PUBLIC HEALTH LAW RESEARCH:
Making the Case for Laws that Improve Health

POLICY BRIEF

Naloxone for Community Opioid Overdose Reversal

June 2015

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Introduction

Drug overdose is the leading cause of injury-related death in the United States, killing more people every year than car crashes. Opioids — both prescription painkillers and heroin — are responsible for most of these deaths. The death rate from prescription opioid-caused overdose nearly quadrupled from 1999 to 2013, while deaths from heroin overdose rose 270 percent between 2010 and 2013. Together, heroin and prescription pain medications take the lives of almost 25,000 Americans per year — nearly 70 people per day. They also cause hundreds of thousands of non-fatal overdoses and an incalculable amount of emotional suffering and preventable health care expenses.

Nearly all opioid overdose deaths are preventable by the timely administration of the medication naloxone. This medicine, which requires a prescription, is not a controlled substance and rapidly reverses opioid overdose in most cases. While naloxone has been used in hospitals and ambulances for decades, the rising tide of overdose deaths has resulted in calls to make it more available to laypeople and first responders. Since 2010, states have moved rapidly to change law, regulation, and policy to increase access to this lifesaving medication. These legal changes include immunity protections for medical professionals who prescribe and dispense the medication and people who administer it, as well as individuals who call 911 to report an overdose. Many laws also permit the medication to be dispensed to any person who is either at risk of overdose or may be in a position to assist in an overdose, even if they have not been examined by the prescriber. Initial evaluations suggest that increased naloxone access can reduce fatal overdose as well as health care expenditures from emergency visits and hospitalizations while likely reducing the emotional trauma caused by losing a friend or loved one to overdose.

Policy Implications

Opioid overdose is a medical emergency. Naloxone has been used for decades to reverse it and restore normal respiration. Over the past 15-20 years, community groups and, later, governmental organizations have worked to increase community access to the medication so that naloxone is available when and where it is needed to reverse potentially fatal opioid overdoses. Increased naloxone access is supported by a large number and variety of organizations, including the World Health Organization, the American Medical Association, the American Public Health Association, and the National Association of Boards of Pharmacy. It is a key component of the federal government's response to the overdose epidemic, and is supported by agencies including the Centers for Disease Control and Prevention (CDC), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Office of National Drug Control Policy.

It is undisputed that, if administered in time, naloxone reverses opioid overdose in the vast majority of cases. A variety of data suggest that individuals who are trained in opioid overdose identification and response, including naloxone administration, are willing to and capable of administering naloxone in an emergency. Medical risks regarding naloxone administration are low, and in most if not all cases are much lower than failing to administer the medication in the event of opioid overdose. The sooner naloxone is administered and respiratory depression is reversed, the better outcomes are likely to be. It therefore makes sense to increase access to the medication, and to fund robust evaluations to ensure that increased access has the intended effect, that any negative consequences are addressed, and that best practices are identified and publicized.

Unfortunately, naloxone is often not available when and where it is needed. There are a number of actions government at all levels can take to address this problem. At the federal level, agencies including SAMHSA and CDC should fund both naloxone access and training programs and systematic evaluations. The Centers for Medicare and Medicaid Services should ensure that the medication is covered by both Medicare and Medicaid, without prior authorization or other barriers. Because one of the greatest barriers to broader access is the fact that naloxone is a prescription medication, both FDA and Congress should strongly consider taking action to make it available over-the-counter or otherwise modify the prescription requirement.

At the state level, states can and should pass laws and modify regulations to ensure that naloxone is available to all who may need it. This may include making it available through community-based organizations and at pharmacies without a patient-specific prescription, ensuring that people at high risk of overdose such as those receiving high-dose opioid painkillers or leaving correctional institutions or drug treatment facilities are provided naloxone at no or minimal cost, and providing education to clinicians to raise awareness of the importance of prescribing and dispensing naloxone to individuals at risk of overdose. They should also pass and publicize comprehensive overdose Good Samaritan laws so that people who witness overdoses are not punished for calling for help. Localities should also consider whether equipping firefighters and law enforcement officers in their jurisdictions with the medication might meaningfully decrease time to naloxone administration, possibly improving outcomes.

Naloxone alone will not stop the overdose epidemic. However, existing evidence supports rapid scale-up of programs to increase access to the medication, of which legal and policy changes are a key component.

Research and Evidence

Opioid overdose is a serious and growing public health problem.

The number of Americans lost to opioid overdose has been increasing for nearly two decades, in an epidemic that impacts people from all ages, races, and geographic areas (Rossen, Khan, & Warner, 2014; Chen, Hedegaard, & Warner, 2014). Fatal poisonings, most of which are caused by drug overdose, have increased by nearly 600 percent in the past three decades, and are now the leading cause of injury death in the United States (Warner et al., 2011). Although this increase has been driven mainly by opioid painkillers (Okie, 2010; Modarai et al., 2013), which took the lives of over 16,000 Americans in 2013, recent data show a marked increase in heroin-related deaths as well (Pollini et al., 2011; Jones, 2013; Rudd et al., 2014; Warner, 2015; Hedegaard, Chen, & Warner, 2015). Heroin-related fatalities rose to over 8,000 in 2013, a nearly four-fold increase since 2000, while prescription opioid-related deaths appear to have plateaued (Rudd et al., 2014; Hedegaard, Chen, & Warner, 2015). Evidence strongly suggests that the increase in heroin deaths is at least partly the result of prescription opioid users transitioning to heroin use (Rudd et al., 2014; Dasgupta et al., 2014; Peavy et al., 2012).

Naloxone has been used for decades to reverse opioid overdose. It is a prescription medication, but is not a controlled substance and has no abuse potential.

Opioid overdose causes decreased levels of consciousness and respiratory depression. It becomes life threatening when breathing is depressed to the point that insufficient oxygen is available to permit the brain and other organs to function effectively, a state called hypoxia (Bouillon, Bruhn, Roepcke, & Hoeft, 2003; Pattinson, 2008; White & Irvine, 1999). Early intervention is critical, as hypoxia can cause cell death within minutes, and the risk of irreversible damage increases with the amount of time the person remains hypoxic (Michiels, 2004). Because most people do not overdose alone, equipping people who use opioids and the friends and family members of those at risk of opioid overdose with the tools to quickly reverse it can reduce the risk of overdose death as well as damage to the brain and other organs (Galea et al., 2006).

Opioid overdose, whether caused by heroin or prescription painkillers, can typically be reversed by administering a medication called naloxone (Chamberlain & Klein, 1994). Naloxone, commonly known by the brand name Narcan, was approved by the Food and Drug Administration (FDA) in 1971. It is a prescription medicine but not a controlled substance, and it has no potential for abuse (Chamberlain & Klein, 1994). It displaces opioids from the brain receptors to which they attach, reversing their effects and restoring normal respiration (Chamberlain & Klein, 1994; Lewanowitsch & Irvine, 2002). It is stocked by nearly every hospital and has been used by paramedics for decades (Barton et al., 2002). While medical professionals typically inject it into a victim's vein, most community groups provide the equipment to inject it into a muscle or to spray it into the nose of a person who is suffering an overdose (Doe-Simkins, Walley, Epstein, & Moyer, 2009). An easy-to-use

auto-injector device (brand name Evzio) was approved in 2014 (Food and Drug Administration, 2014).

There is a growing interest in training and equipping more people to administer naloxone to reverse opioid overdose.

Because people who use drugs (PWUD) are already "on the scene" of an overdose, experts have suggested reducing time to naloxone administration by equipping them with naloxone for more than twenty years (Strang, Darke, Hall, Farrell, & Ali, 1996). By the mid-1990's, naloxone was being distributed to heroin users in Italy (Simini, 1998), Germany, and the United Kingdom (Coffin et al., 2003). The first programs to dispense naloxone to PWUD in the United States were launched in the late 1990's and early 2000's, with the first documented programs operating in Chicago in 1996 and San Francisco in 2001 (Bigg & Maxwell, 2002; Seal et al., 2005; Centers for Disease Control and Prevention, 2012).

By the mid-2000s, community programs in several states including New Mexico, Massachusetts and New York had begun distributing naloxone and overdose rescue training to PWUD and the friends and family members of people at high risk of overdose (Galea et al., 2006; Doe-Simkins, Walley, Epstein, & Moyer, 2009; Maxwell, Bigg, Stanczykiewicz, & Carlberg-Racich, 2006; Clark, Wilder, & Winstainley, 2014; Piper et al., 2008). As of 2014, over 150,000 laypeople had received training and naloxone kits, and participants reported reversing more than 26,000 overdoses (Wheeler, Jones, Gilbert & Davidson, 2015). Naloxone access initiatives have since expanded beyond PWUD, with many states taking action to encourage the provision of naloxone by physicians, pharmacists, and community organizations to anyone at risk of opioid overdose (Bailey & Wermeling, 2014; Zaller et al., 2013; Davis, Webb, & Burris, 2013). There is also increasing movement to equip non-medical first responders such as firefighters and law enforcement officers with naloxone, although evidence supporting the efficacy of this intervention is not yet available (Davis, Ruiz, Glynn, Picariello, & Walley, 2014).

Laypeople are willing to and capable of recognizing opioid overdose and administering naloxone.

A 1999 survey of heroin injectors reported that 89 percent said that they would have used naloxone at the last overdose they witnessed if they'd had it available (Strang et al., 1999). Since then, tens of thousands of lay people have been trained in recognizing and responding to overdose, including administering naloxone (Wheeler, Jones, Gilbert & Davidson, 2015; Clark, Wilder, & Winstanley, 2014). Recent data show that PWUD who received naloxone from one such program were highly likely to administer it during an overdose (Rowe et al., 2015).

Overdose prevention programs typically train people receiving naloxone kits to reduce overdose risk as well as recognize and appropriately respond to overdose (Clark, Wilder, & Winstanley, 2014). Although the level of evidence is relatively low, most reviews report that people who receive naloxone training increase their level of relevant knowledge (Haegerich, Paulozzi, Manns, & Jones, 2014). A study of mostly homeless people who inject drugs in Los Angeles found that a single training session significantly increased knowledge of appropriate overdose response (Wagner et al.,

2010), and a study of people trained in overdose response at six sites in the United States reported that they were significantly more likely to recognize and respond to overdose (Green, Heimer, & Grau, 2008). Recent evidence suggests that a very brief education session is sufficient (Behar, Santos, Wheeler, Rowe, & Coffin, 2015), and a recent study found no significant difference in rescue behaviors or reversal rates between naloxone administered by people who had received formal training versus those who had not (Doe-Simkins et al., 2014).

Medical risks associated with naloxone administration are low, particularly compared to inaction.

No medication is completely safe. However, naloxone has a low risk of serious side effects. The most common stem from the withdrawal symptoms the medication can cause, and include shivering, sweating, and aggressiveness (Buajordet, Naess, Jacobson, & Brors, 2004; Kelly et al., 2005). While these can be uncomfortable, they are generally not life-threatening (Wermeling, 2015). While there are some reports of life-threatening injuries post-naloxone administration, they are rare (Osterwalder, 1996; Enteen et al., 2010; Yokell et al., 2011) and almost always reported in medically complex, post-operative settings where naloxone is administered in amounts higher than those typically used in the community (Boajordet, Naess, Jacobson, & Brors, 2004; Kelly et al., 2005). It is not clear whether these adverse effects, which have included acute lung injury (pulmonary edema), are the result of naloxone administration or events related to the overdose itself (Kelly et al., 2005; Osterwalder, 1996).

Additionally, it appears that individuals who receive naloxone but do not receive additional medical care are not at increased risk of negative outcomes. A 2003 study of 5 years of data in San Diego found no deaths in the 12 hours after patients who were administered naloxone by EMS refused transport to the hospital (n=998) (Vilke, Sloane, Smith, & Chan, 2003). A 2005 study from Finland found no life-threatening events in the 12 hours after overdose patients (n=84) were treated pre-hospital and refused further treatment, which lead the authors to conclude that permitting "presumed heroin overdose patients to sign out after pre-hospital care with naloxone is safe" (Boyd et al., 2006). Likewise, a 2011 retroactive study of 20 months of data from San Antonio found no evidence that any patients who had been administered naloxone and refused transport died in the next 48 hours (n=542) (Wampler et al., 2011).

Laws can act as a barrier to increased naloxone access.

A number of laws and regulations hamper access to naloxone. Because it is a prescription medication, it can be dispensed only on the order of a medical professional authorized to issue prescriptions (Davis, Webb, & Burris, 2013). Further, state medical practice laws typically discourage or prohibit the prescription or distribution of medications to a person other than the person to whom they are to be administered (a process referred to as third-party prescription) or to a person the physician has not examined (Davis, Webb, & Burris, 2013). These restrictions have often prevented naloxone from being available when and where it is needed outside of the medical setting.

Additionally, some prescribers may refrain from prescribing naloxone because of concerns that it might increase their risk of civil liability, although there is no evidence that these concerns are

justified (Beletsky et al., 2007; Burris et al., 2009). Similarly, people present at the scene of an overdose may be afraid to call 911 because of fear of being charged with a crime, particularly where they are using illegal drugs or using prescribed medication other than as prescribed (Enteen et al., 2010; Tobin, Davey, & Latkin, 2005; Sherman et al., 2008).

Many states have modified law and regulation to increase access to naloxone by laypeople and non-medical first responders such as police and firefighters.

While making naloxone available over the counter would likely solve many of these access problems, only the FDA has the authority to make that change. However, states have taken a number of steps to increase access to naloxone, beginning with New Mexico in 2001. As of May 2015, 30 other states and the District of Columbia have also modified law to make it easier for lay people to access naloxone. These changes vary, but most permit individuals otherwise authorized to prescribe naloxone to prescribe it not only to their own patients, but also to family members, caregivers, and others (Davis, Webb, & Burris, 2013). Many states also permit naloxone to be prescribed via a standing order, in which one prescriber issues a prescription for naloxone to be provided to any person who meets certain criteria, as opposed to a named individual. Nearly all of these laws provide limited immunity to medical professionals who prescribe naloxone and lay people who administer it in an overdose (Davis, 2015). An increasing number also authorize law enforcement officers and other non-medical first responders such as firefighters to carry naloxone and administer it in an overdose (Davis, et al., 2014; Davis, Ruiz, Glynn, Picariello, & Walley, 2014).

New Mexico was also the first state, in 2007, to amend its laws to encourage overdose witnesses to summon aid in the event of an overdose by providing limited criminal immunity to overdose witnesses who summon emergency help for an overdose victim. As of May 2015, 22 other states and the District of Columbia have also passed such laws (Davis, 2015). These laws, which are often referred to as "Good Samaritan" laws, provide limited criminal immunity (typically from minor drug-related crimes) for both the overdose victim and the person who calls for help, although some of the more recent laws expand the protection to offenses such as probation and parole violations.

Increased access to naloxone does not appear to increase drug use or risky behavior.

Although data are limited, access to naloxone does not appear to encourage risky behavior, likely because naloxone overdose reversal removes the user's "high" and, depending on the opioid that was taken and the amount of naloxone administered, can put the victim into withdrawal, an extremely unpleasant experience. A study in England reported that 94 percent of heroin users said that having access to naloxone would not increase the dose of drugs that they used (Stran et al., 1999). A small study from San Francisco found that heroin users who received naloxone and overdose education reported a statistically significant decrease in heroin injection six months after the intervention (Seal et al., 2005), and a study in Los Angeles noted that a majority of individuals trained in overdose prevention reported that their drug use decreased three months after the training (Wagner et al., 2010).

Researchers evaluating the Massachusetts Overdose Education and Naloxone Distribution program found that "training active substance users in overdose management and distributing naloxone rescue

kits does not lead opioid users to increase their overall opioid use" (Doe-Simkins et al., 2014). According to a recent systematic review, two studies reported that participants in opioid overdose prevention programs reported a decrease in calling 911, while two reported an increase and one found no change (Clark, Wilder, & Winstanley, 2014).

Naloxone access programs may reduce overdose-related morbidity and mortality.

Evidence of the effectiveness of naloxone access programs in reducing fatal overdose and overdose-related morbidity is limited, but existing data point to a positive effect (Clark, Wilder, & Winstanley, 2014). The best evidence comes from a study in Massachusetts, which showed that communities with higher access to naloxone and overdose training had significantly lower opioid overdose death rates than those did not (Walley et al., 2013). A systematic review of published literature found that 11 of 18 studies reported a survival rate of 100 percent after naloxone was administered in the community setting; the others reported a range of 83-96 percent (Clark, Wilder, & Winstanley, 2014).

Initial evidence from a comprehensive overdose prevention program (Project Lazarus) in one county in North Carolina found a striking decrease in overdose deaths in that county after the program was initiated (Albert et al., 2011). Researchers have suggested that reduction in heroin deaths in Chicago may be partly attributable to a naloxone distribution program in that city, although that finding is merely observational (Maxwell, Bigg, Stanczykiewicz, Carlberg-Racich, 2006).

Naloxone access programs may reduce health care costs.

Naloxone is available in a number of different formulations, with widely varying costs. Evzio, the recently approved auto-injector, retails for $450-$600 (Beletsky, 2015). According to the manufacturer, the majority of state Medicaid programs provide coverage for Evzio, co-pay assistance is available to bring the out-of-pocket cost to less than $30 for most commercially insured patients, and programs are available to provide Evzio at no cost to individuals without drug coverage and qualifying harm reduction and law enforcement agencies (communication with kaléo, June 19, 2015). Community overdose programs reported costs in the range of $15 per kit of injectable naloxone and $30 per kit of intranasal naloxone in 2013 (Coffin & Sullivan, 2013). The price of the medication has recently increased by as much as a factor of 2 to 3, however, reducing the ability of some community organizations to distribute the medication and prompting protests from government officials in several states (Goodman, 2014).

Emergency department visits are expensive, as is follow-up care for patients with lasting damage caused by hypoxia. In a 2013 study, the provision of naloxone kits to heroin users was found to be robustly cost-effective even under extremely conservative assumptions (Coffin & Sullivan, 2013). A separate study noted that the cost of treating people who had overdosed in Rhode Island hospitals could have paid for more than 61,000 naloxone kits at the then-current cost of $15 (Yokell et al., 2011).

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Additional Resources

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Websites

Public Health Law Research: Naloxone Overdose Prevention Laws Map
Public Health Law Research: Good Samaritan Overdose Prevention Laws Map
Network for Public Health Law: Legal Interventions to Reduce Overdose Mortality: Naloxone Access and Overdose Good Samaritan Laws
Network for Public Health Law: Legal Interventions to Reduce Overdose Mortality: Emergency Medical Services Naloxone Access
Substance Abuse and Mental Health Administration: Opioid Overdose Prevention Toolkit