



Emergency Department Intervention with Buprenorphine for Opioid Use Disorder Patients

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Literature adapted from Ruben Strayer, MD and A. Herring, et al

“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.”

Overdose deaths in the United States have exceeded peak mortality from guns, HIV and motor vehicle accidents. This is now the leading cause of overall death of Americans under age 50. American physicians have now begun to curtail their opioid prescribing after the 700% increase that led to a prescription opioid addiction epidemic followed by a heroin epidemic and now to an illicitly manufactured fentanyl epidemic. There are still millions of Americans who still misuse opioids and they end up in the emergency department frequently with misuse harms that include apnea and cardiac arrest.

Emergency providers are uniquely positioned to intervene on addiction harms because the emergency department is where they are encountered. Patients afflicted with opioid misuse live across a spectrum of disease that can be categorized according to how revealed their misuse is. Do they realize they misuse opioids and if so, will they inform healthcare providers? Among revealed opioid misusers, there is a spectrum of willingness to enter into addiction treatment. Many aren't interested in treatment and we can only offer help when they are ready for it.

There are a series of best practices that have emerged to guide the management of patients at all points along the misuse spectrum, from completely unrevealed misuse to the patient who is fully revealed as a misuser and willing to move to recovery. Also, the spectrum includes the opioid naïve patient who presents with acute pain from fracture or kidney stone to the chronic pain patient who takes hundreds of morphine milligram equivalents daily in the form of prescription and street opiates and repeatedly presents after overdose.

The most important way that emergency providers can make an impact in the epidemic is to keep opioid naïve patients opioid naïve so that fewer patients with acute pain are sent down the path to misuse by our prescriptions. Many of us were taught that you couldn't trigger addiction with a script for 20 Percocets but we now know that was marketing. We know that some fraction of opioid naïve patients who fill a prescription for opioids will develop addiction arising from that prescription.

Once opioid addiction develops, it can be managed but there seems to be a permanent or long-lasting derangement of brain chemistry with profound implications for the patient and their loved ones. Preventing the development of addiction is crucial. This means doing an explicit calculation of the likelihood of benefit and harm every time you consider writing for opioids. The benefit of an opioid

prescription is the degree to which opioids ameliorate suffering from pain after safer pharmacologic and non-pharmacologic analgesics have been optimized.

There are two types of harms. The immediate harms include nausea, constipation, itching, dysphoria, confusion, falls, inability to work or drive, traffic accidents and overdose. The second types of harms are the long-term use and misuse harms which are often life-changing or life-ending.

You can predict the likelihood of misuse harms with risk factors. Patients with existing substance use including alcohol and tobacco, psychiatric disease, childhood trauma, social isolation, disability and adolescents or young adults are more likely to develop misuse and should be prescribed opiates with particular caution.

If you decide the likelihood of benefits outweighs harms and you want to send an opioid naïve person home with opioids, the most important way you can decrease the likelihood of that patient developing misuse from your prescription, is to write for a small dose for a brief duration. The duration is crucial. The likelihood of long term use correlates linearly with the number of days' supply of the first opioid prescription. Give no more than a 3 day supply and tell your patient to flush any unused pills, especially if there are any children or teenagers around the home.

- **Hydrocodone and oxycodone seem to be more prone to abuse than alternatives.** You would do best to write for less-euphoriant non-combination preparations like immediate release morphine tabs, such as **Morphine IR 15 mg q 4-6 hours.**

Existing misusers can be grouped according to their degree of being revealed (how apparent their use disorder is) and willingness to pursue treatment.

Unrevealed patients may present with acute pain and without reports of chronic pain or daily opioid use but strike you as deceptive. You can risk-stratify these patients using red and yellow flags for opioid misuse and using the state prescription drug monitoring program but note that a negative PDMP query doesn't mean the patient should receive an opioid script. If the PDMP query is negative, go back and do a calculation of the likelihood of benefit and harm for that patient.

- **A positive PDMP query moves the patient from unrevealed to revealed.** The right way to use a positive query is to open a compassionate dialogue with the patient and try to move that revealed patient from unwilling to willing towards treatment.

Partially revealed patients present with an exacerbation of chronic pain and usually report a history of daily opioid use. Many of these patients are being prescribed opioids by one or more doctors. It is important to recognize that, excluding end-of-life pain, patients with chronic pain are either being harmed by opioids or at very high risk of harm by opioids. The data and national guidelines tell us that patients with chronic pain are more likely to be harmed by opioids than helped. In this group, opioids should be avoided in the emergency department and by prescription. Treat symptoms with non-opioid alternatives. When appropriate, express concern that the

patient is being harmed by opioids and encourage them to move to treatment. *“My job is to manage your pain at the same time I manage the potential for pain medications to harm you.”*

Many of us see patients who present after opioid overdose. These patients are fully revealed as opioid misusers but come in a spectrum of willingness to be treated for addiction. Most of them are unwilling, especially if they are in acute withdrawal after naloxone administration. Engage these patients. Establish rapport by asking how they got started with narcotics. Some of them are keen to tell their stories. Ask them if they would like to stop? If they are, give them some options.

If they are not willing to stop, move to harm reduction mode. Encourage safe injection practices such as not licking needles, using only when others are around and screening for HIV/HCV. Give them a handout on harm reduction strategies and discharge with take-home naloxone. Take a supportive stance and tell them you have an open door if they decide to change their mind.

For overdose patients who get up and walk out, you can say, *“Hey, I know you have a complicated life and I know you wish things were different. When you are ready to make a change, come back. We can help and we’re always open.”*

The last type of patient is the patient who is willing to enter into addiction treatment. When you see one of these patients, you have the opportunity to save a life by initiating medication-assisted addiction therapy in the ED and bridging that patient to outpatient MAT.

Medication assisted therapy (MAT) comes in three forms; naltrexone, methadone and buprenorphine.

- **Naltrexone in its depot form with the brand name Vivitrol is a once monthly injection that blocks the actions of opioids.** It is basically long-acting Narcan. It is medically imposed abstinence therapy. There is a role for Vivitrol and some patients are great candidates for it. However, most people with opioid addiction will not be interested in or succeed with this therapy because it involves withdrawal which is feared by patients. It does not address the most important cause of relapse, the deranged brain chemistry that causes craving.
- **Methadone is a long-acting full mu receptor agonist that patients with opioid use disorder receive by presenting themselves daily to a clinic.** Methadone is effective but is prone to abuse. As a full agonist, it is very dangerous in overdose among a variety of other toxicities. The need to present daily to a clinic is a benefit to some patients who require high engagement but is a barrier for many other patients, especially women who commonly feel threatened at clinics.
- **Buprenorphine is a partial opioid agonist which means that there is a ceiling effect to both its euphoriant potential and toxicity.** Buprenorphine is remarkably safe in overdose. You can still die by overdosing on buprenorphine, especially with coingestants. However, it is much safer than methadone. Buprenorphine has a higher affinity for the mu receptor than just about all other opioids. This is important. If you have oxycodone or heroin, the

buprenorphine will replace them on the mu receptor but because a partial agonist is replacing a full agonist, the patient will withdraw.

Buprenorphine is a highly effective treatment for relieving withdrawal symptoms for most opioid dependent patients. However, if the patient is not already in withdrawal, buprenorphine will precipitate withdrawal. Because it is a partial agonist, you do not get high in the same way you do with other opioids. When you have buprenorphine in your system, oxycodone and heroin won't work because buprenorphine has much higher receptor affinity.

Buprenorphine at its best abolishes withdrawal and cravings and protects the patient from overdose and other opioid abuse harms. However, it is not perfect. Buprenorphine is prone to abuse, especially when it is crushed and injected. The preferred preparation is the combination of buprenorphine and naloxone, trade named Suboxone. This is widely misunderstood. The naloxone component is completely inert when Suboxone is taken under the tongue as intended. The naloxone only acts as a mu receptor antagonist when the drug is injected. The purpose of the naloxone in Suboxone is only to prevent abuse by injection. It has no other effect. It does make the drug a bit more expensive than the generic SL Buprenorphine so I am tending to write the patients a script for Buprenorphine alone that goes by the trade name of Subutex.

Buprenorphine is slow in onset which further reduces abuse potential. Like methadone, it has a long dose-dependent duration of action. Because of the ceiling effect, it can be used safely in high doses to prolong the dosing interval to 3-5 days. This is somewhat theoretical though and of course a prescription for twice daily dosing is best (it helps with the learned behavior of addiction as well).

All of us can dose buprenorphine to treat opioid withdrawal in the ED. To prescribe buprenorphine for addiction requires a special addendum to your DEA license called an X waiver. For physicians, this requires an application process and eight hours of training. Everyone can write for oxycodone, a massively dangerous abuse-prone opioid. But in order to prescribe buprenorphine, a comparatively safe opioid that treats addiction, you have to jump through a series of hoops, so few doctors do.

Most of us haven't seen many opioid-dependent patients presenting to the ED who are willing to enter into addiction treatment. That is probably because, until recently, we haven't had much to offer them besides a piece of paper with some phone numbers. That is no longer true. Now we can initiate the most effective treatment for opioid addiction in the emergency department.

- **American physicians and policy makers have for decades taken a view of addiction as a moral failing and that addicts have made bad choices.** This has led to the stigmatization of not only opioid addiction but also medication assisted therapy which is viewed as replacing one addiction with another.
- This is inconsistent with science and has informed decades of misguided policies. The data is abundant and unambiguous. Abstinence does not work for most people addicted to opioids. Their brains have been hijacked by opioids and it seems that in many cases, this is irreversible

or takes a very long time to reverse. When patients addicted to opioids are randomized to MAT plus counseling versus counseling alone, the patients with MAT stay in treatment. Cochrane concludes that adding psychosocial support to medication assisted therapy does not add additional benefits.

- **Opioid addiction is not a failure of willpower.** It is a disease of deranged brain chemistry and the treatment is an opioid agonist. Medication assisted therapy is not substituting one addiction for another. It is replacing addiction with dependence. The difference between addiction and dependence is *everything*. People addicted to opioids who are successfully transitioned to MAT stop dying. They stop spending all day, every day, terrified of withdrawal and trying to acquire opioids. They stop injecting street drugs with dirty needles and exposing themselves to these harms. They stop having their lives ruined and they can return to their lives and families. They also stop spreading HIV, Hep B and C, and stop getting endocarditis and sepsis. This is a win for all of us.

The best way to manage willing addicts who present themselves to the emergency department for addiction treatment is to initiate buprenorphine treatment in the ED. This is an entirely new thing for us. It is not complicated.

It is called the warm handoff and it involves three steps.

- **First you need the right patient.** This is a patient who is dependent on opioids and is in withdrawal. If the patient is not in withdrawal, buprenorphine can precipitate withdrawal. Most pathways of buprenorphine initiation use the clinical opiate withdrawal scale (COWS). This takes about 90 seconds to perform. The higher score, the better. Most say that you should not initiate buprenorphine until the score is 8 or 9.
- **Treat the patient with buprenorphine.** You do not need an X-waiver to do this.
- **Once the initiation is complete, the last step is follow-up.** This is usually sending the patient to a buprenorphine capable clinic, such as Operation PAR. The case managers know how to educate and follow up on this with the patient. Eventually we will be able to transport the patient to Operation PAR with security's new fancy vehicle. Also eventually, we will have Peer Specialists on call to assist with the patients follow up to Operation PAR.
- **Discharge the patient.** If you have an X waiver, you can send the patient home with a few more days of buprenorphine. This is great if you can, but not completely necessary. You can write the patient a prescription for Buprenorphine for pain (which is off label) without an X waiver. Ideally however, we should all try to get our X waiver.

The classic dosing of buprenorphine on day number one is 4-8 mg sublingual.

The ceiling effect means that higher doses prolong the duration of action without causing dangerous adverse effects. We don't have any literature on this in the ED yet but if initiating buprenorphine in high doses like 32 mg turns out to be safe, it will allow us to cover patients for several days with a dose given in the emergency

department. The addict who is therapeutic on buprenorphine is safe from withdrawal, cravings and overdose.

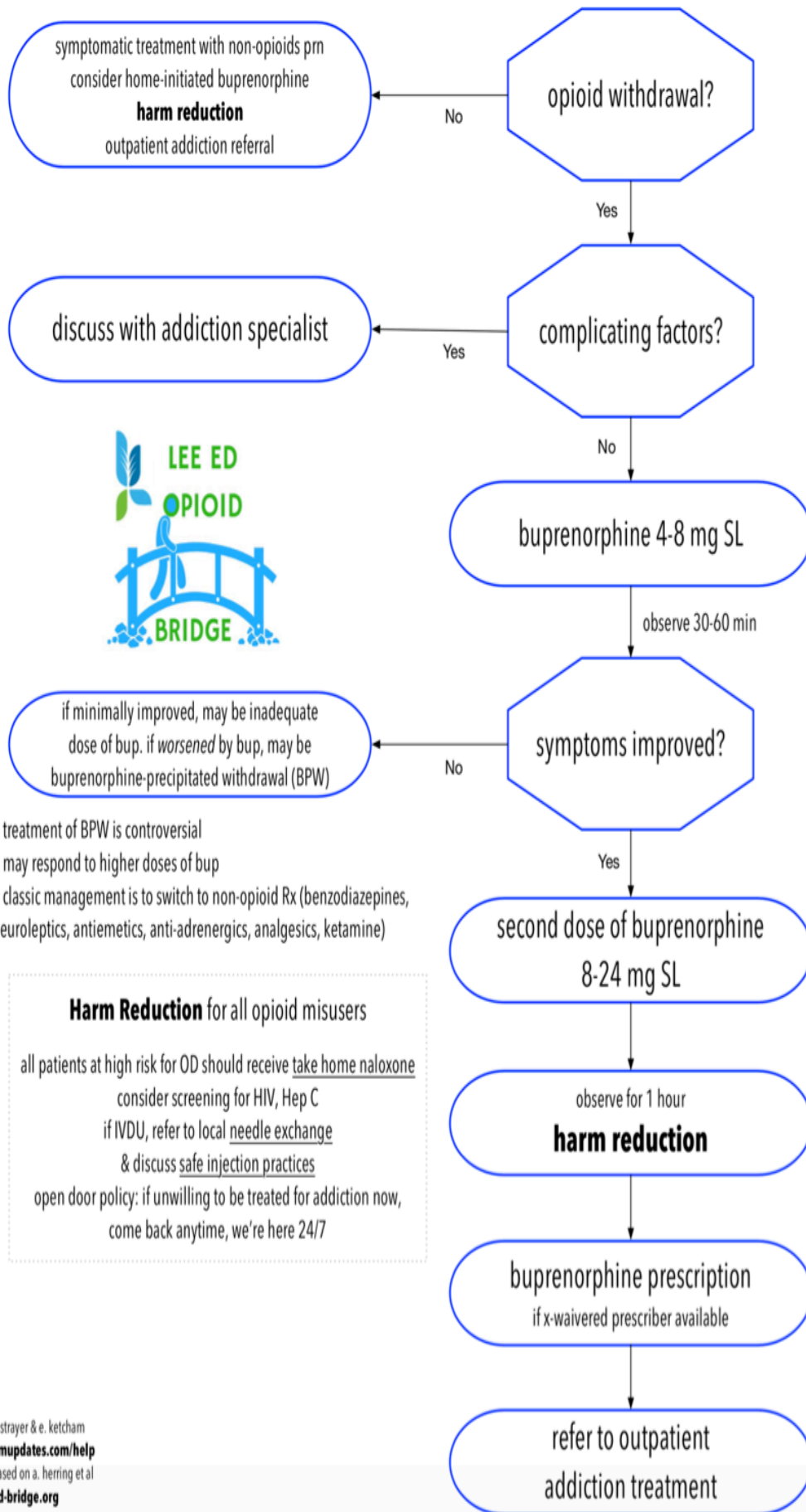
The biggest concern about buprenorphine initiation by emergency doctors is the potential for abuse. Many are concerned about the ED becoming a Suboxone dispensary, attracting even more unsavory patients to the ED and concerned about patients selling Suboxone on the street. The early experience with ED buprenorphine initiation suggests these concerns are probably overblown. In the era of super-fentanyls, Suboxone diversion is probably a public health win. However, buprenorphine does have potential for abuse and street value and Suboxone abuse and diversion is an important concern. This is why some argue that we should be writing a script for buprenorphine/naloxone rather than just buprenorphine.

There is a possibility that high-dose buprenorphine will be demonstrated to be safe and effective for ED initiation. This might prolong the days of therapeutic benefit from a single high dose of buprenorphine. Until then, we need to verify that the patient can get a prescription or immediate follow-up, otherwise the patient will start to withdraw and give up. If your patient can't establish follow-up, we can encourage them come back to the ED (obviously not ideal). The law allows you to dispense more buprenorphine without an X waiver for up to 72 hours (called the 3 day rule). You can dose the patient in the ED on days 1, 2 and 3 without an X waiver. This is long enough in most settings to establish the next link in the chain of recovery. **The dose on days 2 and 3 is 16 mg, or more.**

We know this works. France essentially solved its heroin overdose epidemic in the 1990s by empowering all of the general practitioners to prescribe buprenorphine. Overdose deaths fell by 80%. Baltimore saw similar improvements in opioid death and disease by expanding access to MAT.

Gail D'Onofrio and her group at Yale demonstrated that you can make huge gains in treatment retention by starting buprenorphine in the emergency department. Even the surgeon general says we should be doing this so this is not a novel or unsupported approach. We should be doing this for this patient population and it is vital to make an impact for our community's public health.

Emergency Department Initiation of Buprenorphine for Opioid Use Disorder



if inadequate withdrawal, buprenorphine will precipitate withdrawal
score on clinical opiate withdrawal scale COWS should be ≥ 8 , the higher the better

severe medical disease or very intoxicated/alterd (e.g. acutely ill, liver failure)
using methadone or extended-release opioid
naloxone-precipitated withdrawal
taking high dose prescription opioids daily

- the higher the daily dose of opioids the patient usually uses, and the more severe the withdrawal, the higher the initial dose of bup
- if borderline/inconsistent withdrawal symptoms, dose 2-4 mg every 1-2h
- if vomiting, may use 0.3 mg IV/IM every 30-60 min

- if symptoms not improved with 8 mg bup, patient may be in buprenorphine-precipitated withdrawal and effect of higher buprenorphine dose is uncertain
- bup can cause nausea - if primary symptom is nausea, treat with ondansetron 8 mg

- the bigger the initiation dose of buprenorphine, the longer the patient is protected from withdrawal, cravings, and street opioid overdose
- high dose (total dose of 16-32 mg in ED) preferred if patient not able to be seen by bup prescriber or fill prescription in next 12-24 hours
- do not initiate high dose if patient is heavy user of alcohol or benzodiazepines, medically complex, older age - for risk of respiratory depression

buprenorphine/naloxone 8/2 mg
1 tab/strip BID SL
dispense x 1 week

72 hour rule: patient may return to ED for up to 3 days
administer 16 mg SL on days 2 & 3



- treatment of BPW is controversial
- may respond to higher doses of bup
- classic management is to switch to non-opioid Rx (benzodiazepines, neuroleptics, antiemetics, anti-adrenergics, analgesics, ketamine)

Harm Reduction for all opioid misusers

all patients at high risk for OD should receive take home naloxone
consider screening for HIV, Hep C
if IVDU, refer to local needle exchange
& discuss safe injection practices
open door policy: if unwilling to be treated for addiction now,
come back anytime, we're here 24/7

