

**Exploring Naloxone Uptake and Use
Public Meeting
July 1 and 2, 2015

Summary Report**

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Exploring Naloxone Uptake and Use

July 1 and 2, 2015, Public Meeting

Meeting Summary

The Problem

The United States is experiencing an opioid overdose epidemic. In 2013, more than 16,000 people died from a prescription opioid overdose—about one death every 33 minutes.¹ Overall, overdose deaths in the United States now outnumber deaths from motor vehicle crashes.² The increase in opioid prescriptions during the last decade has contributed to this epidemic. Whereas in the 1990s opioids were used primarily to treat end-of-life and acute cancer pain, they are now also being prescribed to treat non-cancer pain associated with osteoarthritis, rheumatoid arthritis, lower back problems, fibromyalgia, and dental surgery. Unfortunately, treatment capacity remains limited. A March 2015 *American Journal of Public Health* article titled [National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment](#) concluded that there are “significant gaps between treatment need and capacity . . . at the state and national levels.”

As summarized in this report, numerous efforts are underway to reduce the risk of death from opioid overdose. Local community-based organizations have taken the lead in this effort. They have helped reduce overdose deaths among their clients, mostly illicit drug users, by making the prescription drug naloxone available, often at low or no cost, to their clients and clients’ friends and family members. During the past several years, state and federal public health organizations have launched a variety of programs around the country with the goal of stemming the overdose epidemic. Nevertheless, presenters and participants at this meeting expressed concern that many of the efforts underway to reduce opioid overdose are not reaching the U.S. population in general; that certain populations remain at high risk; and that the broad U.S. population needs more information about the risk of opioid overdose, the causes and signs of addiction and overdose, available drug treatment options, and the availability of naloxone to reverse overdose.

The Centers for Disease Control and Prevention (CDC) describes persons at increased risk for prescription opioid overdose as disproportionately male, non-Hispanic white, poor and rural, people who increase their opioid dose (as dose increases, risk of overdose increases), and people who doctor- and pharmacy-shop, hoping to obtain additional pills.³

Naloxone

Naloxone is an opioid receptor antagonist that can rapidly reverse the overdose of either prescription (e.g., OxyContin) or illicit (e.g., heroin) opioids. Historically, naloxone has been most commonly used by trained medical personnel in hospital emergency departments and on ambulances. However, with the rise in prescription opioid use and the associated rise in overdose deaths, naloxone, preceded or followed by a 911 call, has assumed a larger role in the outpatient setting and is increasingly being used by non-medical personnel to reverse overdose.

¹ Grant Baldwin, Director, Division of Unintentional Injury Prevention, Centers for Disease Control and Prevention (CDC).

² Michael Botticelli, Director, National Drug Control Policy, Executive Office of the President.

³ Grant Baldwin, CDC.

The only naloxone therapy with an indication for bystander use is an injectable medicine—Evzio, a take-home auto-injector approved by the Food and Drug Administration (FDA) in April 2014. Although intranasal versions of naloxone are also available, they are not FDA-approved and so their safety and efficacy compared to injectable versions are not known—the intranasal versions are created from the generic injectable naloxone and packaged and distributed in kit form. Applications for two intranasal formulations have been submitted to FDA for marketing approval and are undergoing FDA expedited review.

The Public Meeting

On July 1 and 2, 2015, representatives from academia, government, community-based organizations, industry, and patient advocacy groups came together at FDA’s White Oak campus in Silver Spring, Maryland, to discuss a variety of scientific, legal, regulatory, logistical, and clinical issues surrounding the use of naloxone. This was the second federal public meeting on this topic; the first was a one-day workshop at FDA on [April 12, 2012](#)⁴ to discuss the value of wider availability of naloxone, beyond the more common medical settings, to reduce the incidence of opioid overdose deaths and to hear from the public on related issues of concern.

The overarching topics discussed at the 2015 public meeting, titled ***Exploring Naloxone Uptake and Use***, included identifying which populations are most at risk for opioid overdose, what progress has been made since the 2012 meeting in expanding the availability of naloxone, and what public health organizations around the country can do to keep up the momentum achieved since 2012 to ensure the growth and sustainability of existing programs while expanding naloxone availability to new populations.

The 2015 meeting was organized through a collaboration of FDA, the National Institute of Drug Abuse (NIDA), the CDC, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Health Resources and Services Administration (HRSA). Detailed information about the meeting, including most slide presentations, a web cast, the full transcript, and this summary report, are available on FDA’s [2015 Naloxone Meeting](#) web page.⁵ The following summary highlights key themes and findings, organized primarily around the meeting agenda.

Meeting Summary

Peter Lurie, Associate Commissioner, Office of Public Health Strategy and Analysis (FDA), welcomed attendees, noting how much progress had been made since the first meeting in 2012 and crediting those accomplishments to “the hard work and dedication of people in this very room, people who pioneered these programs, who were willing to advocate for them, to actually carry them out. . . .”

Michael Botticelli, Director of the Office of National Drug Control Policy (ONDCP), Executive Office of the President, and Grant Baldwin, Director, Division of Unintentional Injury Prevention at CDC, provided introductory remarks. They set the stage by describing the extent of non-medical use of opioids in the

⁴ See more about the 2012 workshop on FDA’s web page at <http://www.fda.gov/Drugs/NewsEvents/ucm277119.htm>. Accessed, September 2015.

⁵ See FDA’s web page at <http://www.fda.gov/drugs/newsevents/ucm442236.htm> for more information on the 2015 meeting. Accessed, September 2015.

United States today, including the use of prescription opioids, and the dramatic increase in opioid-related deaths during the past decade.

Michael Botticelli noted that although the numbers of overdoses from prescription opioid use dropped slightly in 2013, the reduction was offset by an increase in heroin use and deaths—some individuals move from prescription opioids to heroin when opioids are no longer easy to obtain. He expressed his concern that so many people are still unaware of the existence of naloxone—what it does and how to obtain it—emphasizing that although much has been achieved since the 2012 meeting, more work is needed. He emphasized that his office, ONDCP, will continue to support the many efforts of the people present at this meeting. The U.S. [National Drug Control Strategy](#) has noted the importance of naloxone since 2012.⁶

Grant Baldwin provided the context of the meeting, giving attendees an in-depth review of the latest statistics on the public health burden of prescription drug- and heroin-related overdoses (see his slide presentation for details on use, geographic locations of highest use, overdose, and overdose fatalities, among other details).

I. Naloxone Use Today—Recent Trends

Naloxone use among illicit drug users, first responders, and family members is growing as a direct result of an increase in the number of programs that address opioid education, overdose, and treatment at national, state, and local levels. The [World Health Organization](#) has issued guidelines on community management of opioid overdose.⁷ Local and national policies for the use of naloxone have expanded in the United Kingdom (U.K.). State and local programs in the United States have expanded recently as well. With this increase in use have also come changes in the market structure and pricing trends for naloxone.

- Naloxone is increasingly available in the United States, in different formulations.
 - According to the IMS data, sales of the 0.4 milligram per milliliter strength (primarily used in vials) make up about 70 to 80 percent of the total sold in a given year; sales of the one milligram per milliliter strength (reported to be used intranasally as well as by injection) make up the rest. These formulations have had sales on the order of hundreds of thousands to millions per year since April 2014 (launch of Evzio).
 - For Evzio, wholesaler distribution has increased since its launch, rising from less than 1,000 per quarter initially to more than 2,500 per quarter at the beginning of 2015. Evzio sales remain well below the sales of other formulations.
- The share of outpatient use of naloxone has risen sharply since 2009.
 - Sales of naloxone from wholesalers to outpatient settings increased by 72 percent during the last 5 years while sales to inpatient or emergency room settings declined by 12 percent.
- The number of sites/persons dispensing naloxone has increased.

⁶ The *National Drug Control Strategy* is available at https://www.whitehouse.gov/sites/default/files/ondcp/2012_ndcs.pdf. Accessed, October 2015.

⁷ See World Health Organization at http://www.who.int/substance_abuse/publications/management_opioid_overdose/en/. Accessed, October 2015.

- A June 2015 CDC [Morbidity and Mortality Weekly Report](#) showed a 243% increase in the number of sites that provide naloxone, a 183% increase in the number of laypersons providing naloxone kits, and a 160% increase in the number of overdose reversals. Of 26,000 reversals since the mid-1990s, 8,000 took place in 2013.⁸
- The Chicago Recovery Alliance was the first organization to distribute naloxone in the U.S. and has been doing so for 18 years. To date, they have distributed naloxone to over 38,000 people and received more than 6,000 reports of peer-reversals with naloxone.
- New York has a sizable program, including an initiative called Learning to Cope. This initiative makes naloxone and training available to prisoners⁹ and their families just before their release from prison.
 - Prisoners with a history of drug use are at greatest mortality risk during the first couple of weeks after release from prison. This is the population targeted in the study.
 - Prisoners due for release were identified and given “standard care” or standard care plus naloxone kits.
 - Although the final results have not been tabulated, the findings so far from interviews are that “two to three uses of naloxone [are happening] on another person for each time it’s used on the individual to whom we’ve assigned it.”
 - No evidence was found that providing naloxone was associated with a safety risk.
- A number of states have very active community drug addiction/public health organizations that are making naloxone and treatment options available to drug users and their families, individuals on opioid pain therapy and their families, and others who may come in contact with individuals at risk of overdose. Presenters described efforts under way in North Carolina, New York, Massachusetts, Ohio, and Rhode Island.
- Many presenters advocated wider naloxone availability.
 - Community-based advocacy groups have been the leaders in making naloxone available among certain populations (e.g., illicit drug users who can obtain it, for example, from needle exchange programs).
 - For many reasons (historical, political, legal, financial, organizational), naloxone has been and remains much less available to individuals at increased risk who are not considered part of the drug user category (e.g., individuals on opioids for long-term for pain or their families; individuals and their families who are in treatment for addiction disorder; individuals leaving prison; and individuals in rural communities with limited access to public health facilities). At the time of the meeting, only 19 states included the FDA-approved auto injector Evzio on their Medicaid formulary.
- There was a call from several presenters and speakers in the Open Public Hearing for a broad public health intervention to reach these additional populations more comprehensively.

⁸ See the report at <http://stacks.cdc.gov/view/cdc/31626#relatedDocuments>. Accessed, October 2015.

⁹ Prisoners are also the focus of a study underway in England. See the presentation by John Strang (day-one transcript, beginning on page 77) for a detailed analysis of the prisoner release study, the N-ALIVE prison release trial.

II. Identifying Patients in Need and Getting Naloxone to Them—National Programs

A number of national efforts have been successful in identifying patients at risk of overdose. In two examples, since 2012, SAMSHA and the U.S. Department of Veterans Affairs (VA) have launched large programs to help identify individuals who should have access to naloxone. Both programs make a range of information available to the public and support co-prescribing (see Section IV).

- SAMHSA has an [Opioid Overdose Toolkit](#), available online,¹⁰ that provides a variety of information about prescribing naloxone and other issues of interest to communities, families, first responders, and those in treatment. The toolkit also can help prescribers minimize the risk of opioid overdose through adherence to clinical practices. The number of people accessing the toolkit has increased significantly in recent years. Since the launch of the toolkit in August 2013, there have been 56,430 downloads of the entire toolkit or sections of it. It will be updated in the near future, so suggestions for input were invited. SAMHSA is also exploring the identification of optimal distribution points for naloxone in rural or resource-poor areas or to reach other specific populations at risk.
- The VA has an extensive program, launched two years ago, that includes prescribing naloxone and providing overdose education. The VA experience is an example of how to quickly move from community-based best practices to a large medical system framework.
 - The VA effort was built on the experience and knowledge of other organizations, including community-based groups around the country, on what was learned at the workshop on opioid overdose in 2012, and on information gathered from discussions with colleagues with similar experience in Scotland.
 - The program is based on prevention education. The VA provides a kit containing prevention and safety information, information on the use of the naloxone, two doses of naloxone, a face shield for rescue breathing, and disposable gloves. Prescribers receive example prescription forms to use with their patients and information on how to identify a patient who is a likely candidate for receiving a kit. Videos on the program are available on YouTube.
 - As of July 1, 2015, the VA had 79 reported opioid overdose reversals with over 5,400 kits dispensed. In many cases, the kits are being used to reverse overdoses in individuals other than those who originally received the kit.

III. Clinical, Legal, and Other Barriers

According to presenters and comments made during the public sessions, a number of barriers remain to making naloxone more widely available.

Prescription Status

- Some asserted that naloxone's prescription status is a barrier that prevents the medication from reaching locations where it may be needed most, such as public parks, bars, and specific neighborhoods.

¹⁰ Information about the Toolkit is available at <http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit-Updated-2014/SMA14-4742>. Accessed, October 2015.

- Many people at highest risk (nonprescription opioid and other illicit drug users) don't necessarily access the traditional medical system.
- Within the traditional medical system, many patients and prescribers are unaware of or uncertain about naloxone. Physician acceptance of naloxone use could be a focus of future interventions.
 - Patients at risk who see medical professionals may feel uncomfortable asking for naloxone even when they know about it, because that might identify them as drug users.
 - Doctors may not know about it or may feel uncomfortable offering it.
 - In a North Carolina health professional education program, prescribers identified not knowing how to discuss the topic with their patients and not wanting to offend patients as obstacles to naloxone provision; some prescribers insisted that opioid misuse is not an issue in their practice (Project Lazarus).
 - One public commenter suggested making education about overdose and naloxone use a mandatory component of becoming an addiction-certified physician. Establishing a program for distribution of naloxone to people at risk could become a requirement for accreditation by the Joint Commission or the Commission on Accreditation of Rehabilitation Facilities (CARF).¹¹

Legal issues

- The legal situation with regard to reporting overdoses and prescribing naloxone remains in flux. All states have a civil Good Samaritan law, providing some civil immunity to people who stop at an emergency situation and render aid in good faith. However, overdose witnesses are typically concerned about possible criminal action, not civil liability. Fear of arrest and/or prosecution for drug use can prevent overdose witnesses from calling for emergency help.
- As of July 2015, 33 states had passed laws providing limited criminal liability to people who call 911 to report an overdose. These laws vary from state to state in terms of whom they cover and the extent of coverage.
 - Many of the laws provide immunity from prosecution, but not arrest, to those summoning emergency assistance in the case of an overdose.
 - Most of the laws only provide protection from minor drug law violations, but some extend the protection to other crimes.
 - In general, more recently passed laws provide more protection, with some newer laws providing protection from arrest as well as probation and parole violations, in addition to protection from prosecution.
- The majority of states have also taken steps to remove legal and regulatory barriers to naloxone access and remove any possible liability for prescribing, dispensing, or administering naloxone in good faith.
 - At the time of the meeting, 39 states had enacted naloxone access laws, which provide civil or criminal immunity for naloxone administration by licensed health care providers or lay responders.

¹¹ CARF is an international, independent, nonprofit accreditor of health and human services organizations.

- The majority of states permit naloxone to be prescribed to people other than a prescriber’s patients, and most states permit it to be prescribed via standing or protocol order. Approximately a dozen states explicitly permit naloxone to be dispensed by laypeople, in addition to traditional pharmacies.
- Increasing costs are a barrier.
 - In the late 1990s, a 10cc vial of naloxone cost \$1.43 and a 1cc vial, as little as 20 cents.
 - Recent price increases (in January 2014) for the 0.4 milligram per milliliter strength and (in September 2014) for the one milligram per milliliter strength were 50 and 60 percent, respectively.
 - In 2014, 25 percent of all generic injectable molecules had at least one formulation with a month-to-month price increase of 60 percent or more.
- The price of naloxone has strained public health budgets as well as those of community-based harm reduction organizations.

IV. *Naloxone Co-prescribing*

Co-prescribing naloxone alongside the opioids provided in community-based office settings was recommended by many presenters and commenters during the open segment of the meeting.

- There was agreement that co-prescribing involves more than writing a prescription. Ideally, it entails provider education, substance-use assessments, overdose prevention toolkits, patient and family education, and referral to treatment programs, among other elements.
 - A number of community programs (e.g., Project Lazarus in North Carolina) have been working to educate prescribers, some of whom have not supported co-prescribing programs because they think they might be enabling patients.
 - The risk of prescription opioid abuse can be minimized by using appropriate patient screening, rational prescribing, and abuse-deterrent formulations. With a good script on how to talk to patients and to families, co-prescribing can be made much more understandable.
 - Offering to co-prescribe can be the beginning of a conversation to address the critical elements of a potential drug problem (e.g., risks of using opioids, risk of overdose, naloxone use, and treatment options) and can even be useful in identifying patients who wish to end long-term opioid use.
- Awareness of naloxone availability and comfort with prescribing the drug appear to be key hurdles for prescribers. One suggestion was to create a Drug Enforcement Administration (DEA) program that ensures that all prescribers who obtain DEA numbers are made aware of the availability of naloxone and their ability to co-prescribe it.
- Clinicians can use Prescription Drug Monitoring Programs (PDMPs), available in all but one state, to help guide their opioid/naloxone prescribing decisions. PDMPs collect, monitor, and analyze electronically transmitted prescribing and dispensing data submitted by pharmacies and dispensing practitioners. The data are used to support state efforts in education, research, enforcement, and abuse prevention. Physicians can look up patient opioid use, including prescribing by other practitioners, before writing a prescription.

Targeted vs universal availability

There was extensive discussion around who should receive naloxone—should everyone (universal prescribing) or should only certain (targeted) populations? Researchers agree that individuals at risk can be classified as having a relative risk of overdose or an absolute risk of overdose and that both would need to be taken into account in any targeted program.

- Obvious **targeted** populations would be patients on chronic pharmaceutical opioids for pain, persons who inject opioids, those with diagnosed substance use disorders, persons who have overdosed previously, and prisoners with an opioid use history who are soon to be released (and whose tolerance is low).
 - Generally, other indicators of increased risk, indicating that a person might be targeted for co-prescribing, include *high* opioid dose, longer duration of treatment, larger supplies of therapy, concomitant benzodiazepine prescriptions, getting controlled substances from multiple providers or multiple pharmacies, some types of mental health disorders, and underlying respiratory conditions.
- **Universal** co-prescribing of naloxone can serve many goals. In a recent research project in San Francisco, preliminary findings indicated that patients are appreciative of naloxone prescriptions; pharmacists and prescribers strongly favor prescribing naloxone to patients on opioids; and naloxone seems to help providers engage patients in a dialogue about opioid safety.
 - When providers are advised to offer naloxone to all patients on opioids, they automatically self-select those they believe are at higher risk for overdose.
 - Universal co-prescribing of naloxone could help reach those individuals typically not included in research projects on how to identify persons at risk. These individuals include, for example, children and teenagers who might accidentally or intentionally gain access to and overdose on an opioid drug prescribed to others.
- Pricing is critical in discussions around targeted vs universal coverage and may limit the ability of programs or health systems to provide universal coverage.

V. The Importance of Training in Naloxone Use

There was broad agreement that training or instruction is needed to be able to use naloxone successfully. Training should cover issues such as how to identify an overdose, how to use the delivery device, how to maintain respiratory integrity during and after naloxone administration, and that those who administer the naloxone should stay with the patient until emergency personnel arrive. A number of states have launched programs to train persons receiving naloxone as well as trainers who can train others. Several programs to educate pharmacists in the use of naloxone are underway.

- Even though a number of good training curricula exist, they tend to be tailored to specific topics (e.g., injectable vs intranasal use; how best to maintain respiratory integrity). SAMHSA is developing a standardized model overdose prevention education curriculum.
 - It is critical that trainings and the programs that deliver them are designed to eliminate active or inadvertent biases against drug users or their families.
- SAMHSA also launched the **Opioid Overdose Prevention Challenge**, a competition with a prize to develop a computer application that builds on the toolkit.

- Rhode Island has assembled a list of best practices—and they have doubled their naloxone distribution through a variety of methods and programs.
 - Trainings should target specific groups, including, for example, illicit drug users, health care professionals, pharmacists, emergency room bedside coaches, or addiction treatment providers.
 - Place-based training (e.g., specific to high-risk locations like parks, certain bars, parts of town, etc.) is also recommended.
 - A 2013 statewide pharmacy-based naloxone training program was launched in Rhode Island via a collaborative pharmacy practice agreement. This model involves pharmacists receiving overdose prevention education, which qualifies them to initiate a prescription for naloxone or honor a request for naloxone directly from a patient or caregiver.
 - The Rhode Island non-profit NOPE-RI trained 66 credentialed trainers in overdose prevention, naloxone administration, and the Good Samaritan law. These trainers are training others, mostly police and emergency personnel.
- Since 2008, Massachusetts has funded community coalitions using SAMHSA block grants with support from the State Bureau of Substance Abuse Services, and the state recently launched a pharmacy training program modeled after the program in Rhode Island.
- Community coalitions can add real value by providing another source of advocacy, outreach, and training to support programs in development.
- Partnering with treatment providers is crucial because their patients may be at greater risk of overdose.

VI. Use by EMS, Police, and Fire Departments

As first responders, emergency medical service (EMS) personnel, police, and fire departments play a critical role in responding to life-threatening emergencies. In 2013, according to the database that captures EMS activities (NEMESIS), 113,153 patients received naloxone through EMS.

- Barriers to naloxone use by EMS, police, and fire departments remain. Coordinating these community services is critical.
 - State and local laws and regulations vary with respect to who may carry naloxone. There are four levels of providers (emergency medical response, emergency medical technician (EMT), advanced EMT, and paramedic), with paramedics receiving the most training on different drugs.
 - In some locations, only paramedics can carry naloxone. In half the states, basic EMTs cannot administer naloxone (even though there is no particular evidence of EMTs using naloxone improperly).
 - It is estimated that police arrive before EMS 80% of the time (sometimes, EMS cannot enter a house until law enforcement arrives). As a result, police administration of naloxone is very important. Yet, in some locations, local health directors have stated that law enforcement personnel are not allowed to carry naloxone.

- Liability issues remain due to lack of consistency and clarity of laws and policies. In South Carolina, a naloxone law, but not a Good Samaritan law, related to naloxone was passed. Research indicates that no liability lawsuits against prescribers have been brought to date.
- It can be difficult to find a prescriber who is willing to write a standing order.
- The National EMS [Scope of Practice Model](#), developed by the National Highway Traffic Safety Administration, serves as the overall guidance for basic EMTs to administer medicine.¹² However it currently does not include administration of naloxone. Plans are to begin an update in 2016, and including naloxone will be one of the considerations.
- Rural areas face substantial barriers to naloxone use.
 - Approximately 80 percent of the land mass in the United States is rural. Urban centers, however, have about 80 percent of the EMS workforce.
 - Rural areas can face numerous obstacles to quick response, including geography, long distances, low population density, call volumes, and lack of availability of training and education for EMS personnel. Many communities have only volunteer fire departments.
 - Not all EMS are staffed with paramedics—especially in rural areas. There is a need to train more basic EMTs in the use of naloxone, and the focus of additional training should be on rural areas.
- New York State has implemented a pilot to expand naloxone use in rural parts of the state; the pilot includes training. To date, 2,000 EMTs have been trained in naloxone use, and there have been 223 opioid overdose reversals.
- Law enforcement must be involved as naloxone programs are being developed and implemented. New programs to train law enforcement are continually being established.
 - At the time of the meeting, there were approximately 570 law enforcement training programs up and running, mostly along the East Coast, sponsored by the Harm Reduction Coalition. HRC is willing to share their materials, including videos.
 - The Justice Department released its [Law Enforcement Toolkit](#) in October 2014 in response to state and local requests for help and the Attorney General’s directive to explore how to include naloxone in their practices and policies.¹³
 - The Toolkit contains samples and templates such as standard operating procedures and training materials that agencies could adopt and make their own.
 - Users of the Toolkit can also obtain assistance with training or in identifying presenters (funding is available to support short-term requests).
- A number of funding options are available for start-up programs.

¹² See the *Scope of Practice Model* at <https://www.nremt.org/nremt/downloads/Scope%20of%20Practice.pdf>. Accessed, October 2015.

¹³ This toolkit is available at <https://www.bjatrainning.org/tools/naloxone/Naloxone-Background>. Accessed, October 2015.

- HRSA’s Federal Office of Rural Health Policy is making funding available to some rural communities, focusing on the purchase and placement of naloxone, training, and treatment programs in remote areas.
- Funding can sometimes be obtained through state prosecutors, who may be willing to make asset forfeiture dollars available.
- Byrne Justice Assistance grants are formula funding grants to local communities and states.
- The Harold Rogers Prescription Drug Monitoring Program solicitation can fund community and statewide programs (e.g., law enforcement naloxone programs).
- Public health departments can sometimes also provide funding.
- A number of suggestions were made about how to obtain buy-in for state and local naloxone programs.
 - All the stakeholders in a community must come to the table to resolve issues because in the end, this is a community problem that must be dealt with in the community.
 - EMS, law enforcement managers, and top public health officials are especially important. One suggestion was to start with the police. New York State has trained 3,200 New York state troopers in the use of naloxone and has had 73 reversals. North Carolina also has conducted extensive outreach to the law enforcement community with notable successes.
 - Standardization of practices would be very helpful. A place to start might be at the state Offices of Emergency Medical Services.
 - [Getnaloxonenow.org](http://getnaloxonenow.org) is a web-based educational site funded by NIH’s National Institute on Drug Abuse.¹⁴ Training modules for bystanders and first responders (e.g., police, fire fighters, and basic EMTs, not paramedics) are available for download.

VII. *New Naloxone Products/Formulations*

FDA is reviewing two applications for the approval of intranasal versions of naloxone. Representatives of Adapt Pharma and Indivior summarized how their intranasal naloxone devices work and updated meeting attendees on the status of their applications at FDA. FDA presented on the process for moving a prescription product to over-the-counter use (OTC switch) and described a possible new regulatory program currently under consideration at FDA. The pros and cons of making naloxone available OTC were discussed as was the possibility of allowing pharmacists to make naloxone available.

- Community-based organizations face a number of barriers when trying to obtain sufficient amounts of naloxone.
 - Its prescription status is a barrier. A non-profit organization has to have some sort of medical/legal infrastructure (e.g., a prescriber who is willing to work with them) to even

¹⁴ This web page contains extensive information on naloxone and overdose prevention. See <http://www.getnaloxonenow.org/>. Accessed, October 2015.

purchase naloxone because as lay people they cannot sign up for a contract to purchase a pharmaceutical. (Passing standing order legislation would help alleviate this obstacle.)

- Financial barriers are increasing. Funding is seldom dedicated to purchase naloxone, and prices continue to rise.

Over-the-counter availability

- There was some support for FDA changing naloxone’s status from prescription to OTC. Under this scenario, naloxone could be made available in the local drugstore for whoever wished to purchase it, with no requirement for a prescription. This approach has a number of advantages, including that patients or their family members could initiate the process themselves, without a prescription, potentially widening distribution. It would also help patients who may feel uncomfortable discussing their situations with their physicians. A number of related issues were considered.
 - An OTC switch is a process governed by FDA regulations, and particular studies would have to be done, for example, to gather data on consumer label comprehension.
 - To qualify for OTC use, it must be demonstrated that it would be easy to use naloxone without the guidance of a medical professional (a “learned intermediary”). It must also be demonstrated that the user can correctly diagnose the condition.
 - Usually, the application holder requests a switch from prescription to OTC use. An outside party could also do that through the petition process, but the petitioner must provide a full development program and complete data to support the switch. No outside party has so far produced data to support such a switch.
- Other drawbacks were noted.
 - A new label needs to be developed and tested (i.e., additional studies, some involving 500 to 600 individuals).
 - Current OTC labels are very small and may not be able to contain all of the information needed for a naloxone product (e.g., how to recognize an overdose, adverse effects).
 - OTC products typically do not qualify for medical insurance reimbursement.
 - There is concern that making naloxone available OTC and not maintaining the distribution approaches through community-based organizations might limit naloxone availability to the population that needs it most free of charge.
 - In 2015, Pennsylvania passed Act 139, allowing third-party prescribing (e.g., to potential witnesses, police, firefighters, staff of substance use treatment programs, and staff of homeless shelters). Physicians can now prescribe by standing order so a physician doesn’t have to be present for training and dispensing. Broad immunity from liability for prescribers and for those who administer naloxone is also included. This Act has resulted in dramatic increases in availability (e.g., naloxone was provided to 457 people in the first 5 months of 2015 compared to 157 in all of 2014) and in reversals (104 so far this year).
 - Some questioned whether illicit drug users would feel comfortable going into the pharmacy to purchase an OTC product.

Possible new FDA regulatory framework

- FDA is considering a new regulatory framework, the Nonprescription Safe Use Regulatory Expansion program (NSURE).
 - NSURE could allow the use of innovative technologies (e.g., smart phone apps, computer kiosks at the point of purchase, vending machines, or websites) to help educate consumers about issues related to novel switch programs.
 - The framework for this new program is still in development, and it will likely take several years before it is in place.

Role for pharmacies

- Could pharmacies play a larger role in making naloxone more available?
 - A variety of approaches are being implemented at pharmacies (e.g., collaborative practice agreements with physicians, state-wide naloxone protocols allowing pharmacists to prescribe naloxone, authority to distribute without a prescription). Rhode Island and Massachusetts both have implemented similar programs.
 - The Drug Policy Alliance has partnered with the California Pharmacy Association to co-sponsor a bill to create pharmacy naloxone access. However, legal, policy, and cost barriers often remain, and approaches vary from state to state.
 - Pharmacies can suffer when reimbursement rates fail to keep up with product price increases. Washington State has developed model legislation, and something similar to this legislation might help iron out some of the price/reimbursement variability from state to state.
 - Stigma could discourage some pharmacies or pharmacists from selling naloxone to *suspect* individuals. Similarly, prospective purchasers may not feel comfortable purchasing the product in pharmacies.

VIII. Measuring Progress and Impact

- It is important to have as much evidence as possible to inform policy decisions.
- The VA system is studying the impact of education and training regarding opioid overdose prevention and recognition, opioid overdose rescue response, and the distribution of naloxone kits for outpatient administration of opioid reversal.
 - Outreach to prescribers, pharmacists, and others in the VA system and tracking of kit offers and distribution, reversal reports, and follow-up treatment takes place via electronic communication and is stored in the VA data warehouse.
 - Multiple pilots are under way to educate and inform prescribers (e.g., focus groups, visits by VA *detailers* who can help identify patients with increased risk for overdose and plan intervention strategies).
- An important area of additional research is what happens after an overdose reversal. Are referrals being made to emergency care or drug treatment?
- A lot of research is underway around community-based naloxone distribution, especially around the impact of increased education on overdose and knowledge of, and skills at, using naloxone. For example, John Strang (U.K.) described a randomized trial under way in the U.K., the N-ALIVE

prison release trial, which examined distribution of naloxone to prisoners upon their release. Although the researchers now question whether the primary outcome was well chosen and all data have not been analyzed, the program has succeeded in expanding the use of naloxone among the study population.¹⁵

- Many studies are descriptive, so it will be important going forward to do more rigorous studies. Needs include:
 - Baseline data, control or comparison groups, randomization, adequate statistical testing, larger sample sizes, longitudinal data, and accounting for multiple interventions
 - Qualitative studies to understand how different policies and programs are being implemented
 - Research to understand how best to reach different types of opioid-using populations and the different types of responders currently involved in naloxone provision
 - Assessments of trends in availability, cost, and introduction of new products (e.g., how these factors could change the dynamics of implementation, patient and provider behaviors, and health outcomes)
 - Best practices in implementation of naloxone programs and their uptake
 - Quantitative studies to measure impact on outcomes
 - Studies of people who are receiving opioids for pain with no other histories of substance abuse disorders to be able to understand the impact in various populations (the vast majority of available research now looks at heroin users)
- Data sources can be a challenge. Poison control data are useful, but sometimes hard to access. State-based surveillance systems can provide data, including EMS or pre-hospital data, emergency department data, and data from PDMPs.
- In addition to data, it is important to develop standard definitions and standardize the methods and approaches used to identify specific activities and impacts on health outcomes.

At the end of the two-day meeting, Kimberly Jeffries Leonard, Deputy Director, Center for Substance Abuse Treatment, SAMHSA, provided closing comments. She praised the successes to date and underscored SAMHSA's continued support.

IX. General Conclusions

- There was broad general agreement among meeting participants and attendees that naloxone should be made widely available to persons at risk for overdose and to those who might witness an overdose.
- The number of states with programs that support overdose prevention and treatment has greatly increased since 2012. Nevertheless, many states and communities still lack programs to make

¹⁵ John Strang (U.K.) describes this study in detail in the day-one transcript, beginning on page 77.

naloxone and treatment follow-up available—rural areas where resources may be geographically distant face special barriers. Ensuring that multiple methods of delivery are available will help ensure that naloxone reaches the many populations at risk.

- A large national educational effort would contribute substantially to informing the U.S. public about the risks of overdose, the availability of naloxone and guidance for use, the causes of addiction disease, and treatment options. Such a program could also help sustain and build more of the momentum gathered since the FDA workshop on naloxone in 2012.
- There was broad support for co-prescribing naloxone, with some supporting universal co-prescribing and others recommending a more risk-based approach. National recommendations on who should receive naloxone would be useful.
- A new distribution model may be needed. The cost of naloxone is preventing some programs from initiating or expanding opioid overdose prevention efforts. Some presenters recommended specific federal budget allocations via state block grant programs and other state-based initiatives to increase access to naloxone through community-based programs.
- Training in the use of naloxone and addiction treatment options should be part of any program to make naloxone available.
- More standardization within and among the states with regard to naloxone use is needed (e.g., Good Samaritan laws, the role pharmacists can play, broader EMT training and use, immunity laws, and laws to allow wider naloxone access to laypeople).
- The policy environment around overdose prevention and naloxone use is rapidly changing. Rigorous research using standardized approaches and definitions is critical to inform policy development and implementation.
- Continued collaboration among all stakeholders is critical for achieving additional progress.