Alcohol, Other Drugs, and Health: Current Evidence

JULY-AUGUST 2025

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Grayken Center for Addiction
Boston Medical Center

INTERVENTIONS & ASSESSMENTS

Both Oral and Extended-release Injectable Naltrexone Effective for Alcohol Use Disorder When Initiated at Hospital Discharge

Patients with alcohol use disorder (AUD) are frequently hospitalized, but the vast majority do not receive medication for AUD (MAUD) at discharge. Starting MAUD in the hospital can help to address this treatment gap. Naltrexone is an effective treatment for AUD, but there are no trials comparing the oral and long-acting injectable (LAI) formulations among patients being discharged from general medical hospitals. In this open-label, randomized clinical trial conducted at an urban academic hospital in Massachusetts, 2016–2020, investigators compared oral with LAI naltrexone administered on discharge to hospitalized patients with AUD. The primary outcome was percentage of heavy drinking days (HDD) in the last 30 days at three-month follow up, assessed via self-report and alcohol biomarkers derived from blood specimens.

- Of 248 patients randomized, 217 (88 percent) completed the three-month follow up; 199 patients were male, the mean age was 49 years, and 116 were unhoused (i.e., ≥1 night in the last three months).
- At three-month follow-up, there was a significant decline in percentage of HDD from baseline among patients receiving oral (-38 percent) and LAI naltrexone (-46 percent); the difference between the two formulations was not significant.
- The difference in odds of hospitalization or ED visit over the three months for oral versus LAI naltrexone was not significant.

Comments: This study confirmed that naltrexone decreases HDD, and that initiating naltrexone on hospital discharge is feasible and effective. The similar efficacy of the oral and LEI naltrexone formulations emphasizes the importance of tailoring medication recommendations to patient preference, availability, cost, and post-discharge follow-up logistics.

Elliott Brady, MD, MPH* & Darius A. Rastegar, MD

* 2024–2025 Rich Saitz Editorial Intern & Addiction Medicine Fellow, Montefiore Einstein Addiction Medicine Fellowship Program

Reference: Magane KM, Dukes KA, Fielman S, et al. Oral vs extended-release injectable naltrexone for hospitalized patients with alcohol use disorder: a randomized clinical trial. *JAMA Intern Med*. 2025; 185(6):635–645.

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HEALTH OUTCOMES

Two Studies Investigate the Impact of Buprenorphine Dose and Duration Among Pregnant Patients With Opioid Use Disorder

In the US, opioid use disorder (OUD) during the perinatal period contributes to substantial maternal morbidity and mortality and adverse neonatal outcomes, including neonatal opioid withdrawal syndrome (NOWS). Medications for OUD, buprenorphine and methadone, are the standard of care for pregnant patients with OUD. However, real-world data on the impact of buprenorphine dose and consistency of administration throughout pregnancy are limited. Two recent observational studies examined associations between buprenorphine dose during pregnancy and neonatal and/or maternal outcomes.

In France, Marc et al conducted a retrospective electronic health record analysis of 75 non-preterm infants (³37 weeks gestation) admitted to two neonatal intensive care units (NICU) for treatment of NOWS (Lipsitz score of ≥4), born to mothers treated with buprenorphine during pregnancy, 2010–2020.

- The infants were grouped into three antenatal buprenorphine dose exposure categories: high-dose (³12mg), low-dose (2–11mg), and very low-dose (<2 mg).
- Duration of NOWS, hospital length of stay, and required total amount of morphine to treat NOWS were all significantly higher among infants whose mothers received high-dose buprenorphine, compared with those who received low or very low doses.

In the US, Jarlenski et al conducted a retrospective analysis of Pennsylvania Medicaid administrative data of 2925 pregnant patients with an OUD diagnosis, a live birth, and two or more buprenorphine prescriptions during pregnancy or postpartum, 2009–2019. Patients who received methadone were excluded.

- Group-based trajectory modeling identified eight patient longitudinal buprenorphine dose and duration trajectories.
- Compared with patients receiving higher and longer-duration buprenorphine doses initiated pre-pregnancy and continued (mean daily dose, 22.35 mg), those who initiated or discontinued buprenorphine during pregnancy were more likely to have discontinued buprenorphine 90-days postpartum and more likely to have experienced a non-fatal overdose.
- Receipt of high-dose buprenorphine and for longer duration during pregnancy was not associated with increased odds of neonatal abstinence syndrome or low infant birth weight, compared with receipt of moderate (mean daily dose, 14.76 mg) or low-dose (mean daily dose, 6.97 mg) buprenorphine initiated pre-pregnancy, or with shorter treatment duration.

Comments: Buprenorphine should be continued in patients with OUD who are pregnant and postpartum. The dose may need to be increased or adjusted (split) due to physiologic changes resulting from pregnancy using a patient-centered approach. In France, it is typical for lower doses of buprenorphine to be used, and fentanyl appears to minimally contribute to the nation's drug supply and overdoses; fentanyl emerged in Pennsylvania in 2017. In Marc et al, NOWS was determined and monitored using the Lipsitz score, while in the US, standard of care is moving from the Finnegan Neonatal Abstinence Scoring Tool (FNAST) to the Eat, Sleep, Console (ESC) care approach. Use of ESC, a function-based approach, results in shorter hospital lengths of stay and lower pharmacologic interventions for neonates with NOWS.

Ximena A. Levander, MD

References: Marc B, Marion D, François B, Lakshmipriya L. Is buprenorphine maternal dose associated with neonatal opioid withdrawal syndrome severity? *Am J Addict.* 2025;34(1):15–20.
Jarlenski M, LoCiganic WH, Chen Q, et al. Association between buprenorphine dose and outcomes among pregnant persons with opioid use disorder. *Am J Obstet Gynecol.* 2025;233(1):59.e1-59.e15.

Split Dosing of Methadone During Pregnancy Improves Outcomes

Methadone has been shown to improve outcomes for pregnant persons with opioid use disorder (OUD) and their newborns. Physiologic changes during pregnancy alter the metabolism of methadone, so it is often split into two or three doses when administered to pregnant patients. Researchers conducted a systematic review of studies looking at split dosing of methadone during pregnancy to evaluate the impact on maternal, fetal, and neonatal outcomes.

- Eight studies were included in this analysis: one case study, three case series, three cohort studies, and one clinical trial.
- Two studies demonstrated increased methadone clearance and metabolism during pregnancy.
- Two studies looked at fetal measures with split dosing compared with single dosing and reported improved outcomes.
- Four studies looked at measures of maternal drug use with split dosing and reported improved outcomes.
- Four studies looked at neonatal outcomes and observed no increase in adverse outcomes with higher doses or split dosing.

Comments: This review shows that the evidence is sparse, but it supports the practice of split dosing of methadone during pregnancy among people with OUD.

Darius A. Rastegar, MD

Reference: Khan NZ, Hand DJ, Qian E, et al. Split-dosing of methadone during pregnancy and postpartum period: a systematic review of outcomes. *J Addict Med*. 2025 [Epub ahead of print]. doi:10.1097/ADM.0000000000001470.

Higher Methadone Doses at Day Seven Associated With Improved Opioid Treatment Program Retention at Day 30

Methadone is an effective treatment for opioid use disorder and higher doses are associated with improved treatment retention. However, the optimal dosing strategy during treatment induction has not been established. Recent reports suggest that more rapid up-titration during hospital admission is safe and effective, but there is less evidence to support this approach in the outpatient setting. This study assessed data from a network of 64 opioid treatment programs in the US between 2020 and 2023, using binary logistic regression to investigate the association between methadone dose at day seven of treatment and 30-day treatment retention.

- The cohort included 14,489 participants; the overall 30-day retention rate was 88 percent.
- Participants who were younger, male, and unemployed were less like to be retained in treatment for 30 days or longer.
- Analyses demonstrated a significant dose-response relationship, with higher day-seven doses predicting increased 30-day treatment retention (91 percent among patients receiving ≥70 mg methadone on day seven, versus 80 percent among those receiving <30 mg).

Comments: This study adds to other reports supporting more rapid up-titration of methadone when initiating treatment. The main concern is patient safety (i.e., overdose risk) during treatment initiation, which this study did not assess. We need more research to find the right balance between efficacy and safety.

Darius A. Rastegar, MD

Reference: Sherrick RC. Relationship between methadone induction dosing and retention in treatment in opioid treatment programs. *J Addict Med*. 2025 [Epub ahead of print]. doi:10.1097/ADM.0000000000001473.

Hospital Addiction Consultations Associated With Increased Receipt of Medications for Opioid and Alcohol Use Disorder and Reduced Hospital Readmission

Substance use disorder (SUD) often causes and complicates hospitalization and is associated with increased readmission rates. Addiction consultation services have the potential to increase medication initiation for SUD and improve outcomes. This observational study at a US academic medical center from 2019 to 2023 evaluated the association between addiction consultation and initiation and continuation of medications for opioid and alcohol use disorder (MOUD/MAUD), and the association between consultation and medication provision with 30-day hospital readmission.

- Of 19,697 SUD admissions (10,453 unique patients), 12,792 had AUD, 7795 had OUD, and 2568 had both. Addiction consultation occurred in 43 percent of admissions.
- Among admissions with OUD and addiction consultation, 84 percent had MOUD prescribed during hospitalization, compared with 49 percent without consultation. Among admissions with AUD, 33 percent had inpatient MAUD prescribed, compared with 6 percent without consultation.
- Discharge prescriptions for OUD and AUD were higher for admissions with consultations, although results were less clear for OUD prescriptions because methadone data were not captured.

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Hospital Addiction Consultations Associated With Increased Receipt of Medications for Opioid and Alcohol Use Disorder and Reduced Hospital Readmission *(continued from page 3)*

- The 30-day readmission rate was significantly reduced for admissions with consultation compared with those without (17 percent versus 20 percent; adjusted rate ratio, 0.82). Results were similar for OUD and AUD, and more pronounced for new initiation of medication for SUD.

Comments: This observational study enhances the rationale for hospital addiction consultation by finding associations between consultation and important outcomes. Most study biases would likely disfavor consultation, strengthening these positive findings. The large number of hospitalized patients who might benefit from addiction consultation may preclude the development of comprehensive access to these services and may require dissemination of these practices across services and specialties, especially hospitalists.

Joseph Merrill, MD, MPH

Reference: Lambert E, Regan S, Wakeman SE. The impact of addiction consultation and medication for opioid or alcohol use disorder on hospital readmission. *J Gen Intern Med*. 2025 [Epub ahead of print]. doi: 10.1007/s11606-024-09301-9.

Greater Testing and Oversight of Medical Cannabis is Needed Before It is Rescheduled in the US

The US Department of Health and Human Services has recommended that cannabis be rescheduled from Schedule I to Schedule III given its "currently accepted medical use."* Access to medical cannabis is currently a result of state-level political processes rather than Food and Drug Administration (FDA) approval or clinical guideline development. Due to cannabis's Schedule I status, insurance plans do not cover its certification or purchasing costs. Locations that certify medical cannabis may charge in the hundreds of dollars per visit with subsequent cash-only purchases due to federal financial restrictions. By linking Arkansas claims, physician licensing, and state medical cannabis application data, this study identified qualifying conditions in medical claims data and determined the association between the medical cannabis certifying physician and patient encounters with traditional medical care.

- Within two years of initiation in the state, medical cannabis was approved for 3.4 percent of adult Arkansans by 12.5 percent of medical-licensed physicians.
- Posttraumatic stress disorder and four pain diagnoses were the most frequent qualifying conditions.
- Seven high-volume certifying physicians—each with >1000 certifications and who certified more than a third of all certified Arkansans—demonstrated limited patient contact. Conversely, low-volume certifying physicians had seen and diagnosed a greater proportion of patients with qualifying conditions.

* As defined by the US Drug Enforcement Administration, Schedule I substances have "no currently accepted medical use." Schedule III substances have "a moderate to low potential for physical and psychological dependence."

Comments: These findings suggest that "cash-only payment" certification sites are highly financially beneficial for these physicians, reminiscent of opioid "pill mills." Before cannabis is rescheduled and widely adopted as a medical therapeutic by the FDA, it should undergo appropriate testing, monitoring, and guideline development—like any other medical intervention—to optimize its impact and avoid undesirable outcomes.

Susan L. Calcaterra, MD, MPH, MS

Reference: Thompson JW, Martin B, Goudie A, et al. Arkansas medical marijuana certifications: higher-volume physicians associated with less evidence of care coordination. *Health Aff (Millwood)*. 2025;44(3):351–360.

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About the journal: *ASCP* provides a forum for clinically relevant research and perspectives that contribute to improving the quality of care for people with unhealthy alcohol, tobacco, or other drug use and addictive behaviors across a spectrum of clinical settings.
***ASCP* is the official journal of the Grayken Center for Addiction at Boston Medical Center.**

We are seeking submissions to our upcoming special series:
"Beyond the four walls:
Innovative approaches to promoting equity in addiction treatment"
This Collection seeks to highlight innovative approaches to substance use and substance use disorder (SUD) treatment initiation and sustained care that extend beyond traditional clinical contexts.
The editors are interested in all submissions that address the above goals but would particularly like to encourage research conducted in such settings in the Global South and in countries where research into substance use and SUD care has been historically low.
Submissions are desired by 15 December 2025.

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