



Contents lists available at ScienceDirect

Journal of the American Pharmacists Association

journal homepage: www.japha.org

COMMENTARY

Pharmacists are missing an opportunity to save lives and advance the profession by embracing opioid harm reduction

Lucas G. Hill*, Kirk E. Evoy, Kelly R. Reveles

ARTICLE INFO

Article history:

Received 14 April 2019

Accepted 24 June 2019

ABSTRACT

More than 70,000 Americans died as a result of a drug overdose in 2017, and a substantial majority of those deaths involved an opioid. Supply-reduction interventions, such as prescription monitoring programs, tamper-resistant formulations, and prescribing limits have failed to reverse rising rates of opioid-related morbidity and mortality. Instead, they may be contributing to this trend by forcing people with opioid use disorder to an increasingly potent illicit market with scant resources for sterile injection. Pharmacists are recognized by governmental authorities, public health experts, and other health professionals as key partners in opioid harm reduction. This is reflected by the proliferation of state laws supporting pharmacy-based access to naloxone, an opioid antagonist that can rapidly reverse the effects of an opioid overdose. Expanded authority to distribute naloxone without an outside prescription, coupled with the provision of sterile syringes and evidence-based medications for opioid use disorder, represents a powerful opportunity for pharmacists to save lives while advancing the role of the profession. However, numerous studies have documented a lack of readiness among pharmacists to dispense naloxone and little willingness to provide sterile syringes. As a profession, it is imperative that we ensure all pharmacists receive adequate education regarding opioid harm reduction interventions and ongoing support to implement these interventions within their practices.

© 2019 American Pharmacists Association®. Published by Elsevier Inc. All rights reserved.

A crisis of opioid-related death

In 2017, the number of Americans who died due to a drug overdose exceeded 70,000 for the first time in history.¹ Two-thirds of these deaths involved opioids, with synthetic opioids contributing in most cases. From 2016 to 2017, drug overdose deaths rose 12%, driven largely by the increased prevalence of illicitly manufactured fentanyl in the U.S. heroin supply. This continued a dramatic rise in overdose deaths due to illicit opioids since 2010.² In response to this crisis, supply-reduction strategies that aim to decrease the availability of opioids for misuse and diversion have proliferated. However, a recent analysis found that supply reduction strategies may be less effective than a harm-reduction approach at reducing

opioid-related death.³ Examples of supply-reduction and harm-reduction strategies pertinent to community pharmacy practice are presented in Table 1.

A frequently cited supply-reduction intervention in pharmacy is the implementation of prescription-monitoring programs (PMPs). PMPs are state-level databases containing dispensing data for controlled substances which can be searched by pharmacists and prescribers to identify concerning patterns of use. A recent systematic review sought to evaluate the impact of PMPs on nonfatal and fatal drug overdoses, and the findings were not encouraging.⁴ Although several studies suggested an association between PMP implementation and reduced rates of fatal overdose due to prescription opioids, a few also found compensatory increases in heroin overdose mortality rates. Notably, PMP use may promote a mindset among pharmacists that prioritizes law enforcement activities rather than compassionate patient care.⁵ This is a concerning shift in provider identity that could undermine public health efforts.

The development of tamper-resistant opioid formulations represents another well-meaning attempt to prevent prescription opioid misuse, and this approach has been strongly encouraged by the Food and Drug Administration (FDA).⁶ A

Disclosure: The authors declare no relevant conflicts of interest or financial relationships.

* **Correspondence:** Lucas G. Hill, PharmD, BCPS, BCACP, Clinical Assistant Professor, University of Texas at Austin College of Pharmacy, 2409 University Avenue, Stop A1910, PHR 2.222G, Austin, TX 78712.

E-mail address: lucas.hill@austin.utexas.edu (L.G. Hill).

ORCID

Lucas Hill: <https://orcid.org/0000-0001-5958-0159>.

<https://doi.org/10.1016/j.japh.2019.06.019>

1544-3191/© 2019 American Pharmacists Association®. Published by Elsevier Inc. All rights reserved.

Key Points**Background:**

- The United States is in the midst of a drug overdose crisis that is increasingly driven by illicit opioids and which supply-reduction interventions have not adequately addressed.
- Almost every U.S. state has recognized an expanded role for pharmacists in distributing naloxone, an opioid antagonist, to prevent opioid-related deaths.

Findings:

- Many pharmacists are not prepared to dispense naloxone without an outside prescription or to provide adequate patient education regarding its use.
- Most pharmacists are not willing to sell sterile syringes without a prescription, indicating limited knowledge regarding the benefits of harm reduction interventions.

popular example is the crush-resistant technology that was applied in Opana ER to deter intranasal and intravenous use. Paradoxically, the technology seems to have inadvertently increased the dangerous practice of administering multiple injections per injection episode by simply requiring a greater volume of diluent.⁷ In 2017, the FDA requested voluntary removal of Opana ER from the U.S. market owing to risks related to illicit injection, including outbreaks of human immunodeficiency virus, hepatitis C virus, and thrombotic microangiopathy.^{8–10} At this time, there is a lack of efficacy data supporting public health benefits of tamper-resistant opioid formulations, and their high cost represents a substantial burden on payers and patients with a medical indication for use.¹¹

In 2016, the Centers for Disease Control and Prevention (CDC) issued a guideline to deter primary care providers from prescribing opioids for chronic pain.¹² The guideline contained 12 broad recommendations, most based on low-quality evidence with high heterogeneity, including suggestions to avoid chronic daily morphine milligram equivalents (MME) greater than 90 and initial opioid prescriptions exceeding a 7-day supply. Crucially, these recommendations were offered with caveats for patient-specific factors to be considered by the treating clinician. However, several U.S. states have prohibited initial opioid prescriptions for more than 7 days, and a growing number of insurers and pharmacies are implementing duration and dose limits that are cumbersome to override.¹³ Opponents of these policies note that opioid prescribing was

already decreasing in the United States for several years before the release of the CDC guideline and has continued to fall annually, yet the overall rate of opioid overdose death has risen dramatically due to increasing illicit use.^{14,15} These concerns prompted the authors of the CDC guideline to release a public clarification addressing commonly overlooked nuances and discouraging policies that prevent clinicians from making patient-specific decisions regarding opioid therapy.¹⁶

As the U.S. health care system has been restricting access to prescription opioids, the justice system has been seeking to decrease the available supply of illicit opioids. As described by legal and medical experts, the “Iron Law of Prohibition” dictates that this sort of interdiction invariably leads to a proliferation of more potent and dangerous substances.¹⁷ This effect is clearly displayed by the gradual replacement of heroin with illicitly manufactured fentanyl in the illicit drug supply. These more potent opioids can produce similar effects in much smaller quantities, reducing the likelihood of detection at legal ports of entry and during interstate transport. This increased potency also amplifies overdose risk for people who use illicit opioids.

An opportunity to save lives and advance the profession

Recognizing the unintended consequences of supply-reduction interventions applied in isolation, a growing number of health professionals are embracing harm-reduction strategies. As a philosophy, harm reduction prioritizes the minimization of negative consequences associated with risky behaviors rather than seeking to force abstinence from those behaviors.¹⁸ In the context of opioids, a spectrum of strategies may be used in the pursuit of harm reduction. The American Pharmacists Association (APhA) House of Delegates recently expanded official APhA policies supporting harm-reduction education and practice to ensure patient-centered care for people who inject drugs.¹⁹

An increasingly common harm-reduction strategy for prevention of fatal opioid overdose is the distribution of naloxone for layperson administration, paired with the provision of opioid overdose prevention and response education to ensure layperson competence. Naloxone, a potent opioid receptor antagonist, can rapidly reverse the effects of an opioid overdose. Harm-reduction coalitions have been leaders in naloxone distribution for decades.²⁰ Based in part on the success of these programs, every U.S. state and the District of Columbia has enacted naloxone access legislation.²¹ The exact specifications of these laws vary, but nearly all include some form of expanded authority for pharmacists to provide naloxone directly to patients without an outside prescription. This represents a vital test of the pharmacy profession’s ability to unite and address emerging public health crises.

A substantial body of evidence supports the effectiveness of opioid overdose education and naloxone distribution to laypersons. State-level enactment of a naloxone access law has been associated with increased naloxone dispensing and a 14% reduction in fatal opioid overdose rates.^{22–24} Granting pharmacists direct authority to dispense naloxone appears to be the most effective component of these laws and has been independently associated with a significant reduction in overdose mortality.²⁵ Prescribing of naloxone in primary care settings has been associated with a 47% reduction in opioid-related emergency department visits as well.²⁶ Furthermore,

Table 1

Common supply reduction and harm reduction strategies for opioids

Supply-reduction strategies	Harm-reduction strategies
Prescription-monitoring programs	Naloxone distribution and education programs
Tamper-resistant formulations	Sterile syringe distribution and education
Prescription dose and duration limits	Agonist and partial agonist treatment

countering concerns about patient backlash to being offered naloxone, multiple studies have shown that patients are receptive to engagement on this topic.^{27,28}

Despite legislation to expand pharmacy-based naloxone access, many pharmacists are not prepared to dispense naloxone without an outside prescription. In Indiana, only about half of surveyed pharmacies stocked naloxone and fewer than one-fourth had ever dispensed it.²⁹ Importantly, chain pharmacies and pharmacies that had completed naloxone training in the preceding 2 years were more likely to stock naloxone than other pharmacies. Similarly in Pennsylvania, only half of surveyed pharmacies stocked naloxone. In those that stocked naloxone, one-third of surveyed pharmacists responded incorrectly to questions assessing their understanding of the statewide standing order.³⁰ In addition to assessing whether pharmacies stocked naloxone, recent studies in California and Texas assessed through telephone audit whether the pharmacist on duty would dispense naloxone without an outside prescription.^{31,32} In California, only one-fourth of pharmacies contacted would provide naloxone, whereas in Texas 84% were willing. Although the Texas study showed divergently positive results compared with other states, it still demonstrated a substantial gap in naloxone accessibility, with 30% of pharmacies not having naloxone immediately available.

In addition to these studies demonstrating poor accessibility of naloxone in pharmacies, several recent surveys have identified pervasive stigma and knowledge deficits among pharmacists related to opioid overdose prevention and reversal.³³⁻³⁶ A study in Massachusetts was the latest to raise serious concerns regarding the readiness of pharmacists to dispense naloxone and provide vital patient education.³⁷ Nearly one-third either thought that or weren't sure whether naloxone could be used to reverse an overdose due to barbiturates or alcohol. The majority of respondents were unaware that available naloxone formulations differed in strength, or that pregnant women could safely receive naloxone. Furthermore, only 4% of surveyed pharmacists demonstrated the knowledge necessary to thoroughly educate potential overdose responders, with most missing key components such as providing rescue breathing and placing victims in the recovery position.

More than just naloxone

Several recent analyses have demonstrated that injection use of opioids is becoming more prevalent, and that rates of related complications, such as infective endocarditis and hepatitis C, are rising.³⁸⁻⁴¹ A key strategy for prevention of these complications that has been endorsed by the CDC is widespread implementation of syringe service programs that provide sterile injection equipment and training to people who inject drugs.^{42,43} However, these programs are not legally allowed to operate in 15 U.S. states, and they face substantial barriers to successful implementation in others.⁴⁴ Pharmacies could serve as a valuable access point for sterile injection equipment and education, but fewer than one-third of community pharmacists indicate that they are willing to sell syringes to people they suspect of illicit drug use.⁴⁵⁻⁴⁷ This is notably inconsistent with a recently enacted APhA policy strongly supporting the provision of sterile injection

equipment, which suggests that sentiments around this issue may be evolving.¹⁹

Managed use of opioids, including transition to safer pharmaceutical alternatives (e.g., methadone, buprenorphine), has the potential to prolong and improve the lives of many people with opioid use disorder.⁴⁸ However, access to these medications remains grossly inadequate due to substantial regulatory barriers that limit their prescribing. As opioid-related morbidity and mortality continue to rise, these regulatory barriers have been criticized by leading addiction experts who advocate for widespread integration of medication-based treatment of opioid use disorder in primary care.⁴⁹⁻⁵¹ Pharmacists can support patient access to treatment by maintaining an adequate stock of buprenorphine-containing products and offering administration of extended-release naltrexone.

The time is now

Supply-reduction interventions have failed to turn the tide of fatal opioid overdoses and may instead be contributing to their rise. Embracing opioid harm reduction in community pharmacies has the potential to save lives while also advancing the role of the profession in addressing public health crises. However, many pharmacists are not prepared to dispense naloxone or provide thorough patient education, and pharmacists' willingness to provide access to sterile syringes is concerning low. As a profession, we must address this deficit by ensuring that all licensed pharmacists receive adequate education regarding opioid harm reduction interventions and ongoing support to implement these interventions within their practices. Numerous resources are available to achieve this goal, including a resource guide for engaging in opioid overdose prevention discussion that was developed by the Pain, Palliative Care, and Addiction Special Interest Group of the APhA Academy of Pharmacy Practice and Management.⁵² Student pharmacists should also receive foundational education regarding these topics in the required curriculum, and this knowledge should be reinforced through exposure to preceptors who provide patient-centered care for people who use illicit opioids. Finally, pharmacists must earn reimbursement for providing opioid harm reduction interventions in a community pharmacy setting to incentivize the availability of these services. It is essential that we meet this challenge and prepare to face future crises as the most accessible health professionals in the United States.

References

- Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep.* 2018;67(5152):1419–1427.
- Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—United States, 2000–2014. *MMWR Morb Mortal Wkly Rep.* 2016;64(50–51):1378–1382.
- Pitt AL, Humphreys K, Brandeau ML. Modeling health benefits and harms of public policy responses to the US opioid epidemic. *Am J Public Health.* 2018;108(10):1394–1400.
- Fink DS, Schleimer JP, Sarvet A, et al. Association between prescription drug monitoring programs and nonfatal and fatal drug overdoses. *Ann Intern Med.* 2018;168(11):783–790.
- Chiarello E. The war on drugs comes to the pharmacy counter: Frontline work in the shadow of discrepant institutional logics. *Law Soc Inq.* 2015;40(1):86–122.

6. U.S. Food and Drug Administration. Abuse-deterrent opioid analgesics. Available at: <https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/abuse-deterrent-opioid-analgesics>. Accessed June 13, 2019.
 7. Broz D, Zibbell J, Foote C, et al. Multiple injections per injection episode: high-risk injection practice among people who injected pills during the 2015 HIV outbreak in Indiana. *Int J Drug Policy*. 2018;52:97–101.
 8. U.S. Food and Drug Administration. FDA requests removal of Opana ER for risks related to abuse, 2017. Available at: <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm562401.htm>. Accessed April 4, 2019.
 9. Conrad C, Bradley HM, Broz D, et al. Community outbreak of HIV infection linked to injection drug use of oxycodone—Indiana, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(16):443–444.
 10. Peters PJ, Pontones P, Hoover KW, et al. HIV infection linked to injection use of oxycodone in Indiana, 2014–2015. *N Engl J Med*. 2016;375(3):229–239.
 11. Curfman GD, Beletsky L, Sarpatwari A. Benefits, limitations, and value of abuse-deterrent opioids. *JAMA Intern Med*. 2018;178(1):131–132.
 12. Dowell D, Haegerich TM, Chou R. Guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*. 2016;315(15):1624–1645.
 13. Davis CS, Lieberman AJ, Hernandez-Delgado H, Suba C. Laws limiting the prescribing or dispensing of opioids for acute pain in the United States: a national systematic legal review. *Drug Alc Dep*. 2019;194:166–172.
 14. Bohnert ASB, Guy Jr GP, 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;169:367–375.
 15. Mundkur ML, Gordon AJ, Kertesz SG. Will strict limits on opioid prescription duration prevent addiction? Advocating for evidence-based policymaking. *Subst Abuse*. 2017;38(3):237–238.
 16. Dowell D, Haegerich T, Chou R. No shortcuts to safer opioid prescribing. *N Engl J Med*. 2019;380(24):2285–2287.
 17. Beletsky L, Davis CS. Today's fentanyl crisis: prohibition's iron law, revisited. *Int J Drug Policy*. 2017;46:156–159.
 18. Harm Reduction Coalition. Principles of harm reduction. Available at: <http://harmreduction.org/about-us/principles-of-harm-reduction/>. Accessed June 13, 2019.
 19. American Pharmacists Association. Actions of the 2019 American Pharmacists Association House of Delegates. Available at: https://www.pharmacist.com/sites/default/files/audience/2019_Report_of_the_APhA_House_of_Delegates-FINAL.pdf. Accessed June 13, 2019.
 20. Wheeler E, Jones TS, Gilbert MK, Davidson PJ. Opioid overdose prevention programs providing naloxone to laypersons—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(23):631–635.
 21. Network for Public Health Law. Legal interventions to reduce overdose mortality: naloxone access and overdose Good Samaritan laws. Available at: https://www.networkforphl.org/_asset/qz5pvn/legal-interventions-to-reduce-overdose.pdf. Accessed June 25, 2018.
 22. McClellan C, Lambdin BH, Ali MM, et al. Opioid-overdose laws association with opioid use and overdose mortality. *Addict Behav*. 2018;86:90–95.
 23. Freeman PR, Hankosky ER, Lofwall MR, Talbert JC. The changing landscape of naloxone availability in the United States, 2011–2017. *Drug Alc Dep*. 2018;191:361–364.
 24. Xu J, Davis CS, Cruz M, Lurie P. State naloxone access laws are associated with an increase in the number of naloxone prescriptions dispensed in retail pharmacies. *Drug Alc Dep*. 2018;189:37–41.
 25. Abouk R, Pacula RL, Powell D. Association between state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose. *JAMA Intern Med*. 2019;179(6):805–811.
 26. Coffin PO, Behar E, Rowe C, et al. Nonrandomized intervention study of naloxone coprescription for primary care patients receiving long-term opioid therapy for pain. *Ann Intern Med*. 2016;165:245–252.
 27. Behar E, Rowe C, Santos G-M, Murphy S, Coffin PO. Primary care patient experience with naloxone prescription. *Ann Fam Med*. 2016;14(5):431–436.
 28. Han JK, Hill LG, Koenig ME, Das N. Naloxone counseling for harm reduction and patient engagement. *Fam Med*. 2017;49(9):730–733.
 29. Meyerson BE, Agley JD, Davis A, et al. Predicting pharmacy naloxone stocking and dispensing following a statewide standing order, Indiana 2016. *Drug Alc Dep*. 2018;188:187–192.
 30. Graves RL, Andreyeva E, Perrone J, Shofer FS, Merchant RM, Meisel ZF. Naloxone availability and pharmacy staff knowledge of standing order for naloxone in Pennsylvania pharmacies. *J Addict Med*. 2018.
 31. Puzantian T, Gasper JJ. Provision of naloxone without a prescription by California pharmacists 2 years after legislation implementation. *JAMA*. 2018;320(18):1933–1934.
 32. Evoy KE, Hill LG, Groff L, Mazin L, Carlson CC, Reveles KR. Naloxone accessibility without a prescriber encounter under standing orders at community pharmacy chains in Texas. *JAMA*. 2018;320(18):1934–1937.
 33. Freeman PR, Goodin A, Troske S, Strahl A, Fallin A, Green TC. Pharmacists' role in opioid overdose: Kentucky pharmacists' willingness to participate in naloxone dispensing. *J Am Pharm Assoc*. 2017;57:S28–33.
 34. Thompson EL, Rao PSS, Hayes C, Purtill C. Dispensing naloxone without a prescription: survey evaluation of Ohio pharmacists [e-pub ahead of print]. *J Pharm Pract*. 2018. <https://doi.org/10.1177/0897190018759225>.
 35. Do V, Behar E, Turner C, Geier M, Coffin P. Acceptability of naloxone dispensing among pharmacists [e-pub ahead of print]. *J Pharm Pract*. 2018. <https://doi.org/10.1177/0897190018798465>.
 36. Thornton JD, Lyvers E, Scott VG, Dwibedi N. Pharmacists' readiness to provide naloxone in community pharmacies in West Virginia. *J Am Pharm Assoc*. 2017;57:S12–18.
 37. Melaragni F, Levy C, Pedrazzi J, Andersen M. Assessing pharmacists' readiness to dispense naloxone and counsel on responding to opioid overdoses. *J Am Pharm Assoc*. 2019;59(4):550–554.e2.
 38. Zibbell JE, Asher AK, Patel RC, et al. Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004 to 2014. *Am J Public Health*. 2018;108(2):175–181.
 39. Powell D, Alpert A, Pacula RL. A transitioning epidemic: how the opioid crisis is driving the rise in hepatitis C. *Health Aff*. 2019;38(2):287–294.
 40. Fleischauer AT, Ruhl L, Rhea S, Barnes E. Hospitalizations for endocarditis and associated health care costs among persons with diagnosed drug dependence—North Carolina, 2010–2015. *MMWR*. 2017;66(22):569–573.
 41. Hartman L, Barnes E, Bachmann L, Schafer K, Lovato J, Files DC. Opiate injection-associated infective endocarditis in the southeastern United States. *Am J Med Sci*. 2016;352(6):603–608.
 42. Centers for Disease Control and Prevention. Managing HIV and hepatitis C outbreaks among people who inject drugs: a guide for state and local health departments, 2018. Available at: <https://www.cdc.gov/hiv/pdf/programresources/guidance/cluster-outbreak/cdc-hiv-hcv-pwid-guide.pdf>. Accessed June 13, 2019.
 43. Winkelstein E. Guide to developing and managing syringe access programs, 2010. Available at: <https://harmreduction.org/wp-content/uploads/2011/12/SAP.pdf>. Accessed June 13, 2019.
 44. American Foundation for AIDS Research. Syringe service programs and the opioid epidemic, 2017. Available at: <https://www.amfar.org/ssp-opioid-epidemic/>. Accessed June 13, 2019.
 45. Goodin A, Fallin-Bennett A, Green T, Freeman PR. Pharmacists' role in harm reduction: a survey assessment of Kentucky community pharmacists' willingness to participate in syringe/needle exchange. *Harm Reduct J*. 2018;15(1):4.
 46. Pollini RA. Self-reported participation in voluntary non-prescription syringe sales in California's Central Valley. *J Am Pharm Assoc*. 2017;57(6):677–685.
 47. Chiarello E. Nonprescription syringe sales: resistant pharmacists' attitudes and practices. *Drug Alc Dep*. 2016;166:45–50.
 48. Laroche MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. *Ann Intern Med*. 2018;169(3):137–145.
 49. Fiscella K, Wakeman SE, Beletsky L. Buprenorphine deregulation and mainstreaming treatment for opioid use disorder: X the X waiver. *JAMA Psychiatry*. 2018;76(3):229–230.
 50. Wakeman SE, Barnett ML. Primary care and the opioid-overdose crisis—buprenorphine myths and realities. *N Engl J Med*. 2018;379(1):1–4.
 51. Samet JH, Botticelli M, Bharel M. Methadone in primary care—one small step for Congress, one giant leap for addiction treatment. *N Engl J Med*. 2018;379(1):7–8.
 52. American Pharmacists Association. Let's talk about naloxone—it saves lives. Available at: <https://www.pharmacist.com/sites/default/files/audience/LetsTalkAboutNaloxone.pdf>. Accessed June 13, 2019.
- Lucas G. Hill, PharmD, BCPS, BCACP**, Clinical Assistant Professor, College of Pharmacy, University of Texas, Austin, TX
- Kirk E. Evoy, PharmD, BCACP, BC-ADM, CTTS**, Clinical Assistant Professor, College of Pharmacy, and Ambulatory Care Clinical Pharmacist, University Health System, University of Texas, Austin, TX
- Kelly R. Reveles, PharmD, PhD, BCPS**, Assistant Professor, College of Pharmacy, University of Texas, Austin, TX