Alcohol, Other Drugs, and Health: Current Evidence

JANUARY-FEBRUARY 2025

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Grayken Center for Addiction
Boston Medical Center

INTERVENTIONS & ASSESSMENTS

Semaglutide and Liraglutide Associated with Reduction in Alcohol and Substance Use Disorder-related Hospitalizations

Preliminary research on the effectiveness of GLP-1 agonists for the treatment of substance use disorder (SUD) is raising hope for improved pharmacotherapy. This large Swedish observational cohort study evaluated whether patients with alcohol use disorder (AUD) diagnoses receiving GLP-1 agonists had a lower risk of hospitalization for AUD or SUD, compared with when they were not receiving these medications. Researchers also assessed the risk of hospitalization associated with receipt of medications approved for AUD (i.e., naltrexone, acamprosate, disulfiram).

- The cohort included 227,866 people with an AUD diagnosis, of whom 133,210 experienced AUD-related hospitalization, 138,390 experienced SUD-related hospitalization, and 6726 were prescribed GLP-1 agonists. Median GLP-1 cohort follow-up was 8.8 years.
- Periods of semaglutide and liraglutide receipt were associated with a lower risk of AUD hospitalization, compared with periods when these medications were not prescribed (adjusted hazard ratio [aHR], 0.64 and 0.72, respectively).
- Receipt of both medications was also associated with a lower risk of SUD hospitalization, compared with periods when these medications were not prescribed (aHR, 0.68 [semaglutide] and 0.78 [liraglutide]).
- Receipt of AUD medication in general was not associated with a lower risk of AUD or SUD hospitalization, although receipt of naltrexone was associated with a reduced risk of both (aHR, 0.86 for both).

Comments: This study provides additional rationale for testing GLP-1 agonists for the treatment of AUD. Bias in any comparison of GLP-1 agonists and approved AUD medications would be present if approved AUD medications were initiated at a time of worsening AUD, or if GLP medications were initiated at a time of relative AUD stability, both of which are plausible in this study. Placebo and comparative trials of GLP-1 agonists are needed.

Joseph Merrill, MD, MPH

Reference: Lähteenvuo M, Tiihonen J, Solismaa A, et al. Repurposing semaglutide and liraglutide for alcohol use disorder. *JAMA Psychiatry*. 2025;82(1):94–98.

Alcohol, Other Drugs, and Health: Current Evidence **is a project of the Grayken Center for Addiction at Boston Medical Center, produced in cooperation with Boston University. Initially supported by a grant from the National Institute on Alcohol Abuse and Alcoholism, the newsletter was supported by grant no. R25-DA013582 (PI: Jeffrey Samet) from the National Institute on Drug Abuse (NIDA) until July 2022. The content is solely the responsibility of the authors and does not necessarily represent the official views of Boston Medical Center, NIDA, or the National Institutes of Health.**

Long-acting Injectable Naltrexone and Buprenorphine-naloxone Well-tolerated in Youth With Opioid Use Disorder One Month Post-initiation

Medication for opioid use disorder (MOUD) is prescribed at relatively low rates in youth with OUD. This study examined adverse events one month after initiation of MOUD in youth aged 15–21 who were transitioning from residential to outpatient OUD treatment. Participants (N=199) were categorized into one of three groups based on their residential discharge regimen: no medication (n=71), sublingual buprenorphine-naloxone (n=59), or long-acting injectable naltrexone (LAI-naltrexone; n=69).

- The LAI-naltrexone cohort reported the most adverse events overall; 62 percent experienced an injection site reaction, accounting for 43 percent of total adverse events in this group.
- When excluding injection site reactions (since these were unique in this study to the mode of administering LAI-naltrexone), there was no significant difference between adverse events across groups.
- Nonfatal overdoses occurred in six participants: five in the no medication cohort, one in the buprenorphine-naloxone cohort, and none in the LAI-naltrexone cohort.

Comments: Both sublingual buprenorphine-naloxone and LAI-naltrexone appear to be relatively well-tolerated in youth one-month post-initiation, but MOUD remains underutilized in youth despite proven reduction in opioid-related morbidity and mortality in the general population. These medications should be strongly considered by clinicians when treating adolescents and young adults with OUD. Future studies could focus on assessment of adverse events further down respective treatment timelines.

Emily Nields, DO

Reference: Terplan M, O'Grady KE, Monico LB, et al. Adverse events at 1 month following medication initiation for opioid use disorder among adolescents and young adults. *Subst Use Addctn J*. 2025;46(1):72–77.

HEALTH OUTCOMES

Methadone Remains Superior to Buprenorphine for Opioid Use Disorder Treatment Retention, Even as Fentanyl Dominates the Drug Supply

Compared with buprenorphine, methadone is associated with superior treatment retention among people with opioid use disorder (OUD). Historically, studies involved populations with heroin or prescription opioid use. Today, high potency opioids, including illicitly manufactured fentanyl and its analogues, pervade the drug supply. This retrospective observational study used nine linked population-level administrative databases in British Columbia, Canada to assess the risk of treatment discontinuation and mortality among people with OUD initiating buprenorphine or methadone during a time when fentanyl became dominant in the illicit drug supply (2010–2020).

- The study examined 30,891 individuals initiating methadone or buprenorphine for OUD treatment.
- The risk of treatment discontinuation within 24 months was greater among recipients of buprenorphine versus methadone (89 percent versus 82 percent; adjusted hazard ratio [aHR], 1.58).
- The risk of mortality was low with both buprenorphine and methadone (0.08 percent versus 0.13 percent, respectively; aHR, 0.57).

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Methadone Remains Superior to Buprenorphine for Opioid Use Disorder Treatment Retention, Even as Fentanyl Dominates the Drug Supply *(continued from page 2)*

Comments: Receipt of methadone continues to be associated with greater OUD treatment retention than buprenorphine, even as illicitly manufactured fentanyl has become widespread in the drug supply. It is notable that in Canada, both methadone and buprenorphine are available in office-based settings. In contrast, methadone for OUD treatment can only be obtained in the US in an opioid treatment program, which may limit the generalizability of these findings to populations with less restrictive access to methadone.

Susan L. Calcaterra, MD, MPH, MS

Reference: Nosyk B, Min JE, Homayra F, et al. Buprenorphine/naloxone vs methadone for the treatment of opioid use disorder. *JAMA*. 2024;332(21):1822–1831.

Factors Associated With Return to Alcohol Use Following Liver Transplant

Return to alcohol use after liver transplant (LT) is associated with an increased risk of graft loss and mortality; many patients with alcohol-associated liver disease (ALD) are required to demonstrate a period of sobriety prior to LT. This US multicenter retrospective cohort study investigated factors associated with return to alcohol use among adults who received LT for ALD between January 2018 and December 2020, with at least one available phosphatidylethanol (PEth; a direct alcohol biomarker) test to assess alcohol use pre- and post-transplantation.

- The study population (N=233) was 70 percent male, with median age of 52; 27 percent identified as Hispanic/Latino. Eighty-nine percent of patients had a diagnosis of alcohol use disorder; 32 percent had a diagnosis of substance use disorder.
- Over a median of 555 days of follow-up, 26 patients returned to alcohol use (6.9 cases per 100 person-years). The mean PEth value for those returning to alcohol use was 244 ng/mL, suggesting hazardous levels of drinking; the median time to return to use was 348 days.
- Psychiatric comorbidities were associated with an increased risk of return to alcohol use (hazard ratio [HR], 2.83), and younger age with a decreased risk (HR, 0.96).
- Non-Hispanic White patients had an increased risk of return to alcohol use (HR, 3.79), with a shorter time to return to use, compared with non-White patients.
- Thirty-three percent of patients had fewer than six months of sobriety before LT; this was not associated with an increased risk of return to alcohol use, nor with time to return to use.

Comments: These findings suggest that mandated periods of sobriety prior to LT receipt may not be reliable predictors of post-LT return to alcohol use or survival among patients with ALD. Moreover, patients with psychiatric comorbidities should be identified and offered additional support pre- and post-LT. The association with race/ethnicity suggests that racial bias may be a factor in LT eligibility; this potential disparity should be investigated.

Nicolas Bertholet, MD, MSc

Reference: Torosian K, Shahrvini B, Johnson WM Jr, et al. Psychosocial predictors of return to alcohol use after liver transplant: a multicenter cohort study. *Alcohol Clin Exp Res*. 2024;48(11):2137–2144.

Characterizing Xylazine-associated Wounds

Xylazine is a non-opioid veterinary sedative. It has been increasingly found as an adulterant with illicitly manufactured fentanyl, leading to concerns that it causes skin and soft tissue injury in people who use drugs. Researchers in Philadelphia, PA aimed to characterize xylazine-associated wounds to inform identification, management, and research. Patients (N=29) were adult inpatients or those seen in the emergency department between April 2022 and February 2023 with xylazine exposure (confirmed via urine drug test) and a wound-related chief complaint.

- Overall, 15 patients were male and their mean age was 39 years; 16 patients were experiencing unstable housing or street homelessness; 28 had non-medical opioid use, and 23 had injection drug use (IDU).
- The largest 59 wounds were characterized: 53 were on the extremities; 41 involved extensor aspects of the limbs. Twelve wounds were small in size (<1 cm), 33 were medium (1 cm to the size of a hand), and 14 were large (larger than the size of a hand).
- Of 57 photographed wounds, 34 had wound beds of predominantly devitalized tissue (eschar or slough), six were blisters, five had granulation tissue, and 12 had mixed tissue. Devitalized tissue was more commonly seen in medium or large wounds.
- Per patient report, 28 wounds were acute (<1 month present), 12 were subacute (1–3 months), and 12 were chronic (>3 months). Compared with acute wounds, subacute and chronic

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Characterizing Xylazine-associated Wounds *(continued from page 3)*

wounds were more commonly medium or large in size and/or had devitalized wound beds.
- Of the 39 wounds with patient-reported etiology, 34 were at sites of IDU.

Comments: These findings suggest that untreated xylazine-associated wounds progress from small multifocal blisters to larger confluent areas of eschar and slough. Wounds tend to be located at sites of IDU, but may also be present in people who use opioids via other routes.

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

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

Reference: Lutz L, McFadden R, Xu L, et al. Wound characteristics among patients exposed to xylazine. *JAMA Dermatol*. 2025;161(1):75–80.

Wounds Attributed to Xylazine Exposure Are Associated With Subcutaneous Injection Drug Use and Healthcare Stigma

People who use drugs (PWUD) are at risk of soft tissue infections and chronic wounds. As the illicit drug supply has become increasingly adulterated with xylazine in some areas, there has also been a rising incidence of skin wounds among PWUD. Researchers surveyed PWUD at three Massachusetts community-based syringe service programs to better understand their experiences with xylazine wounds. Participants were adults who reported having any wounds related to substance use in the past year; those who reported having wounds consistent with illustrations of typical xylazine wounds were considered to have "xylazine wounds."

- The cohort included 171 PWUD; 63 percent were male, and 91 percent had injection drug use (IDU). Overall, 80 percent of the cohort reported xylazine exposure; 148 (87 percent) reported xylazine wounds.
- PWUD with xylazine wounds reported high rates of healthcare stigma (74 percent), inadequate pain treatment (58 percent), and inadequate withdrawal treatment (58 percent).
- Participants with IDU who reported xylazine wounds were more likely to report subcutaneous injection than those with non-xylazine wounds (30 percent versus 5 percent, respectively).

Comments: This study provides some insight into the experiences of PWUD with xylazine-associated wounds. It is still not clear to what extent xylazine or specific drug use practices (like subcutaneous injection) are responsible for the development of these wounds. Increased access to patient-centered treatment and wound management education among PWUD who are at risk for developing wounds is needed.

Darius A. Rastegar, MD

Reference: Jawa R, Ismail S, Shang M, et al. Drug use practices and wound care experiences in the age of xylazine adulteration. *Drug Alcohol Depend*. 2024;263:112390.

Prenatal Cannabis Exposure Modestly Associated With Decreased Birth Weight

Cannabis use is becoming more prevalent in the US, including among persons who are pregnant. Moreover, the potency of cannabis has been increasing. This raises concerns about the potential effect of prenatal cannabis exposure (PCE) on birth outcomes. Researchers used data from the Michigan Archive for Research on Child Health from 2017 to 2022 to prospectively investigate the association between PCE and birth outcomes while adjusting for other factors.

- Of the 584 pregnant persons in the cohort, 90 (15 percent) reported cannabis use during pregnancy. Those who reported use were younger, more likely to identify as non-Hispanic Black, to report high school as their highest level of education, or to have government insurance; they were less likely to be obese, smoke tobacco, or use alcohol.
- In adjusted analyses, PCE was associated with lower birth weight ($\beta = -0.3$), but not with other measured birth outcomes: pre-term birth, gestational age, five-minute Apgar score, and neonatal intensive care unit admission.

Comments: This study shows an association between PCE and modestly lower birth weights, but not other birth outcomes. This information can be used to counsel persons who are pregnant or may potentially become pregnant.

Darius A. Rastegar, MD

Reference: Vanderziel A, Anthony JC, Barondess D, et al. Estimating the effects of prenatal cannabis exposure on birth outcomes. *Am J Addict*. 2025;34(1):21-29.

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Many others periodically reviewed (see www.aodhealth.org).

Contact Information:
Alcohol, Other Drugs, and Health: Current Evidence
Boston Medical Center
801 Massachusetts Ave., 2nd floor
Boston, MA 02118
aodhce@bu.edu