

Rational Perioperative Opioid Management in the Era of the Opioid Crisis: Comment

To the Editor:

The Kharasch *et al.*¹ editorial is very timely because there is pain with its physical, psychologic, socioeconomic, and spiritual constituents and then there is suffering attributable to pain's physical, psychologic, socioeconomic, and spiritual consequences.^{1,2} It is ironic that the evolving opioid epidemic may have created an anomaly. Herein overregulated medical practices to contain overzealous prescription of analgesics may be paradoxically inducing iatrogenic pain and thence iatrogenic suffering leading to iatrogenic suicide ideations, behaviors, attempts, and completions. Can it be safely said that no one ideates, behaves, or attempts to commit suicide unless in pain and suffering? Even those who ritually or culturally presume their completion of life as an indication to take the leap of faith toward ending that life may be suffering as a result of spiritual pain associated with futility of existence within the matrix when existence within the matrix spiritually reveals itself as eternally purposeless to them.³

One of the biggest questions regarding analgesic overdosing incidents has been about when, how, and why to delineate and differentiate these incidents into intentional (suicidal) overdosing *versus* unintentional (accidental) overdosing.⁴ Essentially, each overdosing incident should always be appropriately categorized as suicidal or accidental even if such categorization may seem difficult to impossible after completed suicides. Appropriate categorization can ensure that true incidence of intentional self-harm does not get obscured by falsely higher incidence being deemed to accidental overdosing incidents. Exploration about intent to self-harm may be especially important after near-fatal overdosing incidents so that the survivors can appropriately receive self-directed violence (suicide) prevention management.

Correspondingly, the overcautiously defensive health-care providers may have to also understand that undertreated pain-induced suffering can also lead to self-directed violence wherein providers and their conscience may

feel burdened, especially when their patients' dependence on analgesics may have been iatrogenic and their dependent patients' helplessness during evolving policy-based withdrawals from analgesics may be iatrogenic too. Thus, shouldn't the healthcare providers be aware of and concerned about iatrogenicity playing a role in their patients' suicide ideations, behaviors, attempts, and completions? Moreover, in the presence of unreasonable and inexplicable limited access to buprenorphine, which has low abuse potential as the first-line analgesic to counter pain and suffering, do over-the-counter cannabidiol (CBD) oil and legalized marijuana for recreational and medical purposes become a win-win situation for healthcare providers as well as patients aiming to overcome undertreated pain and suffering?⁵⁻⁷

Summarily, there may not be any clear-cut answer for healthcare providers managing pain patients. However, it has been, is, and will always be about striking and then maintaining the delicate balance between (1) prompt diagnosis and management of pre-existing pain, suffering, and self-directed violence among their patients, and (2) astute prevention and containment of iatrogenic pain, suffering, and self-directed violence among their patients.

Competing Interests

The authors declare no competing interests.

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References

1. Kharasch ED, Avram MJ, Clark JD: Rational perioperative opioid management in the era of the opioid crisis. *ANESTHESIOLOGY* 2020; 132:603–5
2. Bueno-Gómez N: Conceptualizing suffering and pain. *Philos Ethics Humanit Med* 2017; 12:7
3. Somasundaram O, Tejus Murthy AG, Raghavan DV: Jainism - Its relevance to psychiatric practice; with special reference to the practice of Sallekhana. *Indian J Psychiatry* 2016; 58:471–4
4. Connery HS, Taghian N, Kim J, Griffin M, Rockett IRH, Weiss RD, Kathryn McHugh R: Suicidal motivations reported by opioid overdose survivors: A cross-sectional study of adults with opioid use disorder. *Drug Alcohol Depend* 2019; 205:107612

5. Fishman MA, Scherer A, Topfer J, Kim PSH: Limited access to on-label formulations of buprenorphine for chronic pain as compared with conventional opioids. *Pain Med* 2020; 21:1005–9
6. VanDolah HJ, Bauer BA, Mauck KF: Clinicians' guide to cannabidiol and hemp oils. *Mayo Clin Proc* 2019; 94:1840–51
7. Hill KP: Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: A clinical review. *JAMA* 2015; 313:2474–83

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To the Editor:

We read with interest the recent editorial by Kharasch *et al.*¹ concerning opioid management. We agree with their assessment of “opioid phobia,” and we would say “not so fast with opioid-free anesthesia.” There is no doubt that opioids are highly addictive drugs, as shown by recurring waves of opioid abuse since the nineteenth century. We appreciate that those promoting opioid-free anesthesia are well intentioned. However, neither the elimination nor the reduction of perioperative opioids have been clearly associated with decreased long-term use and abuse. As noted by Kharasch *et al.*, the increase in prescription opioids in the attempt to address inadequate perioperative pain management was a major factor in the evolution of the opioid abuse crisis.¹ Ironically, perioperative pain continues to be undertreated at this time. Despite the potential advantages of multimodal analgesia, opioids remain an invaluable class of analgesics in the treatment of moderate to severe perioperative pain, and indiscriminate use of well-intentioned opioid free anesthesia may actually perpetuate inadequate perioperative pain control. Additionally, opioids are a distinctive component of balanced anesthesia. As reiterated in the recent review by Egan,² opioids work synergistically with primary anesthetics to achieve immobility, unconsciousness, and control of adrenergic responses. Elimination of opioids from a balanced anesthetic necessitates increased

reliance on other anesthetic drugs, which may have unintended consequences.

Although the solution to the current opioid abuse crisis is clearly complex and multifaceted, we highlight three significant issues that we believe have received insufficient attention.

First, there is an urgent need for evidence-based guidance for providers about optimal perioperative use of opioids for specific surgical procedures and groups of patients. In reality, providers, frequently do not know how to best use opioids. Recent clinical guidance documents published by professional organizations (*e.g.*, enhanced recovery after surgery, American Society for Enhanced Recovery) have endorsed multimodal analgesia and reduction in the use of opioids but typically have not provided granular guidance regarding specific opioids and doses. In the absence of evidence-based recommendations, opioid-free anesthesia is attractive because, by default, the need to titrate opioids for a range of patients and procedures is eliminated. We suggest that many, if not most, patients would be better served by receiving optimal doses of opioids in the setting of multimodal analgesia, rather than no opioids. For example, appropriate use of intraoperative methadone has been shown to reduce postoperative analgesic requirements.³ Postprocedural dosing protocols and smaller prescription quantities may result in less consumption of opioids without impairing pain control.^{4,5} Health care providers need practical evidence-based guidance for both intraoperative and postoperative opioid administration that addresses the wide array of procedures currently performed.

Second, numerical pain scores should be replaced by functional pain assessment. The numerical pain score inadequately reflects the complicated nature of pain and has been implicated in perpetuating excessive administration of opioids.⁶ Functional pain assessment can include meaningful parameters of the recovery process such as participation in physical therapy, sleeping, eating, and engagement in social interactions. Development and endorsement of practical perioperative pain assessment tools should involve interdisciplinary input from multiple specialties including psychiatry, rehabilitation medicine, physical therapy, and pain medicine. We cannot evaluate our efforts to transform the use of opioids without better methodology for pain assessment. The medical community should rapidly abandon numerical pain scores by developing and adopting better systems for measuring the “fifth vital sign.”

Third, patients must be more engaged in pain management and safe opioid use. Ultimately, it is the patient who takes the opioids home to their community and is faced with decisions about use, sharing, storage, and disposal. Most patients do not appreciate the complex interactions between the central and peripheral nervous systems that produce pain, and have little knowledge of how to manage pain, much less opioids. Patients need education about pain as part of their recovery process. Patients also need a practical understanding of their medications in term of mechanisms, dosing, toxicity, and responsible stewardship. Simple tools such as medication scheduling

and tracking apps, more objective pain self-assessment strategies, and improved disposal opportunities could help patients with safer opioid behavior and should be reinforced throughout the recovery process. As the medical community learns more about patient behaviors, we must simultaneously empower patients with knowledge and tools to be better guardians of both personal and community health.

The opioid crisis is humbling, as we realize that incorrect assumptions and lack of evidence-based practice contributed to a wave of addiction in our communities. Clearly, decisive action is needed, but we must not be rash in addressing our failures. A scientific and thoughtful approach is critical to advancing our practice in safe and meaningful ways. Anesthesiologists have a central role in the perioperative surgical home and in pain management and have a unique opportunity to support the medical community with better evidence-based guidance for opioid administration and prescription, meaningful pain assessment, and patient education and empowerment.

The opioid epidemic is a painful reminder that what we do matters.

Competing Interests

The authors declare no competing interests.

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References

1. Kharasch ED, Avram MJ, Clark JD: Rational perioperative opioid management in the era of the opioid crisis. *ANESTHESIOLOGY* 2020; 132:603–5
2. Egan TD: Are opioids indispensable for general anaesthesia? *Br J Anaesth* 2019; 122:e127–35
3. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Marymont JH, Shear T, Parikh KN, Patel SS, Gupta DK: Intraoperative methadone for the prevention of postoperative pain: A randomized, double-blinded clinical trial in cardiac surgical patients. *ANESTHESIOLOGY* 2015; 122:1112–22
4. Howard R, Fry B, Gunaseelan V, Lee J, Waljee J, Brummett C, Campbell D Jr, Seese E, Englesbe M, Vu J: Association of opioid prescribing with opioid consumption after surgery in Michigan. *JAMA Surg* 2019; 154:e184234
5. Howard R, Waljee J, Brummett C, Englesbe M, Lee J: Reduction in opioid prescribing through evidence-based prescribing guidelines. *JAMA Surg* 2018; 153:285–7
6. 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? *Br J Anaesth* 2018; 120:435–8

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Rational Perioperative Opioid Management in the Era of the Opioid Crisis: Reply

In Reply:

We thank the authors^{1,2} of these letters to the editor for their thoughtful reading of our editorial.³ The diversity of the opinions expressed in these responses reflects the diversity of issues enmeshed in the current crisis.

Chakraborty and Gupta¹ challenge readers to recognize that the complexities of opioid use are more than matched by the complexities of suffering. They suggest that efforts to contain over-prescription of opioids to treat pain may inadvertently result in pain and suffering that can, in turn, lead to suicidal ideations and worse. To use opioids compassionately with the goal of reducing suffering while not placing patients and community members at undue risk is a major challenge. We believe anesthesiologists can help patients during the highly stressful and painful intraoperative and immediate postoperative period by carefully using these powerful medicines. Although beyond the scope of the original editorial, we feel that informed and comprehensive care of the individual in pain will bring the best outcomes with the least risk.

Shishido and Bowdle² amplify and extend some of the themes in our editorial, and we could not have said things any better than they did. To optimize opioid use guided by meaningful clinical endpoints and evidence is a far more patient-centric and medically justified approach to the treatment of pain than arbitrarily abandoning use of these analgesics. Special attention should be paid to their recommendation that patients be more engaged in the management of their pain and the safe use of the opioids they are prescribed to treat that pain. Preanesthesia clinics could be the place for patient education about postoperative pain, pharmacotherapy, and opioid stewardship and not just a place for preoperative screening and evaluations. Although some hospitals and

surgery centers may be looking to shrink their preoperative clinics and replace in-person evaluations with phone calls or less for all but the sickest, we need to avoid missing both a need and an opportunity. Anesthesiologists should endeavor to both improve patient care and enhance their value to their patients and their institutions by meeting this important patient need.

Competing Interests

Dr. Kharasch is the Editor-in-Chief of *ANESTHESIOLOGY*, and his institution receives salary support from the American Society of Anesthesiologists (Schaumburg, Illinois) for this position. Dr. Avram is the Assistant Editor-in-Chief of *ANESTHESIOLOGY*, and his institution receives salary support from the American Society of Anesthesiologists for this position. Dr. Avram also has a financial relationship with the Department of Anesthesiology, North Shore University Evanston Hospital (Evanston, Illinois) for research consultation. Dr. Clark is a consultant for Teikoku Pharma USA (San Jose, California).

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References

1. Gupta D, Chakraborty S: Rational perioperative opioid management in the era of the opioid crisis: Comment. *ANESTHESIOLOGY* 2020; 133:940–1
2. Shishido S, Bowdle A: Rational perioperative opioid management in the era of the opioid crisis: Comment. *ANESTHESIOLOGY* 2020; 133:941–2
3. Kharasch ED, Avram MJ, Clark JD: Rational perioperative opioid management in the era of the opioid crisis. *ANESTHESIOLOGY* 2020; 132:603–5

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Implications of Practice Variability: Comment

To the Editor:

I read with interest the Editorial by Sessler¹ on the implications of practice variability. There is considerable interpatient variability in the response to surgical stress,

hemodynamic perturbations, anesthetics, fluids, vasopressors, inotropic therapy, extracorporeal-circulation, hemotherapy, ischemia-reperfusion, and others, and also considerable interindividual variation in the incidence and severity of the perioperative complications. Although personalized or precision medicine is gaining implementation generally in disease prevention and treatment, the potential of precision perioperative medicine remains to be fully explored and implemented, such as in hemodynamic optimization, anesthetic regimens, pharmacologic therapy, pain management, mechanical ventilation, and other organ protective strategies.² The guideline- and protocol-based perioperative approach constitutes the antithesis of precision medicine in perioperative practice. Nevertheless, the proponents of precision perioperative medicine embrace the notion that most of the standardized therapies are designed for an average patient and are insensitive to the wide heterogeneity wherein different subsets of patients respond differently to an allocated treatment. In addition, they cite an assortment of confounding factors ranging from Hawthorne effect to the impact of a heightened vigilance in modulating the outcomes under evaluation while adhering to a protocol. Moreover, the lack of firm evidence on the results of protocolized interventions, such as early goal-directed therapy in sepsis, accentuates the debate furthermore.³ Interestingly, the theory of refuting a free pass to the clinical pathways on evidence to preclude the extrapolation of the same to procedures and populations they were never investigated upon begets the need of a robust context-appropriate evidence.¹ As precision medicine evolves across diverse clinical settings, the lack of acknowledgment to this evolving paradigm shift under the preconceived notion that the standardized approach is sacrosanct in perioperative practice is a disfavor to the speciality when the impetus to execute precision medicine in other clinical fields is captivating society.

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The author declares no competing interests.

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This letter was sent to the author of the original article referenced above, who declined to respond.—Evan D. Kharasch, M.D., Ph.D., Editor-in-Chief.

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References

1. Sessler DI: Implications of practice variability. *ANESTHESIOLOGY* 2020; 132:606–8