



## AMA Journal of Ethics®

July 2024, Volume 26, Number 7: E551-561

### POLICY FORUM: PEER-REVIEWED ARTICLE

## How Should the Use of Opioids Be Regulated to Motivate Better Clinical Practice?

Ellen L. Edens, MD, MPE, MA, Gabriela Garcia Vassallo, MD, and Robert Heimer, PhD

### Abstract

This article describes historical and political reasons for—and devastating consequences of—US opioid prescribing policy since the 1990s, which has restricted opioid prescribing for pain less than for treating opioid use disorder (OUD) treatment. This article considers merits and drawbacks of a new diagnostic category and proposes a regulatory and clinical framework for prescribing long-term opioid therapy for pain and for prescribing opioids to treat OUD.

*The American Medical Association designates this journal-based CME activity for a maximum of 1 AMA PRA Category 1 Credit™ available through the AMA Ed Hub™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.*

### Approved Uses of Opioids

There are 2 US Food and Drug Administration (FDA)-approved uses for opioid medications: the treatment of moderate to severe pain and opioid use disorder (OUD). Current best practices call for limiting opioid prescribing for pain to acute situations, terminal illness, and certain chronic conditions wherein other medications or treatments are ineffective.<sup>1,2</sup> Conversely, clinical guidelines for treating OUD call for expanding access to long-term medications, with opioid agonists or partial agonists—limited in the United States to methadone and buprenorphine—being first-line treatment.<sup>3</sup> Contrary to available evidence, current US regulatory policies restrict access to opioids for OUD treatment more than for to opioids prescribed for pain.

Treatment guidelines for the management of chronic pain with opioids and for OUD have fluctuated over time due to changing drug policies and **historical developments** that impact medical practice and disproportionately affect minoritized communities through treatment disparities and stigma.<sup>4,5,6,7,8</sup> While the use of opioids to control pain has long been recognized,<sup>9</sup> their use in treating OUD remains controversial, highlighted by the misnomer “medication-assisted treatment.”<sup>10</sup> Opioid-agonist medications for OUD are not assisting treatment; they *are* the first-line treatment. In this paper, we explore the impact of treatment guideline fluctuations on patients and clinicians and provide an

ethical analysis for maximizing benefits and minimizing risks arising from long-term opioid prescribing for pain and for OUD.

### Not New

To gain insight into our current situation and identify potential treatment improvements for the future, it is crucial to possess a basic understanding of the historical context of opioid use in the United States. Modern opioid use emerged in the 19th century with the isolation of morphine. Its use for the treatment of acute trauma was advanced by the invention of the hypodermic syringe, leading to its widespread battlefield use during the Crimean War and US Civil War.<sup>11</sup> An unregulated patent medicine market and physician prescribing, mostly to women, throughout the second half of the 19th century increased opioid dependence within the general US population.<sup>11</sup> Concurrently, while people with narcotic dependence, mostly White, were considered medically ill and in need of treatment and were treated in psychiatric facilities, individuals with cocaine dependence, who were putatively disproportionately Black, were vilified; they were described as murderers, perverts, and drug fiends and were incarcerated—or worse.<sup>12</sup>

Initial efforts to reduce opioid misuse arose through public concern about morphine. Arguably, the early 20th-century US progressive and temperance movements did more to reduce opiate importation and consumption than did enactment of state laws designed to limit access.<sup>13</sup> Government efforts to control and regulate the influx and distribution of products containing opium and cocaine included the Pure Food and Drug Act of 1906 and the Harrison Narcotics Tax Act of 1914.<sup>14,15</sup> The former, the first law at the federal level to regulate dangerous goods, required product labeling and allowed the federal government to set purity standards covering 10 addictive ingredients. Misrepresentation of the latter statute as a prohibitive act by law enforcement had dire consequences, including **increased stigma** directed against people using the regulated drugs and the assumption that addiction was a moral failing.<sup>16</sup> Two Supreme Court rulings in 1919 upheld that opioids could not be used to treat OUD.<sup>17,18,19</sup> Within 4 years, and against the backdrop of a wave of prosecutions against prescribing physicians, “maintenance clinics” providing morphine were shuttered nationally and life expectancies of patients with OUD plummeted.<sup>13,20,21</sup> Between 1935 and 1974, 2 large federal facilities devoted to treating people with addiction were operated jointly by the US Public Health Service and the Federal Bureau of Prisons (so-called “narcotic farms”).<sup>22</sup> Treatment was provided to both those who were voluntarily seeking treatment and those serving drug-related sentences, highlighting the long-standing tug-of-war between conceptualizing addiction as a medical condition deserving of treatment or as a moral failing deserving of punishment. In 1962, a Supreme Court ruling held that addiction was a disease and not an act deserving of punishment.<sup>23</sup>

In the 1960s, the United States saw an increase in illegally trafficked opioids, and heroin addiction became widespread among young American men.<sup>11</sup> Heroin use further increased with easy access to the drug among soldiers serving in the Vietnam War.<sup>11,13</sup> In response, small trials using medications for OUD (MOUD) treatment were conducted and demonstrated the potential effectiveness of methadone, a long-acting full agonist.<sup>24,25</sup> Treatment centers, largely operating under investigational new drug regulations, scaled up methadone treatment from a handful of patients in 1968 to 73 000 by 1973.<sup>26</sup> Fears of inappropriate use, diversion, and profiteering, however, led to the creation of the current closed system under the Narcotic Addict Treatment Act of 1974, in which only clinics registered with the Substance Abuse and Mental Health Services Administration can dispense methadone and patients, especially early in

treatment, are required to visit almost daily to obtain their medication.<sup>27</sup> In the 50 years since the passage of this act, the burdensome regulations have limited access to and acceptability of methadone and stigmatized it—even as it has become all but universally recognized as safe and effective.<sup>28,29,30,31,32,33</sup> These regulations were relaxed only at the start of the COVID-19 pandemic.<sup>34</sup>

During the period when methadone was being underutilized to treat OUD, there was one positive development. In 1966, the long-acting, partial agonist buprenorphine was discovered, along with its analgesic properties,<sup>35</sup> and, as early as 1978, its potential use for treating narcotic addiction was reported.<sup>36</sup> Buprenorphine ultimately proved to be an excellent candidate for MOUD,<sup>37</sup> given its safety profile, lower abuse potential, and effectiveness. However, even with these advantages and its Schedule III drug classification, the Drug Addiction Treatment Act of 2000 mandated that prescribers undergo extensive training and limited the number of patients they could treat.<sup>38</sup> These restrictions were substantially more onerous than those required to prescribe opioids for pain. Moreover, widespread stigma directed toward both patients using buprenorphine and prescribers remains a barrier to expanded prescribing, with people of color disproportionately denied access to MOUD.<sup>39</sup>

Meanwhile, the use of opioids to treat pain increased. Until the 1980s, opioid use focused primarily on acute pain and palliation of terminal diseases like cancer.<sup>40</sup> Beginning at that time, however, there was growing recognition that patients experiencing pain healed more slowly when their pain went untreated.<sup>41,42</sup> To promote more liberal prescribing of opioids for pain, interested physicians and physician administrators had to overcome decades of fear of prosecution and lack of training in medical schools. Nonetheless, pain became a “fifth vital sign” in assessing patient health.<sup>43,44</sup> As it provided effective pain relief in certain circumstances, long-term opioid therapy (LTOT) increased, including for conditions with little evidence of benefit. This range of conditions for which opioids were prescribed—combined with the development of synthetic opioids, time release formulations, and aggressive marketing strategies from the pharmaceutical industry<sup>45</sup>—led to a fivefold increase in morphine milligram equivalents prescribed between 1999 and 2010.<sup>46</sup> Opioid overdose deaths rose in parallel, increasing nearly fourfold during the same period.<sup>47,48</sup> The exponential rise in opioid overdose deaths prompted efforts—reminiscent of a century prior—to reduce access to opioids. Guidelines recommending a limit to opioid prescribing were promulgated as early as 2009, while other supply-side efforts to reduce opioid use relied on law enforcement, civil litigation, and reformulation of high concentration opiates to be more tamper resistant.<sup>49</sup> After peaking in 2012, high-dosage opioid prescribing fell almost 50% by 2017.<sup>50</sup>

Nevertheless, total opioid overdose deaths continued to rise. Although the consequence of a supply-side only approach should have been anticipated, little was done initially to provide demand-side increases in the availability—or to promote the acceptability—of either form of MOUD.<sup>51</sup> Between 2010 and 2015, deaths involving heroin tripled, and from 2014 to 2015, deaths from fentanyl and its congeners increased 72%.<sup>52</sup> As recently as 2016, the Centers for Disease Control and Prevention (CDC) prescribing guideline seemed to prioritize tapering or discontinuation of prescribing, with referral to treatment for OUD being the last of 12 recommendations.<sup>6</sup> Moreover, the guideline offered no indication of which forms of treatment should be promoted or discouraged.<sup>6</sup> Individuals dependent on opioids increasingly turned to illegal drug markets, and

outbreaks of HIV and hepatitis increased.<sup>53</sup> Between the release of the CDC guideline in 2016 and 2021, annual opioid overdose deaths roughly doubled to over 80 000.<sup>54</sup>

### **Influences on Patients and Clinicians**

Interwoven throughout the history of opioids outlined above is the intersection of law and health care. Negative consequences arise when medical treatment is stipulated by an impersonal legal system and the sociocultural powers that drive it. These regulations have struggled to keep pace with current evidence, instead being informed by a misplaced belief that a chronic condition like OUD can be cured through short-term abstinence. A proper understanding of drug control and prohibition legislation, which is beyond the scope of this short report, places the spotlight on political strategies, such as propaganda and mass incarceration, that were utilized to demonize people who use drugs and make draconian legislation palatable to the majority.<sup>55,56</sup> These laws set the stage for reliance on a criminal justice approach, which disproportionately affects the most vulnerable and takes precedence over a public health perspective. This approach has also allowed medical professionals, even those acting in good faith, to become targets of the criminal justice arm of drug control efforts, just as they had in the 1920s following Supreme Court interpretations of the Harrison Narcotics Tax Act.<sup>57,58,59</sup> To say that this approach has failed—with over 80 000 opioid-related deaths in 2021<sup>54</sup>—feels like an understatement.

### **Guidelines for Better Practice**

In 2022, responding to the tidal wave of opioid deaths, the CDC revised its 2016 guidelines on the use of opioids for chronic pain to emphasize patient-centered care, slow tapering of opioids with consideration of a switch to buprenorphine, and assessment for OUD with initiation of or referral to treatment.<sup>2</sup> Correspondingly, and prompted by the COVID-19 pandemic, MOUD regulations saw the first major relaxation in mandated methadone treatment practices since 1975, including termination of the moratorium on mobile methadone units in 2021, and a substantial easing of the Drug Addiction Treatment Act's restrictions on buprenorphine prescribing.<sup>60,61</sup> In parallel, the US Department of Health and Human Services' Overdose Prevention Strategy has incorporated harm reduction principles and best practices as 1 of its 4 pillars. The expanded distribution of naloxone kits and fentanyl test strips to prevent overdose—along with the establishment of safe injection sites, sterile syringe programs, and funding for research on innovative harm reduction approaches—represents a significant and encouraging policy advance aimed at addressing the current opioid crisis.

Nonetheless, while opioids are less likely to be initiated for treating pain than in the past,<sup>62</sup> the range of FDA-approved opioid formulations available for treating chronic pain remains wide, which is not the case for OUD treatment. OUD treatment is limited in the United States to just 2 opioid-agonist formulations (and one opioid antagonist), and there is little discussion of (or research dollars going toward) expanding options for those who do not tolerate or accept the current FDA-approved choices. The FDA, mandated to prioritize safety, seems to assume that approved medications for OUD will be misused or diverted.

Consistent with this assumption, the FDA has put in place onerous risk evaluation and mitigation strategies (REMS) requirements that limit access to lifesaving medications. For instance, the stringent requirements imposed on 6-month subcutaneous buprenorphine implants in 2016, including a skills assessment for clinicians, arguably reflected contemporary bias against people treated with MOUD and their prescribers.

Despite a buprenorphine implant being a simple outpatient procedure similar to an etonogestrel implant (an implantable birth control medication), no such clinician assessment was required for contraceptive implants. The buprenorphine implants were withdrawn in 2020 due to low uptake, not safety concerns.<sup>63</sup> The FDA's approach to long-acting injectable buprenorphine products also involves restricting distribution and access through REMS certification for specialty pharmacy distributors and clinics. This approach lacks flexibility and risk tolerance compared to opioids for pain and potentially overlooks the high prevalence of substance use disorders in the general population receiving controlled substances for non-SUD indications. The consequences of stringent regulations for public health, clinician training, and public health literacy are not adequately considered.<sup>28</sup>

Outside the United States, however, there are a greater number of options for treating OUD. In Canada, for example, as early as 2018, slow-release oral morphine (SROM), a 24-hour formulation, became a guideline-recommended second- or third-line treatment for OUD, based upon moderate-quality evidence.<sup>64</sup> And, in 2019, recognizing that the emergence of fentanyl might require further alternative treatments, a Canadian guideline review committee published guidance on the use of injectable opioid agonist treatments for OUD.<sup>65</sup> The committee recommended that individuals with severe OUD who inject opioids and who have not adequately benefited from oral opioid agonist treatments be considered for injectable diacetylmorphine or hydromorphone treatment,<sup>65</sup> and the government approved both treatment options.<sup>66</sup> Similarly, several countries in the European Union offer alternatives to methadone and buprenorphine, including SROM and diacetylmorphine.<sup>67</sup>

Recent moves in the United States to bring guidance, legislation, funding, practice, and treatment access more in line with the evidence base for both chronic pain and OUD are indeed promising and have helped moderate the ethical quandaries we have described. Yet they remain insufficient. More flexible, patient-centered access to MOUD should be made available. Additionally, a clear path forward to expanding the number of MOUD options should be outlined. As early as 2019, the National Academies of Sciences, Engineering, and Medicine proposed exactly this solution—but noted that many of these options would require changes to the Harrison Narcotics Tax Act of 1914.<sup>28</sup> As of this writing, these changes have not been made.

### **Ethics and Evidence**

There is now an ethical imperative to rethink our approach to the management of opioid prescribing. Conceptualizing chronic pain treated with LTOT as different than OUD, from both clinical and regulatory perspectives, is problematic and has led to a 2-tiered system that confuses clinicians, patients, and regulators.

Both OUD and long-standing debilitating pain are chronic conditions with strong evidence bases for appropriate treatment. Opioids have evidence of benefit for relief of acute pain and treatment of OUD.<sup>37,68</sup> In contrast, accumulating evidence supports alternatives to LTOT for most chronic pain conditions.<sup>2</sup> For those currently prescribed such treatment, however, tapering opioids to discontinuation is often difficult, risks substantial harm, and forces clinicians to fit patients' experiences into regulatory—rather than clinical—boxes. Illustratively, researchers are now proposing a new diagnostic category instead of using the robustly validated OUD diagnostic criteria in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* for patients on LTOT who demonstrate an inability to taper prescription opioids despite

awareness of the high risk of harm and low functional benefit<sup>69</sup> because the stigma of OUD attached to patients and prescribers is substantial and reflected in regulations.<sup>70</sup> Proponents of the new diagnosis recommend excluding not only *DSM-5* criteria of tolerance and withdrawal, which are currently excluded in the case of long-term opioid prescribing for pain, but also the criterion of “persistent desire or unsuccessful efforts to reduce use” because difficulty tapering is also “normal, expected” in the context of LTOT. Exclusion of this latter criterion “better aligns with patients’ experience on LTOT” and helps patients avoid a “stigmatizing and confusing experience of being incorrectly diagnosed with OUD.”<sup>69</sup> Generally, meeting 3 of the well-validated SUD criteria is sufficient to diagnose mild OUD. Yet, rather than working to change discrepant regulations between prescribing opioids for pain and prescribing opioids for OUD, those in favor of creating LTOT as a new diagnosis tend to discount the continuum of severity already embedded in *DSM-5* diagnostic criteria.

We propose that approaching both chronic pain and OUD as the chronic conditions they are provides an ethical and practical framework for addressing these diagnostic inconsistencies. This framework would include complete evaluation and diagnostic workup; patient-centered consent, with discussion of **risks and benefits** of various treatment options; monitoring for safety; and reevaluation of the clinical plan at regular intervals. It would also require regulatory bodies and research funding agencies to consider other opioid formulations for OUD and less restrictive REMS and distribution requirements. It would also require expanding the number and kind of settings in which MOUD treatment can be prescribed and dispensed. Chronic conditions require consideration of pathophysiology and related evidence-base treatments, relative harm, an integrated and collaborative health care system, and a treatment team that leverages patient characteristics and preferences to maximize patient self-management. Conceptualizing and managing both OUD and chronic pain requiring LTOT as chronic medical conditions could help address diagnostic inconsistencies, clinical confusion, and stigma experienced by patients.

## References

1. Use of Opioids in the Management of Chronic Pain Work Group. *VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain*. US Department of Veterans Affairs; US Department of Defense; 2022. Accessed February 26, 2024. <https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOpioidsCPG.pdf>
2. 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(3):1-95.
3. Perry C, Liberto J, Milliken C, et al; VA/DoD Guideline Development Group. The management of substance use disorders: synopsis of the 2021 US Department of Veterans Affairs and US Department of Defense clinical practice guideline. *Ann Intern Med*. 2022;175(5):720-731.
4. Tsai AC, Kiang MV, Barnett ML, et al. Stigma as a fundamental hindrance to the United States opioid overdose crisis response. *PLoS Med*. 2019;16(11):e1002969.
5. Chau V; Office of Behavioral Health Equity. The opioid crisis and the Black/African American population: an urgent issue. Substance Abuse and Mental Health Services Administration; 2020. Accessed February 26, 2024. <https://store.samhsa.gov/sites/default/files/pep20-05-02-001.pdf>

6. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep.* 2016;65(1):1-49.
7. Nuckols TK, Anderson L, Popescu I, et al. Opioid prescribing: a systematic review and critical appraisal of guidelines for chronic pain. *Ann Intern Med.* 2014;160(1):38-47.
8. Courtwright DT. The cycles of American drug policy. *History Faculty Publications* No. 25. University of North Florida; 2015. Accessed February 26, 2024. [https://digitalcommons.unf.edu/cgi/viewcontent.cgi?article=1025&context=ahis\\_facpub](https://digitalcommons.unf.edu/cgi/viewcontent.cgi?article=1025&context=ahis_facpub)
9. Wood HC. The indispensable uses of narcotics: the therapeutic uses of narcotic drugs. *J Am Med Assoc.* 1931;96(14):1140-1144.
10. Robinson SM, Adinoff B. The mixed message behind “medication-assisted treatment” for substance use disorder. *Am J Drug Alcohol Abuse.* 2018;44(2):147-150.
11. Courtwright DT. *Dark Paradise: A History of Opiate Addiction in America.* Harvard University Press; 2001.
12. The use of narcotic drugs in the south. *Med Rec.* 1914;37:127-128.
13. Musto DF. *The American Disease: Origins of Narcotic Control.* 3rd ed. Oxford University Press; 1999.
14. Pure Food and Drug Act, Pub L No. 59-384, 34 Stat 768 (1906).
15. Harrison Narcotics Tax Act, Pub L No. 63-223, 38 Stat 785 (1914).
16. Jordan A, Mathis ML, Isom J. Achieving mental health equity: addictions. *Psychiatr Clin North Am.* 2020;43(3):487-500.
17. *Webb v United States*, 249 US 96 (1919).
18. *United States v Doremus*, 249 US 86 (1919).
19. Waldorf D, Orlick M, Reineman C. *Morphine Maintenance: The Shreveport Clinic, 1919-1923.* Drug Abuse Council; 1974.
20. Musto DF, Ramos MR. Notes on American medical history: a follow-up study of the New Haven morphine maintenance clinic of 1920. *N Engl J Med.* 1981;304(18):1071-1077.
21. Herzberg D. *White Market Drugs: Big Pharma and the Hidden History of Addiction in America.* University of Chicago Press; 2020.
22. Musto DF. Appendix B: drug abuse research in historical perspective. In: Institute of Medicine. *Pathways of Addiction: Opportunities in Drug Abuse Research.* National Academy Press; 1996:284-294.
23. *Robinson v California*, 370 US 660 (1962).
24. Dole VP, Nyswander M. A medical treatment for diacetylmorphine (heroin) addiction. A clinical trial with methadone hydrochloride. *JAMA.* 1965;193(8):646-650.
25. Dole VP, Nyswander ME, Warner A. Successful treatment of 750 criminal addicts. *JAMA.* 1968;206(12):2708-2711.
26. Rettig RA, Yarmolinsky A, eds; Institute of Medicine. *Federal Regulation of Methadone Treatment.* National Academy Press; 1995.
27. Narcotic Addict Treatment Act, Pub L No. 93-281, 88 Stat 124 (1974).
28. Leshner AI, Mancher M, eds; National Academies of Sciences, Engineering, and Medicine. *Medications for Opioid Use Disorder Save Lives.* National Academies Press; 2019.
29. Hall NY, Le L, Majmudar I, Mihalopoulos C. Barriers to accessing opioid substitution treatment for opioid use disorder: a systematic review from the client perspective. *Drug Alcohol Depend.* 2021;221:108651.

30. Brown BS, Benn GJ, Jansen DR. Methadone maintenance: some client opinions. *Am J Psychiatry*. 1975;132(6):623-626.
31. Hunt DE, Lipton DS, Goldsmith DS, Strug DL, Spunt B. "It takes your heart": the image of methadone maintenance in the addict world and its effect on recruitment into treatment. *Int J Addict*. 1985;20(11-12):1751-1771.
32. Stancliff S, Myers JE, Steiner S, Drucker E. Beliefs about methadone in an inner-city methadone clinic. *J Urban Health*. 2002;79(4):571-578.
33. Zaller ND, Bazazi AR, Velazquez L, Rich JD. Attitudes toward methadone among out-of-treatment minority injection drug users: implications for health disparities. *Int J Environ Res Public Health*. 2009;6(2):787-797.
34. Substance Abuse and Mental Health Services Administration. FAQs: provision of methadone and buprenorphine for the treatment of opioid use disorder in the COVID-19 emergency. Substance Abuse and Mental Health Services Administration; 2020. Accessed February 26, 2024. <https://www.samhsa.gov/sites/default/files/faqs-for-oud-prescribing-and-dispensing.pdf>
35. Sivils A, Lyell P, Wang JQ, Chu XP. Suboxone: history, controversy, and open questions. *Front Psychiatry*. 2022;13:1046648.
36. Jasinski DR, Pevnick JS, Griffith JD. Human pharmacology and abuse potential of the analgesic buprenorphine: a potential agent for treating narcotic addiction. *Arch Gen Psychiatry*. 1978;35(4):501-516.
37. Heidbreder C, Fudala PJ, Greenwald MK. History of the discovery, development, and FDA-approval of buprenorphine medications for the treatment of opioid use disorder. *Drug Alcohol Depend Rep*. 2023;6:100133.
38. Lanham HJ, Papac J, Olmos DI, et al. Survey of barriers and facilitators to prescribing buprenorphine and clinician perceptions on the Drug Addiction Treatment Act of 2000 waiver. *JAMA Netw Open*. 2022;5(5):e2212419.
39. Madden EF. Intervention stigma: how medication-assisted treatment marginalizes patients and providers. *Soc Sci Med*. 2019;232:324-331.
40. Manders KL. Integrated approach to the management of pain. A National Institutes of Health consensus report synopsis. *Indiana Med*. 1986;79(12):1053-1055.
41. Max MB. Improving outcomes of analgesic treatment: is education enough? *Ann Intern Med*. 1990;113(11):885-889.
42. Practice guidelines for acute pain management in the perioperative setting. A report by the American Society of Anesthesiologists Task Force on Pain Management, Acute Pain Section. *Anesthesiology*. 1995;82(4):1071-1081.
43. Booss J, Drake A, Kerns RD, Ryan B, Wasse L. Pain as the 5th Vital Sign Toolkit. US Department of Veterans Affairs; 2000. Accessed February 27, 2024. <https://www.va.gov/painmanagement/docs/toolkit.pdf>
44. Mularski RA, White-Chu F, Overbay D, Miller L, Asch SM, Ganzini L. Measuring pain as the 5th vital sign does not improve quality of pain management. *J Gen Intern Med*. 2006;21(6):607-612.
45. Crow D. US opioid prescriptions in record decline. *Financial Times*. April 19, 2018. Accessed February 27, 2024. <https://www.ft.com/content/895f30a6-434f-11e8-803a-295c97e6fd0b>
46. FDA analysis of long-term trends in prescription opioid analgesic products: quantity, sales, and price trends. *FDA News*. March 1, 2018. Accessed February 27, 2024. <https://www.fdanews.com/ext/resources/files/2018/03-06-18-Opioids.pdf?1520649147>



47. Warner M, Hedegaard H, Chen LH. Trends in drug-poisoning deaths involving opioid analgesics and heroin: United States, 1999-2012. Centers for Disease Control and Prevention; 2014. Accessed February 27, 2024. [https://www.cdc.gov/nchs/data/hestat/drug\\_poisoning/drug\\_poisoning\\_deaths\\_1999-2012.pdf](https://www.cdc.gov/nchs/data/hestat/drug_poisoning/drug_poisoning_deaths_1999-2012.pdf)
48. Jalal H, Buchanich JM, Roberts MS, Balmert LC, Zhang K, Burke DS. Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. *Science*. 2018;361(6408):eaau1184.
49. Becker WC, Fiellin DA. Abuse-deterrent opioid formulations—putting the potential benefits into perspective. *N Engl J Med*. 2017;376(22):2103-2105.
50. Bohnert ASB, Guy GPJ Jr, Losby JL. Opioid prescribing in the United States before and after the Centers for Disease Control and Prevention’s 2016 opioid guideline. *Ann Intern Med*. 2018;169(6):367-375.
51. Dasgupta N, Creppage K, Austin A, Ringwalt C, Sanford C, Proescholdbell SK. Observed transition from opioid analgesic deaths toward heroin. *Drug Alcohol Depend*. 2014;145:238-241.
52. Beletsky L, Davis CS. Today’s fentanyl crisis: prohibition’s iron law, revisited. *Int J Drug Policy*. 2017;46:156-159.
53. Heimer R, Hawk K, Vermund SH. Prevalent misconceptions about opioid use disorders in the United States produce failed policy and public health responses. *Clin Infect Dis*. 2019;69(3):546-551.
54. Drug overdose death rates. National Institute on Drug Abuse. Updated June 30, 2023. Accessed February 27, 2024. <https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>
55. Alexander M. *The New Jim Crow: Mass Incarceration in the Age of Colorblindness*. New Press; 2010.
56. Reinerman CL. *Crack in America: Demon Drugs and Social Justice*. University of California Press; 1997.
57. Anson P. Doctors and pharmacists targeted in DEA surge. *Pain News Network*. April 2, 2018. Accessed February 27, 2024. <https://www.painnewsnetwork.org/stories/2018/4/2/doctors-and-pharmacists-arrested-in-dea-surge>
58. Foxhall K. DEA enforcement versus pain practice. *Pract Pain Manag*. 2005;5(6):1.
59. Trehan AB. Fear of prescribing: how the DEA is infringing on patients’ right to palliative care. *Univ Miami Law Rev*. 2007;61(3):961-996.
60. Consolidated Appropriations Act, 2023, Pub L No. 117-328, 136 Stat 4459, 5681 (2022).
61. Substance Abuse and Mental Health Services Administration. Opioid Treatment Program (OTP) guidance. Substance Abuse and Mental Health Services Administration; 2020. Accessed February 27, 2024. <https://www.samhsa.gov/sites/default/files/otp-guidance-20200316.pdf>
62. AMA Substance Use and Pain Care Taskforce. 2021 overdose epidemic report: physicians’ actions to help end the nation’s drug-related overdose and death epidemic—and what still needs to be done. American Medical Association; 2021. Accessed February 27, 2024. [https://end-overdose-epidemic.org/wp-content/uploads/2021/09/AMA-2021-Overdose-Epidemic-Report\\_92021.pdf](https://end-overdose-epidemic.org/wp-content/uploads/2021/09/AMA-2021-Overdose-Epidemic-Report_92021.pdf)
63. DeVarney KB. Probuphine notice October 2020. Titan Pharmaceuticals. October 19, 2020. Accessed February 27, 2024. [https://www.titanpharm.com/Probuphine\\_Notice\\_October\\_2020](https://www.titanpharm.com/Probuphine_Notice_October_2020)

64. Canadian Research Initiative in Substance Misuse. *CRISM National Guideline for the Clinical Management of Opioid Use Disorder*. Canadian Institutes of Health Research; Canadian Research Initiative in Substance Misuse. Accessed February 27, 2024. [https://crism.ca/wp-content/uploads/2018/03/CRISM\\_NationalGuideline\\_OUD-ENG.pdf](https://crism.ca/wp-content/uploads/2018/03/CRISM_NationalGuideline_OUD-ENG.pdf)
65. Fairbairn N, Ross J, Trew M, et al. Injectable opioid agonist treatment for opioid use disorder: a national clinical guideline. *CMAJ*. 2019;191(38):E1049-E1056.
66. Government of Canada approves new treatment options for opioid use disorder and supports research, treatment and harm reduction projects in Ontario. News release. Government of Canada; May 15, 2019. Accessed August 30, 2023. <https://www.canada.ca/en/health-canada/news/2019/05/government-of-canada-approves-new-treatment-options-for-opioid-use-disorder-and-supports-research-treatment-and-harm-reduction-projects-in-ontario.html#>
67. Opioid agonist treatment—the current situation in Europe (*European Drug Report 2023*). European Monitoring Centre for Drugs and Drug Addiction. Updated June 16, 2023. Accessed February 27, 2024. [https://www.emcdda.europa.eu/publications/european-drug-report/2023/opioid-agonist-treatment\\_en](https://www.emcdda.europa.eu/publications/european-drug-report/2023/opioid-agonist-treatment_en)
68. Phillips JK, Ford MA, Bonnie RJ, eds; National Academies of Sciences, Engineering, and Medicine. *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*. National Academies Press; 2017:chap 2.
69. Becker WC, Frank JW, Edmond SN, Starrels JL. When harms outweigh benefits of long-term opioid therapy for pain: need for a new diagnostic entity, research and improved treatments. *Addiction*. 2024;119(1):4-5.
70. Drexler K, Edens EL, Trafton JA, Compton WM. In the balance: no new diagnosis needed in addition to opioid use disorder to study harms associated with long-term opioid therapy. *Addiction*. 2024;119(1):6-8.

**Ellen L. Edens, MD, MPE, MA** is an associate professor of psychiatry at the Yale School of Medicine in New Haven, Connecticut. She is also an addiction psychiatrist at the VA Connecticut Healthcare System and the Substance Use Disorder Program lead for VA National Expert Consultation and Specialized Services. Her clinical expertise is in chronic pain, opioid prescribing, and management of opioid use disorder.

**Gabriela Garcia Vassallo, MD** is an assistant professor of psychiatry at the Yale School of Medicine in New Haven, Connecticut. She is also the director of the Opioid Treatment Program at the VA Connecticut Healthcare System and serves as VA site training director for the Yale Addiction Psychiatry Fellowship. Her professional and research interests include expanding access to evidence-based treatment for opioid use disorders, the integration of harm reduction strategies into clinical care, and the education of health care trainees in substance use disorders.

**Robert Heimer, PhD** is a professor of epidemiology and pharmacology at the Yale School of Medicine in New Haven, Connecticut. Dr Heimer has conducted research at the intersection of infectious diseases and substance use for 3 decades. His areas of investigation have included HIV and hepatitis C epidemiology and prevention science, syringe exchange and other harm reduction measures, overdose prevention and resuscitation, and treatment of people with opioid use disorder.

**Citation**

*AMA J Ethics.* 2024;26(7):E551-561.

**DOI**

10.1001/amajethics.2024.551.

**Conflict of Interest Disclosure**

Dr Edens reports being an advisory board member for Aspire 365, a health care delivery system. Drs Garcia Vassallo and Heimer disclosed no conflicts of interest.

*The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.*