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ORIGINAL RESEARCH

Pain Management and Sedation

Emergency department-initiated buprenorphine protocols: A national evaluation

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Abstract

Objective: Emergency department-initiated buprenorphine (BUP) for opioid use disorder is an evidence-based practice, but limited data exist on BUP initiation practices in real-world settings. We sought to characterize protocols for BUP initiation among a geographically diverse sample of emergency departments (EDs).

Methods: In December 2020, we reviewed prestudy clinical BUP initiation protocols from all EDs participating in CTN0099 Emergency Department-INitiated bupreNOrphine VAlidaTION (ED-INNOVATION). We abstracted information on processes for identification of treatment-eligible patients, BUP administration, and discharge care.

Results: All participating ED-INNOVATION sites across 22 states submitted protocols; 31 protocols were analyzed. *Identification of treatment-eligible patients*: Most EDs 22 (71%) relied on clinician judgment to determine appropriateness of BUP treatment with only 7 (23%) requiring decision support tools or diagnosis checklists. Before BUP initiation, 27 (87%) protocols required a documented Clinical Opiate Withdrawal Scale (COWS) score; 4 (13%) required a clinical diagnosis of withdrawal with optional COWS score. Twenty-seven (87%) recommended a minimum COWS score of 8 for ED-initiated BUP. *BUP administration*: Initial BUP dose ranged from 2–16 mg (mode = 4). For continued withdrawal symptoms, 27 (87%) protocols recommended an interval of 30–60 minutes between first and second BUP dose. Total BUP dose in the ED ranged from 8 to 32 mg. *Discharge care*: Twenty-eight (90%) protocols recommended a BUP

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prescription (mode 16 mg daily) at discharge. Naloxone prescription and/or provision was suggested in 23 (74%) protocols.

Conclusions: In this geographically diverse sample of EDs, protocols for ED-initiated BUP differed between sites. Future work should evaluate the association between this variation and patient outcomes.

KEYWORDS
buprenorphine protocol, emergency department, opioid use disorder, opioid withdrawal

1 | INTRODUCTION

1.1 | Background

From 1999 to 2018, the opioid epidemic claimed over 446,000 lives in the United States.[1] In 2020, there was a 21% increase in fatal overdoses, two thirds of which were opioid related.[2] Medications for opioid use disorder (MOUD), particularly methadone and buprenorphine, reduce mortality, increase treatment retention, decrease opioid misuse, and reduce craving and withdrawal.[3–5] Despite benefit, the majority of patients with opioid use disorder (OUD) do not receive MOUD.[6–8]

The emergency department (ED) is an important setting to identify patients with OUD and initiate buprenorphine (BUP).[6,9,10] From 2005 to 2014, opioid-related visits in the United States to EDs doubled.[11] In 2015, a randomized controlled trial demonstrated that ED-initiated BUP increased engagement in treatment at 30 days, reduced opioid misuse, and was cost effective compared to brief intervention with a referral or referral alone.[10,12] Although there has been a modest increase in ED BUP prescribing, few ED clinicians indicate high readiness to initiate BUP.[13,14]

When experience is lacking, clinical protocols may help facilitate adoption of ED-initiated BUP.[14–16] Most research on BUP has not been conducted in EDs, and existing protocols for BUP initiation in other settings may not reflect the unique needs of the ED and/or its patient population. The recently released guideline published by the Substance Abuse and Mental Health Services Administration (SAMHSA) on ED-initiated BUP suggests dosing that is lower and less frequent than the emergency medicine literature.[17–23] Instead, the SAMHSA guideline mirrors dosing regimens from clinical trials and observational studies in office-based settings.[3,24,25]

Although patients presenting for office-based BUP initiation are not physiologically different from those in the ED, context matters. For example, often the individuals with OUD who use the ED represent vulnerable populations, lacking other sources of healthcare access. They are more often uninsured or underinsured, and many have coexisting mental health issues and unstable housing.[17,26,27] ED patients often have more acute illnesses compared to those in office-based settings and may require more intense treatment and monitoring. In addition to these patient-related differences, EDs are faced with mounting pressures caused by unprecedented crowding; thus, enhancing throughput has become a priority. Minimizing repeat visits is essential to reduce unnecessary volume and to eliminate any potential additional insurance copays. Given the differences between the office and ED settings, it is not surprising that BUP protocols for office-based inductions may not translate well to the ED. To date, EDs have developed their own protocols but only few have made them publicly available.[18,19]

1.2 | Importance

The generation of site-specific evidence-based protocols may be an important strategy to streamline implementation and enhance the adoption of ED-initiated BUP.[14] Understanding variations and similarities in BUP initiation protocols across a diverse sample of EDs can help guide recommendations for protocol development and future research on best practices.

1.3 | Goals of this investigation

We sought to characterize a national sample of ED-initiated BUP clinical protocols on (1) identification of treatment-eligible patients, (2) ED BUP administration, and (3) discharge care with the goals of providing recommendations for key components of an ED-initiated BUP protocol based on similarities across protocols analyzed, as well as lay the groundwork for research to evaluate best practices.

2 | METHODS

2.1 | Study design

We analyzed ED BUP initiation protocols for all EDs enrolled in the National Institute on Drug Abuse Clinical Trials Network (NIDA CTN) 0099 Emergency Department-INitiated BupreNOrphine VAlidaTION Trial Network (ED-INNOVATION) study (ClinicalTrials.gov: NCT04225598).[28] The ED-INNOVATION protocol has been published elsewhere.[28] Briefly, the study has 2 components: (1) an implementation phase using implementation facilitation to enhance adoption of ED-initiated BUP and (2) a randomized controlled trial comparing the

effectiveness of 2 BUP formulations, sublingual (SL-BUP) and a 7-day extended-release injectable (CAM2038, XR-BUP) among patients with OUD on the primary outcome of engagement in formal addiction treatment at 7 days.[28,29] As part of the implementation facilitation phase but before initiation of any associated support efforts, all sites were required to submit their clinical BUP initiation protocols for review by the lead research team before October 31, 2020.

2.2 | Site selection

ED-INNOVATION sites were chosen based on a formal application process that took place in June 2019. Site selection was based on (1) the prevalence of patients with International Classification of Diseases, 10th revision codes for the prior 12 months related to overdose, OUD, and other opioid-related diagnoses using a predetermined list of codes including those in the F11 (opioid related disorders) and T40 (poisoning by, adverse effects of and underdosing of narcotics and psychodysleptics [hallucinogens]) categories; (2) presence of ED investigators with demonstrated experience conducting research; (3) an electronic health record that can be queried routinely to assess opioid-related diagnoses and provision of ED-initiated BUP; (4) ability to have SL-BUP and store extended release BUP under investigational drug status in the ED; and (5) availability of community clinicians and programs for referral for ongoing MOUD (methadone or BUP) treatment. Sites were chosen independently of whether they had a completed protocol for ED-initiated BUP. They were selected to reflect a mix of rural/urban/suburban; community/academic; geographic location; and size. Thirty sites were chosen from 69 applications. After initial site selection, 1 site dropped out and 4 were added, resulting in 33 sites, all of which submitted clinical BUP protocols for review. All sites were approved for participation in ED-INNOVATION by the Western Institutional Review Board.

2.3 | Procedures

Two investigators independently reviewed all submitted clinical BUP protocols using a standardized data abstraction survey created in Qualtrics (Qualtrics, Provo, UT) that collected data on (1) identification of treatment eligible patients, (2) ED BUP administration, and (3) discharge care. These 3 elements were chosen a priori based on a review of the literature on BUP initiation both in the ED and other clinical settings.[18,19,30,31] Specific variables of interest under each section were identified, and questions were drafted and used to review each protocol (Web Appendix 1). After independent review of 5 protocols, data abstractors met to clarify and revise the questions, and all previously reviewed protocols were re-reviewed. Chart abstractors were not blinded to the study objective. Survey results were exported to Excel and reviewed for disagreements then reexamined to see if consensus could be reached. When consensus could not be achieved, a third investigator acted as the final arbitrator.

The Bottom Line

This study demonstrates that variability exists across emergency department-initiated buprenorphine protocols across a sample of 31 geographically diverse sites; however, most protocols used a similar framework of identifying eligible patients, further assessing eligibility, providing buprenorphine, and discharging patients with harm reduction and referral to care. Future research could best test and define the specific steps within that framework.

2.4 | Analysis

This study is descriptive with no formal hypothesis being tested. Descriptive measures used to describe the data include frequencies and percentages for nominal and ordinal categorical variables and mean, mode, minimum, maximum, and total range where appropriate for continuous variables. Interrater reliability after initial data abstraction was calculated for categorical and ordinal variables using either unweighted or weighted Cohen's kappa, respectively.

3 | RESULTS

3.1 | Site characteristics

All sites (n = 33) EDs participating in ED-INNOVATION submitted protocols for lead team review. Among the 4 new sites added to the study, 2 were from the same health system, had the same study staff, and used the same protocol as their original sites. Therefore, 31 protocols were analyzed, representing EDs from 22 states (Figure 1) and a variety of practice settings.

Two sites had previously participated in a clinical trial with the lead research team on ED-initiated BUP (CTN-0069, NCT03023930), during which feedback was provided on their ED-initiated BUP protocols.[29] The lead research team, as an ED participating in clinical trial enrollment, also submitted a clinical protocol for review. The remaining 28 sites submitted protocols with no prior lead team feedback, although all had access to the lead team's protocol for reference.

3.2 | Identification of treatment-eligible patients

Six (19%) protocols had guidelines for universal screening for substance use disorders; 2 (6%) recommended using chief complaints or triage screening and 4 (31%) used either a site-specific assessment or other screening tools such as the NIDA Quick Screen or Screening and Brief Intervention and Referral to Treatment screening tool.[32,33] (Table 1).

In 22 of 31 (71%) protocols, identification of patients with OUD was performed based on clinical judgment; only 7 (23%) expected

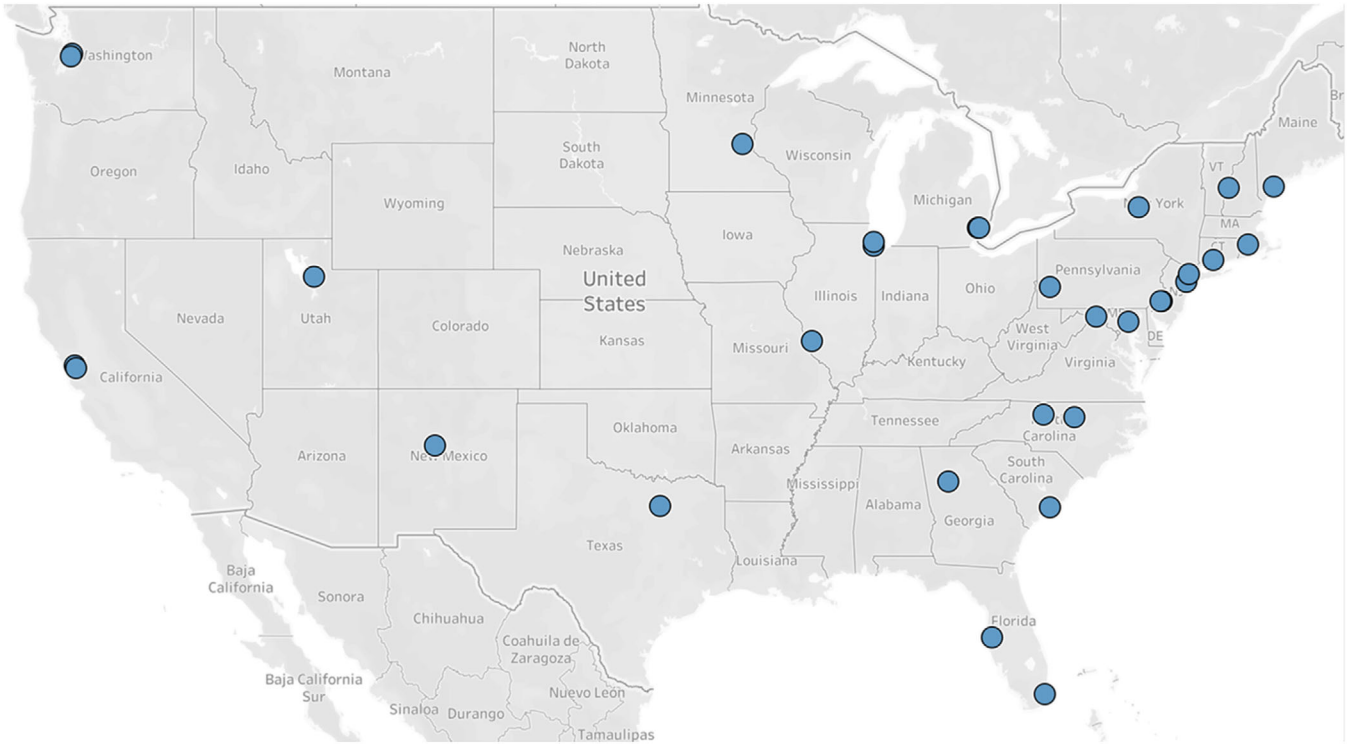

FIGURE 1 Location of emergency department sites that were selected to participate in CTN 0099 ED-INNOVATION (n = 33). Sites that submitted protocols and were selected to participate in the National Institute on Drug Abuse Clinical Trials Network (NIDA CTN) 0099 Emergency Department-INitiated BupreNOrphine VAlidaTION Trial Network (ED-INNOVATION) study are indicated by blue circles (n = 33). The 33 sites represented 22 states; overlapping circles include 2 in California, 2 in Illinois, 2 in Michigan, 2 in New Mexico, 3 in Pennsylvania, and 2 in Washington. Abbreviations: BUP, buprenorphine; COWS, Clinical Opiate Withdrawal Scale; ED, emergency department; OUD, opioid use disorder

documentation of the specific Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria to diagnose OUD.[34] All 31 protocols required determination of a patient's severity of withdrawal: 27 (87%) required a documented Clinical Opiate Withdrawal Scale (COWS) score, and 4 (13%) required a clinical diagnosis of withdrawal with optional COWS score. Among the protocols with required or optional COWS score: 30 (97%) recommended or required a minimum COWS score before ED BUP initiation; 27 (87%) recommended a minimum COWS score of 8 with 3 (10%) or without 24 (77%) objective signs; and the remaining 3 protocols recommended a minimum COWS score of 5, 11, or 12.

Nineteen (61%) protocols listed the minimum number of hours since last opioid use to help inform eligibility for ED BUP initiation: most commonly 8 (26%) requiring 12 hours since short-acting opioid use, 7 (23%) requiring 24 hours since long-acting opioids, and 13 (42%) requiring 48–72 hours since last methadone use. Twenty-one (68%) protocols listed contraindications to ED BUP initiation: 16 (52%) included recent (24 hours to 2-week) methadone use; 11 (35%) included severe medical illness including liver disease; 9 (29%) included altered mental status and/or intoxication; 6 (19%) included pain, trauma, and/or planned surgeries; and 5 (16%) included alcohol and/or benzodiazepine withdrawal or use.

Pregnancy determination before ED BUP initiation was required or recommended in 21 (68%) protocols. In 9 (29%) protocols, other labs such as urine toxicology, liver function tests, complete blood count, and basic/complete metabolic panel were required or recommended if clinically indicated.

Twenty-one (68%) protocols mentioned ancillary staff involvement, including 12 (39%) that used social workers, 11 (35%) that used peer counselors/advocates, and 7 (23%) that used care managers.

3.3 | ED BUP administration

Twenty-eight (90%) protocols specified using SL-BUP in the ED; among those, 3 (10%) also suggested the use of intramuscular or intravenous routes of administration in certain circumstances. The remaining 3 (10%) protocols did not specify the mode of BUP administration. Fifteen (48%) protocols specified using the buprenorphine/naloxone combination product; among those, 6 (19%) additionally allowed buprenorphine monotherapy use. The remaining 16 (52%) protocols did not specify formulation. (Table 2).

Initial recommended BUP dose ranged from 2–16 mg (mode = 4). In 14 (45%) protocols, first BUP dose varied by COWS score: 11 (35%) protocols specified 4 mg BUP for COWS score 8–12 and 8 mg for COWS score 13+.

Additional recommendations for BUP dosing were specified in 28 (90%) protocols ranging from 4 to 24 mg. For continued withdrawal

TABLE 1 Identification of treatment-eligible patients before ED BUP administration (n = 31 site protocols)

	# of site protocols	% of site protocols
a) Inclusion criteria for ED BUP administration:	31	100%
OUD determination	22	71%
Formal OUD screen using DSM-5	7	23%
Active withdrawal	31	100%
COWS score	27	87%
Clinical diagnosis of withdrawal, optional COWS score	4	13%
Time elapsed since last opioid use:	19	61%
Methadone	16	52%
Long-acting opioids excluding methadone	9	29%
Short-acting opioids	9	29%
Heroin	5	16%
b) Minimum COWS score required before ED BUP initiation	30	97%
Minimum COWS score of 8	27	87%
c) Contraindications to ED BUP administration:	21	68%
Recent methadone use	16	52%
Severe medical illness including liver disease	11	35%
Altered mental status and/or intoxication	9	29%
Pain, trauma, and/or planned surgeries	6	19%
Alcohol and/or benzodiazepine withdrawal or use	5	16%
Other	9	29%
d) Other evaluations before BUP administration:		
Pregnancy determination	21	68%
Other labs required or when clinically indicated	9	29%
e) Guidelines for identifying patients for ED buprenorphine	6	19%
f) Ancillary staff for ED BUP	21	68%

Number of site protocols that provided guidelines related to identification of treatment-eligible patients: (a) inclusion criteria, (b) minimum COWS score, (c) absolute contraindications to ED BUP ("other" contraindications included, but were not limited to, naloxone induced withdrawal, BUP allergy, lack of patient willingness to initiate BUP, and exacerbation of psychiatric illness or active psychosis), (d) other evaluations (other labs included urine toxicology, liver function tests, complete blood count (CBC), basic/complete metabolic panel [BMP/CMP], and otherwise not specified), (e) guidelines to identify patients, and (f) ancillary staff.
Abbreviations: BUP, buprenorphine; COWS, Clinical Opiate Withdrawal Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th edition; ED, emergency department; OUD, opioid use disorder

TABLE 2 Details of ED BUP administration (n = 31 site protocols)

	# of site protocols	% of site protocols
a) Variable initial buprenorphine dose based on COWS score	14	45%
Dose based on COWS score 8–12, 13+	12	39%
b) Time frame between buprenorphine dose 1 and 2	29	94%
30–60 min	27	87%
<30 or >60 min	2	6%
c) Maximum total buprenorphine dose in ED	29	94%
8 mg	5	16%
12 mg	5	16%
16 mg	11	35%
24 mg	2	6%
32 mg	6	19%
d) Precipitated withdrawal guidelines	10	32%
e) Ancillary medications for symptoms of:	9	29%
Muscle aches and pains	8	26%
Nausea	9	29%
Abdominal cramps and diarrhea	8	26%
Other	7	23%

Number of site protocols that provided details related to administration of BUP in the ED: (a) initial ED BUP dose dependent on or independent of the patient's COWS score, (b) time frame between the initial BUP dose and a second BUP dose, (c) maximum total BUP dose, (d) precipitated withdrawal guidelines, and (e) ancillary medications for symptomatic management of withdrawal–"other" ancillary medications included clonidine (23%), antihistamines (16%), gabapentin (3%), antipsychotics (3%), and methadone (3%).
Abbreviations: BUP, buprenorphine; COWS, Clinical Opiate Withdrawal Scale; ED, emergency department.

symptoms, 27 (87%) protocols recommended an interval of 30–60 minutes between the first and second BUP dose (range 20–360 minutes). The maximum total BUP dose in the ED was specified in 29 (94%) protocols and ranged from 8 mg to 32 mg (mode 16 mg).

In terms of worsening or perceived precipitated withdrawal, 9 (29%) protocols described ancillary medications for continued withdrawal symptoms. The most frequently listed medications were ondansetron, loperamide, clonidine and nonsteroid anti-inflammatory drugs. Ten (32%) protocols included specific guidelines for precipitated withdrawal; among those, 5 (16%) recommended additional BUP for precipitated withdrawal, and 5 (16%) recommended ancillary medications without additional BUP.

3.4 | Discharge care

Treatment for patients presenting with low COWS scores varied. Twenty-two (71%) protocols included recommendations for management of patients with low COWS scores. Among those, 12 (39%) recommended discharging the patient from the ED with a prescription for

TABLE 3 Discharge care after ED BUP administration (n = 31 site protocols)

	# of site protocols	% of site protocols
a) Policy for low COWS score	22	71%
Discharge from ED for home induction	12	39%
Hold in ED until COWS score increases	3	10%
Both discharge and hold in ED	7	23%
b) Home induction instructions provided	12	39%
c) Buprenorphine prescription at discharge	28	90%
4 mg	2	6%
8 mg	4	13%
12 mg	2	6%
16 mg	21	68%
24 mg	3	10%
32 mg	3	10%
Depends on ED dose/Other	4	13%
d) Naloxone provided and/or prescribed	23	74%
e) Harm reduction education	5	16%

Number of sites with guidelines related to discharge care instructions: (a) policy for low COWS score, (b) provision of home BUP induction instructions, (c) BUP prescription at discharge (note that some site protocols allowed several dosages to be prescribed at discharge), (d) naloxone for overdose prevention, and (e) harm reduction education.

home initiation of BUP; 7 (23%) provided the option of either discharging or holding in the ED; and 3 (10%) recommended holding the patient in the ED until withdrawal worsened. (Table 3).

Referral to outpatient treatment was addressed by all but one (97%) protocol, although only 2 (6%) explicitly mentioned a warm handoff. A BUP prescription provided at discharge was recommended by most, 28 (90%), ranging from 4–32 mg daily; the remaining 3 (10%) protocols did not include information on a discharge prescription of BUP. When prescribed, the most frequent dose (mode) of BUP was 16 mg daily (recommended in 13 [42%] protocols) and 8 mg twice a day (recommended in 8 [26%]). Seventeen (55%) protocols advised a prescription sufficient until the patient's follow-up appointment; 4 (13%) specified a range between 3 and 14 days; and 7 (23%) did not mention a set length of time for the prescription at discharge. If no DATA2000 waivered clinicians were present to prescribe BUP, 14 (45%) protocols recommended having the patient return to the ED daily for subsequent doses for up to 3 days, 3 (10%) recommended a loading dose in the ED up to 32 mg, and 5 (16%) mentioned finding a waivered clinician.

Naloxone prescription and/or provision was suggested in 23 (74%) protocols. Other specific harm reduction education, such as explicit overdose education, was mentioned in only 5 (16%) protocols.

3.5 | Interrater reliability

Kappa values for categorical and ordinal survey questions ranged from 0.37 to 1.0. Only 1 out of 40 survey question had a kappa value <0.41 and only 5 had a kappa <0.61. In general, observers agreed on data abstraction conclusions; agreement between observers was moderate to near perfect. Only 3 disagreements between the data abstractors could not be resolved and required adjudication by a third reviewer.

3.6 | LIMITATIONS

Our findings may be subject to selection bias. Although the ED-INNOVATION sites represented a geographically diverse sample, they may not accurately reflect the spectrum of ED BUP initiation practices across the country. Sites had to apply for inclusion in the CTN study, implying that prior work had been completed on ED-initiated BUP or at least contemplated. Furthermore, ED-INNOVATION sites had access to the lead research team's ED BUP initiation protocol during the implementation facilitation phase and were encouraged to review that protocol when creating or modifying their own site-specific clinical protocols. Additionally, the lead research team also submitted a protocol for review, and 2 sites had participated in a prior CTN study during which feedback was given on their respective ED-initiated BUP protocols; thus, at least 3 protocols were not in early protocol development. Despite this limitation, the presence of significant variability in the analyzed protocols suggests that sites developed BUP initiation procedures that were adapted to their unique settings.

Beyond the generalizability of sites themselves, individual protocols varied in structure and level of detail, potentially precluding consistent interpretation by our investigative team.

Finally, the protocols themselves may not accurately reflect clinical practice, but prior qualitative research suggests that clinicians less experienced at BUP initiation would likely lean heavily on protocols if they existed and that the absence of protocols is a major barrier to adoption of ED-initiated BUP.[14]

4 | DISCUSSION

Our study demonstrated considerable variability in protocols related to all 3 steps of ED-initiated BUP: (1) identification of treatment-eligible patients, (2) BUP administration, and (3) discharge care.

4.1 | Identification of treatment-eligible patients

In most protocols, clinical judgment rather than formal diagnostic criteria was used to determine the presence of OUD in treatment-eligible ED patients. Furthermore, protocols often did not note the involvement of other multidisciplinary team members, such as social workers, health advocates, or other peer counselors/coaches or what training in psychosocial interventions they used to motivate patients with OUD to engage in treatment. The most consistent finding across protocols was the evaluation of withdrawal, either by clinical gestalt

or a formal structured instrument such as the COWS, which grades withdrawal severity on a scale of 0–36 based on signs and symptoms such as heart rate, pupil size, restlessness, and yawning.[35] A clinical diagnosis of OUD and formal evaluation of withdrawal is consistent with SAMHSA Treatment Improvement Protocol Series 63 (TIP 63), the American Society of Addiction Medicine (ASAM) and American College of Emergency Physicians (ACEP) guidelines that recommend initiating BUP in patients experiencing opioid withdrawal.[3,24,31]

Most protocols recommended a minimum COWS score of 8 before starting BUP, consistent with ACEP guidelines but lower than SAMHSA Treatment Improvement Protocol (TIP) 63′s recommendation of COWS score ≥12 and ASAM National Practice Guidelines recommendation of COWS score 11–12. [3,24,31] Several individual ED protocols also used a lower COWS score of 5 or 6 for BUP initiation. Initiating BUP in ED patients with lower COWS score is appealing because it leverages the "teachable moment" of the ED experience when patients may have a heightened interest in behavior change while avoiding the need to have patients return to the ED later in worse withdrawal, potentially exposing them to increased costs and long ED wait times.

Overall, protocols varied in their listed contraindications to ED-initiated BUP. The most common contraindication was recent methadone use, likely due to the risk of BUP-precipitated withdrawal.[3,24] Other listed contraindications, such as alcohol and/or benzodiazepine withdrawal or use, may be viewed as complicating factors of withdrawal or a misunderstanding of risk.[36] Although SAMHSA listed BUP allergy as its only contraindication, only 4 sites did so in their protocols.[24]

Pregnancy was not a contraindication to ED-initiated BUP in any protocol; however, pregnancy was mentioned in most protocols as a special consideration or as a required lab test before initiation, likely because of prior recommendations to use BUP monotherapy in pregnancy to avoid prenatal exposure to naloxone and to provide appropriate, rapid follow-up.[37] Recent guidelines from the American College of Obstetricians and Gynecologists, SAMHSA, ASAM, and ACEP recommend the use of both BUP monotherapy and combination product in pregnancy given similar outcomes and safety profiles.[3,24,31,37]

4.2 | ED BUP administration

Protocols varied in the initial and total dose of ED BUP administered in the ED to patients in opioid withdrawal. For patients with clinical signs of opioid withdrawal, most protocols suggest administering 4–8 mg of BUP independent of initial COWS score. Most protocols that used tiered scoring used a COWS vof <13 as a proxy for mild withdrawal and a COWS score of 13 or higher as a proxy for moderate or severe withdrawal. Among those protocols, most would administer 4 mg for a lower COWS range and 8 mg for a higher COWS range. These initiation doses differ from what is suggested by both SAMHSA and ASAM, which both recommend a lower initial BUP dose of 2–4 mg.[3,24] More recent ED literature has also shown that higher doses of BUP (>12 mg during an ED visit) in patients experiencing opioid withdrawal can be tolerated in select patients. [27,38,39]

Although the lower limit of the COWS for ED initiation differed between protocols, ranging from 5 to 12, most (61%) recommended unobserved (home) initiation for those not in adequate withdrawal for ED BUP initiation. Unobserved BUP initiation has several advantages.[40] It is less resource intensive, requires shorter ED lengths of stay, and adds individual patient flexibility as to how and when to start treatment.[40] One barrier to unobserved initiation for ED patients is the need for a DATA2000 X-waivered clinician to prescribe BUP that may not be available 24/7 in many EDs; however, the new Practice Guideline by the Department of Health and Human Services decreases this barrier substantially by allowing those who treat up to 30 patients to submit an alternative notification of intent in place of the required waiver training.[41] Patient-level barriers are also a factor including the need for transportation to the pharmacy to pick up the medications, lack of valid identification, medication preauthorization, or lack of insurance altogether. The ED INNOVATION randomized controlled trial seeks to test if these patient- and clinician-level barriers to follow-up care are affected by different formulation of buprenorphine such as a long acting 7-day injectable BUP compared to the standard sublingual preparation.[28]

For patients initiated on BUP in the ED with continued withdrawal symptoms after the first BUP dose, most protocols recommended an additional 4–8 mg of BUP, with only a few suggesting higher additional doses of 12 mg or greater. In total, most protocols set the maximum ED BUP dose to 16 mg, although the range was wide at 8 mg to 32 mg. Although 8 mg of BUP for withdrawal was the day 1 limit set by the Food and Drug Administration label for Suboxone (buprenorphine/naloxone), studies have ended day 1 of BUP on a higher total dose.[27,38,39,42] Although the ideal indications for and safety of higher day 1 doses of BUP in patients coming to the ED is under investigation, a higher maximum BUP dose may be beneficial not only for withdrawal relief but also for patients with barriers to follow-up care such as prolonged wait time for postdischarge follow-up or prior authorizations.[27,30] On the whole, variability in initial and maximum ED doses of BUP and the timing between doses in ED BUP initiation protocols underscore both the flexibility of BUP initiation across different EDs settings and a lack of consensus on best practices.

Lastly, although precipitated withdrawal is a rare event, only 10 (32%) protocols provided guidelines on how to manage these occurrences.[21] Half of those protocols recommended additional BUP and the other half supportive medications only. Neither SAMHSA TIP 63 or ASAM guidelines contain information on managing precipitated withdrawal.[3,24] ACEP recommends both additional BUP and ancillary medications for targeted symptoms but acknowledges the limited published data on the rapid effectiveness of additional BUP.[31,43]

4.3 | Discharge care

For patients presenting to the ED in mild or no opioid withdrawal, most protocols recommended discharging the patient for unobserved

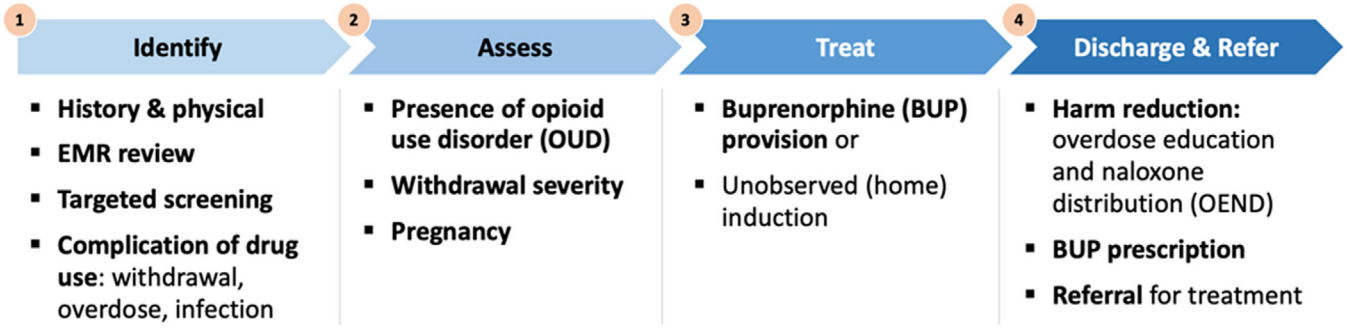

FIGURE 2 Framework for ED-initiated buprenorphine
Abbreviation: EMR, electronic medical record

initiation with BUP.[40,44,45] A few protocols suggested holding a patient with a low COWS score in the ED until withdrawal worsens. Given that EDs have been faced with increased crowding and boarding times, this strategy could compound existing logistical challenges that have already been shown to result in worse objective clinical end points.[46,47]

For patients initiated on BUP in the ED, most protocols recommended prescribing 16 mg of BUP per day on subsequent days regardless of the dose the patient received in the ED. This dose recommendation is consistent with ASAM recommendations of a daily treatment dose of at least 16 mg and SAMHSA recommendations of 4–24 mg.[3,24] It is concerning that some protocols neither mentioned providing a BUP prescription at discharge nor specified a treatment duration (ie, days of coverage with the prescription). Post-ED discharge is a tenuous time for many patients with OUD, especially those who were treated for a non-fatal opioid overdose.[48,49] During this time, it is critically important that patients amenable to treatment are provided with sufficient medication until they can be linked to comprehensive addiction treatment. Providing BUP for these patients can both treat their OUD and help prevent recurrent overdose.[50] In combination with BUP, the provision of naloxone and harm reduction education are essential program components to provide at discharge to improve patient safety, reduce overdose death, and prevent injection and drug use complications such as hepatitis and HIV.[51,52] Most protocols did mention the provision or prescribing of naloxone, a recommended best practice.[53,54] Conversely, very few protocols mentioned other risk reduction measures such as education on safe injection practices.

4.4 | Summary and recommendations for protocol development

In summary, the ED is a unique setting in which to treat patients with OUD. In fact, some have argued that withholding care for those with substance use disorders in the ED is a violation of federal law.[55]

Our study aimed to describe the landscape of ED-initiated BUP protocols in a geographically diverse sample of EDs in the United States. Protocols differed regarding identification of treatment-eligible patients, ED BUP administration, and discharge care, demonstrating both the flexibility of BUP initiation in the ED setting and the realities of carving out a lifesaving strategy with little previous guidance.

Although variation existed across the 31 protocols, most used a similar flow of patients from ED presentation to discharge. We therefore recommend the following evidence-based framework (Figure 2), consistent with the recently released ACEP *Consensus Recommendations on the Treatment of Opioid Use Disorder in the Emergency Department*[56]: (1) identification of patients; (2) Assessment of OUD, withdrawal severity, and pregnancy; (3) treatment with buprenorphine initiation or instructions for unobserved (home) induction; and (4) discharge with overdose education and naloxone distribution, buprenorphine prescription, and referral for follow-up care.

Different EDs may tailor the specifics of each step of the framework to the unique needs of their ED, which is reflected in the variability demonstrated across the 31 protocols. Current and future research should evaluate how variations in screening techniques, BUP dosing, and harm reduction strategies affect patient outcomes and support dissemination of ED-BUP initiation practices to continue to drive innovation that improves patient outcomes.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Ethan Cowan and Clara Zhang Guo conceived and designed the study methods with input from all authors. Clara Zhang Guo and Ethan Cowan reviewed all protocols, David Fiellin arbitrated discrepancies, and Clara Zhang Guo analyzed the data once aligned upon. Clara Zhang Guo and Ethan Cowan drafted the manuscript, and all authors

contributed to revisions. Clara Zhang Guo takes responsibility for the paper.

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WEB APPENDIX A

Extraction Elements for ED Buprenorphine Initiation Protocol Survey	
Identification of treatment-eligible patients	a. Inclusion criteria that must be met before ED BUP administration: OUD determination, active withdrawal, and time since last opioid use b. Minimum COWS value before ED BUP initiation c. Absolute contraindications to ED BUP d. Other required evaluations (pregnancy determination, other labs) e. Screening guidelines for patient identification f. f) Involvement of ancillary staff, such as social work, care managers, and peer counselors, for patient identification and/or care coordination
Buprenorphine administration	a. BUP dosing b. Time frame between BUP dose 1 and 2 for signs and symptoms of worsening withdrawal c. Maximum total BUP dose either explicitly written or calculated by observers based on the site's dosage escalation protocol d. Presence and details of precipitated withdrawal guidelines e. e) Use of ancillary medications
Discharge care	a. The presence of a policy in place for low COWS score b. Provision of home induction instructions c. BUP prescription at discharge d. Naloxone provision and/or prescription e. e) Harm reduction education including overdose instructions or other support pamphlets