Emergency Department
Medication-Assisted Treatment of Opioid Addiction

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About the Author
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About this Paper
These protocols will be submitted to specialty societies for endorsement and publication in 2017.

Contents
I. Introduction ........................................................................................................................................ 3
II. Emergency Department: Low-Risk Providers Treating High-Risk Patients ......................... 4
   Low-Risk Providers ......................................................................................................................... 4
   An Opportunity to Reach High-Risk Patients ............................................................................... 4
   Shifting the Focus to Emergency Treatment of Addiction ....................................................... 6
III. What Can We Do? The Case for Medication-Assisted Treatment of Addiction ..................... 8
   Why Retention in Treatment is the Best Outcome for Short-Term Studies ............................ 9
   Exposure to MAT Improves Survival .......................................................................................... 9
IV. Bringing MAT to the Emergency Department: What Has Been Done So Far .................... 11
   Initiation of Buprenorphine MAT at the Yale New Haven Hospital ED .................................... 11
   ED Use of Buprenorphine for the Treatment of Acute Opioid Withdrawal ............................ 13
V. Treatment of Opioid Addiction: The Basics ........................................................................... 14
I. Introduction

Beginning in the late 1990s, the use of opioids in the United States expanded on an unprecedented scale. In parallel to this increase, opioid-related overdose deaths nearly quadrupled. In 2013, the number of people abusing or misusing opioid pain relievers reached nearly two million, with an additional 517,000 abusing heroin.¹ Opioid pain reliever-associated deaths reached 16,200, and drug overdose deaths became the leading cause of injury death in the US. By 2014 there were over 47,000 drug overdose deaths, surpassing deaths due to motor vehicle crashes and firearms. In California alone, 4,521 people died from a drug overdose in 2014.² That year, the US Centers for Disease Control and Prevention (CDC) added opioid overdose prevention to its list of top five public health challenges and declared the “worst drug overdose epidemic in US history.”³

Deaths due to opioid addiction continue to rise, despite multiple policy interventions at the federal, state, and local levels. Many of these policy efforts have focused on prevention. Prevention is essential, but prevention won’t help the millions of people already addicted to opioids. The death rate for young white Americans, driven by opioid-related deaths, has risen to alarming levels not seen since the height of the AIDS epidemic.⁴ In a tragic reversal of decades of improvement, the impact of preventable mortality from opioid and substance use is of such magnitude that the overall life expectancy for certain demographic groups in the US is actually declining.

Despite the magnitude of excess deaths from untreated opioid addiction, access to treatment remains limited. Merely 24% of patients with opioid use disorder receive medication-assisted treatment (MAT) despite decades of evidence supporting its efficacy.⁵ Eliminating the disparity between patients with opioid use disorder and access to MAT has become a national priority.
II. Emergency Department: Low-Risk Providers Treating High-Risk Patients

The emergency department should not be oversimplified as a pipeline of inappropriate opioid prescribing to be shut off, but instead considered a potential portal to bring high-risk patients into treatment for opioid addiction.

Low-Risk Providers

Until recently, policy responses to the opioid epidemic have largely focused on the emergency department’s role as a pipeline for opioid prescriptions. The focus on restricting opioid prescribing in the ED has persisted despite data showing EDs are responsible for only 5% of the opioid pain relievers in most communities. While EDs may account for 5%-20% of total opioid prescriptions, EDs tend to prescribe small pill counts of low strength, immediate-release opioids, so the actual contribution of opioid morphine equivalents into a community is quite low. In a study of patients who died of prescription drug abuse, it was found that ED prescribers accounted for only 1.5% of pills prescribed to patients in the 12 months before their death. The authors concluded that although patients who subsequently die from substance abuse frequently present to the ED, they are receiving most of their pills elsewhere.

An Opportunity to Reach High-Risk Patients

Doctor shopping, drug seeking, and malingering are not problems that distract from the treatment of “true” emergencies; rather, they are symptoms of the medical disease of addiction that should be treated with the same level of urgency as any other.

Opioid addiction is a devastating medical disease with an associated long-term mortality that exceeds that of myocardial infarction by a significant margin. While after 10 years, survivors of a myocardial infarction have standardized mortality rates approximately double that of the general population, patients with heroin addiction have been found to have a standardized mortality rate of 6 to 50 times that of the general population, depending on study methodologies. In a 30-year follow-up of patients admitted to the California Civil Addict Program, 50% had died; other studies have shown a similarly deadly trajectory to opioid addiction. From this same cohort, it was estimated that on
average, opioid addiction resulted in loss of over 18 years of potential life before age 65.\textsuperscript{10} (See Table 1.)

Table 1. Long-Term Mortality of Patients with Opioid Addiction\textsuperscript{11}

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Duration of follow-up (years)</th>
<th>Deaths (%)</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauer et al.</td>
<td>2008</td>
<td>Austria</td>
<td>5</td>
<td>25</td>
<td>269</td>
</tr>
<tr>
<td>Sanchez-Carbonell &amp; Seus</td>
<td>2000</td>
<td>Spain</td>
<td>11</td>
<td>30</td>
<td>138</td>
</tr>
<tr>
<td>Fridell &amp; Hesse</td>
<td>2006</td>
<td>Sweden</td>
<td>15</td>
<td>24</td>
<td>125</td>
</tr>
<tr>
<td>Davstad et al.</td>
<td>2009</td>
<td>Sweden</td>
<td>18</td>
<td>45</td>
<td>157</td>
</tr>
<tr>
<td>Vaillant et al.</td>
<td>1973</td>
<td>USA</td>
<td>20</td>
<td>23</td>
<td>100</td>
</tr>
<tr>
<td>Oppenheimer et al.</td>
<td>1994</td>
<td>UK</td>
<td>22</td>
<td>34</td>
<td>128</td>
</tr>
<tr>
<td>Jimenez-Treviño et al.</td>
<td>2011</td>
<td>Spain</td>
<td>25</td>
<td>50</td>
<td>214</td>
</tr>
<tr>
<td>Hser et al.</td>
<td>2001</td>
<td>USA</td>
<td>33</td>
<td>49</td>
<td>581</td>
</tr>
<tr>
<td>Nehkant et al.</td>
<td>2005</td>
<td>UK</td>
<td>33</td>
<td>22</td>
<td>86</td>
</tr>
<tr>
<td>Stenbacka et al.</td>
<td>2010</td>
<td>Sweden</td>
<td>37</td>
<td>50</td>
<td>1,705</td>
</tr>
</tbody>
</table>

The ED is clearly a setting at risk for an increased prevalence of opioid misuse and use of multiple doctors for controlled prescriptions, or “doctor shopping.”\textsuperscript{12} However, users of multiple doctors account for less than 1\% of all patients with opioid prescriptions.\textsuperscript{13} Therefore, using patient drug monitoring programs to identify people using multiple prescribers would be expected to have a small effect on the overall pipeline of opioids into the community.\textsuperscript{14}

However, if the use of multiple prescribers is considered a symptom of disease in the individual patient, it helps identify high-risk patients in need of treatment and care. Doctor shopping, frequent ED visits, and evidence of diversion are all strongly associated with increased risk of death from opioid overdose.\textsuperscript{15} (See Figure 1.)
Shifting the Focus to Emergency Treatment of Addiction

In summary, shutting down ED provision of short-duration opioids is unlikely to have a significant impact on the individual patient’s risk of death or the overall volume of diverted opioids in a community. In contrast, identifying and treating addiction provides an opportunity to intervene in a patient population at very high risk for subsequent opioid overdose death.\(^\text{16}\)

The ED should be conceptualized as a patient-centered, open-access setting that can provide an unparalleled combination of all-hours ease of access and capacity for technically advanced, complex care. This ease of access may be particularly important for people struggling with substance use disorders who have difficulty keeping clinic appointments.\(^\text{17}\) Substance use disorders are often accompanied by other medical and/or social issues. EDs have broad medical capability and increasingly are equipped to assist with social issues such as housing, legal assistance, and domestic violence.\(^\text{18}\)

The California Society of Addiction Medicine (CSAM) recently drafted a statement of support for ED-initiated addiction treatment:

“The emergency department is a health care setting in which patients with opioid use disorders commonly present, seeking more opioids to maintain their addiction, seeking help with opioid withdrawal, or in some tragic instances, needing emergency resuscitation for opioid overdose. Emergency physicians are thus uniquely positioned to intervene to help patients with opioid use disorders at a critical moment in the addiction cycle.” —David Kan, president-elect, CSAM
Figure 1. Association of Frequent ED Visits and Subsequent Prescription Drug Death

### Association of Frequent ED Visits and Subsequent Prescription Drug Death

<table>
<thead>
<tr>
<th>ED Visits in Previous Year</th>
<th>Adjusted odds ratio for prescription drug overdose death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
</tr>
</tbody>
</table>

Adjusted odds ratio for prescription drug overdose death.
III. What Can We Do? The Case for Medication-Assisted Treatment of Addiction

“Good evidence shows that opiate substitution treatment, primarily with methadone and buprenorphine, is effective across a range of outcomes, including reducing all-cause mortality, improving physical and mental health, and decreasing illicit drug use, criminal activity, and risk of HIV infection.”

The bottom line: treatment with buprenorphine reduces mortality among patients with opioid addiction.

In a recent study of over 150,000 National Health Service patients treated for opioid dependence, followed for a total of 442,950 patient years, treatment of opioid dependence with buprenorphine was found to reduce risk for opioid overdose death by one half versus patients with no treatment or psychosocial treatment only. In a study of 33,923 Medicaid patients diagnosed with opioid dependence in Massachusetts, mortality during the four-year study period (2003-2007) was double among patients receiving no treatment versus patients treated with buprenorphine. Additionally, patients treated with buprenorphine experienced a 75% reduced mortality versus patients treated with psychosocial interventions alone. Among the highest risk patients who inject heroin, treatment with methadone or buprenorphine for at least five cumulative years is associated with a reduction in mortality at 25 years from 25% to 6%. The association between treatment and improved survival is likely multifactorial and mediated through reduced risk of HIV infection, improved social functioning, reduced criminality, and establishment of long-term contact with health professionals. Importantly, survival benefit is not affected by cessation of injection drug use.
Figure 2. Survival from First Injection of Heroin: Probability of Not Dying Before Long-Term Cessation by Exposure to Opiate Substitution to Treatment\textsuperscript{25}

Why Retention in Treatment is the Best Outcome for Short-Term Studies
Medication-assisted treatment (MAT) with buprenorphine or methadone has a powerful effect on reducing long-term mortality among patients with an opioid use disorder. This effect is not dependent on cessation of illicit opioid use or drug injection. The key intervention is initiating and sustaining MAT with buprenorphine or methadone; the longer people stay in treatment (assuming alternating episodes of relapse and return to treatment), the greater the survival benefit.\textsuperscript{26}

Exposure to MAT Improves Survival
Almost any amount of participation in opioid agonist MAT likely adds a meaningful chance of improving patient survival. At the very least, if a patient can be convinced to go into treatment for one week, that is one week their chance of death from overdose is reduced.\textsuperscript{27} Thus retention in treatment is considered the most meaningful outcome in short-term studies of intervention for addiction. (See Figures 3 and 4.)
Figure 3. Mortality Rate Ratio While on MAT with Opiate Substitution Versus Not on Treatment

Figure 4. Probability That MAT with Opiate Substitution Treatment Reduces Overall Mortality by Duration of Treatment
IV. Bringing MAT to the Emergency Department: What Has Been Done So Far

Initiation of Buprenorphine MAT at the Yale New Haven Hospital ED

Emergency physician Gail D’Onofrio and her staff at the Yale New Haven Hospital recognized the potential of the ED as a critical point of access for patients suffering from opioid use disorders. In 2009, she began a groundbreaking program that screened ED patients for opioid use disorder, combined with a brief negotiation interview and ED initiation of buprenorphine (Screening, Brief Intervention, and Referral to Treatment [SBIRT] + buprenorphine). Six years later, the results of their work with 329 opioid-dependent patients were published in the Journal of the American Medical Association, and they were stunning. The rates of participation in addiction treatment in the SBIRT + buprenorphine arm were more than double that of the patients who received screening and referral only (78% vs. 37%). Furthermore, their ED was not overwhelmed with malingering patients seeking buprenorphine, nor was there a significant incidence of buprenorphine-related complications—precipitated withdrawal or overdose (D’Onofrio personal communication). D’Onofrio’s work strongly suggests that ED-initiated MAT with buprenorphine is both feasible and efficacious.30

The Yale New Haven Emergency Department team utilized a pragmatic model. A simple screening tool (the Mini-International Neuropsychiatric Interview) was used to target any ED patient meeting DSM-IV criteria for opioid dependence. Patients were then randomized into one of three groups: (1) referral to addiction treatment, (2) brief intervention and referral to addiction treatment, or (3) ED initiation of buprenorphine/naloxone MAT plus referral to a primary care buprenorphine clinic, where they could continue to receive the medication.

Patients in the buprenorphine group received SBIRT and were then assessed for withdrawal using the Clinical Objective Withdrawal Scale (COWS). If the patient was in moderate to severe withdrawal, 8 mg of sublingual buprenorphine was administered in the ED, and the patient was given a prescription for an adequate amount of buprenorphine to last until a primary care follow-up appointment within 72 hours (8 mg day one, 16 mg per day for days two and three). If the patient was not in active
withdrawal or had mild symptoms, a prescription was given to the patient to cover 72 hours of home-initiated MAT (buprenorphine sublingual tablets: 8 mg day one, 16 mg on days two and three). By the third day, longitudinal primary care and addiction treatment was initiated at an outpatient clinic. In the Yale ED, not all physicians had obtained their Drug Enforcement Administration (DEA) "X" waiver to allow prescribing of buprenorphine. To assist enrolling patients, the physicians with a DEA "X" waiver rotated remote on-call coverage to be able to call in the buprenorphine prescriptions as needed.

Summary of the Yale ED MAT Study


Lead Author
Gail D’Onofrio, MD, chair, Department of Emergency Medicine, Yale New Haven Hospital

Study Design
Randomized clinical trial involving 329 opioid-dependent patients who were treated at the Yale New Haven Hospital ED from April 7, 2009, through June 25, 2013.

Treatment Arms
1. Screening and referral to treatment (referral) [n = 104].
2. Screening, brief intervention, and referral to community-based treatment services (brief intervention) [n = 111].
3. Screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for follow-up within 72 hours. Buprenorphine regimen was 8 mg SL tablet first day then 16 mg on days 2 & 3. Buprenorphine was administered in the ED for patients in moderate to severe withdrawal. In patients with mild symptoms the three-day supply was prescribed for at-home unsupervised induction [n = 114].

Primary Outcome
Enrollment in addiction treatment at 30 days.

Results
Primary outcome: 78% of the buprenorphine group were engaged in treatment at 30 days versus 37% in the referral group and 45% in the brief intervention group.
ED Use of Buprenorphine for the Treatment of Acute Opioid Withdrawal

Does use of buprenorphine by emergency physicians lead to cases of precipitated withdrawal?

Once the word gets out that the ED has buprenorphine, will ED visits increase as patients present seeking buprenorphine?

A study by Berg et al. suggests that concerns about harm (precipitated withdrawal or drug seeking) are likely unfounded. In a retrospective chart review of 158 patients treated at a single ED with buprenorphine for opioid withdrawal, the authors found no instances of precipitated opioid withdrawal (a potential medical complication of buprenorphine), and a greater than 50% reduction (17% vs. 8%) in return-rate to the same emergency department for a drug-related visit within one month, compared to return-visit rate for usual care (no pharmacologic management or supportive therapies such as anti-nausea medications and sedatives).\textsuperscript{31}
V. Treatment of Opioid Addiction: The Basics

Pharmacotherapy and psychosocial therapy are the two main modalities for the treatment of opioid addiction. Medications approved for use in the treatment of opioid addiction include:

- Agonist maintenance with methadone
- Partial-agonist maintenance with buprenorphine or buprenorphine plus naloxone
- Antagonist maintenance using naltrexone
- Detoxification with tapering doses of methadone and buprenorphine

Medication combinations that are not approved but are commonly used off-label for detoxification from opioid addiction include:

- Clonidine
- Antispasmodic medications (loperamide, dicyclomine, diphenoxylate/atropine)
- Nonsteroidal anti-inflammatory drugs (NSAIDs) (ibuprofen)
- Sedatives (trazodone or diphenhydramine)

Psychosocial therapy, including individual counseling, peer group mutual-help programs, or other community-based treatment programs, is also an important component of the treatment of opioid addiction. While the evidence is still unclear about which behavioral approaches are most effective when combined with MAT, only three of eight studies in a review by the American Society of Addiction Medicine found a positive benefit to behavioral therapy in addition to medication. Therefore, medication should not be withheld if behavioral treatment is not easily available.
VI. Buprenorphine in the ED: Background and Initial Considerations

Buprenorphine is a unique medication with pharmacologic properties that are unfamiliar to most emergency clinicians:34

- High-affinity, low intrinsic activity mu opioid receptor agonism
- Kappa opioid receptor antagonism
- Anti-hyperalgesic, long-acting analgesia

Buprenorphine is a partial agonist at the mu opioid receptor, where it has a very high affinity but low intrinsic activity. Its high affinity means it will out-compete and displace full opioid agonists such as heroin, morphine, methadone, and others from the mu opioid receptor, while its low intrinsic activity results in less euphoria and lower abuse potential, with reduced withdrawal discomfort. Importantly, buprenorphine demonstrates a protective ceiling effect in respiratory depression that greatly enhances its safety profile versus full mu opioid agonists. (See Figure 5.)

Figure 5. Comparison of the Respiratory Effects of Intravenous Buprenorphine and Fentanyl in Humans and Rats

While buprenorphine alone does not cause life-threatening respiratory depression even at high doses in adults, there are several important safety considerations that should not be overlooked. Buprenorphine can potentiate the dangerous respiratory depression produced by sedatives such as benzodiazepines or alcohol. Additionally, small children appear more susceptible to buprenorphine-induced respiratory depression, and deaths have occurred after massive overdoses.

Patients tend to like the effects of buprenorphine, often describing an even, clear-headed state. This may result from reduction in stress and drug craving produced by buprenorphine via kappa opioid receptor (KOR) antagonism. KOR antagonism blocks the actions of endogenous dynorphins released during the stress response. Kappa opioid receptor antagonists, like buprenorphine, may promote resilience and help counteract the stress hypersensitivity often seen in addiction. Finally, there is sufficient agonism to produce a reinforcing, withdrawal-reduction effect that likely increases medication compliance.

Buprenorphine is an excellent first-line analgesic for chronic and acute pain. As an analgesic, buprenorphine produces pain relief similar to a full mu opioid receptor agonist with no analgesic ceiling effect. Moreover, buprenorphine has anti-nociceptive properties important in patients with chronic, centralized pain syndromes. Contrary to common perception, buprenorphine can be used in combination with full mu opioid receptor agonists, and patients using buprenorphine can be continued on buprenorphine when admitted for surgery, or when requiring analgesia for acute injury, and receive opioid agonists or additional buprenorphine doses for pain management. Buprenorphine does not lead to bioaccumulation of metabolites and can be used in the elderly or in patients with renal failure without dose adjustment.35

**Buprenorphine Has Important Potential Side Effects**

- High-affinity, low intrinsic mu agonism can result in precipitated withdrawal when used in opioid-tolerant patients who have not waited a sufficient length of time from their last opioid agonist dose, due to displacement of the full mu agonists from the receptor site.
To avoid precipitated withdrawal in patients on long-acting opioids such as OxyContin, MS Contin, and methadone, slowly reduced daily methadone to 30 mg or less for at least a week, then discontinue completely. Wait for the development of withdrawal symptoms (typically at least 36 hours) before first dose of buprenorphine.

To avoid precipitated withdrawal in patients on short-acting opioids such as morphine, oxycodone, and heroin, discontinue completely, then wait 12-24 hours for the development of withdrawal symptoms before first dose of buprenorphine. It may be easiest for some patients to take their last dose in the evening. Then begin buprenorphine the next day.

Management of unexpected precipitated withdrawal:

- Increase dose of buprenorphine
  - 2-4 mg oral every hour till symptoms have improved
  - 0.3 mg IV or IM every 30 minutes till symptoms have improved
- Anti-emetics for nausea
  - Ondansetron, prochlorperazine, metoclopramide, etc.
- NSAIDs for arthralgias and myalgias
- Nausea, vomiting.
- Constipation.
- Other less common unpleasant effects include headache, insomnia, leg edema, and itching.

Buprenorphine Dosing

- Analgesia

  Buprenorphine is a DEA Schedule III narcotic. Any clinician with authority to prescribe DEA Schedule III medications may prescribe buprenorphine in intravenous, intramuscular, transmucosal, or transdermal preparations for the treatment of pain, without a waiver.

  - Parenteral Buprenex: 0.3 mg IV/IM q 30 minutes, duration 6-8 hours
    - Analgesic equivalent = 10 mg IV morphine for opioid naïve.
  - Transdermal patch Butrans: 5-20 mcg per hour
    - May be administered either in the ED or prescribed.
• Prescriptions may be written or called in.
• No DEA “X” waiver is required.

• **Transmucosal film Belbuca buccal film:** 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg buprenorphine per film administered daily or every 12 hours.
  • No DEA “X” waiver is required.

• **Opioid Maintenance**
  • Sublingual (SL) tablets Subutex (buprenorphine alone) or Suboxone (buprenorphine + naloxone): 2-8 mg every 6-8 hours*
    i. Induction: 2-8 mg SL up to 16 mg in first 24 hours after sufficient abstinence from opioids with clinical symptoms of mild-to-moderate withdrawal.
    ii. Maintenance: typical dosing is 4-32 mg SL tablet daily or every other day.
  • There are multiple preparations of buprenorphine currently available for treatment of addiction, including:
    • Generic buprenorphine and buprenorphine/naloxone
    • Branded products, including
      o Suboxone (buprenorphine/naloxone)
      o Zubsolv (buprenorphine/naloxone)
      o Bunavail (buprenorphine/naloxone)
    • Buprenorphine implant
      o Probuphine (6-month implantable buprenorphine)
    • Preparations in Phase-3 trials, including
      o Buprenorphine 1-week injectable depot shot
      o Buprenorphine 4-week injectable depot shot

• **Opioid Withdrawal**
  Under the “three-day rule” any opioid (including all formulations of buprenorphine) can be administered in the ED for the treatment of acute withdrawal without a DEA “X” waiver, for no more than three consecutive days.36
Regulation of Buprenorphine Prescribing

In other countries, such as France, any physician with opioid prescribing authority can prescribe any formulation of buprenorphine. Here in the US, in 2000, Congress enacted DATA 2000, which created the DEA “X” license system and permits physicians to prescribe certain approved opioid-based medications specifically for the treatment of opioid addiction. Buprenorphine/naloxone (Suboxone), buprenorphine (Subutex), the implant (probuphine), and high-dose buccal film (Bunavil) are covered under this statute.

Buprenorphine for the treatment of addiction can only be prescribed by a physician with a DEA DATA 2000 “X” waiver. While another administrative burden for the busy clinician, it is feasible that all prescribing clinicians in a given ED could be expected to complete this training if they are properly incentivized. The eight-hour training can be completed in its entirety online. DATA 2000 caps the number of patients a physician can treat at any one time to 30 through the first year following certification, expandable to 275 patients thereafter for physicians with additional specialty training in addiction medicine. (Health and Human Services Final Rule, 81 Fed. Reg. 44711)

“Rescue” buprenorphine (including induction) can be prescribed by any clinician with a valid DEA license to prescribe opioids.

The “three-day rule” provides an exception to the DATA 2000 waiver requirement. Title 21 C.F.R. § 1306.07(b) allows a practitioner who is not certified as a “waivered DATA 2000 physician” to administer (but not prescribe) narcotic drugs to a patient for the purpose of relieving acute withdrawal symptoms while arranging for the patient’s referral for treatment, under the following conditions: (1) no more than one day’s medication may be administered or given to a patient at one time, (2) this treatment may not be carried out for more than 72 hours, and (3) this 72-hour period cannot be renewed or extended. The physician without a waiver can administer buprenorphine only in the ED; additional doses cannot be dispensed or prescribed for use at home. Additional doses can only be provided when the patient returns to the ED for a subsequent visit; treatment may continue over a total duration of no more than three days.
Buprenorphine can be administered or prescribed for the treatment of pain by any clinician with DEA Schedule III prescribing authority.

Buprenorphine can be administered in any formulation for the treatment of pain without need for a DEA “X” waiver. Transdermal patches and buccal film preparations are specifically FDA-approved for treatment of pain and may be prescribed for pain in a patient with addiction without the need for a DEA waiver. Tablet formulations of buprenorphine (Suboxone and Subutex) are only FDA-approved for the treatment of addiction. Nevertheless, off-label use of the sublingual tablet formulations of buprenorphine (Suboxone and Subutex) for the treatment of pain is not prohibited under DEA requirements; thus, sublingual tablets can be prescribed for pain by any provider with DEA Schedule III prescribing authority without a DATA 2000 “X” waiver.37

Buprenorphine prescriptions can be remotely refilled by fax or phone by any physician with the appropriate prescribing authority (see Table 2).

21 C.F.R. § 1306.21:

Prescriptions for Schedule II-V controlled substances (such as buprenorphine) may be written, faxed, or orally transmitted.

Buprenorphine can be initially prescribed to an ED patient over the phone by any physician with the appropriate prescribing authority (see Table 2).

Controlled Substances Act, 21 U.S.C. §§ 802(52-54)(A):

Under the Ryan Haight Act, at least one face-to-face encounter must occur before a controlled substance can be prescribed unless the encounter meets the federal definition of telemedicine. Because most EDs are registered with the DEA, this allows a buprenorphine provider to be consulted via phone or other form of communication (telemedicine) for an ED patient seen by another provider. The buprenorphine provider can then call in or fax a buprenorphine prescription.
Table 2. Buprenorphine Formulations, FDA Approval Status, and DEA DATA 2000 “X” Waiver Requirements

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Doses Available</th>
<th>Indication</th>
<th>DEA DATA 2000 “X” Waiver Required?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral (Buprenex)</td>
<td>0.3 mg IV/IM every 30 minutes, duration 6-8 hours</td>
<td>Pain</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Analgesic equivalent = 10 mg IV morphine for opioid naïve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transdermal patch (Butrans)</td>
<td>Buprenorphine: 5, 7.5, 10, 15, and 20 mcg/hour, every 7 days</td>
<td>Pain</td>
<td>No</td>
</tr>
<tr>
<td>Low-dose buccal film (Belbuca)</td>
<td>Buprenorphine: 75, 150, 300, 450, 600, 750, 900 mcg, twice daily</td>
<td>Pain</td>
<td>No</td>
</tr>
<tr>
<td>High-dose buccal film (Bunavail)</td>
<td>Buprenorphine/naloxone, daily: 2.1 mg/0.3 mg, 4.2 mg/0.7 mg, and 6.3 mg/1 mg</td>
<td>Addiction</td>
<td>Yes for addiction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Off-label for pain</td>
<td>No for pain or 3-day rule</td>
</tr>
<tr>
<td>Sublingual tablets (Subutex, Suboxone, Zubsolv)</td>
<td>Dosed daily for addiction; divided doses for pain. Buprenorphine: 2 mg, 8 mg Buprenorphine/naloxone: 2 mg/0.5 mg, 8 mg/2 mg; 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg, 8.6 mg/2.1 mg, 11.4 mg/2.9 mg</td>
<td>Addiction</td>
<td>Yes for addiction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Off-label for pain</td>
<td>No for pain or 3-day rule</td>
</tr>
<tr>
<td>Sublingual film (Suboxone)</td>
<td>Buprenorphine/naloxone: 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg</td>
<td>Addiction</td>
<td>Yes for addiction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Off-label for pain</td>
<td>No for pain or 3-day rule</td>
</tr>
<tr>
<td>Implant (Probuphine)</td>
<td>80 mg (equivalent to &lt;8 mg sublingual daily)</td>
<td>Addiction</td>
<td>Yes</td>
</tr>
<tr>
<td>Compounded</td>
<td>Many options</td>
<td>Pain</td>
<td>No</td>
</tr>
</tbody>
</table>
Buprenorphine can be initiated in the ED without complex psychosocial intake and evaluation.

In the ideal system, psychosocial interventions and supports would be adequately funded and widely accessible. The unfortunate reality is that such supports are often not available, or available only after a waitlist delay. The core interventions of addiction treatment can be provided in the ED without additional staff. Properly trained ED staff can introduce and explain the neurobiological model of addiction and recovery, and potentially initiate medication-assisted treatment. Feasible low-cost models to expand the extent of substance abuse services may utilize volunteers or paid substance use counselors embedded in the ED itself.

Buprenorphine induction does not need to occur under direct medical observation.

The concept of a home induction is well established and common. Patients can be easily instructed to abstain from opioids and then initiate buprenorphine once withdrawal has commenced. Self-evaluation of opioid withdrawal state can be supported by use of the Subjective Opioid Withdrawal Score (SOWS). Precipitated withdrawal is unusual, easily treated, and rarely harmful. It is not medically necessary to initiate buprenorphine under direct supervision.38

Buprenorphine can be initiated in the ED even if next-day follow-up is not available.

Although a warm handoff to an addiction care coordinator in the ED with next-day follow-up in a comprehensive addiction clinic is ideal, it is not currently practical in many systems. The alternative has been referred to as “interim” treatment, where the patient is waitlisted for entry into a comprehensive program, but MAT with buprenorphine is initiated with a skeleton set of supports as a bridge to optimal treatment.39 Because of its long action, a single dose of buprenorphine in the ED can help with withdrawal symptoms for up to three days.
Substance use treatment does not necessarily require highly trained medical staff or inpatient treatment.

Addiction counselors, health educators, case managers, nurses, and/or health advocates can provide a backbone of community-based psychosocial and addiction-related care for patients in an ED providing buprenorphine MAT.

Trained nonmedical staff can implement many of the interventions for addiction. Peer counselors may naturally form therapeutic alliances with certain populations of patients with substance use disorders more readily than traditional medical staff. Utilization of low-cost personnel is a strategy to both promote patient acceptance and to help expand care with a limited budget. Such staff can be embedded in the ED, where addiction-related interventions can occur in the midst of regular operations, both reaching the patients and partnering with emergency clinicians to facilitate treatment and arrange timely discharge of patients with complex psychosocial needs. Project Assert, originally developed by Dr. Ed Bernstein at Boston Medical Center, is an example of this model. This type of program can work closely with peer supported, self-directed recovery programs such as the Wellness Recovery Action Plan, faith-based programs, and 12-step programs.\textsuperscript{40}

**Emerging technology and communication tools may provide an avenue for care coordination out of the ED not previously possible.**

- Mobile phone applications can support patients in recovery with abstinence tracking systems, relapse trigger alerts, and connection with other people in recovery for support. An example is the Hazelden mobile app Field Guide to Life that provides first-year support to people newly recovering from addiction and was recognized with the White House Behavioral Health Patient Empowerment Challenge Award in 2013.
- Messaging and telemedicine can allow check-ins and support without a face-to-face encounter.
- Take-home “E-pill” secure pill dispensers can provide controlled at-home access to medications such as buprenorphine.\textsuperscript{41}
- Telemedicine programs are being developed to provide medication supervision with counseling.
Social instability does not exclude patients from eligibility for ED-initiated buprenorphine treatment of addiction.

Ideally, a whole-person approach to care is developed that addresses the complex psychosocial needs of many ED patients with substance use disorders. However, such services are not always available. Isolated buprenorphine MAT can be an important stand-alone harm reduction intervention. Homeless patients have been successfully treated for opioid dependence with buprenorphine.\textsuperscript{42}
VII. Practical Questions to Consider When Developing an ED Buprenorphine MAT Program

1. What are the appropriate selection criteria for initiation of buprenorphine MAT in the ED?
   
   i. **Suggested inclusion criteria**
      
      - Patient is at least 18 years old.
      - Patient meets DSM-5 criteria for opioid use disorder.
      - Access to follow-up care within 3-7 days.
      - No known allergy/hypersensitivity to buprenorphine or naloxone.

   ii. **Potential factors that complicate treatment**
      
      - Patient has serious, uncontrolled psychiatric problems such as suicidality or psychosis.
      - Patient currently using more than 30 mg/day of methadone (may have greater difficulty stabilizing on buprenorphine).
      - Patient with complex, severe, chronic pain on high-dose daily opioids may require a titration of the opioid, and may benefit from a multidisciplinary set of complex care services—potentially better accomplished with an outpatient provider and frequent follow-up.
      - Comorbid substance use disorders are common in patients with opioid use disorder and should not exclude patients from eligibility for ED MAT. However, these patients may have more complex needs benefiting from close coordination of additional resources with ED-based care.
      - While very rare and reversible, there may be a risk of hepatotoxicity due to buprenorphine in patients with liver disease. As a result, some authors recommend liver testing—transaminases and bilirubin—prior to initiating buprenorphine treatment. Additionally, patients whose serostatus is unknown and who have risk factors should be screened for hepatitis B and C.43

2. Does the induction have to occur in the ED?
   
   No. Home induction is an established method of induction that can eliminate the need for a prolonged ED stay.
3. What are the potential negative impacts of initiating ED MAT: Buprenorphine?

- **Precipitated withdrawal.** While unpleasant, precipitated withdrawal is easily treated and does not pose a significant health threat. The general principle of treatment is simply to give more buprenorphine. Adjuncts such as clonidine, metoclopramide, dicyclomine, ondansetron, and NSAIDs can also be used.

- **Malingering and buprenorphine abuse/misuse.** The few EDs that have begun use of buprenorphine for the treatment of withdrawal and addiction have not noted increased “buprenorphine seeking.” In general, buprenorphine is less “likeable” than full mu opioid agonists such as hydrocodone or morphine, and is thought to have a reduced abuse potential. Frequently, diverted buprenorphine is used for its intended purpose—to treat withdrawal symptoms. Patients who tried illicit buprenorphine were twice as likely to be retained in treatment compared to buprenorphine-naïve patients.44

- **Overdose.** On its own, buprenorphine presents a very low risk for clinically significant respiratory depression. Importantly, the risk is significantly less than commonly prescribed analgesics such as codeine, hydrocodone, morphine, or tramadol. However, in combination with sedatives, alcohol, and/or other opioids, fatal overdose can occur. Additionally, fatal overdoses in small children have also been described after massive ingestions.45
VIII. Buprenorphine in the ED: Implementation

Overview

- Leading Resource Development in Your Community
- Key Partnerships
- Funding
- Buprenorphine Inclusion on the Hospital Formulary

Leading Resource Development in Your Community

Mental health and substance use disorder treatment has long been underfunded. Proven strategies remain underutilized, and access to critical services is commonly limited. The ED has emerged as the final safety net for patients without alternative access to care for a myriad of disorders from low back pain and diabetes to schizophrenia and addiction.

It is an exciting time for emergency clinicians to take a leading role in the development of innovative programs that deliver high-quality MAT services to patients in need. At this time, there is no single solution to the problem of addiction, nor is there a clear optimal role for the ED. Perhaps the first test for any ED MAT program should simply be this: Will this program have a positive impact on individual patients? The health care system? The larger community?

Given the burden of preventable deaths, scarcity of outpatient resources for addiction treatment and MAT is not an excuse to ignore addiction and substance use disorders among ED patients. Innovative strategies that increase the capacity of EDs to independently assist patients with substance use disorders are urgently needed.

Key Partnerships

Core Partners

- Emergency physicians willing to obtain DEA "X" waivers and prescribe buprenorphine to treat patients with opioid use disorder
- Primary care clinicians willing to obtain DEA "X" waivers and accept patients for ongoing treatment (or treatment centers willing to partner with EDs to accept referrals)
• Nursing staff to assist in all aspects of care including patient identification and administration of medications
• Pharmacy staff able to dispense and seek payment for needed medications

Helpful Partners for Expanding Scope of ED-Based Addiction Services
• Additional staff trained to provide support, education, and coaching to patients in the ED about recovery and MAT (e.g., health advocates, substance use counselors, case managers).
• Pain and/or addiction specialists able to manage difficult-to-treat cases or give virtual advice and support (note: the Clinician Consultation Center Warm Line offers free clinical advice Monday-Friday 7 AM-3 PM Pacific Time, 855.300.3595; the Providers’ Clinical Support System assigns free mentors).
• Care managers able to assist coordination of medical services and supportive care, including (ideally) follow-up phone calls.

Funding
Medicaid programs include medication-assisted treatment for addiction with buprenorphine for its beneficiaries; in California, buprenorphine sublingual tablets are available to Medi-Cal beneficiaries without need for prior authorization approval. The California Drug Medi-Cal Organized Delivery System (DMC-ODS) is in the process of rolling out to counties across California, and provides funding and infrastructure for the full spectrum of addiction treatment services. Hospital community benefit funds may be sought to support start-up costs. Partnerships with local nonprofits and philanthropic foundations may also yield addition sources of funding.
Buprenorphine Inclusion in the Hospital Formulary
Buprenorphine should be made available on hospital formularies in sublingual, transdermal, and parenteral formulations. The indications for use are (1) analgesia and acute opioid withdrawal management for general emergency providers and (2) opioid detoxification and initiation of opioid substitution therapy for physicians with a DEA DATA 2000 “X” waiver.

Getting started: recruit champions in other departments.
A hospital committee or working group on pain and/or addiction is a great place to start building support to bring buprenorphine to the ED. Primary care, surgical, and medical specialty practices will be affected by incorporating buprenorphine into ED practice. Champions from partner services should be recruited early on to build a broad base of support. The medical, surgical, and anesthesia services should have a plan for managing patients using buprenorphine, including developing protocols to allow some patients to continue their baseline buprenorphine dose during an inpatient stay.

While there remains some controversy, several studies suggest that some patients do better, with shorter hospital stays and better pain management, if the buprenorphine is continued, with opioid agonists or additional buprenorphine doses used to manage acute pain. Data 2000 waivers are not required for physicians prescribing buprenorphine for pain and to prevent withdrawal during an inpatient stay. As the prevalence of buprenorphine use in the general population increases, learning how to treat pain in patients on buprenorphine is a skill that inpatient services need to develop regardless of ED practice.

Use evidence from the medical literature to build the case for buprenorphine.
The pharmacy and therapeutics committee members should be provided with the literature that supports use of buprenorphine. Buprenorphine should be included on hospital formularies for three main reasons:

1. Buprenorphine has superior clinical efficacy for pain treatment in patients with a history of chronic opioid use. Small studies report improved pain scores on patients transitioned from high-dose opioid agonists to buprenorphine.
   Buprenorphine has no ceiling effect on analgesia at clinically meaningful doses
and is a potent analgesic compared to morphine, with 0.3 mg IV equivalent to 10 mg morphine.⁴⁷

2. Buprenorphine has a superior side effect profile compared to traditional full opioid agonists, including less sedation and respiratory depression (an advantage in the elderly and patients with sleep apnea or other respiratory disorders), less impact on the sphincter of Oddi (an advantage in pancreatitis, and biliary disease), and its kappa antagonism results in less impact on mood disorders and less hyperalgesia, with its partial agonism resulting in less of a “high” sensation and less abuse potential.

3. Buprenorphine is considered the gold standard for the treatment of opioid use disorder, equivalent in efficacy to methadone, superior to naltrexone, and far superior to nonmedical treatment (retention rate in treatment with buprenorphine is 67% compared to 12% with a social model alone). Its lack of impact on respiration (lower overdose risk) and the ability to prescribe outside of opioid treatment programs are advantages compared to methadone. Buprenorphine is a World Health Organization essential medicine for the treatment of opioid addiction and withdrawal.⁴⁸

**Helpful references for use of buprenorphine without a waiver**

- Parenteral buprenorphine for acute pain⁴⁹
- Sublingual buprenorphine for acute pain⁵⁰
- Sublingual and transdermal buprenorphine for pain⁵¹
- Buprenorphine for treatment of acute withdrawal⁵²

**Helpful references for use of buprenorphine by waived physicians for addiction**

- Buprenorphine for detoxification⁵³
- Buprenorphine initiated in the ED for long-term opioid substitution treatment of opioid addiction⁵⁴

**Anticipate and address common concerns.**

*The DEA will not investigate or punish physicians just for prescribing sublingual buprenorphine off-label for pain.* The DEA has been very clear that buprenorphine in any formulation can be prescribed for pain to any patient. Specifically, the DEA clarified that general providers can prescribe all formulations of buprenorphine for the indication
of pain in patients who carry the diagnosis of addiction, even when using sublingual formulations that are off-label for pain.\textsuperscript{55} There are currently many physicians who prescribe sublingual buprenorphine for large numbers of patients with chronic pain.\textsuperscript{56}

\textit{Precipitated withdrawal}. Precipitated withdrawal is an awful experience for patients, and is seen frequently in the ED after naloxone reversals. Guidelines are needed to ensure physicians review prior opioid use and understand how to assess withdrawal severity before buprenorphine is administered or prescribed. Methadone, due to its long and complex half-life, may be initially excluded from the protocol until physicians are more experienced. Twelve hours after the last dose of heroin or short-acting opioid is typically sufficient; however, because of variability in metabolism, patients should always wait until objective signs of withdrawal develop before taking intermediate or higher-dose buprenorphine (buccal, sublingual, or parenteral formulations). The transdermal patch has such a gradual onset and is such a low dose that it can generally be placed on any patient not on methadone, even without waiting for withdrawal symptoms. See \textit{Buprenorphine: Everything You Need to Know} for a more detailed description of the patch induction process.

\textit{Keep pain and addiction separate}. Don’t let potentially stigmatized concerns around buprenorphine for addiction prevent use of buprenorphine for analgesia. If the institution is not ready to start treating addiction in the ED, start with a focus on pain treatment and work toward a system of buprenorphine MAT as physicians gain more experience.

\textit{Define the target patient population for treatment of pain with buprenorphine}. Consider starting with a tight focus on high-risk patients (e.g., heroin injection or illicit prescription opioid use) and extending to a broader patient base over time, depending on institutional attitudes.

\textit{Develop parameters and protocols for use in the ED to allay fears that there will be unrestrained, “out-of-control” use}. For example, treat severe pain with IV or IM buprenorphine, followed by placement of a transdermal patch in the ED and a brief prescription of sublingual tablets, with arrangement for outpatient follow-up within a
week. Patients need clear instructions about whether they need to follow up only with an outpatient provider, or if refills will be given in the ED.

**Develop a cost analysis.**

Make estimates about total patients treated with buprenorphine, so pharmacists can calculate any potential changes in cost compared to usual care. Buprenorphine sublingual tablets without naloxone and parenteral formulations are inexpensive; sublingual tablets with naloxone, patches, and buccal film are much more expensive. Working with pharmacists in advance of project launch will help ensure claims are processed appropriately (e.g., to third-party payers, managed care, or state Medi-Cal). Pharmacists need to know that California Medi-Cal covers sublingual buprenorphine without the need for authorization. Buprenorphine prescription for pain in any form, if given as a prescription to fill as an outpatient, usually requires an authorization from Medi-Cal, and private insurance often requires prior authorization. (See Table 3.) If the emergency department develops a program to dispense naloxone to all high-risk patients, the pharmacist may need to consider the expense of atomizers (not billable to Medi-Cal); naloxone in its injectable form, which can be converted to intranasal with an atomizer, is relatively inexpensive.

**Finally, if at an impasse, reach out and appeal to concern for the “big picture” of the opioid epidemic.**

The opioid epidemic is daily national news. If a local administrator is blocking progress, reach out to partners in the system who may champion the effort. Alternatively, developing an analysis based on ED data, documenting the number of times patients come in repeatedly with addiction, may help make the case that these patients are coming in anyway; adding capacity for MAT allows them to be treated more effectively and can decrease return visits.
**Table 3. Buprenorphine Formulary Details**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Indication and (dose strength)</th>
<th>Waiver Needed to Prescribe?</th>
<th>Where Is Drug Dispensed?</th>
<th>Payment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral (IV or IM): Buprenex</td>
<td>Pain or acute withdrawal in ED (high dose)</td>
<td>No</td>
<td>ED</td>
<td>Bundled as part of ED payment.</td>
<td>At times under shortage.</td>
</tr>
<tr>
<td>Sublingual tablet or film:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subutex (buprenorphine alone) or</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suboxone (buprenorphine + naloxone)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zubsolv tablet (buprenorphine + naloxone)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bunavail strips (buprenorphine + naloxone)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sublingual tablet or film:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subutex or Suboxone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zubsolv tablet (buprenorphine + naloxone)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bunavail strips</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Sublingual tablet or film:**
  - **Subutex (buprenorphine alone)**
  - **Suboxone (buprenorphine + naloxone)**
  - **Zubsolv tablet (buprenorphine + naloxone)**
  - **Bunavail strips (buprenorphine + naloxone)**

- **Indication and (dose strength):**
  - Pain or acute withdrawal in ED (high dose)

- **Waiver Needed to Prescribe?**
  - No

- **Where Is Drug Dispensed?**
  - Administered in ED or prescribed

- **Payment**
  - Covered by all types of Medi-Cal.

- **Comments**
  - Requires documentation on Rx of opioid use disorder or opioid dependence.
  - Schedule III (see above).
<table>
<thead>
<tr>
<th>(buprenorphine + naloxone)</th>
<th>Buccal film: Belbuca</th>
<th>Pain or acute withdrawal in ED (medium dose)</th>
<th>No</th>
<th>Administered in ED or prescribed</th>
<th>California Medi-Cal and most insurers require prior authorization.</th>
<th>Advantage over SL tablets — much smaller doses allow for more gradual tapers.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transdermal patch: Butrans</td>
<td>Pain or acute withdrawal in ED (low dose)</td>
<td>No</td>
<td>Administered in ED or prescribed</td>
<td>Bundled as part of ED payment if administered in ED. Medi-Cal and most insurers require prior authorization.</td>
<td>Low-dose patch alone will not be sufficient for some opioid-tolerant patients.</td>
<td></td>
</tr>
<tr>
<td>Implant: Probuphine</td>
<td>Addiction: maintenance</td>
<td>Yes</td>
<td>Prescribed (must be inserted by trained physician)</td>
<td>Authorization required.</td>
<td>Minimal risk of diversion, reduces need for compliance, long-acting medication (6 months).</td>
<td></td>
</tr>
</tbody>
</table>
Putting It Together: Steps to Create a Pilot ED Buprenorphine Program

1. **Identify a clinical champion** in your emergency department. This could be a physician or other clinician who can lead skill development, training, and implementation.

2. **Create a planning team.** Nursing, pharmacy, and social work representation is essential. Additional team members from outside the ED include but are not limited to primary care clinicians and specialists in addiction and pain medicine. Consider developing a core leadership group responsible for getting the project up and running, with a larger interest group including a broad array of potential partners and allies. Leadership from hospital- and outpatient-based services may be involved.

3. **Create a business plan.** The initial plan need not be overly complicated but should answer the basic questions:
   a. What costs will the pilot incur above current operating costs?
      i. What costs can be expected to be reimbursed through patient insurance coverage?
      ii. What are the requirements to assure payment capture?
      iii. Are there billing procedures that need to be built into the electronic health record?
   b. What funding sources are available for costs not directly billable to the patient?
      i. Hospital or community benefit funds?
      ii. Foundation grants?
      iii. Hospital or physician group training budgets?
   c. How will services impact staff resources? In a fixed staffing model, how will program operations add or potentially decrease work demands on ED staff?
      i. Potential reductions in work demands include:
         1. Reduced conflict and negotiation with patients
2. Reduced malingering / drug seeking
3. Shorter lengths of stay

ii. Potential increases in work demand include:
1. Patient education around addiction and treatment
2. Increased ED visits due to patients seeking buprenorphine
3. Complications of ED induction such as precipitated withdrawal
4. Follow-up ED visits after induction

4. **Develop a brief overview document that communicates program goals and interventions.** A clearly written, one-page overview of what problem the program seeks to address, what the program goals are, who is involved, and how it will operate can be used to communicate and build support of the program.

5. **Obtain administrative leadership buy-in and formal endorsement.** Addiction is a medical disease with tremendous cultural baggage. Many misplaced fears and stigmatized attitudes prevent clinicians from recognizing addiction as a medical disease with predictable symptoms that are disease-related, not character flaws. Public support from hospital leadership may help reduce the stigma associated with addiction treatment.

   a. Review the overview document at departmental meeting(s), obtain buy-in from frontline clinical staff, and address any potential clinical concerns.

   b. Upon emergency departmental endorsement, consider pursuing formal endorsement of the program by the medical staff through the medical executive committee. Further endorsement by the hospital CEO may enhance buy-in from clinical and administrative staff.
IX. Program Options for ED-Integrated Buprenorphine MAT

Introduction

The basic components of an ED MAT program with buprenorphine:

1. Team of committed and prepared emergency clinicians
2. Inpatient and outpatient pharmacy with adequate medication stocks and collaborating pharmacists
3. Outpatient providers able to accept patients for ongoing buprenorphine treatment
4. Clinical care pathways:
   a. Patient identification
   b. Induction with buprenorphine
      i. In the ED
      ii. At home
   c. Maintenance—what will be the role of ED services after initiation?
      i. For crisis care only?
      ii. As interim site for waitlisted patients awaiting entry into a community-based care setting?
      iii. As an integrated site for long-term maintenance?

The following care pathways will attempt to describe the step-by-step operational details of an ED MAT program with buprenorphine. The pathways are intended to be a starting point for pilot development that programs will tailor to their unique environments. Three approaches to ED-initiated MAT with buprenorphine are presented, from a basic model to a more complex and resource-intensive intervention.
Models for an ED MAT buprenorphine program

ED MAT Clinical Pathway 1.0: The Basic Model
In this pathway, a small number of ED providers develop informal referral connections to outpatient sites for ongoing care. Need for additional training is minimal. Patient care is worked into the usual workflow. No extra staff is needed.

ED MAT Clinical Pathway 2.0: The Initiate and Refer Model
In this pathway, a team of providers is supported by care management staff, and referrals to outpatient care are formalized. There is robust communication between an outpatient clinic and the referring ED. Multiple ED physicians have their DATA 2000 DEA "X" waiver. Substance abuse counselors or social workers are available to identify patients, engage them, and perform intake assessments for the ED MAT program.

ED MAT in the ED Clinical Pathway 3.0: The Expanded Model
Most or all of ED physicians have DEA “X” waivers, there is global buy-in from nursing and social services staff, and there are dedicated addiction counselors in the ED. The ED acts as a hub, accepting referrals from outside providers to initiate buprenorphine MAT as well as offer ongoing maintenance therapy for patients waiting to enter outpatient care.

Note: The Emergency Medical Treatment and Active Labor Act mandates EDs to care equally for all patients presenting for care based on medical need. Therefore, traditional appointments cannot be honored. However, most EDs have low-acuity areas with predictable times of low patient demand that are ideal times to offer specialty addiction services within the ED. These services can be staffed by emergency clinicians from other specialties—for example, primary care, addiction medicine, or psychiatry.
Figure 6. MAT in the ED Clinical Pathway 1.0: The Basic Model

<table>
<thead>
<tr>
<th>Emergency Physician</th>
<th>Pharmacy Partner</th>
<th>Outpatient Buprenorphine Providers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Informal recruitment of patients</strong></td>
<td><strong>Inpatient</strong> pharmacy for ED administration</td>
<td><strong>Intake process</strong></td>
</tr>
<tr>
<td>May or may not have formal departmental policy or guideline</td>
<td><strong>Outpatient</strong> pharmacy for home prescriptions</td>
<td>• Phone</td>
</tr>
<tr>
<td>May focus on high-risk patients such as injection drug users</td>
<td><strong>Areas for coordination</strong></td>
<td>• Drop-in</td>
</tr>
<tr>
<td><strong>Common buprenorphine options</strong></td>
<td>Billing procedures</td>
<td>• ED-arranged appointment</td>
</tr>
<tr>
<td><strong>For addiction</strong></td>
<td>• Prescribed</td>
<td>• Patient-arranged appointment</td>
</tr>
<tr>
<td>Short 3- to 7-day courses of Suboxone or Subutex (8 mg day 1, 16 mg days 2-7)</td>
<td>• ED- administered</td>
<td><strong>Availability</strong></td>
</tr>
<tr>
<td><strong>For pain (administered in ED)</strong></td>
<td>Stocking buprenorphine</td>
<td>• How many referrals per month can be accepted?</td>
</tr>
<tr>
<td>Butrans 7-day 20 mcg/hour patch or Subutex (as above)</td>
<td>• IV/IM</td>
<td>• Any special requirements or target populations?</td>
</tr>
<tr>
<td>(can also act as opioid agonist bridge to formal induction to MAT at outpatient partner site)</td>
<td>• Sublingual tablets</td>
<td><strong>Communication</strong></td>
</tr>
<tr>
<td><strong>For pain or withdrawal in ED</strong></td>
<td>• Transdermal (optional)</td>
<td>Point person for feedback, problem-solving, and system development</td>
</tr>
<tr>
<td>Buprenex 0.3 mg IM or IV</td>
<td>• Buccal (optional)</td>
<td></td>
</tr>
<tr>
<td>Butrans 7-day patch</td>
<td>Prescribing</td>
<td></td>
</tr>
<tr>
<td>Suboxone or Subutex 2-8 mg SL</td>
<td>• Registering DEA &quot;X&quot;-waivered MDs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Telehealth prescribing by phone or fax</td>
<td></td>
</tr>
</tbody>
</table>
MAT in the ED Clinical Pathway 1.0: The Basic Model

In situations where recruiting resources is a challenge, a basic model program can be developed by an ED champion.

Key Components

1. A prescribing ED physician and program champion.
2. At least one emergency physician should obtain a DEA “X” waiver and be available on-call to provide support and to call in prescriptions as needed. This physician should be comfortable with indications, contraindications, and principles of addiction treatment with buprenorphine.
   - Simplified induction
     Suboxone or Subutex, 8 mg SL on day 1 after withdrawal symptoms have developed, then day 2-7, increase dose by 2 mg every 2 hours as needed for withdrawal symptoms up to 16 mg per 24 hours.
   - Supportive medications
     Clonidine 0.1 mg PO every 2 hours as needed. TDNTE 1.2 mg/24 hours. Caution about orthostasis.
     Loperamide 4 mg PO as needed up to 16 mg per day
     Gabapentin 600 mg PO three times a day
     Ibuprofen 400 mg PO every 6 hours
3. Collaborating pharmacy.
4. At minimum, sublingual tablet formulations of buprenorphine should be available to be administered and/or prescribed from the ED.
5. Referral sites for ongoing treatment of addiction.
6. The availability of providers willing to accept referred patients from the ED for ongoing buprenorphine treatment (e.g., primary care clinic, addiction program, pain specialty clinic) will dictate the volume of patients that can be initiated by the ED. Some systems are exploring an addiction clinic in the ED itself.

For Consideration

Treating pain and opioid withdrawal using buprenorphine can serve as a bridge to formal addiction treatment. If the patient has acute pain, or acute exacerbation of chronic pain, the transdermal buprenorphine patch can be administered in the ED as an analgesic treatment.
In an opioid-dependent patient, a 20 mcg/hour 7-day patch will provide a window of stable opioid agonism therapy during which the patient can seek formal induction into opiate substitution therapy at an outpatient clinic. ED prescribers who lack a DEA “X” waiver may administer or prescribe transdermal formulations of buprenorphine.

The DEA has formally stated that non-waivered providers with DEA Schedule III narcotic prescribing authority can prescribe any formulation of buprenorphine off-label for pain. Despite this, some pharmacies may be hesitant to fill prescriptions of Suboxone and Subutex from a non-DEA “X” waivered physician and will require this waiver for generic buprenorphine only or buprenorphine/naloxone combination tablets, Suboxone, and Subutex (sublingual strip formulations), Zubsolv (sublingual tablet formulation), Bunavail (BEMA strips) as they are only FDA-approved for the treatment of addiction. For this reason, reaching out to local pharmacies and discussing these issues in advance can be beneficial. In addition, writing the indication on the prescription (“pain” or “opioid dependence”) may help the prescription to be managed appropriately.

**Opioid Detoxification with Buprenorphine**

Studies of patients in California and elsewhere with opioid addiction have demonstrated an instantaneous reduction in mortality after buprenorphine-assisted detoxification, justifying its use in the ED even when access to long-term maintenance is not available. While any provider can treat acute withdrawal, following this acute administration of buprenorphine with a prescribed detoxification treatment plan requires a DATA 2000 “X” waiver. In a study of over 300 patients in California, Evans et al. found a standardized mortality ratio (SMR) of 6.1 for patients not in treatment. Detoxification lowered this mortality risk by more than 50%, to SMR 2.4. Detoxification followed by medication-assisted therapy was the best option, resulting in an SMR of 1.8.\textsuperscript{vii}

**Going "Cold Turkey" Is Dangerous**

*Buprenorphine detoxification is a harm reduction strategy when long-term buprenorphine MAT is not available.*
When a patient with opioid addiction (e.g., an injection heroin user) is seen in the ED, their predicted discharge mortality is far greater than a patient discharged from an inpatient ward after myocardial infarction. There are two typical ED approaches to a patient with opioid addiction: (1) addressing the acute medical issues and avoiding the problem of opioid addiction or (2) advising the patient to “get off drugs” and providing a phone number, which may or may not provide timely access to addiction treatment.

The first approach results in the continued abuse of opioids. What few providers realize is that the risks associated with advising a patient to quit may be even higher. While counterintuitive, if an opioid-addicted patient takes the ED provider’s advice and attempts unsupervised detoxification without medical assistance (the so-called “cold turkey” approach), they will experience tremendous anxiety, negative mood states, and physical suffering. This suffering often occurs away from their typical social environment of use, leaving them isolated and feeling sick “trying to kick it.” As they cut down or stop use, their physiologic tolerance to opioid-induced respiratory depression declines. Not surprisingly, socially isolated, psychologically desperate, physically suffering patients tend to overshoot their declining tolerance, which often results in overdose and death.

**ED Buprenorphine Detoxification**

Gradual withdrawal of buprenorphine, combined with clonidine and gabapentin, reduces the suffering and pain that accompanies the transition off of opioid physical dependence. Unfortunately, the long-term neurocognitive changes produced by opioid addiction and the enabling social circumstances are not meaningfully addressed by detoxification. As a result, patients remain extremely vulnerable to relapse after detoxification and should be offered long-term MAT if at all possible. Detoxification is generally considered only for those patients who have demonstrated sustained psychosocial stability. Therefore, if offered from your emergency department, every reasonable effort should be made to develop long follow-up for all patients started on buprenorphine detoxification. Only physicians with a DEA DATA 2000 waiver may prescribe buprenorphine for the purpose of supporting opioid detoxification.
**Who Is Eligible for ED-Initiated Detoxification?**
ED buprenorphine detoxification is best reserved for high-risk opioid-dependent patients without a regular medical provider who could supervise either an opioid taper or maintenance of opioid substitution therapy. Patients already on methadone or buprenorphine should not be started on a buprenorphine detoxification plan. ED initiation of detoxification is most appropriate for patients taking illicit opioids (either opioid pain relievers purchased on the street or heroin) without any regular medical provider. These are high-risk patients without any other options.

**The Detoxification Guideline**

**Initiation** Ideally, patients should be in acute withdrawal. At this point, 4 mg SL buprenorphine can be administered and the patient discharged home with a prescription for buprenorphine taper. The ideal duration of buprenorphine detoxification taper has not been established. Emergency providers may be most comfortable with short tapers of seven days, but longer tapers can be used.\(^\text{lx}\)

If the patient is not in withdrawal, they should be advised to not take any opioid and wait 12-24 hours for the development of withdrawal symptoms. Once in significant withdrawal, they can begin with a 4 mg SL dose. That first day, patients can titrate up every two hours with an additional 2 mg up to 8 mg total in the first 24 hours. The patient should be advised to avoid any benzodiazepines, muscle relaxants, alcohol, or other drugs that could lead to excessive sedation or respiratory depression.

Buprenorphine dosing once withdrawal has begun:

- **Day 1**: 4 mg SL, then wait 2 hours and take additional 2 mg SL as needed up to a total of 8 mg
- **Day 2-3**: Stabilize on dose from day 1
- **Day 4-7**: Reduce dose by 1-2 mg a day as tolerated

**Supportive medications**: Clonidine 0.1 mg PO every 4 hours as needed, Loperamide 4 mg PO as needed up to 16 mg per day, Gabapentin 600 mg PO three times a day, Ibuprofen 400 mg PO every 6 hours

Detoxification is a difficult, painful, and stressful time. Access to psychosocial supports and care coordination should be maximized.
Figure 5. Buprenorphine Detoxification

High-risk Opioid use disorder

- Using illicit opioids
- No primary care or other longitudinal provider
- Not already on methadone or buprenorphine

Outpatient buprenorphine maintenance available?

No

Buprenorphine detoxification

Discontinue opioid (usually 12-24 hours) until feeling significant signs of withdrawal

Maximize any psychosocial supports available to patient

Yes

Initiate buprenorphine and refer for maintenance therapy

---

**Buprenorphine dosing**

**Day 1** 4mg SL

wait 2 hours and take additional 2 mg SL as needed up to total 8mg

**Day 2-3** stabilize on dose from day 1

**Day 4-7** reduce dose by 1-2mg a day

---

**Supportive medications**

- **Clonidine** 0.1mg PO every 4 hrs as needed
- **Loperamide** 4mg PO as needed up to 16mg per day
- **Gabapentin** 600mg PO three times a day
- **Ibuprofen** 400mg PO every 6 hours
MAT in the ED Clinical Pathway 2.0: Initiate and Refer

In this model, buprenorphine MAT is initiated in the ED. This model is based on the model used at the Yale New Haven Hospital by Dr. Gail D’Onofrio and her team. It involves an organized program of patient recruitment, selection, and motivational counseling followed by induction onto buprenorphine in the ED or at home, with outpatient follow-up within 72 hours.

In essence, this is an augmented version of the basic model where the structural components of the program are solidified with formal institutional buy-in, departmental policies, and formalized handoffs to outpatient providers.

Step 1: Patient Identification and Inclusion
The most basic requirements for inclusion are that the patient has an opioid use disorder (see Appendix A) and a desire to begin medication-assisted treatment with buprenorphine.

- **Who identifies the patient?** Patient identification can be done by frontline clinical staff such as nurses, doctors, or physician assistants. Patients may be referred to the ED by outside providers.

- **Who formally initiates treatment?** Ultimately, only a physician can prescribe buprenorphine for the treatment of opioid use disorder. Nurses and other staff such as emergency technicians and substance abuse counselors may expedite care through an intake and assessment process.

- **What patient group will have the greatest benefit from treatment?** Patients at risk for death from opioid overdose should be prioritized; risk factors include:
  - Injection heroin and nonmedical pain reliever abuse
  - History of overdose and/or substance abuse
  - History of mental illness
>100 mg morphine equivalents/day
- Medicaid/low-income patients
- Frequent ED visits (>3 last year; ED visits with disposition of leaving without treatment or against medical advice)
- Multiple opioid prescriptions in last year and multiple prescribers

**Suggested Communication Interventions**

- **Talk to patients broadly and openly about addiction to break down stigma on the part of patients and clinicians.** Daily discussion of addiction helps break down stigmatized attitudes and promotes a nonjudgmental medical approach. Getting the word out to the larger health system and the community that the ED is a setting for getting help, versus a setting for hiding addiction and hoping to “score,” may be a benefit to beginning an ED MAT program. Public signage and patient handouts should be considered part of a communications plan.

- **Provide an overview of buprenorphine treatment and what it entails, discussing risks, benefits and expectations.** Widespread patient education about the neurobiological model of addiction, buprenorphine treatment, and the treatment program can be provided to any patient receiving opioids. For patients identified with addiction, individually tailored educational materials can then be used.

**Step 2: Clinical Evaluation**

The key actions here are to determine stage of withdrawal and to assess for contraindications for treatment with buprenorphine.

- **Review contraindications.** CDC has developed a buprenorphine treatment checklist of factors that may complicate treatment (see Appendix B).

- **Evaluate recent use and level of withdrawal using COWS (see Appendix C):**
  - Patients without recent use or withdrawal:
    - Can be started with 2 mg buprenorphine.
    - Titration can occur in the ED or at home.
- Patients with recent use and mild or no withdrawal can be given a prescription for home induction. Alternatively, a patient can choose to wait for withdrawal symptoms to worsen and then induce in the ED.
  - Patients with mild-to-moderate withdrawal (COWS 8 or greater):
    - ED initiation can start with 4 mg buprenorphine SL.
    - Titrate to relief of symptoms in ED Q 1-2 hours up to 16 mg.
    - Follow ED administration with home induction.

**Home Induction**

**Overview** Office-based induction is recommended primarily as a measure to prevent precipitated withdrawal. However, home induction is far less complicated in many respects, and some authors have suggested that limiting induction to office-based, directly observed protocols is an unnecessary barrier to treatment. Advocates of home induction consider it a more patient-centered approach that promotes self-management of addiction. Limited data suggest that with adequate instruction, patients can reasonably be expected to follow needed safety precautions and, with a simple algorithm, avoid inducing precipitated withdrawal.

**Step 1: The Emergency Department Visit**

After selection for buprenorphine treatment, the ED visit is an opportunity to promote self-management of opioid addiction and to empower the patient with specific local resources for support outside of the ED. At this point it will be important to explain the trajectory of care for the patient and clarify the ongoing role of the ED. In some scenarios, the ED will only be involved for the initial visit; in other systems the ED may play an ongoing role before longitudinal care at an outpatient site is established.

**Step 2: The Take-Home Kit**

The home induction kit should prepare and guide the patient through the first three days of treatment. It may include information on when and how to use buprenorphine and
adjunctive medications such as clonidine or loperamide, how to self-assess withdrawal, pitfalls and common mistakes, a step-by-step guide to dosing, and a guide to additional treatment resources. The contents of an example kit are presented in Figure 6, below.

**Step 3: Buprenorphine Dose Escalation**

There are a number of strategies to stabilize on buprenorphine. A simple approach utilizing 2 mg buprenorphine sublingual tablets is presented.

**Day 1** The patient is given a script for a total of 20, 2 mg buprenorphine sublingual tablets and instructed to wait for withdrawal symptoms to develop to mild-to-moderate severity (see Appendix D, SOWS >17). At this point, 2 mg buprenorphine is taken; repeat doses are taken every 2 hours till symptoms of withdrawal are improved (maximum of 16 mg in first 24 hours). There are numerous potential adjunctive medications, including clonidine 0.1-0.2 mg Q 4 hours), gabapentin (600 mg TID), and loperamide (2-4 mg Q 4 hours) that may be used to reduce withdrawal symptoms.

**Day 2** The day 1 total is taken as a single dose in the AM; repeat doses are taken every 2 hours till symptoms of withdrawal are improved (maximum of 24 mg).

**Step 4: Follow-Up**

The patient should be evaluated in a partner clinic setting or in the ED by day 3. If withdrawal symptoms are adequately controlled, the maintenance dose is established as the total dose from day 2. Titration can continue as needed up to a total daily dose of 24-32 mg. At this point the patient enters the maintenance phase of treatment.
Figure 7. Example Home Induction Kit

<table>
<thead>
<tr>
<th>Instruction sheet</th>
<th>What the section addresses</th>
</tr>
</thead>
<tbody>
<tr>
<td>What’s in the tool kit?</td>
<td>Guides when/how to use medications in the kit</td>
</tr>
<tr>
<td>When to start Suboxone</td>
<td>Guides the timing of treatment initiation</td>
</tr>
<tr>
<td>Things not to do</td>
<td>Warns against common mistakes or misunderstandings</td>
</tr>
<tr>
<td>How to take Suboxone</td>
<td>Facilitates correct dosing method</td>
</tr>
<tr>
<td>Plan</td>
<td>Guides treatment, provides support, and facilitates follow-up</td>
</tr>
<tr>
<td>What was taken</td>
<td>Facilitates keeping track of dosing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medications</th>
<th># Pills</th>
<th>Medication</th>
<th>Dose (mg)</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine/naloxone</td>
<td>10</td>
<td>2/0.5</td>
<td>Initiate buprenorphine treatment (day 1)</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine/naloxone</td>
<td>4</td>
<td>8/2</td>
<td>Buprenorphine treatment (days 2–3)</td>
<td></td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>6</td>
<td>200</td>
<td>↓ Withdrawal symptoms (pain)</td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td>6</td>
<td>0.1</td>
<td>↓ Withdrawal symptoms (anxiety)</td>
<td></td>
</tr>
<tr>
<td>Loperamide hydrochloride</td>
<td>6</td>
<td>2.0</td>
<td>↓ Withdrawal symptoms (diarrhea)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 8. MAT in the ED Clinical Pathway 2.0: The Yale Model — ED Induction

1. **Assess for contraindications**
   - Evaluate withdrawal

2. **Buprenorphine 2mg SL**
   - **Mild withdrawal**
     - Wait 2 hours
     - Reassess
   - **Mild to moderate withdrawal**
     - 4mg buprenorphine
     - Reassess
     - In 1-2 hrs
     - Repeat up to 16mg total

3. **Withdrawal symptoms and cravings tolerable**
   - Continued induction at home

4. **No recent use & No withdrawal (<8)**
   - Reassess
   - In 1-2 hrs
   - Repeat dose
   - (≈8+)
   - Abstinence

5. **At least 12-24 hours abstinence**
   - Take home doses prescribed

6. **Continued induction at home**

7. **COWS**
   - Mild withdrawal
   - Wait 2 hours
   - Reassess
   - In 1-2 hrs
   - Repeat dose
   - 4mg buprenorphine

8. **Continued induction at home**

9. **Discharge**
   - Home induction
   - Opioid use disorder & desire to start buprenorphine to quit or reduce use
Figure 9. MAT in the ED Clinical Pathway 2.0: The Yale Model — Home Induction

- Safety: Storage, driving, interactions
- Avoidance of precipitated withdrawal
- Follow up plan
- ED Rx: 20, 2mg SL buprenorphine tablets
- Day 1:
  - Begin when SOWS > 17
  - 2mg SL buprenorphine
  - Repeat 2mg Q 2 hrs
  - Max 16 mg first 24 hrs
- Day 2:
  - Total from day #1 in AM or BID
  - 2mg SL buprenorphine
  - Repeat 2mg Q 2 hrs
  - Max 24 mg
- Partner clinic follow up
- Abstinence timing
- Use of SOWS
- Adjunct withdrawal medications
- Interim ED maintenance
- Day 3
- Verbal and written instructions given during ED visit
MAT in the ED Clinical Pathway 3.0: The ED as Hub for Coordination of Addiction Services

For patients unable to enter into an alternative site of care, the ED may be the only option available. In this case, the alternative to ED-based care is that the patient returns to unassisted self-treatment of their addiction, with a high risk of relapse and harm.

The expanded model of care is designed to meet the needs of these patients. In this system, the ED is a fully integrated hub for medication-assisted addiction treatment in the community. Patients gain 24/7 access to care for initiation and maintenance of care in addition to assistance with crisis and relapse.

Most or all ED physicians should have DEA “X” waivers. There is global buy-in from nursing and social services staff, with dedicated addiction counselors embedded in the ED. The ED is able to accept referrals from outside providers to initiate buprenorphine MAT as well as offer ongoing maintenance therapy for patients who are delayed entering outpatient care.

Key Components

1. **Systemwide, interdisciplinary committee for addiction treatment.** A systemwide committee allows a forum to build partnerships and manage ongoing communication between hospital- and community-based services. Recommended participants include emergency physicians, primary care providers, hospitalists, pain specialists, addiction specialists, hospital administrators, and social service providers.

2. **ED addiction services should be linked to regional opioid harm reduction efforts whenever possible.** As providers reign in opioid prescribing, patients may abruptly experience discontinuation of a long-term pattern of opioid prescribing from any number of sources — the ED, primary care, and specialty clinics. As medical “refugees,” some patients will inevitably turn to illicit opioids such as heroin or diverted pharmaceutical opioids. The ED can act as a hub to
link opioid-dependent patients to clinicians equipped to either help them taper to a safer dose or switch them to a safer option like buprenorphine.

3. **Integrated care management.** To maximize the benefits of MAT with buprenorphine and to limit futile care, duplicated care, or at worst, diversion enabling, expanded care models should include integrated care management. Ideally, when a patient presents to the ED, medical record access should enable real-time discovery of where a patient is within their treatment plan. This may include participation with treatment contracts and contingency management treatment.

4. **Embedded addiction counselors and social services in the ED.** This may take many forms, from peer-based volunteer services to trained addiction counselors and mental health professionals. For comprehensive care, the ED provider will need additional staff and some type of clinical space that can be used for psychosocial interventions that are impractical for a busy emergency physician.

**Considerations Around Prolonged ED Treatment with Buprenorphine**

1. There should be clarity regarding alternative sites of treatment. Patients should be supported to take responsibility to access available outpatient sites of care and should not utilize the ED simply out of convenience.

2. A regularly updated wait list at partner clinics may clarify which patients have demonstrated follow through versus patients who were unable or unwilling to comply with steps needed to establish care at an alternative site.

3. At every visit, an attempt should be made to transfer care to an outpatient longitudinal site of care.

4. Possible relapse should be evaluated at every visit using a patient drug monitoring database and, if available, an ED visit database.

5. Patients receiving buprenorphine should not also receive opioid pain relievers from the ED.

6. Patients should be encouraged to present to the ED when there is maximal capacity to provide adjunctive psychosocial support. For example, an ED might
have a weekly day when an embedded buprenorphine maintenance clinic operates out of a low-acuity treatment area.

**Buprenorphine Prescribing in the ED Beyond Initiation**

**Day 3 return ED visit** Patients unable to obtain follow-up in a partner outpatient setting may use the emergency department for interim maintenance therapy. During the initial week, the buprenorphine dose can be escalated in increments of 2-4 mg per day up to a total of 24 mg/day.

**Day 7 return ED visit** On return to the ED, the patient may either need continued dose adjustment or demonstrate that they have achieved an optimal dose. If available, the patient should transition to an alternative outpatient provider for ongoing treatment. If none are available, the ED may act as the provider of last resort to maintain opioid agonist therapy as patients await outpatient care. The patient can be maintained with one-week supplies of buprenorphine. Longer prescriptions may be considered with appropriate supports in place.
Figure 10. MAT in the ED Clinical Pathway 3.0: The ED as Hub for Coordination of Addiction Services

Day 3
Interim ED maintenance

Continued withdrawal symptoms?

YES
Administer 4mg buprenorphine
In addition to total day#2 dose

ED Rx:
Up to 36, 2mg SL buprenorphine tablets

Days 4-6 increase dose by 2-4mg per day.
Max 32 mg / day

NO
Daily dose established

Continued ED maintenance until alternate provider is established

Day 7
Return to ED
X. Further Resources

ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use

TAP 30: Buprenorphine: A Guide for Nurses

TIP 40: Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction

The Facts About Buprenorphine for Treatment of Opioid Addiction [for patients]

The Drug Medi-Cal Organized Delivery System (DMC-ODS)

DSM-5 Opioid Use Disorder Patient Evaluation Sheet
http://www.buppractice.com/printpdf/19556 (PDF)

DSM-5 Opioid Use Disorder Diagnostic Criteria and Explanation
XI. Appendices

Appendix A: DSM-5 Opioid Use Disorder Diagnostic Criteria

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. 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.
10. Tolerance, as defined by either of the following:
   a) A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
   b) A markedly diminished effect with continued use of the same amount of an opioid. Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
   a) The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal).
   b) Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

Severity Scoring
Mild: 2-3 symptoms
Moderate: 3-5 symptoms
Severe: 6 or more symptoms
Appendix B: CDC Recommended Buprenorphine Treatment Checklist

1. Does the patient have a diagnosis of opioid dependence?
2. Are there current signs of intoxication? Is there a risk for severe withdrawal?
3. Is the patient interested in buprenorphine treatment?
4. Does the patient understand the risks and benefits of buprenorphine treatment?
5. Can the patient be expected to adhere to the treatment plan?
6. Is the patient willing and able to follow safety procedures (e.g., ongoing abuse of alcohol and/or benzodiazepines)?
7. Does the patient agree to treatment after a review of the options?
8. Can the needed resources for the patient be provided (either on- or offsite)?
9. Is the patient psychiatrically stable? Is the patient actively suicidal or homicidal; has he or she recently attempted suicide or homicide? Does the patient exhibit emotional, behavioral, or cognitive conditions that complicate treatment?
10. Is the patient pregnant?
11. Is the patient currently dependent on or abusing alcohol?
12. Is the patient currently dependent on benzodiazepines or other sedative-hypnotics?
13. What is the patient’s risk for continued use or continued problems? Does the patient have a history of multiple previous treatments or relapses, or is the patient at high risk for relapse to opioid use? Is the patient using other drugs?
14. Has the patient had prior adverse reactions to buprenorphine?
15. Is the patient taking other medications that may interact with buprenorphine, such as full opioid agonists or benzodiazepines?
16. Does the patient have medical problems that are relative contraindications to buprenorphine treatment, such as chronic pain on high-dose, full opioid agonist therapy? Are there physical illnesses that complicate treatment, such as HIV treated with antiretrovirals (ARVs) or tuberculosis treated with rifampin?
17. What kind of recovery environment does the patient have? Are the patient’s psychosocial circumstances sufficiently stable and supportive?
18. What is the patient’s level of motivation? What stage of change characterizes this patient?
Appendix C: COWS (Clinical Opiate Withdrawal Scale), Used in Observed Inductions

### Clinical Opiate Withdrawal Scale (COWS)

**Flowsheet for measuring symptoms over a period of time during buprenorphine induction.**

For each item, write in the number that best describes the patient’s signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Date:</th>
</tr>
</thead>
</table>

**Buprenorphine Induction:**

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc. Times of Observation:

<table>
<thead>
<tr>
<th>Resting Pulse Rate: Record Beats per Minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = pulse rate 80 or below</td>
</tr>
<tr>
<td>1 = pulse rate 81-100</td>
</tr>
<tr>
<td>2 = pulse rate 101-120</td>
</tr>
<tr>
<td>4 = pulse rate greater than 120</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sweating: Over Past 1/2 Hour not Accounted for by Room Temperature or Patient Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = no report of chills of flushing</td>
</tr>
<tr>
<td>1 = subjective report of chills or flushing</td>
</tr>
<tr>
<td>3 = beads of sweat on brow or face</td>
</tr>
<tr>
<td>4 = sweat streaming off face</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Restlessness Observation During Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = able to sit still, but is able to do so</td>
</tr>
<tr>
<td>3 = frequent shifting or extraneous movements of legs/arms</td>
</tr>
<tr>
<td>5 = Unable to sit still for more than a few seconds</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pupil Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = pupils pinned or normal size for room light</td>
</tr>
<tr>
<td>1 = pupils possibly larger than normal for room light</td>
</tr>
<tr>
<td>2 = pupils moderately dilated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Base or Joint Aches or Pain Presenting Previously, only the Additional Component Attributed to Opiate Withdrawal is Scored</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = not present</td>
</tr>
<tr>
<td>1 = mild diffuse discomfort</td>
</tr>
<tr>
<td>2 = patient reports severe diffuse aching of joints/muscles</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Runny Nose or Tearing Not Accounted for by Cold Symptoms or Allergies</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = not present</td>
</tr>
<tr>
<td>1 = nasal stuffiness or unusually moist eyes</td>
</tr>
<tr>
<td>2 = nose running or tearing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GI Upset: Over Last 1/2 Hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = no GI symptoms</td>
</tr>
<tr>
<td>1 = stomach cramps</td>
</tr>
<tr>
<td>2 = nausea or loose stool</td>
</tr>
<tr>
<td>3 = vomiting or diarrhea</td>
</tr>
<tr>
<td>5 = multiple episodes of diarrhea or vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tremor Observation of Outstretched Hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = no tremor</td>
</tr>
<tr>
<td>1 = tremor can be felt, but not observed</td>
</tr>
<tr>
<td>2 = slight tremor observable</td>
</tr>
<tr>
<td>4 = gross tremor or muscle twitching</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Yawning Observation During Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = no yawning</td>
</tr>
<tr>
<td>1 = yawning once or twice during assessment</td>
</tr>
<tr>
<td>2 = yawning three or more times during assessment</td>
</tr>
<tr>
<td>4 = yawning several times/minute</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anxiety or Irritability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = none</td>
</tr>
<tr>
<td>1 = patient reports increasing irritability or anxiousness</td>
</tr>
<tr>
<td>4 = patient so irritable or anxious that participation in the assessment is difficult</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gooseneck Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = skin is smooth</td>
</tr>
<tr>
<td>3 = piloerection of skin can be felt or hairs standing up on arms</td>
</tr>
<tr>
<td>5 = prominent piloerection</td>
</tr>
</tbody>
</table>

**Score: 5-12 = Mild**  
**13-24 = Moderate**  
**25-36 = Moderately Severe**  
**More than 36 = Severe Withdrawal**  

*Source: Wesson et al. 1999.*

The National Alliance of Advocates for Buprenorphine Treatment  
PO Box 333 * Farmington, CT 06034 * MakeContact@naabt.org  
naabt.org  

59  
Herring
Appendix D: SOWS (Subjective Opiate Withdrawal Scale), Used in Home Inductions

Assessment of Withdrawal from Opioids

The Subjective Opiate Withdrawal Scale (SOWS)

Date ......................................................... Time .........................................................

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>NOT AT ALL</th>
<th>A LITTLE</th>
<th>MODERATELY</th>
<th>QUITE A BIT</th>
<th>EXTREMELY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 I feel anxious</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2 I feel like yawning</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3 I am perspiring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4 My eyes are teary</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5 My nose is running</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6 I have goosebumps</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7 I am shaking</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8 I have hot flushes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9 I have cold flushes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10 My bones and muscles ache</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11 I feel restless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12 I feel nauseous</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13 I feel like vomiting</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14 My muscles twitch</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>15 I have stomach cramps</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16 I feel like using now</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Appendix E: Emergency Department Initiation of Buprenorphine for Opioid Use Disorder: Provider Guidelines

1. Patient identification
2. Confirm patient has an opioid use disorder
3. Evaluate if the patient is in opioid withdrawal
4. ED screening orders
5. Buprenorphine administration
6. Buprenorphine prescription
7. Discharge instructions

Andrew Herring, MD
October 2016
Andrew.a.herring@gmail.com
**Patient identification**
Any of the following can be used to clinically identify a patient who should be evaluated for presence of an opioid use disorder and eligibility for ED initiation of buprenorphine.

- a. Explicit request for assistance with opioid use disorder. (e.g., “I need help to get clean.”)
- b. Statement of intent to attempt abstinence. (e.g., “I am never using again.”)
- c. Admitted or clinically obvious history of injection opioid use
- d. Opioid overdose
- e. Behavior in the ED that suggests drug seeking. (e.g., repeated visits requesting IV hydromorphone for chronic pain.)
- f. Admitted or obvious use of illicit opioids
- g. Clinical gestalt that an opioid use disorder may be present
- h. Patients with severe liver disease (transaminases > 5x normal) should be followed by GI
- i. Patients with active alcohol, benzodiazepine, and/or barbiturate use disorders and psychiatric instability are generally NOT considered good candidates for treatment.

**Confirm Patient has an Opioid Use Disorder**

2-minute Rapid Opioid Dependence Screen (RODS)

Evaluate if the patient is in opioid withdrawal

Opiate Withdrawal Timeline

<table>
<thead>
<tr>
<th>Symptoms Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔️ Nausea</td>
</tr>
<tr>
<td>✔️ Vomiting</td>
</tr>
<tr>
<td>✔️ Stomach Cramps</td>
</tr>
<tr>
<td>✔️ Diarrhea</td>
</tr>
<tr>
<td>✔️ Goosebumps</td>
</tr>
<tr>
<td>✔️ Depression</td>
</tr>
<tr>
<td>✔️ Drug Cravings</td>
</tr>
</tbody>
</table>

NOTE:

Short-acting opioids (Heroin, Norco, Percoset, Morphine IR, snorted Oxy) wait 8-12 hours
Long-acting opioids (Oxycodone, MS Contin) wait 16-24 hours
* Methadone wait at least 48 hours *

<table>
<thead>
<tr>
<th>Symptom</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling sick</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Stomach cramps</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Muscle spasms or twitching</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling cold</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Heart pounding</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Muscular tension</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Aches and pains</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Yawning</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Runny/watery eyes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

SCORING

<table>
<thead>
<tr>
<th>&lt; 10</th>
<th>Don’t give buprenorphine yet</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10</td>
<td>Give buprenorphine now</td>
</tr>
</tbody>
</table>

(10-20) Moderate withdrawal

(20-30) Severe withdrawal

Recommended ED screening order set

- Urine pregnancy test
- Rapid HIV test
- Hepatitis A,B,C screening
- Liver function tests
- If possible: consultation with social worker and substance abuse counselor

ED Buprenorphine order for patients at least in moderate withdrawal

- Buprenorphine 4mg sublingual tablet x1 now
  or
- Buprenorphine/naloxone sublingual tablet x 1 now

ED orders for adjunctive medications to ease symptoms of withdrawal

- Ibuprofen 400mg PO
- Ondansetron 4mg PO
- Clonidine 0.1 mg PO [hold if BP < 90/60 or HER < 60]
- Loperamide 4mg PO

ED prescription

```
“Subutex”
Buprenorphine

2mg

“Suboxone”
Buprenorphine / Naloxone

2mg/0.5mg

8mg/2mg

“Buprenorphine 2 mg sublingual tablet
1-4 tablets under the tongue
every 1-3 hours as needed for withdrawal
Dispense #20 No Refills

Buprenorphine/naloxone 2mg/0.5mg sublingual tablet
1-4 tablets under the tongue
every 1-3 hours as needed for withdrawal
Dispense #20 No Refills
```

Prescribing Notes:

- Buprenorphine is a schedule III drug.
- Prescribing for opioid detoxification or maintenance requires a DEA DATA 2000 X waiver
- Day one maximum = 8mg (4 x 2mg tablets)
- Day two maximum = 16mg (8 x 2mg tablets)
- Day three maximum = 16mg (8 x 2mg tablets)
- Alternatively, 8mg tablets can be prescribed, then broken in half for dose titration.
Patient Instructions for Beginning Buprenorphine Treatment

**Day One:** Before taking a buprenorphine tablet you want to feel lousy from your withdrawal symptoms. Very lousy. It should be at least 12 hours since you used heroin or pain pills [oxycontin (snorted), vicodin, etc…), 16 hours since oxycontin (swallowed), and at least 48 hours since you used methadone.

Wait it out as long as you can. The worse you feel when you begin the medication the more satisfied you will be with the whole experience. If you take the buprenorphine too soon, it can make you feel worse rather than better.

You should have at least 3 of the following feelings: • Twitching, tremors or shaking • Joint and bone aches • Bad chills or sweating • Anxious or irritable • Goose pimples

<table>
<thead>
<tr>
<th>Very restless, can't sit still</th>
<th>Heavy yawning</th>
<th>Enlarged pupils</th>
<th>Runny nose, tears in eyes</th>
<th>Cramps, nausea, vomiting, or diarrhea</th>
</tr>
</thead>
</table>

First dose: 4 mg of Buprenorphine (Bup) under the tongue. This is two 2mg tablet

\[
\begin{align*}
N_2 &+ N_2 \\
2 mg &+ 2 mg \\
= &4 mg
\end{align*}
\]

Put the tablets under your tongue. Keep it there. If you swallow Bup tablets they will not work, the medicine is best absorbed through the thin skin on the bottom of your tongue.

It takes about 20-45 minutes for the medication to be absorbed and have an effect. Feel better? Good, the medicine is working. Still feel lousy after 45 minutes? Don’t worry, you may need more medication.

At 1-3 hours (60-180 minutes) after your first dose, see how you feel. If you feel fine after the first 4 mg, don’t take any more, this may be all you need. If you have withdrawal feelings, take another 2 mg dose.

Later in the day (6-12 hours after the first dose), see how you feel again. If you feel fine, don’t take any more. If you have withdrawal feelings, take another 2 mg dose under your tongue.

**Do not take more than 8 mg of Bup on the first day.**

Most people feel better after the 4-8 mg on the first day. Still feel really bad, like a bad withdrawal? Call the study doctor right away. You can call or page any time during the day if you are having difficulty.
**Day One Summary:** No medication until you feel significant withdrawal. 4 mg under your tongue, wait 1-3 hours. If still feel sick, take 2 mg. Wait 1-3 hours. If still sick, take 2 mg again. Do not take more than 8 mg on Day 1.

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Dose</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>4 mg</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Dose if needed</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>2 mg</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; Dose if needed</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
<td>2 mg</td>
</tr>
</tbody>
</table>

**Day Two: The right dose depends on how you felt on Day One**

<table>
<thead>
<tr>
<th>Day One</th>
<th>Day Two</th>
</tr>
</thead>
<tbody>
<tr>
<td>If the total on Day One was 4 mg</td>
<td>If you took 4 mg on Day 1 and feel fine the next morning, then take 4 mg again on Day 2. If you took 4 mg on Day 1 and feel some withdrawal the next morning, then try starting with 8 mg on the morning of Day 2. Later in the day on Day 2, see how you feel. If you feel fine, there is no need to take more. If you still feel withdrawal, you can try taking another 4 mg dose.</td>
</tr>
<tr>
<td>If the total on Day One was 8 mg</td>
<td>If you took 8 mg on Day 1 and feel fine the next morning, then take 8 mg again on Day 2. This will be your new daily dose. If you took 8 mg on Day 1 and feel some withdrawal the next morning, then try starting with 16 mg on the morning of Day 2.</td>
</tr>
</tbody>
</table>

How’s it going? Still feel really bad? Call: YOUR RESOURCE

★ No more than 8 mg on Day
**Day Two Summary**: 8-16 mg total, depending on how much you took on Day 1.

<table>
<thead>
<tr>
<th>Time</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Dose</td>
<td></td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Dose if needed</td>
<td></td>
</tr>
</tbody>
</table>

= Total mg taken on Day One

= Total mg taken on Day
Day Three:
The right dose for you on Day 3 depends on how you felt on Day 2. Did you still feel unwell, like you were in some withdrawal by the evening or night of Day 2? Or did you feel like the medication was too strong, leaving you too groggy or sedated? Different people need different doses of Bup.

If you felt comfortable at the end of Day 2, repeat the dose you took on Day 2. This is your new daily dose.

If felt too tired, groggy, or over sedated on Day 2, try taking a lower dose on Day 3. Take 4 mg less on Day 3 than you took on Day 2.

Day Three Summary: Take the total Day 2 dose under your tongue in the morning. You can try a little less if the Day 2 dose felt too strong.

Follow up:
★ Come to the ?? Clinic.
★ You must bring a valid, government-issued photo identification card to this visit.
★ You can reach a nurse to discuss this appointment during the day, Monday, Wednesday and Friday at: ??
★ If you have an urgent medication related problem BEFORE your follow up visit: Call ?? or Return to ED??

<table>
<thead>
<tr>
<th>Time</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Dose</td>
<td></td>
</tr>
<tr>
<td>2nd Dose</td>
<td></td>
</tr>
<tr>
<td>(if needed)</td>
<td></td>
</tr>
</tbody>
</table>

= Total mg taken on Day Three.
Endnotes


3. CDC, "Vital Signs."


Brady et al., "Emergency Department Utilization."

Rosie Cornish et al., "Risk of Death During and After Opiate Substitution Treatment in Primary Care: Prospective Observational Study in UK General Practice Research Database," BMJ 341 (October 26, 2010): c5475, doi:10.1136/bmj.c5475.


Kimber et al., "Survival and Cessation."

Cornish et al., "Risk of Death"; Clark et al., "Evidence"; Kimber et al., "Survival and Cessation."


48 Mattick et al., "Buprenorphine Maintenance."


52 Berg et al., "Evaluation of the Use of Buprenorphine."


54 D’Onofrio et al., "Emergency Department-Initiated Treatment."

55 Heit, Covington, and Good, "Dear DEA."

56 Daitch et al., "Conversion."


58 Deegenhardt et al., "Mortality Among Regular or Dependent Users"; Smolina et al., "Long-Term Survival."

59 Evans et al., "Mortality."

D’Onofrio et al., "Emergency Department-Initiated Treatment."

Cunningham et al., "Comparison of Induction Strategies"; Lee et al., "Clinical Case Conference"; Lee, Vocci, and Fiellin, "Unobserved 'Home' Induction"; Gunderson et al., "Unobserved versus Observed."

Cunningham et al., "Comparison of Induction Strategies."