Alcohol, Other Drugs, and Health: Current Evidence

NOVEMBER-DECEMBER 2024

TABLE OF CONTENTS

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***Hosted by* Honora L. Englander & Marc R. Larochelle**

Learn more on page 5

INTERVENTIONS & ASSESSMENTS

Buprenorphine/naloxone Was Superior to Extended-release Naltrexone for Opioid Use Disorder Treatment Retention Among Medicaid Patients

The comparative effectiveness of buprenorphine/naloxone (SL-BUP) and extended-release naltrexone (XR-NTX) for opioid use disorder (OUD) treatment has been the subject of clinical trials and observational studies. This observational study evaluated the relative treatment retention and overdose risk of SL-BUP and SR-NTX among New Jersey and California Medicaid patients from 2016 to 2019.

- The cohort included 1755 patients who were initiated on XR-NTX and 9886 initiated on SL-BUP who had not received medication for OUD (MOUD) in the preceding 90 days.
- The cumulative risk of treatment discontinuation or death within six months was 76 percent for patients receiving XR-NTX and 62 percent for those receiving SL-BUP, with a significant risk difference of 14 percent favoring SL-BUP.
- The cumulative risk of overdose or death within six months was 3.9 percent for patients receiving XR-NTX and 3.3 percent for those receiving SL-BUP, with a statistically insignificant risk difference of 0.5 percent favoring SL-BUP.

Comments: SL-BUP has significant advantages over XR-NTX for OUD treatment, primarily its comparative ease of initiation, though some carceral settings favor its use. This study demonstrates that even among patients who initiate XR-NTX, real-world treatment retention is lower than among those receiving SL-BUP. While no differences in overdose risk were seen in this study, reliance on Medicaid claims data to identify overdose likely underestimates these events and limits medication comparisons.

Joseph Merrill, MD, MPH

Reference: Ross RK, Nunes EV, Olfson M, et al. Comparative effectiveness of extended-release naltrexone and sublingual buprenorphine for treatment of opioid use disorder among Medicaid patients. *Addiction*. 2024 Nov;119(11):1975–1986.

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HEALTH OUTCOMES

High Risk of Mortality in the Week Following a Non-fatal Opioid Overdose

Patients with opioid use disorder have an increased risk of overdose. This prospective observational study in Oslo, Norway aimed to assess subsequent all-cause mortality in patients 18–70 years of age following receipt of naloxone from emergency medical services (EMS) for an opioid overdose from 2014 to 2018.

- The cohort included 890 people (76 percent male, mean age 38) treated for 1764 overdoses (3142 person-years).
- Overall, 112 people (13 percent) died during the study period; none within two days of the index non-fatal overdose. The most common cause of death was overdose (53 percent).†
- Standardized mortality ratio (SMR)* calculations showed that women and men in the cohort were, respectively, 32 and 25 times more likely to die than women and men in the general population over the study period.
- The crude mortality rate (CMR)** was 3.6/100 person-years over the study period and highest within seven days of EMS attendance (22.2/100 person-years).
- In adjusted analyses, mortality risk was highest within the first seven days post-overdose, especially among individuals with severe overdose symptoms (i.e., Glasgow Coma Scale = 3/15 and/or a respiration rate of ≤6 per minute).

* SMR is calculated by dividing the observed age- and sex-specific mortality rate in the cohort by the expected sex- and age-specific mortality rate in the general population.
** CMR is calculated by dividing total number of deaths during the follow-up period by the total person-years contributed by all participants.
† Categorized as "accidental poisoning" by the European Shortlist for Causes of Death, 2012 (ICD 10).

Comments: This study shows that the risk of mortality in the week after a non-fatal overdose is very high, particularly among individuals with severe overdose symptoms. The fact that no deaths occurred within two days of EMS attendance indicates that deaths were likely not due to rebound opioid toxicity. Prescription opioid medications and heroin were more common causes of opioid overdose than fentanyl in this cohort; the risk for those with fentanyl use in the US is likely higher. Results indicate an urgent need for targeted interventions for this high-risk group. A non-fatal overdose should be treated like other medical emergencies and patients should have immediate access to evidence-based treatment.

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

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

Reference: Eide D, Gjersing L, Danielsen AW, et al. Heightened mortality risk after a non-fatal opioid overdose: risk factors for mortality in the week following emergency treatment. *Addiction*. 2024;26:1–8.

Interprofessional Addiction Consultation Services Improved Receipt of Medications for Opioid Use Disorder Following Hospitalization

Hospitalization presents an opportunity to initiate medications for opioid use disorder (MOUD) among adults with OUD. This stepped-wedge cluster randomized clinical trial evaluated whether interprofessional addiction consultation services (ACS) implemented across six New York public hospitals increased MOUD initiation (in the 14 days following hospital discharge) and MOUD engagement (for the 30 days following initiation) among hospitalized adults with OUD, compared with usual care.

(continued page 3)

Interprofessional Addiction Consultation Services Improved Receipt of Medications for Opioid Use Disorder Following Hospitalization *(continued from page 2)*

- Within 14 days of hospital discharge, MOUD initiation was 11 percent among patients who received ACS versus 7 percent among those who received usual care.
- Patients hospitalized during the ACS treatment period had 7.96 times higher odds of initiating MOUD, compared with those hospitalized in the usual care period.
- At 30 days following initiation, MOUD engagement was 7 percent among patients who received ACS versus 5 percent among those who received usual care; at six months, it was 3 percent versus 2 percent, respectively.

Comments: Hospital-based clinicians have an important role to play in identifying patients with OUD and offering and initiating MOUD. However, MOUD treatment initiation is just one element the OUD care cascade; the benefits of MOUD are realized with ongoing treatment engagement in the outpatient setting. Identifying ways to expand in-hospital OUD treatment provision and to improve community-based OUD services are urgently needed to support people with OUD. MOUD initation and treatment retention are both essential to reduce the morbidity and mortality associated with untreated OUD.

Susan L. Calcaterra, MD, MPH, MS

Reference: McNeely J, Wang SS, Rostam Abadi Y, et al. Addiction consultation services for opioid use disorder treatment initiation and engagement: a randomized clinical trial. *JAMA Intern Med*. 2024;184(9):1106–1115.

In a US Cohort of People With Injection Drug Use, Primary Care Engagement Was Not Associated With Initiation or Continuation of Medications for Opioid Use Disorder

In the US, a small fraction of adults with opioid use disorder (OUD) receive effective medications for OUD (MOUD). Primary care clinicians can help facilitate initiation of MOUD by prescribing buprenorphine. Researchers used 2014–2020 data from a prospective cohort of individuals with injection drug use in Baltimore, Maryland to investigate the association of engagement in primary care with initiation and continuation of MOUD.* They included as index visits all visits where a participant reported: a) any past 6-month opioid use non-medically; and b) no use of MOUD in the past 6 months.

- There were 360 individuals and 789 study visits included in the analysis; at 490 index visits (62 percent) participants reported primary care engagement. At follow up visits, 17 percent had initiated methadone and 10 percent initiated buprenorphine.
- In adjusted analyses, there was no significant association between engagement in primary care and initiation or continuation of MOUD, including buprenorphine.

* This study assessed initiation and continuation of buprenorphine or methadone; in the US, methadone cannot be prescribed in primary care.

Comments: It is disappointing to see that primary care clinicians have not stepped up to address an important medical problem that affects their patients and for which there is a very effective treatment. Offering buprenorphine for OUD in the primary care setting should be supported and expected.

Darius A. Rastegar, MD

Reference: Sosnowski DW, Feder KA, Genberg BL, et al. Association of primary care engagement with initiation and continuation of medication treatment for opioid use disorder among persons with a history of injection drug use. *Drug Alcohol Depend*. 2024;262:111383.

Higher-potency Cannabis Use in Adolescents is Associated With Mental Health Problems

Higher-potency cannabis is increasingly available, and its use is associated with anxiety and psychosis in adults. Researchers used baseline assessments from a trial in England and Wales to examine the association between higher-potency cannabis use and mental health in adolescents 13–14 years of age. Cannabis potency was correlated with probable depressive disorder, probable anxiety disorder, and auditory hallucinations using standardized questionnaires.

- Of 6672 participants, 38 (0.6%) reported low-potency cannabis use and 171 (2.6%) high-potency cannabis use.* Compared with low-potency use, high-potency use was more common among those who smoked combustible cigarettes, drank alcohol, were a gender minority, and came from a socioeconomically deprived household.
- In unadjusted analyses, low-potency cannabis use was associated with depression and anxiety, but not hallucinations. High-potency use was associated with all three.
- In adjusted analyses, the association between low-potency cannabis use and the three outcomes was no longer significant. High-potency use was still associated with depression (adjusted odds ratio [aOR], 1.59) and hallucinations (aOR, 1.56), but the association with anxiety was no longer significant.

(continued page 4)

Higher-potency Cannabis Use in Adolescents is Associated With Mental Health Problems

(continued from page 3)

*Potency was estimated by images used in prior research to facilitate participant identification of cannabis type. Low-potency was defined as typically <10 percent Δ^9-tetrahydrocannabinol (THC), 1–2 percent cannabidiol (CBD); high-potency as typically >10 percent THC, <1 percent CBD.

Comments: This study suggests that higher-potency cannabis use may lead to more mental health problems in adolescents. Regulations limiting cannabis potency and interventions addressing cannabis use in adolescents may help to mitigate these harms.

Darius A. Rastegar, MD

Reference: Hines LA, Cannings-John R, Hawkins J, et al. Association between cannabis potency and mental health in adolescence. *Drug Alcohol Depend*. 2024;261:111359.

Canadian Youth Experience Low Rates of Outpatient Physician Follow-up After Substance Use-related Emergency Department Visits

Emergency departments (EDs) across the US and Canada have seen an increase in substance use-related visits among youth. Researchers used population-level data in the province of Ontario, Canada to investigate the proportion and predictors of outpatient physician follow-up visits 60 days after a substance use-related ED encounter in youth aged 10–24, both before and during the COVID-19 pandemic (April 2017 –May 2021).

- During the study period, 64,236 youth had at least one ED visit related to substance use.
- Visits for alcohol (49 percent) and cannabis (32 percent) use were the most common. Visits for sedatives were the least common (9 percent); sedatives were the only substance for which there were more visits among females than males.
- Compared with prior to the pandemic, there was a higher prevalence of ED visits for all substances except alcohol during the pandemic. However, alcohol-related ED visits were associated with the greatest increase in the relative risk (RR) of having repeat ED visits or hospitalizations (RR, 1.65), and follow-up with a mental health or addiction treatment provider (RR, 1.42), compared with visits for other substance use.
- Rates of follow-up physician care for any substance use was 33 percent pre-pandemic versus 42 percent during the pandemic (adjusted odds ratio [aOR], 1.34). Sedative presentations had the highest rates of follow-up care (65 percent).
- Receipt of mental health services in the year before the substance use-related ED visit was most strongly associated with follow-up physician care for substance use within 60 days (aOR, 6.86).

Comments: Despite improvements made during the COVID-19 pandemic, continuity of substance use-related care from the ED to outpatient physician follow-up in Canadian youth is poor. The authors propose that increased utilization of virtual care may account for the increased rates of follow-up during the pandemic. Future studies should focus on identifying barriers to substance use care within the health system. Until such obstacles are further elucidated and remedied, substance use interventions for youth in the ED setting should be maximized.

Emily Nields, DO

Reference: Rosic T, Cloutier P, Myran D, et al. Physician follow-up of pediatric and young adult emergency department visits for substance use in Ontario, Canada. *J Adolesc Health*. 2024;75(5):757–765.

Together for Hope: Shaping the Future of Addiction Care 2025 — Save the Date + Call for Abstracts!
Wednesday, April 16 - Thursday, April 17
DCU Center, Worcester

After a successful inaugural event earlier in 2024, BMC's Grayken Center for Addiction is widening the reach of its second annual addiction conference. Together for Hope 2025 will bring together substance use disorder experts and people with lived experience from all across Massachusetts. We encourage you to join us and participate in impactful conversations about shaping the future of addiction care.

The conference invites individuals from all backgrounds and areas of expertise to contribute their unique insights, ideas, and stories about recent, innovative work from you and your team in four key theme areas of recovery, harm reduction, youth and families, and addiction treatment.
Please consider submitting an abstract describing your work before the deadline of Feb. 6, 2025.

Contact: Kris Warren | grayken.center@bmc.org

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Hosted by addiction medicine specialists Honora L. Englander, MD (Oregon Health & Science University) and Marc R. Larochelle, MD, MPH (Boston Medical Center/ Boston University Chobanian & Avedisian School of Medicine), each episode of "Behind the Evidence" offers thoughtful discussion of one or more recent significant publications in the clinical addiction literature. Through author interviews and expert insights, "Behind the Evidence" will appeal to clinicians, as well as anyone who is interested in the latest developments in addiction medicine research.

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Addiction Science & Clinical Practice
Addictive Behaviors
AIDS
Alcohol
Alcohol & Alcoholism
Alcohol: Clinical & Experimental Research
American Journal of Drug & Alcohol Abuse
American Journal of Epidemiology
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American Journal of Preventive Medicine
American Journal of Psychiatry
American Journal of Public Health
American Journal on Addictions
Annals of Internal Medicine
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Journal of Studies on Alcohol
Journal of Substance Abuse Treatment
Journal of the American Medical Association
Journal of Viral Hepatitis
Lancet
New England Journal of Medicine
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Psychiatric Services
Substance Abuse
Substance Use & Misuse

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

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