

## **Editorial**

### **Postoperative pain management: time to get back on track**

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Opioid use in the UK has increased significantly over the last 20 years, with the 34% increase in number of opioid items dispensed in primary care dwarfed by the far greater rise of 127% in the oral morphine equivalent dose of those prescriptions [1]. It is now estimated that 5% of the UK population take opioids, while nearly 10% of the population take some form of dependence-forming medicines [2], a term that encompasses opioids, gabapentinoids, benzodiazepines and Z drugs. Dependence and addiction to opioids have been well-recognised since Victorian times [3]. Prescribed opioid misuse is now a phenomenon seen in developed countries with the US and Canada being the worst affected [4]. Persistent postoperative opioid use has been identified as a contributor to this rise in opioid prescriptions. Studies, mainly undertaken in North America, have demonstrated that 0.6% to 26% opioid-naïve patients, and 35% to 77% patients with previous opioid exposure, continue to take opioids for more than 3 months postoperatively when healing is complete and acute pain would have ceased [5].

In addition to patient factors, four main risk factors for prolonged opioid use have been identified: the use of modified-release opioid preparations; the duration of the initial opioid prescription (but, interestingly, not the dose); the use of repeat prescriptions; and surgery [5, 6]. This joint supplement from *Anaesthesia* and the *British Journal of Surgery* includes invited reviews on the current state of enhanced recovery after surgery (ERAS) and fast-track surgery [7], and on the use of scoring systems and patient-reported outcome measures (PROMS) to improve the quality of patient recovery [8]. All of these processes are commendable and have led to improvements in the quality of peri-operative care. However, has the introduction of fast-track surgery, scoring systems and the use of patient satisfaction outcome measures inadvertently contributed to the phenomena of persistent post-operative opioid use and opioid-induced ventilatory impairment?

### **Long-acting opioids**

One of the cornerstones of ERAS is the use of analgesia to attenuate the stress response from surgery and promote restoration of function, thus expediting patient discharge from hospital [7]. At the same time that the benefits of enhanced recovery were being extolled, Purdue Pharma, and subsequently its subsidiaries, were beginning to promote the modified-release opioid, oxycodone (OxyContin®, Purdue Pharma, Stamford, CT, USA) [3]. Purdue Pharma's subsidiaries and sister companies include Mundipharma and Napp Pharmaceuticals. Studies were published that created a narrative that OxyContin® was essential in fast-track surgery [4, 9-11]. The study by Reuben et al. has been retracted since its disgraced author admitted

fabricating results in multiple studies in what has been acknowledged as one of the widest-ranging cases of academic fraud [4]; while the study by Sunshine et al. was sponsored by Purdue Pharma [9]. The study by de Beer et al. [10] demonstrated the superiority of controlled-release oxycodone in promoting mobilisation after lower limb arthroplasty, reducing length of stay and costs, when compared with intravenous patient-controlled analgesia or epidural analgesia, while other placebo-comparison studies demonstrated the superiority of controlled-release oxycodone in reducing one or more of the following: pain scores; subsequent opioid consumption; length of stay and costs [4, 11]. Based on these studies, and with aggressive marketing by Purdue Pharma, modified-release oxycodone became, and continues to be, an integral part of many enhanced recovery programmes [4]. With the benefit of hindsight, it not surprising that the use of an oral opioid analgesic is superior to placebo or patient-controlled analgesia, with the requisite drips, pumps and supplemental oxygen, in promoting mobility and thus reduced length of stay. In 2007, Purdue Pharma were found guilty of perpetuating misleading claims that OxyContin® was superior to other opioids by not being addictive. Three senior executives were also found guilty and the company was ordered to pay costs and damages of over \$600 million [3]. Purdue Pharma is now facing an avalanche of class action claims and has just filed for bankruptcy. Current evidence shows that not only is oxycodone just as addictive as other opioids, it is actually more likeable by patients with a higher abuse liability [12].

As well as the use of modified-release opioid preparations being the strongest predictor of subsequent sustained opioid use [6], their use also carries similar risks to the use of a continuous opioid or patient-controlled analgesia (PCA) ‘background’ infusion in opioid-naïve patients for causing opioid-induced ventilatory impairment [13, 14]. In 2018, the Australian and New Zealand College of Anaesthetists and its Faculty of Pain Medicine joined the US Food and Drug Administration (FDA), the American Pain Society and the American Academy of Pain Medicine in stating that modified-release opioid analgesics are not recommended for use in treating acute pain or postoperative pain [13]. This advice is also in alignment with the recommendations of the US Center for Disease Control and Prevention (CDC), who advise that, when opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids (i.e. not extended-release preparations) and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids [15]. Moreover, the CDC and the US OxyContin® product licence state that modified-release oxycodone should be reserved for use in patients for whom alternative treatment options (e.g. non-opioid analgesics or immediate-release opioids) are

ineffective, not tolerated, or would otherwise be inadequate to provide sufficient management of pain [13, 15]. Thus, the widespread and continued use of OxyContin as an integral part of enhanced recovery after surgery pathways can only be described as a pseudoaxiom (a false principle or rule handed down from generation to generation of medical providers and accepted without serious challenge or investigation).

### **Unidimensional pain scores**

At the same time as Purdue Pharma were gaining a licence to market OxyContin, the American Pain Society introduced the “*Pain as the Fifth Vital Sign*” campaign. The premise was that pain scores should be recorded routinely on an inpatient’s chart and that unrelieved pain should be seen as a ‘red flag’ for escalation [3]. It is now recognised that this campaign encouraging repeated pain assessment using unidimensional scores, such as the numeric rating scale (NRS), contributed to the burgeoning use of opioids [3, 16], with some studies failing to find a significant improvement in acute pain management [17]. Aiming for ‘no worse than mild pain’ [18] using the NRS as a tool was associated with increased opioid use and opioid-induced over-sedation [19], despite the fact that opioids have relatively little effect on movement-related pain [20], a primary focus of ERAS programmes to hasten mobilisation.

In 2017, the Joint Commission (the US’s healthcare regulatory agency) recognised the dangers of unidimensional pain scores in driving unrealistic patient expectations and subsequent opioid dependence and recommended the use of multimodal scoring systems that include restoration of function, rather than reliance on unidimensional pain intensity scales to guide inpatient administration of opioids [21]. Subsequently, the “*Pain as the Fifth Vital Sign*” campaign has been discredited and is no longer being promoted [16], and the American Pain Society has been inundated with lawsuits over its links to opioid pharmaceutical companies and dissolved due to bankruptcy in June 2019.

### **Opioid-induced ventilatory impairment**

As well as prescribed opioids being a risk factor for persistent post-operative opioid use, it is increasingly being recognised that prescribed opioids are a major cause of death or hypoxia caused by opioid-induced ventilatory impairment both in hospital and in the community [15].

Whilst risk factors such as obstructive sleep apnoea, use of modified-release opioid preparations, increased sensitivity to opioids with age and concurrent use of sedatives such as gabapentinoids have been identified, many instances of opioid-induced ventilatory impairment occur in people with no risk factors. More worrisome is that standard track and trigger tools are not sensitive enough to provide early warning of impending opioid-induced ventilatory impairment. Therefore, the Australian and New Zealand College of Anaesthetists and its Faculty of Pain Medicine [14] have recommended that: opioids should not be titrated to unidimensional pain scores alone; slow-release opioids should be avoided; for opioid naïve patients, initial doses of opioid should be based on the patient's age; and there must be regular assessment of a patient's level of sedation whenever opioids are administered.

### **Patient satisfaction**

In 2001, the Institute of Medicine in the USA deemed that the US health delivery system did not provide consistent, high-quality medical care to all people. Subsequently, the US Congress directed the Centre for Medicare and Medicaid Services to design a patient satisfaction survey to promote adoption of best practice. Failure to comply led to financial penalties. Three of the 22 questions concerned pain management: (1) During this hospital stay, did you need medicine for pain? (2) During this hospital stay, how often was your pain well controlled? (3) During this hospital stay, how often did hospital staff do everything they could to help you with your pain?

As a result many clinicians felt obliged to administer more opioids than necessary in order to satisfy the patient reported satisfaction scores, and these specific patient reported outcome measures are now being removed from the US's Hospital Consumer of Healthcare Providers and Systems Survey [22].

### **Addiction**

These three pseudoaxioms pale into insignificance when compared with the fact that for over three decades, drug companies and doctors promoted the false concept that addiction to prescribed opioids is rare. This particular medical myth was based on a single letter comprising five sentences that was published in 1980, entitled: "*Addiction rare in patients treated with narcotics*". In 2017, a bibliometric analysis identified that it had been cited 608 times, with 439 of these publications citing it as evidence that addiction was rare in patients (including those with chronic pain) treated with opioids. Thus, this frequently and uncritically

cited letter created a narrative that allayed prescribers' concerns about the risk of addiction with opioid therapy [23].

In summary, these various pseudoaxioms have had unintended consequences and have directly contributed to the dual issue of persistent post-operative opioid use and opioid-induced ventilatory impairment. To promote the safe development of recovery after surgery, and reduce the risk of both prolonged postoperative opioid use and ventilatory impairment, we need to apply the lessons from North America and Australasia and encourage multidisciplinary care with multimodal analgesia, both in hospital and at home [24]. Surgical analgesic regimens need to be constructed using the concept of procedure-specific pain management, with increased use of regional anaesthesia techniques when appropriate [25], rather than relying on the World Health Organization's pain ladder that was devised for the treatment of end-of-life cancer pain. Additional opioid analgesia needs to be titrated to function, not purely unidimensional pain intensity scores, with immediate-release formulations of opioids based on patients' age, with no place for the routine use of modified-release opioid preparations [14]. All patients on opioids need to be carefully monitored for signs of opioid-induced ventilatory impairment and over-sedation. Discharge analgesia needs more thought than it has received previously, with procedure-specific guidance determining the amount of analgesia a patient is given, with non-opioids as well as limited opioids. Additional education to medical and nursing staff will be required to ensure compliance. In addition, patients must be taught how to use, wean and dispose of their post-discharge analgesia safely, and provision must be made to identify those who are requesting repeat opioid prescriptions, either to address their persistent pain or to tackle inappropriate opioid continuation [24]. Through good intentions, postoperative pain management has left patients vulnerable to opioid risk; clinicians' acknowledgement and awareness of that risk, together with simple measures, must get it back on track.

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## References

1. Curtis HJ, Croker R, Walker AJ, Richards GC, Quinlan J, Goldacre B. Opioid prescribing trends and geographical variation in England, 1998-2018: a retrospective database study. *Lancet Psychiatry* 2019; 6: 140-50.
2. Cartagena Farias J, Porter L, McManus S, et al. Prescribing patterns in dependence forming medicines. London: NatCen; 2017.  
[http://phrc.lshtm.ac.uk/papers/PHRC\\_014\\_Final\\_Report.pdf](http://phrc.lshtm.ac.uk/papers/PHRC_014_Final_Report.pdf) (accessed 19/08/2019).
3. deShazo RD, Johnson M, Eriator I, Rodenmeyer K. Backstories on the US opioid epidemic. Good intentions gone bad, an industry gone rogue, and watch dogs gone to sleep. *American Journal of Medicine* 2018; 131: 595-601
4. Levy N, Mills P. Controlled-release opioids cause harm and should be avoided in management of postoperative pain in opioid naïve patients. *British Journal of Anaesthesia* 2019; 122: e86-90.
5. Kent ML, Hurley RW, Oderda GM, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative-4 Joint Consensus Statement on persistent postoperative opioid use: definition, incidence, risk factors, and health care system initiatives. *Anesthesia and Analgesia* 2019; 129: 543-52.
6. Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use - United States, 2006-2015. *Morbidity and Mortality Weekly Report* 2017; 66: 265-9.
7. Kehlet H. Enhanced postoperative recovery: good from afar - but far from good? *Anaesthesia* 2020; **this supplement**.
8. Myles PS. More than just morbidity and mortality - quality of recovery and long-term functional recovery after surgery. *Anaesthesia* 2020; **this supplement**.

9. Sunshine A, Olson NZ, Colon A, et al. Analgesic efficacy of controlled-release oxycodone in postoperative pain. *Journal of Clinical Pharmacology* 1996; 36: 595-603.
10. de Beer Jde V, Winemaker MJ, Donnelly GA, et al. Efficacy and safety of controlled-release oxycodone and standard therapies for postoperative pain after knee or hip replacement. *Canadian Journal of Surgery* 2005; 48: 277-83.
11. Rothwell MP, Pearson D, Hunter JD, et al. Oral oxycodone offers equivalent analgesia to intravenous patient-controlled analgesia after total hip replacement: a randomized, single-centre, non-blinded, non-inferiority study. *British Journal of Anaesthesia* 2011; 106: 865-72.
12. Wightman R, Perrone J, Portelli I, Nelson L. Likeability and abuse liability of commonly prescribed opioids. *Journal of Medical Toxicology* 2012; 8: 335-40.
13. Australian and New Zealand College of Anaesthetists. Position statement on the use of slow-release opioid preparations in the treatment of acute pain. 2018. <http://www.anzca.edu.au/resources/endorsed-guidelines/position-statement-on-the-use-of-slow-release-opio> (accessed 19/08/ 2019).
14. Australian and New Zealand College of Anaesthetists. Statement on principles for identifying and preventing opioid-induced ventilatory impairment (OIVI). 2018. <http://www.anzca.edu.au/resources/endorsed-guidelines/oivi-statement> (accessed 12/09/2019).
15. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016. *Morbidity and Mortality Weekly Report* 2016; 65: 1-49.
16. Levy N, Sturgess J, Mills P. “Pain as the fifth vital sign” and dependence on the “numerical pain scale” is being abandoned in the US: Why? *British Journal of Anaesthesia*. 2018; 120: 435-8.



17. Mularski RA, White-Chu F, Overbay D, Miller L, Asch SM, Ganzini L. Measuring pain as the 5th vital sign does not improve quality of pain management. *Journal of General Internal Medicine* 2006; 21: 607-12.
18. Moore RA, Straube S, Aldington D. Pain measures and cut-offs - 'no worse than mild pain' as a simple, universal outcome. *Anaesthesia* 2013; 68: 400-12.
19. Vila H, Jr., Smith RA, Augustyniak MJ, et al. The efficacy and safety of pain management before and after implementation of hospital-wide pain management standards: is patient safety compromised by treatment based solely on numerical pain ratings? *Anesthesia and Analgesia* 2005; 101: 474-80.
20. Gilron I, Orr E, Tu D, O'Neill JP, Zamora JE, Bell AC. A placebo-controlled randomized clinical trial of perioperative administration of gabapentin, rofecoxib and their combination for spontaneous and movement-evoked pain after abdominal hysterectomy. *Pain* 2005; 113: 191-200.
21. The Joint Commission. R<sup>3</sup> Report. Pain assessment and management standards for hospitals. 2017.  
[https://www.jointcommission.org/assets/1/18/R3\\_Report\\_Issue\\_11\\_Pain\\_Assessment\\_2\\_11\\_19\\_REV.pdf](https://www.jointcommission.org/assets/1/18/R3_Report_Issue_11_Pain_Assessment_2_11_19_REV.pdf) (accessed 19/08/2019).
22. Rummans TA, Burton MC, Dawson NL. How good intentions contributed to bad outcomes: the opioid crisis. *Mayo Clinic Proceedings* 2018; 93: 344-50.
23. Leung PTM, Macdonald EM, Stanbrook MB, Dhalla IA, Juurlink DN. A 1980 letter on the risk of opioid addiction. *New England Journal of Medicine* 2017; 376: 2194-5.
24. Levy N, Mills P, Rockett M. Post-surgical pain management: time for a paradigm shift. *British Journal of Anaesthesia*. 2019; 123: e182-186

25. Joshi GP, Van de Velde M, Kehlet H; PROSPECT Working Group Collaborators. Development of evidence-based recommendations for procedure-specific pain management: PROSPECT methodology. *Anaesthesia* 2019; 74: 1298-1304.