

SAMHSA
Opioid Overdose
TOOLKIT

Facts for Community Members

Five Essential Steps for First Responders

Information for Prescribers

Safety Advice for Patients & Family Members

Recovering from Opioid Overdose



ACKNOWLEDGMENTS

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SCOPE OF THE PROBLEM

Opiate overdose continues to be a major public health problem in the United States. It has contributed significantly to accidental deaths among those who use, misuse or abuse illicit and prescription opioids. In fact, U.S. overdose deaths involving prescription opioid analgesics increased to about 17,000 deaths a year in 2010 [1, 2], almost double the number in 2001 [1]. This increase coincided with a nearly fourfold increase in the use of prescribed opioids for the treatment of pain [3].

WHAT ARE OPIOIDS? Opioids include illegal drugs such as heroin, as well as prescription medications used to treat pain such as morphine, codeine, methadone, oxycodone (Oxycontin, Percodan, Percocet), hydrocodone (Vicodin, Lortab, Norco), fentanyl (Duragesic, Fentora), hydromorphone (Dilaudid, Exalgo), and buprenorphine (Subutex, Suboxone).

Opioids work by binding to specific receptors in the brain, spinal cord and gastrointestinal tract. In doing so, they minimize the body's perception of pain. However, stimulating the opioid receptors or "reward centers" in the brain also can trigger other systems of the body, such as those responsible for regulating mood, breathing and blood pressure.

HOW DOES OVERDOSE OCCUR? A variety of effects can occur after a person takes opioids, ranging from pleasure to nausea, vomiting, severe allergic reactions (anaphylaxis) and overdose, in which breathing and heartbeat slow or even stop.

Opioid overdose can occur when a patient deliberately misuses a prescription opioid or an illicit drug such as heroin. It also can occur when a patient takes an opioid as directed, but the prescriber miscalculated the opioid dose or an error was made by the dispensing pharmacist or the patient misunderstood the directions for use.

Also at risk is the person who takes opioid medications prescribed for someone else, as is the individual who combines opioids — prescribed or illicit — with alcohol, certain other medications, and even some over-the-counter products that depress breathing, heart rate, and other functions of the central nervous system [4].

WHO IS AT RISK? Anyone who uses opioids for long-term management of chronic cancer or non-cancer pain is at risk for opioid overdose, as are persons who use heroin [5]. Others at risk include persons who are:

- Receiving rotating opioid medication regimens (and thus are at risk for incomplete cross-tolerance).
- Discharged from emergency medical care following opioid intoxication or poisoning.
- At high risk for overdose because of a legitimate medical need for analgesia, coupled with a suspected or confirmed history of substance abuse, dependence, or non-medical use of prescription or illicit opioids.
- Completing mandatory opioid detoxification or abstinent for a period of time (and presumably with reduced opioid tolerance and high risk of relapse to opioid use).
- Recently released from incarceration and a past user or abuser of opioids (and presumably with reduced opioid tolerance and high risk of relapse to opioid use).

Tolerance develops when someone uses an opioid drug regularly, so that their body becomes accustomed to the drug and needs a larger or more frequent dose to continue to experience the same effect.

Loss of tolerance occurs when someone stops taking an opioid after long-term use. When someone loses tolerance and then takes the opioid drug again, they can experience serious adverse effects, including overdose, even if they take an amount that caused them no problem in the past.

FACTS FOR COMMUNITY MEMBERS

STRATEGIES TO PREVENT OVERDOSE DEATHS

STRATEGY 1: Encourage providers, persons at high risk, family members and others to learn how to prevent and manage opioid overdose. Providers should be encouraged to keep their knowledge current about evidence-based practices for the use of opioid analgesics to manage pain, as well as specific steps to prevent and manage opioid overdose.

Federally funded Continuing Medical Education courses are available to providers at no charge at <http://www.OpioidPrescribing.com> (six courses funded by the Substance Abuse and Mental Health Services Administration) and on MedScape (two courses funded by the National Institute on Drug Abuse).

Helpful information for laypersons on how to prevent and manage overdose is available from Project Lazarus at <http://projectlazarus.org/> or from the Massachusetts Health Promotion Clearinghouse at <http://www.maclclearinghouse.org>.

STRATEGY 2: Ensure access to treatment for individuals who are misusing or addicted to opioids or who have other substance use disorders. Effective treatment of substance use disorders can reduce the risk of overdose and help overdose survivors attain a healthier life. Medication-assisted treatment, as well as counseling and other supportive services, can be obtained at SAMHSA-certified and DEA-registered opioid treatment programs (OTPs), as well as from physicians who are trained to provide care in office-based settings with medications such as buprenorphine and naltrexone.

Information on treatment services available in or near your community can be obtained from your state health department, state alcohol and drug agency, or from the federal Substance Abuse and Mental Health Services Administration (see page 7).

STRATEGY 3: Ensure ready access to naloxone. Opioid overdose-related deaths can be prevented when naloxone is administered in a timely manner. As a narcotic antagonist, naloxone displaces opiates from receptor sites in the brain and reverses respiratory depression that usually is the cause of overdose deaths [5]. *During the period of time when an overdose can become fatal, respiratory depression can be reversed by giving the individual naloxone [4].*

On the other hand, naloxone is *not* effective in treating overdoses of benzodiazepines (such as Valium, Xanax, or Klonopin), barbiturates (Seconal or Fiorinal), clonidine, Elavil, GHB, or ketamine. It also is not effective in overdoses with stimulants, such as cocaine and amphetamines (including methamphetamine and Ecstasy). However, if opioids are taken in combination with other sedatives or stimulants, naloxone may be helpful.

Naloxone injection has been approved by FDA and used for more than 40 years by emergency medical services (EMS) personnel to reverse opioid overdose and resuscitate persons who otherwise might have died in the absence of treatment [6].

Encourage providers and others to learn about preventing and managing opioid overdose.

Ensure access to treatment for individuals who are misusing or addicted to opioids or who have other substance use disorders.

FACTS FOR COMMUNITY MEMBERS

Naloxone has no psychoactive effects and does not present any potential for abuse [1, 4]. Injectable naloxone is relatively inexpensive. It typically is supplied as a kit with two syringes, at a cost of about \$6 per dose and \$15 per kit [7].

For these reasons, it is important to determine whether local EMS personnel or other first responders have been trained to care for overdose, and whether they are allowed to stock naloxone in their drug kits. In some jurisdictions, the law protects responders from civil liability and criminal prosecution for administering naloxone. So-called “Good Samaritan” laws are in effect in 10 states and the District of Columbia, and are being considered by legislatures in at least a half-dozen other states [8]. Such laws provide protection against prosecution for both the overdose victim and those who respond to overdose. To find states that have adopted relevant laws, visit the CDC’s website at: [http://www.cdc.gov/HomeandRecreational Safety/Poisoning/laws/immunity.html](http://www.cdc.gov/HomeandRecreationalSafety/Poisoning/laws/immunity.html).

STRATEGY 4: Encourage the public to call 911. An individual who is experiencing opioid overdose needs immediate medical attention. An essential first step is to get help from someone with medical expertise as quickly as possible [9, 10]. Therefore, members of the public should be encouraged to call 911. All they have to say is, “Someone is not breathing” and give a clear address and location.

STRATEGY 5: Encourage prescribers to use state Prescription Drug Monitoring Programs (PDMPs). State Prescription Drug Monitoring Programs (PDMPs) have emerged as a key strategy for addressing the misuse and abuse of prescription opioids and thus preventing opioid overdoses and deaths. Specifically, prescribers can check their state’s PDMP database to determine whether a patient is filling the prescriptions provided and/or obtaining prescriptions for the same or similar drug from multiple physicians.

While a majority of states now have operational PDMPs, the programs differ from state to state in terms of the exact information collected, how soon that information is available to physicians, and who may access the data. Therefore, information about the program in a particular state is best obtained directly from the state PDMP or from the board of medicine or pharmacy.

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FACTS FOR COMMUNITY MEMBERS

RESOURCES FOR COMMUNITIES

Resources that may be useful to local communities and organizations are found at the following websites:

Substance Abuse and Mental Health Services Administration (SAMHSA)

National Treatment Referral Helpline
1-800-662-HELP (4357) or 1-800-487-4889
(TDD — for hearing impaired)

National Substance Abuse Treatment Facility Locator:
<http://www.findtreatment.samhsa.gov/TreatmentLocator> to search by state, city, county, and zip code

Buprenorphine Physician & Treatment Program Locator:
http://www.buprenorphine.samhsa.gov/bwns_locator

State Substance Abuse Agencies:
<http://findtreatment.samhsa.gov/TreatmentLocator/faces/abuseAgencies.jspx>

Center for Behavioral Health Statistics and Quality (CBHSQ):
<http://www.samhsa.gov/data/>

SAMHSA Publications: <http://www.store.samhsa.gov>
1-877-SAMHSA (1-877-726-4727)

Centers for Disease Control and Prevention (CDC)

<http://www.cdc.gov/Features/VitalSigns/PainkillerOverdoses>
<http://www.cdc.gov/HomeandRecreationSafety/Poisoning>

White House Office of National Drug Control Policy (ONDCP)

State and Local Information: <http://www.whitehouse.gov/ondcp/state-map>

Association of State and Territorial Health Officials (ASTHO)

Prescription Drug Overdose: State Health Agencies Respond (2008):
<http://www.astho.org>

National Association of State Alcohol and Drug Abuse Directors (NASADAD)

State Issue Brief on Methadone Overdose Deaths:
<http://www.nasadad.org/nasadad-reports>

National Association of State EMS Officials (NASEMSO)

National Emergency Medical Services Education Standards:
<http://www.nasemso.org>

American Association for the Treatment of Opioid Dependence (AATOD)

Prevalence of Prescription Opioid Abuse: <http://www.aatod.org/>

*Resources that
may be useful
to local communities
and organizations...*

FIVE ESSENTIAL STEPS FOR FIRST RESPONDERS

Overdose is common among persons who use illicit opioids such as heroin and among those who misuse medications prescribed for pain, such as oxycodone, hydrocodone, and morphine. The incidence of opioid overdose is rising nationwide. For example, between 2001 and 2010, the number of poisoning deaths in the United States nearly doubled, largely because of overdoses involving prescription opioid analgesics [1]. This increase coincided with a nearly fourfold increase in the use of prescribed opioids for the treatment of pain [3].

To address the problem, emergency medical personnel, health care professionals, and patients increasingly are being trained in the use of the opioid antagonist naloxone hydrochloride (naloxone or Narcan), which is the treatment of choice to reverse the potentially fatal respiratory depression caused by opioid overdose. (Note that naloxone has no effect on non-opioid overdoses, such as those involving cocaine, benzodiazepines, or alcohol [11].)

Based on current scientific evidence and extensive experience, the steps outlined below are recommended to reduce the number of deaths resulting from opioid overdoses [2, 4, 7, 12-14].

STEP 1: CALL FOR HELP (DIAL 911)

AN OPIOID OVERDOSE NEEDS IMMEDIATE MEDICAL ATTENTION.

An essential step is to get someone with medical expertise to see the patient as soon as possible, so if no EMS or other trained personnel are on the scene, dial 911 immediately. All you have to say is: "Someone is not breathing." Be sure to give a clear address and/or description of your location.

STEP 2: CHECK FOR SIGNS OF OPIOID OVERDOSE

Signs of **OVERDOSE**, which often results in death if not treated, include [11]:

- Face is extremely pale and/or clammy to the touch
- Body is limp
- Fingernails or lips have a blue or purple cast
- The patient is vomiting or making gurgling noises
- He or she cannot be awakened from sleep or is unable to speak
- Breathing is very slow or stopped
- Heartbeat is very slow or stopped.

Signs of **OVERMEDICATION**, which may progress to overdose, include [11]:

- Unusual sleepiness or drowsiness
- Mental confusion, slurred speech, intoxicated behavior
- Slow or shallow breathing
- Pinpoint pupils
- Slow heartbeat, low blood pressure
- Difficulty waking the person from sleep.

Because opioids depress respiratory function and breathing, one telltale sign of a person in a critical medical state is the "death rattle." If a person emits a "death rattle" — an exhaled breath with a very distinct, labored sound coming from the throat — emergency resuscitation will be necessary immediately, as it almost always is a sign that the individual is near death [13].

FIVE ESSENTIAL STEPS FOR FIRST RESPONDERS

STEP 3: SUPPORT THE PERSON'S BREATHING

Ideally, individuals who are experiencing opioid overdose should be ventilated with 100% oxygen before naloxone is administered so as to reduce the risk of acute lung injury [2, 4]. In situations where 100% oxygen is not available, rescue breathing can be very effective in supporting respiration [2]. Rescue breathing involves the following steps:

- Be sure the person's airway is clear (check that nothing inside the person's mouth or throat is blocking the airway).
- Place one hand on the person's chin, tilt the head back and pinch the nose closed.
- Place your mouth over the person's mouth to make a seal and give 2 slow breaths.
- The person's chest should rise (but not the stomach).
- Follow up with one breath every 5 seconds.

STEP 4: ADMINISTER NALOXONE

Naloxone (Narcan) should be administered to any person who shows signs of opioid overdose, or when overdose is suspected [4]. Naloxone injection is approved by the FDA and has been used for decades by emergency medical services (EMS) personnel to reverse opioid overdose and resuscitate individuals who have overdosed on opioids.

Naloxone can be given by intramuscular or intravenous injection every 2 to 3 minutes [4, 13-14]. The most rapid onset of action is achieved by intravenous administration, which is recommended in emergency situations [13]. The dose should be titrated to the smallest effective dose that maintains spontaneous normal respiratory drive.

Opioid-naive patients may be given starting doses of up to 2 mg without concern for triggering withdrawal symptoms [2, 4, 7, 14].

The intramuscular route of administration may be more suitable for patients with a history of opioid dependence because it provides a slower onset of action and a prolonged duration of effect, which may minimize rapid onset of withdrawal symptoms [2, 4, 7].

DURATION OF EFFECT. The duration of effect of naloxone is 30 to 90 minutes, and patients should be observed after this time frame for the return of overdose symptoms [4, 13-14]. The goal of naloxone therapy should be to restore adequate spontaneous breathing, but not necessarily complete arousal [4].

More than one dose of naloxone may be needed to revive someone who is overdosing. Patients who have taken longer-acting opioids may require further intravenous bolus doses or an infusion of naloxone [4].

Comfort the person being treated, as withdrawal triggered by naloxone can feel unpleasant. As a result, some persons become agitated or combative when this happens and need help to remain calm.

SAFETY OF NALOXONE. The safety profile of naloxone is remarkably high, especially when used in low doses and titrated to effect [2, 4, 13, 17]. When given to individuals who are not opioid-intoxicated or opioid-dependent, naloxone produces no clinical effects, even at high doses. Moreover, while rapid opioid withdrawal in tolerant patients may be unpleasant, it is not life-threatening.

Naloxone can safely be used to manage opioid overdose in pregnant women. The lowest dose to maintain spontaneous respiratory drive should be used to avoid triggering acute opioid withdrawal, which may cause fetal distress [4].

FIVE ESSENTIAL STEPS FOR FIRST RESPONDERS

STEP 5: MONITOR THE PERSON'S RESPONSE

All patients should be monitored for recurrence of signs and symptoms of opioid toxicity for at least 4 hours from the last dose of naloxone or discontinuation of the naloxone infusion. Patients who have overdosed on long-acting opioids should have more prolonged monitoring [2, 4, 7].

Most patients respond by returning to spontaneous breathing, with minimal withdrawal symptoms [4]. The response generally occurs within 3 to 5 minutes of naloxone administration. (Rescue breathing should continue while waiting for the naloxone to take effect. [2, 4, 7])

Naloxone will continue to work for 30 to 90 minutes, but after that time, overdose symptoms may return [13, 14]. Therefore, it is essential to get the person to an emergency department or other source of medical care as quickly as possible, even if he or she revives after the initial dose of naloxone and seems to feel better.

SIGNS OF OPIOID WITHDRAWAL. The signs and symptoms of opioid withdrawal in an individual who is physically dependent on opioids may include, but are not limited to, the following: body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness, and increased blood pressure. In the neonate, opioid withdrawal may also include convulsions, excessive crying, and hyperactive reflexes [13].

NALOXONE-RESISTANT PATIENTS. If a patient does not respond to naloxone, an alternative explanation for the clinical symptoms should be considered. The most likely explanation is that the person is not overdosing on an opioid but rather some other substance or may even be experiencing a non-overdose medical emergency. A possible explanation to consider is that the individual has overdosed on buprenorphine, a long-acting opioid partial agonist. Because buprenorphine has a higher affinity for the opioid receptors than do other opioids, naloxone may not be effective at reversing the effects of buprenorphine-induced opioid overdose [14].

In all cases, support of ventilation, oxygenation, and blood pressure should be sufficient to prevent the complications of opioid overdose and should be given priority if the response to naloxone is not prompt.

SUMMARY:

Do's and Don'ts in Responding to Opioid Overdose

- **DO** support the person's breathing by administering oxygen or performing rescue breathing.
- **DO** administer naloxone.
- **DO** put the person in the "recovery position" on the side, if he or she is breathing independently.
- **DO** stay with the person and keep him/her warm.
- **DON'T** slap or try to forcefully stimulate the person — it will only cause further injury. If you are unable to wake the person by shouting, rubbing your knuckles on the sternum (center of the chest or rib cage), or light pinching, he or she may be unconscious.
- **DON'T** put the person into a cold bath or shower. This increases the risk of falling, drowning or going into shock.
- **DON'T** inject the person with any substance (salt water, milk, "speed," heroin, etc.). The only safe and appropriate treatment is naloxone.
- **DON'T** try to make the person vomit drugs that he or she may have swallowed. Choking or inhaling vomit into the lungs can cause a fatal injury.

NOTE: All naloxone products have an expiration date, so it is important to check the expiration date and obtain replacement naloxone as needed.

Opioid overdose is a major public health problem, accounting for almost 17,000 deaths a year in the United States [15]. Overdose involves both males and females of all ages, ethnicities, and demographic and economic characteristics, and involves both illicit opioids such as heroin and, increasingly, prescription opioid analgesics such as oxycodone, hydrocodone, fentanyl and methadone [3].

Physicians and other health care providers can make a major contribution toward reducing the toll of opioid overdose through the care they take in prescribing opioid analgesics and monitoring patients' response, as well as through their acuity in identifying and effectively addressing opioid overdose. Federally funded CME courses are available at no charge at <http://www.OpioidPrescribing.com> (six courses funded by the Substance Abuse and Mental Health Services Administration) and on MedScape (two courses funded by the National Institute on Drug Abuse).

OPIOID OVERDOSE

The risk of opioid overdose can be minimized through adherence to the following clinical practices, which are supported by a considerable body of evidence [2, 7, 16-17].

ASSESS THE PATIENT. Obtaining a history of the patient's past use of drugs (either illicit drugs or prescribed medications with abuse potential) is an essential first step in appropriate prescribing. Such a history should include very specific questions. For example:

- "In the past 6 months, have you taken any medications to help you calm down, keep from getting nervous or upset, raise your spirits, make you feel better, and the like?"
- "Have you been taking any medications to help you sleep? Have you been using alcohol for this purpose?"
- "Have you ever taken a medication to help you with a drug or alcohol problem?"
- "Have you ever taken a medication for a nervous stomach?"
- "Have you taken a medication to give you more energy or to cut down on your appetite?"

The patient history also should include questions about use of alcohol and over-the-counter (OTC) preparations. For example, the ingredients in many common cold preparations include alcohol and other central nervous system (CNS) depressants, so these products should not be used in combination with opioid analgesics.

Positive answers to any of these questions warrant further investigation.

TAKE SPECIAL PRECAUTIONS

WITH NEW PATIENTS. Many experts recommend that additional precautions be taken in prescribing for new patients [7, 17]. These might involve the following:

1. **Assessment:** In addition to the patient history and examination, the physician should determine who has been caring for the patient in the past, what medications have been prescribed and for what indications, and what substances (including alcohol, illicit drugs and OTC products) the patient has reported using. Medical records should be obtained (with the patient's consent) directly from past caregivers.
2. **Emergencies:** In emergency situations, the physician should prescribe the smallest possible quantity (typically not exceeding 3 days' supply) and arrange for a return visit the next day. The patient's identity should be verified by asking for proper identification.
3. **Non-emergencies:** In non-emergency situations, only enough of an opioid analgesic should be prescribed to meet the patient's needs until the next appointment. The patient should be directed to return to the office for additional prescriptions, as telephone orders do not allow the physician to reassess the patient's continued need for the medication.

INFORMATION FOR PRESCRIBERS

STATE PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs) have emerged as a key strategy for addressing the misuse and abuse of prescription opioids and thus preventing opioid overdoses and deaths. Specifically, prescribers can check their state's PDMP database to determine whether a patient is filling the prescriptions provided and/or obtaining prescriptions for the same or similar drugs from multiple physicians.

While many states now have operational PDMPs, the programs differ from state to state in terms of the exact information collected, how soon that information is available to physicians, and who may access the data. Therefore, information about the program in a particular state is best obtained directly from the PDMP or from the state board of medicine or pharmacy.

SELECT AN APPROPRIATE MEDICATION. Rational drug therapy demands that the efficacy and safety of all potentially useful medications be reviewed for their relevance to the patient's disease or disorder [2, 17].

When an appropriate medication has been selected, the *dose*, *schedule*, and *formulation* should be determined. These choices often are just as important in optimizing pharmacotherapy as the choice of medication itself. Decisions involve (1) dose (based not only on age and weight of the patient, but also on severity of the disorder, possible loading-dose requirement, and the presence of potentially interacting drugs); (2) timing of administration (such as a bedtime dose to minimize problems associated with sedative or respiratory depressant effects); (3) route of administration (chosen to improve compliance/adherence as well as to attain peak drug concentrations rapidly); and (4) formulation (e.g., selecting a patch in preference to a tablet, or an extended-release product rather than an immediate-release formulation).

Even when sound medical indications have been established, physicians typically consider three additional factors before deciding to prescribe an opioid analgesic [2, 17]:

1. The **severity of symptoms**, in terms of the patient's ability to accommodate them. Relief of symptoms is a legitimate goal of medical practice, but using opioid analgesics requires caution.
2. The patient's **reliability in taking medications**, noted through observation and careful history-taking. The physician should assess a patient's history of and risk factors for drug abuse before prescribing any psychoactive drug and weigh the benefits against the risks. The likely development of physical dependence in patients on long-term opioid therapy should be monitored through periodic check-ups.

3. The **dependence-producing potential of the medication**. The physician should consider whether a product with less potential for abuse, or even a non-drug therapy, would provide equivalent benefits. Patients should be warned about possible adverse effects caused by interactions between opioids and other medications or substances, including alcohol.

At the time a drug is prescribed, patients should be informed that it is illegal to sell, give away, or otherwise share their medication with others, including family members. The patient's obligation extends to keeping the medication in a locked cabinet or otherwise restricting access to it and to safely disposing of any unused supply (visit <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm> for advice from the FDA on how to safely dispose of unused medications).

EDUCATE THE PATIENT AND OBTAIN INFORMED CONSENT. Obtaining informed consent involves informing the patient about the risks and benefits of the proposed therapy and of the ethical and legal obligations such therapy imposes on both physician and patient [17]. Such informed consent can serve multiple purposes: (1) it provides the patient with information about the risks and benefits of opioid therapy; (2) it fosters adherence to the treatment plan; (3) it limits the potential for inadvertent drug misuse; and (4) it improves the efficacy of the treatment program.

Patient education and informed consent should specifically address the potential for physical dependence and cognitive impairment as side effects of

INFORMATION FOR PRESCRIBERS

opioid analgesics. Other issues that should be addressed in the informed consent or treatment agreement include the following [17]:

- The agreement instructs the patient to stop taking all other pain medications, unless explicitly told to continue by the physician. Such a statement reinforces the need to adhere to a single treatment regimen.
- The patient agrees to obtain the prescribed medication from only one physician and, if possible, from one designated pharmacy.
- The patient agrees to take the medication only as prescribed (for some patients, it may be possible to offer latitude to adjust the dose as symptoms dictate).
- The agreement makes it clear that the patient is responsible for safeguarding the written prescription and the supply of medications, and arranging refills during regular office hours. This responsibility includes planning ahead so as not to run out of medication during weekends or vacation.
- The agreement specifies the consequences for failing to adhere to the treatment plan, which may include discontinuation of opioid therapy if the patient's actions compromise his or her safety.

Both patient and physician should sign the informed consent agreement, and a copy should be placed in the patient's medical record. It also is helpful to give the patient a copy of the agreement to carry with him or her, to document the source and reason for any controlled drugs in his or her possession. Some physicians provide a laminated card that identifies the individual as a patient of their practice. This is helpful to other physicians who may see the patient and in the event the patient is seen in an emergency department.

EXECUTE THE PRESCRIPTION ORDER. Careful execution of the prescription order can prevent manipulation by the patient or others intent on obtaining opioids for non-medical purposes. For example, federal law requires that prescription orders for controlled substances be signed and dated on the day they are issued. Also under federal law, every prescription order must include at least the following information:

- Name and address of the patient
- Name, address and DEA registration number of the physician
- Signature of the physician
- Name and quantity of the drug prescribed
- Directions for use
- Refill information
- Effective date if other than the date on which the prescription was written.

Many states impose additional requirements, which the physician can determine by consulting the state medical licensing board. In addition, there are special federal requirements for drugs in different schedules of the federal Controlled Substances Act (CSA), particularly those in Schedule II, where many opioid analgesics are classified.

Blank prescription pads — as well as information such as the names of physicians who recently retired, left the state, or died — all can be used to forge prescriptions. Therefore, it is a sound practice to store blank prescriptions in a secure place rather than leaving them in examining rooms.

NOTE: The physician should immediately report the theft or loss of prescription blanks to the nearest field office of the federal Drug Enforcement Administration and to the state board of medicine or pharmacy.

MONITOR THE PATIENT'S RESPONSE TO TREATMENT. Proper prescription practices do not end when the patient receives a prescription. Plans to monitor for drug efficacy and safety, compliance, and potential development of tolerance must be documented and clearly communicated to the patient [2].

Subjective symptoms are important in monitoring, as are objective clinical signs (such as body weight, pulse rate, temperature, blood pressure, and levels of drug metabolites in the bloodstream). These can serve as early signs of therapeutic failure or unacceptable adverse drug reactions that require modification of the treatment plan.

Asking the patient to keep a log of signs and symptoms gives him or her a sense of participation in the treatment

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program and facilitates the physician's review of therapeutic progress and adverse events.

Simply recognizing the potential for non-adherence, especially during prolonged treatment, is a significant step toward improving medication use [18]. Steps such as simplifying the drug regimen and offering patient education also improve adherence, as do phone calls to patients, home visits by nursing personnel, convenient packaging of medication, and periodic urine testing for the prescribed opioid as well as any other respiratory depressant.

Finally, the physician should convey to the patient through attitude and manner that any medication, no matter how helpful, is only part of an overall treatment plan.

When the physician is concerned about the behavior or clinical progress (or the lack thereof) of a patient being treated with an opioid analgesic, it usually is advisable to seek a consultation with an expert in the disorder for which the patient is being treated *and* an expert in addiction. Physicians place themselves at risk if they continue to prescribe opioids in the absence of such consultations [17].

CONSIDER PRESCRIBING NALOXONE ALONG WITH THE PATIENT'S INITIAL OPIOID PRESCRIPTION.

With proper education, patients on long-term opioid therapy and others at risk for overdose may benefit from having a naloxone kit to use in the event of overdose [4].

Patients who are candidates for such kits include those who are:

- Taking high doses of opioids for long-term management of chronic malignant or non-malignant pain.
- Receiving rotating opioid medication regimens (and thus are at risk for incomplete cross-tolerance).
- Discharged from emergency medical care following opioid intoxication or poisoning.
- At high risk for overdose because of a legitimate medical need for analgesia, coupled with a suspected or confirmed history of substance abuse, dependence, or non-medical use of prescription or illicit opioids.
- Completing mandatory opioid detoxification or abstinence programs.
- Recently released from incarceration and a past user or abuser of opioids (and presumably with reduced opioid tolerance and high risk of relapse to opioid use).

It also may be advisable to suggest that the at-risk patient create an "overdose plan" to share with friends, partners and/or caregivers. Such a plan would contain information on the signs of overdose and how to administer naloxone or otherwise provide emergency care (as by calling 911).

DECIDE WHETHER AND WHEN TO END OPIOID THERAPY.

Certain situations may warrant immediate cessation of prescribing. These generally occur when out-of-control behaviors indicate that continued prescribing is unsafe or causing harm to the patient [2]. Examples include altering or selling prescriptions, accidental or intentional overdose, multiple episodes of running out early (due to excessive use), doctor shopping, or engaging in threatening behavior.

When such events arise, it is important to separate the patient as a person from the behaviors caused by the disease of addiction, as by demonstrating a positive regard for the person but no tolerance for the aberrant behaviors.

In such a situation, the essential steps are to (1) stop prescribing, (2) tell the patient that continued prescribing is not clinically supportable (and thus not possible), (3) urge the patient to accept a referral for assessment by an addiction specialist, (4) educate the patient about signs and symptoms of spontaneous withdrawal and urge the patient to go to the emergency department if withdrawal symptoms occur, and (5) assure the patient that he or she will continue to receive care for the presenting symptoms or condition [17].

Identification of a patient who is abusing a prescribed opioid presents a major therapeutic opportunity. The physician should have a plan for managing such a patient, typically involving work with the patient and the patient's family, referral to an addiction expert for assessment and placement in a formal addiction treatment program, long-term participation in a 12-Step mutual help program such as Narcotics Anonymous, and follow-up of any associated medical or psychiatric comorbidities [2].

In all cases, patients should be given the benefit of the physician's concern and attention. It is important to remember that even drug-seeking patients often have very real medical problems that demand and deserve the same high-quality medical care offered to any patient [2, 17].

TREATING OPIOID OVERDOSE

In the time it takes for an overdose to become fatal, it is possible to reverse the respiratory depression and other effects of opioids through respiratory support and administration of the opioid antagonist naloxone (Narcan) [13]. Naloxone is approved by the FDA and has been used for decades to reverse overdose and resuscitate individuals who have overdosed on opioids.

The safety profile of naloxone is remarkably high, especially when used in low doses and titrated to effect [4, 13]. If given to individuals who are not opioid-intoxicated or opioid-dependent, naloxone produces no clinical effects, even at high doses. Moreover, while rapid opioid withdrawal in tolerant patients may be unpleasant, it is not typically life-threatening.

Naloxone should be part of an overall approach to opioid overdose that incorporates the following steps.

RECOGNIZE THE SIGNS OF OVERDOSE. An opioid overdose requires rapid diagnosis. The most common signs of overdose include [2]:

- Pale and clammy face
- Limp body
- Fingernails or lips turning blue/purple
- Vomiting or gurgling noises
- Cannot be awakened from sleep or is unable to speak
- Very little or no breathing
- Very slow or no heartbeat

Signs of **OVERMEDICATION**, which may progress to overdose, include [2]:

- Unusual sleepiness or drowsiness
- Mental confusion, slurred speech, intoxicated behavior
- Slow or shallow breathing
- Pinpoint pupils
- Slow heartbeat, low blood pressure
- Difficulty waking the individual from sleep

Because opioids depress respiratory function and breathing, one telltale sign of an individual in a critical medical state is the "death rattle." Often mistaken for snoring, the "death rattle" is an exhaled breath with a very distinct, labored sound coming from the throat. It indicates that emergency resuscitation is needed immediately [4].

SUPPORT RESPIRATION. Supporting respiration is the single most important intervention for opioid overdose and may be life-saving on its own. Ideally, individuals who are experiencing opioid overdose should be ventilated with 100% oxygen before naloxone is administered to reduce the risk of acute lung injury [2, 4]. In situations where 100% oxygen is not available, rescue breathing can be very effective in supporting respiration [4]. Rescue breathing involves the following steps:

- Verify that the airway is clear.
- With one hand on the patient's chin, tilt the head back and pinch the nose closed.
- Place your mouth over the patient's mouth to make a seal and give 2 slow breaths (the patient's chest should rise, but not the stomach).
- Follow up with one breath every 5 seconds.

INFORMATION FOR PRESCRIBERS

ADMINISTER NALOXONE. Naloxone (Narcan) should be given to any patient who presents with signs of opioid overdose, or when overdose is suspected [4]. Naloxone can be given by intramuscular or intravenous injection every 2 to 3 minutes [4, 13-14].

The most rapid onset of action is achieved by intravenous administration, which is recommended in emergency situations [13]. Intravenous administration generally is used with patients who have no history of opioid dependence. Opioid-naïve patients may be given starting doses of up to 2 mg without concern for triggering withdrawal symptoms [4].

The intramuscular route of administration may be more suitable for patients with a history of opioid dependence because it provides a slower onset of action and a prolonged duration of effect, which may minimize rapid onset of withdrawal symptoms [4].

Pregnant patients. Naloxone can be used safely to manage opioid overdose in pregnant women. The lowest dose to maintain spontaneous respiratory drive should be used to avoid triggering acute opioid withdrawal, which may cause fetal distress [4].

MONITOR THE PATIENT'S RESPONSE. Patients should be monitored for re-emergence of signs and symptoms of opioid toxicity for at least 4 hours following the last dose of naloxone (however, patients who have overdosed on long-acting opioids require more prolonged monitoring) [4].

Most patients respond to naloxone by returning to spontaneous breathing, with mild withdrawal symptoms [4]. The response generally occurs within 3 to 5 minutes of naloxone administration. (Rescue breathing should continue while waiting for the naloxone to take effect.)

The duration of effect of naloxone is 30 to 90 minutes. Patients should be observed after that time for re-emergence of overdose symptoms. The goal of naloxone therapy should be restoration of adequate spontaneous breathing, but not necessarily complete arousal [4, 13-14].

More than one dose of naloxone may be required to revive the patient. Those who have taken longer-acting opioids may require further intravenous bolus doses or an infusion of naloxone [4]. Therefore, it is essential to get the person to an emergency department or other source of acute care as quickly as possible, even if he or she revives after the initial dose of naloxone and seems to feel better.

SIGNS OF OPIOID WITHDRAWAL: Withdrawal triggered by naloxone can feel unpleasant. As a result, some persons become agitated or combative when this happens and need help to remain calm.

The signs and symptoms of opioid withdrawal in an individual who is physically dependent on opioids may include (but are not limited to) the following: body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness, and increased blood pressure [13]. Withdrawal syndromes may be precipitated by as little as 0.05 to 0.2 mg intravenous naloxone in a patient taking 24 mg per day of methadone.

In neonates, opioid withdrawal also may produce convulsions, excessive crying, and hyperactive reflexes [13].

NALOXONE-RESISTANT PATIENTS: If a patient does not respond to naloxone, an alternative explanation for the clinical symptoms should be considered. The most likely explanation is that the person is not overdosing on an opioid but rather some other substance or may even be experiencing a non-overdose medical emergency. A possible explanation to consider is that the individual has overdosed on buprenorphine, a long-acting opioid partial agonist. Because buprenorphine has a higher affinity for the opioid receptors than do other opioids, naloxone may not be effective at reversing the effects of buprenorphine-induced opioid overdose [4].

In all cases, support of ventilation, oxygenation, and blood pressure should be sufficient to prevent the complications of opioid overdose and should be given the highest priority if the patient's response to naloxone is not prompt.

NOTE: All naloxone products have an expiration date. It is important to check the expiration date and obtain replacement naloxone as needed.

LEGAL AND LIABILITY CONSIDERATIONS

Health care professionals who are concerned about legal risks associated with prescribing naloxone may be reassured by the fact that prescribing naloxone to manage opioid overdose is consistent with the drug's FDA-approved indication, resulting in no increased liability so long as the prescriber adheres to general rules of professional conduct. State laws and regulations generally prohibit physicians from prescribing a drug such as naloxone to a third party, such as a caregiver. (Illinois, Massachusetts, New York, and Washington State are the exceptions to this general principle.) More information on state policies is available at <http://www.prescribeprevent.org/> or from individual state medical boards.

CLAIMS CODING AND BILLING

Most private health insurance plans, Medicare, and Medicaid cover naloxone for the treatment of opioid overdose, but policies vary by state. The cost of take-home naloxone should not be a prohibitive factor. Not all community pharmacies stock naloxone routinely but can always order it. If you are caring for a large population of patients who are likely to benefit from naloxone, you may wish to notify the pharmacy when you implement naloxone prescribing as a routine practice.

The codes for Screening, Brief Intervention, and Referral to Treatment (SBIRT) can be used to bill time for counseling a patient about how to recognize overdose and how to administer naloxone. Billing codes for SBIRT are as follows:

Commercial Insurance: CPT 99408 (15 to 30 minutes)

Medicare: G0396 (15 to 30 minutes)

Medicaid: H0050 (per 15 minutes)

RESOURCES FOR PRESCRIBERS

Additional information on prescribing opioids for chronic pain is available at the following websites:

<http://www.opioidprescribing.com>. Sponsored by the Boston University School of Medicine, with support from SAMHSA, this site presents course modules on various aspects of prescribing opioids for chronic pain. To view the list of courses and to register, go to <http://www.opioidprescribing.com/overview>. CME credits are available at no charge.

<http://www.pcass-o.org> or <http://www.pcassb.org>. Sponsored by the American Academy of Addiction Psychiatry in collaboration with other specialty societies and with support from SAMHSA, the Prescriber's Clinical Support System offers multiple resources related to opioid prescribing and the diagnosis and management of opioid use disorders.

<http://www.medscape.com>. Two course modules sponsored by the National Institute on Drug Abuse and posted on MedScape can be accessed at <http://www.medscape.org/viewarticle/770687> and <http://www.medscape.org/viewarticle/770440>. CME credits are available.

WHAT ARE OPIOIDS?

Opioids include illicit drugs such as heroin and prescription medications used to treat pain such as morphine, codeine, methadone, oxycodone (Oxycontin, Percodan, Percocet), hydrocodone (Vicodin, Lortab, Norco), fentanyl (Duragesic, Fentora), hydromorphone (Dilaudid, Exalgo), and buprenorphine (Suboxone).

Opioids work by binding to specific receptors in the brain, spinal cord and gastrointestinal tract. In doing so, they minimize the body's perception of pain. However, stimulating the opioid receptors or "reward centers" in the brain also can trigger other systems of the body, such as those responsible for regulating mood, breathing, and blood pressure.

A variety of effects can occur after a person takes opioids, ranging from pleasure to nausea, vomiting, severe allergic reactions (anaphylaxis) to overdose, in which breathing and heartbeat slow or even stop.

Opioid overdose can occur when a patient misunderstands the directions for use, accidentally takes an extra dose, or deliberately misuses a prescription opioid or an illicit drug such as heroin. Also at risk is the person who takes opioid medications prescribed for someone else, as is the individual who combines opioids — prescribed or illicit — with alcohol, certain other medications, and even some over-the-counter products that depress breathing, heart rate, and other functions of the central nervous system [4].

PREVENTING OVERDOSE

If you are concerned about your own use of opioids, don't wait! Talk with the health care professional/s who prescribed the medications for you. If you are concerned about a family member or friend, urge him or her to do so as well.

Effective treatment of opioid use disorders can reduce the risk of overdose and help a person who is misusing or addicted to opioid medications attain a healthier life. An evidence-based practice for treating opioid addiction is the use of FDA-approved medications, along with counseling and other supportive services. These services are available at SAMHSA-certified and DEA-registered opioid treatment programs (OTPs) [19-20]. In addition, physicians who are trained to provide treatment for opioid addiction in office-based and other settings with medications such as buprenorphine/naloxone and naltrexone may be available in your community [21].

IF YOU SUSPECT AN OVERDOSE

An opioid overdose requires immediate medical attention. An essential first step is to get help from someone with medical expertise as soon as possible.

Call 911 immediately if you or someone you know exhibits any of the symptoms listed below. All you have to say: "Someone is unresponsive and not breathing." Give a clear address and/or description of your location.

Signs of **OVERDOSE**, which is a life-threatening emergency, include:

- Face is extremely pale and/or clammy to the touch
- Body is limp
- Fingernails or lips have a blue or purple cast
- The patient is vomiting or making gurgling noises
- He or she cannot be awakened from sleep or is unable to speak
- Breathing is very slow or stopped
- Heartbeat is very slow or stopped.

Signs of **OVERMEDICATION**, which may progress to overdose, include:

- Unusual sleepiness or drowsiness
- Mental confusion, slurred speech, intoxicated behavior
- Slow or shallow breathing
- Pinpoint pupils
- Slow heartbeat, low blood pressure
- Difficulty waking the person from sleep.

WHAT IS NALOXONE?

Naloxone (Narcan) is an antidote to opioid overdose. It is an opioid antagonist that is used to reverse the effects of opioids. Naloxone works by blocking opiate receptor sites. It is not effective in treating overdoses of benzodiazepines (such as Valium, Xanax, or Klonopin), barbiturates (Seconal or Fiorinal), clonidine, Elavil, GHB, or ketamine. It also is not effective in treating overdoses of stimulants such as cocaine and amphetamines (including methamphetamine and Ecstasy). However, if opioids are taken in combination with other sedatives or stimulants, naloxone may be helpful.

IMPORTANT SAFETY INFORMATION. Naloxone may cause dizziness, drowsiness, or fainting. These effects may be worse if it is taken with alcohol or certain medicines. Use naloxone with caution. Do not drive or perform other possibly unsafe tasks until you know how you react to it.

If you experience a return of symptoms (such as drowsiness or difficulty breathing), **get help immediately**.

REPORT ANY SIDE EFFECTS

Get emergency medical help if you have any signs of an allergic reaction after taking naloxone, such as hives, difficulty breathing, or swelling of your face, lips, tongue, or throat.

Call your doctor or 911 at once if you have a serious side effect such as:

- Chest pain, or fast or irregular heartbeats;
- Dry cough, wheezing, or feeling short of breath;
- Sweating, severe nausea, or vomiting;
- Severe headache, agitation, anxiety, confusion, or ringing in your ears;
- Seizures (convulsions);
- Feeling that you might pass out; or
- Slow heart rate, weak pulse, fainting, or slowed breathing.

If you are being treated for dependence on opioid drugs (either an illicit drug like heroin or a medication prescribed for pain), you may experience the following symptoms of opioid withdrawal after taking naloxone:

- Feeling nervous, restless, or irritable;
- Body aches;
- Dizziness or weakness;
- Diarrhea, stomach pain, or mild nausea;
- Fever, chills, or goosebumps; or
- Sneezing or runny nose in the absence of a cold.

This is not a complete list of side effects, and others may occur. Talk to your doctor about side effects and how to deal with them.

STORE NALOXONE IN A SAFE PLACE

Naloxone is usually handled and stored by a health care provider. If you are using naloxone at home, store it in a locked cabinet or other space that is out of the reach of children or pets.

SUMMARY: HOW TO AVOID OPIOID OVERDOSE

1. Take medicine only if it has been prescribed to you by your doctor.
2. Do not take more medicine or take it more often than instructed.
3. Call a doctor if your pain gets worse.
4. Never mix pain medicines with alcohol, sleeping pills, or any illicit substance.
5. Store your medicine in a safe place where children or pets cannot reach it.
6. Learn the signs of overdose and how to use naloxone to keep it from becoming fatal.
7. Teach your family and friends how to respond to an overdose.
8. Dispose of unused medication properly.

READ MORE AT <http://www.drugs.com/cdi/naloxone.html>.

RECOVERING FROM OPIOID OVERDOSE

RESOURCES FOR OVERDOSE SURVIVORS AND FAMILY MEMBERS

Survivors of opioid overdose have experienced a life-changing and traumatic event. They have had to deal with the emotional consequences of overdosing, which can involve embarrassment, guilt, anger, and gratitude, all accompanied by the discomfort of opioid withdrawal. Most need the support of family and friends to take the next steps toward recovery.

While many factors can contribute to opioid overdose, it is almost always an accident. Moreover, the underlying problem that led to opioid use — most often pain or substance use disorder — still exists and continues to require attention [2].

Moreover, the individual who has experienced an overdose is not the only one who has endured a traumatic event. Family members often feel judged or inadequate because they could not prevent the overdose. It is important for families to work together to help the overdose survivor obtain the help that he or she needs.

FINDING A NETWORK OF SUPPORT

As with any disease, it is not a sign of weakness to admit that a person or a family cannot deal with the trauma of overdose without help. It takes real courage to reach out to others for support and to connect with members of the community to get help. Health care providers, including those who specialize in treating substance use disorders, can provide structured, therapeutic support and feedback.

If the survivor's underlying problem is pain, referral to a pain specialist may be in order. If it is addiction, the patient should be referred to an addiction specialist for assessment and treatment, either by a physician specializing in the treatment of opioid addiction, in a residential treatment program, or in a federally certified Opioid Treatment Program (OTP). In each case, counseling can help the individual manage his or her problems in a healthier way. Choosing the path to recovery can be a dynamic and challenging process, but there are ways to help.

In addition to receiving support from family and friends, overdose survivors can access a variety of community-based organizations and institutions, such as:

- Health care and behavioral health providers
- Peer-to-peer recovery support groups such as Narcotics Anonymous
- Faith-based organizations
- Educational institutions
- Neighborhood groups
- Government agencies
- Family and community support programs.

RECOVERING FROM OPIOID OVERDOSE

RESOURCES

Information on opioid overdose and helpful advice for overdose survivors and their families can be found at the following websites:

Substance Abuse and Mental Health Services Administration (SAMHSA)

- National Treatment Referral Helpline 1-800-662-HELP (4357) or 1-800-487-4889 (TDD — for hearing impaired)
- National Substance Abuse Treatment Facility Locator: <http://www.findtreatment.samhsa.gov/TreatmentLocator> to search by state, city, county, and zip code
- Buprenorphine Physician & Treatment Program Locator: http://www.buprenorphine.samhsa.gov/bwns_locator
- State Substance Abuse Agencies: <http://findtreatment.samhsa.gov/TreatmentLocator/faces/abuse-Agencies.jsp>

Centers for Disease Control and Prevention (CDC):

<http://www.cdc.gov/Features/VitalSigns/PainkillerOverdoses>

National Institutes of Health (NIH), National Center for Biotechnical Information: <http://www.ncbi.nlm.nih.gov>

The Partnership at Drug-Free.org: <http://www.drugfree.org/uncategorized/opioid-overdose-antidote>

Project Lazarus: <http://projectlazarus.org>

Harm Reduction Coalition: <http://harmreduction.org>

Overdose Prevention Alliance: <http://overdosepreventionalliance.org>

Toward the Heart: <http://towardtheheart.com/naloxone>

REFERENCES

REFERENCES

1. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. CDC WONDER Online Database, 2012.
2. Beletsky LB, Rich JD, Walley AY. Prevention of fatal opioid overdose. *JAMA*. 2013;308(180): 1863–1864.
3. Harvard Medical School. Painkillers fuel growth in drug addiction: Opioid overdoses now kill more people than cocaine or heroin. *Harvard Ment Hlth Let*. 2011;27(7):4–5.
4. BMJ Evidence Centre. Treatment of opioid overdose with naloxone. *British Medical Journal*. Updated October 23, 2012. [Accessed March 24, 2013, at <http://www.bmj.com>]
5. Enteen L, Bauer J, McLean R, Wheeler E, Huriaux E, Kral AH, Bamberger JD. Overdose prevention and naloxone prescription for opioid users in San Francisco. *J Urban Health*. 2010 Dec;87(6):931–941.
6. Seal KH, Thawley R, Gee L et al. Naloxone distribution and cardiopulmonary resuscitation training for injection drug users to prevent heroin overdose death: A pilot intervention study. *J Urban Health*. 2005;82(2):303–311.
7. Coffin PO, Sullivan SD. Cost effectiveness of distributing naloxone to heroin users for lay overdose reversal. *Ann Intl Med*. 2013;158:1–9.
8. Banta-Green C. Good Samaritan overdose response laws: Lessons learned from Washington State. Washington, DC: Office of National Drug Control Policy, Executive Office of the President, The White House, March 29, 2013. [Accessed at <http://www.whitehouse.gov/blog/2013/03/29/good-samaritan-overdose-response-laws-lessonslearned-washington-state>]
9. Strang J, Manning V, Mayet S et al. Overdose training and take-home naloxone for opiate users: Prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. *Addiction*. 2008;103(10): 1648–1657.
10. Green TC, Heimer R, Grau LE. Distinguishing signs of opioid overdose and indication for naloxone: An evaluation of six overdose training and naloxone distribution programs in the United States. *Addiction*. 2008;103(6): 979–98.
11. Hardman E, Limbird LE, eds. *Goodman and Gilman's the Pharmacologic Basis of Therapeutics, 11th ed*. New York, NY: McGraw-Hill, 2006, pp. 576–578.
12. Centers for Disease Control and Prevention (CDC). Community-based opioid overdose prevention programs providing naloxone — United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2012;261(6):101–105.

REFERENCES

13. Rx List [Accessed March 24, 2013, at <http://www.rxlist.com>]
14. Drugs.com [Accessed March 24, 2013, at <http://www.drugs.com>]
15. Centers for Disease Control and Prevention (CDC). CDC grand rounds: Prescription drug overdoses — A U.S. epidemic. *MMWR Morb Mortal Wkly Rep.* 2012;61(1):10–13.
16. Isaacson JH, Hopper JA, Alford DP, Parran T. Prescription drug use and abuse. Risk factors, red flags, and prevention strategies. *Postgrad Med.* 2005;118:19.
17. Finch JW, Parran TV, Wilford BB, Wyatt SA. Clinical, legal and ethical considerations in prescribing drugs with abuse potential. In Ries RK, Alford DP, Saitz R, Miller S, eds. *Principles of Addiction Medicine, Fifth Edition.* Philadelphia, PA: Lippincott, Williams & Wilkins, Ch. 109, in press 2013.
18. Michna E, Ross EL, Hynes WL, et al. Predicting aberrant drug behavior in patients treated for chronic pain: Importance of abuse history. *J Pain Symptom Manage.* 2004;28:250.
19. National Treatment Referral Helpline 1-800-662-HELP (4357) or 1-800-487-4889 (TDD for hearing impaired)
20. National Substance Abuse Treatment Facility Locator: <http://www.findtreatment.samhsa.gov/TreatmentLocator> to search by state, city, county, and zip code
21. Buprenorphine Physician & Treatment Program Locator: http://www.buprenorphine.samhsa.gov/bwns_locator
22. Bazazi AR, Zaller ND, Fu JJ, Rich JD. Preventing opiate overdose deaths: Examining objections to take-home naloxone. *J Health Care Poor Underserved.* 2010 Nov;21(4):1108–1112.



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