Opioid use disorder (addiction) and overdose from opioid analgesics and heroin constitute a significant public health problem in New York City (NYC). Overdose deaths from opioids are increasing—even though they’re preventable. Between 2000 and 2013, opioid analgesic overdose deaths increased 256%. Heroin overdose deaths doubled between 2010 and 2013 after declining for several years.

Of the 782 NYC overdose deaths in 2013, 215 involved opioid analgesics and 420 involved heroin.

Although opioid use disorder has serious consequences, many New Yorkers with this chronic health condition do not receive effective treatment. Medication-assisted treatment (eg, buprenorphine and methadone) for opioid use disorder is a life-saving tool—with benefits to patients and the community (Boxes 1 and 2, Figure). Buprenorphine is an office-based treatment that can be integrated into primary care along with management of patients’ other health issues. Despite buprenorphine’s many benefits, it remains underutilized. By following the guidance in this publication, you can make treatment for opioid use disorder more available to those who need it and be part of the public health effort to reverse the epidemic of opioid use disorder and overdose.

To incorporate buprenorphine treatment into your practice, follow these steps:
1. Learn to recognize opioid use disorder.
2. Obtain training and a waiver to prescribe buprenorphine.
3. Prescribe buprenorphine to patients with opioid use disorder.
4. Provide ongoing management of patients with opioid use disorder.

Continuing education training and mentorship from experienced clinicians are also available online (Resources).

WHAT ARE OPIOIDS?
- Opioids are drugs that bind to specific receptors in the brain and relieve pain. The group includes both heroin and opioid analgesics.
- Opioid analgesics are medications legally prescribed as painkillers, such as morphine, oxycodone, and hydrocodone.
STEP 1. LEARN TO RECOGNIZE OPIOID USE DISORDER

- Ask nonjudgmental, open-ended questions about a patient’s functioning with his or her family, at work or school, and in social situations.
- Be aware of signs associated with opioid intoxication such as drowsiness, slurred speech, memory impairment, and pupillary constriction.
- Screen for drug use. Ask “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?” If the response is ≥1, use one of several validated screening tools available, such as the DAST-10 (Box 3). See Resources—Clinical Tools for other options.
- For patients who respond “Yes” to ≥3 questions on the DAST-10, use criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (Box 4) to assess for mild, moderate, or severe opioid use disorder (this term replaces the previous DSM terms “opioid abuse” and “opioid dependence”).

BOX 1. BUPRENORPHINE FAQS

- How does buprenorphine work?
  Buprenorphine is a partial opioid agonist, attaching to the same receptors in the brain as other opioids (eg, opioid analgesics, heroin, methadone), but producing only weak morphine-like effects, without the euphoria or respiratory depression triggered by full opioid agonists. These effects increase with dosage, but plateau at a moderate dosage. As a partial opioid agonist, buprenorphine at a moderate dosage enables patients to discontinue use of other opioids without experiencing withdrawal symptoms.

- How is buprenorphine taken?
  Buprenorphine is available in tablet or film and is generally administered once daily under the tongue. The tablets completely dissolve within 5 to 10 minutes, and the film dissolves even more rapidly. Buprenorphine is available in 2 formulations:
  - Buprenorphine and naloxone (because naloxone precipitates withdrawal symptoms when injected, but not when taken orally, it is included in the formulation as a deterrent to intravenous use of buprenorphine)
  - Buprenorphine only

The buprenorphine/naloxone combination is preferable in all cases, except when the patient is hypersensitive to naloxone or pregnant (see Review safety considerations, page 4).

- What about overdose?
  Buprenorphine’s weak morphine-like effects increase with dosage, but plateau at a moderate dosage (the “ceiling effect”), making it difficult for a person to overdose on buprenorphine alone. Fatal overdose is still possible if other central nervous system depressants, such as benzodiazepines or alcohol, are taken along with buprenorphine.

BOX 2. BUPRENORPHINE MISUSE*: MYTHS AND FACTS

MYTH: Buprenorphine is just as likely to be misused as other opioids.

FACT: Risk of misuse is lower with buprenorphine than with full opioid agonists. Buprenorphine is long-acting and exhibits a ceiling effect, limiting euphoria. The naloxone in the coformulated buprenorphine works to deter injection: it’s an opioid antagonist that produces withdrawal symptoms if injected, but not when it’s absorbed sublingually, as indicated.

MYTH: People who’ve used buprenorphine without a prescription are not candidates for buprenorphine treatment.

FACT: The most common reasons for buprenorphine misuse are self-treatment of withdrawal symptoms and lack of access to treatment. Most patients who’ve misused buprenorphine in the past will still be appropriate treatment candidates, but it’s important to evaluate the circumstances before prescribing buprenorphine.

*Using someone else’s buprenorphine or using buprenorphine in ways other than prescribed.
**BOX 3. DRUG USE QUESTIONNAIRE (DAST-10)**

The following questions concern information about your potential involvement with drugs, excluding alcohol and tobacco, during the past 12 months. Carefully read each statement and decide if your answer is “YES” or “NO.”

When the words “drug abuse” are used, they mean the use of prescribed or over-the-counter medications used in excess of the directions and any non-medical use of any drugs. The various classes of drugs may include, but are not limited to, cannabis (eg, marijuana, hash), solvents (eg, gas, paints, etc), tranquilizers (eg, Valium), barbiturates, cocaine, and stimulants (eg, speed), hallucinogens (eg, LSD), or narcotics (eg, heroin). Remember that the questions do not include alcohol or tobacco.

Please answer every question. If you have difficulty with a statement, then choose the response that is mostly right.

These questions refer to the past 12 months only.

1. Have you used drugs other than those required for medical reasons? Yes No

2. Do you abuse more than one drug at a time? Yes No

3. Are you always able to stop using drugs when you want to? Yes No

4. Have you had “blackouts” or “flashbacks” as a result of drug use? Yes No

5. Do you ever feel bad or guilty about your drug use? Yes No

6. Does your spouse (or parent) ever complain about your involvement with drugs? Yes No

7. Have you neglected your family because of your use of drugs? Yes No

8. Have you engaged in illegal activities in order to obtain drugs? Yes No

9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs? Yes No

10. Have you had medical problems as a result of your drug use (eg, memory loss, hepatitis, convulsions, bleeding, etc)? Yes No

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**BOX 4. DSM-5 CRITERIA FOR OPIOID USE DISORDER**

Ask opioid users if they have experienced these symptoms in the past year:

- Taking the substance in larger amounts or for longer than you meant to,
- Wanting to cut down or stop using the substance but not managing to,
- Spending a lot of time getting, using, or recovering from use of the substance,
- Cravings and urges to use the substance,
- Not managing to do what you should at work, home, or school because of substance use,
- Continuing to use, even when it causes problems in relationships,
- Giving up important social, occupational, or recreational activities because of substance use,
- Using substances again and again, even when it puts you in danger,
- Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance,
- Needing more of the substance to get the effect you want (tolerance),
- Development of withdrawal symptoms, which can be relieved by taking more of the substance.

2-3 symptoms: mild opioid use disorder
4-5 symptoms: moderate opioid use disorder
6+ symptoms: severe opioid use disorder

* Persons who are prescribed medications such as opioids may exhibit these two criteria, but would not necessarily be considered to have opioid use disorder.
STEP 2. OBTAIN TRAINING AND A WAIVER TO PRESCRIBE BUPRENORPHINE

To prescribe buprenorphine, you must meet the following 3 criteria13:

• Be a licensed physician (MD or DO).
• Have any of the following credentials:
  • completion of at least 8 hours of a specific continuing medical education (CME) training (online or in person) from an approved organization on prescribing buprenorphine (Resources),
  • subspecialty board certification related to addiction, or
  • investigator role in 1 or more clinical trials leading to Food and Drug Administration approval of a narcotic for drug maintenance or detoxification.
• Have the capacity to refer patients to counseling. In NYC, you can meet this criterion by referring patients to 800-LIFENET, or 311.

If you meet all 3 criteria, you can obtain a waiver to prescribe buprenorphine from the Drug Enforcement Administration. Once you’re qualified, you may have a maximum of 30 patients on buprenorphine at any one time during the first year. After 1 year following the initial notification, you can submit a second notification to enable you to treat up to 100 patients. Call the Center for Substance Abuse Treatment (CSAT) at 866-BUP-CSAT/866-287-2728 or visit http://buprenorphine.samhsa.gov/training.html for information about the waiver process.

If you are not able to prescribe buprenorphine, go to http://buprenorphine.samhsa.gov/bwns_locator/index.html or call 866-BUP-CSAT/866-287-2728 or LIFENET (800-LIFENET) to find a buprenorphine prescriber.

STEP 3. PRESCRIBE BUPRENORPHINE TO PATIENTS WITH OPIOID USE DISORDER

The treatment goals for opioid use disorder are to block the euphoric effects of opioids, alleviate physical withdrawal symptoms and reduce psychological cravings, and help patients regain or acquire the ability to function in their personal, community, and work lives.

Talk with your patient

Buprenorphine may be a good choice for patients who:
• meet the DSM-5 criteria for opioid use disorder,
• can be expected to be reasonably adherent to the treatment plan, based on provider’s experience,
• have been educated about the risks and benefits of buprenorphine treatment,
• are willing to follow safety precautions for buprenorphine treatment,
• have agreed to buprenorphine treatment after a review of treatment options.

Draft a treatment agreement

• A written agreement (Resources) will help establish mutual trust and clarify expectations of patient involvement in buprenorphine treatment.7

Review safety considerations*

• Sedatives/hypnotics (eg, benzodiazepines, alcohol): If a benzodiazepine or other central nervous system (CNS) depressant is medically necessary, monitor the patient for side effects—particularly sedation and respiratory depression. The combination of buprenorphine and other CNS depressants can be fatal.7
• Hepatic impairment: Evidence demonstrates a low risk of hepatotoxicity; consider monitoring liver function during treatment.14
• HIV: Buprenorphine is associated with reduced opioid use, increased initiation of antiretroviral therapy, and increased CD4 counts,13 and has been effectively and safely integrated into HIV treatment settings.16 Clinical data haven’t shown hepatotoxicity or pharmacodynamic interactions when buprenorphine is used with antiretroviral therapy, including atazanavir/ritonavir,15 which increases plasma concentrations of buprenorphine and its metabolite norbuprenorphine.17
• Pregnancy: Methadone remains the standard of care in the United States, but buprenorphine (without naloxone) may be used as first-line treatment for pregnant women who’ve been maintained successfully on buprenorphine or are unwilling to take methadone.18
• Lactation: Breastfeeding is not contraindicated.7 While small amounts of buprenorphine and norbuprenorphine are secreted into breast milk, adverse events have not been reported among breastfed infants of mothers treated with sublingual buprenorphine.19,20
• Adverse events: The most common adverse events are rashes, hives, and pruritus. Bronchospasm, angioneurotic edema, and anaphylactic shock have also been reported. Buprenorphine products should not be given to those who are hypersensitive to buprenorphine or naloxone.7
• Illicit substances: There is no medical rationale for discontinuing buprenorphine for most patients who continue to use other drugs:
  • There have been no documented adverse interactions between buprenorphine and cocaine or marijuana, but patients who use cocaine may need additional interventions.21-24
• Some patients who use multiple substances might need a higher level of care, such as a specialized addiction treatment program; others may benefit from continued management with buprenorphine in the general medical setting.

*See product information for full safety information.

**Assess severity of withdrawal**

Typically, patients must show at least mild withdrawal symptoms before beginning buprenorphine or they risk developing a precipitated or severe withdrawal.\(^1,2^5\) A score of \(\geq 5\) on the standardized Clinical Opiate Withdrawal Scale (COWS) (**Resources**) is the recommended threshold\(^2,5\); higher scores reduce the chances of precipitating withdrawal.

**Determine location of treatment initiation**

Several studies have established the safety of home inductions. Office-based prescribers will likely find home inductions more feasible and can consult published guidance.\(^2,6-28\)

**Determine optimal dosage**

The average daily buprenorphine dosage is 16 mg/day.\(^2^9\) Few patients require—and many health plans will not pay for—dosages higher than 24 mg/day. Underdosing can result in craving and withdrawal symptoms, which could cause patients to drop out of treatment, and dosages that are too high can cause sedation.\(^7\)

• Initiate treatment according to the package insert.
• Monitor patients for approximately 2 weeks after initiating therapy until you’ve determined the adequate buprenorphine dosage.
• Substances that inhibit the 3A4 enzyme (eg, macrolide antibiotics, protease inhibitors) can increase plasma levels of buprenorphine. Substances that induce the 3A4 system (eg, phenobarbital) may have the opposite effect.\(^7\)

For patients who are switching from methadone,

• Coordinate to taper the patient to 30 to 60 mg of methadone before starting buprenorphine.

**STEP 4. PROVIDE ONGOING MANAGEMENT OF PATIENTS WITH OPIOID USE DISORDER**

• Tailor frequency of return visits to the patient and degree of clinical stability. Weekly or more frequent visits may be needed for a patient early in treatment or during unstable periods. Longer visit intervals, such as monthly, may be appropriate for the stable patient. Incorporate the following into follow-up visits:
  • relapse prevention counseling,\(^7\)
  • assessment of adherence to prescribed buprenorphine,\(^7\)
  • urine toxicology as an adjunct to assess drug use and, if appropriate, buprenorphine adherence,\(^7\)
  • assessment for mood, anxiety, or personality disorders.\(^7\)
• Offer referral to counseling or a 12-step program. These services can help the patient manage psychological or psychosocial problems that could interfere with treatment gains.\(^7\)
• Provide a clear protocol for refilling prescriptions to ensure continuous treatment.
• Remain attentive to frequent requests for early refills or reports of lost medication. These could be signs of misuse, which might indicate self-treatment of withdrawal and a need to increase prescribed dosage. Requests for more medication could also signal diversion to individuals who do not have access to a buprenorphine prescription or who are self-treating opioid withdrawal.\(^11,1^2\)
• If the patient continues to misuse opioids during maintenance treatment,
  • discuss treatment goals in a nonjudgmental manner, emphasizing a collaborative relationship, and minimize confrontation.
  • intensify treatment by reducing follow-up intervals, reassessing the medication dosage, and referring for more intensive psychosocial counseling or specialized addiction treatment.

**INTEGRATE BUPRENORPHINE TREATMENT INTO PRACTICE WORKFLOW**

• Assign a staff member such as a nurse or clinical pharmacist to coordinate the buprenorphine program, keep an electronic registry of buprenorphine patients, and manage refill requests.
• Plan for referral or on-site psychosocial counseling; in settings where a behavioral specialist and primary care physician provide collaborative care, group visits may be a feasible approach.
• Ensure coverage by a waivered physician during vacations to minimize disruptions in treatment.
Reducing dosage and discontinuing treatment

Make the decision to discontinue buprenorphine treatment in partnership with the patient after assessing quality of life and social functioning. People who’ve been opioid dependent for short periods may be able to discontinue buprenorphine therapy; those who’ve been using opioids over long periods with a history of relapse will likely need long-term treatment. Abrupt discontinuation or rapid dosage taper may result in opioid withdrawal syndrome, so work closely with the patient on a tapering schedule to avoid relapse. Refer to the package insert for full prescribing information, including dosing and safety. Be prepared to reinitiate treatment if necessary.

SUMMARY

Buprenorphine is a life-saving office-based treatment for opioid use disorder. Integrating buprenorphine prescribing into your practice will make treatment for opioid use disorder more available to those who need it and reduce stigmatization that may deter people from seeking care.

Buprenorphine Treatment Finder:
866-BUP-CSAT/866-287-2728
http://buprenorphine.samhsa.gov/bwns_locator/index.html

RESOURCES

Clinical Tools
- DAST-10: http://smchealth.org/sites/default/files/docs/1309587937DRUGUSEQUESTIONNAIRE.pdf
- ASSIST: www.who.int/substance_abuse/activities/assist/en/

General Information About Buprenorphine:
http://buprenorphine.samhsa.gov/index.html

Buprenorphine Training Courses
- Substance Abuse and Mental Health Service Administration (SAMHSA): 866-BUP-CSAT/866-287-2728; http://buprenorphine.samhsa.gov/training.html
- American Academy of Addiction Psychiatry: www.aapa.org
- American Osteopathic Academy of Addiction Medicine: www.aoaam.org
- American Psychiatric Association: www.psychiatry.org
- American Society of Addiction Medicine: www.asam.org

Buprenorphine Waiver Process and Forms:
http://buprenorphine.samhsa.gov/howto.html

Physician-Patient Sample Treatment Agreement:
www.ncbi.nlm.nih.gov/books/NBK64238/

PCSS-MAT Mentoring Program for Prescribers:
http://pcssmat.org/mentoring/

LIFENET (a free, confidential help line for New York City residents; 24 hours a day/7 days a week):
In English: 800-LIFENET/800-543-3638
In Spanish: 877-AYUDESE/877-298-3373
In Korean and Chinese (Mandarin and Cantonese dialects): 877-990-8585
For other languages, call 800-LIFENET and ask for an interpreter.
TYT hard of hearing, call 212-982-5284
REFERENCES


