

## Treatment of OUD in the Emergency Department

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### Abstract

From the late 1900s to the early 2000s, various pharmaceutical companies encouraged healthcare providers to treat patients with opioids, suggesting that they were highly effective and non-addictive [1]. This resulted in a significant rise in the rate of opioid prescribing. Along with increasing prescribing rates, came increasing rates of opioid misuse, abuse, and overdose. Opioid overuse deaths and opioid use disorder (OUD) in the United States have dramatically increased over the past decade, with approximately 128 people dying every day from an overdose of prescription or illicit opioids

**Keywords:** opioid use disorder; emergency; HIV

### Introduction

From the late 1900s to the early 2000s, various pharmaceutical companies encouraged healthcare providers to treat patients with opioids, suggesting that they were highly effective and non-addictive [1]. This resulted in a significant rise in the rate of opioid prescribing. Along with increasing prescribing rates, came increasing rates of opioid misuse, abuse, and overdose. Opioid overuse deaths and opioid use disorder (OUD) in the United States have dramatically increased over the past decade, with approximately 128 people dying every day from an overdose of prescription or illicit opioids [2]. Due to direct and indirect effects of the COVID-19 pandemic, U.S. Emergency Departments (EDs) have seen a 30% increase in opioid overdose related visits [3]. The initial response of the healthcare system was to reduce or stop prescribing opioids, however logical this approach did not lead to a solution. In addition to expanded prescribing, the opioid crisis was escalated by the improved purity of heroin and the introduction of synthetic opioids such as fentanyl. The decrease in prescribed opioids led to a surge in the production and consumption of illicit opioids further amplifying the crisis. As patients were no longer able to obtain prescribed opioids, many turned to illicit opioids to manage their pain and/or dependence. These illicit substances are often cheaper to obtain, and contain unregulated levels of potent opioids, such as fentanyl, making them extremely dangerous.

To adequately address the OUD crisis, ED's can serve a much-needed role in initiating and maintaining long-term treatment of OUD. The ED is highly trafficked by patients grappling with OUD and exhibiting high-risk behaviors. Treatment for such patients often is based on utilizing an opioid agonist or antagonist treatment (OAT) with or without psychosocial treatment [4]. Currently, only one third of patients seen in the ED for opioid overdose in 2023 received treatment within the following year [5]. As the

ED is the primary point of contact for patients with high-risk opioid use, ED physicians have a unique opportunity to play a role in mitigating the opioid crisis. Based on these factors, ED-initiated OUD treatment should be developed and applied, rather than supporting the traditional route of referring patients to an outpatient or inpatient OUD treatment facility from the ED.

### Treatment Options:

Opioid use disorder (OUD) is a chronic, relapsing illness of a problematic pattern of opioid use, including use despite adverse consequences. This disorder manifests with physical and psychological symptoms. Physical symptoms of acute intoxication include decreased level of consciousness, respiratory depression, and miosis. Long-term use leads to the development of tolerance, in which patients no longer exhibit acute effects at their typical dose [6]. Psychological symptoms include maladaptive behaviors related to obtaining and using opioids. Successful recovery is possible with evidence-based, long-term treatment of OUD using opioid agonist treatment (OAT) with or without concurrent psychosocial treatment (7). OATs relieve withdrawal symptoms and eliminate cravings and are associated with higher rates of success and retention compared to abstinence-based therapies [8]. Treatment of OUD with OATs is also associated with lower rates of HIV/Hepatitis C transmission, opioid overdose and all-cause mortality [9]. Buprenorphine and methadone are the first-line OATs recommended for OUD. The goal of treatment is once-daily dosing with no withdrawal between doses [10].

### Methadone

Methadone is a full opioid receptor agonist that treats withdrawal symptoms of OUD and opioid cravings. It has been proven to reduce the likelihood of dying from an overdose by up to 50% [11]. Methadone is also associated with higher treatment retention rates than buprenorphine due to methadone's action as a full opioid receptor agonist [12]. Methadone is subject to stricter prescribing regulations compared to other OATs due to the fact it's a full opioid receptor agonist. This raises concern about overdose potential. It is only prescribed by providers at designated opioid treatment programs (OTP) registered under the Drug Enforcement Administration (DEA) and certified by the Substance Abuse and Mental Health Service Administration [13]. Providers were required to complete special training and submit waivers to the DEA. Methadone is administered as a directly observed therapy (DOT), meaning individuals must travel to an OTP and be witnessed taking the medication. Methadone is a DOT in order to prevent a patients' ability to take the drug home to prevent risk of relapse and/or overdose [14]. The highly regulated method of administration of methadone has been criticized as an act of "exceptionalism" given the fact that other full opioid agonists, such as oxycodone, are prescribed without the same constraints [15]. Patients are required to travel to an OTP daily for the first 90 days of treatment. Physical distancing related to the COVID-19 pandemic pushed lawmakers to relax methadone prescribing regulations for the first time since it's FDA approval for OUD in the mid-1960's [16]. Under the new guidelines, providers were granted the ability to prescribe up to 28 days of take-home doses [17]. Many states are working to maintain these more relaxed guidelines as no adverse effects were reported [18]. Another criticism of the strict prescribing regulations of methadone is that they are becoming increasingly obsolete [19]. Specifically, they have remained unchanged for the past 50 years with all patients receiving the same initial dose of 30 mg daily for the first 90 days of treatment. Public health professionals argue that this dose is miniscule against the highly potent illicit fentanyl and fentanyl analogues available today. The aforementioned criticism regarding strict and obsolete methadone prescribing practices call for policies that make prescribing practices more accessible and individualized.

### **Methadone in the ED:**

Methadone is long-acting, meaning most can miss a single day's dose with no or minimal withdrawal symptoms [20]. Therefore, patients who present to the ED after having missed a single dose of methadone without signs of withdrawal may be discharged. ED physicians are allowed to administer methadone in the ED for management of acute opioid withdrawal given the lethality of withdrawal. Initiation of OATs in the ED for the purpose of management therapy has sparked the attention of public health professionals and lawmakers as a means mitigate the opioid crisis. This topic has become increasingly relevant as illicit opioids continually become more potent and prevalent [21]. A 2019 study found that over half of the patients who died of opioid overdose had a previous ED visit relating to opioid withdrawal or overdose [22]. However, in 2023 only 18% of individuals with OUD were receiving treatment [23]. This calls for intervention from ED providers to initiate treatment in vulnerable patients with untreated OUD. Recently, the DEA established the "72-Hour Emergency Rule" allowing non-OTP providers to administer methadone for opioid withdrawal for up to 72 hours while arranging continuity of care [24]. Current literature describes use of the "72-Hour Emergency Rule" in the ED setting to address opioid withdrawal in patients unable to make it to an OTP clinic due to another acute medical issue or weather emergency [25].

### **Buprenorphine**

Buprenorphine is a partial opioid receptor agonist used as a long-term preventative medication that decreases recurrence of opioid overdose [26]. As a partial opioid receptor agonist, buprenorphine causes minimal euphoria and has a lower potential for overdose compared to methadone.

Buprenorphine is subject to strict prescribing regulations due to its opioid agonist effects, but regulations are less strict compared to those of methadone. Only providers who have obtained Drug Addiction Treatment Act of 2000 (DATA) waivers may prescribe buprenorphine [27]. This creates a disproportionate number of patients seeking treatment compared to the number approved prescribers, which leads to long wait times for initiation or continuity of care [28] This is particularly alarming as any delay in care of OUD could be lethal. The Biden Administration responded to this issue in April 2022 by eliminating the training requirements for prescribers for treatment of up to 30 patients at a time [29]. The DATA waiver is still required. These updated prescribing guidelines granted ED physicians the ability to administer buprenorphine for management of acute opioid withdrawal.

### **Buprenorphine in the ED:**

ED physicians are allowed to initiate buprenorphine at time of discharge for patients with OUD who have not yet begun treatment. Buprenorphine works to manage OUD similar to methadone, but is viewed as the safer option due to the "ceiling effect". The "ceiling effect" is a phenomenon in which further increases above 24 mg in dosage do not illicit respiratory and cardiovascular depression, as would be seen with methadone [30] Initiation of buprenorphine in the ED with referral to outpatient treatment has been associated with increased treatment engagement 30 days after discharge compared to referral-only interventions [31].

The American College of Emergency Physicians (ACEP) and the American Academy of Emergency Medicine have addressed this association by recommending ED physicians initiate buprenorphine with outpatient follow-up care to patients with OUD who have not yet begun treatment [32]. Buprenorphine is also subject to the "72-Hour Emergency Rule", in which a dose can be administered daily for three consecutive days [33]. A few EDs have taken care one step further by collaborating with community providers to increase accessibility of buprenorphine in their communities. Penn Presbyterian Medical Center (PPMC) established the Center for Opioid Recovery and Engagement (CORE) ED Buprenorphine Program which offers buprenorphine treatment to patients who self-identify as having OUD [34]. Under the guidelines of this program, OUD identification involves patient self-identification of OUD or ED providers will assess accordingly. ED providers identify patients based on presentation for OUD-related illnesses such as cellulitis or using the Clinical Opiate Withdrawal Scale (COWS). When deemed a candidate for outpatient treatment, a referral is made to multidisciplinary providers within the University of Pennsylvania Healthcare System who continue buprenorphine therapy. This includes family medicine, internal medicine and psychiatric providers. Furthermore, referrals are made based on patients home or work locations, transportation and insurance. The result of the program was 68% of patients who received ED-initiated buprenorphine with referral were in treatment, compared to less than 5% before the start of the program. The actions of this ED proved that simple measures of collaboration have significant effects in connecting patients to outpatient care from the ED.

### **Acute OUD Treatment:**

#### **Naloxone**

Naloxone is an opioid antagonist used as the primary overdose reversal agent in the acute setting. However, the efficaciousness of naloxone against more potent opioids such as fentanyl and fentanyl analogs have its limitations [35]. This led to an increase in naloxone products with a higher dose. The Surgeon General of the United States Public Health Services issued an advisory in 2018 calling for increased access to naloxone [36]. The FDA responded by approving an over-the-counter naloxone nasal spray in 2023 [37]. Additionally, KLOXXADO, a higher dose form of naloxone, was approved

in 2021. The approval of KLOXXADO was initially met with opposition for two reasons [38]. Firstly, those opposed to KLOXXADO are weary that EMS responders are administering more doses of naloxone as a result of availability bias. This would result in the administration of multiple doses of naloxone out of caution rather than observing clinical signs and symptoms of opioid overdose. This is potentially concerning as side effects of naloxone include pulmonary edema, seizures, arrhythmias and respiratory depression [39]. Secondly, some argue that KLOXXADO is not the panacea for opioid overdoses because patients being treated for a suspected opioid overdose may be experiencing a polysubstance overdose. This could include but is not limited to benzodiazepines, alcohol, contamination of illegal opioids with non-opioid depressants, or other sedative agents [40]. Despite initial apprehension, the distribution of naloxone upon being discharged from the ED is associated with decreased risk of mortality from OUD, but is not commonly practiced (41). Reasons cited for the lack of distribution include lack of time, physician knowledge, and institutional support. A retrospective study of nine EDs in a health system indicated that only 16.3% of patients received take-home naloxone at the time of discharge after being treated for opioid overdose. This data calls for the standardization of treatment protocol to allow ED providers to easily distribute naloxone at the time of discharge and educate patients of its use in a timely manner.

### Conclusion:

Based on multiple social- and health care system-related factors, ED providers have a unique opportunity to initiate and maintain effective care as they meet high-risk patients with OUD at their most vulnerable moments. Life-saving maintenance therapies exist, however under the current system of outpatient clinic OUD care, the issue of access and consistent follow up remains. Creating standardized treatment approaches specifically made for ED physicians to initiate OUD treatment during times of crisis, such as after a near fentanyl overdose, would be an effective measure to address the OUD crisis.

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