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Review

Approach to buprenorphine use for opioid withdrawal treatment in the emergency setting

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ABSTRACT

Introduction: Opioid use disorder (OUD) is increasing in prevalence throughout the world, with approximately three million individuals in the United States affected. Buprenorphine is a medication designed, researched, and effectively used to assist in OUD recovery.
Objective: This narrative review discusses an approach to initiating buprenorphine in the emergency department (ED) for opioid-abuse recovery.
Discussion: Buprenorphine is a partial mu-opioid receptor agonist with high affinity and low intrinsic activity. Buprenorphine's long half-life, high potency, and 'ceiling effect' for both euphoric sensation and adverse effects make it an optimal treatment alternative for patients presenting to the ED with opioid withdrawal. While most commonly provided as a sublingual film or tablet, buprenorphine can also be delivered via transbuccal, transdermal, subdermal (implant), subcutaneous, and parenteral routes. Prior to ED administration, caution is recommended to avoid precipitation of buprenorphine-induced opioid withdrawal. Following the evaluation of common opioid withdrawal symptoms, a step-by-step approach to buprenorphine can by utilized to reach a sustained withdrawal relief. A multimodal medication-assisted treatment (MAT) plan involving pharmacologic treatment, as well as counseling and behavioral therapy, is essential to maintaining opioid remission. Patients may be safely discharged with safe-use counseling, close outpatient follow-up, and return precautions for continued management of their OUD. Establishing a buprenorphine program in the ED involves a multifactorial approach to establish a pro-buprenorphine culture.
Conclusions: Buprenorphine is an evidence-based, safe, effective treatment option for OUD in an ED-setting. Though successfully utilized by many ED-based treatment programs, the stigma of 'replacing one opioid with another' remains a barrier. Evidence-based discussions on the safety and benefits of buprenorphine are essential to promoting a culture of acceptance and optimizing ED OUD treatment.

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1. Introduction

For over three decades following the publication of the infamous single-paragraph letter declaring '*addiction is rare among long-term opioid users*', the opioid industry has boomed to a multi-billion dollar market [1]. In the midst of continually growing opioid use, the medical community has not only recognized the addictive power of opioids, it has witnessed the emergence of a nationwide opioid use disorder (OUD) epidemic effecting individuals of every gender, race, and socioeconomic status. Current estimates suggest three million individuals in the United States are currently or have previously suffered from an OUD [2], with drug overdose deaths surpassing 70,000 people in the United States in 2018 [3].

While OUD management may not be the primary focus of emergency physicians, it is an inevitable and unavoidable component of the emergency department (ED) setting. As with any disease or ailment, it is the responsibility of emergency clinicians to not only recognize individuals suffering from OUD, but to also provide safe, therapeutic treatment alternatives for the patient in search of assistance.

Buprenorphine is a medication designed, researched, and effectively used to assist in OUD recovery and should be considered an optimal tool in the emergency physician's armamentarium. The objective of this article is to provide an overview of buprenorphine, the benefits of buprenorphine use in combatting OUD, how it can be effectively utilized in the ED setting, and the necessary steps to establish a pro-buprenorphine treatment program.

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2. Discussion

2.1. What is buprenorphine?

Buprenorphine is a semisynthetic derivative of the baine, a molecule first isolated from the opium poppy (*Papaver somniferum*). Developed in 1978, buprenorphine was first used to treat chronic pain conditions. In addition to its analgesic effect, buprenorphine is also utilized to reduce cravings for pure (full agonist) opioids in individuals suffering from OUD. Buprenorphine is currently approved in the United States for the use of OUD and in the treatment of moderate/severe chronic pain where it has repeatedly been shown to be a safe, effective treatment option [4,5].

2.2. Mechanism of action

Buprenorphine is a partial agonist with a high affinity and low intrinsic activity for the mu-opioid receptor. Buprenorphine is approximately 25–100× as potent as morphine and nearly as potent as fentanyl [6-8]. The average onset for sublingual buprenorphine is 30 to 60 min, with peak effect at 1 to 4 h [6]. The higher binding affinity and slower dissociation rate of buprenorphine compared to other opioids results in a longer duration of action compared to other opioids [9]. The duration of effect is dose-dependent, ranging from 6 to 12 h for low doses (<4 mg) and 24 to 72 h for higher doses (>16 mg) [6]. These three qualities - high potency, lower intrinsic activity, and extended duration - make buprenorphine a favorable candidate for OUD treatment.

Individuals using buprenorphine to prevent relapse and suffering from opioid cravings will experience the agonistic effects including decreased craving, sedation, miosis, and mild respiratory depression [10]. In contrast to other opioids, buprenorphine demonstrates a 'ceiling effect' on respiratory depression and euphoria, though not on analgesia [11,12]. This 'ceiling effect' results in fulfillment of opioid craving and suppression of withdrawal similar to other opioids, but with less respiratory and central nervous system (CNS) depression and a decreased potential for abuse compared to other full agonist opioids [13]. By reducing opioid cravings, patients are able to focus on the counseling and therapy that allows them to successfully maintain addiction remission and improve their quality of life [14].

Buprenorphine is also an effective analgesic for moderate to severe pain in a variety of pain presentations [8,15,16]. Parenteral buprenorphine (<3 mg) has demonstrated a greater analgesic effect than intravenous morphine (10 mg) following abdominal surgery [17]. In patients presenting with cancer pain, transdermal buprenorphine has also shown to be just as effective as transdermal fentanyl, oral morphine, or oral oxycodone [18]. The utility of buprenorphine for acute pain management in the ED setting is an area in need of additional research.

2.3. Major types of buprenorphine

Buprenorphine is predominantly used as a sublingual film or tablet. Though less common in an ED setting, buprenorphine can also be delivered via transbuccal, transdermal, subdermal (implant), subcutaneous, and parenteral routes (see Table 1). The abuse potential of buprenorphine in the outpatient setting is countered by the prescribing of combined delivery of naloxone in 4-to-1 (buprenorphine-to-naloxone) ratios for the sublingual and oral options. As naloxone is poorly absorbed through the oral route, its antagonistic effects are only demonstrated when attempts are made to alter the medications into an injectable or aerosolized solution.

In June 2018, the FDA approved the first generic version of suboxone for OUD management [19,20]. This generic version is poised to offer increased therapeutic buprenorphine availability to individuals unable to afford the tradename versions.

2.4. Pharmacokinetics

Sublingual administration is considered the optimal route of administration for opioid withdrawal (OW) treatment based on the ease of use and efficient absorption rate. Buprenorphine can be absorbed across the gastrointestinal mucosa but undergoes extensive first-pass metabolism, making gastrointestinal absorption suboptimal [8,21]. Buprenorphine bioavailability is approximately one-fourth when given via the buccal route and one-half via the sublingual route [22].

Following absorption and systemic distribution, buprenorphine is metabolized via hepatic glucuronidation to semi-active metabolites [23,24]. Both buprenorphine and its metabolites undergo further hepatic metabolism to minimally active metabolites with minor sedating and anti-analgesic effects [24]. These metabolites along with the parent compound are predominantly eliminated in the feces, with the remaining 10–30% excreted in urine [25].

Buprenorphine should be used cautiously with hepatic CYP3A4 enzyme competing substrates and inhibitors, which may alter metabolism and lead to unwanted and unpredictable systemic concentrations. CYP3A4 substrates include statins, amiodarone, haloperidol, macrolides, azole antifungals (fluconazole, ketoconazole), calcium channel blockers, grapefruit juice (bergamottin), methylprednisolone, and protease inhibitors. At therapeutic doses, buprenorphine and its metabolites are effectively metabolized without enzymatic inhibition and can be safely used with few drug interactions [26].

2.5. Adverse effects of buprenorphine

The adverse effects of buprenorphine consumption are in part dependent on the co-consumption of opioids at the time of administration. Due to the higher affinity compared to other opioids, buprenorphine has the potential to precipitate withdrawal symptoms when given to individuals intoxicated with other opioids which are displaced during buprenorphine administration [27,28]. This is equally concerning in patients on high-dose methadone in which single doses of buprenorphine have been shown to precipitate withdrawal [29].

OW symptoms typically occur 4–6 h after short-acting opioids and 12–24 h after long-acting opioids, with peak withdrawal symptoms occurring at 36–72 h [6,30]. Prior to initiating buprenorphine treatment, a

Table 1
Buprenorphine alternatives. Buprenorphine is available in sublingual, buccal, transdermal, subcutaneous, and parenteral forms

Buprenorphine alternatives			
Trade Name	Components	Route	Dosing/combinations
Suboxone	Buprenorphine/naloxone	Sublingual, Buccal film	2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg
Suboxone	Buprenorphine/naloxone	Sublingual, tablet	2 mg/0.5 mg, 8 mg/2 mg
Subutex	Buprenorphine	Sublingual, tablet	2–8 mg tablets
Bunavail	Buprenorphine/naloxone	Buccal film	2.1 mg/0.3 mg, 4.2 mg/0.7 mg, 63/1.0 mg
Zubsolv	Buprenorphine/naloxone	Sublingual, tablet	1.4 mg/0.36 mg, 5.7 mg/1.4 mg, 11.4 mg/2.9 mg
Sublocade	Buprenorphine extended-release	Subcutaneous injection	100 mg, 300 mg
Buprenex	Buprenorphine	Parenteral injection	0.3 mg
Probuphine	Buprenorphine	Subdermal implant	80 mg per 6-month implant
Butrans	Buprenorphine	Transdermal patch	7.5, 10, 15, and 20 μg/h per 7-day patch

full analysis of OW should involve a Clinical Opioid Withdrawal Symptoms (COWS) assessment in order to avoid the development of precipitated OW (see Table 2) [31].The most common side effects of OW are tachycardia, dilated pupils, restlessness and agitation, nausea and vomiting, anxiety, excessive yawning, tremors, rhinorrhea, muscle/joint aches, goose-flesh skin, and diaphoresis [10]. As opposed to abstinence-induced OW, precipitated OW can result in the sudden-onset of serious adverse effects such as retching vomiting, visual or auditory hallucinations, delirium, rhabdomyolysis, hemodynamic instability, and seizures [32,33].

Co-ingestion of buprenorphine with other sedatives can also cause adverse effects. Caution should be used when buprenorphine is co-administered with central nervous system (CNS) depressants such as alcohol and benzodiazepines, as these may precipitate worsening respiratory depression [11,34].

Immunosuppression is a commonly reported adverse effect of opioids [8,35]. High potency opioids such as hydromorphone and fentanyl can cause opioid-induced immunosuppression by reducing antibody production, cytokine expression, natural killer cell activity, and phagocytosis [8,35]. Buprenorphine is believed to have less of an immunosuppressive effect and may even restore immune function in chronic opioid users [36-38].

Buprenorphine results in prolongation of the QT interval. Though relatively safe, buprenorphine should be used cautiously with other QT prolonging medications such as fluoroquinolones (moxifloxacin), macrolides, antipsychotics, tricyclic antidepressants, and selective serotonin receptor antagonists (SSRIs). Evidence has demonstrated the QT prolongation in buprenorphine is less than that of methadone, suggesting buprenorphine may be the optimal maintenance therapy in patients with heart conditions [6,39-41].

In addition to the common adverse effect, buprenorphine has several black box warnings depending on the route of administration, listed in Table 3. [42].

2.6. Specific population considerations

2.6.1. Pregnant/breastfeeding

A 2016 meta-analysis comparing methadone and buprenorphine use during pregnancy found no difference between the groups with respect to congenital malformations [43]. Additionally, the overall incidence of congenital anomalies was similar to what would be expected in the general population, suggesting both methadone and buprenorphine are safe during pregnancy. As compared to methadone, which requires daily visits to opioid treatment facilities, buprenorphine can be prescribed for daily home use making it an optimal choice for pregnant patients. A 2017 American Congress of Obstetricians and Gynecologists (ACOG) opinion statement supported the use of buprenorphine during pregnancy for OUD [44].

A recent 2017 study also found efficacy in using buprenorphine to treat newborn infants suffering from neonatal abstinence syndrome after being exposed to opioids in utero [45]. As compared to oral morphine, infants who received sublingual buprenorphine experienced a nearly 50% drop in days requiring treatment (15 days versus 28 days) and a one-third decrease in hospital stay duration (21 days versus 33 days) [45].

Several studies have demonstrated that the amount of buprenorphine taken during pregnancy and breastfeeding is relatively small and unlikely to result in abnormal infant development [46,47]. The safety of buprenorphine is further supported by both ACOG and the American Academy of Pediatrics (AAP), which support buprenorphine use for OUD during breastfeeding regardless of maternal dose [44,48].

Table 2
Common Opioid Withdrawal Symptoms (COWS). COWS offers a numerical score of opioid withdrawal severity based on both subjective and objective measures. The cumulative score is used to assess severity of opioid withdrawal and safety of initiating buprenorphine treatment.

Common opioid withdrawal symptoms	
Symptoms	Score
Heart rate (>80)	0–4
Diaphoresis	0–4
Dilated pupils	0–5
Anxiety/irritability	0–4
Restlessness	0–5
Yawning	0–5
Bone/joint pain	0–4
GI upset	0–5
Tremor (outstretched hands)	0–4
Gooseflesh skin	0–5
Runny nose/tearing	0–4

<5 - no withdrawal; 5–12 - mild withdrawal;
13–24 - moderate withdrawal; >24 severe withdrawal.

Table 3
Black box warnings of buprenorphine alternatives. Each formulation of buprenorphine - sublingual, buccal, transdermal, subcutaneous, and parenteral forms – carries unique adverse risks that should be assessed prior to safe utilization

Buprenorphine blackbox warnings	
Type	Warning
Buccal (film)	Chewing, swallowing, snorting, or injecting extract from film will result in uncontrolled, potentially deadly, delivery; concomitant use of benzodiazepines or opioids may cause sedation, respiratory depression, coma, death; accidental exposure among children can result in severe toxicity
Intradermal (implant)	Increased risk of implant migration, expulsion, nerve damage, embolism, death
Subcutaneous (solution, extended release)	Severe toxicity if injected intravenously; tissue damage, thromboembolism
Transdermal (patch, extended release)	Chewing, swallowing, snorting, or injecting extract from film will result in uncontrolled, potentially deadly, delivery; concomitant use of benzodiazepines or opioids may cause sedation, respiratory depression, coma, death; accidental exposure among children can result in severe toxicity

2.6.2. Geriatric patients

Geriatric patients often struggle with polypharmacy due to multiple comorbidities and decreased organ function, resulting in variations in opioid metabolism. Unlike other opioids which have increased half-lives due to age-related decreases in metabolism and organ dysfunction, the half-life of buprenorphine remains relatively unchanged at ages >65 years [49-51]. Additionally, buprenorphine has less of an effect on polypharmacy associated with CYP450 interactions compared to other opioids [51,52].

Further, buprenorphine is associated with a decreased fracture risk among geriatric patients compared to other opioids [53]. This is presumably due to the decreased CNS sedating effects of buprenorphine at therapeutic doses. An expert consensus panel has endorsed buprenorphine as the recommended opioid option among elderly patients [51].

2.6.3. Liver failure patients

Liver enzyme conjugation of buprenorphine is relatively preserved in cirrhosis, and efficient metabolism has been demonstrated in severe liver disease, even at high doses [54-56]. Buprenorphine is considered a safe opioid alternative in patients with liver disease/cirrhosis [8,52,57].

2.6.4. Renal failure patients

Due to the predominant hepatic metabolism, stool excretion, and unchanged pharmacokinetics during dialysis, buprenorphine can be used at normal therapeutic doses in patients with renal dysfunction on dialysis [51,58]. Buprenorphine's large volume of distribution and high protein-binding limit the efficacy of dialysis in the treatment of patients suffering from buprenorphine overdose [42].

2.7. Pediatric warnings

Data does not support the use of buprenorphine in patients <16 years old. Moreover, recent data from the American Academy of Pediatrics showed a concerning incidence of buprenorphine exposures among pediatric populations [59]. Data collected from the United States poison control center between 2007 and 2016 found over 11,000 children had been exposed to buprenorphine, the majority of which were unintentional uses in children under 6 years old [59]. This research highlights the potential danger in opioid prescribing and need to exercise caution with any patient being prescribed buprenorphine who has children in the house or living community.

2.8. Role of buprenorphine in the emergency department

The majority of emergency physicians recognize the importance of utilizing non-opioid analgesic alternatives to prevent opioid misuse and addiction development. Several clinicians have recognized the ED as a unique setting of high-volume OUD/OW presentations and taken the additional step of initiating addiction management for the multitude of patients suffering from opioid addiction. Despite a community stigma that often views buprenorphine as a glorified opioid - a substitution of one addiction for another - utilizers of ED-based buprenorphine programs recognize the unique opportunity for intervention where the ED is often the first place OUD patients present following overdose or withdrawal. Among the supporters of OUD intervention and buprenorphine utilization, emphasis is placed on the differentiation of opioid dependence versus addiction, the former allowing patients to return to functional lives free of high-risk, drug-seeking behavior [60].

Research has shown that buprenorphine can be used as a safe means of treating OW that results in fewer ED visits compared to symptomatic treatment alone [61]. A landmark study investigating OUD treatment in the ED setting has shown ED-initiated buprenorphine was associated with increased engagement in outpatient opioid addiction treatment programs, as well as reduced illicit opioid use in those who continued the treatment transition to outpatient care [62].

A recent multicenter retrospective cohort study analyzed the benefits of medications for OUD by examining the records of over 17,000 patients (excluding cancer patients) who were seen following a nonfatal opioid overdose [63]. As compared to patients who received naltrexone (an opioid-receptor antagonist) which showed no benefit over withholding medication treatment, buprenorphine was associated with decreases in both all-cause mortality (adjusted hazard ratio, 0.63 [95% confidence interval (CI), 0.46 to 0.87]) and opioid-related mortality (adjusted hazard, 0.62 [95% CI, 0.41 to 0.92]). A surprising finding from this study was that only about one-third of the opioid overdose patients received prescriptions for either buprenorphine or methadone in the year that followed the overdose [63]. These results indicate that although effective, buprenorphine is still highly underutilized.

An Oakland-based opioid addiction program received national attention after obtaining a government grant that provided the resources needed to successfully initiate OUD treatment directly from the ED [64]. These government funds effectively allowed the program to offer continuous, patient-centered buprenorphine therapy [64]. This comprehensive treatment program reinforces the effectiveness of an ED-based OUD program when given the resources and support necessary to combat the opioid epidemic.

2.9. Appropriate ED management of opioid withdrawal with buprenorphine

Buprenorphine treatment in the ED begins with recognition of OW. Patients suffering from OW are identified by a constellation of symptoms - increasing type and severity - that are quantitatively measured using a COWS assessment (see Table 2) [31]. Each of the symptoms is scored based on severity, with the cumulative score used to assess the safety of buprenorphine initiation. In order to avoid precipitating OW, buprenorphine should not be given within 24 h of long-acting opioid use and only once conclusive evidence of OW has been noted. Variation in practice exists among providers regarding the specific COWS score to use in defining OW. Ultimately, higher COWS scores and an increased number of objective signs such as diaphoresis, runny nose, and gooseflesh skin provide added certainty of OW and the reassurance that buprenorphine administration will not result in induced OW. A COWS score > 7 is believed to provide sufficient confidence in an established OW. If uncertain of OW despite COWS >7, consider starting with a lower dose of buprenorphine or delaying initiation until a higher COWS score is noted (COWS >8) [65]. Prior to buprenorphine administration, all patients should have a documented initial COWS score and time of first assessment, along with patient-reported last opioid usage including type, amount, and route of administration.

Once OW has been established, buprenorphine can be administered using a stepwise approach. The following pathway and dosing recommendations are an adaptation based on a cumulative, evidence-based literature review on ED buprenorphine administration. Compared to other buprenorphine stepwise approaches, this is a conservative approach taking additional precautions to avoid precipitating OW. Fig. 1 provides a step-by-step approach to opioid withdrawal (OW) management for patient presenting to the ED.

Though consistent with other stepwise approaches, this approach has not yet been formally tested.

1) Assess for sufficient OW (COWS>7); if uncertainty regarding withdrawal or last opioid use, observe an additional hour and reassess for an increasing COWS score.
2) Once OW is reliably established, administer 4 mg buprenorphine sublingually; allow 20–40 min for withdrawal symptom resolution (typical onset 30–60 min, sublingual).
3) Reassess for OW at 1–2 h intervals; repeat 4 mg dose as needed until OW symptoms are no longer observed and the patient confirms subjective symptom resolution (typical first day doses range from 8 to 16 mg).
4) Observe for 1–2 h after the final buprenorphine dose prior to discharge to evaluate for safety.
5) Provide patient with outpatient multimodal medication-assisted treatment (MAT) clinic information for planned follow up within 48–72 h. An x-waivered provider (see below) should prescribe a three-day course of buprenorphine equal to the total dose required to achieve OW resolution in the ED (typically 8–16 mg). The total dose can be taken once daily or divided in two separate treatments administered sublingually twice a day. If hospital regulations permit, consider discharging the patient with a bridging dose of buprenorphine (2–4 mg) to prevent symptom relapse in patients who are at risk of prescription filling delays.

Caution is recommended with patients presenting with opioid use in the previous 24 h. Based on the results of a 158 patient retrospective chart review, the risk of ED-initiated buprenorphine-induced OW is negligible [61]. However, in the event of induced OW, treat with a non-opioid regimen. While it may seem intuitive to treat with opioids, the high potency buprenorphine administered will block therapeutic relief of the precipitated OW. Consider alternatives such as clonidine (0.1–0.2 mg PO) [66] or a fast-acting benzodiazepine such as lorazepam (1–2 mg PO) [65].

2.10. Prescribing buprenorphine from the emergency department

Buprenorphine administration in the ED can be done by any licensed provider without further certification. Under the Drug Addiction Treatment Act of 2000 (DATA 2000), however, only physicians who receive an x-waiver qualification can treat outpatient opioid dependency with narcotic medications (buprenorphine) approved by the FDA. In order to qualify for the x-waiver, clinicians must have a valid medical license, an

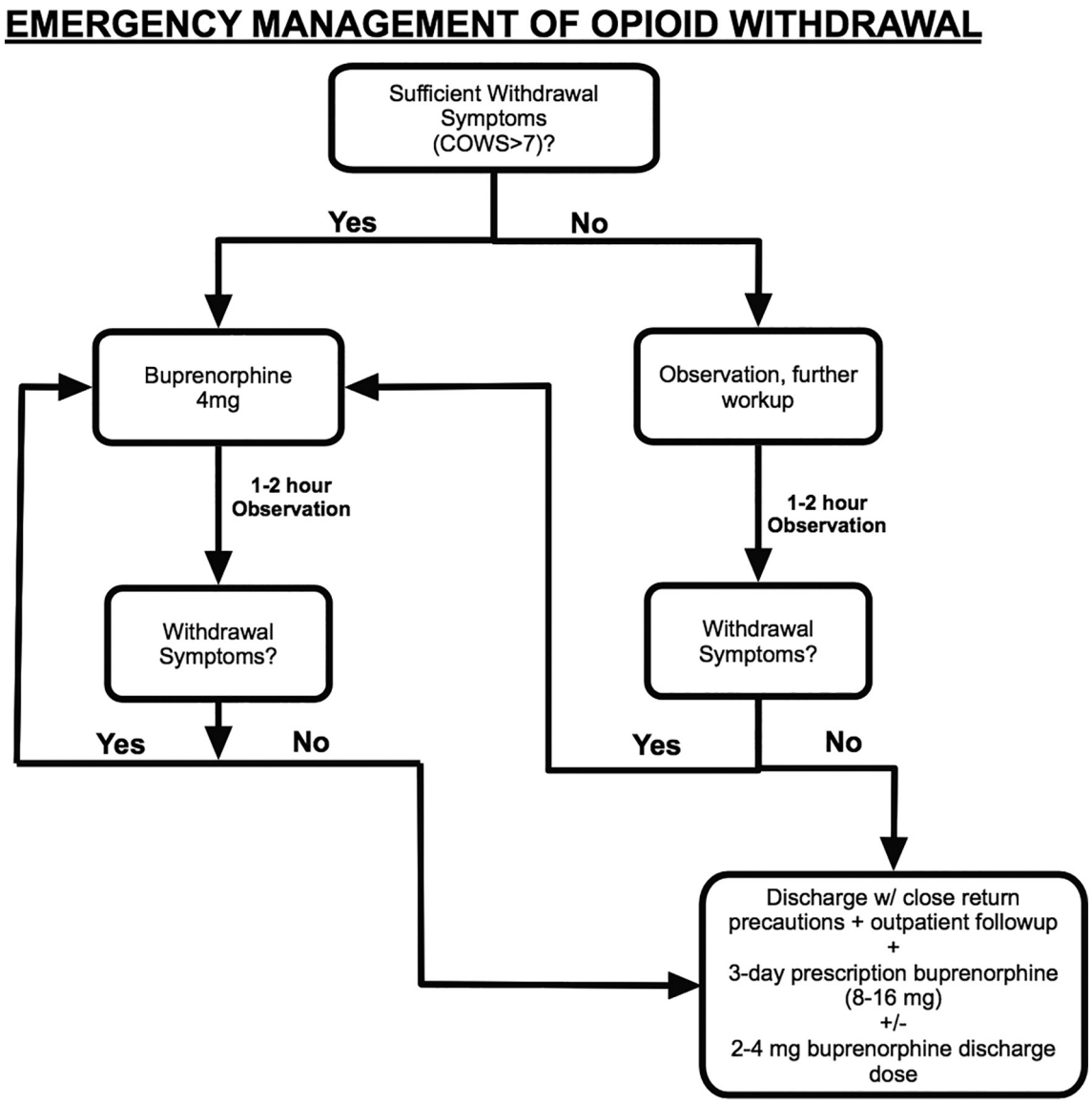

Fig. 1. Emergency Management of opioid withdrawal. A step-by-step approach to buprenorphine can by utilized to reach a sustained withdrawal relief.

active DEA number, and complete an 8-hour training course covering buprenorphine utilization and OUD treatment management. A link to the course can be found on the American Society of Addiction Medicine (www.asam.org) or through the Providers Clinical Support System (www.pcssnow.org). Once completed, the waiver entitles the applicant to prescribe buprenorphine to up to 30 patients at a time (i.e., DEAX-qualified). In order to treat over 30 patients, after one year the x-waivered clinician can apply to the Substance Abuse and Mental Health Services Administration (SAMSHA), which allows treatment of up to 100 patients at a time. A further federal application is necessary to prescribe to higher patient volumes (up to 275 patients at a time) [67]. Note that the patient cap applies only to active prescriptions, not total prescriptions. This cap has limited effect on ED buprenorphine prescribers who would only be expected to have several three-day prescriptions active at any given time.

2.11. Discharge and outpatient follow-up

Buprenorphine as part of opioid maintenance therapy (OMT) is not the cure-all for OUD. Only when combined with a multimodal MAT plan involving counseling and behavioral therapy can successful remission be maintained [68]. It is essential to provide patients being discharged with the name, telephone number, and address of local opioid addiction centers or a primary care physician specialized in treating opioid use disorder. A listing of national buprenorphine treatment practitioners can be found using the SAMSHA practitioner locator (https://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator). Alternatively, patients can register to an anonymous buprenorphine provider matching system that facilitates patient-provider contact (www.treatmentmatch.org).

When prescribing buprenorphine, stress to the patient the importance of continued outpatient therapy and the need for reassessment within 48–72 h to ensure adequate dosing and titration of buprenorphine to prevent relapse [2,14]. Provide the patient with education material on buprenorphine management as well as literature on opioid addiction and recovery. Ensure the patient has access to local pharmacy prescription pickup. A listing of local pharmacies with buprenorphine availability can be found at the SAMSHA website (https://www.samhsa.gov/bupe/lookup-form). Counsel the patient on the dangers and risk of injury associated with concomitant benzodiazepine and alcohol use in which buprenorphine may potentiate the sedating effects, and caution against driving or operating heavy machinery [69,70].

Emergency clinicians should also consider the unique position many of the OUD/OW patients may have in combatting the opioid crisis. A

patient motivated to start outpatient MAT treatment may also serve as a positive impact on other opioid users within their circle of acquaintances. Promote patient outreach in their community by supplying addiction treatment literature, as well as a prescription for a naloxone kit.

Lastly, advise the patient to return to the ED for further treatment and evaluation if unable to establish outpatient treatment. Emergency clinicians may administer buprenorphine for up to three consecutive days ("72-hour rule") while the patient establishes outpatient treatment [71].

2.12. Implementing an ED-based buprenorphine treatment program

Emergency clinicians motivated to start a buprenorphine treatment program may do so by considering the entire flow of OUD management within the community from the patient to the health care providers and administrators to the governing bodies.

The success of any buprenorphine treatment program is reliant on a culture of acceptance that must be established across the ED. Many clinicians are unaware of buprenorphine or have incorrect assumptions about its use and benefits. Establishing a focus group or hospital committee to provide evidence-based information on the efficacy and safety of OUD treatment within the ED and outpatient settings is a first step in creating awareness and stimulating interest. Developing a hospital-tailored training guide that facilitates education and utilization can assist, and materials to facilitate discussion at all levels can be found at ed-bridge.org.

Support from hospital administration can be established by presenting a cost model that stresses the research-based financial implications and potential cost savings associated with ED-based substance abuse disorder programs. Several studies focusing on screening, brief intervention, and referral to treatment (SBIRT) initiatives among Medicaid patients presenting to the ED for substance use disorder have estimated potential savings between $2000 to $6000 per patient year [72,73]. Many programs were implemented at a total cost of less than $100 per patient initiated in treatment [74-76]. A further administrative decision to incentivize clinicians to obtain the x-waiver qualification can promote interest and involvement at the clinician level.

Adequate training of health care clinicians is necessary for buprenorphine utilization. Although not all clinicians require x-waiver certification, all members of the team must be involved in the screening, recognition, and stepwise management of presenting OUD patients. Educational training sessions incorporating health care faculty across the spectrum - nursing staff, physicians, physician assistants, social workers, case managers, health educators – can be utilized to build a common understanding of buprenorphine management. Training videos for clinicians at all levels can be found at SHOUT: Supporting Hospital Opioid Use Treatment (https://www.projectshout.org/webinars) or Project ASSERT: Alcohol & Substance Abuse Services, Education, and Referral to Treatment (https://www.bu.edu/bniart). Educational handouts and training documents should be readily available to healthcare staff including treatment flow charts, outpatient program listings, available prescribing pharmacies, and specific patient communication instructions to empower patients motivated to move forward with outpatient MAT.

Sufficient in-hospital pharmacologic resources must also be available. Develop close communication with hospital pharmacists to establish a plan for increased buprenorphine usage prior to program implementation. Talk with pharmacy leadership to ensure buprenorphine is on the formulary. Utilize a buprenorphine monograph similar to the one found at SHOUT.org (https://www.projectshout.org/toolkit). Estimate anticipated ED utilization so that buprenorphine is available and easily accessible on the pharmacy registry. Discuss the specific formulations available, indications for use (analgesia versus OW), stock supply quantities, and any challenges that may prevent quick, efficient access to patients presenting to the ED. Further discussion with pharmacy directors regarding a planned inpatient guide to buprenorphine management would also assist those patients requiring inpatient admission for opioid withdrawal (an example of an inpatient guide can be found at https://www.projectshout.org/toolkit).

Outpatient treatment transition must also be established for continued OUD management. Discharge prescriptions rely on at least one x-waivered provider be available at all times in the ED. Additionally, proper lines of outpatient treatment programs and local pharmacy supply must be available for prescriptions. Communicate directly with pharmacies and with MAT program administrators to ensure patients are provided with accurate and up-to-date treatment options and specific times and days when treatments are available. The hospital social work staff is essential for addressing any of the patient's other social or economic disparities or insurance lags that may hinder successful continuation of outpatient treatment.

Identifying ED patients who will benefit from addiction management is essential to addressing OUD. Patients with OUD who may benefit from MAT may not necessarily present intoxicated or in OW [77]. Educate clinicians to screen for and recognize the red flags of high-risk characteristics of OUD. Transition of care can be further facilitated by obtaining patient education materials from outpatient partners that describe how to access their buprenorphine treatment services.

Most importantly, become involved in the community as an ED OUD treatment advocate. Reach out to other institutions with well-established buprenorphine treatment programs to share thoughts and ideas on how programs can be most effective (https://ed-bridge.org/connect or https://medicine.yale.edu/edbup). Connect with the community of providers associated with the National Alliance of Advocates for Buprenorphine Treatment who can provide recommendations and support based on their advocacy in the field (https://www.naabt.org/providers.cfm). Finally, become a local community advocate by attending town hall meetings or reaching out to local and state legislation in order to voice your support (http://openstates.org/find_your_legislator).

3. Conclusions

Buprenorphine is a high potency mu-opioid partial agonist with lower intrinsic activity and longer duration than other opioids, making it an optimal treatment option for OUD in the ED. Research demonstrating successful transition of buprenorphine initiation to outpatient treatment programs has reinforced the safety and efficacy of buprenorphine utilization in the ED setting. Though many programs have successfully implemented ED-based buprenorphine treatment programs, the stigma of 'replacing one opioid with another' remains a barrier to universal buprenorphine program implementation. Evidence-based discussions on the benefits of buprenorphine treatment that emphasize the difference between opioid addiction and dependence are essential to promoting a culture of buprenorphine acceptance and optimizing OUD patient treatment.

Conflicts of interest

None.

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