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Prevention of Fatal Opioid Overdose

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Opioid overdose is a burgeoning public health crisis, accounting for at least 16 000 deaths annually in the United States.¹ Opioid overdose occurs across sex, ethnic, age, and geographic strata and involves both medical and nonmedical opioid use. To date, federal government response has focused primarily on monitoring and securing the drug supply.¹ This Viewpoint suggests various steps necessary to support a more comprehensive approach.

During the time it typically takes some overdoses to turn fatal, it is possible to reverse the respiratory depression and other effects of opioids with the antagonist naloxone. Community-based organizations, health care institutions, and local and state agencies have begun to train and equip potential nonmedical bystanders to recognize and reverse overdose events using first aid techniques and emergency supplies of naloxone.^{2,3} As the number of such initiatives has increased, the 53 000 program trainees have tracked more than 10 000 reports of overdose rescues in the United States.² These efforts have targeted drug users (syringe access programs, drug treatment centers, correctional facilities),¹ physicians (to “coprescribe” naloxone along with opioids),⁴ and first responders (ie, fire and police).³ The concept has also gained traction among policy makers, including the Office of the National Drug Control Policy and professional organizations.⁵

Despite the mounting supportive evidence, the number of these programs remains limited in many communities with elevated rates of fatal overdose.² Multiple barriers limit the diffusion of this innovation: the price of naloxone has sky-rocketed in the context of a severe shortage; few prescribers are aware of and are willing to facilitate overdose prevention education and naloxone access; funding for program activities and evaluation research

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remains sparse; and the Food and Drug Administration (FDA)–approved formulation of naloxone is suboptimal for out-of-hospital use.

In April 2012, an interagency hearing on naloxone access was convened by the FDA and brought together practitioners, regulators, researchers, and people personally affected by overdose. Although the meeting underscored numerous regulatory hurdles, decisive action is necessary to advance overdose prevention programs beyond the proof-of-concept phase (Table).

The FDA must ensure that adequate supplies of naloxone are available to meet the increasing demand. Like many sterile injectable products, naloxone is in chronic shortage. Most naloxone programs experience challenges in obtaining naloxone because of cost increases or suppliers' inability to fill orders.¹ As existing programs scale up and more jurisdictions adopt these measures, federal action can help expand naloxone supply, such as by fast-tracking importation licenses.

Health care practitioners are optimally positioned to facilitate opioid overdose prevention. Equipping clinicians and providing incentive for them to screen patients for overdose risk and to educate patients, their families, and caregivers about recognizing and responding to overdoses is an important step, alongside community-based education about opioid overdose and naloxone distribution. Explicitly integrating overdose prevention, including naloxone coprescription, into the FDA-industry cooperative strategy for evaluation and mitigation of opioid risk also could be helpful.⁴

Clinicians may be unclear about legal risks associated with prescribing naloxone⁶ and may be concerned about the possibility of facilitating risky drug use⁶; yet there is no evidence of such disinhibition.⁷ Prescribing naloxone to manage opioid overdose is consistent with its FDA-approved indication, precipitating no increased liability as long as prescribers adhere to general rules of professional conduct.⁷ Some states have passed laws indemnifying clinicians from risk of malpractice lawsuits perceived to arise from prescription of naloxone. Others have introduced Good Samaritan laws shielding lay bystanders and persons experiencing overdose from possible civil liability (flowing from providing first aid) and criminal drug charges when 911 is called.⁷ Using evidence-based model legislation, federal coordination can help disseminate these legal protections to encourage clinician engagement, lay responder rescue, and help-seeking.

In out-of-hospital settings, the administration of injectable drugs carries the risk of needle-stick injury and presents logistical barriers, such as the absence of a sterile syringe and delay in preparation.³ FDA action is needed to fast-track approval of naloxone delivery systems that are safe and user-friendly for nonmedical responders. Administration of intranasal naloxone via aftermarket nasal atomizers is an “off-label” system increasingly used by out-of-hospital emergency medical personnel and by community-based programs.³ The lack of FDA approval limits the implementation of intranasal formulations and devices: nasal atomizers are difficult to stock and seldom covered by insurance. FDA approval of intranasal naloxone is predicated on research demonstrating such a formulation to be “substantially equivalent” to the current formulation. Federal funding is needed to clear this hurdle because naloxone is an off-patent, generic medication not widely considered to be a promising investment by major pharmaceutical companies. Use of an autoinjector—a safe and effective method for delivery of epinephrine—represents another alternative that would require FDA approval.

Federal agencies are uniquely situated to address national public health crises through increasing awareness, funding, and coordinated action. Community-based organizations, state and local health departments, and professional societies have taken the lead in

developing, implementing, and publicizing overdose education and naloxone distribution as a component in a comprehensive response to this veritable epidemic.⁵ The federal government should actively support research and programmatic action on overdose education and naloxone access.

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Table

Potential Federal Action to Improve Prevention of Fatal Overdose

Barrier/Limiting Factor	Remedial Federal Action	Agency in Charge
Naloxone shortage and high cost	Allow temporary importation from qualifying foreign manufacturers	FDA
Lack of health care training to screen for and address problematic opioid use, opioid overdose risk, and underutilization of out-of-hospital naloxone	Monitor supply and demand Provide funding for dissemination of overdose prevention and management education, including naloxone distribution to potential bystanders through community-based and addiction treatment programs	FDA SAMHSA, CDC
Lack of health care training to screen for and address problematic opioid use, opioid overdose risk, and underutilization of out-of-hospital naloxone	Require Opioid REMS programs to cover overdose prevention and the role of naloxone	FDA
Lack of prescriber incentives to deliver overdose prevention and management education	Create and disseminate existing practitioner training and toolkits (such as the materials available at http://prescribetoprevent.org/) to facilitate opioid overdose prevention. Materials should be tailored to priority settings and populations, including chronic pain therapy, drug treatment facilities, and emergency departments	SAMHSA, AHRQ, national professional association
Lack of public awareness about risk factors, signs and symptoms, and appropriate response to overdose	Reimburse overdose prevention education interventions and cover naloxone prescription and delivery devices	CMS
Prescriber concern about legal risks to self and patients from naloxone prescription; bystander reluctance to call 911	Formulate and disseminate model legislation providing legal immunity to naloxone prescribers and lay responders to change police behaviors and encourage witnesses to call 911	DOJ, Bureau of Justice Assistance
Lack of public awareness about risk factors, signs and symptoms, and appropriate response to overdose	Conduct public awareness campaigns about risk factors, signs and symptoms, and response to overdose	FDA, CDC, ONDCP
Research	Evaluate community-based naloxone access initiatives, Good Samaritan laws, and interventions targeting drug users and possible bystanders on overdose risk behaviors	NIH, CDC, DOJ
Lack of public awareness about risk factors, signs and symptoms, and appropriate response to overdose	Evaluate the effects of education, brief interventions, laws and regulations, and other interventions on clinician practice and patient overdose morbidity and mortality outcomes	NIH, CDC, DOJ
Lack of public awareness about risk factors, signs and symptoms, and appropriate response to overdose	Provide funding for program evaluation and clinical research on intranasal and autoinjector devices	NIH, CDC, SAMHS

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Barrier/Limiting Factor	Remedial Federal Action	Agency in Charge
Explore alternative models of naloxone access	Such models may include a new "over-the-counter-plus" class of drugs and pharmacist naloxone prescription	FDA, national professional associations

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare & Medicaid Services; DOJ, Department of Justice; FDA, Food and Drug Administration; NIH, National Institutes of Health; ONDCP, Office of the National Drug Control Policy; SAMHSA, Substance Abuse and Mental Health Services Administration.