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MANAGEMENT OF OPIOID USE DISORDER IN THE EMERGENCY DEPARTMENT: A WHITE PAPER PREPARED FOR THE AMERICAN ACADEMY OF EMERGENCY MEDICINE

Reuben J. Strayer, MD,* Kathryn Hawk, MD, MHS,† Bryan D. Hayes, PHARMD,‡§ Andrew A. Herring, MD,‖ Eric Ketcham, MD, MBA,¶** Alexis M. LaPietra, DO,†† Joshua J. Lynch, DO,‡‡ Sergey Motov, MD,§§ Zachary Repanshek, MD,‖‖ Scott G. Weiner, MD, MPH,¶¶ and Lewis S. Nelson, MD***

*Department of Emergency Medicine, Maimonides Medical Center, Brooklyn, New York, †Department of Emergency Medicine, Yale School of Medicine, New Haven, Connecticut, ‡Department of Emergency Medicine, Harvard Medical School, Boston, Massachusetts, §Department of Pharmacy, Massachusetts General Hospital, Boston, Massachusetts, ‖Department of Emergency Medicine, University of California at San Francisco, Highland Hospital-Alameda Health System, Oakland, California, ¶Department of Emergency Medicine, Santa Fe & Espanola, New Mexico, **Department of Behavioral Health, Addiction Medicine, Presbyterian Healthcare System, Santa Fe & Espanola, New Mexico, ††Department of Emergency Medicine, Saint Joseph's Regional Medical Center, Paterson, New Jersey, ‡‡Department of Emergency Medicine, Jacobs School of Medicine and Biomedical Sciences, University of Buffalo, Buffalo, New York, §§Department of Emergency Medicine, Maimonides Medical Center, Brooklyn, New York, ‖‖Department of Emergency Medicine, Lewis Katz School of Medicine, Temple University, Philadelphia, Pennsylvania, ¶¶Department of Emergency Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, and ***Department of Emergency Medicine, Rutgers New Jersey Medical School, Newark, New Jersey

Reprint Address: Reuben J. Strayer, MD, Department of Emergency Medicine, Maimonides Medical Center, Brooklyn, NY

INTRODUCTION

Over 2 million Americans misuse prescription or illicitly obtained opioids, and opioid overdose deaths rose to a record 47,600 in 2017, representing a nearly 600% increase in 18 years (1,2). Because patients with opioid use disorder (OUD) are often socioeconomically and functionally marginalized, the primary point of contact with health care for many is the emergency department (ED). Emergency clinicians are therefore ideally positioned to address the current opioid addiction and overdose epidemic by preventing the development of OUD, identifying patients affected by OUD, and initiating the most effective treatments and harm-reduction practices.

As the scope of the epidemic has broadened, a crucial shift in therapeutic strategy has occurred: whereas people with OUD were commonly referred to detoxification programs, and the use of medication to treat addiction was largely confined to specialist-run clinics, there is now broad consensus discouraging abstinence-based therapy, which usually results in dangerous relapse, in favor of medication-centered treatment initiated at any point of patient contact (3–13).

Most currently practicing emergency clinicians were not trained to initiate medication for addiction treatment (MAT), also known as medication-assisted therapy, medications for opioid use disorder (MOUD), opioid agonist treatment (OAT), or opioid substitution treatment. This guideline aims to provide evidence-based recommendations for clinicians in acute care settings managing patients being harmed—or at risk to be harmed—by opioids.

Q1. How can Emergency Clinicians Prevent the Development of OUD in Opioid-Naïve Patients Who Present with Acute Pain?

Emergency clinicians are charged with providing effective pain relief for opioid-naïve patients presenting to

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Table 1. Opioid Harms

Constipation, nausea, itching
Dysphoria, confusion, falls, occupational dysfunction, automobile crashes
Lethargy, respiratory depression
Immunosuppression, hypogonadism
Opioid-induced hyperalgesia
Opioid misuse, overdose, addiction
Diversion and unintentional ingestion by children

the ED with a variety of acutely painful conditions while managing the potential for analgesics to cause harm.

For opioid-naïve patients who present to the ED with moderate or severe acute pain, opioids may be appropriately administered as part of a multimodal analgesic strategy tailored to the patient and painful condition.

Emergency clinicians' prescriptions are a comparatively small contribution to overall opioid prescribing in the United States (14). However, ED-based opioid prescriptions may have a disproportionate impact on the development of long-term use because an opioid prescription arising from the ED is more likely to be the patient's *first* opioid prescription. Even short courses of opioid therapy are associated with dependence, with one study showing 6% of patients still filling opioid prescriptions 1 year after an initial 3-day prescription, among a host of corroborating literature demonstrating the link between the first prescription for pain and long-term use (15–26). Therefore, emergency clinicians should carefully evaluate the potential benefit and harm whenever an opioid prescription is considered, recognizing that preventing long-term use centers on *keeping opioid-naïve patients opioid naïve* (27,28).

Opioids cause a spectrum of harms, ranging from the discomfort of mild nausea and pruritis to the devastating consequences of misuse, overdose, and addiction (Table 1). The likelihood and importance of these harms, as applied to a particular patient, should be weighed against the expected analgesic benefit of an opioid added to effective nonpharmacologic and nonopioid analgesic modalities. The decision to prescribe outpatient opioids should follow from a discussion of these benefits and harms with the patient and take into account known risk factors for opioid misuse, recognizing that many patients without risk factors still develop harmful long-term use (Table 2).

The development of long-term use correlates linearly with the number of days' supply of the first prescription (15). Therefore, if an outpatient opioid prescription is judged to be necessary and appropriate, the most important strategy to mitigate the risk of misuse is to prescribe a small number of tablets (usually no more than 3 days' worth, or 9–12 tablets).

Table 2. Risk Factors for Long-Term Use of Opioids

Existing substance use (including alcohol and tobacco)
Psychiatric disease
Social isolation, disability
Adolescents and young adults

Hydrocodone and oxycodone, despite their prevalence, are more euphoric than other opioids, and the most frequently prescribed preparations are combined with acetaminophen (29,30). Not only does this coformulation limit the dose of acetaminophen, an effective analgesic, but it also introduces the risk of acetaminophen-induced hepatotoxicity if the total daily dose of acetaminophen exceeds 4 g. Immediate-release morphine sulfate tablets are effective and likely less abuse-prone than the aforementioned alternatives.

Extended-release and long-acting opioid preparations should not be prescribed by acute care providers except under unusual circumstances (31,32). Codeine and tramadol are burdened by a host of unique drug interactions and toxicities and are also best avoided (33–36).

Emergency clinicians should avoid prescribing opioids for painful syndromes commonly associated with opioid misuse, such as back pain, dental pain, and headache (37–41).

Emergency clinicians who discharge patients with an opioid prescription must discuss safe household storage and disposal of unused pills, especially if the patient lives with children or adolescents. Opioids (and all medications) should be stored in their original package, optimally within a locked container, out of the reach of children. Unneeded opioids should be disposed of at a Drug Enforcement Administration (DEA)-approved controlled substance public disposal location (many pharmacies and police stations participate—listings can be found on the DEA website) (42). If a take-back or disposal program is unavailable or inconvenient, high-risk substances such as opioids should be disposed of in household trash after mixing with an unpalatable substance and placed in a sealed container, or, specifically in the case of opioids, flushed down the toilet (43).

Q2. What is Opioid Withdrawal Syndrome?

(Q2, Q3, and Q4 cover abstinence-related opioid withdrawal. For opioid withdrawal syndrome precipitated by naloxone or buprenorphine, refer to the relevant sections below.)

Opioid withdrawal syndrome (OWS) is a constellation of signs and symptoms experienced by those with opioid dependence whose mu-opioid receptors are left vacant from the cessation of exposure to opioids. The effects associated with OWS are typically extremely uncomfortable and very distressing.

Signs and symptoms of OWS include anxiety and irritability; gastrointestinal distress including abdominal cramping, vomiting, and diarrhea; and diffuse somatic pain that ranges from mildly distressing to unbearable. OWS often includes dysphoria, depression, and hopelessness that makes the condition particularly difficult to tolerate. Physical findings may include mydriasis, piloerection, diaphoresis, and yawning, along with typically minor signs of autonomic excess (e.g., hypertension, tachycardia). An intense craving for opioids often makes it difficult for these patients to cooperate with medical care, but patients should have a normal mental status.

Classically, OWS is not considered life-threatening, but dangerous consequences can be caused by hyperadrenergic tone, particularly in older or frail patients, and especially when OWS is precipitated by naloxone or buprenorphine (44,45). Patients with OWS are most at risk, however, if their withdrawal symptoms are not adequately treated, as they are likely to self-treat with dangerous illicitly obtained opioids, exposing themselves to overdose and other harms. Patients with opioid dependence often have concomitant medical illness requiring treatment that they may refuse if their OWS is not alleviated.

Q3. Should Patients with Opioid Withdrawal be Treated with Opioid Agonist Therapies or Nonagonist Therapies?

OAT should be the first-line treatment for patients with OWS in the ED. OAT, as compared with therapies that do not utilize opioid agonists, treats the underlying etiology of the OWS, manages the symptoms of OWS much more quickly and effectively, and can be continued long term, which allows the immediate transition from withdrawal to sustainable addiction treatment.

In some settings, OAT may not be available or a patient may not be amenable to OAT. In these cases, OWS should be treated with medications that are not opioid agonists.

Q4. How is OWS Treated with Agonists or Nonagonists?

Agonist treatment of OWS is best initiated in the ED using buprenorphine or methadone. Buprenorphine is preferred for most patients given its safety benefits compared with methadone (Q8). Treatment of OWS with buprenorphine in the ED is equivalent to initiation of buprenorphine as a treatment for OUD (Q19). Methadone should be used to treat OWS if buprenorphine is not available or in patients withdrawing from methadone (especially if they plan to return to methadone therapy). Most patients will have significant relief of OWS with 20-mg methadone by mouth (p.o.) or, if the patient is vomiting, 10 mg intramuscular (i.m.) methadone (Q46) (46).

In scenarios where OAT cannot be utilized due to either availability or patient preference, treatment should be tailored to the patient's symptoms (Table 3). Agitation can be treated with antipsychotics, antihistamines, or benzodiazepines. Gastrointestinal effects can be treated with antiemetics, antidiarrheal agents, and antispasmodics, and dyspepsia can be treated with H2 antagonists. Severe pain related to OWS is unlikely to be alleviated by acetaminophen or nonsteroidal antiinflammatory drugs, although there is little downside to trying these medications. Ketamine, haloperidol, and baclofen are nonopioid medications that may provide analgesia. Autonomic dysfunction that leads to many of the findings of OWS, such as hypertension, diaphoresis, irritability, and restlessness, may be treated with alpha-2 agonists; clonidine has been the traditional medication used from this class. Lofexidine has recently been approved by the U.S. Food and Drug Administration (FDA) for treatment of OWS, and may provide marginally better symptomatic relief with fewer side effects compared with clonidine, but is dramatically more expensive (47).

Q5. How can Emergency Clinicians Protect the Health of OUD Patients Apart from Initiating Buprenorphine?

Harm reduction is a public health-based strategy to reduce the negative consequences associated with a particular disease or behavior for individuals and their

Table 3. Nonagonist Treatment of OWS

Dysautonomia
Clonidine 0.1 mg p.o. q1–3h
Dexmedetomidine start at 0.2 μg/kg/min i.v.
Lofexidine 0.2–0.4 mg p.o. q6–12h
Pain
Ibuprofen 400–600 mg p.o. q4–6h
Ketorolac 10–15 mg i.v./i.m. q4–6h
Acetaminophen 500–1000 mg p.o. q4h up to 4 gm daily
gabapentin 200–400 mg p.o. q6–8h
Baclofen 10 mg p.o. q8h
Tizanidine 4–8 mg p.o. q6–h
GI distress
Ondansetron 4–8 mg p.o./i.v. q4–6h
Promethazine 25–50 mg i.v./i.m.
Metoclopramide 10–20 mg i.v. q6–8h
Diphenhydramine 50 mg i.v. q6–8h
Hydroxyzine 50–100 mg p.o./i.m. q4–6h
Loperamide 4 mg p.o. q4h
Dicyclomine 20 mg p.o. q6h
Agitation
Lorazepam 2–4 mg p.o./i.v. q2–4h
Diazepam 10–20 mg i.v. q30–60 min
Midazolam 2–5 mg i.m./i.v. q2h
Haloperidol 2–10 mg i.v./i.m./p.o. q4–6h
Droperidol 1–5 mg i.v./i.m. q4–6h
Olanzapine 5–10 mg i.m. q4h
Ziprasidone 10–20 mg i.m. q4h
Ketamine 0.25 mg/kg i.v. over 20 min q2h

OWS = opioid withdrawal syndrome; p.o. = per os (by mouth); q = every; i.m. = intramuscular; GI = gastrointestinal.

communities. Although it is most often associated with drug use, it also applies to clinicians' attempts to manage conditions such as diabetes and hypertension, with the goal of encouraging individuals to be as healthy as possible by *meeting patients where they are*—even if they don't follow the optimal treatment plan—through teaching the skills necessary to maximize quality of life and minimize morbidity.

EDs increasingly care for patients after opioid overdose; they have a 1-year mortality of over 5% (48,49). Harm reduction, as it pertains to OUD, promotes health both for patients who are ready to move to recovery (with medications and treatment engagement) and those who are not, by providing access to knowledge and resources to keep the patient as healthy as possible, recognizing that the door to recovery remains open as long as the patient is alive.

Overdose prevention and naloxone distribution, initiated in the late 1990s by harm-reduction organizations, is recognized as an important health care intervention for high-risk patients. Naloxone distribution has received wide support from many federal and national organizations, including the U.S. Surgeon General, who in April 2018 released an advisory encouraging the wide distribution of naloxone to individuals who use opioids, as well as to their friends and families (50–52). Clinicians may be concerned about the possibility of increased risky opioid use if naloxone is available in the community. Evidence does not suggest that this *parachute effect* occurs significantly, and to the extent it does occur, it is likely outweighed by the public health benefits from overdose rescue. Limited evidence demonstrates that opioid use is decreased or unchanged where naloxone distribution occurs, and we recommend ED-based naloxone distribution as further research is ongoing (53,54). Localities with high naloxone dissemination have lower opioid-related mortality, and people who have been rescued from overdose may be particularly receptive to addiction treatment (55). PrescribeToPrevent.org provides ED-specific guidance on naloxone preparations, prescribing and billing, patient instructions, and sample protocols.

Emergency clinicians can reduce morbidity and mortality in people with ongoing opioid use by offering screening for pregnancy, hepatitis C, and human immunodeficiency virus, and with frank discussions around safe injection practices (Table 4) (56). Many municipalities offer syringe service programs that not only reduce the devastating consequences of contaminated needle use but are often integrated with social work, case management, and treatment referral services that can improve patient outcomes (57,58). Limited data indicate that these programs, along with supervised consumption sites, reduce the dangers of illicit substance use as well as the community harms of public injecting and unsafely disposed syringes, without increasing drug use, trafficking, or crime (59–63).

Table 4. Safe Injection Practices

Avoid using alone. If you overdose, you want someone around to help.
Be cautious if you haven't used in a while. You're more likely to overdose.
Avoid mixing. Many overdoses happen when heroin or painkillers are mixed with other drugs like benzos, methadone, antidepressants, or alcohol.
Always do a tester shot to make sure a new batch isn't too strong.
Make an overdose plan. Be prepared with naloxone, and have a phone on hand in case you need to call 911.
Don't be afraid to call 911. If you're with someone who you think is overdosing, call 911. The law provides substantial protection from prosecution.
Always use new equipment, and never share equipment. Many communities anonymously provide free syringes and drug use equipment.
Never lick needles, always use sterile water, and discard cotton after every use.

Q6. What is the Relative Efficacy of MAT Compared with Abstinence-Based Treatment Programs in Reducing Morbidity and Mortality in Patients with OUD?

Stigma and bias among clinicians, the public, payers, policy-makers, and even the patients themselves toward people with substance use disorder has led to acceptance of the abstinence-based treatment standard historically adopted for this disease. Although this approach (which includes most "detox," "rehab," and 12-step programs) may be valid for certain substance use disorders, such as stimulants, the availability of mechanism-based and evidence-based pharmacologic agents strongly differentiates the treatment of OUD. The stigma is often manifest in the misguided belief that the use of buprenorphine or methadone is "replacing one addiction with another." Buprenorphine or methadone therapy uses one opioid (that is pharmaceutical and legal) to replace another (that may not be either); even this description of MAT undervalues its personal and societal benefits, however. Addiction is a *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM 5)-defined diagnosis that is distinguished from dependence fundamentally by behavior, and effective treatments reduce the harmful behaviors associated with drug use that can have significant health, work, family, and legal consequences (64). Buprenorphine or methadone treatment reduces or eliminates harms arising from the desperate behavior caused by the fear of running out of opioids and developing withdrawal, as well as the harms associated with using, and especially injecting, chemicals purchased on the street of uncertain identity and potency.

Because there are several widely varying forms of behavioral therapy, there is confusion in the literature

and little consistency in treatment practices (65). Behavioral therapy alone without an agonist (i.e., detoxification) is not generally effective in maintaining abstinence. Though the addition of behavioral therapy to an opioid agonist may improve retention in long-term treatment, counseling does not convey significant added value in short-term morbidity or mortality (66,67). Therefore, providers should not link the initiation of MAT to the immediate availability of, or patient willingness to participate in, counseling. Furthermore, patients who request detoxification treatment (often originating from a stigma-based desire to be "drug-free") should be advised of the much higher likelihood of relapse when treatment does not include the use of opioid agonists. Additionally, especially at a time when the street opioid supply has been contaminated with illicit fentanyl and its analogues, patients should be educated about how dangerous relapse is. These conversations may frame buprenorphine as a treatment for addiction similar to insulin as a treatment for diabetes.

United States federal law requires that patients being treated with MAT receive behavioral counseling, however, emergency clinicians meet this requirement by referring the buprenorphine-initiated patient to outpatient addiction care (68).

Q7. How do Naltrexone, Methadone, and Buprenorphine Compare as Treatments for OUD?

There are limited head-to-head comparisons on the safety or effectiveness of these three evidence-based pharmacological approaches to managing patients with OUD (69,70). However, the data on each are sufficiently robust to draw conclusions on their comparative effectiveness, and specifically, on their practical utility in the management of patients in the ED.

Naltrexone, a long-acting opioid receptor antagonist, competitively inhibits the agonist effects of opioid agonists. It is most commonly administered for OUD treatment in its i.m. depot formulation, which provides effective antagonism for about 1 month; however, as a competitive antagonist, the use of high doses of potent opioids can overcome this blockade. Unlike agonist therapies, naltrexone does not address the altered neurochemistry that causes opioid cravings and relapse. Patients must have not taken opioids for several days prior to administration to prevent the development of precipitated opioid withdrawal; this creates a significant barrier to initiation, as withdrawal is what many OUD patients want desperately to avoid, and essentially eliminates its use in the ED setting.

Buprenorphine and methadone are long-acting opioid agonists with a significant pharmacological distinction: methadone is a full opioid receptor agonist and buprenorphine is an opioid receptor partial agonist (Q8). Both are effective at treating opioid withdrawal and at reducing opioid use and harm (69–74). Methadone, as a full agonist, is significantly more prone to abuse than buprenorphine and is far more dangerous in overdose. Methadone also provides less opioid receptor "blockade" effect compared with buprenorphine; receptor blockade protects patients against overdose with other opioids.

Buprenorphine and methadone are also distinguished by their regulatory status. Methadone for the treatment of OUD can be dispensed (not prescribed) only through federally regulated opioid treatment programs (OTPs); initiating methadone as a treatment for addiction is therefore not possible from the ED. Buprenorphine may be prescribed by any provider with a Drug Addiction Treatment Act (DATA) 2000 waiver and administered in the ED for 72 h by waivered or nonwaivered clinicians, making it significantly more accessible and relevant to emergency care (Q15).

Q8. What are the Pharmacologic Features of Buprenorphine that Make it Well Suited to Treat OUD?

Buprenorphine is a mu-opioid receptor *partial agonist* that binds with a *higher affinity* than nearly every other opioid and *dissociates slowly*. Due to the partial agonism, binding to the opioid receptor evokes only limited clinical effects, and as the dose is escalated, a maximal response is reached, a *ceiling effect*. Even at high doses in opioid-naïve patients, respiratory depression and euphoria are minimal compared with that from full opioid agonists (75).

In patients with abstinence-induced opioid withdrawal, buprenorphine's partial agonism is generally sufficient to replace the loss of agonism as the concentrations of full agonist fall, quelling the clinical manifestations of withdrawal.

Due to the high mu-opioid receptor binding affinity of buprenorphine, full agonist opioids have limited ability to displace the buprenorphine. This explains why administration of a full agonist opioid, such as heroin, after buprenorphine results in reduced clinical effect, often referred to as *buprenorphine blockade* (76). This opioid receptor blockade protects buprenorphine-using patients from overdose and limits euphoria and reward from full agonists, though buprenorphine blockade can be partially overcome with high doses of full agonists. It also highlights the difficulty in using opioids to manage acute pain in a patient on buprenorphine maintenance treatment (Q42).

Buprenorphine exhibits slow dissociation from the opioid receptor and a long elimination half-life, allowing buprenorphine to be dosed once per day or even less

Table 5. Buprenorphine Preparations†

Dosage Form	Trade Name(s)	Medication(s)	Available Dose(s)	Approximate Price per Dose*
Buccal film	Belbuca	Buprenorphine	75 μg, 150 μg, 300 μg, 450 μg, 600 μg, 750 μg, 900 μg	$6–15
	Bunavail	Buprenorphine/naloxone	2.1/0.3 mg, 4.2/0.7 mg, 6.3/1 mg	$9–18
Sublingual film	Suboxone	Buprenorphine/naloxone	2/0.5 mg, 4/1 mg, 8/2 mg, 12/3 mg	$5–20
	Generic		2/0.5 mg, 8/2 mg	$4–9
Sublingual tablet	Zubsolv	Buprenorphine/naloxone	0.7/0.18 mg, 1.4/0.36 mg, 2.9/0.71 mg, 5.7/1.4 mg, 8.6/2.1 mg, 11.4/2.9 mg	$5–20
	Generic	Buprenorphine/naloxone		$4–10
	Generic	Buprenorphine	2/0.5 mg, 8/2 mg 2 mg, 8 mg	$4–9
Subcutaneous implant	Probuphine Implant Kit	Buprenorphine	74.2 mg	$1500
Transdermal patch (weekly)	Butrans	Buprenorphine	5 μg/h, 7.5 μg/h, 10 μg/h, 15 μg/h, 20 μg/h	$80–215
	Generic	Buprenorphine	5 μg/h, 7.5 μg/h, 10 μg/h, 15 μg/h, 20 μg/h	$65–170
Solution for injection	Buprenex	Buprenorphine	0.3 mg/mL (1 mL)	$18
	Generic	Buprenorphine	0.3 mg/mL (1 mL)	$14
Subcutaneous prefilled syringe	Sublocade	Buprenorphine	100 mg/0.5 mL (0.5 mL), 300 mg/1.5 mL (1.5 mL)	$1200–1900

* Prices based on estimated Average Wholesale Price.
† Not all products carry indication for OUD (see text).

frequently, though twice a day (b.i.d.) or three times a day (t.i.d.) dosing is sometimes used, especially early in buprenorphine therapy (75).

Q9. What are the Important Harms Associated with Buprenorphine Use and Buprenorphine Abuse?

In opioid-dependent patients who are not in withdrawal, administration of buprenorphine may result in precipitated opioid withdrawal because a partial agonist (buprenorphine) displaces the full agonist (heroin, for example) from the receptor. Initiating buprenorphine treatment therefore requires that the patient already be sufficiently in withdrawal, or past the period of physical withdrawal, to avoid buprenorphine-precipitated withdrawal (BPW).

Buprenorphine administered by the intravenous route is more psychoactive and rewarding than by the proper, sublingual route (77). To prevent surreptitious self-administration of intravenous buprenorphine, the preferred outpatient formulation contains naloxone (Q11). When opioid-dependent patients use buprenorphine/naloxone formulations by the sublingual route prior to the development of moderate withdrawal, precipitated opioid withdrawal may occur due to the buprenorphine, not due to the naloxone.

In opioid-naïve adults or especially children, at very high doses (relative to body weight), the partial agonism may still cause clinically consequential adverse opioid effects, including dangerous respiratory depression, especially when used with other sedating medications such as benzodiazepines (78–80). Despite the potential risk, buprenorphine is substantially safer than any of the full agonist opioids.

Buprenorphine, as with other opioids, induces hyperalgesia, in which the sensitivity to painful stimuli increases with ongoing opioid exposure (81).

Q10. Which Immediate-Release Buprenorphine Preparations are Commonly Used in Acute Care Settings to Treat OUD?

Buprenorphine is available in several formulations, some in combination with naloxone (Table 5) (82). The most commonly used preparations in the ED are sublingual film and sublingual tablets; clinically, there is little difference in effects or patient-oriented outcomes between them, nor between sublingual preparations and the less commonly used buccal preparations (83–85). Lower-dose preparations (Belbuca [BioDelivery Sciences International, Raleigh, NC], Butrans [Purdue Pharma L.P., Stamford, CT]) are indicated for pain, not OUD treatment.

Buprenorphine is also available in an intravenous form, as a 0.3-mg/mL solution for injection. This formulation is FDA approved only for acute pain management, but can be used for opioid withdrawal when vomiting interferes with sublingual administration. Access to intravenous buprenorphine is not required, however, as sublingual administration is almost always effective, even in the setting of vomiting.

Q11. What are the Roles for Buprenorphine Mono-Product and the Combination Product with Naloxone?

Naloxone is added to some products as an abuse deterrent. Naloxone's bioavailability via oral, sublingual, and

buccal routes is near zero; therefore, the naloxone component has no clinical effect when buprenorphine-naloxone is taken sublingually or buccally as intended (86). However, if the medication is crushed or dissolved in solution and injected or aerosolized, the mu-receptor antagonist properties of naloxone would counteract clinical effects of the buprenorphine (or other opioids), and possibly precipitate opioid withdrawal. Evidence is conflicting on the abuse-deterrent efficacy of adding naloxone to sublingual buprenorphine (87).

The FDA approved generic buprenorphine/naloxone sublingual film in 2018, with an approximate price of $4 for the 2/0.5-mg film and $9 for the 8/2-mg film (88,89). A variety of programs are available in many settings to support the medication cost for patients both in the initial treatment period and long term; providing 1 week's supply of buprenorphine to patients who will have difficulty obtaining a prescription facilitates success during the vulnerable transition period (90).

In the ED there is no concern for misuse because doses administered are directly observed. The buprenorphine mono-product and buprenorphine–naloxone combination preparation are therefore equivalent and interchangeable in this context.

Q12. What Long-Acting Forms of Buprenorphine are Available?

Long-acting preparations, such as the transdermal patch, subcutaneous implant, and subcutaneous prefilled syringe (for depot injection), have the potential to improve adherence with their less frequent administration (weekly for the patch, monthly for the subcutaneous injection, and biannually for the implant) (91). Currently, the transdermal patch is FDA approved only for chronic pain and not approved for the treatment of OUD. The implant's daily transmucosal dose equivalency is too low to be effective for most patients with OUD. Although the direct medication cost of the depot subcutaneous injection is high, the benefits for patients at high risk for medication noncompliance with a transmucosal formulation may be great enough to justify the administration of the depot injectable product in the ED.

Q13. Which Buprenorphine Preparation Should be Used in Pregnancy?

Buprenorphine (with or without naloxone) is safe during pregnancy to treat OUD, and its use in pregnant women is increasing (92–94). Historically, buprenorphine mono-product has been recommended during pregnancy for concern of the untoward effects of naloxone as a teratogen or, if crushed and injected, potential consequences of precipitated withdrawal on the fetus. However, a series of cohort studies demonstrate the safety of the combination product during pregnancy, with no difference in the rate of birth anomalies between the buprenorphine mono-product and the buprenorphine-naloxone combination (95–99). A pregnant patient with OUD should therefore generally be treated with the product determined to be best suited for her if she were not pregnant.

Neonatal OWS, until recently referred to as neonatal abstinence syndrome, is common after delivery of children by mothers who were using buprenorphine or methadone, although it is less severe with buprenorphine (100,101). Limited evidence suggests that higher buprenorphine doses used during pregnancy do not increase the severity of neonatal OWS (102). Women on agonist therapy for opioid addiction should continue MAT while breastfeeding; both methadone and buprenorphine are minimally transferred to breast milk.

Q14. Is it Necessary to Have Psychiatry or Addiction Specialists Available for Consultation to Initiate Buprenorphine in the ED?

Emergency clinicians can and should acquire the skills required to identify OUD patients who would benefit from MAT, initiate or prescribe buprenorphine, and refer to outpatient addiction care. Specialist addiction consultation is of benefit in some situations, such as those with complicated psychiatric or medical comorbidities, but is not required to initiate buprenorphine in the ED.

Q15. Is it Necessary to Have DATA 2000-Waivered Physicians in the ED to Initiate Buprenorphine?

DATA 2000 mandates that physicians obtain an addendum to their DEA registration, known as an "X-waiver," to *write an outpatient prescription* for buprenorphine to treat addiction. An X-waiver is not required to *administer* buprenorphine in the ED (or on inpatient units); all physicians may treat opioid withdrawal and initiate buprenorphine therapy in the ED or hospital. Under the "3-day rule," patients may return to the ED daily to receive buprenorphine administered in the ED for the primary treatment of OUD/addiction for up to 2 days after the first day, for a total of 72 h (103). Therefore, though the capacity to provide an outpatient buprenorphine prescription adds strength and flexibility in managing patients with OUD, departments that do not have any X-waivered providers may still effectively initiate buprenorphine and refer for ongoing treatment, using return ED visits as a bridge to outpatient care as needed.

Buprenorphine may be administered for opioid dependence if it is a secondary concern. For example, patients who are hospitalized for the treatment of cellulitis may

receive buprenorphine without an available X-waivered clinician.

Buprenorphine may be prescribed by any DEA-registered clinician for the treatment of chronic pain; currently this is rarely done from the ED.

Emergency clinicians may obtain an X-waiver through an 8-h training program. Although current U.S. regulations stipulate that special training is necessary to prescribe buprenorphine for addiction, this should not discourage nonwaivered physicians from treating OUD with buprenorphine in the ED. We support proposals to remove the waiver requirement to prescribe buprenorphine for the treatment of OUD/addiction (104–107).

Q16. How Robust Must Outpatient Follow-Up Resources be to Initiate Buprenorphine in the ED?

DATA 2000 requires that when initiating buprenorphine for treatment of OUD, the provider must refer to appropriate counseling once the patient is discharged. Stronger transitions such as an arranged appointment and provider-to-provider communication ("warm handoff") make successful linkage to comprehensive outpatient addiction care more likely; however, a simple phone number referral to addiction services on discharge satisfies the DATA 2000 mandate. Poor availability of comprehensive addiction care and outpatient counseling services should not dissuade emergency clinicians from treating patients with OUD with buprenorphine (Q35).

Q17. What Other Regulatory Requirements Pertain to ED-Initiated Buprenorphine?

DATA 2000 limits the number of patients to whom a single provider can prescribe buprenorphine *at any one time* to 30 patients in the first year, which can be increased (by application) to 100 and 275 patients in the second and third year, respectively. As this pertains only to active prescriptions, and most ED prescriptions will be for a limited supply until further outpatient treatment can be obtained, it is unlikely that an emergency clinician would approach these limits through their ED practice. Contemporary electronic health records (EHRs) can report on specific medication use, which satisfies the DEA reporting mandates. Practitioners who work in settings without an electronic health record, or with an EHR incapable of medication reporting, should keep a log of patients to whom buprenorphine is administered or prescribed for addiction, including dose and quantity. No specific written consent is required to treat OUD patients with buprenorphine.

"Telebup" programs, where DATA 2000-waivered providers assess patients and prescribe buprenorphine remotely, expand MAT access to underserved regions. DEA-registered providers (including nurse practitioners and physician assistants) without a waiver may link the patient to a waivered provider (who must have a license to practice medicine in the state where the physical encounter is taking place) using a telemedicine video portal. The waivered provider remotely assesses the patient and prescribes buprenorphine (108).

When prescribing buprenorphine, the diagnosis of OUD should be documented (109). The DSM-5 criteria for OUD is met by most patients presenting to the ED with complications of opioid use (Table 6) (64,110).

Q18. How Should ED Patients be Screened for OUD?

EDs disproportionately provide care to patients with OUD and other substance use disorders, who may present for emergency care with concerns directly related or unrelated to their opioid use, and their presentation may reveal their misuse of opioids or not (5). Identifying OUD in ED patients when opioid misuse is not explicit in their presentation, linking their signs and symptoms to opioid misuse, initiating harm reduction practices,

Table 6. Summarized DSM-5 Criteria for Opioid Use Disorder

2 or more of the following:
Opioids are often taken in larger amounts or over a longer period than was intended
There is a persistent desire or unsuccessful efforts to cut down or control opioid use
A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects
Craving, or a strong desire or urge to use opioids
Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home
Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids
Important social, occupational, or recreational activities are given up or reduced due to opioid use
Recurrent opioid use in situations in which it is physically hazardous
Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
Exhibits tolerance as demonstrated by increased amounts of opioids needed to achieve desired effect; diminished effect with continued use of the same amount
Exhibits withdrawal as demonstrated by symptoms of opioid withdrawal syndrome; opioids taken to relieve or avoid withdrawal

DSM-5 = *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (64).

and moving appropriate patients to addiction treatment has the potential to significantly improve health outcomes.

A variety of opioid misuse screening tools are available, though tools developed for clinic environments may not perform well in the ED (111–113). The abbreviated National Institute on Drug Abuse Quick Screen uses a single drug use question: "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" can be asked by any staff member in an acute care environment (114,115). Patients who screen positively should be assessed more specifically for substance use disorders and offered appropriate treatment and harm reduction measures.

Q19. Which Patients Should be Considered for ED-Based Buprenorphine Initiation?

All patients with OUD who are not already in a MAT program (methadone, buprenorphine, or naltrexone) should be considered for ED-initiated buprenorphine. The more the patient is being harmed by opioids, the more the potential benefit of buprenorphine treatment. Nearly all people who use street opioids should therefore be offered buprenorphine, as should patients who present after nonfatal overdose, having demonstrated the highest risk. Patients experiencing opioid withdrawal are particularly susceptible to opioid harms, and prompt treatment with buprenorphine is indicated in this group.

Q20. In which Patients Should ED-Based Buprenorphine Initiation be Avoided, or Used with Particular Caution?

Buprenorphine predominantly causes harm in two ways: BPW and buprenorphine toxicity. BPW is more likely in patients with insufficiently severe opioid withdrawal and in patients who take long-acting opioids, especially methadone (Q21). Patients with opioid withdrawal who are on methadone maintenance should generally be treated with methadone rather than buprenorphine (Q46).

Buprenorphine toxicity is similar to toxicity associated with full agonist opioids, but consequential respiratory depression is much less likely than with full agonists (Q8). Buprenorphine is more likely to cause dangerous respiratory depression in patients taking central nervous system depressants such as benzodiazepines or alcohol, patients with advanced cardiorespiratory disease or sleep apnea, or the very old or young. Sedative-intoxicated patients should be observed for a period of metabolism and reassessed for appropriateness of buprenorphine treatment.

The likelihood of harm from buprenorphine must be weighed against the likelihood of harm from withholding buprenorphine. The latter will, in many cases, cause the patient to use full agonist opioids that are almost always more dangerous than buprenorphine. The patients who are most likely to be harmed by buprenorphine are usually at the highest risk to be harmed by full agonists (especially street opioids) and are therefore also the most likely to benefit from buprenorphine treatment (Q36).

Q21. How can Sufficient Spontaneous (Abstinence-Induced) Opioid Withdrawal be Assured, so that BPW is Avoided?

Avoiding BPW is an important consideration in initiating buprenorphine therapy. The 36-point Clinical Opiate Withdrawal Scale (COWS) is most often used as a measure of OWS severity, with minimum recommended COWS scores ranging from 8 to 13 to initiate buprenorphine treatment. The more severe the patient's OWS, the less likely BPW will occur and the better buprenorphine therapy will be received. Patients who use long-acting opioids and patients who have more "subjective" features driving their COWS score should wait until the development of a higher COWS score ($\geq$13) or the development of objective signs of OWS.

As a rule of thumb, patients who use short-acting opioids (e.g., heroin) should wait 8–12 h since last use; patients who use extended-release opioids (e.g., Oxycontin [Purdue Pharma L.P.], MS Contin [Rhodes Pharmaceuticals L.P., Coventry, RI]) should wait 24 h, and patients who use methadone should wait > 72 h.

Q22. What Ancillary Testing Should be Done Prior to or during ED-Initiated Buprenorphine?

Once an appropriate patient has been identified using a directed history and physical examination, no ancillary tests are required to initiate buprenorphine. Downstream addiction providers will often test their patients for pregnancy, human immunodeficiency virus, and hepatitis C, liver function, and urine toxicology; however, this does not need to be done in the acute care setting and should not delay the first dose of buprenorphine.

OUD patients often have co-occurring medical, psychiatric, and social concerns, and many of these patients benefit from a more comprehensive assessment to identify and manage these conditions; however, such an assessment is not needed in advance of or during buprenorphine initiation.

Q23. How Should Emergency Clinicians Dose Buprenorphine?

Pathways developed for office-based psychiatry practice classically call for small initiation doses (2 mg), but ED

experience suggests that larger doses on day #1 may be superior, as larger doses are safe and more likely to extinguish cravings and extend buprenorphine's duration of action (116). We recommend 4–8 mg sublingual (s.l.) buprenorphine as the first dose, based on the severity of withdrawal (Figure 1).

If, 30–60 min after the first dose, the patient feels entirely better and has reliable access (via prescription or clinic appointment) to the second dose on day #2, initiation is complete. If the patient is still experiencing OWS after the first dose or may not be able to obtain the second dose before withdrawal or cravings recur, we recommend administration of additional buprenorphine to bring the total day #1 dose to 16–32 mg, with a target of 16 mg appropriate for most ED patients who present with OWS. Doses higher than 16 mg offer increased relief of withdrawal, extended protection from cravings, and protection from toxicity from full agonist opioids. However, the risk of over-sedation and respiratory depression is increased at higher doses, especially if the patient uses other sedatives. Although high-dose buprenorphine initiation has been demonstrated to be safe in a variety of settings, there is at present little ED-based literature to support this practice (117–120).

At the time of reassessment after the first dose, if the patient's signs and symptoms are not improved or worsen, the provider should consider non-OWS etiologies (e.g., sedative/alcohol withdrawal, intoxication, infection) as well as precipitated withdrawal (Q39).

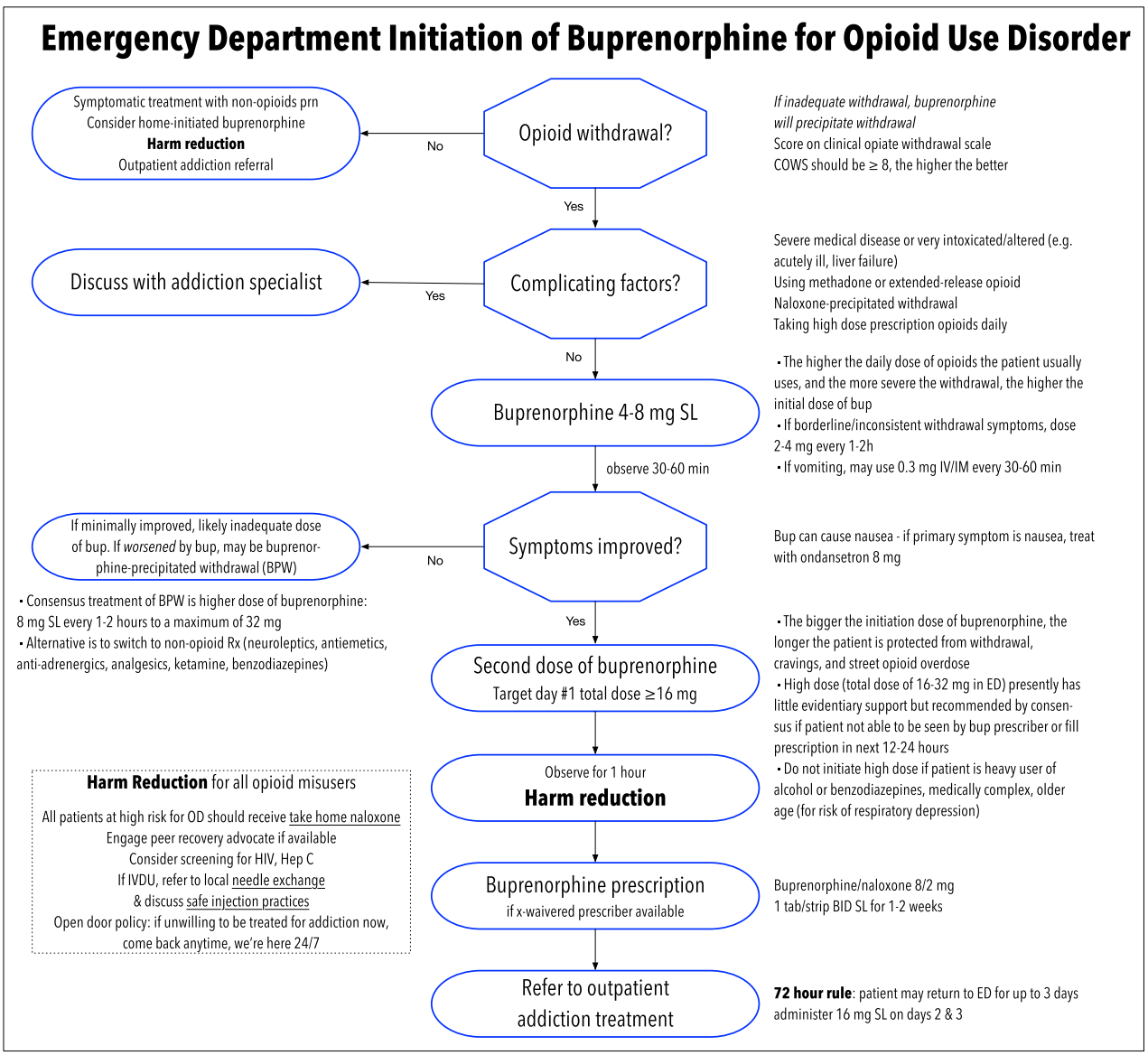


Figure 1. Emergency department initiation of buprenorphine for opioid use disorder. COWS = Clinical Opiate Withdrawal Scale; SL = sublingual; IM = intramuscular; ED = emergency department; OD = overdose; HIV = human immunodeficiency virus; IVDU = intravenous drug user; BID = twice a day.

Q24. How Long Should ED-Initiated Buprenorphine Patients be Observed, and what Adverse Effects can Occur?

Though serious adverse events when using buprenorphine to treat OUD are rare, we recommend that patients be observed for 30–60 min after each administered dose to monitor for over-sedation. The most common adverse effect is nausea, which can be difficult to distinguish from nausea related to OWS. The usual antiemetics, such as ondansetron 4–8 mg, are effective. Longer periods of observation are prudent for patients with complicating factors such as serious co-occurring medical disease, older age, or nonopioid co-intoxication. Although the treatment of patients with OUD does not require hospital admission, OUD patients with unstable medical, psychiatric, or social illness may benefit from inpatient management.

Q25. How can Buprenorphine be Initiated in Patients Not Yet in Sufficient Withdrawal?

Opioid-dependent patients who do not demonstrate signs of moderate-to-severe OWS are at risk for BPW if initiated too early. The preferred approach for many of these patients is *home initiation* with a prescription for buprenorphine (Q32), specific instructions, and outpatient follow-up. Alternatively, insufficiently withdrawing patients can be observed in the ED for the development of moderate OWS or placed in an ED-based observation pathway (121). This group includes patients who present with opioid intoxication. Like many intoxicated patients, they should be observed for a period of time to allow metabolism and be reassessed for suitability for OUD treatment when sober.

Q26. How can Buprenorphine be Initiated in Patients Who Have Completed Their Period of Physical Withdrawal?

Patients who have been abstinent for longer than a few days to weeks may be "fully detoxed" and no longer experiencing OWS. However, most still experience dangerous cravings, which contribute to relapse. These patients are no longer physically dependent on opioids and therefore not at risk for BPW; they may be treated promptly with buprenorphine and referred for comprehensive addiction care, ideally with a buprenorphine prescription. Tolerance may be reduced in this group, therefore, an initial dose of 2–4 mg s.l. is reasonable. However, patients who have completed physiologic withdrawal within the last 1–2 weeks may not yet have significantly decreased tolerance, and augmenting the first dose based on patient response, with a goal of 8–16 mg on day number one, may prove optimal when studied further.

Q27. How can Buprenorphine be Initiated in Patients Who Decline Buprenorphine in the ED?

Patients may decline buprenorphine due to misconceptions about MAT (e.g., "replacing one addiction with another") that can be addressed in the ED. Some patients who decline buprenorphine wish to continue to use street opioids. These patients should be offered harm reduction services (Q5) and encouraged to return to the ED when they are ready to transition to recovery. Other patients decline buprenorphine based on an unwillingness to endure the period of time until development of sufficient opioid withdrawal that is conventionally required to initiate buprenorphine. These patients may be successfully transitioned to buprenorphine over a period of 4–8 days using very small, gradually increased doses as they continue to use full agonist opioids (9,122–125). This *microdosing* technique allows for buprenorphine initiation without withdrawal, but at present has a limited evidentiary base and is therefore of uncertain effectiveness.

Q28. What is the Appropriate Disposition for Patients Treated with Buprenorphine in the ED?

Very few patients treated with buprenorphine require inpatient management for their OWS or OUD. Hospitalization may be required to manage co-occurring severe alcohol or sedative use disorder, or coincident medical, psychiatric, or social concerns.

Q29. Which Patients Discharged from the ED after Buprenorphine Initiation Should Receive a Buprenorphine Prescription?

Unless immediate follow-up with a buprenorphine prescriber is available, most patients treated with buprenorphine in the ED should have their treatment extended with a buprenorphine prescription to avoid gaps in therapy that allow relapse to street opioid use (111,125,126).

Providers may be concerned that buprenorphine prescribed or dispensed out of the ED will be sold on the black market. Although this practice is illegal and not condoned, concerns around buprenorphine diversion should not discourage prescribing. This is because illegally obtained buprenorphine is primarily used for its intended purpose of preventing opioid withdrawal in patients with OUD and not as an abused substance (127–130).

If buprenorphine cannot be prescribed (e.g., because no waivered prescribers are available), cannot be filled, or is determined to be inappropriate, patients should be instructed to return to the ED as needed for further administered doses as covered by the 3-day rule (Q15).

Q30. How can Providers Improve the Likelihood that a Patient Will be Able to Fill a Prescription for Buprenorphine?

The ability to pay for buprenorphine should be discussed with patients. Depending on the insurer and state, some buprenorphine formulations may require prior authorization, which is sometimes difficult to arrange from the ED, but social work, case management, and pharmacy services may be able to coordinate patient resources with payers and pharmacies, as well as facilitate transportation if needed. Delays and denials are reduced by developing streamlined prescribing and dispensing processes with local pharmacies and the hospital outpatient pharmacy (131).

Different insurances cover different formulations and may require specific indications; if the EHR allows, we recommend a standardized discharge prescription that includes language to improve the odds of success, including the DEA-X number directly on the prescription to assist the pharmacy (Figure 2).

Many patients have difficulty filling their first buprenorphine prescription; a charity buprenorphine program, which provides an initial supply of buprenorphine tablets, is a powerful discharge strategy if available.

Q31. What is the Appropriate Prescribed Dose of Buprenorphine?

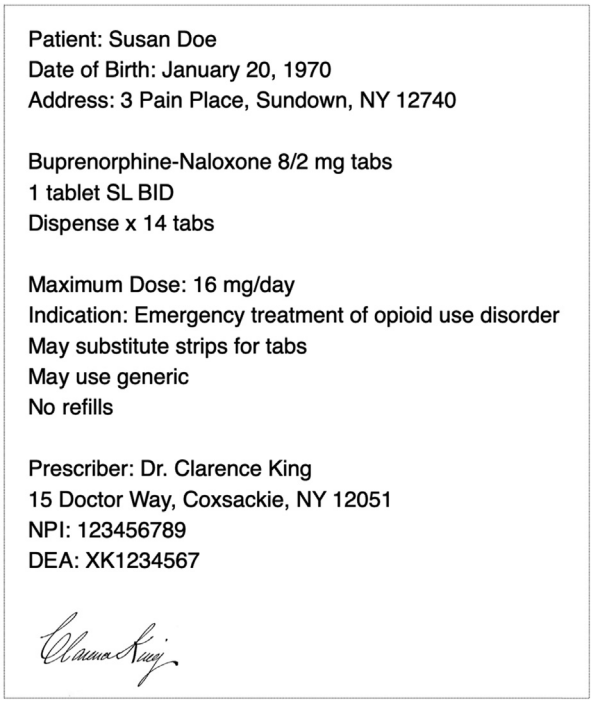
Most patients stabilize on 8–24 mg/day. For simplicity, we recommend 16 mg per day as an initial prescription for most patients discharged after initiation of buprenorphine in the ED.

Q32. How can Buprenorphine be Prescribed for Home Initiation, for Patients Who do Not Receive Buprenorphine in the ED?

We recommend a simplified home initiation regimen of 4 mg once the patient is in adequate withdrawal, followed by 4 mg every 2 h as needed for ongoing withdrawal symptoms, to a maximum of 24 mg on day #1, followed by 8 mg twice per day on days #2 and beyond. Patients should be advised to return to the ED or a buprenorphine provider if symptoms worsen after taking a dose. Providing a home initiation patient information handout is recommended; home initiation mobile apps have been developed to guide patients, and other resources also exist.

Q33. How Should Patients be Linked to Outpatient Comprehensive Addiction Care?

The stronger the link to ongoing care, the more likely the patient will succeed. An ideal *warm handoff* includes provider-to-provider verbal communication to establish explicit and exact follow-up details, including a plan for contingencies such as inability to fill a prescription or get to an appointment. If synchronous transfer of care is infeasible, a written or voicemail referral should include patient name and date of birth, insurance status, co-occurring substance use, mental health, medical and social conditions, what medications were given to the patient and prescribed from the ED, test results, and follow-up plan. Prearranged standing weekly appointments or walk-in hours with local treatment centers that are available to ED patients facilitate access to outpatient care.


Patient: Susan Doe
Date of Birth: January 20, 1970
Address: 3 Pain Place, Sundown, NY 12740

Buprenorphine-Naloxone 8/2 mg tabs
1 tablet SL BID
Dispense x 14 tabs

Maximum Dose: 16 mg/day
Indication: Emergency treatment of opioid use disorder
May substitute strips for tabs
May use generic
No refills

Prescriber: Dr. Clarence King
15 Doctor Way, Coxsackie, NY 12051
NPI: 123456789
DEA: XK1234567

Figure 2. Sample buprenorphine prescription. SL = sublingual; BID = twice a day; NPI = National Provider Identifier; DEA = Drug Enforcement Agency.

Advocates referred to as peers, recovery coaches, or advisors may offer essential support to patients striving to establish addiction services (132,133). Bridge clinics, which can be staffed by emergency clinicians, offer flexible scheduling to smooth the transition from emergency to outpatient care (5,134). Patients should be encouraged to return to the ED promptly if existing support is failing.

Q34. What Discharge Instructions Should be Given to Patients Initiated with Buprenorphine in the ED?

Discharge instructions after buprenorphine initiation should be directed at a fifth-grade reading level and include visual guidance where possible. Relevant topics

Table 7. Nonopioid Analgesics and Modalities for Chronic Pain Management in the ED

Nonopioid	Nonpharmacologic
Ketamine	Physical therapy and exercise
Haloperidol	Osteopathic manipulative therapy
Gabapentin	Treatment of a coexisting mood disorder
Lidocaine 4% or 5% topical patch	Biofeedback
Ketorolac or ibuprofen + acetaminophen	Cognitive behavior therapy
Trigger point injection	Transcutaneous electrical nerve stimulation
Regional anesthesia:	
Lower paracervical blocks (for headache or orofacial pain)	
Sphenopalatine ganglion block (for headache)	

ED = emergency department.

include a description of how buprenorphine works and why opioid substitution treatment is more effective than abstinence, specific guidance on sublingual administration, cautions around BPW, and warnings regarding concomitant use of sedatives. In addition to follow-up appointment details, advice on safe medication storage, particularly regarding children and theft, and dangerous side effects and indications for return to the ED should be included.

Q35. Should Emergency Clinicians Use Buprenorphine to Treat OUD Patients Who are Unwilling or Unlikely to Continue with Long-Term Buprenorphine Treatment or Enter into Outpatient Addiction Care?

Clinicians may be reluctant to use buprenorphine in the ED to treat opioid withdrawal when follow-up care with an outpatient buprenorphine prescriber or addiction clinic is not assured. However, though ongoing comprehensive addiction care is the goal for all OUD patients, the balance of benefit and harm strongly favors buprenorphine therapy for almost all patients not already in a methadone program who present for care in opioid withdrawal (135,136). Buprenorphine is markedly safer than full agonists (such as methadone or hydromorphone) if the patient uses street opioids or sedatives after discharge (137–139). The alternative, which is to discharge the patient without treating withdrawal or to use comparatively ineffective nonagonists (e.g., clonidine) to treat withdrawal, impels the patient to use street opioids, which have become progressively dangerous due to unpredictable adulteration with fentanyl, among other critical hazards (140–143). Even if it is likely that the patient will ultimately return to street opioids, buprenorphine provides comparative safety from overdose, craving, and withdrawal during its therapeutic interval, as well as a period for the patient to contemplate recovery (144).

Initiating buprenorphine in patients who do not have immediate access to comprehensive addiction care makes successful transition to recovery significantly more likely than waiting for the establishment of such care (145,146). Psychosocial counseling, when added to buprenorphine, does not improve outcomes over buprenorphine treatment alone (4,67,72). The initiation of buprenorphine treatment should therefore not be withheld for concern that the patient will not have access to behavioral treatments or support. Note that U.S. regulations stipulate that a referral to outpatient addiction care is required whenever buprenorphine is initiated or prescribed out of the ED (Q16).

Q36. Should Emergency Clinicians Use Buprenorphine to Treat OUD Patients Who, in Addition to Opioids, Use Sedatives Such as Alcohol or Benzodiazepines, Other Recreational Substances, or Have Concomitant Psychiatric Illness?

The likelihood of harm from buprenorphine increases with concomitant sedative use, but treating these patients with buprenorphine is much safer than the patient using

Table 8. Likelihood of Benefit and Harm in Patients Taking Daily Opioids for Chronic Pain

Benefit Likely Exceeds Harm	Harm Likely Exceeds Benefit
Single prescriber	Multiple prescribers
Stable dose	Escalating dose
Low dose	High dose (>90 MME/day)
Infrequent visits for breakthrough pain	Frequent visits for breakthrough pain
High occupational/social function	Use of CNS depressants or stimulants
No opioid misuse	Poor occupational/social function
No evidence of addiction	Evidence of misuse (uses higher doses than prescribed, uses prescribed opioids in a way other than as prescribed, uses non-prescribed opioids or other psychotropic medications, uses illicit/street drugs)
	Evidence of addiction (compulsive use, use despite harmful consequences)

MME = morphine milligram equivalents; CNS = central nervous system.

Table 9. Excerpts From the AAEM Analgesia Guideline

When patients present to the ED with an exacerbation of chronic pain, the clinician should favor nonpharmacological and nonopioid analgesic treatments, as opioids are more likely to cause harm rather than benefit in these cases.
For patients with chronic pain, opioids should be prescribed by a single physician who will provide ongoing care, and who can use opioids as part of an analgesic care plan that includes specific functional goals as well as a patient–provider agreement.
When oral opioids are administered or prescribed, morphine may be preferred, as it may be less abuse prone than other opioids such as oxycodone and hydrocodone, and is of similar analgesic efficacy.
Opioid prescriptions should be limited to 2–3 days of an immediate-release opioid formulation.
When opioids are prescribed for outpatient analgesia, patients should be counseled on relevant opioid harms, including the risk of developing tolerance and dependence.

AAEM = American Academy of Emergency Medicine; ED = emergency department.

full opioid agonists concomitantly with sedatives. The FDA recommends that buprenorphine "should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system" (147). Psychiatric disease and use of other recreational substances such as cocaine are common among OUD patients and do not contraindicate buprenorphine treatment. They do indicate the need to implement coordinated addiction and psychiatric treatment modalities in addition to buprenorphine therapy.

Q37. Should Emergency Clinicians Use Buprenorphine to Treat OUD Patients Who Have Been in Buprenorphine Treatment in the Past, but Have Now Returned to Street or Prescription Opioid Misuse?

Like many chronic diseases, opioid addiction is characterized by relapse that is often due to psychosocial stressors or interruptions in access to treatment. Relapse is not a failure of therapy, and many patients with a history of relapse during buprenorphine therapy will move to sustained recovery with subsequent treatment attempts (148). Prior exposure to buprenorphine increases the likelihood of future success in buprenorphine treatment, and a history of relapse during buprenorphine (or any other) treatment for addiction should not discourage reinitiation of buprenorphine for an otherwise suitable patient (4,136).

Q38. How Should Emergency Clinicians Counsel OUD Patients (or Their Loved Ones) Who are Concerned that Buprenorphine Therapy is 'Replacing One Addiction with Another' or Concerned About Long-Term Buprenorphine Use?

Clinicians, families, and OUD patients themselves often believe that opioid addiction is the result of bad choices or a failure of willpower that can be overcome with determination and coaching, similar to how victims of emotional trauma benefit from peer support groups and psychosocial therapy. In fact, opioid addiction is an organic brain syndrome that induces neurochemical changes, which for many OUD patients requires long periods of agonist treatment to reverse, if they are reversible at all. Morbidity and mortality in OUD patients arise from *acquisition harms,* the risky (and sometimes illegal) actions desperately carried out to ensure continued supply of opioids and prevent withdrawal; *injection harms* from injecting nonsterile compounds with nonsterile needles; and *street drug harms* resulting from using illicitly manufactured and unregulated chemicals of unknown potency and safety. These *addiction harms* are abolished by transitioning patients to MAT, which, rather than substituting one addiction for another, *replaces addiction with dependence*. Like people who take daily insulin or thyroxine, people who take daily prescribed buprenorphine are dependent on buprenorphine; however, buprenorphine-maintained OUD patients are freed from addiction harms and often able to return to much more normal, productive, healthy lives.

Though some buprenorphine-maintained patients are able to cease buprenorphine therapy and successfully achieve abstinence recovery, it is more common for OUD patients who are weaned from MAT to relapse, which is very dangerous (73,149). Many, if not most, patients on buprenorphine maintenance are best served by, and do very well on, indefinite agonist treatment; the Substance Abuse and Mental Health Services Administration recommends that "Patients should take buprenorphine as long as they benefit from it and wish to continue" (150,151).

Q39. How Should BPW be Managed in the ED?

It is preferable to prevent BPW rather than treat it, by assuring that an opioid-dependent person is in an adequate state of spontaneous (abstinence-related) withdrawal prior to initiation of buprenorphine. However, unpredictable pharmacology and patient variability will lead to occasional cases of BPW, even with appropriate care. A patient may also present to the ED with BPW from using either prescribed or nonprescribed buprenorphine.

The optimal treatment of BPW is an active area of inquiry and there are, at present, minimal clinical data to

guide practice; recommendations are therefore based predominantly on consensus. Scant data suggest that BPW is less likely to develop when higher doses of buprenorphine are initially used, and many experts report successful treatment of BPW using higher doses of buprenorphine (152,153). The sole relevant guideline stipulates a maximum dose of 16 mg, however, higher doses (24–32 mg) are considered safe and may be effective when lower doses fail to alleviate BPW symptoms (138,154,155).

If a patient who experiences BPW declines higher doses of buprenorphine, BPW can be treated with nonagonist therapies such as clonidine, ondansetron, and loperamide (Table 3). For mild cases of BPW, it may be prudent to hold further treatments of any sort in favor of observation. Another attempt to initiate buprenorphine can be made after a period where the patient continues to metabolize the full agonist opioids in their system, with the hope that the next attempt to treat with buprenorphine will not precipitate withdrawal.

Q40. How Should Emergency Clinicians Manage Patients Who Have Naloxone-Precipitated Withdrawal?

Abstinence-related opioid withdrawal is generally gradual in onset, moderate in peak intensity, and persists for several days. Withdrawal precipitated by the administration of naloxone (NPW), usually to a patient with a presumed opioid overdose, peaks more quickly in intensity and is of greater severity. Naloxone delivered intravenously precipitates an abrupt and severe withdrawal syndrome and is complete by about 45 min. After administration of naloxone by the intranasal or i.m. route, the severity of withdrawal is moderate and lasts about 75 min (156). Given the increasing availability of naloxone for bystander use, the need to manage NPW in the ED is likely going to increase.

The optimal treatment of a patient with NPW remains undefined, but is guided by both the clinical severity and expected duration. The initial approach includes verbal encouragement and assurance that the effects will be short lived. Maintaining professional composure despite a patient's disruptive behavior (due to their discomfort and craving) is important to promote de-escalation.

Symptomatic care may prove sufficient until the naloxone effect abates. Pharmacologic therapies include antiemetics, short-acting benzodiazepines, and antipsychotics such as haloperidol (116). Ketamine may be useful in the management of severe withdrawal that is inadequately responsive to traditional nonagonist treatments (157,158). Due to concern for aspiration, caution must be exercised in administering sedating medications to patients who are actively vomiting (156).

Autonomic effects, such as tachycardia and hypertension, can be improved using an alpha-2 agonist sympatholytic such as clonidine or lofexidine (p.o.) or dexmedetomidine (i.v.) (159–161). Lofexidine is recently approved and has not yet been shown to be cost effective (116).

Cravings associated with precipitated opioid withdrawal are most effectively mitigated through the administration of an opioid agonist. However, the presence of naloxone on the mu-opioid receptor will limit the effect of an opioid agonist. Although higher doses of an agonist such as fentanyl can overcome the opioid receptor blockade, the duration of the agonist effect may exceed that of naloxone, resulting in potentially dangerous recrudescence of opioid intoxication (162).

Buprenorphine, given its high receptor affinity, may successfully compete with naloxone and mitigate the precipitated OWS. There are few data to support this use, but buprenorphine has been reported to quell withdrawal in a single ED patient who had received intranasal naloxone after a fentanyl and heroin overdose, patients with *naltrexone*-precipitated opioid withdrawal, and in a case of planned NPW done to facilitate buprenorphine initiation (163–165). Successful use of buprenorphine in this context simultaneously alleviates the effects of NPW and bridges the patient to buprenorphine maintenance recovery. However, such treatment carries the theoretical risk of replacing NPW with longer-lasting BPW, as well as the risk of dangerous respiratory depression if the patient used nonopioid sedatives in addition to opioids. Providers considering the use of buprenorphine to treat NPW must be prepared to manage BPW and respiratory depression, and should proceed only after explicit patient consent, given the paucity of literature on this practice.

Effective treatment of patients with NPW not only alleviates suffering and makes the immediate use of dangerous street opioids less likely, it allows the clinician to engage the patient in harm-reduction efforts (Q5) and facilitates a discussion of a possible move to recovery with MAT.

Q41: How Should Prescription Drug Monitoring Programs be Used in Emergency Care?

Prescription drug-monitoring programs (PDMPs) are state-administered databases that report a patient's history of dispensed controlled substance prescriptions, including opioids and benzodiazepines (166). PDMPs are now in place in all 50 states, and many of the limitations of PDMPs that were present in the past (e.g., delayed time from prescription fill to appearing in the database and lack of interstate data sharing) are largely resolved (167,168). Several states now mandate PDMP

access, and at least 25 states require that the PDMP be checked prior to the first opioid prescription a given clinician prescribes to a patient (169,170). Despite their ubiquity and state-based mandates, the role of PDMPs in EM practice remains unclear.

Prior work suggests that ED clinicians who intend to prescribe opioids to patients are not accurate in their determination of which patients have obtained multiple opioid prescriptions from multiple providers, highlighting how PDMP access supplements information available to the clinician (171). Other studies demonstrate that viewing PDMP information is not associated with reductions in ED opioid prescribing, perhaps indicating enhanced confidence when the clinician writes an opioid prescription (172–174).

PDMPs have several limitations that may undermine their efficacy in acute care settings. Firstly, interpretation of a PDMP profile is in part subjective, which leads to inconsistent decision-making about opioid prescribing and creates a situation where the clinician must be both the "judge and jury" for a patient in pain (175,176). There have been attempts to reduce this subjectivity by providing numerical scores that correlate with overdose death risk, but they have not been validated prospectively (177). A second limitation is that PDMPs capture only prescriptions that are written for a specific individual. They do not report controlled substances obtained from diverted sources; one study found that only 36% of patients with self-reported nonmedical use of prescription opioids had a reported prescription in the PDMP (178). The third limitation is that, because methadone for OUD is obtained through federally regulated OTPs, it does not appear on the PDMP. Lastly, diverted or illicit opioid use is, of course, not reflected in the PDMP; many people who use heroin or illicitly obtained prescription opioids will have reassuring PDMP queries.

As a result, the PDMP should be used as a tool that is specific only for certain types of aberrant medication-related behavior, such as those patients who obtain multiple prescribed controlled substances from multiple providers or receive large amounts of prescribed opioids that are then diverted. The PDMP should be accessed prior to a prescription written for an opioid or benzodiazepine, to detect and avoid multiple simultaneous opioid prescriptions or dangerous drug combinations. A PDMP query may influence MAT initiation decisions and is recommended prior to administering or prescribing buprenorphine (and is required by law in some states).

If OUD or diversion is suspected from the PDMP profile, sharing that information with the patient and referring them to the appropriate treatment resources is indicated (179). Even with a concerning profile, opioid prescribing may still be appropriate for a patient with pain; PDMP data should be used as one part of a complete evaluation that also takes into account other clinical factors. Conversely, given that some opioid-naïve patients who are prescribed opioids will progress to long-term use, a PDMP profile without prior opioid prescriptions may highlight even higher stakes for that patient than a patient with existing misuse—a careful calculation of the benefits and harms of prescribing an opioid is indicated in the service of *keeping opioid naïve patients opioid naïve* (Q1) (15,27).

Q42. How Should Emergency Clinicians Manage Patients Maintained on Buprenorphine Who Have Acute Pain from Illness or Injury?

There are several strategies to provide additional analgesia for patients maintained on buprenorphine. The best strategy is to maximize nonpharmacologic and nonopioid analgesic modalities such as nonsteroidal antiinflammatory drugs, acetaminophen, and local/regional anesthesia techniques where applicable. This can progress to parenteral nonopioids such as intravenous lidocaine, dexmedetomidine, and especially analgesic-dose ketamine, which has demonstrated effectiveness in severe acute pain (180–182).

Additionally, the daily buprenorphine dose can be divided into smaller, more frequent dosing, which augments buprenorphine's analgesic effect. Whereas daily (q.d.) or b.i.d. is usual therapy for OUD, the total daily s.l. buprenorphine dose can be split to t.i.d. or q.i.d. when enhanced analgesia is required (183,184). Augmenting the divided daily dose with additional buprenorphine by the s.l., i.v., or i.m. route may be effective, though high doses (16–32 mg) may be required (185). Experience and data are limited, but it is reasonable to supplement the patient's divided daily dose with additional 2–8 mg s.l. buprenorphine every 1–2 h, or 0.3–0.6 mg i.v./i.m. buprenorphine every 10–20 min. Patients receiving significantly augmented doses of buprenorphine should be monitored for hypoventilation.

Alternatively, or in addition to nonopioid analgesia and divided/augmented buprenorphine, providers may add a high-affinity full-agonist opioid such as fentanyl to the patient's usual buprenorphine dose. Hydromorphone is often recommended in this context but is more euphoric than alternatives, which may make it more likely to precipitate relapse in the OUD patient in buprenorphine-maintained recovery. Due to profound tolerance often present in OUD patients and the buprenorphine blockade effect from partial agonism, buprenorphine-maintained patients may require very high doses of full agonist opioid to achieve a therapeutic effect, especially if their daily buprenorphine dose is $\geq$ 16 mg/day (185,186). Because most emergency clinicians are not willing to titrate full agonist opioids to

these doses in a clinically relevant time frame, and due to the as-yet unquantified relapse risk inherent in this practice, we recommend focusing on nonopioid modalities and optimizing buprenorphine dosing in this patient group. If full agonists are used, as with any patient receiving high opioid doses, ventilation should be closely monitored.

Buprenorphine-maintained patients being discharged with acutely painful conditions should be managed with maximal nonopioid analgesia in addition to dividing their daily buprenorphine dose to t.i.d.-q.i.d. If these strategies are thought to be inadequate for pain control, outpatient analgesia should be coordinated with the patient's buprenorphine prescriber.

It is important for acute care clinicians to recognize the shift in expert consensus around preoperative analgesic planning for buprenorphine-maintained patients. Whereas these patients were previously weaned from buprenorphine in anticipation of treating operative pain with full agonist opioids, recent guidance recommends the continuation of at least 8 mg s l. buprenorphine per day throughout the preoperative and postoperative period, supplementing analgesia with nonopioid and full agonist modalities, similar to the strategies described above (187–190).

Q43. How Should Emergency Clinicians Manage Acute Moderate or Severe Pain in a Patient with a History of OUD, now in Abstinence Recovery (Not Taking Methadone or Buprenorphine)?

Despite the evidence to support MAT in patients in recovery from OUD, many patients opt for nonpharmacological management through counseling, peer support, or 12-step programs. Balancing the priority to do no harm while still providing effective pain management in patients in abstinence-based opioid addiction recovery is a complex and poorly understood clinical problem. Exposing these patients to opioids may precipitate relapse, as may the stress and trauma of an acute painful event or poorly controlled pain (191,192).

Nonopioid and nonpharmacological pain management strategies are strongly favored in this group (Table 7). If opioids are required to treat pain inadequately managed with opioid alternatives, a very short course of a less euphoriant opioid (e.g., favoring oral morphine over hydromorphone and oxycodone) should be utilized (Q1) (193). A short course of analgesic dose buprenorphine, which is less euphoriant than full agonists, may also be effective and appropriate. Optimal dosing of buprenorphine for analgesia in nontolerant patients is uncertain but significantly lower than that used to treat OUD; 250–500 μg s l. b.i.d. is reasonable but may require splitting 2 mg tablets or strips into quarters or eighths (194). Note that currently this is an off-label indication, and the existing buprenorphine products for pain are indicated only for patients with chronic pain requiring around-the-clock analgesia.

An empathetic and honest discussion that carefully delineates the likely potential benefits and harms that accompany the use of an opioid should frame a shared decision-making process. The value of formal informed consent is unknown, but given the risk associated with the use of opioids in this patient group, it is suggested (195).

Q44. How Should Emergency Clinicians Treat Exacerbations of Chronic Pain in Patients Who Take Daily Prescription Opioids?

Patients may present to acute care settings with exacerbations of their chronic pain, or acute-on-chronic pain. Patients taking daily prescription opioids should optimally be managed by a single provider who monitors opioid effectiveness and harm under a formal patient–provider agreement (196,197). Guidelines across a variety of disciplines stipulate that acute care providers managing patients with chronic pain should avoid administering opioids or altering existing opioid regimens, and rather use multimodal nonopioid and nonpharmacologic analgesic treatments until the patients can be evaluated by their pain medicine provider (196,198,199).

Current evidence and guidelines suggest that patients with chronic pain are more likely to be harmed than benefited by opioid therapy (31,200–205). Table 7 presents treatment options for emergency clinicians caring for patients with chronic pain (198,206).

The American Academy of Emergency Medicine (AAEM) and the American College of Emergency Physicians guidelines for emergency clinicians managing chronic pain recommend that clinicians avoid prescribing opioids for acute exacerbations of chronic pain, that existing opioid prescriptions not be refilled, and that lost, destroyed, or stolen opioid prescriptions not be replaced. If opioids are prescribed for exacerbations of chronic pain, acute care clinicians should prescribe a small number of immediate-release tablets after a discussion with the patient's primary analgesic provider when possible.

Patients who take daily prescribed opioids for chronic nonterminal pain live on a spectrum of opioid benefit and harm (Table 8). Patients who are stably benefiting from their ongoing opioid therapy should be managed similarly to patients who are stably benefiting from any prescription therapy, whereas patients who are likely being harmed by daily opioid use should be counseled on these harms and encouraged to take steps with their prescribing provider(s) to mitigate them. These steps may include slowly reducing their daily opioid dose or being treated for addiction.

Q45. How Should Emergency Clinicians Manage Pain at the End of Life?

Many patients undergoing palliative or hospice care report under-treatment of their pain at the end of life. Opioid harms—especially long-term use harms—are less important in this context, and end-of-life pain should be treated aggressively in a multimodal approach that often includes opioids. Patients with pain at the end of life may benefit from early engagement of hospice or palliative care services (207–209).

Q46. How Should Emergency Clinicians Manage Patients on Methadone Maintenance Who Have Missed Their Usual Methadone Dose?

Methadone is a long-acting full mu-receptor agonist effective in the treatment of OUD and is dispensed at designated clinics (OTPs) where patients on methadone maintenance treatment (MMT) receive their daily dose. Methadone can be prescribed for addiction only by credentialed clinicians in the context of an OTP, but can be prescribed *for pain* without these constraints, and methadone prescribed for pain contributes disproportionately to opioid overdose mortality (210). Patients on MMT may present to the ED for an unrelated concern that caused them to miss their daily dose, or because they missed one or more doses and are requesting that a dose be dispensed in the ED.

Methadone is more abuse-prone and far more dangerous than buprenorphine and most other full agonist opioids; clinicians must therefore approach the patient with missed methadone dose with more caution (211). Methadone metabolism varies across patients, but most patients can miss a single day's dose of methadone with no or minimal opioid withdrawal while awaiting their next clinic visit. Patients who miss their clinic dose and present without evidence of withdrawal can therefore be discharged with reassurance.

If significant withdrawal is present, we recommend treatment with 10 mg i.m. or 20 mg p.o., both of which are safe, and sufficient to ameliorate OWS (46). The i.m. route is advantageous in this context for guaranteed absorption, especially in the vomiting patient. Patients should generally not be administered their full daily dose even after dose confirmation with the OTP, particularly if discharge is anticipated. This is because the actual methadone dose the patient takes may be different than the prescribed clinic dose; providing the prescribed clinic dose may therefore result in dangerous toxicity. Furthermore, although a withdrawal-suppression dose may be administered in the ED, because the ED is not an OTP, it is not authorized to provide the patient's full "OUD treatment" dose.

Nonagonists can also be used to manage withdrawal (Table 3), however, we do not recommend that patients be discharged with objective signs of OWS, as they are at high risk to self-treat with street opioids. Additionally, the threshold to administer methadone to treat MMT patients apprehended by law enforcement should be low, as these patients may be unable to access their daily dose for some time.

Q47. How Should Emergency Clinicians Manage Patients on Methadone Maintenance Who Have Acute Moderate-To-Severe Pain from Intercurrent Illness or Injury?

Methadone does not have the degree of opioid "blockade" of buprenorphine. After a discussion with the patient's OTP, if the patient is to be admitted to the hospital, the patient should receive their daily dose of methadone, which can be divided b.i.d. or t.i.d. to improve its analgesic effect, and additional opioid or nonopioid analgesia can be used to treat pain. Patients on daily methadone are often hyperalgesic (more sensitive to pain) and often have a narrow therapeutic window (the effective analgesic dose of an opioid is close to the dose that causes dangerous toxicity); the treatment of acute severe pain in MMT patients therefore requires careful titration, ideally in a closely monitored setting. A multimodal analgesic strategy (Table 7) is advised, and involvement of a pain or addiction specialist may be helpful.

Q48. How can ED Administrators Encourage Best Practices Related to Opioid Prescribing and Reduction of Opioid-Related Harms?

Patterns of opioid prescribing result from learned behaviors, such as during training or arising from departmental culture. Efforts to change opioid-prescribing behavior in Emergency Medicine has predominantly taken three forms: benchmarking reports, guidelines, and clinical "nudges."

Benchmarking reports show providers their prescribing habits compared with their peers; presenting individual and comparison prescribing data can result in significant practice improvements (212–214). When benchmarking, it is ideal to standardize reporting with a defined denominator, for example, the number of patients discharged by that provider or per 100 patients discharged by similar prescribers. A comparison of pill counts per prescription can also be valuable. Focus should be on providers who are above or below one standard deviation from the mean. *Transparent* reports that allow providers to compare their prescribing practices openly to their peers may have a greater effect than *anonymized* reports (215).

National, regional, hospital, and departmental guidelines can be helpful to standardize care and promulgate best practice recommendations, and have been linked to decreased opioid use (216–223). Multiple societies have released opioid-prescribing guidelines relevant to emergency medicine; key recommendations from the AAEM guideline are excerpted in Table 9 (31,198,199,224,225). Opioid prescribing policies summarized on publicly displayed posters can reassure patients that they are not being treated differently than others (226,227). [Such posters should not be presented to patients prior to a medical screening examination (e.g., in the waiting room) so as not to discourage patients from seeking care (228,229)].

"Nudges" are behavioral design decisions, commonly in the EHR, which lead clinicians to adopt best practices (230). EHR alerts can remind providers to check their prescription drug monitoring program so as to consider alternatives in patients already taking daily opioids and avoid prescribing an opioid to patients taking benzodiazepines. Similar nudges can remind clinicians to engage at-risk patients (such as patients on high daily opioid doses, who take benzodiazepines, or present after nonfatal overdose) with harm-reduction efforts such as take-home naloxone. Similarly, defaulting the number of opioid tablets to align with current recommendations can significantly reduce the number of pills given per prescription (231,232). These interventions often require larger system cooperation and information technology support (134).

The goal of an opioid prescribing best practice program is not to reduce opioid *use* but to reduce opioid *harms*. Opioid harms related to acute care mainly arise, not from the administration of opioids in the department to opioid-naïve patients in severe acute pain, but from injudicious outpatient prescribing, as well as the suboptimal management of existing daily opioid users. Providers should not be encouraged to blindly reduce their use of opioid analgesia, so as not to result in the undertreatment of pain.

CONCLUSION

Since the beginning of emergency medicine, EDs have treated the consequences of opioid misuse such as infections, trauma, respiratory depression, and cardiac arrest. The ED management of opioid addiction itself, however, has classically consisted of a piece of paper with phone numbers on it and a quick discharge. This approach was often inadequate and based in stigma and a lack of understanding of OUD. Until recently, few frontline providers had the resources or expertise to meaningfully intervene in the often-devastating natural history of this disease.

In response to the current epidemic, many EDs have taken important steps to improve the care of this vulnerable population. Strategies and protocols that account for the capabilities and limitations of acute care environments have been successfully developed and implemented (111,233,234). An increasing number of EDs have improved opioid-prescribing practices, treat opioid withdrawal patients with buprenorphine, and dispense take-home naloxone to at-risk patients and their companions.

Many questions remain: What is the optimal dosing of buprenorphine in spontaneously withdrawing patients? What is the best strategy for managing OUD patients who wish to be treated with buprenorphine but are not in spontaneous withdrawal? What is the best approach to NPW and BPW? Is buprenorphine of benefit in the treatment of chronic pain patients taking high doses of prescribed opioids, or in opioid-naïve patients with acute, severe pain? What is the role of hospitals and EDs in advanced harm-reduction practices that could reach more patients, such as needle exchange, supervised consumption sites, or prescription hydromorphone?

As emergency-driven addiction care evolves, we anticipate the use of higher doses of buprenorphine at the index visit, which may overcome buprenorphine and NPW and safely extend buprenorphine's therapeutic interval—and protection—to several days (120). As more providers obtain waivers (or the waiver requirement is abolished), home initiation protocols, which permit motivated patients to await spontaneous withdrawal and begin treatment in their own quarters, could become more common. Microdosing initiation pathways open buprenorphine therapy to opioid-dependent people unable or unwilling to tolerate a period of withdrawal (122,123). Long-acting injectable or implantable buprenorphine preparations may be administered during an emergency visit, providing weeks of therapy at the moment the patient is available and possibly the most receptive (235). Emergency clinicians will increasingly obtain specialized addiction training to run addiction or bridge clinics, extending the meaning and reach of the specialty to accommodate the changing face of the American health care system and the challenges of the people it serves (236).

The history of medicine is, in part, the history of physicians stretching the scope of their practice to answer the pressing needs of their times (237).

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