

# Consensus Recommendations on the Treatment of Opioid Use Disorder in the Emergency Department



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The treatment of opioid use disorder with buprenorphine and methadone reduces morbidity and mortality in patients with opioid use disorder. The initiation of buprenorphine in the emergency department (ED) has been associated with increased rates of outpatient treatment linkage and decreased drug use when compared to patients randomized to receive standard ED referral. As such, the ED has been increasingly recognized as a venue for the identification and initiation of treatment for opioid use disorder, but no formal American College of Emergency Physicians (ACEP) recommendations on the topic have previously been published. The ACEP convened a group of emergency physicians with expertise in clinical research, addiction, toxicology, and administration to review literature and develop consensus recommendations on the treatment of opioid use disorder in the ED. Based on literature review, clinical experience, and expert consensus, the group recommends that emergency physicians offer to initiate opioid use disorder treatment with buprenorphine in appropriate patients and provide direct linkage to ongoing treatment for patients with untreated opioid use disorder. These consensus recommendations include strategies for opioid use disorder treatment initiation and ED program implementation. They were approved by the ACEP board of directors in January 2021. [Ann Emerg Med. 2021;78:434-442.]

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## INTRODUCTION

In 2019, the National Safety Council announced that for the first time in history, a person in the United States was more likely to die of an unintentional opioid overdose than in a motor vehicle collision.<sup>1</sup> After a brief decrease in opioid-associated mortality from 2017 to 2018 of 1.7% (47,600 to 46,802), the US Centers for Disease Control and Prevention (CDC) reported 50,042 deaths in 2019, an increase of 9.4%, with even greater increases in overdose deaths projected due to the coronavirus disease 2019 (COVID-19) pandemic.<sup>2</sup> Provisional reporting by the CDC reveals new increases in rates of drug overdose in all US states, with an overall increase in drug overdose deaths of 26.8% and 19 states showing increases of more than 30% between August 2019 and August 2020.<sup>2</sup> Increased availability of highly potent illicit fentanyl and fentanyl analogues and the social isolation and treatment interruption associated with the COVID-19 pandemic represent drivers of the worsening opioid crisis, augmenting existing barriers and treatment gaps in the opioid cascade of care, a quality measurement framework that includes treatment engagement, medication initiation, retention,

and remission.<sup>3-6</sup> The treatment of opioid use disorder with buprenorphine or methadone has been associated with improved quality of life, reduced drug use, diminished HIV/Hepatitis C transmission, reduced opioid overdose, and decreased all-cause mortality.<sup>7-12</sup> With only 18% of individuals with opioid use disorder receiving medication for opioid use disorder treatment within the past year,<sup>13</sup> opioid overdose remains the leading cause of unintentional death for adults under the age of 50 in the United States, claiming an average of approximately 130 lives every day.<sup>14</sup>

## The Opioid Crisis and Emergency Departments

The first 2 decades of this millennium were characterized by dramatic increases in rates of opioid prescription, opioid overdose, and opioid-related utilization of inpatient and emergency department (ED) care.<sup>15-17</sup> As the opioid crisis has worsened, ED visits for opioid-related adverse drug events, complications of injection drug use, and opioid withdrawal have become increasingly common, resulting in ED visits for opioid-related presentations more than doubling between 2010 and 2018.<sup>18,19</sup> Patients who survive an opioid overdose are 100 times more likely to die

by drug overdose in the following year and 18 times more likely to die by suicide compared to the general population.<sup>20</sup> One-year mortality following an ED visit for opioid overdose is 4.7% to 5.5%.<sup>12,21,22</sup> Despite the extraordinarily high mortality, only one third of patients seen in the ED for nonfatal overdose received medication for opioid use disorder in the following year.<sup>12</sup> Importantly, compared to patients who did not receive medication for opioid use disorder after overdose, those who received buprenorphine had a significant reduction in mortality (adjusted hazard ratio 0.63; confidence interval [CI] 0.46 to 0.87), as did those receiving methadone (adjusted hazard ratio 0.47; CI 0.32 to 0.71).<sup>12</sup> Analysis of another cohort of 6,451 commercially insured patients discharged from an ED after nonfatal opioid overdose found that only 16.6% of patients received treatment for opioid use disorder in the 90 following days.<sup>23</sup>

Emergency physicians have an opportunity to provide evidence-based interventions and improve the care of patients with untreated opioid use disorder. Evidence strongly supports the initiation of pharmacotherapy for patients with untreated opioid use disorder at any and all points of contact with the health care system; this has been advocated by the Surgeon General, the National Institute on Drug Abuse, the Substance Abuse and Mental Health Services Administration (SAMHSA), the National Academy of Sciences, and the American College of Emergency Physicians (ACEP).<sup>24-29</sup> The ED is often the only contact individuals with opioid use disorder have with the health care system, and initiating treatment during the visit can make an enormous contribution to improving access to lifesaving care for people with opioid use disorder.

### **Fundamentals: Opioid Use Disorder and Food and Drug Administration (FDA)-Approved Medications**

Opioid use disorder is a chronic disease characterized by changes in brain function whose pathophysiology, like that of most chronic diseases, is heavily influenced by genetic and environmental factors.<sup>30</sup> The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for diagnosing opioid use disorder relate to loss of control, physiologic changes, and personal consequences, and the presence of these criteria defines mild (2 to 3 criteria), moderate (4 to 5), or severe (6 or more) disease.<sup>31</sup> As with many chronic diseases, pharmacotherapy plays a central, not adjunctive, role in treatment of opioid use disorder. Individuals with moderate to severe opioid use disorder are eligible for initiation of medication for opioid use disorder.

There are 3 medications approved by the FDA for the treatment of OUD. In the ED, initiation of treatment is

driven by a combination of federal regulation, patient characteristics, and pharmacological properties. Naltrexone is a long-acting, competitive  $\mu$ -opioid receptor antagonist that is used in the treatment of both opioid use disorder and alcohol use disorder.<sup>32</sup> Naltrexone results in precipitated opioid withdrawal in patients dependent on opioid agonists, and patients must be abstinent from opioids for at least 7 to 10 days prior to administration by any route.<sup>26</sup> Naltrexone does not treat opioid withdrawal and is not as effective at reducing mortality for patients with opioid use disorder as agonist opioid treatment.<sup>12</sup>

Methadone is a synthetic  $\mu$ -opioid receptor full agonist used for treatment of chronic pain and for opioid use disorder. Although therapeutic use of methadone is generally safe, rapid dose escalation results in potentially fatal respiratory depression. Additionally, high doses may cause a similar effect, which is enhanced by combination with sedatives.<sup>32</sup> Methadone is effective for the management of opioid withdrawal, and, as a full agonist, it does not cause precipitated withdrawal. Physicians can administer methadone in the ED or hospital for the treatment of opioid withdrawal, but the use of methadone for the treatment of opioid use disorder is limited to patients enrolled in regulated opioid treatment programs.<sup>33</sup>

Buprenorphine, a synthetic partial  $\mu$ -opioid receptor agonist, is primarily used for the treatment of opioid use disorder, though it is also prescribed for pain. The  $\mu$ -opioid receptor affinity is sufficiently strong to prevent other opioids from binding, exerting a “blocking effect.” As a partial agonist, buprenorphine has a ceiling effect on respiratory depression, meaning sedation and respiratory depression is diminished, and it has a similar plateau in analgesic efficacy.<sup>32</sup> Due to its high affinity and partial agonism at the  $\mu$ -opioid receptor, buprenorphine can behave as an antagonist by displacing a full agonist bound to the opioid receptor, leading to precipitated opioid withdrawal in opioid-dependent patients. In patients with abstinence-related withdrawal or withdrawal precipitated by naloxone, buprenorphine provides a sufficient agonist effect to ameliorate the withdrawal syndrome.

### **CONSENSUS RECOMMENDATION SCOPE**

These recommendations provide evidence-based assistance for emergency physicians treating ED patients with opioid withdrawal and initiating treatment for opioid use disorder with direct linkage to ongoing addiction care.

### **METHODS**

ACEP staff solicited applications from experts in the ACEP Pain Management and Addiction Medicine Section

to develop a consensus guideline that was conceived by ACEP and supported through a grant from SAMHSA. ACEP staff reviewed and approved applications and credentials for the 10 responding physicians with expertise in emergency and addiction medicine, medical toxicology, administration, and research from diverse practice settings. Consistent with the patient/population, intervention, comparisons, and outcomes (PICO) framework, experts identified a research question focused on ED practices to improve outcomes of patients with opioid use disorder to guide the literature search and consensus recommendations.<sup>34</sup> Recommendations were discussed and reviewed iteratively by all members throughout the process. All members attested to meeting International Committee of Medical Journal Editors guidelines. These consensus recommendations were reviewed and approved by the ACEP board of directors on January 28, 2021.

### Literature Review

A rapid review was conducted to inform the development of an evidence-based consensus guideline. The authors worked with a medical librarian to identify key words and phrases as well as inclusion and exclusion criteria to be applied in database searches. The librarian then performed searches in the MEDLINE and Scopus databases on July 27, 2020, and August 14, 2020, using the following key words/phrases or variations and combinations of the key words/phrases: addiction treatment, analgesics, opioid, buprenorphine, naloxone drug combination, buprenorphine/naloxone, clonidine, harm reduction, heroin, lofexidine, medication for opioid use disorder, medication-assisted treatment, methadone, naloxone, opiate substitution treatment, opioid addiction, opioid overdose, opioid use disorder, opioid withdrawal, opioid-related disorders, precipitated withdrawal, suboxone, survival analysis, and thiorphan. All searches were limited to studies of adult humans. Additional publications were identified by reviewing the reference lists of selected publications and by consulting with content experts and were used to tailor the literature search.

Resulting titles and abstracts were audited independently by 2 reviewers (JH and MW) to determine if the article addressed the PICO elements of treating withdrawal or initiation of treatment for opioid use disorder in ED patients with opioid use disorder or opioid withdrawal with a focus on the outcomes: mortality, morbidity (including accepting treatment for medical care not related to opioid use disorder), and linkage to opioid use disorder treatment. Exclusion criteria included initiation of opioid use disorder treatment in the

outpatient setting, even if follow-up measurements included ED visits; economic impact, even if this involved the ED; and take-home naloxone, if this was the only intervention reported.

**Data collection and processing.** Multiple reports of single trials were deduplicated by the medical librarian and subsequently exported to Rayyan.<sup>35</sup> The 2 primary reviewers (JH and MW) initially reviewed titles and abstracts independently, with subsequent inclusion of articles by consensus. In case of disagreement, the full text of the manuscript was examined. Disagreements in which consensus could still not be reached were resolved with a third reviewer (KH). All included manuscripts were subsequently made available to all experts on the consensus panel, who performed their own individual assessments of quality and bias.

**Rapid literature review results.** Seven hundred seventy-six articles published between January 1, 1970, and August 14, 2020, were identified in the searches. After the inclusion and exclusion criteria were applied, 60 articles were made available to consensus experts (Table E1, available at <http://www.annemergmed.com>).

### RESULTS AND RECOMMENDATIONS

Based on the literature review, clinical experience, and expert consensus, we recommend that ED clinicians treat opioid withdrawal and offer buprenorphine with direct linkage to ongoing medication for opioid use disorder treatment for patients with untreated opioid use disorder.

There is strong evidence demonstrating reduced morbidity and mortality for patients with opioid use disorder who are treated with opioid agonist treatment outside of the ED setting.<sup>7-12</sup> Initiating buprenorphine in the ED is effective for engaging patients in formal addiction treatment. In a randomized controlled trial, 78% (89 of 114; 95% CI 70% to 85%) of ED patients with opioid use disorder who received buprenorphine in the ED with referral for ongoing buprenorphine were engaged in formal addiction treatment at 30 days, compared to the 37% (38 of 102; 95% CI 28% to 47%) and 45% (50 of 111; 95% CI 36% to 54%) of patients who received brief intervention with standard or facilitated referral, respectively.<sup>36</sup> The buprenorphine group reduced the number of days of illicit opioid use per week from 5.4 days (95% CI 5.1 to 5.7) to 0.9 days (95% CI 0.5 to 1.3), versus reductions from 5.4 days (95% CI 5.1 to 5.7) to 2.3 days (95% CI 1.7 to 3.0) in the referral group and from 5.6 days (95% CI 5.3 to 5.9) to 2.4 days (95% CI 1.8 to 3.0) in the brief intervention group.<sup>36</sup> An analysis from the health care perspective using cost-effectiveness acceptability

curves found that at all positive willingness-to-pay values, ED-initiated buprenorphine treatment was more cost-effective than brief intervention with standard or facilitated referral.<sup>37</sup> Many EDs have instituted buprenorphine programs, which, alongside the broad state-wide implementation by the California Bridge Project,<sup>38</sup> have provided evidence of feasibility in ED populations.<sup>39-41</sup> Massachusetts adopted legislation (Chapter 208 of the Acts of 2018) requiring acute care hospitals that provide emergency services to have protocols and the capacity to initiate opioid agonist therapy to patients who present after opioid-related overdoses.<sup>42,43</sup> The use of buprenorphine has increased from 12.3 per 100,000 ED visits in 2002 to 2003 to 42.8 per 100,000 ED visits in 2016 to 2017 (odds ratio for linear trend 3.31; 95% CI 1.04 to 10.5).<sup>44</sup>

### Patient Selection

Individuals can be identified during their visit by direct history taking, review of electronic health record, physical examination, or screening techniques. In light of the widely recognized treatment gap and the high mortality of patients with untreated opioid use disorder, all patients meeting criteria for opioid use disorder who are not currently enrolled in treatment should be offered treatment and assessed for active suicidal ideation.<sup>13,18,20</sup>

Although concomitant use of buprenorphine and sedatives increases the risk of adverse outcomes, including overdose and death, medication for opioid use disorder should not be denied to patients with this high-risk use. In 2017, an FDA advisory specifically addressed this issue, stating that “buprenorphine should not be withheld from patients taking benzodiazepines or other medications that depress the central nervous system (CNS), despite potential side effects, given the potential harm of untreated opioid use disorder.”<sup>45</sup> When initiating buprenorphine, patients should be educated about the risks of concomitant use of benzodiazepines, sedatives, opioid analgesics, and alcohol.

### Enhancing Patient Motivation to Start Treatment

Using nonstigmatizing language and normalizing the process of ED initiation of buprenorphine and referral to ongoing treatment increases the likelihood that an individual will accept treatment. The Brief Negotiation Interview,<sup>46</sup> which includes asking permission to discuss their drug use, providing feedback, and enhancing motivation by eliciting patients' reasons to change and negotiating next steps, is effective. Integration into the flow of the ED and the electronic record with decisional support will improve success.<sup>47,48</sup>

### Protocols

Although specific protocols may vary among EDs, most include assessment for (1) moderate to severe opioid use disorder using questions derived from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria; (2) the degree of opioid withdrawal by the Clinical Opiate Withdrawal Scale; and (3) pregnancy. Depending on the degree of withdrawal, the patient should be offered treatment with buprenorphine in the ED or provided a prescription for unobserved (home) induction.<sup>49,50</sup> Patients should be discharged with a prescription for sufficient buprenorphine until an outpatient appointment to an opioid treatment provider or program (ideally within 1 week).<sup>51,52</sup> If no Drug Addiction Treatment Act of 2000 (DATA 2000)-waivered provider is available, a plan for access to medication under the “3-day rule” should be made (further information can be found in the section on ED Administration of Buprenorphine). The inclusion of harm reduction strategies (including overdose education and naloxone distribution) or prescriptions is also an essential component of the ED visit.<sup>53</sup> Sample protocols are available online, in EM textbooks, and on the ACEP Emergency Medicine Quality Network Opioid Initiative website.<sup>38,49,50,54-56</sup> In contrast to traditional outpatient induction protocols and FDA labeling,<sup>26</sup> ED-based protocols often start with administration of at least 8 mg of buprenorphine for patients with clinical signs of opioid withdrawal, and some protocols include an option for 24 mg or more during the ED visit based on provider experience, buprenorphine and/or specialist consultation, or other factors.<sup>38,49,50,54-56</sup>

### Referrals

Each patient with ED-initiated buprenorphine should be provided with a direct specific referral (when possible, with an appointment time) to a provider that aligns with the patient's insurance and other preferences. EDs should engage their community stakeholders in protocol development and enhance bidirectional communication to improve the continuity of care of patients with opioid use disorder. As with all chronic diseases, EDs are dependent on local resources. When no connection to local treatment providers exists, champions should consider online treatment provider resources such as the SAMHSA treatment finder website,<sup>57</sup> which includes information about treatment services offered and payment/insurance. The addition of health advocates or navigators in the ED who assist with motivating patients to accept treatment and navigating their paths to treatment may facilitate

better outcomes.<sup>39,58</sup> Whether these individuals are social workers, counselors, or peers, success depends on their ability to be integrated into the fabric of the ED.<sup>59</sup> A process of reviewing the fidelity of these interventions to ensure that they are evidence based should be in place.

### Documentation

When prescribing buprenorphine for opioid use disorder, the diagnosis of opioid use disorder should be included on the patient's medical record. Adding the diagnosis of opioid use disorder in the ED can expedite the referral process for many outpatient treatment providers and further support insurance preauthorization requests. This diagnosis should be supported by ED documentation.<sup>31,60</sup>

### Implementation Tips

Sustained success is built on the inclusion of multidisciplinary champions in developing protocols, normalizing the care of individuals with addiction, and developing monitoring and feedback systems to the staff. The inherent nature of ED care means that staff often only observe the negative consequences of untreated addiction rather than the successes that patients can have with evidence-based treatment. Leadership involvement in setting expectations for initiating treatment of opioid use disorder and providing referral for long-term addiction care is critical for departmental practice change.<sup>47,61,62</sup> Integrating decision support into the electronic health record is highly effective for streamlining the process of ED-initiated buprenorphine with referral for ongoing treatment and is integral for patient and provider satisfaction. A pilot test of a user-centered clinical decision support integrated within the electronic health record more than doubled prescription rates of ED-initiated buprenorphine and naloxone while doubling the number of unique physicians adopting the practice.<sup>48,63</sup>

### DATA 2000 Training/DEA X-waiver

DATA 2000 permitted US physicians to obtain a Drug Enforcement Administration (DEA) DATA waiver (by applying to SAMHSA after completing an approved 8-hour course) to treat patients with opioid use disorder using buprenorphine, the only schedule III, IV, or V medication that is FDA-approved for the treatment of opioid use disorder.<sup>64,65</sup> Once SAMHSA approves the physician's application, the physician receives an X-waiver designation from the DEA.

In all, DATA 2000 enables physicians to prescribe buprenorphine for opioid use disorder to be filled by patients at a pharmacy rather than obtaining medication from a traditional opioid treatment program. The Comprehensive Addiction Recovery Act of 2016 allowed for qualifying physician assistants and nurse practitioners to obtain X-waivers after completing 24 hours of approved coursework.<sup>66</sup> Patient limits have been incorporated into both laws, but they refer only to outpatients in longitudinal care and are unlikely to be a limitation to emergency clinicians prescribing only from the ED. Legislative and regulatory efforts are underway to reduce or eliminate the expectation for training and certification prior to prescribing buprenorphine for patients with opioid use disorder.<sup>67,68</sup> On April 28, 2021, the Department of Health and Human Services released new practice guidelines exempting state licensed, DEA-registered clinicians treating up to 30 patients at one time from completing the 8 (or 24) hour DATA 2000 training previously required to obtain an X-waiver.<sup>69</sup> As patients count towards a clinician's 30 patient limit until care is transferred to another clinician or 30 days from prescription end, most EM clinicians can practice under this exemption unless prescribing outside of traditional EM setting. Importantly, physicians must still apply for a X-waiver by filing a Notice of Intent with SAMHSA, who may take up to 45 days to approve the application.<sup>69</sup>

### ED Administration of Buprenorphine

An emergency physician has historically been able to administer buprenorphine in the ED under the "3-day rule" without having obtained an X-waiver.<sup>70</sup> A patient may be discharged and return to the ED repeatedly within 72 hours to receive medication from the same or a different provider. The dose is not specified; however, the medication must be administered to the patient while in the ED. The "3-day rule" was recently modified in the Further Continuing Appropriations Act, 2021, and Other Extensions Act, which was signed into law on December 11, 2020.<sup>71</sup> The Act requires the Attorney General (who will delegate this responsibility to the DEA), within 180 days, to revise current regulations governing the 3-day rule to allow practitioners to dispense not more than a 3-day supply of medication to one person or for one person's use *at one time* for the purpose of initiating maintenance treatment or detoxification treatment (or both) without a DATA 2000 waiver.

Patients with opioid use disorder who are being admitted to the hospital for a medical condition may be initiated and maintained on medication for opioid use

disorder treatment while hospitalized without restriction, even without a DATA waiver.

### Special Populations

Historically, buprenorphine as a single agent (without naloxone) was considered the preferred formulation for pregnant patients requiring medication for opioid use disorder, although recent investigation has revealed no adverse events with the combined buprenorphine/naloxone product.<sup>72</sup> The American College of Obstetrics and Gynecology recommends the use of either formulation.<sup>73</sup> The addition of naloxone to buprenorphine is intended to reduce intravenous use, misuse, diversion, and street value, though it does have a higher cost to the uninsured patient. Buprenorphine is approved for patients aged 16 years and older and should be considered for adolescents with opioid use disorder.<sup>33</sup> It is important to check local regulations and hospital policy before prescribing to adolescents. Buprenorphine can be safely used in geriatric patients with opioid use disorder; however, as it is an opioid, dosing may need to be adjusted and education should be provided to the patient and family regarding the risk of concomitant use of sedating medications.

### Stigma and Language

Patients report feeling heavily stigmatized during health care interactions, sometimes leading to distrust and an unwillingness to seek medical care.<sup>74-76</sup> Best practices support the avoidance of stigmatizing and derogatory terms such as “abuse,” “addict,” and being “clean.”<sup>74,75</sup> Language should be patient-centered, professional, and objective. For example, person-centered language such as “person who injects drugs” and “patient with an opioid use disorder” avoid negative connotations and conflation of the individual with specific behaviors to facilitate the development of a therapeutic alliance with the patient.

Given the evidence supporting a central role of pharmacotherapy in the treatment of opioid use disorder, many professionals are making a concerted effort to move away from the term “medication-assisted treatment,” replacing it with more accurate terminology, “medication for opioid use disorder.”<sup>26,74,27</sup> Those who desire to preserve the medication-assisted treatment acronym often use “medication for addiction treatment.”<sup>77</sup> The updated terminology conveys that medication, or the option of it, is essential for treating patients with opioid use disorder, while the term “medication-assisted treatment” implies that medication is more of an adjunctive therapy.<sup>77-79</sup> Stigma is often unwitting, unrecognized, and unaddressed by physicians, and stigmatizing attitudes, language, and

behaviors are often solidified during training. Raising awareness of nonpatient-centered language, attitudes, and behaviors among all members of the health care team is essential to transforming ED culture and care of opioid use disorder.

### CONCLUSION

Detecting and offering evidenced-based treatments for patients with opioid use disorder is aligned with the goals of emergency medicine to intervene on high-mortality disease processes. The window of opportunity to begin lifesaving pharmacotherapy may be fleeting. The ED’s 24-hour, 365-day accessibility ideally positions it as a cornerstone of care to close the enormous treatment gap for patients with opioid use disorder.<sup>61</sup>

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### Future Meetings of the American College of Emergency Physicians

The following are the planned sites and dates for the future annual meetings of the American College of Emergency Physicians:

October 25-28, 2021	Boston, MA
October 1-4, 2022	San Francisco, CA
October 9-12, 2023	Philadelphia, PA