Reducing Opioid Overdose Deaths by Expanding Naloxone Distribution and Addressing Structural Barriers to Care

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See also Razaghizad et al., p. 1516.

ncreasing access to naloxone is a key component of efforts to decrease time to overdose rescue and reduce fatal opioid overdose. The past decade has seen substantial efforts to expand naloxone availability through three primary channels: (1) emergency medical services and other uniformed first responders responding to an overdose; (2) pharmacies, both via traditional prescriptions and non-patient-specific prescription mechanisms; and (3) overdose education and naloxone distribution (OEND) programs.

In an umbrella review, Razaghizad et al. (p. 1516) focus on the last of these channels by evaluating evidence regarding the effects of OEND programs on a variety of outcomes, including knowledge regarding opioid overdose response, overdose management behaviors, population-level overdose mortality, and cost effectiveness. Qualitatively synthesizing evidence from six systematic reviews, the authors conclude that OEND programs generally

produce beneficial outcomes across all domains considered, although the authors' ratings for the strength of the evidence are often "limited" or "moderate."

Improvement in knowledge regarding opioid-related overdose risk factors, symptoms, and response strategies was the only domain receiving the authors' highest confidence rating. Despite variation in context, specific curricula, and participants, studies consistently find that the "OE" component of OEND programs achieves its goals. Of note, the review does not evaluate whether programs that require education as a condition of naloxone receipt provide naloxone to fewer individuals compared with distribution mechanisms in which such training is optional or highly compressed. If educational requirements are sufficiently onerous to deter individuals from obtaining naloxone, such training may be a net negative, particularly in light of the past decade's dramatic increases in opioid overdose

combined with the approval and availability of naloxone products specifically designed for use by laypeople in the United States.

It is more challenging to evaluate the extent to which improved knowledge might translate to improved overdose management behaviors and health outcomes, although self-reported data suggest that OEND programs are effective in improving participants' use of recommended overdose response strategies. However, most of the underlying studies contributing to the evidence base in this domain rely solely on pre-post comparisons among OEND participants, and several lack even preperiod or baseline data.

Furthermore, the ability of OEND programs to improve health outcomes is affected by factors outside their control. In particular, OEND program participants' behaviors are fundamentally shaped by the "risk environment" in which they exist. In the United States and many other countries, this risk environment is greatly affected by both stigma against people who use drugs and the continued criminalization of many manifestations of opioid use disorder, including the possession of drugs and drug paraphernalia.

This is highlighted in the data on whether program participants report calling emergency medical services when witnessing an overdose. Particularly in the US context, rates of summoning emergency medical services following an overdose incident are often strikingly low, including among OENDtrained individuals (e.g., 10%–30%).² Of course, disinclination to call emergency medical services for assistance following an overdose is not a failure of OEND but, rather, reflects well-documented concerns among people who use drugs that law enforcement's accompaniment of

emergency medical services will result in serious legal and social consequences, including arrest for drug or drug paraphernalia possession, homicide charges, or parole violations; loss of housing; and involvement of child protective services. 3-5 Although nearly all states have enacted overdose Good Samaritan laws intended to mitigate these concerns, laws are typically limited to minor drug crimes and are undermined by the fact that people who use drugs largely do not trust police to follow the law. 3

Given that education and training are unlikely to address these deeply rooted concerns, and in the absence of structural changes that comprehensively address the perceived and actual risks of calling 911, the "ND" component of OEND programs has elevated importance. Unfortunately, Razaghizad et al. did not examine how effective OEND programs are at providing naloxone, particularly to individuals who may be unlikely or unable to access it from pharmacies.

The extent and specifics of naloxone distribution through OEND programs are likely key factors in their ability to produce population-level reductions in opioid-related overdose mortality. Indeed, the one study with a credible causal inference design that contributes to the "moderate" evidence rating for this outcome finds a dose-dependent relationship between community OEND enrollment and, hence, naloxone kits distributed and lower opioid-related overdose deaths. ⁶ Although it is certainly suggestive that OENDs with broad implementation can help reduce community rates of opioid overdose deaths, it is unclear whether this one study's findings would generalize to the other forms of OEND, particularly those that do not provide naloxone to those at greatest risk or in great enough

quantities to significantly improve the likelihood that it will be immediately available at opioid overdoses throughout the community.

Indeed, one challenge to synthesizing the evidence on OEND programs is that the programs vary widely in their setting, participants, intervention design, and perhaps most importantly—volume of naloxone distributed to the communities they serve. A recent study of 247 US syringe service programs offering OEND found that they distributed more than 702 000 naloxone doses in 2019, but more than half of all doses were distributed by just 14 (6%) programs. 7 It is likely that this varied implementation generates differential effects, and better understanding the determinants and consequences of this heterogeneity can help guide the development and dissemination of effective overdoseprevention strategies. These types of details may be outside the scope of an umbrella review of systematic reviews, but they are key for identifying gaps in populations reached, potential barriers for successful implementation, and which aspects of OEND are most important for their ultimate goal of reducing fatal opioid overdose.

Overall, the evidence Razaghizad et al. evaluated provides additional support for the proposition that OEND programs improve overdose-related outcomes. The questions then become: what are the barriers to expanding naloxone access through OENDs and other mechanisms, and how can we address them?

In the United States, these barriers largely fall into the categories of financial, regulatory, and stigma. Many programs distribute naloxone without any federal, state, or local funding support, ⁸ and OENDs commonly report challenges with maintaining an adequate supply. ^{7,9} Naloxone distribution efforts also face

persistent regulatory challenges, most notably the lack of an over-the-counter formulation of the medication. 10 Given the extensive evidence that naloxone is safe, effective, and cost effective, it is beyond time to dramatically increase funding for naloxone distribution and reduce barriers to both naloxone distribution and evidence-based prevention and treatment of people with opioid use disorder. Perhaps more challenging to address are concerns voiced by some that naloxone provision promotes riskier opioid use, which persist despite the majority of evidence suggesting that any such impact is far outweighed by the beneficial impacts of increased access to the medication. 11

The conclusions of Razaghizad et al. derive primarily from studies conducted before the stark rise in fentanyl and stimulants as increasing contributors to overdose mortality. The evolution of the overdose crisis only serves to further highlight the need for multifaceted approaches that remove barriers to naloxone in addition to addressing the structural factors that contribute to opioid use disorder and opioid-related harm, including but not limited to structural racism and continued reliance on a failed model that centers criminal-legal, and not public health, approaches to people who use drugs. AJPH

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PUBLICATION INFORMATION

Full Citation: Smart R, Davis CS. Reducing opioid overdose deaths by expanding naloxone distribution and addressing structural barriers to care. *Am J Public Health*. 2021;111(8):1382–1384.

Acceptance Date: April 29, 2021.

DOI: https://doi.org/10.2105/AJPH.2021.306376

CONTRIBUTORS

The authors contributed equally to the conceptualization and writing of this editorial.

ACKNOWLEDGMENTS

This work was supported by the National Institute on Drug Abuse (grant R21DA04595).

Note. The National Institute on Drug Abuse had no role in the preparation, review, approval, or decision to submit this editorial for publication.

CONFLICTS OF INTEREST

The authors report no conflicts of interest relevant to this editorial.

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