Free markets. Real solutions.

R STREET POLICY STUDY NO. 142
May 2018

HARM REDUCTION STRATEGIES FOR CHRONIC PAIN MANAGEMENT IN THE OPIOID EPIDEMIC

Carrie L. Wade and Cory J. Goracke-Postle

CONTENTS

INTRODUCTION

The opioid epidemic is a complex problem with a multitude of contributing factors, including undertreated pain, prescribing practices, illicit drug use and stigmatization. Therefore, solutions that only address one component of the issue risk exacerbating other features of the epidemic in unintended ways. One consideration of particular importance is the impact of current solutions on the chronic pain patient population. These patients are at risk when policies, prescribing guidelines and public perception take a singular approach to such a complex problem. In fact, approaches to address the opioid epidemic that fail to consider the specific needs of this population may backfire and worsen the epidemic itself, causing devastating consequences for these patients and their families. As such, instead of a one-size-fits-all approach, it is worth considering ways in which we can mitigate risks to this population while ensuring their pain management needs are met.

Guidelines have emerged to address how to best manage pain, including appropriate opioid prescribing. The 2016 introduction of the Center for Disease Control (CDC) Guidelines on Opioid Prescribing highlights the association of the prevalence of chronic pain with the opioid addiction epidemic .[1] The confluence of these two factors has driven the ongoing effort to establish the Federal Pain Research Strategy,[2] which is in development through leadership of the NIH Interagency Pain Research Coordinating Committee. While there is general agreement that the opioid epidemic requires a national response to optimize prescribing practices and support for the development of prescribing standards, there is dissatisfaction among some pain management professionals regarding the process by which the guidelines were established. There are also ongoing concerns regarding implementation and interpretation and/or misinterpretation of the guidelines that may impact access for patient populations for whom opioid pharmacotherapy is appropriate and indicated—particularly for the chronic pain population .[3]

While several key important consensus documents reiterate the dual objectives of curtailing the opioid crisis and effectively managing pain for those who rely on opioids as part of their treatments,[4] the importance of maintaining this balance has not been fully captured in the ongoing national conversation. On the contrary, the emphasis appears heavily weighted toward addressing the opioid addiction/overdose problem, while the problem of chronic pain is often lost in

1. "CDC Guideline for Prescribing Opioids for Chronic Pain—United States 2016," Centers for Disease Control and Prevention, 2016. http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm.

2. For more information, see the Committee's website at https://iprcc.nih.gov/FPRS/FPRS.htm.

3. See, e.g., Joseph V. Pergolizzi, Jr. et al., "Comments and Suggestions from Pain Specialists Regarding the CDC's Proposed Opioid Guidelines," *Pain Practice* 16:7 (2016), pp. 794-808. https://doi.org/10.1111/papr.12475; and Alan L. Gordon and Seamus L. Connolly, "Treating Pain in an Established Patient: Sifting Through the Guidelines," *Rhode Island Medical Journal* 100:10 (2017), pp. 41-44. http://www.rimed.org/rimedicaljournal/2017/10/2017-10-41-cont-gordon.pdf.

4. See, e.g., Interagency Pain Research Coordinating Committee, "Federal Pain Research Strategy Overview," National Institutes of Health, 2017. https://iprcc.nih.gov/Federal-Pain-Research-Strategy/Overview; and "CDC Guideline for Prescribing Opioids for Chronic Pain—United States 2016." http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm.

the shuffle. Further, there is growing concern that the chronic pain patient population is increasingly stigmatized, which can introduce additional barriers to medical treatment and contribute to opioid misuse and abuse.

The principles of harm reduction have already been effective to address other national public health emergencies, such as illicit drug use and addiction. Accordingly, they may also be successfully applied to chronic pain management involving opioids.

CHRONIC PAIN RECOGNITION AND INITIAL TREATMENT APPROACH

The term "chronic pain" represents a wide variety of conditions that range from, but are not limited to, rheumatoid arthritis, diabetic neuropathy, low back pain, chronic headache, fibromyalgia and irritable bowel syndrome. Chronic pains have distinct pathologies and are quite often differential in their responsiveness to pain relievers. They are burdensome for the individual, their family members and society as a whole. The presence of chronic pain in patients also increases the risk for depression and anxiety,[5] and it has been estimated that the prevalence of suicide attempts is between two and three times greater in the this population of patients. Suicidal fatalities are twice as common.[6] All of these characteristics underscore the complex problem of chronic pain as a national public health crisis.

The publication of the Institute of Medicine's report on the state of Chronic Pain in the United States in 2011 and the subsequent introduction of the National Pain Strategy by the Office of the Assistant Secretary of Health and Human Services in March of 2016 highlight the nation's increasing attention to the problem of chronic pain.[7] The aforementioned documents report the number of Americans affected by chronic pain at 100 million and the annual national economic burden at 565-600 billion. Although the magnitude of these numbers has been challenged,[8] there is agreement that chronic pain is an important global problem.

Traction for recognition of the importance of pain and pain management first emerged in the 1990s and momentum for public awareness of the problem was achieved in early 2000 when the United States Congress passed H.R. 3244[9] and, with consent of the Executive Branch, declared the "Decade of Pain" (2001-2010). It was anticipated that such recognition would raise awareness of the problem of pain and that expanded support for associated research would materialize.[10]

In 2001, the Joint Commission on Accreditation of Health Care Organizations introduced a requirement that pain be assessed for all patients together with standard vital signs.[11] Advocacy for this practice was engendered during the 1990s by pain management national leadership, which resulted in a comprehensive educational effort to encourage healthcare professionals to assess pain level in all patients and provide treatment as needed.[12] Such an effort is thought to have significantly increased the general understanding of pain and to have revealed the inadequacies in available effective and safe treatments for pain management,[13] particularly for those who suffer chronic pain.

Subsequently, in 2004, the World Health Organization (WHO), the International Association for the Study of Pain (IASP) and the European Federation of IASP Chapters (EFIC) organized the first "Global Day Against Pain" in Geneva Switzerland, where leadership introduced the concept of pain control as a human right.[14] In 2010, the IASP, WHO and EFIC held a second "Global Day Against Pain," which was comprised of 230 representatives from IASP chapters in 64 distinct countries.[15] Here, the international membership of the IASP ratified its commitment to international pain management through the "Declaration of Montreal," which states that access to pain management is a fundamental human right—a principle that was recently

5. Ana Miriam Velly et al., "Epidemiology of pain and relation to psychiatric disorders," *Progress in Neuropsychopharmacology & Biological Psychiatry* (2017). https://doi.org/10.1016/j.pnpbp.2017.05.012.

6. See, e.g., Mélanie Racine, "Chronic pain and suicide risk: A comprehensive review," *Progress in Neuropsychopharmacology & Biological Psychiatry* (2017). https://doi.org/10.1016/j.pnpbp.2017.08.020; Nicole K. Tang et al., "Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links," *Psychological Medicine* 36 (2006), pp. 575-86. https://doi.org/10.1017/S0033291705006859.

7. See, e.g., "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research," *Military Medicine* 181:5 (2016), pp. 397-99. https://doi.org/10.7205/MILMED-D-16-00012; And Office of the Assistant Secretary for Health, "National Pain Strategy: A Comprehensive Population Health Level Strategy for Pain," U.S. Dept. of Health and Human Services, 2016. pp. 13-14. https://iprcc.nih.gov/sites/default/files/HHSNational_Pain_Strategy_508C.pdf.

8. Laxmaiah Manchikanti et al., "Responsible, Safe, and Effective Prescription of Opioids for Chronic Non-Cancer Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines," *Pain Physician* 20:2S (2017), pp. S3-S92. http://www.painphysicianjournal.com/current/pdf?article=NDIwMg==&journal=103.

9. Section 1603 of H. R. 3244 states that: "The calendar decade beginning January 1, 2001, is designated as the 'Decade of Pain Control and Research.'" PL 106–386—Oct. 28, 2000. https://www.congress.gov/106/plaws/publ386/PLAW-106publ386.pdf.

10. Roxanne Nelson, "Decade of pain control and research gets into gear in USA," *The Lancet* 362:9390 (2003), p. 1129. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(03)14505-9/abstract.

11. Peter Lanser and Sabina Gesell, "Pain management: the fifth vital sign," *Healthcare Benchmarks* 8:62 (2001), pp. 68-70. https://www.ahcmedia.com/articles/70942-guest-column-pain-management-the-fifth-vital-sign.

12. Ibid.; and James N. Campbell, "APS 1995 Presidential Address," *The Journal of Pain* 5:1 (Spring 1996), pp. 85-88. http://www.jpain.org/article/S1082-3174(96)80076-6/abstract.

13. Natalia E. Morone et al.,"Pain adversely affects outcomes to a collaborative care intervention for anxiety in primary care," *Journal of General Internal Medicine* 28:1 (2013), pp. 58-66. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3539032.

14. Arthur G. Lipman, "Pain as a Human Right: The 2004 Global Day Against Pain," *Journal of Pain and Palliative Care Pharmacotherapy* 19:3 (2005), pp. 85-100. https://doi.org/10.0180/J354v19n03_16.

15. Michael J. Cousins and Mary E. Lynch, "The Declaration Montreal: access to pain management is a fundamental human right," *Pain* 152:12 (2011), pp. 2673-74. https://insights.ovid.com/pubmed?pmid=21995880.

reaffirmed internationally.[16] Further, the declaration indicated that withholding access to pain management represents non-compliance with the United Nations' 1961 "Single Convention on Narcotic Drugs," which stated that medical narcotics are often necessary for the alleviation of pain.

Following the recognition that chronic pain is a quality-of-life issue that requires proper management, doctors began to increase prescribing of opioid therapies for patients who presented with various forms of pain. More recently, however, as the rates of opioid addiction have escalated, public support for their use has diminished and opioid prescribing practices have come under scrutiny as a primary cause of the current epidemic.

THE CHANGED NATURE OF TODAY'S OPIOID EPIDEMIC

In 2016, the rate of prescription opioid abuse was high—an estimated 15 million people.[17] However, it is important to note that among those adults who reported opioid abuse, 69.9 percent used them without a prescription and 40.6 percent obtained prescription opioids for free from friends or relatives.[18] Such numbers clearly demonstrate that a substantial amount of misuse and abuse has arisen not from individuals using opioids appropriately and under the supervision of a medical professional to treat their pain, but rather from use without any prescription or outside of the prescribed instructions.

It is also important to consider that, in response to concerns regarding opioid over-prescribing that emerged in the 1990s and early 2000s, doctors have recently been more likely to suggest alternative remedies for patients whose pain is manageable by other means. As a result, opioid prescription rates have fallen continuously since their peak in 2010. In fact, although prescriptions had more than quadrupled from 180 morphine milligram equivalents per-capita in 1999 to 782 in 2010, they were down to 640 by 2015. Despite the decrease in prescriptions, however, the number of opioid-related deaths has remained relatively stable (with only minimal changes recently). This is because, since 2010, a disproportionately large increase in deaths now involves heroin and other synthetic opioids obtained without prescriptions. These are cheaper to make and therefore easier to introduce into the illicit market. Heroin overdose deaths had previously remained relatively low from 1999 until 2010. However, from 2010-2015, as prescriptions for opioids were declining, heroin overdose deaths increased four-fold, which included a 20.6 percent increase from 2014 to 2015 alone. In addition, state information from 2016 and 2017 confirms that heroin and fentanyl currently account for more than 50 percent of overdose deaths in some states.[19]

Thus while opioid prescribing certainly had a role in contributing to the opioid epidemic initially, that issue has now been overshadowed by other factors. For this reason, strict limitation or restriction of opioid prescribing alone will not solve the current opioid epidemic. In fact, it may instead have the unintended consequence of limited or ineffective pain management for chronic pain patients who might then turn to illicit drug use for pain control. From a public health perspective, this would represent a transition to riskier behavior with less oversight and regulation. The increased danger to patients could potentially worsen the lethality of the opioid epidemic.

CHRONIC PAIN AS A UNIQUE DISEASE STATE

The global problem of pain has been long recognized by the International Association for the Study of Pain (IASP), which for many decades, together with the World Health Organization (WHO) and others, has spearheaded efforts to develop consensus around research priorities and global prescribing guidelines.[20] It has also worked to codify the very definition of pain itself as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[21] The presentation of acute pain is frequently a key factor that motivates patients to seek medical evaluation and thus it is often an important aspect of diagnosing primary disease. Therefore, pain has traditionally been viewed as a symptom, rather than as its own disease state.

However, for a substantial segment of the population, the transition from acute to chronic pain represents an experience that is clearly independent of additional disease pathology. Under these conditions, residual or ongoing pain is unrelated to any other identifiable primary disease. In these cases, the neurobiological changes that are often associated with such persistent pain may better match an independent

16. Ibid.; and Frank Brennan et al., "Access to Pain Management-Still Very Much a Human Right," *Pain Medicine* 17:10 (2016), pp. 1785-89. https://doi.org/10.1093/pm/pnw222.

17. Center for Behavioral Health Statistics and Quality, "Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health," Dept. of Health and Human Services, 2015. https://www.samhsa.gov/data/sites/default/files/NSDUH-FRR1-2014/NSDUH-FRR1-2014.htm.

18. Beth Han et al., "Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health," *Annals of Internal Medicine* 167:5 (2017), pp. 293-301. https://doi.org/10.7326/M17-0865.

19. Julie K. O'Donnell et al., "Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 - 10 States, July-December 2016," *Morbidity and Mortality Weekly Report* 66:43 (2017), pp. 1197-1202. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5689219.

20. Michael J. Cousins and Mary E. Lynch, "The Declaration Montreal: access to pain management is a fundamental human right," *Pain* 152:12 (2011), pp. 2673-74. https://insights.ovid.com/pubmed?pmid=21995880.

21. Harold Merskey and Nikolai Bogduk, *Classification of Chronic Pain: Description of Pain Syndromes and Definitions of Pain Terms*, 2nd edition (International Association for the Study of Pain, 1994), p. 209. https://locatorplus.gov/cgi-bin/Pwebrecon.cgi?DB=local&v1=1&ti=1,1&Search_Arg=9423059&Search_Code=0359&CNT=20&SID=1.

categorization and, for this reason, it has been proposed that chronic pain should be reclassified as a disease state of its own.[22]

Support for such a push emerged through the advent of imaging capabilities, through which it was established that chronic pain patients have altered brains in terms of changes in basic function, structure and neurochemistry.[23] Such alterations are consistent with a disease-state profile and, in fact, have led to the recognition of other conditions as independent diseases, as in the case of the classification of addiction as a disease.

However, the concept of chronic pain as a disease is not yet universally embraced, particularly by other medical specialties,[24] and thus the proposal remains an area of ongoing debate.[25] However, the implications of such a consensus definition are important not only for how it might impact resource allocation but also as it would help to distinguish chronic pain patients and the pain they experience as a unique category worthy of a unique approach to analgesic therapeutics—one that might safely include, rather than blanketly prohibit supervised and responsible opioid therapy.[26]

Addiction and Opioid Use in Chronic Pain Patients

The characterization of addiction as a disease first came about in 1980 after the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM III) defined substance-use disorders independently from other mental health conditions.[27] As this theory emerged, neuroanatomical and physiological studies confirmed that there was a biological basis for the idea that repeated exposure to drugs of abuse induces changes in the brain that manifest in compulsive-like behaviors.

Likewise, the biological mechanisms underlying the propensity for misuse and transition to opioid addiction have been studied extensively in both human and animal models.[28] During the transition from misuse or abuse of drugs to addiction there are simultaneous alterations in dopamine neurotransmission to the parts of the brain that are primarily responsible for reward processing and in the part primarily responsible for driving brain stress and aversive systems.[29] While the primary alterations in dopamine neurotransmission that result from binge cycles of drug use drive behaviors of increasing drug consumption, it is the resulting pathological stress responses that occur in the extended amygdala that are the hallmark of the transition to an addictive state.

However, particularly with respect to chronic pain patients, it is of key importance to understand that opioid *use* is not the same thing as opioid *misuse* or *abuse*. Opioid misuse is distinct and defined as "taking more or in a different way than prescribed." Opioid abuse is further distinguished as "intentional use for non-medical purposes."[30] Such distinctions are key not only to managing the opioid epidemic but also to ensuring that patients for whom opioid use is indicated and appropriately managed are not prohibited or restricted from access.

An extensive pre-clinical literature demonstrates that self-administration to commonly prescribed analgesic opioids is altered under conditions of chronic pain.[31] For example, analgesic drugs that are typically not addictive, like clonidine, become reinforcing under conditions of chronic pain.[32] Fur-

22. See, e.g., Phillip J. Siddall and Michael J. Cousins, "Persistent pain as a disease entity: implications for clinical management," *Anesthesia & Analgesia* 99:2 (2004), pp. 510-20. https://insights.ovid.com/pubmed?pmid=15271732; John D. Loeser and Ronald Melzack, "Pain: an overview," *The Lancet* 353:9167 (1999), pp. 1607-09. http://www.thelancet.com/journals/lancet/article/PIIS0140673699013112/abstract; David Niv and Marshall Devor, "Chronic pain as a disease in its own right," *Pain Practice* 4:3 (2004), pp. 179-81. http://onlinelibrary.wiley.com/doi/10.1111/j.1533-2500.2004.04301.x/abstract; Jane C. Ballantyne, "Opioids for chronic nonterminal pain," *South Medical Journal* 99:11 (2006), pp. 1245-55. https://www.ncbi.nlm.nih.gov/pubmed/17195420; and Allan I. Basbaum and David Julius, "Toward better pain control," *Scientific American* 294 (2006), pp. 60-67. https://www.scientificamerican.com/article/toward-better-pain-contro.

23. Irene Tracey and M. Catherine Bushnell, "How neuroimaging studies have challenged us to rethink: is chronic pain a disease?", *The Journal of Pain* 10:11 (2009), pp. 1113-20. http://www.jpain.org/article/S1526-5900(09)00712-3/abstract.

24. Ann Margaret Taylor et al., "Is Chronic Pain a Disease in Its Own Right? Discussions from a Pre-OMERACT 2014 Workshop on Chronic Pain," *The Journal of Rheumatology* 42:10 (2015), pp. 1947-53. 10.3899/jrheum.141328.

25. Milton Cohen et al., "Is chronic pain a disease?", *Pain Medicine* 14:9 (2013), pp. 1284-88. https://doi.org/10.1111/pme.12162.

26. See, e.g., Taylor et al. https://doi.org/10.3899/jrheum.141328.

27. Sean M. Robinson and Bryon Adinoff, "The Classification of Substance Use Disorders: Historical, Contextual, and Conceptual Considerations," *Behavioral Sciences* (Basel) 6:3 (2016), p. 18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5039518.

28. George F. Koob and Michel Le Moal, "Neurobiological mechanisms for opponent motivational processes in addiction," *Philosophical Transactions of the Royal Society London: Biological Sciences* 363:1507 (2008), pp. 3113-23. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2607326.

29. See, e.g., Kathleen Chu et al., "Dependence-induced increases in ethanol self-administration in mice are blocked by the CRF1 receptor antagonist antalarmin and by CRF1 receptor knockout," *Pharmacology Biochemistry and Behavior* 86:4 (2007), pp. 813-21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2170886; Nicholas W. Gilpin et al., "Effects of CRF1-receptor and opioid-receptor antagonists on dependence-induced increases in alcohol drinking by alcohol-preferring (P) rats," *Alcoholism, Clinical and Experimental Research* 32:9 (2008), pp. 1535-42. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2583093; Angelo Contarino and Francesco Papaleo, "The corticotropin-releasing factor receptor-1 pathway mediates the negative affective states of opiate withdrawal," *Proceedings of the National Academy of Sciences* USA 102:51 (2005), pp. 18649-54. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1317931; and George F. Koob, "Neurobiological substrates for the dark side of compulsivity in addiction," *Neuropharmacology* 56:Suppl 1 (2009), pp. 18-31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2637927.

30. Stephen Butler, The IMMPACT factor or IMMPACT strikes again! *Pain* 154, 2243-44 (2013). https://www.ncbi.nlm.nih.gov/pubmed/23911698.

31. Thomas J. Martin et al., "Opioid self-administration in the nerve-injured rat: relevance of antiallodynic effects to drug consumption and effects of intrathecal analgesics," *Anesthesiology* 106:2 (2007), pp. 312-22. http://anesthesiology.pubs.asahq.org/article.aspx?articleid=1931186.

32. Eric E. Ewan et al., "Analgesics as reinforcers with chronic pain: Evidence from operant studies," *Neuroscience letters* 557 Pt A, 60-64 (2013). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3858505.

ther, other studies have demonstrated that the establishment of chronic pain itself alters reward pathways, which suggests that pain states may decrease the brain's responses to rewarding stimuli.[33] In animal models, the neurobiology of the reward pathways under strictly controlled conditions of chronic pain can be illuminated. However, the complexity and intrinsic variability of the human experience, which includes sociological and biological factors, results in more diverse patient outcomes.

Since the pain pathways represent an essential warning system to indicate pending damage to an organism, it stands to reason that chronic inhibition of pain signaling through the use of opioids results in compensatory changes that heighten the ability of the patient to detect pain. Such a disruption in homeostasis results in a generalized hypersensitivity called "hyperalgesia." Opioid-induced hyperalgesia is increasingly recognized as an emergent pain state associated with chronic opioid use.

Distinct from—but parallel to—this response, the homeostasis of an emotional state of an individual is thought to be disrupted in both chronic pain patients and patients with opioid use disorder who are in a state of withdrawal or abstinence.[34] These various forms of homeostatic disruption lead to an escalation of emotional distress. Left unaddressed, this condition is thought to render individuals susceptible to addiction. Therefore, it has been suggested that disruption of homeostasis with *either* insufficiently controlled pain (with restricted access to or sub-therapeutic doses of analgesics) or over-controlled pain (with too high a dose of opioid) may lead to an addictive state through the development of hyperkatifeia, or the unstable emotional and behavioral state that underlies addiction.[35] This suggests that, in chronic pain patients in particular, *under-prescribing* of opioids may actually be counterproductive to addiction avoidance. It also reinforces the commonly understood notion that the use of opioids with the appropriate supervision and care of a doctor is always preferable to the risk that people will self-medicate in the absence of that option.

What's more, the concept of addiction is somewhat more problematic with respect to chronic pain patients, as the mechanisms that underlie it are separate from other physiological responses to opioids, such as tolerance and dependence and, in contrast, do not resolve upon cessation.[36]

In 2001, the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine composed the following consensus definitions on Tolerance, Dependence, and Addiction:

> **Tolerance:** Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.
>
> **Physical Dependence:** Physical dependence is a state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist.
>
> **Addiction:** Addiction is a primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm and craving.[37]

All three of these various states may be observed in opioid users, but it is essential to correctly identify which state a particular patient is in and then adjust accordingly, as each requires a different approach.

Indeed, historical conflation of these issues may have unintentionally led to an interpretation that chronic pain patients are "addicted" to opioids, when in fact, that may not be the case. Using a stricter definition of addiction and with careful diagnosis, rates of addiction resulting from pain management are thought to be on the lower end of the spectrum at

33. Anna M.W. Taylor et al., "Mesolimbic dopamine signaling in acute and chronic pain: implications for motivation, analgesia, and addiction," *Pain* 157:6 (2016), pp. 1194-98. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4866581; Keiichi Niikura et al., "Neuropathic and chronic pain stimuli downregulate central mu-opioid and dopaminergic transmission," *Trends in Pharmacological Sciences* 31:7 (2010), pp. 299-305. http://www.cell.com/trends/pharmacological-sciences/fulltext/S0165-6147(10)00062-3.

34. Joseph Shurman et al., "Opioids, pain, the brain, and hyperkatifeia: a framework for the rational use of opioids for pain," *Pain Medicine* 11 (2010), pp.1092-98. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2907890.

35. Ibid.

36. Nora D. Volkow and A. Thomas McLellan, "Opioid Abuse in Chronic Pain--Misconceptions and Mitigation Strategies," *The New England Journal of Medicine* 374:13 (2016), pp. 1253-63. http://www.nejm.org/doi/full/10.1056/NEJMra1507771.

37. "Definitions Related to the Use of Opioids for the Treatment of Pain: Consensus Statement of the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine," American Society of Addiction Medicine, 2001. https://www.asam.org/docs/default-source/public-policy-statements/1opioid-definitions-consensus-2-011.pdf.

8 percent or less with a rate of misuse (taking more or in a different way than prescribed) between 15 to 26 percent.[38]

In light of this, as policies and programs are put into place to address the opioid epidemic, the importance of proper diagnoses is imperative. Evaluation of neurological mechanisms and behavioral responses following the onset of pain shows that while opioid use for pain management does result in dependence and tolerance, it does not guarantee a transition to addiction.

The fact is that there are a variety of populations affected by opioid addiction that can range from acute pain patients to recreational drug users. Each of these populations is distinct and thus requires a thoughtful, targeted approach to address their unique needs in order to be effective. In particular, chronic pain patients are at risk when policies and prescribing guidelines take a singular approach that effectively treats all opioid *users* as *abusers*. Instead, the specific circumstances and needs of this population and their pain must be considered in order to help combat the broader opioid epidemic.

The Problem of Stigmatization

Such a misunderstanding of the distinctions between appropriate and inappropriate use of opioids has also exacerbated the problem of stigmatization around chronic pain patients and even the medical professionals who treat them. This, too, is counterproductive to effective opioid management.

Despite decades-long efforts by the healthcare professional societies and patient advocacy groups to address and reverse stigmatization, patients with pain remain at high risk for being maligned culturally and clinically.[39] Moreover, pain management healthcare professionals may encounter the same risks of social maligning, which can lead to fear of prescribing.[40] Highly publicized cases of lawsuits and criminal prosecution impact policy, medical practice and medication development.[41] The perceived conflict of interest of between pain management and professional research societies and the undue influence of pharmaceutical manufacturers further extends the stigmatization to patients, pain management and research advocacy groups. However, absent a comprehensive description of the full mission and educational, research and consensus-development accomplishments of such independent societies, activist advocacy groups actually do a disservice to pain patients and pain management providers by undermining the ultimate goal, which is a comprehensive approach that may include the use of opioids.[42] All forms of stigmatization may contribute to insufficient diagnosis, the under-treatment of chronic pain[43] and the limited development of alternative pain treatments—all of which are counterproductive both to serving patients and to combating the opioid epidemic.

It has been previously noted that through the process of reviewing the factors that may or may not have contributed to the emergence of the opioid epidemic, the tone of the national conversation frequently shifts to assigning blame—whether to the pharmaceutical industry, various professional societies, healthcare professionals or individuals .[44] However, such a tendency for lawmakers and law enforcement to frame solutions in binary terms frequently misses the complexity of both chronic pain and opioid addiction.[45]

38. David A. Fishbain et al., "What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review," *Pain Medicine* 9:4 (2008), pp. 444-59. https://doi.org/10.1111/j.1526-4637.2007.00370.x; Kevin E. Vowles et al., "Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis," *Pain* 156:4 (2015), pp. 569-76. https://doi.org/10.1097/01.j.pain.0000460357.01998.f1; Bridget A. Martell et al., "Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction," *Annals of Internal Medicine* 146:2 (2001), pp. 116-27. http://annals.org/aim/article-abstract/732048/systematic-review-opioid-treatment-chronic-back-pain-prevalence-efficacy-association?volume=146&issue=2&page=116.

39. See, e.g., Daniel B. Carr, "Patients with Pain Need Less Stigma, Not More," *Pain Medicine* 17:8 (2016), pp. 1391-93. https://doi.org/10.1093/pm/pnw158; Lies De Ruddere and Kenneth D. Craig, "Understanding stigma and chronic pain: a-state-of-the-art review," *Pain* 157:8 (2016), pp. 1607-10. https://doi.org/10.1097/j.pain.0000000000000512; Daniel S. Goldberg, "Pain, objectivity and history: understanding pain stigma," *Medical Humanities* 43:4 (2017), pp. 238-43. https://doi.org/10.1136/medhum-2016-011133; Emily E. Hurstak et al., "The risks of opioid treatment: Perspectives of primary care practitioners and patients from safety-net clinics," *Substance Abuse* 38:2 (2017), pp. 213-21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5568522; Summer J. McGee et al., "Defining Chronic Pain Ethics," *Pain Medicine* 12:9 (2011), pp. 1376-84. https://doi.org/10.1111/j.1526-4637.2011.01192.x; and William Notcutt and Gerda Gibbs, "Inadequate pain management: myth, stigma and professional fear," *Postgraduate Medical Journal* 86:1018 (2010), pp. 453-58. http://pmj.bmj.com/content/86/1018/453.short?rss=1.

40. See, e.g., Pergolizzi, Jr. et al. https://doi.org/10.1111/papr.12475; Alan D. Kaye, "Clinical and Professional Aspects of Opioid Prescribing for Pain Physicians," *Pain Physician* 20 (2017), pp. S1-S2. http://www.painphysicianjournal.com/current/pdf?article=NDIwMQ==&journal=103; Scott M. Fishman, "Pain and politics: DEA, Congress, and the Courts, Oh My!" *Pain Medicine* 7:1 (2006), pp. 87-88. https://doi.org/10.1111/j.1526-4637.2006.00099.x; Frank Brennan, "The US Congressional 'Decade on Pain Control and Research' 2001-2011: A Review," *Journal of Pain & Palliative Care Pharmacotherapy* 29:3 (2015), pp. 212-27. https://doi.org/10.3109/15360288.2015.1047553; and Fontana. http://www.professionalnursing.org/article/S8755-7223(07)00136-6/fulltext.

41. See, e.g., John Tierney, "Richard Paey Is Free," *The New York Times*, September 20, 2007. https://tierneylab.blogs.nytimes.com/2007/09/20/florida-governor-pardons-richard-paey; John Tierney, "Juggling Figures, and Justice, in a Doctor's Trial," *The New York Times,* July 3, 2007. https://mobile.nytimes.com/2007/07/03/science/03tier.html; Brennan. https://doi.org/10.3109/15360288.2015.1047553; Scott M. Fishman, "From balanced pain care to drug trafficking: the case of Dr. William Hurwitz and the DEA," *Pain Medicine* 6:2 (2005), pp. 162-64. https://doi.org/10.0000/j.1526.4637.2005.05028.x; and Jonathan I. Nathan, "Chronic pain treatment: a high moral imperative with offsetting personal risks for the physician—a medical student's perspective," Pain Practice 9:2 (2009), pp. 155-63. https://doi.org/10.1111/j.1533.2500.2008.00257.x.

42. See, e.g., Chuck Raasch, "McCaskill report says top opioid manufacturers gave millions to pain groups," *St. Louis Post-Dispatch*, Feb. 13, 2018. http://www.stltoday.com/news/local/govt-and-politics/mccaskill-report-says-top-opioid-manufacturers-gave-millions-to-pain/article_904a09a9-a9fe-5d0d-a0ed-0ccb778d30fe.html; and David Williams, "President's Response to McCaskill Report," American Pain Society, Feb. 13, 2018. http://americanpainsociety.org/186-president-s-response-to-mccaskill-report.

43. See, e.g., Fishman. https://doi.org/10.1111/j.1526-4637.2006.00099.x; and Fontana. http://www.professionalnursing.org/article/S8755-7223(07)00136-6/fulltext.

44. See, e.g., Arthur G. Lipman, "Opioid abuse, politicians and blame,"*Journal of Pain and Palliative Care Pharmacotherapy* 29:1 (2015), pp. 2-3. https://doi.org/10.3109/15360288.2014.1004012.

45. Ibid.

On the contrary, instead of stigmatization and dismissal, we must seek to more clearly understand the complexities of chronic pain as a disease, the particularities of its effective management and the ways that harm reduction strategies can help to address the related issues.

HARM REDUCTION PRINCIPLES

Given the complexity of addiction and the challenge of how to best manage or treat it, there is a growing interest in the use of harm reduction approaches to mitigate the negative consequences associated with opioid use. Rather than attempting to change or disrupt drug use,[46] harm reduction targets the consequences and behaviors associated with it. These techniques meet users "where they are," as opposed to where others may wish they would be. Extensive literature has found that harm reduction strategies have many beneficial results, such as decreased disease transmission, reduced opioid overdose and increased entry into treatment.[47]

Successes-To-Date

Historically, harm reduction programs have evolved as new threats have emerged. For example, the first clean syringe access programs (SAP) in the mid 1980's came about as the link between injection drug use and HIV was discovered and a lack of access to clean needles exacerbated transmission of the infectious disease. The decreased incidence of HIV following the implementation of these programs lends proof of the efficacy of harm reduction approaches that aim to decrease specific consequences of risk behaviors.

Still, in areas where the threat of negative consequences may not be perceived or the political climate is such that implementation is difficult, harm reduction programs are lacking. Such gaps can reveal community vulnerabilities that may be unexpected. An example related to HIV transmission recently emerged in Scott County, Indiana, which lacked SAPs until an outbreak of HIV concentrated among injection drug users occurred.[48] To control the spread of these viruses, then-Indiana Health Commissioner, Dr. Jerome Adams, implemented syringe access, which brought effective control to the outbreak. While the timing of the implementation in this case has been widely criticized,[49] it is argued that, unfortunately, without such an outbreak, to implement an SAP would not have been possible because the need was not previously appreciated.[50]

Likewise, the availability of SAPs in Vancouver, British Columbia helped decrease needle sharing among HIV-positive injection drug users from 37 percent in 1996 to 2 percent in 2014. Difficult access to clean needles makes it 3.5 times more likely that a person will share them, while access to SAPs makes it less than half as likely that a person will do so.[51] Extending these findings to incidence of HIV supports the idea that decreased needle-sharing results in decreased transmission of infectious diseases. Indeed, in New York City, syringe-exchange rates have correlated strongly with decreases in HIV incidence.[52] In 2002, HIV incidence rates decreased by 300 percent—just ten years after needle distribution increased from 750,000 to 3 million.[53]

Moreover, tangible harm reduction programs like syringe access have had a positive impact in decreasing the stigma associated with drug use in general. Studies have already shown that people who inject drugs are more likely to "trust" healthcare providers in a syringe-access setting than in a clinical one.[54] It is therefore plausible that such increased trust contributes to the successful outcomes that harm reduction programs offer. In fact, several analyses of existing programs conclude that, rather than tacitly tolerating drug use and allowing addiction to take over communities, harm reduction programs actually correlate with increased entry into treatment. In Baltimore, for example, people who visit SAPs are more likely to enter treatment that those who do

46. G. Alan Marlatt and Katie Witkiewitz, "Update on harm-reduction policy and intervention research," *Annual Review of Clinical Psychology* 6 (2010), pp. 591-606. https://doi.org/10.1146/annurev.clinpsy.121208.131438.

47. See, e.g., Christopher Rowe et al., "Neighborhood-Level and Spatial Characteristics Associated with Lay Naloxone Reversal Events and Opioid Overdose Deaths," *Journal of Urban Health* 93:1 (2016) pp. 117-30. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4794468; Katy M. Turner et al., "The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence," *Addiction* 106:11 (2011), pp. 1978-88. https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0034499; Holly Hagan et al., "Reduced injection frequency and increased entry and retention in drug treatment associated with needle-exchange participation in Seattle drug injectors," *Journal of Substance Abuse Treatment* 19:3 (2000), pp. 247-52. https://www.ncbi.nlm.nih.gov/pubmed/11027894; Steffanie A. Strathdee et al., "Needle-exchange attendance and health care utilization promote entry into detoxification," *Journal of Urban Health* 76:4 (1999), pp. 448-60. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3456698; and Miranda W. Langendam et al., "The impact of harm-reduction-based methadone treatment on mortality among heroin users," *American Journal of Public Health* 91:5 (2001), pp. 774-80. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1446673.

48. See, e.g., "Mike Pence's Response to H.I.V. Outbreak: Prayer, Then a Change of Heart," *The New York Times*, Aug. 7, 2016. https://www.nytimes.com/2016/08/08/us/politics/mike-pence-needle-exchanges-indiana.html.

49. See, e.g., Ibid.; Steffanie A. Strathdee and Chris Beyrer, "HIV Outbreak in Indiana," *The New England Journal of Medicine* 373:14 (2015), pp. 1380-81. http://www.nejm.org/doi/full/10.1056/NEJMc1510396.

50. Jerome Adams, "HIV Outbreak in Indiana," *The New England Journal of Medicine* 373:14 (2015), pp. 1379-80. https://doi.org/10.1056/NEJMc1510396 - SA1.

51. Anees Bahji et al., "Increasing awareness about HIV prevention among young people who initiated injection drug use in a Canadian setting, 1988-2014," *International Journal of Drug Policy* 26 (2015), pp. 1258-64. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4666805.

52. Don C. Des Jarlais et al., "HIV infection among persons who inject drugs: ending old epidemics and addressing new outbreaks," *AIDS* 30:6 (2016), pp. 815-26. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4785082.

53. Ibid.

54. Carla Treloar et al., "Trust and people who inject drugs: The perspectives of clients and staff of Needle Syringe Programs," *International Journal of Drug Policy* 27 (2016), pp. 138-45. https://doi.org/10.1016/j.drugpo.2015.08.018.

not,[55] while in Seattle, people who use SAP services are more likely to remain on methadone treatment.[56]

Such successes show great promise as applied to the opioid epidemic, as well. For example, the dramatic increase in drug overdose deaths since 2013 has become a very public topic of concern. Many of these cases also involve synthetic opioids, such as fentanyl and its associated derivatives. In light of this, naloxone distribution for those who are at risk of overdose and fentanyl test strips to reduce the risk of using fentanyl-laced heroin are harm reduction strategies that can mitigate some of the dangers. In fact, recently naloxone distribution programs have been more widely promoted as a response to historical increases in opioid overdose deaths.[57] Consider, for example, that even when administered by people who are not medically trained, Narcan was able to reverse 26,000 opioid overdoses between 1996 and 2014.[58]

Application to Chronic Pain Management

With these successes in mind, consideration of the complexity of the characteristics and unique needs of the chronic pain patient populations can ensure effective and meaningful policies and programs to address the opioid epidemic. Part of that approach must include harm reduction approaches to minimize the risks associated with opioid use in these patients. These risks include, but are not limited to, conversion to addiction, overmedication and overdose for all populations of chronic pain patients who receive opioid medication.

In response to the opioid epidemic, in 2016, the Centers for Disease Control released a series of guidelines for opioid prescribing to reduce the supply of prescription opioids and possible overmedication. Included in these guidelines are recommendations to consider opioids only when the benefits of use outweigh the risks; to establish treatment goals for acceptable pain levels and daily functioning; and associated recommendations for opioid selection, dosing regimen, duration and discontinuation. However, the only harm reduction strategy for chronic pain management found in the report suggests that clinicians should prescribe naloxone alongside opioids if the patient meets a series of risk factors.

That said, some states have initiated strategies that fall within a continuum of harm reduction. For example, in North Carolina, 75 percent of their counties implemented a number of initiatives to address the opioid epidemic including, but not limited to 1) public awareness education regarding opioid overdose; 2) healthcare-professional education regarding pain management; 3) emergency-department training to reduce opioid analgesic prescribing and to ensure use of prescription drug monitoring programs; 4) development of systems to recover unused opioid medications to reduce diversion; 5) patient support groups; 6) expansion of access and use of naloxone; and 7) increasing access to addiction medications such as methadone and buprenorphine.[59] Some of these strategies were associated with lowered overdose mortality, such as provider education and strict emergency department prescribing policies. It is expected that greater effects will be more evident as the implementation time is extended and as barriers to implementation are resolved. Furthermore, advocacy for co-prescription of naloxone with opioid medications has resulted in reduced anticipated overdoses.[60]

Upon review, most harm reduction strategies related to opioid prescribing recommended to date (by the National Safety Council, the CDC, and the Institute of Medicine) address prescribing in acute settings, such as emergency departments or for acute conditions such as post-surgical pain. However, there is a critical need to further consider harm reduction strategies for chronic pain patients for whom opioids are the most effective pain management strategy. Currently, there are minimal harm reduction strategies for this population.

As in the case of chronic pain itself, when considering harm reduction strategies that can mitigate the opioid epidemic, the role that stigmatization plays in exacerbating the problem cannot be overlooked. Stigma is thought to play leading role in creating barriers to accessing medical services, harm reduction services and treatment facilities. Further, drug use creates an environment of social isolation, which increases the likelihood that a person will use drugs in high-

55. See, e.g., Hagan et al. https://www.ncbi.nlm.nih.gov/pubmed/11027894; Strathdee et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3456698; Elise D. Riley et al., "Drug user treatment referrals and entry among participants of a needle exchange program," *Substance Use & Misuse* 37:14 (2002), pp. 1869-86. https://www.ncbi.nlm.nih.gov/pubmed/12511056; Steffanie A. Strathdee et al., "Facilitating entry into drug treatment among injection drug users referred from a needle exchange program: Results from a community-based behavioral intervention trial," *Drug and Alcohol Dependence* 83:3 (2006), pp. 225-32. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2196224.

56. See, e.g., Hagan et al. https://www.ncbi.nlm.nih.gov/pubmed/11027894.

57. Don C. Des Jarlais et al., "Harm reduction: a public health response to the AIDS epidemic among injecting drug users," *Annual Review of Public Health* 14 (1993), pp. 413-50. https://doi.org/10.1146/annurev.pu.14.050193.002213.

58. Eliza Wheeler et al., "Community-Based Opioid Overdose Prevention Programs Providing Naloxone — United States, 2010," *Morbidity and Mortality Weekly Report* 61:6 (2012), pp. 101-05. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378715.

59. Apostolos A. Alexandridis et al., "A statewide evaluation of seven strategies to reduce opioid overdose in North Carolina," *Injury Prevention* 24:1 (2018), pp. 48-54. http://injuryprevention.bmj.com/content/24/1/48.long.

60. Mikiko Y. Takeda et al., "Co-prescription of naloxone as a Universal Precautions model for patients on chronic opioid therapy-Observational study," *Substance Abuse* 37:4 (2016), pp. 591-96. https://www.tandfonline.com/doi/full/10.1080/08897077.2016.1179704.

risk situations where spread of infection or overdose are common.[61]

Communication and language are also thought to have a significant impact on pain management. For example, the use of stigmatizing language around pain and addiction can lead to the undertreatment of pain patients,[62] put them at risk for misusing prescriptions (taking more than prescribed to relieve pain) or seeking illicit sources. Additionally, stigmatized language can prevent people from seeking help in the first place,[63] which increases the likelihood that pain patients will inappropriately self-medicate. To be effective, approaches must therefore guard against stigmatization and use respectful language in order to be tailored specifically for this patient population.

As the CDC guidelines are implemented and as local governments develop customized guidance to address the epidemic, ensuring that health care professionals have the appropriate training, as well as prescribing authority, and dosing and duration flexibility will be essential. From a public health perspective, insufficient pain management may exacerbate the epidemic in ways that have not been fully considered. Concerns have been raised that pain patients whose prescriptions have been limited or curtailed (as in the case of chronic pain patients on established treatment)[64] or denied (as in the case of chronic pain patients with substance-use disorder), may begin or escalate use of prescription opioids illegally or may resort to heroin or other illicit or unregulated alternatives.[65] These high-risk practices may contribute to the escalation in heroin and high-potency illicit opioid use.[66] Therefore, as approaches are proposed and implemented to address the epidemic, such potential adverse impacts must be fully considered.

CONCLUSION

The current state of the opioid epidemic is devastating. The National Institute on Drug Abuse (NIDA) has reported that over 53,000 people died in 2016 from opioid overdose—a 32 percent increase from the previous year. In response to these increasingly alarming statistics, in the fall of 2017, the White House declared the opioid crisis a public health emergency and, in April 2018, the Surgeon General issued a national advisory on the matter.[67] Such recognition of the problem at the highest leadership level provides an important beacon for the development and implementation of comprehensive, data-driven solutions.

Overall, the current data support that prescription opioids provided for the treatment of chronic pain do not comprise a substantial component of the opioid addiction epidemic. In light of this, policies that restrict prescribing across the board can have significant negative impact on these populations and may exacerbate the epidemic from other angles. Further, whereas opioid prescription restriction may have merit in the general population or in acute pain settings, opioids remain a gold standard and essential component of an effective chronic pain management regimen.

Unfortunately treatment for chronic pain that involves opioid use has become controversial, in part due to its conflation with the use of opioids for recreational purposes, the fear of addiction and the worsening of the opioid epidemic. However, it is essential that we do not abandon our moral obligation to meet the needs of the chronic pain patient population, understanding that the goal remains to restore health and quality of life for those in chronic pain. This is a humanitarian objective with broad sociological benefit.

Effectively treating chronic pain patients while addressing the opioid epidemic and mitigating risks to patients is a complex problem that must consider the unique needs of this population in order to be effective. This requires multimodal, complex solutions that engender an "All Hands on Deck" national call to action.[68] And, with strategic design and implementation, harm reduction strategies hold promise to have a significant positive impact when applied to the use of opioids in the treatment of chronic pain.

61. Rusty Souleymanov and Dan Allman, "Articulating Connections between the Harm-Reduction Paradigm and the Marginalisation of People Who Use Illicit Drugs," *British Journal of Social Work* 46:5 (2016), pp. 1429-45. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4985724.

62. Anna P. Goddu et al., "Do Words Matter? Stigmatizing Language and the Transmission of Bias in the Medical Record," *Journal of General Internal Medicine* (2018) pp. 1-7. https://doi.org/10.1007/s11606-017-4289-2.

63. Willem Scholten et al., "Access to treatment with controlled medicines rationale and recommendations for neutral, precise, and respectful language," *Public Health* 153 (2017), pp. 147-53. https://doi.org/10.1016/j.puhe.2017.08.021.

64. See, e.g., Amanda Pfeffer, "Prescription limits driving some patients to street drugs," *CBC*, Oct. 20, 2017. http://www.cbc.ca/news/canada/ottawa/prescription-limits-driving-patients-street-drugs-1.4351816; Kristian Foden-Vencil, "Oregonian Turns To Heroin For Pain Relief After Opioid Prescription Cut," *Oregon Public Broadcasting*, July 18, 2016. https://www.opb.org/news/article/oregon-heroin-opioid-prescription-addiction-treatment; and John Keilman, "Chronic pain patients say opioid crackdown is hurting them," *Chicago Tribune*, June 5, 2017. http://www.chicagotribune.com/lifestyles/health/ct-opioid-patients-backlash-met-20170603-story.html.

65. Pauline Voon et al., "Self-management of pain among people who inject drugs in Vancouver," *Pain Management* 4:1 (2014), pp. 27-35. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3962749.

66. Ibid.

67. Office of the Surgeon General, "Surgeon General Releases Advisory on Naloxone, an Opioid Overdose-Reversing Drug," April 5, 2018. https://www.hhs.gov/about/news/2018/04/05/surgeon-general-releases-advisory-on-naloxone-an-opioid-overdose-reversing-drug.html.

68. Rebecca Cooney, "All hands on deck—addressing the nation's opioid epidemic," *The Lancet United States of Health Blog*, July 27, 2017. http://usa.thelancet.com/blog/2017-07-27-all-hands-deck—addressing-nation's-opioid-epidemic.

ABOUT THE AUTHORS

Carrie L. Wade is a senior fellow and the harm reduction policy director for the R Street Institute, where she is responsible for directing R Street's harm-reduction agenda. Carrie joined R Street in April 2017, having previously worked as a drug-abuse researcher at the University of Minnesota and The Scripps Research Institute in La Jolla, California. Her research has focused largely on the intersection of prescription opioid abuse and chronic pain in animal models of opioid self-administration. In addition, using brain-mapping techniques, she studied the role the basal ganglia performs in the development and maintenance of opioid addiction. Results from these studies have been published in several academic journals.

Carrie's scientific background in the biological mechanisms of opioid addiction led to her interest in how public-health initiatives can prevent incidence of addiction and reduce the negative societal and personal consequences that result from substance use. Her work with the Baltimore Harm Reduction Coalition solidified her goal to promote reasonable and efficient drug policies. Carrie received her bachelor's in neuroscience and Ph.D. in pharmacology from the University of Minnesota. She also holds a master's in public health from Johns Hopkins University.

Cory J. Goracke-Postle is the Director of the Center for Pain Research at the University of Minnesota, where she is responsible for coordinating a consortium of pain experts in their research efforts. She joined the Center for Pain Research following ten years of progressive leadership within the Office of the Vice President for Research at the University of Minnesota, where she oversaw and was responsible for the compliance of the university's pre-clinical portfolio. In that position, her expertise helped to lead pre-clinical research oversight, publish on preclinical pain models and present models for successful research programs at Public Responsibility in Medicine & Research (PRIM&R) conferences.

Cory's scientific background in the mechanisms underlying chronic pain and analgesia led to her interest in utilizing this expertise to address the opioid epidemic by supporting research that focuses on discovery and translation of non-opioid analgesic medication. To that end, she has worked to characterize a new non-opioid analgesic, establishing a molecular role for the molecule in neurotransmission. In her role in the Center for Pain Research, she is working to take these concepts from bench to bedside by coordinating clinical trials, fundraising, and raising awareness and providing education to the public. Cory received her bachelor's in Psychology from the College of Saint Benedict/Saint John's University, her Ph.D. in Neuroscience from the University of Minnesota and completed her Clinical Fellowship at Upsher-Smith Laboratories, Inc.