

Pain Management and Opioid Regulation: Continuing Public Health Challenges

The still-growing US opioid epidemic lies at the intersection of two major public health challenges: reducing suffering from pain and containing the rising toll of harms associated with the use of opioids medications. Responding successfully to these challenges requires a substantial investment in surveillance and research on many fronts and a coordinated policy response by federal and state agencies and stakeholder organizations.

A 2017 report of the National Academies of Sciences, Engineering and Medicine (NASEM) called for improved methods of measuring pain and the effects of alternative modalities of treatment as well as intensive surveillance of opioid-related harms; urged a long-term cultural transformation of how pain is perceived, assessed and treated; and outlined a comprehensive and balanced public health framework to guide Food and Drug Administration approval, monitoring, and review of opioids.

We, authors of the NASEM report, use the articles published in this special section of *AJPH* as a platform for commenting on the public health burden of pain, the role of opioids in managing pain, global disparities in access to opioids for pain management, divergent approaches to opioid regulation, and the challenge of striking a reasonable balance between the needs of patients in pain and the prevention of opioid-related harms. (*Am J Public Health*. 2019;109:31–34. doi:10.2105/AJPH.2018.304881)

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See also Carr et al., p. 17; and also the *AJPH* Pain Management section, pp. 30–72.

The still-growing US opioid epidemic lies at the intersection of two substantial public health challenges: reducing the burden of suffering from pain and containing the rising toll of harms associated with the use of opioid medications. In March 2016, the Food and Drug Administration (FDA) asked the National Academies of Sciences, Engineering and Medicine (NASEM) to update the science on pain research, care, and education since the 2011 publication of the Institute of Medicine (IOM) report *Relieving Pain in America*¹ and to identify actions that the FDA and other organizations could take to respond to the opioid epidemic. The NASEM report *Pain Management and the Opioid Epidemic*, released in July 2017,² concluded that years of sustained and coordinated effort will be required to contain the epidemic and urged the responsible regulatory agencies to maintain a reasonable balance between preserving access to opioids when clinically indicated and mitigating opioid-related harms. We (the committee chair and three of its members) review eight articles published in this issue of *AJPH*, using this platform as an opportunity to amplify the conclusions and recommendations set forth in the NASEM report.

THE PUBLIC HEALTH BURDEN OF PAIN

The 2011 IOM report, the National Pain Strategy,³ and

similar reports in other countries highlight the public health burden of pain in the United States and globally. However, its magnitude, dimensions, and social cost remain poorly measured, particularly for chronic noncancer pain. The 2017 NASEM report highlighted the need for improved methods of measurement for chronic pain and its many comorbidities.²(p50–51) Such information is foundational because understanding the breadth and depth of the chronic pain problem is critical to the formulation of effective solutions. Prevalence estimates for chronic pain vary wildly, ranging from 11% to 40%. The NASEM report referred to an estimate on the basis of 2012 data by Nahin⁴ showing that 11.2% of the adult US population (25.3 million people) were experiencing daily chronic pain (pain every day for the past three months).⁴ The most recent estimate, on the basis of the 2016 National Health Interview Survey, is that 8% of US adults (19.6 million) had “high-impact” chronic pain (referring to limitations in major life domains).⁵

Evidence-based assessment of the impact of pain, especially noncancer chronic pain, has been very difficult because of the inadequacy of the data available. Two of the articles published in the *AJPH* special section suggest frameworks for measuring and then addressing chronic pain. Blyth et al. (p. 35) demonstrate that musculoskeletal pain, particularly lower back pain, is an enormous global problem with an underestimated impact. Nevertheless, quantification remains elusive. For example, the Global Burden of Disease study used days of life lost owing to premature death or disability, but disability from pain is largely lost, as the 10th revision of the *International Classification of Diseases* codes are a poor representation for common pain conditions.⁶ The solution Blyth et al. offer focuses on the development of better diagnostic codes with the inclusion of pain as a disease entity as proposed for use in the 11th revision of the *International Classification of Diseases*.

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Gallagher and Sandbrink (p. 41) call attention to the burden of pain from war, arguing that war-related injuries to soldiers and civilians are diverse and often poorly understood. War injuries feature interaction of combat exposure, psychological disease, and pain. In this regard, the pain of war is an archetypical multidimensional chronic pain condition. Gallagher and Sandbrink properly emphasize stepped and multidisciplinary care as well as Comprehensive Addiction and Recovery Act provisions. A collaborative effort by the Veterans Administration and the Department of Defense (VA/DoD) quantifies pain intensity, disability, and psychological dimensions of pain and emphasizes the use of a diverse range of treatment options while reducing reliance on opioids. Thus, the VA/DoD Opioid Safety Initiative links comprehensive evaluation with comprehensive treatment.

THE ROLE OF OPIOIDS IN MANAGING PAIN

Although it is generally understood that opioids can play an essential role in treating acute postoperative pain and in alleviating the suffering of patients with severe acute pain and cancer-related pain, the management of pain is slowly evolving beyond an opioid-centric approach.⁷ Improved clinical guidelines are needed for use in these settings to maximize benefit and minimize risk, considering the expanding role of nonopioid alternatives (e.g., multimodal postoperative analgesia). At the same time, it is also generally accepted that the US opioid epidemic is largely attributable to the well-documented increase in

prescribing opioids for chronic noncancer pain in the 1990s. The remarkable increase in prescribing (sales of prescription opioids quadrupled between 1999 and 2010) was accompanied by a similarly striking increase in opioid-related overdose deaths and a substantial increase in opioid use disorder.² It should, therefore, come as no surprise that a core component of the US response to the epidemic has been a multipronged effort to reduce clinically unwarranted prescribing of these drugs for chronic noncancer pain.

The NASEM committee emphasized that chronic pain is a complex pathophysiologic condition that develops over time and that its successful management requires an equally complex and time-intensive approach. From this perspective, the committee warned against unwarranted assumptions that the public health burden of chronic noncancer pain can be significantly ameliorated by a greater use of opioids.^{8,9} There is no evidence for this supposition. Rather, some nonopioid pharmacologic treatments are likely to be as effective as opioids, or more so, when used to treat conditions for which they are indicated, and they have a lower profile of harm in many cases. Moreover, nonpharmacologic treatments often have powerful effects in the management of chronic pain.¹⁰ Therefore, a more comprehensive, individualized approach, featuring multiple therapeutic modalities and including nonpharmacologic ones, is preferred.

The committee's conclusions are strongly reinforced by Aldington and Eccleston (p. 46) in their synthesis of the Cochrane Library's 288 systematic reviews of primary randomized controlled trials on the

prevention and treatment of acute and chronic pain. However, the authors' ability to provide clinical guidance was severely limited because of the absence of evidence of enough quality to warrant strong endorsement for any specific analgesic strategy. The authors properly call for high-quality research on the treatment of chronic pain to better inform providers and policymakers. Especially noteworthy is their finding that there is no evidence to support the use of high-dose opioids (200 morphine milligram equivalents/day) for chronic noncancer pain, a fact also emphasized in the Centers for Disease Control and Prevention (CDC) guideline.¹¹ In retrospect, access to such a comprehensive and systematic review of the evidence on this question in the 1990s might have helped avoid the subsequent overprescribing of opioids and the accompanying public health crisis. Going forward, practice should err on the side of minimizing addiction risk and of reducing harm, such as improving access to naloxone for opioid users, until adequate data on and methods for chronic pain treatment are available.¹²

Because of the limited alternatives to opioid analgesics, cannabis-containing products have emerged as a potential analgesic modality. The nation's failure to provide proper infrastructure for cannabis research and the continued classification of cannabis in Schedule I under the Controlled Substances Act have prompted many states to legalize cannabis products despite the direct conflict with federal law. Unfortunately, the net result is that cultivation, distribution, and marketing of cannabis are poorly regulated for both medical and recreational uses. In an admirably concise summary of the

current knowledge about possible benefits and risks of cannabis for pain treatment, Carr and Schatman (p. 50) conclude that the cannabis now being marketed in the legalizing states has not been shown to be effective as an analgesic and has an "uncertain safety profile." Because of the inevitable proliferation of medical use (prescribed or self-initiated), the nation is facing urgent public health challenges—facilitating clinical research, guiding use of cannabis in the treatment of pain through public and professional education, and, eventually, crafting a sound regulatory framework.¹³

GLOBAL DISPARITIES AND DIVERGENT APPROACHES

Although opioids are abundant in certain countries, much of the world is without access to opioids for types of pain that might respond to these drugs (e.g., acute and cancer-related pain). Scholten et al. (p. 52) have attempted to construct an "adequacy of opioid consumption" index to define trends and countrywide differences in opioid consumption across time (up to 2015). They conclude that many countries consume "inadequate" amounts of opioids as benchmarked against 20 of the more developed nations. Although interesting, the article raises many more questions than it answers. One wonders first whether benchmarking against 20 more developed nations is the right reference group. Moreover, although the authors noted that they excluded some opioids used for anesthesia and opioid use disorder treatment, they were apparently unable to identify how opioids were being used

in pain treatment or for which indications opioid use might be particularly low. The analysis was therefore highly limited because of the lack of comparison with any measured medical needs or outcomes.

Nevertheless, perhaps some measure of “adequate” access to pain management could be useful in public health terms. If Scholten et al. had the ability to disaggregate opioid consumption by medical indication, their indices of the adequacy of opioid consumption might have been connected more meaningfully to therapeutic efficacy. The model would also have been improved by considering access to the different modalities of care as well as the risks and harms associated with the various modalities and their relative cost effectiveness. In the absence of such an overall strategy, the author’s “adequacy of opioid consumption” index provides little more than a simple heuristic for variation in medical opioid consumption produced by a combination of national wealth, expenditures on health care, and commercial factors affecting supply and demand; it is not a direct measure of medical need or benefit.

Bhadelia et al. (p. 58) discuss disparities in the availability of palliative care—defined exclusively in terms of opioids—in less well-developed countries. They make the case for expanding the availability of opioids (assuming proper regulation). In the abstract, this is an idea worth exploring because countries without broad access to opioids have the chance to “do it right” and avoid some of the pitfalls the United States has experienced. Yet, the authors acknowledge that the specific types of education and regulation required are unclear and would likely need to be culturally and resource

sensitive. Although offering strong advocacy for pain control, the authors conflate palliative care, pain relief, and the use of opioids. Differences in the goals of end-of-life care, the management of chronic pain in nonpalliative situations, and acute pain care are not acknowledged—nor are access to nonopioid alternatives or the emerging evidence of poorer long-term outcomes for patients chronically consuming opioids. In this sense, the arguments are strikingly like those made for wider use of opioids more than two decades ago in the United States—which had disastrous consequences.

The US experience is a cautionary tale for countries that might have the pennies for generic morphine, oxycodone, and other drugs but that hardly command the resources to deal with the devastating consequences of increased opioid prescribing that the United States and some other countries are now enduring. In the absence of a pain management infrastructure proven to be successful in a country of modest or minimal resources, a precautionary principle clearly applies: considering the experiences of other nations, the expanded use of opioids should be approached cautiously and should incorporate appropriate safeguards, monitor abuse and diversion, and respond quickly and effectively to signs of trouble.

FINDING THE RIGHT BALANCE IN OPIOID REGULATION

Which countries are better off: those that have “too few” opioids (as measured by a presumed need for relief of acute pain and chronic cancer pain) or those that

are awash in opioids being prescribed too readily for chronic noncancer pain and, perhaps, being overprescribed for acute pain and cancer pain and then being diverted to the illegal market? No one is now able to answer this question. Clearly, a balance must be struck, even though the available data are not adequate to the task of measuring palliative benefits of treatment and the harms associated with prescribing, including diversion.

The state of play in the United States is clearly, and quite properly, in the direction of reining in the profligate prescribing that spurred the epidemic, while being respectful of, and responsive to, the needs of individuals whose pain does not respond to alternative modalities of care. Brennan et al. (p. 61) argue that individuals suffering from inadequately treated pain have a “human right” to pain management. The authors’ goal is to show that, in recent years, many international bodies have embraced the concept of a human right of access to pain management and that the right of access to pain management has legal grounding in international human rights documents; this imposes obligations on signatory governments that might be enforceable in domestic courts under some circumstances. Brennan et al. illustrate this broad claim in the context of acute and chronic pain, with a focus on the regulatory challenges posed by the US opioid crisis. The argument potentially implicates a right of access to nonopioid pain management alternatives, although they are generally of modest effectiveness now.²

Although acknowledging that opioids may play a “circumscribed role” in the treatment of chronic noncancer pain, Brennan et al. contend that the right to

access pain treatment implies that “physicians should be able to make the clinical determination of the best treatment options—without inappropriate government interference.”^(p63) We think that even that claim may be too strong as a normative matter. After all, local, state, and federal governments clearly have a strong regulatory interest in this issue, and the medical profession’s failure to establish effective mechanisms for self-policing is evident in the historical increases in opioid prescribing, prosecutions of licensed medical providers in otherwise good standing for demonstrably excessive prescribing, and an ongoing lack of (strong) adherence to prescribing guidelines.^{14–16} Although many commentators, as well as the NASEM report, have expressed legitimate concern about arbitrary restrictions on prescribing (e.g., dose and time), it would be a serious mistake (in the United States, at least) for the courts to constitutionalize a right to opioid medications for any specific indication. These decisions should be left to the FDA and allied agencies and bodies that are charged with measuring and weighing the likely effects of possible regulatory restrictions in the comprehensive public health framework recommended in the 2017 NASEM report.

In their overview of recent reports and federal initiatives on pain policy, Gross and Gordon (p. 66) question the balance in current US regulatory policy. They suggest that policymakers have focused too much on regulating controlled substances, preventing opioid use disorder, and modifying prescribing practices and that they have failed to formulate a coherent analgesic policy. They are certainly right to imply that the regulatory

perspective of the Controlled Substances Act is not focused on facilitating safe and effective analgesia. It is also clear that some of the most visible aspects of the US response to the opioid crisis involve seeking to curtail opioid prescribing and that rules and guidelines can be misapplied and might deter responsible prescribing. For example, there is legitimate concern that the CDC guidelines,¹¹ although intended for outpatient primary care, are being adopted arbitrarily by regulators and health care organizations to reduce opioids unilaterally without addressing the need for expanded resources of integrated pain care. Such unilateral restrictions of opioids may be driving additional people into illicit opioid markets with even greater harm.^{17,18}

However, more aggressive regulation, particularly by the FDA, is not incompatible with a balanced approach to the role of opioids in pain management. The current crisis is rooted in a broad health system failure, and steps need to be taken on all fronts to reduce the supply of and the demand for opioids. In our view, implementation of the National Pain Strategy³—an interagency effort to provide a comprehensive, population health-level strategy for pain management—needs to be aligned with ongoing efforts to ameliorate the opioid crisis. Going forward, stronger FDA regulation can strike a proper balance between the needs of patients in pain and the prevention of opioid-related harms. The NASEM committee recommends a comprehensive and balanced public health framework to guide opioid approval, monitoring, and review, as well as other agency decisions. The FDA should implement this framework with all deliberate speed. Careful regulation should

be embedded in a long-term cultural transformation of how pain is perceived, assessed, and treated, including efforts to develop clinical pain competencies for all health care providers. **AJPH**

CONTRIBUTORS

All of the authors contributed equally to this commentary.

CONFLICTS OF INTEREST

No conflicts of interest.

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