Opioid overdose prevention
Jeffrey Bratberg, Bill McLaughlin, and Scott Brewster

APhA–APPPM
Pharmacists have essential role in opioid overdose prevention

Nearly one-half of opioid painkiller users are unaware that these drugs are as addictive as heroin.1 In 2013, 10.8% of men and 5.8% of women aged 12 years or older reported prescription opioids.5 People who the greatest risk for individuals used have skyrocketed, with most often a benzodiazepine.6–9 The have another drug in their system, heroin overdose are more likely to aged 12 years or older reported 10.8% of men and 5.8% of women for opioids were written in 2012, and opioid overdose was a leading cause of unintentional injury death in 2013.1 Fatal and nonfatal opioid overdose incidence increases parallel the trend in prescription opioid prescribing.4

Meanwhile, heroin use and related deaths have skyrocketed, with the greatest risk for individuals using heroin along with prescribed prescription opioids.5 People who die from prescription opioid or heroin overdose are more likely to have another drug in their system, most often a benzodiazepine.6–9 The majority of opioid overdoses are preventable via naloxone administration, as most overdoses are witnessed by another person.10,11

Pharmacists perform critical, life-saving public health interventions every day, such as dispensing prescriptions for buprenorphine/naloxone and epinephrine auto injectors, recommending nonprescription medications and products, and administering various immunizations throughout the year.12 In general, pharmacists advocate for overdose education and opioid safety,13 and nonprescription syringe sales,14 and some provide a broader array of addiction services and education in community pharmacies.15

Pharmacists are ideally positioned to contribute to the following U.S. Department of Health & Human Services priorities to address opioid overdose, death, and dependence: improving prescribing practices, identifying high-risk individuals, ensuring access to medication-assisted therapy (buprenorphine and methadone), and expanding use of naloxone.16 Pharmacists can incorporate risk-stratified, patient-centered opioid screening and education into existing workflows without compromising efficiency by integrating overdose risk assessment and recommending and/or initiating naloxone during prescription processing.17–20 Pharmacists can focus their interventions on patients at the highest risk of overdose. These high-risk patients include those covered by Medicaid,21 prescribed high doses of opioids,22 with chronic pain,23,24 using long-acting opioids,25 using methadone,26 recently incarcerated,27,28 with a history of overdose,29 and filling buprenorphine prescriptions for medication-assisted therapy.30

Another method pharmacists can use to identify individuals at high risk of misuse, dependence, overdose, and death is the prescription drug monitoring program (PMP). In 49 states, PMPs help prescribers and pharmacists identify patients who use prescription opioids prescribed by multiple prescribers and review controlled substance prescriptions filled at multiple pharmacies.31 Using PMPs, pharmacists can initiate discussions about overdose prevention and may be able to more accurately identify high-risk combinations of opioids and benzodiazepines. However, more research is required to determine the effectiveness of PMPs in reducing fatal and nonfatal opioid overdoses.32,33

Once patients are identified, pharmacists play an important role
in overdose education. Unfortunately, primary care providers, the group that most often prescribes opioids, may not provide overdose education and naloxone distribution (OEND) as often as needed to patients at risk. Therefore, pharmacists can assist in this area by providing overdose education, including how to identify an overdose, perform rescue breathing, contact 911, and administer naloxone, as well as what to do and expect after naloxone administration (e.g., withdrawal symptoms, the need to place the patient in the rescue position). Although lack of time is one of the greatest barriers to providing public health prevention in community pharmacies, effective OEND takes only 5 to 15 minutes on average. Pharmacists can also help educate patients and providers about abuse-deterrent formulations. To reduce prescription opioid diversion and misuse while preserving patient access to effective pain management, pharmaceutical manufacturers have developed formulations aimed at discouraging abuse. These drugs are designed to inhibit snorting and/or injecting and have been effective in reducing some prescription drug abuse. Although the introduction of these products reduces the availability of more easily modifiable prescription opioids, it may also encourage people with abuse risk factors to shift from prescription opioids to heroin.

Pharmacies are ideal locations for increasing community access to naloxone because of their thousands of highly recognizable, public locations with extended hours. Pharmacists are also the most accessible interface between the community and the health care system. Pharmacies are rapidly increasing naloxone access, and this increased distribution is associated with reduced mortality, stable or decreased drug use, and increased participation in treatment programs. The expanded access is also cost-effective when distributed to illicit opioid users and safe. Despite these achievements, prescription drug users require still greater access to naloxone, since naloxone is principally distributed to heroin users, and more than one-half of those who die from opioid overdose use prescription opioids.

Table 1. Resources for opioid overdose prevention

<table>
<thead>
<tr>
<th>Information</th>
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<tr>
<td>Safe medication and syringe disposal</td>
<td>Drug Enforcement Administration drug disposal information (<a href="http://www.deadiversion.usdoj.gov/drug_disposal/">www.deadiversion.usdoj.gov/drug_disposal/</a>)</td>
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<td>Alameda County, CA: Safe Drug Disposal program (<a href="http://www.acgov.org/acute/safedisposal/">www.acgov.org/acute/safedisposal/</a>)</td>
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<td></td>
<td>U.S. Food and Drug Administration (FDA) information on safe disposal of needles and other sharps (<a href="http://www.fda.gov/">www.fda.gov/</a></td>
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<td>MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/ConsumerProducts/Sharps/default.htm)</td>
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<td>Opioid prescribing, overdose, and naloxone education</td>
<td>Provider’s Clinical Support System for Opioid Therapies (<a href="http://pcss-o.org/">http://pcss-o.org/</a>)</td>
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<td>SCOPE of Pain (Safe and Competent Opioid Prescribing Education) (<a href="http://www.scopeofpain.com">www.scopeofpain.com</a>)</td>
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<td>Overdose Prevention Alliance (<a href="http://www.overdosepreventionalliance.org">www.overdosepreventionalliance.org</a>)</td>
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<td>Substance Abuse and Mental Health Services Administration’s (SAMHSA) Opioid Overdose Prevention Toolkit (<a href="http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit-Updated-2014/SMA14-4742">http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit-Updated-2014/SMA14-4742</a>)</td>
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<td>Get Naloxone Now (<a href="http://getnaloxonenow.org">http://getnaloxonenow.org</a>)</td>
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<td>Overdose and naloxone continuing professional development</td>
<td>Prescribe to Prevent (<a href="http://prescribetoprevent.org/">http://prescribetoprevent.org/</a>)</td>
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<td>Opioid Overdose Prevention Toolkit from Pharmacist’s Letter (<a href="http://www.opioidoverdosepreventionforpharmacists.com">www.opioidoverdosepreventionforpharmacists.com</a>)</td>
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<td>College of Psychiatric and Neurologic Pharmacists (<a href="http://cpnp.org">http://cpnp.org</a>)</td>
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<td>Opioid overdose and naloxone epidemiology</td>
<td>Prescription drug overdose at the Centers for Disease Control (CDC) National Center for Injury Prevention and Control (<a href="http://www.cdc.gov/drugoverdose/">www.cdc.gov/drugoverdose/</a>)</td>
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<td>Management of substance abuse at World Health Organization (<a href="http://www.who.int/substance_abuse/env">www.who.int/substance_abuse/env</a>)</td>
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<td>FDA public meeting: Exploring Naloxone Uptake and Use (<a href="http://www.fda.gov/Drugs/NewsEvents/ucm442236.htm">www.fda.gov/Drugs/NewsEvents/ucm442236.htm</a>)</td>
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<td>“Legal Interventions to Reduce Overdose Mortality” by the Network for Public Health Law (<a href="http://www.networkforphl.org/_asset/g25pn/network-naloxone-10-4.pdf">www.networkforphl.org/_asset/g25pn/network-naloxone-10-4.pdf</a>)</td>
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<td>Naloxone administration videos and handouts</td>
<td>Prescribe to Prevent (<a href="http://prescribetoprevent.org/">http://prescribetoprevent.org/</a>)</td>
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<td>Veterans Health Administration on YouTube (<a href="http://www.youtube.com/channel/UCaW28mX6gCpTuWYjyPwD-O">www.youtube.com/channel/UCaW28mX6gCpTuWYjyPwD-O</a>)</td>
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<td>“Naloxone Access: A Practical Guideline for Pharmacists” by the College of Psychiatric and Neurologic Pharmacists (<a href="http://cpnp.org/guideline/naloxone">http://cpnp.org/guideline/naloxone</a>)</td>
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<td>“Opioid Safety and How to Use Naloxone” by the San Francisco Department of Public Health (<a href="http://www.chcf.org/~/media/MEDIA%20LIBRARY%20Files/PDF/N/PDF%20NaloxoneOpioidSafetyProviders.pdf">http://www.chcf.org/~/media/MEDIA%20LIBRARY%20Files/PDF/N/PDF%20NaloxoneOpioidSafetyProviders.pdf</a>)</td>
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Pharmacists and providers have an increased awareness of the severity of the opioid overdose epidemic; the increased risks of prescription opioids, especially when combined with other medications; the role and use of naloxone to reverse opioid-related overdose; and the efficacy of medication-assisted therapies for patients with substance use disorders. Still, the biggest barrier to prescribing naloxone and methadone or buprenorphine for patients with opioid use disorders is the stigma of the treatment. Pharmacists who dispense buprenorphine in their practice have more favorable views on dispensing naloxone and selling syringes to avert blood borne disease transmission and also feel more comfortable providing care to patients with addiction.37–49

Thus, continuing professional education programs on pain, addiction, and overdose prevention should include information on addressing and reducing this stigma to further enhance the pharmacist’s role in opioid overdose prevention.

Pharmacists hold many important roles in opioid overdose prevention. They dispense the majority of prescription opioids from community pharmacies, review PMPs, counsel patients on opioid safety, provide medication lockboxes, and educate patients on and offer drug disposal services. As medication safety and education specialists, pharmacists are also ideally positioned to integrate OEND, as well as harm reduction services such as nonprescription syringe sales, into their practices.

Pharmacists and staff members should be educated on the effects of stigma on overdose prevention services provided to both patients at risk for substance misuse and patients already misusing prescription or illicit opioids.50,51 An increasing number of insurers pay pharmacists to perform annual comprehensive medication reviews, during which pharmacists can discuss naloxone with patients who have risk factors for overdose. With stigma, time, and payment hurdles behind them, pharmacists can reduce opioid overdose and death in their communities. (For a list of resources, see Table 1.)

References


30. Substance Abuse and Mental Health Services Administration; 2014.


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ponent to maximize the euphoric effect. With oral dosage forms, abusers may simply swallow multiple units to increase the dose, or they may manipulate the units to facilitate rapid release and absorption or alternate means of delivery, including snorting (insufflation), smoking, and injection. Extended-release opioids are particularly subject to abuse, as they contain high levels of active ingredient that can be manipulated to release rapidly. The design of abuse-deterrent formulations should take into account potential routes of abuse.

A number of abuse-deterrent oral opioid formulations, based on a range of technologies, have been marketed or are in development.1–3 The most successful of these formulations are physical/chemical barriers, agonist/antagonist combinations, and aversion technology.

Physical/chemical barriers are imparted through formulation and processing, which make the dosage form resistant to crushing, cutting, or grinding and/or make the active ingredient difficult to extract or prepare for injection. These properties are usually created by the inclusion of high-molecular-weight polymers such as polyethylene oxide. This technology has been used in extended-release formulations of hydrocodone bitartrate (Hysingla ER—Purdue and Zohydro ER—Pernix), oxycodone hydrochloride (OxCont-in—Purdue) and oxymorphone hydrochloride (Opana ER—Endo). Extended-release hydromorphone hydrochloride (Exalgo—Mallinckrodt) is also reported to have crush- and extraction-resistant properties from its osmotic “push–pull” technology.

Combining an opioid with an opioid antagonist can reduce the euphoric effects of oral formulations if manipulated for more rapid release or alternate delivery. Talwin NX (Hospira; discontinued) tablets and Suboxone (Reckitt Benckiser) sublingual film (indicated for treatment of opioid addiction, not pain relief) combine naloxone hydrochloride with pentazocine hydrochloride or buprenorphine hydrochloride, respectively. Naloxone has low oral/sublingual bioavailability and thus does not interfere with the action of the opioid when taken as directed. However, if the tablets or films were dissolved for injection, the naloxone would enter the bloodstream directly and diminish or prevent the euphoric effect that otherwise would be attained. Targiniq ER (Purdue), a recently approved extended-release oxycodone hydrochloride tablet, includes naloxone hydrochloride as an abuse deterrent. Embeda (Pfizer) combines morphine sulfate with the antagonist naltrexone hydrochloride. Naltrexone is well-absorbed from the gastrointestinal tract but is sequestered inside the product’s extended-release morphine beads. When swallowed intact, the naltrexone is not released from the formulation; however, if the beads are crushed or dissolved, the antagonist is released to reduce the pharmacological effect of the morphine.

Aversion approaches rely on the inclusion of ingredients that cause discomfort to individuals who manipulate the dosage form prior to use (either orally or via an alternate route of administration) or ingest the intact product at high doses to achieve a euphoric effect. This approach was used to discourage deliberate overdose of Lomotil (Pfizer), an anti diarrheal combining subtherapeutic levels of the anticholinergic atropine sulfate with the active diphenoxylate hydrochloride, which may produce opioid-like effects at high doses. Aversive agents that have been proposed for abuse-deterrent formulations of oral opioids include intensely bitter compounds to discourage mastication; mucous membrane irritants to discourage mastication, insufflation, smoking, or injection; malodorous compounds to deter insufflation; and emetics or discomfort-inducing agents at levels that only exert their effect under overdose conditions. Oxecta (Pfizer; approved but not currently marketed) was an extended-release oxycodone hydrochloride tablet that employed physical/chemical barriers to crushing and extraction and also included the nasal irritant sodium lauryl sulfate as an aversive agent.

The U.S. Food and Drug Administration (FDA) recently issued a guidance for industry describing the agency’s current thinking on the design, performance, and evaluation of studies to demonstrate abuse-deterrent properties of a formulation and their implications in product labeling.3 In the document, FDA described premarket studies including laboratory manipulation and extraction studies, pharmacokinetic studies, and abuse potential studies. The agency also outlined postmarket evaluations including formal studies and/or supportive information such as prescribing patterns, diversion events, attitudes, and practices. Various label statements related to abuse-deterrent properties could be supported, depending on how studies are conducted and their results.

Additional research in the abuse-deterrent technologies described above, as well as other approaches such as prodrug design, are active fields of investigation.1,2 Pharmacists should understand the characteristics of these formulations and their potential impact on methods of abuse as part of a comprehensive approach to managing risk while effectively treating patients suffering from chronic pain.

References


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APhA–ASP Student pharmacist naloxone initiatives support community, profession

Many students at the East Tennessee State University (ETSU) Bill Gatton College of Pharmacy have witnessed first-hand the devastation associated with deaths from opioid overdose in Tennessee and other states raged by prescription drug abuse. The Generation Rx initiative has been active in APhA–ASP chapters in Central Appalachia and across the nation, reaching children, young adults, and providers with innovative, collaborative, and educational programming.1 Expanded access to naloxone, an emergency opioid reversal treatment, has given student pharmacists another avenue to reach those most at risk of death from opioid overdose.

Role of the student pharmacist

In collaboration with the Virginia Department of Behavioral Health and Developmental Services, ETSU student pharmacists and medical and nursing students underwent training as part of Project REVIVE!, a pilot initiative to teach community members to recognize and respond to opioid overdoses by administering intranasal naloxone. ETSU students immediately sought to use their training to help reverse opioid overdoses in southwest Virginia. Student pharmacists learned the signs and symptoms of opioid and heroin overdose and how to administer intranasal naloxone in a life-threatening situation, achieving train-the-trainer certification. More than 150 student pharmacists are now qualified to train laypersons to recognize opioid overdose, ensure the appropriate storage of naloxone, assemble an intranasal naloxone device, and deliver lifesaving treatment.

Call for wider access

Programs like Project REVIVE! have expanded access to naloxone in many different states, as Diana Yap explained in an April 2015 Pharmacy Today article. While states such as Rhode Island, New Mexico, and North Carolina have differing approaches to patient access to naloxone, access is expanding nationwide.2 As of June 2015, 39 states have naloxone access laws and 28 have 911 Good Samaritan laws,3 demonstrating the changing conversation and reduced stigma of naloxone and the disease of addiction.

At a naloxone patient training event in Lebanon, VA, Sarah Melton, PharmD, associate professor of pharmacy practice at ETSU, said, “It’s time for us to take back our own communities and stop these overdose deaths.”4 Melton has been fundamental to the success of both Project REVIVE! and ETSU’s Generation Rx. The empowering approach she described has influenced both student pharmacists and community members, with 10 student pharmacists helping train more than 40 laypersons at this event. In attendance and receiving training was U.S. Senator Tim Kaine (D–VA), who said, “I didn’t fully grasp how [big] of a problem [opioid overdose] was until I was last here in April for a few days and I was hearing about it everywhere I went.” He added that the naloxone training “gives me some idea about some other things we can do.”4

Final-year PharmD candidate Heather Flippin described her interaction with Sen. Kaine as a “privilege” and “inspiring,” and said she was pleased that he was “advocating for our initiative to fight the prescription drug abuse epidemic.”

Bridging the gap and becoming a provider

Like many other student pharmacists across the country, my classmates and I are experiencing some of the most rigorous years of our training, but we are also witnessing an exciting and transformative time in the profession of pharmacy.

Expanded naloxone access and increased pharmacist responsibility over dispensing mark yet another avenue to establishing pharmacists as providers. Where state laws permit, initiatives like Generation Rx and Project REVIVE! provide pharmacists with the opportunity and ability to reach patients and caregivers, and ultimately to save lives. These activities demonstrate the value of pharmacy through advocacy in addressing the epidemic of prescription drug abuse.

References


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