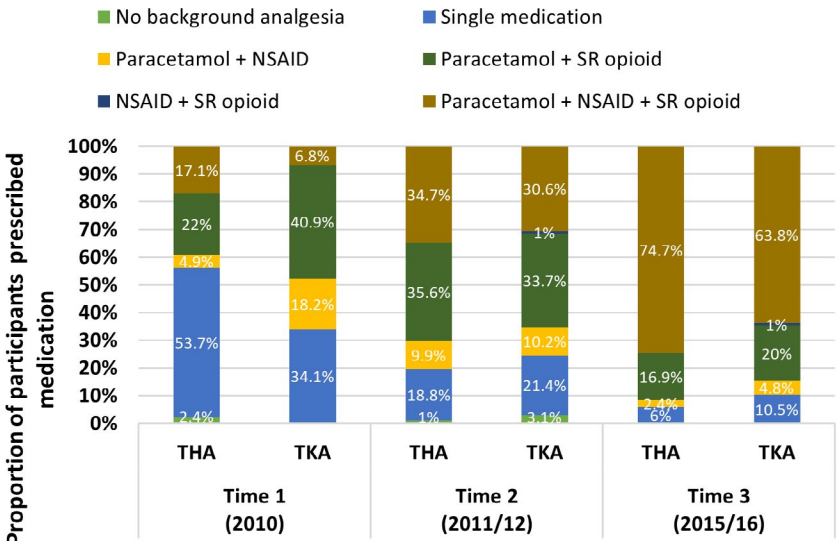


**FIGURE 2** Frequency of prescriptions for background analgesics in multimodal combination at Time 1, 2 and 3 ($n = 472$). Coloured columns represent the proportion of participants with prescriptions for varied combinations of background analgesics at each time point. NSAID, nonsteroidal anti-inflammatory drug; SR, sustained-release; THA, total hip arthroplasty; TKA, total knee arthroplasty

Time 1, they were not required in subsequent years (Fisher's exact = 5.366, $p = 0.031$). Osteoarthritis as the underlying condition was marginally lower at Time 1 (Fisher's exact = 5.743, $p = 0.039$). Patients at Time 2 were interviewed on a significantly later postoperative day compared with patients at Time 1 ($U = 7{,}091.5$, $p = 0.019$) and Time 3 ($U = 15{,}595$, $p = 0.004$). Consequently, where possible, analyses controlled for postoperative day.

## 3.2 | Trends in multimodal prescribing for acute postoperative pain

Patients were prescribed up to three types of analgesic medication in multimodal combination for background pain control: paracetamol; an NSAID; a sustained-release (SR) opioid. Figure 2 describes combined analgesic prescribing for THA and TKA at Time 1, 2 and 3. The number of

analgesics prescribed in multimodal combination did not differ by surgery ($U = 26{,}674.5$, $p = 0.419$). There was a statistically significant increase in the number of analgesics prescribed in combination over time, irrespective of surgical group (Kruskal–Wallis $\chi^2 = 97.148$, $p < 0.001$), from Time 1 to Time 2 ($U = 5{,}848$, $p < 0.001$) and from Time 2 to Time 3 ($U = 2{,}918.5$, $p < 0.001$). Survey year was significantly associated with combined prescribing of all three background analgesics ($\chi^2 = 98.685$, $p < 0.001$). The odds of having a prescription for paracetamol, NSAIDs and SR opioids were over three times higher at Time 2 (OR = 3.6, 95% CI = 1.8–7.5), and 16 times higher at Time 3 (OR = 16.4, 95% CI = 7.9–34), compared to those at Time 1.

Table 2 describes trends in fixed rate versus PRN (pro re nata, as needed) prescribing for background analgesia following THA and TKA. There were statistically significant, but inconsistent patterns of fixed rate prescribing for paracetamol (THA $\chi^2 = 45.772$, $p < 0.001$; TKA $\chi^2 = 59.41$, $p < 0.001$) and SR opioids (THA $\chi^2 = 31.841$, $p < 0.001$) from Time 1. Compared to Time 1, the odds of THA and TKA patients having a fixed prescription for paracetamol declined significantly at Time 2, but were significantly higher at Time 3. The odds of THA patients having a fixed prescription for an SR opioid were significantly greater at Time 3 following a non-significant decline at Time 2. There was a statistically significant increase in fixed rate prescribing of NSAIDS (THA $\chi^2 = 11.127$, $p = 0.004$; TKA $\chi^2 = 8.941$, $p = 0.011$). Patients had significantly greater odds of being prescribed a fixed NSAID by Time 3, compared to those at Time 1. There was no significant association between survey year and fixed prescriptions for SR opioids following TKA ($\chi^2 = 2.32$, $p = 0.314$).

## 3.3 | Trends in multimodal analgesic administration for acute postoperative pain

Trends in the number of multimodal analgesics administered for background pain control following THA and TKA are presented in Figure 3. The number of analgesics administered in multimodal combination did not significantly differ by surgery type ($U = 25{,}545$, $p = 0.957$). There was a statistically significant increase in the number of analgesics administered in multimodal combination from Time 1 (Kruskal–Wallis $\chi^2 = 93.89$, $p < 0.001$). Post-hoc testing revealed that patients were administered a greater number of combined analgesics at Time 2 compared to Time 1 ($U = 4{,}042$, $p < 0.001$), and at Time 3 compared to Time 2 ($U = 11{,}934$, $p < 0.001$). Survey year was significantly associated with receiving combined paracetamol, NSAIDs and SR opioids ($\chi^2 = 78.72$, $p < 0.001$). The odds of receiving these three medications were significantly higher at Time 2 (OR = 5.0, 95% CI = 1.7–14.6) and Time 3 (OR = 20.4, 95% CI = 7.1–58.2), relative to Time 1.

There was no significant difference in the mean ratio of available analgesics administered to THA (56.4%) and TKA (55.7%) patients ($U = 2{,}742$, $p = 0.74$). The ratio of available analgesics administered to patients at Time 1, 2 and 3 are presented in Table 3, irrespective of surgical group. There was a significant increase in the total proportion of all available analgesics administered over time, such that significantly more

**TABLE 2** Proportion and odds ratios of fixed-rate prescribing for background pain control following THA and TKA in 2010, 2011/2012 and 2015/2016

| | THA patients | | | TKA patients | | |
|---|---|---|---|---|---|---|
| | Time 1 | Time 2 | Time 3 | Time 1 | Time 2 | Time 3 |
| Fixed paracetamol | | | | | | |
| *n* (%) | 29 (74.4) | 48 (50.5) | 78 (94) | 31 (70.5) | 47 (51.1) | 100 (96.2) |
| Wald (*p*) | n.a. | 6.2 (0.013)[a] | 8.2 (0.004)[c] | n.a. | 4.5 (0.035)[a] | 15 (<0.001)[d] |
| OR (95% CI) | n.a. | 0.4 (0.2–0.8) | 5.4 (1.7–17.1) | n.a. | 0.4 (0.2–0.9) | 10.5 (3.2–34.5) |
| Fixed NSAIDs | | | | | | |
| *n* (%) | 4 (50) | 36 (75) | 59 (92.2) | 8 (72.7) | 32 (74.4) | 68 (93.2) |
| Wald (*p*) | n.a. | 2 (0.16) | 8.5 (0.004)[c] | n.a. | 0.01 (0.909) | 3.9 (0.047)[a] |
| OR (95% CI) | n.a. | 3 (0.6–13.9) | 11.8 (2.2–62) | n.a. | 1.1 (0.2–4.9) | 5.1 (1.0–25.5) |
| Fixed SR opioids | | | | | | |
| *n* (%) | 11 (73.3) | 45 (63.4) | 74 (97.4) | 18 (85.7) | 49 (74.2) | 74 (83.1) |
| Wald (*p*) | n.a. | 0.5 (0.465) | 7.9 (0.005)[b] | n.a. | 1.1 (0.284) | 0.1 (0.775) |
| OR (95% CI) | n.a. | 0.6 (0.2–2.2) | 13.5(2.2–82.4) | n.a. | 0.5 (0.1–1.8) | 0.8 (0.2–3.1) |

Abbreviations: n.a., reference group = 2010; NSAID, nonsteroidal anti-inflammatory drug; SR, sustained-release; THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a]$p < 0.05$. [b]$p < 0.01$. [c]$p < 0.005$. [d]$p < 0.001$.

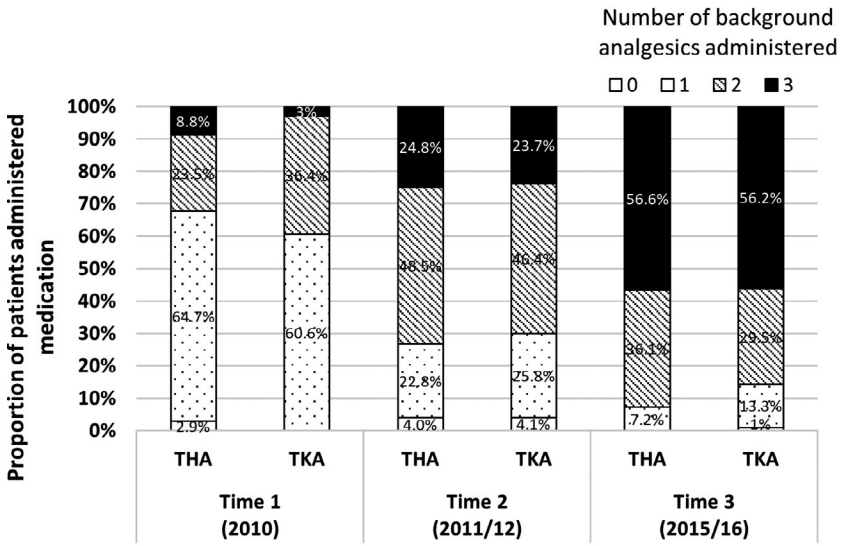


**FIGURE 3** The number of medication types administered to THA and TKA patients for background pain control ($n = 453$). Shaded columns represent the proportion of participants administered no, one, two, or three background analgesics at each time point. THA, total hip arthroplasty; TKA, total knee arthroplasty

analgesic was administered to patients at Time 3 compared to Time 1 ($U = 5{,}293$, $p < 0.001$) and Time 2 ($U = 13{,}541$, $p < 0.001$). This reflected use of prescribed paracetamol, NSAIDs and SR opioids, which were significantly higher at Time 3, compared with Time 1 (paracetamol $U = 4{,}409$, $p < 0.001$; NSAIDs $U = 823$, $p < 0.001$; SR opioids $U = 967$, $p < .001$), and Time 2 (paracetamol $U = 1{,}225$, $p < 0.001$). Use of weak opioids, however, significantly declined from Time 1 (Time 2 $U = 1{,}556$, $p = 0.013$; Time 3 $U = 1{,}289$, $p = 0.013$). Furthermore, patterns in the administration of rescue opioids (IR opioids, PCA) did not vary significantly and remained low throughout the study.

The morphine equivalence dose (mg) of SR opioids, IR opioids and PCA opioids administered during each survey period are reported in Figure 4. There was a significant increase in the dose of SR opioids administered (Kruskal–Wallis $\chi^2 = 67.368$, $p < 0.001$) at Time 2 ($U = 5{,}835$, $p < 0.001$) and Time 3 ($U = 7{,}257$, $p < 0.001$), relative to Time 1. There were no significant differences, however, in morphine equivalent dose of IR (Kruskal–Wallis $\chi^2 = 0.953$, $p = 0.621$) and PCA opioids (Kruskal–Wallis $\chi^2 = 0.248$, $p = 0.884$) between study surveys. The total morphine equivalence dose of all strong opioids and tramadol significantly increased over time (Kruskal–Wallis $\chi^2 = 27.212$, $p < 0.001$). Higher doses of all strong opioids/tramadol were administered at Time 2 ($Mdn = 40.4$ mg, $IQR = 45.5$ mg) compared to Time 1 ($Mdn = 30$ mg, $IQR = 40.75$ mg; $U = 6{,}937$, $p = 0.011$) and at Time 3 ($Mdn = 55.25$ mg, $IQR = 52.5$ mg) compared to Time 2 ($U = 14{,}998$, $p = 0.001$).

**TABLE 3** Mean ratio of prescribed analgesics administered

| | Mean proportion of prescribed medications administered | | | |
|---|---|---|---|---|
| **Analgesic class** | **Time 1** | **Time 2** | **Time 3** | **$p^d$** |
| Paracetamol[a] | 73% | 78.1% | 91% | <0.001 |
| NSAIDS[a] | 58.8% | 75.5% | 85.4% | 0.001 |
| Weak opioids[b] | 29.9% | 27.5% | 16% | 0.025 |
| Strong opioids[c] | | | | |
| IR | 21.5% | 23.8% | 18.9% | ns |
| SR | 59.5% | 82.5% | 87.9% | <0.001 |
| PCA | 34.3% | 33.2% | 22.3% | ns |
| All analgesics | 49.7% | 53.1% | 62% | <0.001 |

*Note:* Missing data: [a]$n = 3$, [b]$n = 7$, [c]IR opioids $n = 4$, SR opioids $n = 20$, PCA opioids $n = 14$, [d]Kruskal–Wallis test.

Abbreviations: IR, immediate release; ns, not significant; NSAID, nonsteroidal anti-inflammatory drug; PCA, patient controlled analgesia; SR, slow release.

## 3.4 | Trends in postoperative pain experience

Prevalence of any acute postoperative pain in the previous 24 hr (pain score > 0) across the three surveys was 95.3% ($n = 450$), with 80.8% ($n = 382$) of all patients reporting moderate-to-severe levels of postoperative pain (pain ≥ 4; see Table 4). There was no significant association between survey year and prevalence of postoperative pain (THA $\chi^2 = 2.134$, $p = 0.344$; TKA Fisher's Exact = 3.713, $p = 0.152$). A significantly lower proportion of TKA patients, however, reported moderate-to-severe levels of acute postoperative pain at Time 2 compared to Time 1 and 3 ($\chi^2 = 11.306$, $p = 0.004$, Cramer's $V = 0.215$, $z_{res} = -2.4$).

Ratings of pain intensity were highly variable (see Figure 5). Two-way ANCOVA revealed a statistically significant reduction in rest pain from Time 1, after controlling for postoperative interview day ($F(2, 340) = 16.215$, $p < 0.001$). Rest pain significantly decreased from Time 1 to Time 2 ($p = 0.031$, $M_{diff} = -0.8$), and from Time 2 to Time 3 ($p < 0.001$, $M_{diff} = -0.9$). There was no statistically

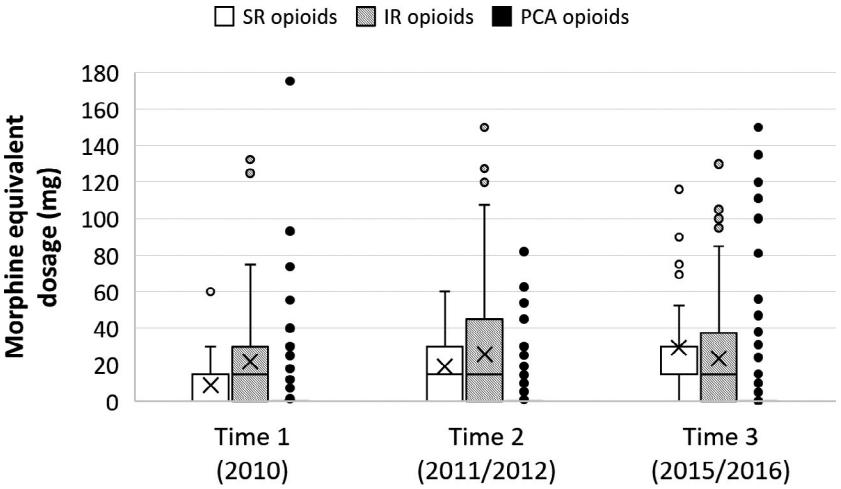


**FIGURE 4** Boxplots of the morphine equivalent dose of slow release (SR), immediate release (IR), and patient controlled analgesia (PCA) opioids administered (mg). Horizontal bars and crosses denote median and mean dosage, respectively

**TABLE 4** Prevalence of pain following THA and TKA surgery: 2010, 2011/2012, 2015/2016

| | Pain prevalence: n (%) | | | | Tests of association |
|---|---|---|---|---|---|
| | 2010 | 2011/2012 | 2015–2016 | Total | *p* |
| Any pain (pain > 0)[a] | | | | | |
| THA | 33 (88.1) | 94 (93.1) | 79 (95.2) | 210 (92.9) | ns[c] |
| TKA | 43 (100) | 93 (94.9) | 104 (99) | 240 (97.6) | ns[d] |
| Moderate-to-severe pain (worst pain ≥ 4)[b] | | | | | |
| THA | 32 (78) | 74 (74) | 64 (77.1) | 170 (75.9) | ns[c] |
| TKA | 39 (92.9) | 76 (77.6) | 97 (92.4) | 212 (86.5) | 0.004[c] |

*Note:* Missing data: [a]$n = 1$, [b]$n = 4$, [c]$p$-value, chi-square test of independence, [d]$p$-value, Fisher's exact test.
Abbreviations: ns, not significant; THA, total hip arthroplasty; TKA, total knee arthroplasty.

significant interaction between surgical group and survey year ($F(2, 340) = 0.417$, $p = 0.659$). One-way ANCOVA revealed a significant effect of survey year on dynamic pain ratings after controlling for interview day ($F(2, 447) = 4.547$, $p = 0.011$). Dynamic pain was significantly less intense at Time 2 compared to Time 1 ($p = 0.015$, $M_{diff} = -0.9$).

Patients typically experienced high levels of activity interference and moderate levels of sleep interference following THA and TKA (see Figure 6). There was a statistically significant decrease in activity interference from Time 1, after controlling for postoperative interview day ($F(2, 428) = 14.329$, $p < 0.001$). Inspection of simple main effects revealed that activity interference significantly decreased from Time 1 to Time 2 ($p = 0.028$, $M_{diff} = -0.9$), and from Time 2 to Time 3 ($p = 0.003$, $M_{diff} = -0.9$). There was no significant interaction between surgical type and survey year in ratings of activity interference ($F(2, 428) = 1.771$, $p = 0.659$). The distribution of sleep interference data did not support two-way analyses, or ANCOVA (Levene's test $p < 0.05$). One-way analyses indicated a statistically significant decrease in sleep interference ($F(2, 198.205) = 14.748$, $p < 0.001$, $\omega^2 = 0.06$), such that sleep interference was significantly less intense at Time 2 ($p < 0.001$, $M_{diff} = -1.6$) and Time 3 ($p < 0.001$, $M_{diff} = -2.2$) compared to Time 1.

## 3.5 | Effect of multimodal analgesia on acute postoperative pain experience

Table 5 describes the intensity of acute postoperative pain and pain interference with activities and sleep, according to number of background analgesics administered in multimodal combination. Patients administered three ($p < 0.001$, $M_{diff} = -1.7$) or two ($p = 0.001$, $M_{diff} = -1.1$) multimodal analgesics reported significantly lower activity interference than patients administered one background analgesic. Patients administered three multimodal background analgesics also reported significantly lower rest pain than patients administered two ($p = 0.02$, $M_{diff} = -0.6$) or one ($p = 0.02$, $M_{diff} = -0.7$) background analgesic. The same pattern was observed for ratings of sleep interference: three versus two background analgesics ($p = 0.016$, $M_{diff} = -0.8$); three versus one background analgesic ($p < 0.001$, $M_{diff} = -1.5$). Data on dynamic pain did not support analysis with two-way

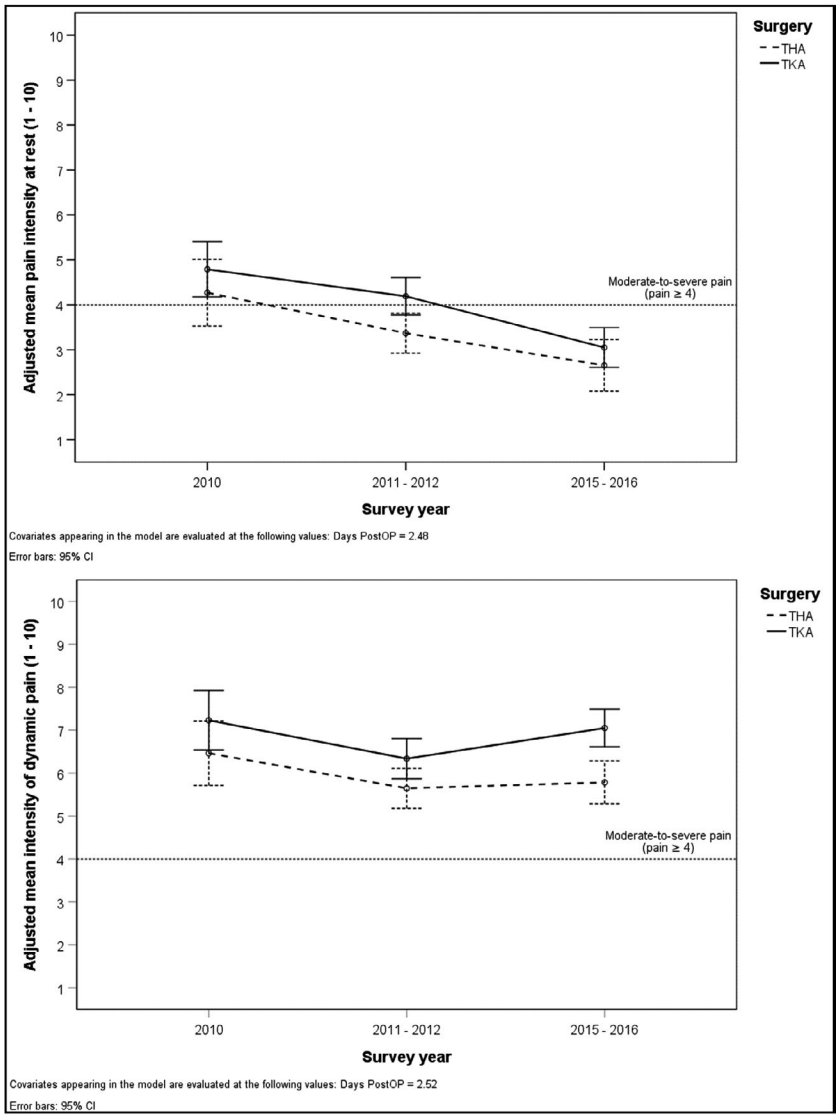


**FIGURE 5** Trends of acute postoperative rest ($n = 471$) and dynamic pain ($n = 469$) intensity following THA and TKA. Dotted lines and solid lines represent THA and TKA patients, respectively. Error bars are 95% CIs of the mean. THA, total hip arthroplasty; TKA, total knee arthroplasty

ANCOVA (Levene's test, $p = 0.021$). However, there was no significant difference between the number of multimodal analgesics administered and unadjusted ratings of dynamic pain ($F(2, 418) = 0.14$, $p = 0.869$). This was confirmed by one-way ANCOVA, controlling for postoperative day ($F(2, 420) = 0.554$, $p = 0.575$).

No significant interactions between surgical group and the number of multimodal medications administered were found after controlling for postoperative interview day: rest pain ($F(2, 317) = 2.499$, $p = 0.543$); activity interference ($F(2, 401) = 1.585$, $p = 0.206$) and sleep interference ($F(2, 402) = 2.022$, $p = 0.134$). Total knee arthroplasty patients reported significantly more intense rest pain ($F(1, 317) = 23.22$, $p = 0.018$, $M_{diff} = 0.6$), dynamic pain ($t(449) = 4.307$, $p < 0.001$, $M_{diff} = 1.0$) and activity interference ($F(1, 401) = 10.067$, $p = 0.002$, $M_{diff} = 0.8$) than THA patients. There was no statistically significant effect of surgical group on sleep interference ($F(1, 402) = 1.083$, $p = 0.299$).

## 3.6 | Trends in opioid-induced side effects and their pharmacological management

Data for adjuvant pain medications were collected in Time 2 and 3 in the context of large, and statistically significant increases in prescribing of gabapentinoids (1.2%–53.2%; $\chi^2 = 67.943$, $p < 0.001$, $\varphi = 0.499$ continuity correction applied) between 2010 and 2016. Despite apparent increases in prescribing, use of adjuvant medications at Time 3 was low (see Figure 7). Although almost all patients surveyed at Time 3 were prescribed an antiemetic medication ($n = 185$, 98.4%), less than one third of patients received it ($n = 59$, 31.4%). Approximately half of all patients were prescribed ($n = 100$, 53.2%) and received ($n = 98$, 52.1%) a gabapentinoid. In addition, there was a considerable discrepancy between rates of laxative prescribing and laxative use. While approximately half the sample had a prescription for laxatives ($n = 90$, 47.9%), laxatives were only administered to 34% of the sample ($n = 64$). Under two-thirds of patients with constipation had a

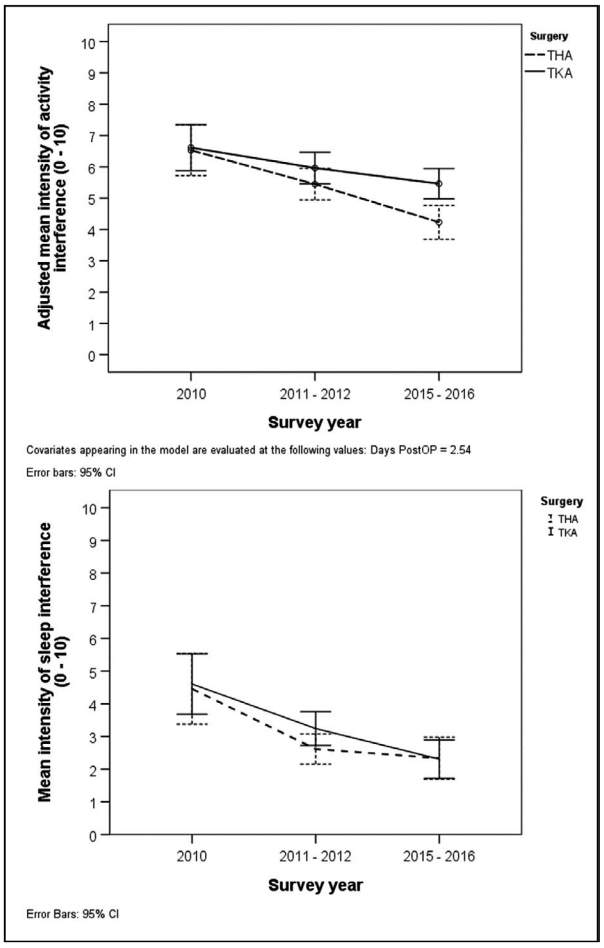


**FIGURE 6** Trend of activity interference among patients who reported pain following THA and TKA: 2010–2016 ($n = 457$). Dotted lines and solid lines represent THA and TKA patients, respectively. Error bars are 95% CIs of the mean. THA, total hip arthroplasty; TKA, total knee arthroplasty

laxative prescription ($n = 28$, 60.9%) and only half the patients with constipation received a laxative ($n = 23$, 50%).

The intensity of past 24-hr medication induced nausea, drowsiness are dizziness are reported in Table 6. Patients experienced high levels of nausea following TKA surgery. Drowsiness was high following both THA and TKA, and was significantly more intense at Time 3 compared with Time 2. Rates of medication induced constipation were significantly lower at Time 3 ($n = 46$, 26.4%), compared to Time 2 ($n = 101$, 51%; $\chi^2 = 22.382$, $p < 0.001$, $\varphi = -2.51$, continuity correction applied).

# 4 | DISCUSSION

## 4.1 | Quality of evidence-based analgesic prescribing

Results from this 6-year observational study, undertaken in the context of increasing international awareness of the importance of multimodal analgesia (Beverly, Kaye, Ljungqvist, & Urman, 2017; Savarese & Tabler, 2017), identified significant and sustained practice change in analgesic prescribing for acute postoperative pain. Over the course of this study, we observed considerable increase in multimodal prescribing from an infrequent practice, to the norm for arthroplasty patients in the hospital. In 2010, 43.5% of surveyed patients were prescribed a single analgesic for background pain control, and rates of prescriptions for paracetamol, NSAIDs and SR opioids in multimodal combination were low (11.8%). Multimodal prescribing had increased significantly by the following year (Time 2) and was very frequent 5 years later (Time 3). At 5 years, less than one-in-ten patients were prescribed a single background analgesic (8.5%) and seven-in-ten patients were prescribed all three background analgesics in multimodal combination.

We considered orders for fixed-rate, rather than PRN analgesics as an indicator of the quality of multimodal prescribing. Fixed prescriptions decrease the complexity of nurses' medication-related decision making, thereby raising the likelihood that analgesics will be administered in multimodal combination and patients will receive sufficient analgesia. Although background analgesics were commonly prescribed as fixed-rate in 2010, we observed increased PRN prescribing in the year immediately following targeted presentations to anaesthetists. We speculate that in the context of a rising number of orders for multimodal medications, the more frequent use of medication 'as needed' may have reflected a cautious initial commitment to multimodal analgesia from prescribers, which was conditioned on pain assessment at bedside. Overall however, there was a statistically significant increase in fixed-rate prescriptions over the course of the study, such that the majority of background analgesics were fixed-rate by 2015/2016, and fixed prescribing for paracetamol and NSAIDS was nearly universal (>92%).

## 4.2 | Quality of evidence-based analgesic administration

The expansion of multimodal prescribing appeared to precipitate a substantial increase in the administration of multimodal analgesics by nursing staff. Analyses revealed significant growth in the rates of multimodal analgesic administration 1 and 5 years following the initial survey. Approximately one-third of patients were administered background medications in multimodal combination in 2010. By 2015/2016, almost all THA and TKA patients surveyed, 88.8%, were administered multimodal analgesics and patients had 20 times the odds, relative to 2010, of being administered paracetamol, NSAIDs and SR opioids in combination. However, this equated to less than six-in-ten patients receiving all three background

**TABLE 5** Intensity of acute postoperative pain by the number of multimodal analgesics received for background pain control

| | Number of background analgesics administered | | | | Main effects |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | *p* |
| Proportion of patients | | | | | |
| *n* (%) | 10 (2.1) | 108 (22.8) | 177 (37.4) | 158 (34.9) | – |
| Rest pain (*M*, *SD*)[a] | | | | | 0.027[e,g] |
| THA | 2.5 (1) | 3.5 (2.3) | 3.4 (2.0) | 3.1 (2.0) | |
| TKA | 5 (2.9) | 4.1 (1.7) | 4.1 (2.3) | 3.3 (1.9) | |
| Total | 3.8 (2.4) | 3.8 (2) | 3.8 (2.2) | 3.2 (1.9) | |
| Dynamic pain (*M*, *SD*)[b] | | | | | ns[f,g] |
| THA | 5.3 (2.2) | 5.8 (2.7) | 5.7 (2.3) | 5.9 (2.5) | |
| TKA | 6.8 (1.6) | 6.9 (2.0) | 7.0 (2.4) | 6.6 (2.2) | |
| Total | 6.1 (2) | 6.4 (2.4) | 6.4 (2.4) | 6.3 (2.4) | |
| Worst activity interference (*M*, *SD*)[c] | | | | | <0.001[e,g] |
| THA | 7.8 (1.7) | 6.1 (2.4) | 4.7 (2.7) | 4.7 (2.5) | |
| TKA | 5.6 (3.2) | 6.7 (2.1) | 6.1 (2.5) | 5.1 (2.3) | |
| Total | 6.6 (2.7) | 6.4 (2.3) | 5.4 (2.7) | 4.9 (2.4) | |
| Worst sleep interference (*M*, *SD*)[d] | | | | | <0.001[e,g] |
| THA | 2.8 (3.2) | 3.6 (3.0) | 2.5 (2.4) | 2.3 (2.5) | |
| TKA | 3.4 (3.4) | 3.5 (2.6) | 3.5 (2.9) | 2.2 (2.7) | |
| Total | 3.1 (3.1) | 3.6 (2.8) | 3 (2.7) | 2.2 (2.6) | |

*Note:* Missing data: [a]$n = 2$, [b]$n = 4$, [c]$n = 16$, [d]$n = 15$, [e]*p*-value, two-way ANCOVA controlling for postoperative interview day; [f]*p*-value, two-way ANOVA; [g]comparison excludes patients who received no background analgesics due to small group size.

Abbreviations: ns, not significant; THA, total hip arthroplasty; TKA, total knee arthroplasty.

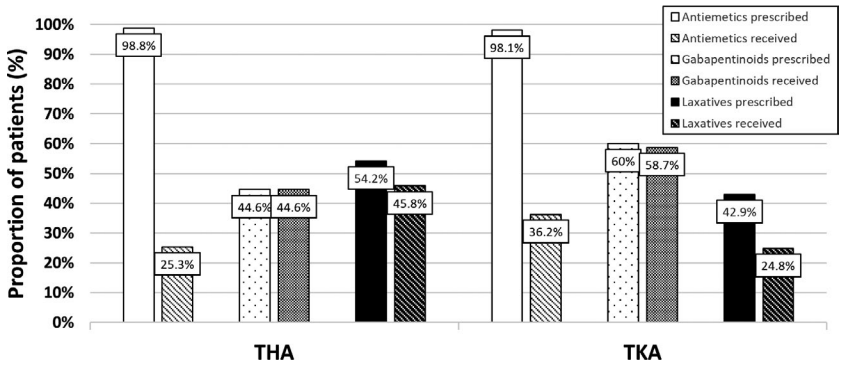


**FIGURE 7** Prescribing and administration of adjuvant analgesics for the pharmacological management of opioid-induced side effects: 2015/2016 ($n = 188$). Shaded columns represent the proportion of participants prescribed or administered: antiemetics; gabapentinoids; and laxatives. THA, total hip arthroplasty; TKA, total knee arthroplasty

medications at year five, indicating that despite the considerable increase in the use of multimodal analgesics throughout the study, there may be room for further improvement. However, with pressure on hospitals to discharge surgical patients after short hospital stays, the need to prescribe and use opioid medications should be balanced against risks of post-discharge opioid misuse (Yorkgitis & Brat, 2018). Although further work needs to be done to understand the optimal way to use multimodal analgesics to reduce opioid use following discharge from hospital, the postoperative use of regional analgesia and anaesthesia should be encouraged to optimize opioid

**TABLE 6** Intensity of nausea, drowsiness and dizziness reported following THA and TKA at Time 1, 2 and 3

| | Intensity of side effect (*Mdn*, *IQR*) | | | Mann–Whitney *U* test | |
|---|---|---|---|---|---|
| | Time 2 (2011/2012) | Time 3 (2015/2016) | Total | *U* | *p* |
| Nausea (0–10)[a] | | | | | |
| THA | 0 (3) | 1 (5) | 0 (3) | 3,700.5 | 0.339 |
| TKA | 2.5 (4) | 2 (7) | 2 (5) | 6,620.5 | 0.166 |
| Drowsiness (0–10)[a] | | | | | |
| THA | 2 (4) | 4 (7) | 3 (5) | 2,742.5 | <0.001 |
| TKA | 3 (4) | 5 (6) | 4 (6) | 4,941.5 | <0.001 |
| Dizziness (0–10)[a] | | | | | |
| THA | 1 (3) | 0 (4) | 0 (3) | 3,969 | 1 |
| TKA | 2 (3) | 2 (4) | 2 (4) | 6,963 | 0.347 |

*Note:* Missing data: [a]$n = 13$.

sparing during admissions (Beverly, Kaye, Ljungqvist, et al., 2017; Chou et al., 2016)..

Growth in the use of multimodal analgesics was reflected in significantly increased paracetamol and NSAID use, measured by the total ratios of available medication administered, and SR opioid use, also measured by the morphine equivalence dose. The lack of significant differences in the use of strong IR and PCA opioids over time indicated the absence of a clinically significant opioid-sparing effect following increased use of multimodal analgesia. While this contrasts with findings from the experimental literature involving major surgery (Elia et al., 2005; Rømsing et al., 2005), the magnitude of the opioid sparing effect from multimodal analgesia may be small (McDaid et al., 2010), and arthroplasty patients are known to have particularly high pain and opioid requirements. In a randomized controlled trial of TKA patients where the multimodal analgesia group was found to use less opioid than the PCA opioid comparison group (Lamplot et al., 2014), there had also been manipulation of intraoperative analgesic medications. This may account for the divergent results relative to the present study.

The finding of greater levels of SR and total opioid-use after the initial survey, suggested the need for the effective management of opioid-induced side effects. This survey, however, suggested critical gaps in the prescribing and administration of adjuvant analgesics. Consensus guidelines recommend the use of prophylactic antiemetics titrated for patients' risk of nausea and vomiting (Gan et al., 2014). However, in 2015/2016, despite the high levels of nausea reported and the wide availability of antiemetic medications, less than one third of patients received an antiemetic. Consideration should be given to whether fixed prescribing could be employed to increase rates of antiemetic administration. Gabapentinoids have been demonstrated to reduce both postoperative opioid requirements and nausea (Axelby & Kurmis, 2020; Zhang, Ho, & Wang, 2011). However, only approximately half the sample had a prescription for, and were administered, a gabapentinoid at 5 years. Finally, analyses suggested that laxatives were both under prescribed and under administered at 5 years. Only half of the patients who reported constipation received a laxative and an additional 40% of constipated patients had no laxative prescription.

## 4.3 | Changes in patients' postoperative pain experience

Findings generally supported past research demonstrating the efficacy of multimodal analgesia for pain reduction (Elia et al., 2005; Lamplot et al., 2014). However, it is important to note that clinically significant mean reductions in pain intensity are commonly considered to be greater than 2 on an 11-point NRS (Childs, Piva, & Fritz, 2005). Use of analgesic medications in multimodal combination was associated with modest, non-clinical reductions in rest pain severity and clinically significant reductions in pain interference with physical activity and sleep. We identified a significant decrease in rest pain and interference of pain on physical activity and sleep following the initial survey, which corresponded to the increased postoperative use of multimodal analgesia. Analyses suggested that growth in the use of multimodal analgesia improved the overall quality of postoperative pain management on the wards. In 2010, management of postoperative rest pain appeared to be suboptimal, with patients reporting a mean intensity of rest pain indicating moderate-to-severe pain (NRS $\geq 4$). The mean intensity of rest pain was mild (NRS $< 4$) in 2015/2016, indicating that on average, patients' postoperative rest pain was well managed.

However, the initial improvement in patients' dynamic pain in the year following the initial survey failed to be sustained 5 years later. Moreover, the finding of high levels of dynamic pain and low use of rescue opioids at all time points

suggested that rescue opioids were under-administered. Findings suggested the presence of a considerable clinical gap in the bedside assessment and management of breakthrough pain, which may explain the failure of improved use of background analgesics (SR opioids, paracetamol and NSAIDS) to reduce worst pain intensity. Although there was a commitment to establish an acute pain service at the hospital site by Time 3, ward staff need to be supported to independently achieve quality standards of pain management whereby patients' pain intensity does not interfere with patients' ability to mobilize, sleep, socialize, etc., and rehabilitate effectively. This intensity is generally considered to be less than 4/10 at rest and with activity, but past research has revealed that patients may be able to cope with higher levels of postoperative pain (van Dijk, Kappen, Schuurmans, & van Wijck, 2015; van Dijk, Kappen, van Wijck, Kalkman, & Schuurmans, 2012). Nurses' decision making for analgesic administration in the clinical work environment is complex, and requires judgments involving clinical experience, patients' reports of pain and patient preferences, and evidence-based knowledge of the safe and effective use of various medications and treatments. Nurses may benefit from the use of clinical support algorithms or aides-mémoires (Botti et al., 2014) to help guide the administration of analgesic medications to surgical patients.

### 4.4 | Limitations

This study had several limitations. First, not all key side-effects of analgesic medications were measured, such that the rates of sedation, overdose and falls remain unknown. Second, potential differences in intra-operative analgesia, including the use of femoral nerve blocks and spinal local anaesthetic, as well as the use of non-pharmacological interventions, were not accounted for and as such, pain scores did not represent the *absolute* effect of multimodal analgesia in the postoperative context. Rather, these results reflect the *relative* contribution of the postoperative use of multimodal analgesics in real-world conditions involving variation in surgeons, anaesthetists and intra-operative procedures. However, the effect of multimodal analgesia under experimental conditions has been reported by numerous authors elsewhere (e.g. Elia et al., 2005; Lamplot et al., 2014; Ong et al., 2010). Further limitations of the observational design included the inability to identify the drivers of practice change. There were multiple stakeholders engaged in translating the data derived from this study and recognition of a significant practice problem by the hospital executive resulting in the establishment of an acute pain service in late 2015. However, the degree to which practice change was driven by increasing general awareness in clinicians of the benefits of multimodal analgesia, the feedback delivered to prescribers, or other factors, was unclear. Future research in other hospital sites should be conducted to explicitly test the efficacy of feeding data back to clinicians to improve the prescribing and use of multimodal analgesics.

## 5 | CONCLUSION

This research identified significant, sustained improvement in the prescription and use of multimodal analgesics for acute postoperative pain on the orthopaedic wards of an Australian private hospital between 2010 and 2016. Following targeted presentations to prescribers, THA and TKA patients were significantly more likely to be prescribed and receive analgesics in multimodal combination. At 5 years after the initial survey, prescribers were significantly more likely to order analgesics in a fixed-rate fashion, potentially reducing the complexity of nurses' decision making regarding the administration of combined medications. Use of multimodal analgesia was associated with statistically significant reduction of rest pain and interference with physical activity, but not opioid sparing or dynamic pain control. However, future research and quality improvement activity that adopts this method should additionally attend to the gaps in the overall quality of pain management highlighted by this survey.

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### CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

### AUTHORS' CONTRIBUTIONS

MB, TB, JC, MD, BR and RdS made substantial contributions to the conception and design of the study. MB and BR contributed to the acquisition of study data. DK completed the data entry and analysis, and drafted the manuscript. All authors discussed the results, commented on the manuscript and revised it critically. All authors gave approval for the manuscript to be published.

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