Ohio's Opioid Drug Epidemic

Ohio is in the grips of a drug overdose epidemic. From 1999 to 2011, Ohio's death rate due to drug overdose increased 440 percent. Unintentional drug overdoses caused 1,765 deaths to Ohio residents in 2011. This is equivalent to 5 Ohioans dying every day or one Ohioan dying every 5 hours. The increase in drug overdose deaths has been driven largely by opioids such as prescription pain relievers and heroin. In 2011, approximately two-thirds (1,154, 65.4 percent) of the fatal drug overdoses involved any opioid (prescription or heroin).[i]

What is Naloxone?

Among the tools available to prevent opioid drug overdose deaths is Naloxone Hydrochloride (also known as Narcan). Naloxone is indicated for the complete or partial reversal of narcotic depression, including respiratory depression, induced by opioids including natural and synthetic opioids, and certain partial opioid antagonist analgesics. When administered during an overdose, Naloxone blocks the effects of opioids on the brain and temporarily restores breathing within minutes.

Naloxone has been used safely by emergency medical professionals for over 40 years and has only one function: to reverse the effects of opioids on the brain and the respiratory system in order to prevent death. Naloxone is a highly specific medication which means that when it is administered in standard doses and in the absence of opioids or agonistic effects of other opioid antagonists, it exhibits essentially no pharmacologic activity. Naloxone is not a controlled substance and has not been shown to produce tolerance or cause physical or psychological dependence. Naloxone is an incredibly safe medication and it is impossible to overdose on Naloxone. The only contraindication for Naloxone is in patients who are known to be hypersensitive to the medication.

Administration of Naloxone varies based upon the setting in which it is administered. While most commonly given by intramuscular injection (IM), it can also be administered intranasally using an atomizer device that delivers a mist to the nasal mucus membrane. The device used for this latter form of administration is not yet FDA approved, but studies show that it is just as effective as IM injection.[ii] In addition, intranasal administration is becoming increasingly common in overdose prevention programs throughout the country, commonly referred to as Naloxone Prescription Programs (OENDPs), because it prevents needle stick injuries and its overall ease of use.

Overdose Education and Naloxone Distribution Programs (OENDPs)

In response to the growing overdose deaths caused by opioids, several states and localities have implemented OENDPs. OENDPs provide overdose training and take-home doses of Naloxone to those who are at high-risk for an overdose. OENDPs provide training in recognizing the signs and symptoms of an overdose, instruction on how to perform rescue breathing, administration of Naloxone and the importance of calling 911. Such programs have been proven effective at reversing opioid overdoses. Since 1996, more than 53,000 individuals have been trained by OENDPs resulting in more than 10,000 overdose reversals using Naloxone. There are approximately 200 sites where Naloxone is being distributed in 16 states.[iii] While there are several different models developed to provide Naloxone to individuals at high-risk for overdose, they all have the same goal: to prevent overdose deaths.

Community Based Naloxone Distribution Model: Project DAWN (Deaths Avoided with Naloxone)

Building on its commitment to stem the dramatic increase in drug overdose deaths in Ohio, the Ohio Department of

Health (ODH), Violence and Injury Prevention Program, allocated seed money and technical assistance to initiate Project DAWN (Deaths Avoided with Naloxone), Ohio's first Overdose Reversal Project. Project DAWN is housed at the Portsmouth City Health Department and serves all of Scioto County. ODH has also provided technical assistance and additional resources to expand the Project DAWN program to Cuyahoga and Montgomery counties.

What is the Structure of Project DAWN?

Project DAWN is modeled after similar programs that have been in operation for years. Upon a arriving at the at Project DAWN site, a trained opioid Overdose Prevention Educator completes a registration form and reviews it with the prospective program participant to make a determination about the individual's eligibility. This registration form follows an influenza vaccine paradigm to ensure proper record keeping for a medical encounter. The form is modeled on patient history forms approved for use in other states: basic identifying and demographic information, risk factors for overdose, medication allergies, and previous overdose history.

The trainer then engages the participant in a brief educational program about overdose prevention and response, known as Opioid Overdose Prevention Training. The training has been designed in accordance with a review of applicable Ohio statutes and case law regarding prescription medications.[iv]

The Opioid Overdose Prevention Training includes:

1. Overdose prevention techniques
2. Recognizing signs and symptoms of overdose
3. Calling 911
4. Airway and breathing assessment/Rescue breathing/ Recovery position
5. Naloxone storage, carrying, and administration in an emergency setting
6. Reporting of overdose to Project DAWN and refill procedures
7. Post-overdose follow-up care

Project DAWN Kit

Upon completion of the program, the participant will be assessed by the trainer on their understanding of the information and their comfort with the basic components of overdose response. After a patient review, a licensed prescriber will issue a prescription to take to a nearby pharmacy to obtain two doses of naloxone or dispense the medication on-site (physician only). If going to a pharmacy, the program participant will receive the rest of their kit containing 2 nasal atomizers, an instructional DVD, a CPR barrier device, and an instructional booklet are provided to the participants at no cost upon their return.

What is the target population for Project DAWN?

Community level programs aimed at reducing opioid drug overdose deaths, such as Project DAWN, target a wide-range of high-risk individuals. These individuals vary from chronic pain patients who may misuse or abuse medications to non-medical users of prescription opioids and heroin users. Additional indications include: those who are opioid naive or have abstained from using opioids (recently released from jail or treatment facility), individuals with certain health conditions (renal dysfunction, COPD, HIV/AIDS) and those who are concurrently using other central nervous system depressants (benzodiazepine, alcohol, anti-depressants). Table 1 provides a complete list of the populations targeted by Project DAWN.

Table 1. Potential indications for prescription Naloxone and risk factor for poisoning[v]		
	Potential Indication/Patient Population	**Documentable Risk Factor for Poisoning**
1	Emergency medical care for opioid poisoning	Increased risk for subsequent unintentional poisoning and self-harm
2	Suspected illicit or nonmedical opioid user	Risk for multiple drug use; continued (multiple) drug use; reduced opioid tolerance among inpatients
3	High-dose opioid prescription (>80 mg morphine equivalence/day)	Patient incorrectly administers opioid resulting in higher risk of toxic levels
4	Any methadone prescription to opioid naïve patient	Low threshold for overdose; inexperience with long-acting opioids
5	Any opioid use and smoking/COPD/emphysema or other respiratory illness or obstruction	Increased risk of respiratory depression due to comorbidities
6	Any opioid use and renal dysfunction or hepatic disease	Prolonged and/or increased serum concentrations of opioid due to decreased metabolism and/or excretion
7	Any opioid use and HIV/AIDS	HIV seropositivity is associated with an increased risk of overdose mortality
8	Any opioid use and known or suspected concurrent alcohol use	Additive effect of multiple central nervous system depressants
9	Any opioid use and concurrent benzodiazepine use or any concurrent sedating medication use	Additive effect of multiple central nervous system depressants
10	Any opioid use and concurrent SSRI or TCA anti-depressant use	Increased toxicological risk for opioid poisoning; higher risk for substance use and self-harm
11	Released prisoners	Relapse to/initiation of nonmedical opioid use; reduced opioid tolerance; risk for multiple substance use
12	Release from opioid detoxification or mandatory abstinence program	Relapse to nonmedical opioid use; reduced opioid tolerance; risk for multiple substance use
13	Voluntary request	Perceived risk for opioid exposure
14	Patients entering methadone maintenance treatment programs (for addiction or pain)	Increased risk for poisoning in first month; risk for multiple substance use

What type of Naloxone is distributed?

Since the target population of Project DAWN includes injection and non-injection drug users, the program uses an intranasal delivery system. The Naloxone provided comes in single dose needleless luer-lock syringes with 2mg per 2 mL solution. The recommended dose is 1 mL in each nostril, for a total of 2 mg of Naloxone administered. Intranasal delivery systems are currently being used by OENDPs in New Mexico, North Carolina (Project Lazarus), New York City, San Francisco, Seattle King County Health Department and Massachusetts.[vi]

Single dose Naloxone

Frequently Asked Questions

Do these programs reduce drug overdose death rates?

A recent evaluation of Massachusetts' overdose education and nasal naloxone distribution (OEND) programs found that opioid overdose death rates were significantly reduced in communities where OEND was implemented. The study of 19 communities found that the higher the cumulative rate of OEND implementation (i.e. more participants that were enrolled), the greater the reduction in death rates.[vii]

Why prescribe Naloxone to an individual at-risk for overdose?

Fatal overdoses can be prevented. Opioid overdoses often occur 1 to 3 hours after the drug was first used.[viii] This provides a sufficient window of time to intervene to prevent an overdose death.

In addition, overdoses are often witnessed. In Ohio, a 2011 review of drug overdose deaths from Scioto County found that 87% of decedents were not alone at the time of their death, with predominantly adult family members or significant others present when they died.[ix] Furthermore, a 2006 study in Baltimore found that 69.7% of drug users reported witnessing an overdose.[x] Most overdoses are witnessed, and the provision of Naloxone can enable these witnesses to respond in a safe and effective manner.

What are the adverse events associated with the administration of Naloxone?

Adverse events associated with Naloxone are usually the result of the individual entering into opioid withdrawal, the medical consequences of long-term drug abuse or health problems unrelated to Naloxone. A review of studies on pre-hospital administration of Naloxone indicates that serious adverse events are rare:

- Buajordet et al. (2004): Study of 1192 administrations by EMS found that found that adverse events reported were mostly related to withdrawal symptoms: confusion (32%), headache (22%), nausea/emesis (9%), aggressiveness (8%), tachycardia (6%), shivering (5%), seizures (4%)[1], sweating (3%), tremor (1%) and miscellaneous. Only 0.03% of overdoses treated with Naloxone were associated with serious complications requiring hospitalization.[xi]

- Yealy et al. (1990): Reported on 813 out-of-hospital patients with depressed levels of consciousness who received out-of-hospital Naloxone by paramedics during a one-year period and found few adverse reactions (0.07%).[xii]

- Enteen et al. (2010): Less than 1% of participants in a Naloxone Prescription Program in San Francisco who attributed overdose reversal to Naloxone reported serious adverse events.[xiii]

From the FDA precautions label for Naloxone: "In addition to naloxone, other resuscitative measures such as maintenance of a free airway, artificial ventilation, cardiac massage, and vasopressor agents should be available and employed when necessary to counteract acute narcotic poisoning. Several instances of hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary edema have been reported. These have occurred in postoperative patients, most of whom had pre-existing cardiovascular disorders or received other drugs which may have similar adverse cardiovascular effects. Although a direct cause-and-effect relationship has not been established, naloxone should be used with caution in patients with pre-existing cardiac disease or patients who have received potentially cardiotoxic drugs." [xiv]

> "What about adverse events? So among the 1300 overdose reports that we've documented, seven of them were deaths. And I can tell you that having reviewed each one of these, in each case, these were people who were dead when the response came about. So the person was already dead. They didn't have any response to the naloxone because their heart wasn't beating anymore."
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> **Dr. Alex Walley, Assistant Professor, Internal Medicine, Boston University**
> Role of Naloxone in Opioid Overdose Fatality Prevention, FDA Hearing, April 12, 2012

Return of Respiratory Depression

One concern with pre-hospital administration of Naloxone is the return of respiratory depression. Two studies have examined this question among those who were administered Naloxone by EMS and refused transport to the hospital.

- Vilke et al. (2003): During a five year period in San Diego, 998 out-of-hospital patients received Naloxone

[1] The authors noted that the majority of patients were severely cyanotic and hypoxic before the Naloxone treatment. This fact may explain the frequency of severe headache and seizures reported.

from EMS and refused transport, against medical advice. A review of medical examiner records found no instances of these individuals dying of opioid poisoning within the 12 hours following Naloxone administration.[xv]

- Boyd et al. (2006): A study out of Finland found "allowing presumed heroin overdose patients to sign out after pre-hospital care with Naloxone is safe. If transported to an ED, a 1-h observation period after Naloxone administration seems to be adequate for recurrent heroin toxicity." [xvi]

While these studies indicate that pre-hospital care with Naloxone may be adequate to reverse an opioid overdose, the abuse of longer acting prescription opioid analgesics (Oxycontin ER, Methadone, Fentanyl) require the activation of emergency medical services to avoid the return of respiratory depression. To that end, all programs that distribute Naloxone include a robust education component emphasizing that many of these drugs have a longer half-life than Naloxone which is why it is critical to call 911 in the event of an overdose.

By our approval of Naloxone prescription by licensees are we abetting illicit drug use?

The premise of this question is that by shielding addicts from the negative consequences of their behavior, prescription Naloxone wrongly reduces the disincentives to reduce drug use and/or seek treatment. This premise is not supported and there is no evidence to suggest that the fear of overdose is a deterrent to drug use.[xvii] However, there is evidence to suggest that surviving an overdose is a traumatic event that is likely to induce remorse and self-reflection. In fact, a study of injection drug users found that one in four IDUs (26.2%) sought drug treatment within 30 days after their last overdose.[xviii]

The same study found that 40.7% of IDUs reported that someone talked to them about drug treatment following their most recent overdose and many of these individuals (45.0%) subsequently sought treatment. Therefore, programs providing Naloxone can serve as a mechanism to educate drug users on the negative consequences of opioid abuse and provide referrals to treatment services.

> "I think it's ethically questionably to withhold vaccine or often other preventive measures because of unproven fears about disinhibition and risk compensation."
>
> **Greg Zimet, Clinical Psychologist, Indiana University School of Medicine**
> Role of Naloxone in Opioid Overdose Fatality Prevention, FDA Hearing, April 12, 2012

The availability of Naloxone has also been associated with a decrease in drug use. Results from an OENDP in San Francisco found that six months following training in Naloxone administration, participants had a statistically significant *decrease* in injection frequency.[xix]

This question also fails to take into account that not every person who overdoses on opioids is drug dependent or an illicit user. As demonstrated by the high-risk categories listed in table 1 above, individuals who are using opioid pain medications to treat legitimate chronic pain may also be at risk for overdose. In this instance, provision of Naloxone provides a safety net to an individual suffering from chronic pain that may inadvertently increase their dose, abstain from use or mix their medications.

Are there cost savings associated with the greater availability of Naloxone?

Naloxone can prevent complications that result in costly drug overdose-related hospital stays.[xx] The cost of an overdose reversal kit is approximately $40, while the average in-patient treatment charge for a drug overdose in Ohio is $10,488. This cost is often paid by taxpayers because in two-thirds of all hospitalizations involving drug-related poisonings, the patient was either uninsured or covered by public insurance.[xxi]

How difficult is it for individuals to learn how to administer the medication and respond to an opioid overdose?

Research shows that programs such as Project DAWN are effective at improving responses to opioid overdoses. Several studies indicate that opioid users can be trained to execute appropriate actions to assist the successful reversal of potentially fatal overdose.[xxii] [xxiii]

In addition, data from Project DAWN in Portsmouth also indicates no difficulty in administering the medication. In fact, 100 percent of participants who administered naloxone reported no difficulty in assembling or administering the medication.[xxiv]

For more information on Project DAWN, please visit: http://www.healthy.ohio.gov/vipp/drug/ProjectDAWN.aspx

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