

Acute Pain Update

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Prior to Covid-19, the World Health Organisation published the 'top 10' leading causes of death in upper- and middle-class income countries and globally in 2019.¹ Opioid related deaths are not on the list. There is however wide acceptance that the USA have an opioid epidemic associated with unnecessary death and 2020 saw a new record of 93,000 deaths because of opioid drug overdose that cost Americans about 3.5 million years of life.² In New Zealand we have witnessed a steady increase in opioid use from 14.4 per 1000 people in 2011 to 16.6 per 1000 in 2016.³

Coroner inquest reports have recorded 325 opioid related deaths over a 5-year period between 2008 and 2012⁴ and Ministry of Health data recorded an average of 37 deaths per year between 2004 and 2011 with the cause of death recorded as 'opioid poisoning'.⁵

Of course 'death' is not the only opioid related harm. A New Zealand study published in 2017 examined medication harm in hospitals and found that opioids (including tramadol) and anticoagulants/antiplatelet agents accounted for 40% of all harm. They were also implicated in the most severe harm; defined as bleeding, hypotension and delirium, confusion and over-sedation.⁶

In the face of growing concern over opioid stewardship, the Australian and New Zealand College of Anaesthetists (ANZCA) has updated and amalgamated two separate college statements on slow-release opioids and identifying and preventing opioid induced ventilatory impairment (OIVI).

PS41 - Position Statement on Acute Pain Management, was developed with the stated purpose to 'advance the standards of care related to the management of acute pain' and to 'develop a framework for the provision of high quality management of acute pain'.

The framework includes provisions for pain education, assessment of analgesic efficacy and adverse events, recommendations for pharmacological therapies, delivery of acute pain services and quality assurance.

Education recommendations are directed to undergraduate medical students, ANZCA and FPM trainees and 'other medical staff' and nurses; acknowledging that anaesthetists play a key role in the education process. There is also acknowledgement of the importance of patient and carer education with explicit emphasis on setting expectations of having well managed pain in the rehabilitation process rather than having 'no pain'.

Assessment of efficacy considers both pain intensity scores and functional assessment.

A	No limitation: the patient is able to undertake the activity** without limitation due to pain
B	Mild limitation: the patient is able to undertake the activity but experiences moderate to severe pain
C	Severe limitation: the patient is unable to complete the activity due to pain

* Adapted from Scott DA & McDonald WM (2008) Assessment, Measurement and History. In: Textbook of *Clinical Pain Management: Acute Pain 2e*. Macintyre PE, Rowbotham D and Walker S (eds). London, Hodder Arnold.

** Activity assessed is relevant activity related to the cause of the 'new' acute pain – e.g., ability to take deep breaths and cough after abdominal surgery or injury, or to flex knee after knee surgery

Scott & McDonald, 2008; Schug et al, 2020

Provision is also made for assessment of anxiety, mood and past experience with a recommendation that these factors should inform non-pharmacological management and that additional opioids to manage these should be avoided.

A large section in the appendix is devoted to opioid induced ventilatory impairment (OIVI) as the most dangerous adverse effect and emphasis is placed on sedation monitoring as an early warning system to identify over-sedation and raise alarm to take appropriate action. The sedation score table below aims to improve on the traditional AVPU – scoring system (A = alert; V = responds to voice; P = responds to pain, and U = unresponsive) that is not sensitive enough for early detecting of OIVI.

Macintyre & Schug, 2021

Table 2: Sedation Scores
0 = wide awake
1 = easy to rouse
2 = easy to rouse but unable to remain awake
3 = difficult to rouse

1. A score of 2 is taken to indicate early OIVI and therefore the aim should be to titrate an opioid so that a patient's sedation score is always less than 2.
2. Note that a sedation score (e.g. 'sedation score less than 2') may be specified in the 'Max Dose/24 hrs' in the PRN section of the ACSQHC *National Inpatient Medication Chart* (NIMC) to indicate the maximum amount to be administered in 24 hrs when prescribing opioids in (Australian Commission on Safety and Quality in Health Care, 2019).

Overall, PS41 provide a good framework and the language has softened from the original position statement of 2018 with an acknowledgement that it not possible to accurately conclude whether the risk of OIVI is higher or lower in specific patient populations. There is an acknowledgement that long acting opioids may have a place in acute pain management where there is a demonstrated need, close monitoring and a clear cessation plan in place.⁷

Analgesic (and opioid) stewardship spans the domains of pre-operative, intra-operative and post-operative care.

Opioid free anaesthesia (OFA), in the context of the current opioid epidemic, has been promoted as an intra-operative strategy that could have a meaningful influence on the problem.⁸ However, despite a surge in research on opioid free anaesthesia, it is still not clear if OFA is any better or safer than an opioid permissive balanced anaesthetic. There are many OFA 'recipes' in use, but apart from a reduction in nausea and vomiting, the benefit remains unclear.⁹ A multicentre, double-blind, randomised, controlled clinical trial comparing opioid free versus opioid anaesthesia on postoperative opioid-related adverse events after major or intermediate non-cardiac surgery (POFA trial study protocol) is hoping to clarify the role of OFA.¹⁰

There are encouraging evidence emerging of effective analgesic modalities that is opioid *sparing* rather than opioid *free*. And interesting strategy out of Auckland, published in January 2021, showed a significant reduction in opioid consumption when intraperitoneal lignocaine was used compared to intravenous lignocaine for laparoscopic colectomy, showing a greater than 50% reduction in opioid use in the first 3 post operative days as well as reduced opioid use for the total length of stay.¹¹

Studies have suggested that over prescribing of opioids was not only a common problem, but likely a significant contributor to opioid availability in the community.¹²⁻¹⁵ It is estimated that 50% of adults who misuse opioids obtain them from family and friends.⁹ Arguably, it is in the post-operative domain of analgesic stewardship where the most gains are to be made to minimise harm.

In 2015, I presented on Methadone and its perioperative utility. Since that presentation, the landscape for the use of long-acting opioids within the first 24h after surgery, has changed and its use is no longer recommended by ANZCA.^{9,16} The position that methadone is considered a long acting opioid and should be avoided in acute pain management, seems at odds with evidence to suggest that methadone is no more unsafe than any other conventional short acting opioid.¹⁷ It is also useful as a rescue analgesic where short acting opioids have failed.¹⁸ A systematic review and meta-analysis published in Pain demonstrated that methadone had an overall opioid sparing effect, introducing the concept of opioid sparing opioids.¹⁹

A surge in accidental deaths involving fentanyl caused regulators to restrict the indications for the use of fentanyl patches, which will likely pave the way for future changes to opioid regulation; including box warnings, smaller pack sizes and changes to the wording in packet inserts of opioids.²⁰

The use of non-steroidal anti-inflammatory drugs (NSAIDs) are a useful strategy to minimise the use of opioids and there are a number of new and strengthened recommendations for their use:⁹

- Celecoxib given as a single pre-operative dose is effective at reducing opioid usage, pain scores at 24 hours and postoperative nausea and vomiting. (New Recommendation, Level I)
- The COX-2 inhibitors do not impair platelet function and are not associated with increased perioperative blood loss. (Strengthened Recommendation, Level I)
- In patients with normal renal function, parecoxib perioperatively does not increase renal failure. (New Recommendation, Level I)
- NSAIDs hasten bowel recovery after colorectal surgery. (New Recommendation, Level I)
- With regard to renal function, celecoxib and naproxen are safer than ibuprofen with long-term use. (New Recommendation, Level II)

There is continued debate on the effect of opioids on cancer and the literature remains conflicting.

More recent studies and meta-analysis has not been able to provide conclusive evidence or recommendations beyond those in existence.^{21,22}

References:

1. <https://www.who.int>
2. Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2021.
3. Health Quality and Safety Commission New Zealand. Atlas of Healthcare Variation - opioids: HQSC New Zealand; 2017
4. Shipton EE, Shipton AJ, Williman JA, *et al.* Deaths from opioid overdosing: implications of coroners' inquest reports 2008-2012 and annual rise in opioid prescription rates: a population-based cohort study. *Pain Ther* 2017;6:203–15
5. <https://www.health.govt.nz>
6. Gillian Robb, Elizabeth Loe, Ashika Maharaj, Richard Hamblin, Mary E Seddon. Medication-related patient harm in New Zealand hospitals. *New Zealand Medical Journal* 2017 Aug 11;130(1460):21-32.
7. PS41 - Position Statement on Acute Pain Management. www.anzca.edu.au
8. Anamourlis PC. Opioid free anaesthesia: A paradigm shift. *South African Family Practice* 2019; 61(2):S21-S24
9. Schug SA, Scott DA, Mott JF, Halliwell R, Palmer GM, Alcock M; APM:SE Working Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine (2020), *Acute Pain Management: Scientific Evidence (5th edition)*, ANZCA & FPM, Melbourne.
10. Beloeil H, Laviolle B, Menard C, Paugam-Burtz C, Garot M, Asehnoune K, Minville V, Cu villon P, Oger S, Nadaud J, Leco eur S, Chanques G, Futier E; SFAR research network. POFA trial study protocol: a multicentre, double-blind, randomised, controlled clinical trial comparing opioid free versus opioid anaesthesia on postoperative opioid-related adverse events after major or intermediate non-cardiac surgery. *BMJ Open*. 2018 Jun 30;8(6):e020873.
11. Wiremu S Macfater Weisi Xia, Ahmed W H Barazanchi, Nicholas J Lightfoot, Maree Weston, Darren Svirskis, Andrew G Hill. Intravenous Local Anesthetic Compared with Intraperitoneal Local Anesthetic in Laparoscopic Colectomy: A Double-Blind Randomized Controlled Trial. *Ann Surg* 2021 Jan 15.
12. Clarke H, Soneji N, Ko DT, Yun L, Wijeyesundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014;348:g1251.
13. 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.
14. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. *JAMA Intern Med*. 2016;176:1286–93
15. Hill MV, McMahan ML, Stucke RS, Barth RJ Jr. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg*. 2017;265:709–14.
16. www.anzca.edu.au Position statement on the use of slow release opioid preparations in the treatment of acute pain.
17. Intraoperative Methadone in Surgical Patients: A Review of Clinical Investigations. Murphy GS, *et al.* *Anesthesiology*. 2019.
18. Clinical pharmacology of methadone for pain. Fredheim OM, Moksnes K, Borchgrevink PC, Kaasa S, Dale O. *Acta Anaesthesiol Scand*. 2008 Aug;52(7):879-89.
19. Intraoperative methadone administration and postoperative pain control: a systematic review and meta-analysis. D'Souza RS, Gurrieri C, Johnson RL, Warner N, Wittwer E. *Pain*. 2020 Feb;161(2):237-243

20. <https://www.tga.gov.au/prescription-opioids-what-changes-are-being-made-and-why>
21. Oscar Diaz-Cambronero, Guido Mazzinari, Juan P Cata. Perioperative opioids and colorectal cancer recurrence: a systematic review of the literature. *Pain Management* 2018 Sep 1;8(5):353-361.
22. Daniel I Sessler, Lijian Pei, Yuguang Huang, Edith Fleischmann, Peter Marhofer, Andrea Kurz, Douglas B Mayers, Tanja A Meyer Treschan, Martin Grady, Ern Yu Tan, Sabry Ayad, Edward J Mascha, Donal J Buggy, Breast Cancer Recurrence Collaboration. Recurrence of breast cancer after regional or general anaesthesia: a randomised controlled trial. *Lancet* 2019 Nov 16;394(10211):1807-1815.