

Emergency Department Naloxone Distribution

Key Considerations and Implementation Strategies

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Introduction

Opioid overdose deaths have quadrupled since 1990,¹ and are now a leading cause of injury and death in the United States, killing more people between 25 to 64 years old than motor vehicle accidents.¹ Most overdose deaths occur in the pre-hospital setting and 78% are unintentional.² In the last few years, there have been multiple federal recommendations to increase availability of naloxone,^{3,4,5} an opioid antagonist and overdose reversal agent, to prevent out of hospital opioid overdose deaths. Naloxone has been distributed from community overdose education and naloxone distribution (OEND) programs since 1996. These programs have been shown to decrease fatal opioid overdose rates,^{6,7} and many states have implemented policies to improve naloxone access.^{8,9,10} In the last several years, some Emergency Departments (EDs) have started ED OEND programs to provide naloxone to patients identified at risk for opioid overdose (Figure 1).^{11,12}

Given the high prevalence of unmet substance abuse needs among ED patients,¹³ and increasing frequency of drug related ED visits,¹⁴ emergency physicians have an opportunity to prevent opioid overdose deaths. ED naloxone distribution is a simple and cost effective way to provide a lifesaving intervention to patients at risk for opioid overdose.^{15,16} While there are many ways to develop an ED program, tailored to your local and institutional needs, there are several key topics every ED OEND intervention must consider for successful implementation:

- 1) **Program Implementation and Utilization:** *Is there support for ED OEND at your institution? What are barriers and facilitators for patients and providers?*
- 2) **Policies and Regulations:** *What are the hospital, insurance, pharmacy, state, and federal regulations?*
- 3) **Cost:** *How much does it cost and what are the methods of reimbursement?*
- 4) **Means of Distribution:** *In what form and by what means will you provide patients with naloxone?*
- 5) **Patient Education:** *What resources do you have to improve education and use?*

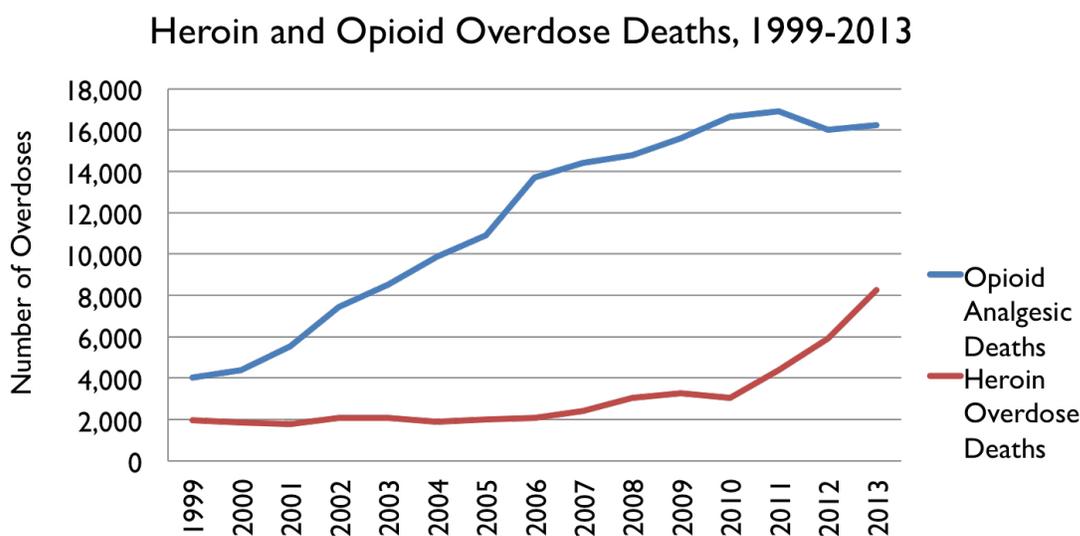


Figure 1: National heroin and opioid overdose deaths, 1999-2013.

DATA SOURCE: National Center on Health Statistics, CDC WONDER

Program Implementation & Utilization

Establishing a program does not guarantee utilization. Hospital, provider and patient factors need to be optimized to ensure adequate program uptake. Primary factors influencing program utilization include knowledge of research evidence; local, and state policies and laws; ED/hospital support, policies, and procedures; professional organizations' policies and guidelines; and cost and payment mechanisms.

To successfully implement a program, you need a champion to coordinate program implementation. Gaining support from your hospital and ED leadership early in the process will help facilitate the development of policy and procedures easily incorporated into daily ED operations. If you are unsure whether providers would be willing to utilize an OEND program, you can perform a pre-program assessment and, if necessary, education. Minimizing the labor required by physicians and nurses can diminish provider utilization barriers and garner support. For example, rather than creating a separate system or additional step to provide a naloxone rescue kit (NRK), incorporate orders into your Electronic Medical Record System (if you have one). This helps integrate the program into usual emergency care (See Figure 2 for an example of how an order can appear in Epic). The policy should be simple, straightforward, and easy to understand. Roles, responsibilities, and expectations for naloxone provision and education should be clearly defined. Prior to program launch, provide education to providers, nurses, nursing assistants, secretaries, and any other relevant ED staff about the program policies and procedures. Provider and staff education can be done at departmental meetings, EM residency conferences, or nursing roll call/change of shift meetings. Have the policy easily accessible for reference where other ED policies are kept. It can also be circulated by email or posted in the department.

Patient barriers to receiving a NRK include stigma, mistrust of medical providers, fear of legal consequences for possession or use, and fear of feeling unpleasant feelings of withdrawal after receiving naloxone. Additionally, patients are often unaccompanied by someone who could use the NRK to save them in case of an overdose. Building patient trust and rapport will improve program acceptability. Soliciting patient feedback about your program will also help improve program quality.

Prominent provider barriers include negative attitudes toward patients presenting with addiction(s) or after an overdose, misinformation or lack of knowledge about naloxone, and lack of clarity about which patients should receive naloxone. Previously, naloxone distribution programs focused on heroin users, however with the rise of prescription opioid use and overdose, we

recommend that naloxone be provided to patients taking more than 100mg morphine equivalents daily, have known opioid abuse/dependency, or who have had an opioid overdose (Significant risk factors for opioid overdose are listed in Figure 3). When you start your program, start with a discrete patient population that is easy to identify as being at risk for future overdose, such as individuals who present after an opioid overdose. Staff training, program monitoring, and staff feedback should be data driven and provided on a regular, ongoing basis.

The screenshot shows an Epic order set titled "Orders from Order Sets" with the main order "Naloxone Kit and Education" and a "Remove" button. Below this are three items:

- naloxone atomizer (MAD) device**: Miscellaneous, Once as needed, Starting Today at 0116, For 1 dose. Provided with naloxone Intranasal Rescue Kit.
- nalOXone injection 2 mg**: 2 mg, Inhalation, Once as needed, opioid reversal, Starting Today at 0116, For 1 dose. For home administration as needed.
- Anchor Recovery Coach (401-415-8833)**: Order details.

Below these items is a link for "Play Overdose Rescue Education Video" with a "STAT, Until discontinued starting Today at 0117 Until Specified" note.

Figure 2: Example Epic order set

Figure 3: Persons at risk for opioid overdose

- 1) Received emergency care for opioid intoxication or poisoning
- 2) Have suspected substance abuse or non-medical opioid use
- 3) Are taking >100mg morphine equivalents/day
- 4) Are receiving an opioid prescription for pain and:
 - a) Are prescribed methadone or buprenorphine.
 - c) Have poorly controlled respiratory disease or infection.
 - d) Have renal dysfunction, hepatic disease, cardiac illness
 - e) Have known or suspected excessive alcohol use or dependency
 - f) Concurrent use of a benzodiazepine or other sedative
 - g) Suspected poorly controlled depression
- 5) Patients in above categories with difficulty accessing emergency medical services.
- 6) Recent incarceration/release from prison with history of opioid use.
- 7) Resumption of opioid use after period of abstinence.

Policies and Regulations

The largest barrier to naloxone availability is fact that naloxone has not been approved for over-the-counter (OTC) sales. Multiple state policies have been used to address this barrier. The Food and Drug Administration (FDA) last considered the issue in 2012 and concluded that more data is necessary before moving forward. While OTC naloxone is still a possibility, it would require a well-organized and funded citizen petition or, more likely, a drug company to take it on. Both options are limited by costs and/or anticipated financial return on investment.

Regulatory issues specific to naloxone

There is significant variability between states.¹⁷ Legal clarity regarding state level protection may encourage prescribing and have wide impact on naloxone availability. While existing¹⁸ laws may be perceived as a barrier to naloxone program implementation, thirty-seven states have successfully amended these regulations and a blueprint exists to help other states wanting to explore this option.¹⁹

Common regulatory barriers limiting Naloxone availability

Access to naloxone is the main barrier faced by patients and programs. As mentioned earlier, its status as a prescription drug (but not a controlled substance) means that a prescriber is necessary. Often providers willing to prescribe are in short supply. Most state practice laws require a treatment relationship between the prescriber and the provider which limits the impact of those providers willing to prescribe. State EMS laws also define the level of first responder who may access naloxone and restrictive policies for carting naloxone may disproportionately affect some areas.²⁰

Liability, real or perceived, associated with naloxone is an issue for prescribers, pharmacists, and bystanders. Prescribers may be concerned with any activity that can be perceived as outside the practice of medicine or standard of care in their area. Pharmacists have concerns about their liability for providing medications without a specific prescription and storing/providing prefilled injection medications. Bystanders may not use naloxone and/or call 911 for overdoses because of perceived criminal liability due to drug possession, syringes, outstanding warrants or parole violations.

Potential regulatory solutions:

- 1) **Third party prescribing:** This statutory change specifically endorses the prescribing of naloxone to one individual with intent for the drug to be administered to another at-risk individual e.g., a family member, roommate or friend. The idea being that victims are unable to administer to themselves and the medication is better suited to be carried by a family member or friend likely to be with the victim. This is currently available in 33 states.²² Most laws include limited liability protection for all parties involved.
- 2) **Standing naloxone orders:** Standing orders outline a formalized hospital, system or statewide process allowing for naloxone to be distributed to an individual without a prescription. The standing order is not patient specific, and the patient may not be known to the prescriber, so the patient needs only to meet criteria to receive the medication from the pharmacist e.g., vaccinations and emergency contraception. Again limited immunity is provided for persons acting in good faith. Typically there is one prescriber for the entire program. This approach is currently available in 24 states.²²
 - a. There are other alternatives to standing orders that may be helpful in some states or situations where they can be amended for this purpose.
 - i. Collaborative practice agreements: These delegate medical management to pharmacists for certain predefined conditions. e.g., Medication Therapy Management (MTM) programs. Some version exists in 48 states.
 - ii. Pharmacist as prescriber: Here the medication is provided and the physician is informed later. Pharmacists may need to maintain additional certification. Some version exists in 8 states.

Cost

Cost can be a significant barrier for many patients and EDs. The two main considerations when planning the budget for your program are the cost of the naloxone and other kit items and the time the healthcare worker spends educating the patient to use the kit.

In the early planning stages, you should explore a variety of sources to fund your program. Hospital or departmental funding, health department program grants and city or county funds may be available. It is important to identify key allies in these areas who can support you in this effort. Your ED Chairman, hospital leadership, health commissioners, medical examiners

or coroners, community based naloxone distribution programs, syringe exchange programs and even law enforcement can advocate for you in this effort. Your local health departments may already have an opioid task force or other resources in place to tackle the epidemic from other angles and they may be eligible for grants that can be utilized for your project.

If your community has already established a naloxone distribution program it would be beneficial to work with them, as they may be aware of local sources of available funding.

Your county medical examiner or coroner can provide compelling data on opioid overdose mortality, which can support requests for funding. The criminal justice system is another resource that is not often considered when looking for healthcare funding. Local police departments, jails, drug courts, your state Attorney General and the United States Attorney's office are often tasked with providing services to opioid users. Drug seizure funds are routinely distributed to police department budgets for drug prevention efforts and may be available to assist your program. In Massachusetts, New York and Ohio, State Attorney Generals have been able to negotiate a six dollar rebate on each vial of naloxone with the naloxone manufacturer

Billing in the ED is divided into two fundamentally different categories: Professional service and facilities.

Depending on your state Medicaid program, it may be possible for you to bill the patient's insurance for the naloxone kit and the education provided to the patient.

Amphastar. This rebate has been available only to programs providing naloxone for overdose prevention and not for general hospital use.

Depending on your state Medicaid program, it may be possible for you to bill the patient's insurance for the naloxone kit and the education provided to the patient. It is vital that you work with a state Medicaid representative to develop a process to do this. Many state Medicaid programs will provide coverage for naloxone and it may be as simple as adding it to your state's outpatient formulary. The next step is to identify an expert in your hospital in ED billing and coding. Billing for the naloxone kits as well as for the education that is provided to the patient can improve the sustainability of your program. Billing in the ED is divided into two fundamentally different categories: Professional service and facilities.²⁴ Professional service codes are determined based on the "complexity and intensity of provider performed work and include the cognitive effort expended by the provider."²⁴ The facility or technical coding guidelines reflect the "volume and intensity of resources utilized by the facility to provide patient care."²⁴ Unlike professional service billing, the Centers for Medicaid and Medicare Services (CMS) does not have any standard guidelines for facility level coding.^{24,25} CMS

even allows hospitals to write their own rules for facility billing as long as they are applied consistently.^{24,25} To be reimbursed for the naloxone kits, you must bill the facility rather than a professional code.

If you want to distribute the Evzio™ auto-injector, Kaléo, the company that produces Evzio™, has some donation community service programs with

hospitals, community and government organizations. There are also special insurance reimbursement and rebate programs. Most insurance plans, including government insurance plans, will cover Evzio™,

Cost (continued)

however some insurance companies will require prior authorization.²⁶ Low income, uninsured patients who do not qualify for Medicare or Medicaid, may be eligible to receive Evzio™ at no cost through the Kaléo Cares Patient Assistance Program.²⁷

The last stage of planning your Emergency Department naloxone program involves ordering and assembling your naloxone kits. Items that may be included in the kit include educational materials, pamphlets or DVDs; nasal atomizers or needle and syringes depending on route of administration, gloves, face shield for rescue breathing and two doses of naloxone. A sample budget is outlined in Table 1.

Naloxone is currently available from three different manufacturers: Amphastar, Hospira and Kaléo. The Amphastar product, a prefilled syringe containing two milligrams of naloxone in a concentration of 2 mg/2mL, is the recommended concentration for intranasal administration. The average cost for a single (2 mg) nasally administered dose of the AmphaStar product is \$33. Next, Hospira manufactures a single dose vial, which is available in the recommended concentration of 0.4/mg for intramuscular administration. The

average cost for a single dose (0.4 mg) of the Hospira intramuscular naloxone is \$15.83. Your hospital may be eligible for a cost discount, check with you pharmacist. Finally, Kaléo manufactures an auto-injector device, which includes two (0.4 mg each) doses of intramuscular naloxone. This product costs \$287.50 per dose, but the cost is significantly reduced if covered by insurance or provided through Kaléo's cost assistance program. The FDA has accepted new drug applications for two pre-assembled nasal products by the pharmaceutical companies Adapt Pharma²⁸ and Indivior PLC.²⁹ These products may become available commercially in the coming year.

The initial purchase of items for your kits should be made only after closely evaluating your patient population to estimate the number of at risk patients seen in your Emergency Department. This will help you purchase an appropriate quantity of materials and naloxone. It is advisable to purchase naloxone on an as needed basis as it has a shelf life of only 2 years. If too much medication is purchased initially, valuable funding may be wasted when the drug reaches its expiration date.

Table 1: Sample Budget

Item	Cost Estimate
Luer-Jet™ Prefilled Syringe - Naloxone 2mg/2 ml vial \$28.50 /vial (2 vials per kit- \$57/kit) NDC NUMBER 76329-3369-1 http://www.amphastar.com/images/Naloxone.pdf	\$57
LMA MAD Nasal™, Nasal Atomizers (2 per kit) http://www.lmana.com/pwpccontrol.php?pwplD=6359	\$6.50
DVDs (with cases)	\$1.25
Teal, Nylon CHECK WALLET bag 7"W X 5.5"H http://www.otco.com/security-bags/zipper-bags/zipper-check-wallet-bags.htm	\$1.19
Quick Reference Guide	\$0.38
Laerdal® Face Shield — http://www.laerdal.com/us/doc/115/Laerdal-Face-Shield	\$1.64
Brochures	\$0.25

Means of Distribution

Providers can provide patients naloxone by direct to patient distribution, writing a prescription, referral to a community organization, or referral to a pharmacy participating in a Collaborative Practice Agreement (see Regulatory section for more information).

Formulations

Currently, naloxone is offered in intramuscular (IM) and intranasal (IN) formulations. It is recommended that you prescribe two doses of whichever formulation you choose. IM formulations can be delivered in the lateral arm or thigh. Intranasal (IN) naloxone has similar efficacy and safety as IM naloxone for reducing overdose and is given as a spray in each nostril.^{30,31}

IM naloxone can also be dispensed as a two single-dose vials, 0.4mg/mL, with a 3cc syringe and 1 inch 23G needle (Image 1). Evzio™ (Image 2) is an FDA approved pre-filled auto-injector that contains a single dose of Naloxone 0.4 mg,³² prescribed in packs of two auto-injectors. IN naloxone is prescribed as a 2mL, prefilled luer-lock needleless syringe with an IN mucosal atomizing device (Image 3).³³

Prescription Writing

An easy way to implement take-home naloxone within any Emergency Department is to write a prescription and provide patients at risk for overdose with written instructions. There are a variety of existing resources available that can be tailored to patients at risk for heroin overdose or at risk for prescription opioid overdose.

How to Distribute

Naloxone distribution programs can vary based on available resources, as well as hospital, pharmacy, city, and state policies and regulations. Providing a prescription and written overdose education instructions is low-impact to the health system and can be implemented immediately. However, there can be barriers associated with patients taking the prescription to pharmacy including pharmacy availability and patient out-of-pocket costs. Providing a patient with naloxone and overdose education as a 'kit' can eliminate these barriers. Kits can be assembled in the pharmacy and either sent to the ED or stored in an ED automated medication management system to be retrieved by nurses after a prescription is written by a physician. Some EDs utilize a standing order policy, where all kits are prescribed by a physician's standing order and can be dispensed at discretion of the nurse, social worker, or a drug counselor.



Image 1: Harm Reduction Coalition's SKOOP: Skills and Knowledge on Overdose Prevention IM naloxone rescue kit with two doses IM naloxone 0.4mg/mL, syringe, needle, and barrier for rescue breathing.



Image 2: Evzio™ autoinjector and trainer



Image 3: Intranasal naloxone 2mg/2mL needleless syringe and MAD.

Patient Education

Patient education should contain information about overdose risk factors, how to avoid an opioid overdose, how to recognize and respond to an overdose, and how to administer naloxone. A combination of in-person counseling and an educational video or handout is best, although not always feasible. Family and friends should be included in the training whenever possible, as they will likely be administering naloxone to your patient in an out of hospital overdose.

In person education can be provided by anyone in the ED: social workers, drug counselors, nurses, pharmacists, or physicians. The advantages of in person education are that it is interactive, questions can be answered in real time, can be tailored to each patient, and can be combined with referral to treatment. The primary barriers to implementation are time required by providers and cost for service provision. If you choose to utilize an overdose educator who can spend at least fifteen minutes providing education, you can bill for this service by documentation of Screening, Brief Intervention and Referral to Therapy (SBIRT). SBIRT is an evidence-based approach used to deliver early intervention and treatment to individuals with problematic use, abuse and dependence on alcohol and illicit drugs. To bill for this service, a healthcare professional must spend a minimum of 15 minute of face-to-face time with the patient and document a screening tool such as the DAST-10, the drug abuse-screening test. In some centers, such as Boston Medical Center, this is provided by hospital employed Health Promotion Advocates (HPAs).

Use of out of hospital resources can help minimize the time and cost barriers. Hospitals in Rhode Island, for

example, can consult a community Recovery Coach (RC) who is trained, certified, and employed by a community recovery organization. The HPAs and RCs both provide overdose education and naloxone training in addition to referral to addiction treatment, but consultation of the community RCs allows for in person training without additional cost to the hospital. This has allowed for OEND implementation at community hospitals in addition to academic centers.

If in-person education is not feasible, there are multiple video and handout resources available for use. Videos can be shown on hospital televisions or a computer on wheels. Handouts can be included in the naloxone kit. Video and handout materials are cheaper, portable, uniform, and can be referenced by patients at home. However they are also less personal, less engaging, and use of handouts alone misses and opportunity for referral to addiction treatment. PrescribetoPrevent.org has a selection of educational videos, handouts, and online training modules tailored to different patient populations. Images 4 and 5 are stills from one of the available educational videos, “Staying Alive on the Outside.” On the following page is an example educational handout that is distributed from Lifespan affiliate EDs in Rhode Island. PrescribetoPrevent.org has several examples of patient educational materials you can use. Of note, Evzio™ provides audible instructions for how to administer naloxone, making it incredibly easy to use, even for people who have no prior training.

Check with your hospital, but your educational materials may need to be approved by your hospital Pharmacy and Therapeutics Committee.

A combination of in-person counseling and a video or handout educational materials is best, although not always feasible.



Images 4 and 5: Still shots from “Staying Alive On the Outside”

Naloxone/911

How to use intranasal naloxone in an overdose

1



Are they breathing? → Call 911 for help

Signs of an overdose:

- Slow or shallow breathing
- Gasping for air when sleeping or weird snoring
- Pale or bluish skin
- Slow heartbeat, low blood pressure
- Won't wake up or respond (rub knuckles on sternum)

All you have to say:

"Someone is unresponsive and not breathing."

Give clear address and location.



2



Airway →

Make sure nothing is inside the person's mouth.

Rescue breathing

Oxygen saves lives. Breathe for them.

One hand on chin, tilt head back, pinch nose closed.

Make a seal over mouth & breathe in

1 breath every 5 seconds

Chest should rise, not stomach

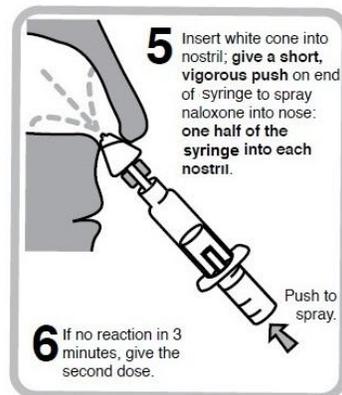
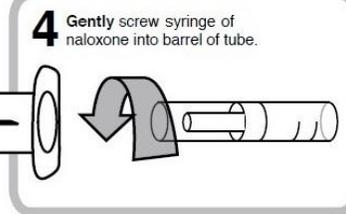
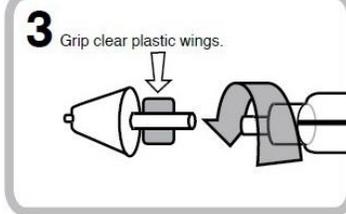
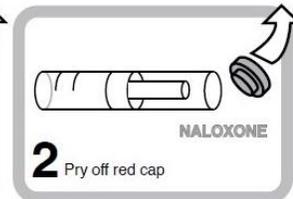
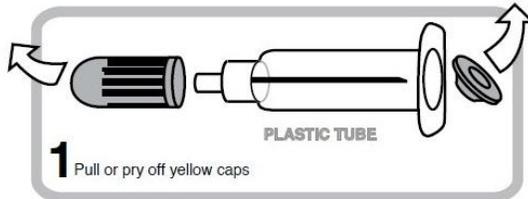


3



Prepare Naloxone

Are they any better? Can you get naloxone and prepare it quickly enough that they won't go for too long without your breathing assistance?



Adapted from: HarmReduction.org

4



Evaluate + support

- Continue rescue breathing
- Place them on their side (rescue position), especially if they are throwing up
- Give another shot of naloxone if they aren't breathing in 3 minutes
- Naloxone wears off in 30-90 minutes
- Comfort them; withdrawal can be unpleasant
- Get them medical care and help them not use more opiate right away
- Encourage survivors to seek treatment if they feel they have a problem

Keep Naloxone at room temperature and away from light.

Anchor Recovery Center
(401) 721-5100
<http://www.anchorrecovery.org/>

How to Avoid Overdose

- Only take medicine prescribed to you
- Call a doctor if your pain gets worse. Do not take more medicine than instructed
- Never mix pain medicine (opioids) with alcohol or sleeping pills
- Dispose of unused medications safely
- Store your medicine in a secure place
- Learn how to use naloxone
- Teach family and friends to recognize and respond to an overdose

Risk Factors for Overdose

- Mixing pain medicine (opioids) with alcohol, benzodiazepines, or other drugs
- Lower tolerance due to a period of not using opioids or drugs (after time in jail, a hospital, detox, or drug-free treatment)
- Using drugs by yourself

Adapted from: prescribtoprevent.org, harmreduction.org, 'Get the SKOOP' overdose prevention brochure

Conclusion

The first steps to setting up an OEND program is to understand the local policies and regulations about standing orders, third party prescribing, collaborative practice agreements, Good Samaritan laws, and provider medication distribution. This will determine the options you have for distribution, whether it be giving naloxone directly to a patient or providing patients with a prescription or referral to a local pharmacy or community organization. If policies allow for direct to patient naloxone

distribution, cost considerations may affect what formulation you decide to use and the components of your kit. Naloxone and SBIRT are billable to the insurance, but state and local departments of health, grants, and hospital funding, should also be considered as potential sources of funding. There are a wide range of educational materials available for both providers and patients. PrescribetoPrevent.org has a repository of materials you can use. If your hospital does not have the capacity to provide in-

person overdose education and naloxone training, there may be local community organizations you can partner with. Finally, when making policies and procedures for your program, make them simple, incorporated into usual emergency care, have clear goals, roles and expectations, and define your patient population. Patients and providers will need continuous education and should have an avenue to provide feedback for program quality improvement.

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