

UC Irvine

Western Journal of Emergency Medicine: Integrating Emergency Care with Population Health

Title

Methadone Initiation in the Emergency Department for Opioid Use Disorder

Permalink

<https://escholarship.org/uc/item/5x22m436>

Journal

Western Journal of Emergency Medicine: Integrating Emergency Care with Population Health, 25(5)

ISSN

1936-900X

Authors

Wolfson, Daniel

King, Roz

Lamberson, Miles

et al.

Publication Date

2024-08-01

DOI

10.5811/westjem.18530

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

Methadone Initiation in the Emergency Department for Opioid Use Disorder

Daniel Wolfson, MD*

Roz King, MSN*

Miles Lamberson, BA*

Jackson Lyttleton, BS*

Colin T. Waters, MD, PhD*

Samantha H. Schneider, MS[†]

Blake A. Porter, PharmD[‡]

Kyle M. DeWitt, PharmD[‡]

Peter Jackson, MD^{§||}

Martha W. Stevens, MD, MSCE*

John Brooklyn, MD^{§¶}

Richard Rawson, PhD^{||#}

Elly Riser, MD, MPH**

*University of Vermont Larner College of Medicine, Department of Emergency Medicine, Burlington, Vermont

[†]Rush University Medical Center, College of Medicine, Chicago, Illinois

[‡]The University of Vermont Medical Center, Department of Pharmacy, Burlington, Vermont

[§]University of Vermont Larner College of Medicine, Department of Psychiatry, Burlington, Vermont

^{||}University of Vermont, Vermont Center for Behavior and Health, Center on Rural Addiction, Burlington, Vermont

[¶]University of Vermont Larner College of Medicine, Department of Family Medicine, Burlington, Vermont

[#]University of California Los Angeles School of Medicine, Los Angeles, California

**University of Vermont Larner College of Medicine, Department of Medicine, Burlington, Vermont

Section Editor: Marc Martel, MD

Submission history: Submitted October 26, 2023; Revision received April 23, 2024; Accepted April 29, 2024

Electronically published August 1, 2024

Full text available through open access at http://escholarship.org/uc/uciem_westjem

DOI: 10.5811/westjem.18530

Introduction: Overdose deaths from high-potency synthetic opioids, including fentanyl and its analogs, continue to rise along with emergency department (ED) visits for complications of opioid use disorder (OUD). Fentanyl accumulates in adipose tissue; although rare, this increases the risk of precipitated withdrawal in patients upon buprenorphine initiation. Many EDs have implemented medication for opioid use disorder (MOUD) programs using buprenorphine. However, few offer methadone, a proven therapy without the risk of precipitated withdrawal associated with buprenorphine initiation. We describe the addition of an ED-initiated methadone treatment pathway and compared its 72-hour follow-up outpatient treatment engagement rates to our existing ED-initiated buprenorphine MOUD program.

Methods: We expanded our ED MOUD program with a methadone treatment pathway. From February 20–September 19, 2023, we screened 20,504 ED arrivals; 5.1% had signs of OUD. We enrolled 61 patients: 28 in the methadone; and 33 in the buprenorphine pathways. For patients who screened positive for opioid use, shared decision-making was employed to determine whether buprenorphine or methadone therapy was more appropriate. Patients in the methadone pathway received their first dose of up to 30 milligrams (mg) of methadone in the ED. Two additional methadone doses of up to 40 mg were dispensed at the time of the ED visit and held in the department, allowing patients to return each day for observed dosing until intake at an opioid treatment program (OTP). We compared 72-hour rates of outpatient follow-up treatment engagement at the OTP (for those on methadone) or at the addiction treatment center (ATC) (for those on buprenorphine) for the two treatment pathways.

Results: Of the 28 patients enrolled in the methadone pathway, 12 (43%) successfully engaged in follow-up treatment at the OTP. Of the 33 patients enrolled in the buprenorphine pathway, 15 (45%) successfully engaged in follow-up treatment at the ATC (relative risk 1.06; 95% confidence interval 0.60–1.87).

Conclusion: Methadone initiation in the ED to treat patients with OUD resulted in similar 72-hour follow-up outpatient treatment engagement rates compared to ED-buprenorphine initiation, providing another viable option for MOUD. [West J Emerg Med. 2024;25(5)668–674.]

BACKGROUND

The opioid crisis in the United States continues unabated with 106,699 drug-involved fatalities in 2021, primarily involving illicitly manufactured high-potency synthetic opioids, and is further complicated by adulterants such as xylazine and gabapentin.¹⁻⁶ Individuals with opioid use disorder (OUD) face the highest risk of death within the first 48 hours following an ED (emergency department) visit for a non-fatal overdose.⁷ The ED identification of patients with OUD and initiation of buprenorphine treatment has proven effective and is supported by the American College of Emergency Physicians and the California Bridge network of hospitals.⁸⁻¹² However, the rising prevalence of fentanyl in the illicit drug supply complicates treatment due to its accumulation in adipose tissue, potentially causing precipitated withdrawal upon buprenorphine initiation.¹³⁻¹⁵ Additionally, abstaining from fentanyl for the required pre-induction period may be difficult for some, leading them to avoid further buprenorphine or favor methadone for their medication for OUD (MOUD).¹⁶⁻²⁰ Methadone, a synthetic full mu-opioid receptor agonist, avoids these complications, as it does not precipitate withdrawal.^{21,22} In response, the University of Vermont Medical Center (UVM) enhanced its existing Start Treatment and Recovery (STAR) program, an ED-based initiative to initiate MOUD in patients with OUD. Originally focused on buprenorphine, the program was expanded to include methadone, adapting to the shifting landscape of opioid use and patient needs. We describe the implementation of an ED-initiated methadone treatment pathway, comparing its 72-hour follow-up outpatient treatment engagement rates to our existing ED-initiated buprenorphine MOUD program.

METHODS

We performed an open trial comparing two MOUD treatment pathways where patients in the ED who met OUD criteria and agreed to treatment chose between initiation onto buprenorphine or methadone. From February 20–September 19, 2023 we screened charts of 20,504 ED arrivals, with 1,051 (5.1%) having signs of OUD. Of these, 903 were determined ineligible, 43 patients declined treatment, and six patients eloped. Patients declining participation due to time constraints or deemed unsuitable for the study at clinician discretion were excluded. Enrollment to initiate MOUD in the STAR program was completed for 61 patients with 28 initiated on methadone and 33 on buprenorphine. Not included in this analysis were an additional 38 patients who were enrolled in STAR but admitted to the hospital (Figure 1). The STAR program coordinators screened patient charts from 9 AM to 9 PM daily and remained on call for enrollments 24/7. They approached identified patients to confirm opioid use, eligibility, and interest in starting MOUD.

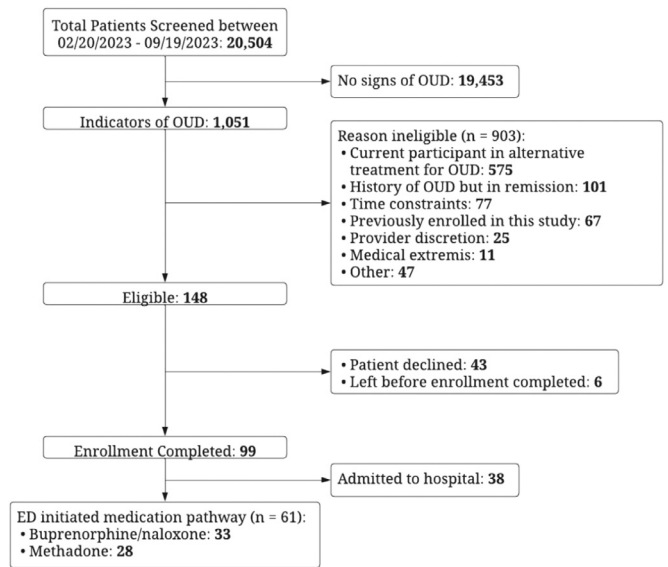


Figure 1. Flow chart of screening of emergency department patients and enrollment in a STAR (start treatment and recovery) program. February 20–September 19, 2023. ED, emergency department; OUD, opioid use disorder.

An emergency clinician then used the *Diagnostic and Statistical Manual of Mental Disorders*, 5th Ed, criteria to confirm the diagnosis of OUD and assess readiness for treatment. Shared decision-making was used to decide on the most appropriate MOUD treatment pathway: methadone or buprenorphine/naloxone. This process involved a discussion between the clinician and the patient that included a review of the risks and benefits of each medication, the severity of OUD, the patient’s prior experience/preference, and clinical factors such as drug interactions or QT prolongation. We compared rates of 72-hour follow-up treatment engagement at the opioid treatment program (OTP) (for those on methadone) or at the UVM Addiction Treatment Center (ATC) (for those on buprenorphine) for the two treatment pathways using a chi-square test Stata/SE 18.0 (StataCorp, College Station, TX).

Patients signed a disclosure agreement allowing access to their electronic health record, which was sent to the OTP/ATC via secure email. Patients received details about their outpatient treatment appointment and were provided with transportation vouchers and a cell phone, when necessary. Patients were linked to an ED peer recovery coach who engaged with them during their ED visit and continued support through phone calls for up to 10 days following discharge.

Methadone Treatment Pathway: Patients receiving methadone were given the standard US Food and Drug Administration-recommended starting dose of 30 milligrams (mg) orally with subsequent dosing of 40 mg on the following days if bridging doses were required until the OTP appointment.²³ The initial dose was reduced to 20 mg for patients with known opioid use in the prior four hours, if they

were currently using other sedatives, or with relevant drug interactions. Methadone was not offered if the patient had a respiratory rate <10 breaths/minute, an allergy to methadone, end-stage liver disease, medical extremis, or a known QTc ≥ 500 milliseconds. Electrocardiograms were not routinely required but were obtained for risk factors in patient history or medications. Basic labs and urine drug screen were obtained. Patients were instructed to follow up at the OTP the next business day. If a patient was initiated on methadone on a weekend or holiday, the appropriate number of additional methadone doses were dispensed and held in a lock box in the ED for observed dosing. The patient was

instructed to return to the ED to receive follow-up doses. Patients returning for re-dosing were not required to check in as an ED patient but were given their methadone dose, observed, and documented by a nurse using a scripted template (Figure 2).²⁴

Buprenorphine/naloxone Treatment Pathway: For patients receiving buprenorphine, the Clinical Opioid Withdrawal Scale (COWS) guided dosing strategies. Patients with a COWS score <8 underwent home initiation. For scores of 8–11, initiation in the ED with 8 mg buprenorphine/naloxone was provided, and for scores >12, a 16 mg dose was administered. All patients received a take-home starter pack with a three-day

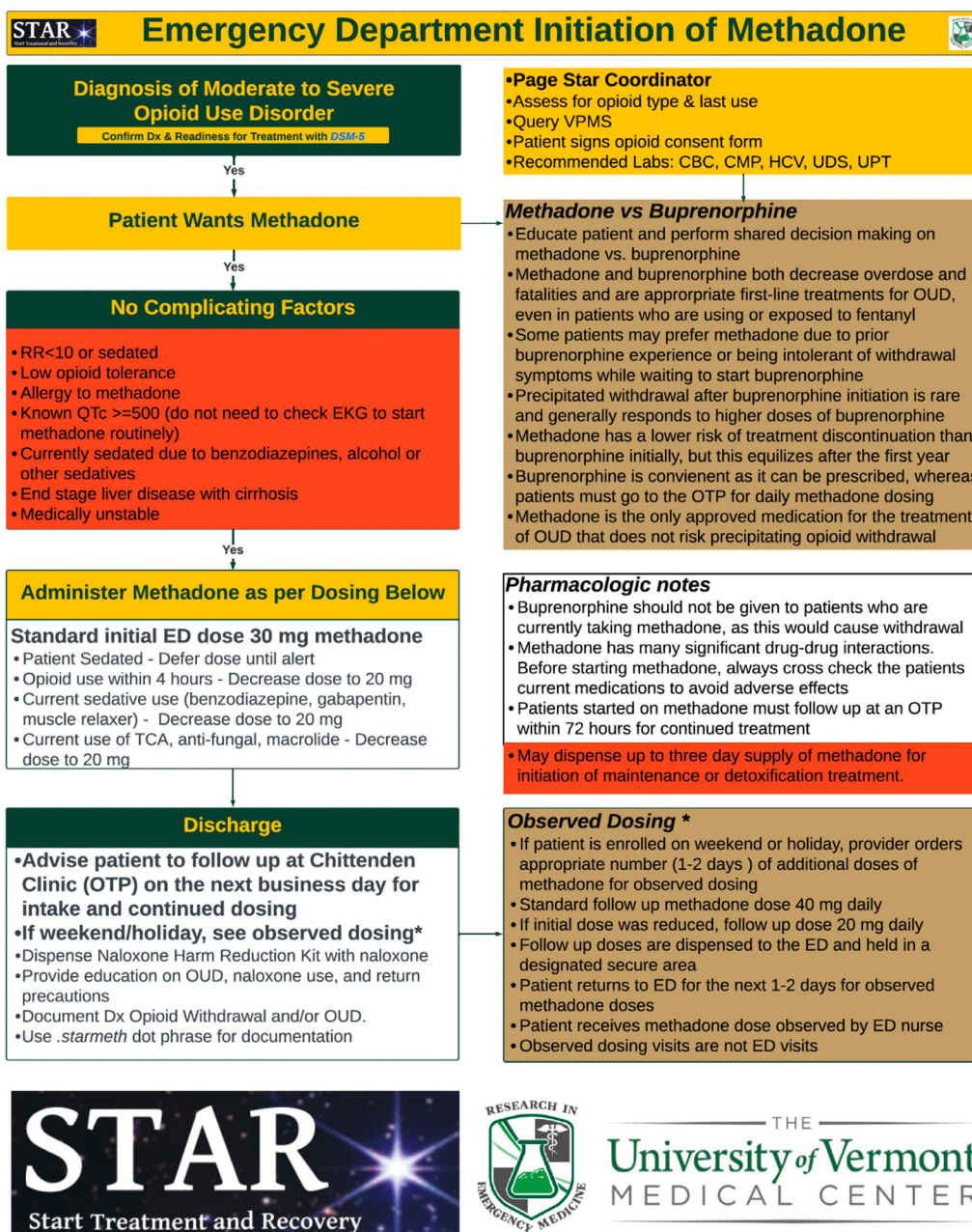


Figure 2. Emergency department initiation of methadone and STAR (start treatment and recovery) pathway.

supply of buprenorphine/naloxone and a follow-up appointment at the ATC within 72 hours (Figure 3).²⁵

Institutional Review Board Review: The University of Vermont Research Protections Office deemed this project to meet criteria for research not requiring review.

RESULTS

Patients enrolled in the methadone or buprenorphine pathways had similar demographics with no significant differences between groups by gender, race, ethnicity, age, mode of ED arrival, or ED disposition. Of the 28 patients in the methadone pathway, 12 (43%) attended the OTP for

ongoing methadone treatment. Of the 33 patients enrolled in the buprenorphine pathway, 15 (45%) attended the ATC for ongoing buprenorphine/ naloxone treatment. The 72-hour rates of successful follow-up outpatient treatment engagement for patients enrolled in the methadone vs buprenorphine pathways were not significantly different (relative risk 1.06; 95% confidence interval CI, 0.60–1.87).

DISCUSSION

We enhanced our ED’s existing buprenorphine-based MOUD program by incorporating a treatment pathway



Figure 3. Emergency department initiation of buprenorphine STAR (start treatment and recovery) pathway.

for initiating methadone. Our findings show that ED-initiation of methadone for OUD is practical and achieves 72-hour follow-up outpatient treatment engagement rates comparable to those of buprenorphine. While previous case studies have documented successful initiation of methadone in the ED, we are one of the first to systematically report on the implementation of a clinical practice pathway for methadone initiation in the ED followed by linkage to ongoing care.^{22,26} Traditionally, methadone has not been used in the ED due to the potential to cause fatal respiratory depression if given in doses exceeding an individual's tolerance; however, the ED is an ideal location to safely monitor patients during methadone initiation.²⁷ Previous federal regulations had restricted the use of methadone to treat OUD to licensed OTPs in the outpatient setting.²⁸ The Easy Medication Access and Treatment for Opioid Addiction Act improved the flexibility of MOUD by allowing practitioners to dispense up to a three-day supply of narcotics, including methadone, for the purpose of initiating maintenance or detoxification treatment.^{29–33}

Patients prefer selecting the optimal treatment pathway through shared decision-making, which involves a thorough comparison of the advantages and disadvantages of buprenorphine vs methadone. This approach fosters informed and collaborative healthcare choices and potentially leads to improved outcomes and adherence.^{22,34} We found most patients will directly say which treatment pathway they prefer due to past experiences of treatment and precipitated withdrawal. Buprenorphine is advantageous and preferred as it is logistically easier to take: there is less risk of respiratory depression; the patient can receive take-home medications and prescriptions; and care can ultimately be managed by the patient's primary care physician without daily trips to the methadone clinic for dosing.¹⁹ However, patients who have experienced buprenorphine-precipitated withdrawal or who cannot tolerate cessation of fentanyl for the required pre-buprenorphine induction time (often 72 hours or longer) may benefit from methadone.³⁵

Although surveys from other institutions indicate physicians have more comfort initiating buprenorphine over methadone (88% vs 45%), our experience shows clinicians readily adopting the methadone treatment pathway.³⁶ To foster clinician acceptance of ED MOUD, we implemented several strategies: sharing testimonials from our ED peer recovery coaches; facilitating one-on-one discussions between project champions and clinicians; and leveraging direct clinical experience. These approaches align with existing research, which demonstrates increased exposure to impacted populations effectively reduces stigma towards them.³⁷ Overcoming these barriers enhanced treatment options through the successful

implementation of a methadone initiation pathway for ED patients with OUD.

LIMITATIONS

Limitations of this study include a small sample size that restricts the generalizability of results and impacts statistical significance. Additionally, the absence of long-term outcome data, such as six-month follow-up metrics, limits insights into the intervention's effectiveness. The exclusion of patients concurrently enrolled in other treatment programs introduced selection bias, potentially affecting the study's applicability to the wider OUD population. Finally, individual clinician biases may have influenced both participant selection and treatment choice, potentially affecting study outcomes.

CONCLUSION

ED initiation of methadone for patients with opioid use disorder is practical, achieves 72-hour follow-up treatment engagement rates comparable to those of buprenorphine treatment, and provides another option for MOUD that benefits some patients.

Address for Correspondence: Daniel Wolfson, MD, University of Vermont Larner College of Medicine, Department of Emergency Medicine, 111 Colchester Ave., Burlington, VT 05401. Email: Daniel.Wolfson@uvmhealth.org

Conflicts of Interest: By the WestJEM article submission agreement, all authors are required to disclose all affiliations, funding sources and financial or management relationships that could be perceived as potential sources of bias. This study was funded by the Substance Abuse and Mental Health Services Administration (SAMHSA) 1H79TI085330 and the 2019 University of Vermont Health Network Innovation Grant. There are no other conflicts of interest or sources of funding to declare.

Copyright: © 2024 Wolfson et al. This is an open access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) License. See: <http://creativecommons.org/licenses/by/4.0/>

REFERENCES

1. Spencer MR, Miniño AM, Warner M. Drug overdose deaths in the United States, 2001–2021. 2022. Available at: <https://www.cdc.gov/nchs/products/databriefs/db457.htm>. Accessed March 23, 2023.
2. National Institute on Drug Abuse. Drug overdose death rates. 2023. Available at: <https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>. Accessed March 23, 2023.
3. O'Donnell J, Tanz LJ, Gladden RM, et al. Trends in and characteristics of drug overdose deaths involving illicitly manufactured fentanyl - United States, 2019–2020. *MMWR Morb Mortal Wkly Rep*. 2021;70(50):1740–6.

4. Mattson CL. Notes from the field: trends in gabapentin detection and involvement in drug overdose deaths — 23 states and the District of Columbia, 2019–2020. *Morb Mortal Wkly Rep.* 2022;71(19):664–6.
5. Kariisa M, Patel P, Smith H, et al. Notes from the field: xylazine detection and involvement in drug overdose deaths - United States, 2019. *Morb Mortal Wkly Rep.* 2021;70(37):1300–2.
6. Friedman J, Montero F, Bourgois P, et al. Xylazine spreads across the US: a growing component of the increasingly synthetic and polysubstance overdose crisis. *Drug Alcohol Depend.* 2022;233:109380.
7. Weiner SG, Baker O, Bernson D, et al. One-year mortality of patients after emergency department treatment for nonfatal opioid overdose. *Ann Emerg Med.* 2020;75(1):13–7.
8. Hawk K, Hoppe J, Ketcham E, et al. Consensus recommendations on the treatment of opioid use disorder in the emergency department. *Ann Emerg Med.* 2021;78(3):434–42.
9. Herring AA. Postoverdose initiation of buprenorphine after naloxone-precipitated withdrawal is encouraged as a standard practice in the California Bridge network of hospitals. *Ann Emerg Med.* 2020;75(4):552–3.
10. Snyder H, Kalmin MM, Moulin A, et al. Rapid adoption of low-threshold buprenorphine treatment at California emergency departments participating in the CA Bridge program. *Ann Emerg Med.* 2021;78(6):759–72.
11. D'Onofrio G, O'Connor PG, Pantalon MV, et al. Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial. *JAMA.* 2015;313(16):1636–44.
12. Bogan C, Jennings L, Haynes L, et al. Implementation of emergency department-initiated buprenorphine for opioid use disorder in a rural southern state. *J Subst Abuse Treat.* 2020;112S:73–8.
13. Huhn AS, Hobelmann JG, Oyler GA, et al. Protracted renal clearance of fentanyl in persons with opioid use disorder. *Drug Alcohol Depend.* 2020;214:108147.
14. Comer SD and Cahill CM. Fentanyl: receptor pharmacology, abuse potential, and implications for treatment. *Neurosci Biobehav Rev.* 2019;106:49–57.
15. D'Onofrio G, Hawk KF, Perrone J, et al. Incidence of precipitated withdrawal during a multisite emergency department-initiated buprenorphine clinical trial in the era of fentanyl. *JAMA Netw Open.* 2023;6(3):e236108.
16. Shearer D, Young S, Fairbairn N, et al. Challenges with buprenorphine inductions in the context of the fentanyl overdose crisis: a case series. *Drug Alcohol Rev.* 2022;41(2):444–8.
17. Spadaro A, Faude S, Perrone J, et al. Precipitated opioid withdrawal after buprenorphine administration in patients presenting to the emergency department: a case series. *J Am Coll Emerg Physicians Open.* 2023;4(1):e12880.
18. Sue KL, Cohen S, Tilley J, et al. A plea from people who use drugs to clinicians: new ways to initiate buprenorphine are urgently needed in the fentanyl era. *J Addict Med.* 2022;16(4):389–91.
19. Schoenfeld EM, Westafer LM, Beck SA, et al. “Just give them a choice”: patients’ perspectives on starting medications for opioid use disorder in the ED. *Acad Emerg Med.* 2022;29(8):928–43.
20. Varshneya NB, Thakrar AP, Hobelmann JG, et al. Evidence of buprenorphine-precipitated withdrawal in persons who use fentanyl. *J Addict Med.* 2022;16(4):e265–8.
21. Bart G. Maintenance medication for opiate addiction: the foundation of recovery. *J Addict Dis.* 2012;31(3):207–25.
22. Church B, Clark R, Mohn W, et al. Methadone induction for a patient with precipitated withdrawal in the emergency department: a case report. *J Addict Med.* 2023;17(3):367–70.
23. Substance Abuse and Mental Health Services Administration (SAMHSA). Tip 63: medications for opioid use disorder. 2021. Available at: <https://store.samhsa.gov/product/tip-63-medications-opioid-use-disorder/pep21-02-01-002>. Accessed February 21, 2024.
24. CA Bridge. Methadone hospital quick start. 2023. Available at: <https://cabridge.org/resource/methadone-hospital-quick-start/>. Accessed May 11, 2023.
25. CA Bridge. Buprenorphine emergency department quick start. 2023. Available at: <https://bridgetotreatment.org/resource/buprenorphine-bup-hospital-quick-start/>. Accessed April 8, 2024.
26. Huo S, Heil J, Salzman MS, et al. Methadone initiation in the emergency department for opioid use disorder: a case series. *J Emerg Med.* 2023;64(3):391–6.
27. Bart G. Maintenance medication for opiate addiction: the foundation of recovery. *J Addict Dis.* 2012;31(3):207–25.
28. Subpart C—Certification and treatment standards for opioid treatment programs. Available at: https://www.govregs.com/regulations/expand/title42_chapterI_part8_subpartC_section8.12. Accessed May 12, 2023.
29. Drug Enforcement Administration. Dispensing of narcotic drugs to relieve acute withdrawal symptoms of opioid use disorder. 2023. Available at: <https://www.federalregister.gov/documents/2023/08/08/2023-16892/dispensing-of-narcotic-drugs-to-relieve-acute-withdrawal-symptoms-of-opioid-use-disorder>. Accessed September 21, 2023.
30. Laks J, Kehoe J, Farrell NM, et al. Methadone initiation in a bridge clinic for opioid withdrawal and opioid treatment program linkage: a case report applying the 72-hour rule. *Addict Sci Clin Pract.* 2021;16(1):73.
31. 21 CFR 1306.07—Administering or dispensing of narcotic drugs. 2024. Available at: <https://www.ecfr.gov/current/title-21/chapter-II/part-1306/subject-group-ECFR1eb5bb3a23fddd0/section-1306.07>. Accessed April 3, 2023.
32. Drug Enforcement Administration. DEA’s commitment to expanding access to medication-assisted treatment. 2022. Available at: <https://www.dea.gov/press-releases/2022/03/23/deas-commitment-expanding-access-medication-assisted-treatment>. Accessed April 3, 2023.
33. BILLS-116hr2281rfs.pdf. 2020. Available at: <https://www.govinfo.gov/content/pkg/BILLS-116hr2281rfs/pdf/BILLS-116hr2281rfs.pdf>. Accessed April 3, 2023.

34. Yarborough BJH, Stumbo SP, McCarty D, et al. Methadone, buprenorphine and preferences for opioid agonist treatment: a qualitative analysis. *Drug Alcohol Depend.* 2016;160:112–8.
35. Silverstein SM, Daniulaityte R, Martins SS, et al. “Everything is not right anymore”: buprenorphine experiences in an era of illicit fentanyl. *Int J Drug Policy.* 2019;74:76–83.
36. Heil J, Ganetsky VS, Salzman MS, et al. Attitudes on methadone utilization in the emergency department: a physician cross-sectional study. *West J Emerg Med.* 2022;23(3):386–95.
37. Corrigan PW and Nieweglowski K. Stigma and the public health agenda for the opioid crisis in America. *Int J Drug Policy.* 2018;59:44–9.