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Optimal postoperative pain management: redefining the role for opioids

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linked, population-level databases, is required. The investigators acknowledge these limitations in their report.

The results of this study, in conjunction with results of studies of pregnancy interval after early loss and with findings of studies using new approaches to study interval after a livebirth, suggest that interpregnancy interval might be less important than previously assumed, at least for women in highincome regions. Rather than adhering to hard and fast rules, clinical recommendations should consider a woman's current health status, her current age in conjunction with her desires regarding child spacing and ultimate family size, and particularly following a loss, her emotional readiness to become pregnant again.

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Center for Perinatal Research, The Research Institute at Nationwide Children's Hospital, Columbus, OH 43215, USA; and Departments of Pediatrics and Obstetrics and Gynecology, College of Medicine, and Division of Epidemiology, College of Public Health, The Ohio State University, Columbus, OH, USA mark.klebanoff@nationwidechildrens.org I have prepared a grant application to the US National Institutes of Health, currently pending, to study the association of interpregnancy interval with pregnancy outcome. I declare no other competing interests.

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Optimal postoperative pain management: redefining the role for opioids

Fear of pain is deeply rooted among patients who are about to have surgery.¹ Satisfactory perioperative pain management is crucial to assuring a good patient experience, optimising postoperative outcomes, and enhancing functional recovery after surgery.² Despite decades of research showing the benefits of various new analgesic strategies, many patients endure severe postoperative pain,³ and this holds true across all age groups and continents, even after surgery widely considered to be minor.⁴ A 2016 study from the USA, which enrolled 799 449 patients, showed that reliance on opioid analgesics as the mainstay for perioperative pain management is still widespread.⁵ This situation is worrying because several countries, most prominently the USA, Canada, and Australia, are struggling with an opioid crisis of unprecedented proportions.⁶ There are an estimated 2 million patients in the USA who have an opioid use disorder,7 with approximately

90 deaths occurring every day in the USA from an opioid overdose.⁸ For many of these individuals, opioid dependency started with a prescription after minor trauma or surgery, highlighting the pivotal role of the health-care system in this epidemic.

In *The Lancet*, a new Series on postoperative pain management and opioids^{3,6,9} details the current state of perioperative pain management with a strong focus on opioids, their role as analgesics, and the problems that accompany their widespread use. Paul Glare and colleagues³ revisit the rationale for the use of opioids and other analgesics: to alleviate acute postsurgical pain and disrupt the transition from acute to chronic postsurgical pain. As the authors explain, it is now firmly established that poorly controlled acute pain after surgery is among the strongest predictors for the development of chronic postsurgical pain, but simply using escalating doses of opioids might only



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worsen the problem. Mark Neuman and colleagues⁶ recount how opioid overprescribing after surgery emerged and delineate prescribing, hospital, and public policy interventions to standardise and decrease the dispensing of opioids after surgery. Both groups of authors^{3,6} advocate for an approach that includes transitional pain clinics for patients at high risk for prolonged opioid use after surgery as a model for the future.¹⁰ Lesley Colvin and colleagues⁹ review the basic mechanisms that underlie the adverse effects of opioid use, including opioid-induced hyperalgesia and tolerance. As our understanding of the limitations of opioid use has grown, multimodal analgesic regimens are increasingly used, helpful in decreasing opioid dose¹¹ and could be the key to avoiding long-term dependence.¹⁰ By combining non-opioid analgesics with targeted regional anaesthetic techniques, multimodal analgesic regimens target multiple sites along the nociceptive pathway with the net effect of limiting opioid dose, improving analgesia, and enhancing safety.¹¹ Better understanding of the basic mechanisms underlying opioid-induced hyperalgesia and tolerance, including the role of the β -arrestin pathway, has led to the development of biased agonists that could provide similar analgesic effects to opioids with fewer side-effects in the future.9

Currently, the best approach is multimodal analgesia. The first component of an effective multimodal analgesic regimen should be one or two simple nonopioid analgesics: in the absence of contraindications, acetaminophen, a non-steroidal anti-inflammatory



drug, or a cyclo-oxygenase-2 inhibitor. An adjuvant analgesic, such as an antiepileptic, $\alpha 2$ agonist, or ketamine, is often added, on the basis of the procedure and patient's risk profile. Advanced techniques such as neuraxial (spinal and epidural) anaesthesia and analgesia, nerve blocks, and wound infiltration should be integrated into the multimodal analgesic regimen whenever feasible. Wound infiltration with local anaesthetic and regional analgesia can provide excellent dynamic pain relief, but care must be taken to align the duration of these advanced analgesic methods with the anticipated time course of pain, and the techniques must be meaningfully integrated into the overall plan of care.¹² Opioids should be used as rescue medication, intravenously for as short a time as possible, and orally as soon as feasible. The perioperative initiation of extended-release transdermal or fast-onset transmucosal opioids to treat acute pain should be avoided.

Research that extends well beyond the immediate postoperative period is needed. Brandal and colleagues¹³ summarised the experiences of one institution in implementing opioid-sparing anaesthesia as part of an enhanced recovery plan in the operating room. Intraoperative opioid use was reduced, but the quantities of opioid medication given at the time of hospital discharge remained unchanged. Changing the analgesic plan in the operating room alone without adopting a comprehensive strategy that extends through recovery from surgery will decrease the effect of opioid-sparing strategies. Clarke and colleagues¹⁴ describe their experience with a transitional pain service consisting of a multidisciplinary team of pain physicians, specialised nurses, and pain psychologists. A cohort of 250 Canadian patients (ranging from 19-81 years; 44.4% female), who had surgery and were at high risk of poor compliance with use of opioid analgesics after surgery, showed a marked reduction in opioid consumption and 26% of long-term opioid users were weaned of the drugs completely, without any negative effect on pain or physical function. Additionally, they saw a reduction in the length of hospital stay with an improvement in quality of life in those managed by the transitional pain service.

Education will need to include patients, hospitals, health-care systems, and the graduate schools where health-care providers are trained. By educating patients about the risks and alternatives to opioids, health-care providers can help empower patients (and themselves) to request alternatives and demand closer attention if they are struggling after surgery. Opioid-free anaesthesia has been put forward as a panacea for the opioid problem, but there is no evidence that opioid-free anaesthesia is superior to multimodal analgesia.¹⁵ For now, opioids remain an essential and reliable tool for treating moderate to severe pain.

Can we reduce or eliminate the transition from acute to chronic pain? Based on systematic reviews, there is preliminary evidence that regional anaesthesia can be protective against chronic postsurgical pain after thoracotomy and mastectomy,16 and ketamine can decrease the risk of chronic postsurgical pain.¹⁷ A wide range of demographic, genetic, clinical, perioperative, psychosocial, and psychophysical risk factors suggest that there might be no one single intervention that can protect all patients.³ In the future, we believe standardised preoperative patient stratification will guide clinicians in designing an optimal and individualised analgesic plan.¹⁸ That treatment plan should start preoperatively, integrate with the care provided in the operating room and during the course of hospitalisation, and be continued after hospital discharge until pain has subsided, in transitional pain clinics when necessary.9

The current debate around opioids calls for education and moderation. The authors of the new *Lancet* Series on postoperative pain management and opioids^{36,9} are to be commended for their comprehensive account of opioids and their current use and misuse in perioperative pain management, for detailing strategies to reduce inappropriate prescribing, and for improving our understanding of the adverse effects and dangers of opioids. Each Series paper has pointed a way forward, and laid out how constructive change can be implemented on many levels from drug discovery to direct communication with patients, all the way to legislative action.

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