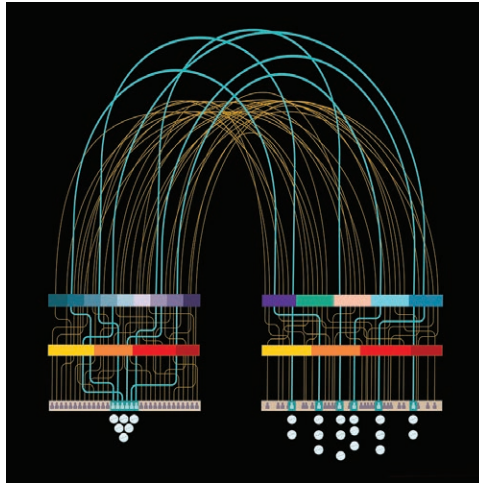


Uncoupling Pain and Opioid Use after Surgery

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Pain is an expected outcome after almost any surgical procedure. Therefore, one important goal in the perioperative period is to pharmacologically mitigate activation of the nociceptive pathway, such that the pain experienced after an operation is minor and short-lived. With this aim in mind, opioids are a useful perioperative tool due to their analgesic efficacy and titratability according to individual patient needs.¹ However, the routine prescription of oral opioids after surgery has been called into question in the wake of the opioid crisis. As a result of this concern, there has been a proliferation of studies that have used administrative databases to investigate prolonged postoperative postdischarge oral opioid use.² These studies, while insightful, do not provide a complete picture. The complexity of the perioperative experience cannot be gleaned from a billing code or a prescription filled. Instead, we need studies with granular, prospective data collection on pain outcomes to enhance our understanding of how to intervene and improve care.

In this issue of *ANESTHESIOLOGY*, Kuck *et al.*³ prospectively investigated rates and predictors of prolonged postoperative surgical site pain as well as opioid use at 3 months in a cohort of patients undergoing a mix of surgical procedures. As in previous studies,⁴ they found that preoperative opioid use was the strongest predictor of prolonged opioid use, with only about 4% of patients being “new” prolonged opioid users at 3 months. Similarly, preoperative pain also predicted the presence of surgical site pain at 3 months, in agreement with previous work indicating that both preoperative and immediate postoperative acute pain are strongly and consistently associated with prolonged pain.⁵



“These data may give insight into an important uncoupling between postoperative postdischarge pain and opioid use and could possibly be explained by other forces driving the use or non-use of opioids.”

postdischarge pain and opioid use and could possibly be explained by other forces driving the use or non-use of opioids, such as patients’ and providers’ fears of addiction or preference for nonopioid adjuvants.

The discrepancy between pain and opioid use also underscores the potentially problematic approach of relying on opioid use as a proxy for pain in perioperative studies. Often, the reason a patient is taking opioids (for surgical site pain *vs.* other pain) is not measured or reported, including in this current study. It may seem obvious that an individual taking opioids for chronic back pain preoperatively would continue to do so the day after undergoing an appendectomy. Similarly, there may be other reasons for new chronic use postoperatively independent of the index procedure. A recent prospective

The importance of this study is that these strong associations were replicated using a prospective, multisite recruitment model, and employed a system that collects perioperative data to gather some of the variables, with the final cohort consisting of 680 patients across 11 institutions.

One particularly interesting finding in their analysis was a seeming disconnect between pain and opioid use at 3 months. The authors found no significant association between these two outcomes at 3 months, *i.e.*, the 14% of patients who reported taking opioids and the 27% of patients who reported persistent pain were not statistically associated. While it is unclear whether an association might have been observed if pain was considered as a continuous variable rather than dichotomous, conceptually we would expect a close relationship between the measures. These data may give insight into an important uncoupling between postoperative

Image: A. Johnson, Vivo Visuals Studio.

This editorial accompanies the article on p. 462. This article has an audio podcast.

Accepted for publication March 6, 2023.

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study demonstrated that in a cohort of surgical patients, “persistent” opioid use was more likely secondary to a new medical condition, recurrent cancer, or a surgical complication rather than surgical site pain.⁶ Thus, identifying whether opioid analgesics are being taken to control surgical site pain is crucial. Without specifically querying patients about the indication for opioid use, targeting preventive perioperative interventions to reduce prolonged opioid use is unlikely to be successful.

Indeed, many previous studies have failed to detect an impact of interventions to mitigate either prolonged opioid use or pain after surgical procedures.^{7,8} The question of how to prevent prolonged pain and opioid use in any given patient requires careful measurement of individual phenotypic differences and inclusion of these phenotypic measures in the analytic plan. For example, is a given preventive strategy more effective among women than men? Among highly anxious patients or those with baseline widespread pain? Without analyzing the differential effect of interventions among individuals, we risk discarding efficacious strategies that may be crucial to individuals with a given risk profile. If the field of perioperative pain management is to evolve into personalization of care, it needs more granular resolution of patient predictors, longitudinal, high-quality outcome measurements, and carefully planned and rational estimation of effect moderation (what works well in whom).

The type of data collected by Kuck *et al.* may allow such resolution in the future. However, obtaining these data is not an easy feat, as demonstrated by the many challenges that were experienced by the study team for this current paper. Prospective data collection is undoubtedly costlier and more time-consuming in comparison to using routinely collected data. In this current study, of 3,505 eligible patients, 680 were included in final cohort. The perioperative period is a stressful time when many patients are understandably overwhelmed. We ask a lot of our patients when we request them to fill out countless surveys before and after a procedure. We therefore need to be thoughtful and selective about what we collect, use validated instruments, and carefully analyze these data. We also need to use new and innovative methodologies to collect relevant phenotypic data and patient-centered outcomes less obtrusively, for example with brief ecologic momentary assessments through a smartphone.

Returning to our goals in the perioperative period, it seems clear that it is overly simplistic to consider using an opioid postoperatively as a failure in care. Similarly, prolonged use does not equate to misuse, as is often suggested or implied. Over the past few years, there has been a notable shift in attitudes toward using opioids for chronic pain, as evidenced by revised guidelines from the Centers for Disease Control and Prevention (Atlanta, Georgia).⁹ It is time for us to acknowledge and be comfortable with the possibility that there may be a subset of patients who benefit from opioids and whose quality of life can be improved

from their short- and long-term use. This statement does not discount the fact that opioids are potentially harmful and that their use requires close oversight by a healthcare provider. However, this balance allows us to respect and alleviate a patient’s pain while simultaneously being mindful of the broader public health implications of these treatment decisions.

Research Support

No funding was received for this manuscript. Dr. Ladha is supported in part by a Merit Award from the Department of Anesthesiology and Pain Medicine at the University of Toronto, Toronto, Canada.

Competing Interests

Dr. Ladha is co-principal investigator of an observational study on medical cannabis funded by Shoppers Drug Mart (Toronto, Canada). Dr. Schreiber is an Editor for ANESTHESIOLOGY.

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References

1. Shanthanna H, Ladha KS, Kehlet H, Joshi GP: Perioperative opioid administration. *ANESTHESIOLOGY* 2020; 134:645–59
2. Jivraj NK, Raghavji F, Bethell J, Wijeyesundera DN, Ladha KS, Bateman BT, Neuman MD, Wunsch H: Persistent postoperative opioid use. *ANESTHESIOLOGY* 2020; 132:1528–39
3. Kuck K, Naik BI, Domino KB, Posner KL, Saager L, Stuart AR, Johnson KB, Alpert SB, Durieux ME, Sinha AK, Brummett CM, Aziz MF, Cummings KC III, Gaudet JG, Kurz A, Rijsdijk M, Wanderer JP, Pace NL; Multicenter Perioperative Outcomes Group Enhanced Observation Study Investigator Group for the Multicenter Perioperative Outcomes Group Enhanced Observation Study Collaborator Group: Prolonged opioid use and pain outcome and associated factors after surgery under general anesthesia: A prospective cohort association multicenter study. *ANESTHESIOLOGY* 2023; 138:462–76
4. Lawal OD, Gold J, Murthy A, Ruchi R, Bavry E, Hume AL, Lewkowitz AK, Brothers T, Wen X: Rate and risk factors associated with prolonged opioid use after surgery. *JAMA Netw Open* 2020; 3:e207367
5. Rosenberger DC, Pogatzki-Zahn EM: Chronic post-surgical pain – Update on incidence, risk factors and preventive treatment options. *BJA Educ* 2022; 22:190–6
6. Barth RJ, Porter ED, Kelly JL, Bessen SY, Molloy LB, Phillips JD, Loehrer AP, Wilson MZ, Ivatury

- SJ, Billmeier SE, Seigne JD, Wong SL, Wilkinson-Ryan I: Reasons for long-term opioid prescriptions after guideline-directed opioid prescribing and excess opioid pill disposal. *Ann Surg* 2023; 277:173–8
7. Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E: Chronic opioid use after surgery: Implications for perioperative management in the face of the opioid epidemic. *Anesth Analg* 2017; 125:1733–40
 8. Carley ME, Chaparro LE, Choinière M, Kehlet H, Moore RA, Kerkhof EVD, Gilron I: Pharmacotherapy for the prevention of chronic pain after surgery in adults: An updated systematic review and meta-analysis. *ANESTHESIOLOGY* 2021; 135:304–25
 9. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R: CDC clinical practice guideline for prescribing opioids for pain — United States, 2022. *MMWR Recomm Rep* 2022; 71:1–95