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# Alcohol, Other Drugs, and Health: Current Evidence

MARCH - APRIL 2026

## INTERVENTIONS & ASSESSMENTS

### Dutasteride as a Promising Option to Decrease Heavy Drinking

Current pharmaceutical options to decrease heavy alcohol use are limited; dutasteride, a 5-alpha-reductase inhibitor—normally used for prostate conditions—might be a good candidate. Researchers conducted a 12-week parallel-group randomized controlled trial among adults aged  $\geq 35$  years with alcohol use disorder (AUD) and heavy alcohol use\* who wanted to decrease or stop their drinking. Participants were randomized to receive either dutasteride 1 mg daily or a placebo. All participants received bi-weekly medical management.

- Participants (N=167) were 95 percent White and 44 percent female; the average age was 56 years.
- Compared with placebo, participants receiving dutasteride experienced greater reductions in the number of heavy drinking days (40 percent decrease with dutasteride versus 23 percent decrease with placebo).
- Participants receiving dutasteride also consumed fewer drinks per week, compared with placebo (32 percent decrease with dutasteride versus 16 percent with placebo).
- Analyses stratified by sex showed statistically significant effects in men but not in women; women receiving placebo had a greater drinking reduction than men receiving placebo.
- There were no serious adverse events and no study withdrawal due to side effects.

\* Defined as  $\geq 24$  drinks in a week for men and  $\geq 18$  drinks in a week for women with at least two heavy drinking days in a week.

*Comments:* Among people with AUD with a drinking reduction goal, dutasteride was well tolerated and significantly reduced heavy drinking and total alcohol use, especially in the men in this cohort, which was predominantly White. Effects were non-significant among women, but women in the placebo group showed a greater decrease. Effect sizes were comparable to currently approved medications. Further study is warranted, especially among racially diverse populations.

Nicolas Bertholet, MD, MSc

*Reference:* Covault J, Tennen H, Feinn R. Dutasteride as a treatment to support reduced drinking: a randomized placebo-controlled trial. *J Addict Med.* 2025 [Epub ahead of print]. doi: 10.1097/ADM.0000000000001609.

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## HEALTH OUTCOMES

### High 12-month Adherence to Buprenorphine Associated with Improved Health Outcomes in Youth with Opioid Use Disorder

Buprenorphine reduces mortality among people with opioid use disorder (OUD), but ideal treatment duration and minimal adherence to achieve protective effects are not well established in youth. This retrospective cohort study examined buprenorphine duration/adherence patterns (defined as trajectories) in 11,649 Massachusetts youth with OUD aged 13–26 and subsequent health outcomes over 12 months, 2014–2022. Weekly buprenorphine adherence was defined as  $\geq 1$  day.

- Four patterns of buprenorphine receipt emerged: 1) high adherence for 12 months (24 percent of the cohort); 2) low adherence for 12 months (28 percent); 3) discontinuation in 3–9 months (16 percent); and 4) discontinuation in  $<3$  months (33 percent).
- Compared with youth with high buprenorphine adherence for 12 months...
  - overdose risk was greater among those with low adherence for 12 months (adjusted hazard ratio [aHR], 1.46), discontinuation in 3–9 months (aHR, 1.82), and discontinuation in  $<3$  months (aHR, 1.76).
  - risk of all-cause ED usage was greater among those with low adherence for 12 months (aHR, 1.09), and discontinuation in  $<3$  months (aHR, 1.08).
  - risk of all-cause inpatient hospitalization was greater among youth in all three of the other trajectories.

*Comments:* These findings warrant clinician encouragement of high adherence to and longer duration of buprenorphine among youth with OUD. Limitations included possible overestimation of weekly adherence and the potential effect of other overdose prevention medications (i.e., naloxone) on beneficial outcomes in the high adherence cohort.

Emily Nields, DO

*Reference:* Hadland SE, Kimmel SD, Yan S, et al. Buprenorphine treatment duration and adherence among youth and subsequent health outcomes. *Pediatrics*. 2025;156(6):e2025071147.

### Opioid Overdose Risk Higher for Individuals Who Utilize Varied Routes of Administration

Opioid overdose is a significant cause of morbidity in the US. Previous studies have found that people who inject opioids are at higher risk of overdose than those who use other routes of administration. Researchers in Baltimore, Maryland used data from a cohort of individuals who have injected drugs to investigate the association between within-person variation in route of administration (i.e., injection, nasal inhalation, or smoking), and the risk of non-fatal overdose.

- The study included 1121 unique participants with 4396 visits between 2014 and 2022; the past six-month prevalence of self-reported overdose was 12 percent.
- Utilizing all three routes of opioid administration was associated with a higher risk of overdose compared with: injection alone (adjusted odds ratio [aOR], 2.4), nasal inhalation alone (aOR, 2.9), and injection and smoking (aOR, 4.2).
- The study found similar results for cocaine use via varied routes associated with an increased risk of self-reported overdose.

(continued page 3)

## Opioid Overdose Risk Higher for Individuals Who Utilize Varied Routes of Administration *(continued from page 2)*

*Comments:* This study suggests that people utilizing varied routes of opioid administration have an increased risk of overdose. It makes sense that individuals who utilize only one route would have a more predictable response. It is possible that administration by varied routes is a marker for a more severe use disorder. Another potential factor is that overdose may prompt a change in route of administration. In any case, it would

be reasonable to counsel individuals who utilize varied routes of opioid administration on the potential increased risk.

Darius A. Rastegar, MD

*Reference:* Lucia M, Feder KA, Kirk GD, et al. Association of route of drug administration with self-reported non-fatal overdose: a cohort study of Baltimore City adults who have injected drugs. *Drug Alcohol Depend.* 2025;277:112962.

## Observational Study Finds Association Between Adolescent Use of MDMA and Anxiety in Adulthood

There is a positive association between the use of 3,4-methylenedioxymethamphetamine (MDMA) and mental health conditions. However, causal associations remain problematic given the lack of longitudinal prospective data on the long-term effects of MDMA exposure. Researchers analyzed a subset of data from the Victorian Adolescent Health Cohort Study (Australia), following a cohort of students from age 15 to 35 (waves 2-10). They examined the association between any young adulthood MDMA use, frequency of use, and persistence of use with development of depression and anxiety at age 35.\* To address confounding in estimating causal relationships, researchers used doubly robust inverse probability treatment weighting (IPTW) methods.

- Of 1329 participants, 55 percent were female; 25 percent reported any young adulthood MDMA use (5 percent classified as “frequent” and 10 percent as “persistent”).
- By age 35, 12 percent of the cohort had depression and 11 percent had anxiety.

- Any MDMA use compared with no MDMA use during young adulthood raised the odds of past 12-month adulthood anxiety by age 35 (adjusted odds ratio [aOR], 1.73). “Frequent” and “persistent” use also increased the odds of adulthood anxiety (aOR, 2.56 and 2.05, respectively).
- There was limited evidence of an association between any category of young adulthood MDMA use and depression in adulthood.

\* MDMA use was categorized as “any,” frequent” (greater than monthly), and “persistent” (across two or more waves).

*Comments:* The use of IPTW methods is a newer statistical approach for observational data that uses propensity scores to attribute the outcome of interest to exposure. These results highlight the value in prospective longitudinal data collection and analyses to guide public health messaging and awareness around MDMA use and longer-term outcomes.

Ximena A. Levander, MD

*Reference:* Bryant Z, Morley K, Kerr JA, et al. The relationship between 3,4- methylenedioxymethamphetamine (MDMA) use in young adulthood and anxiety or depressive disorders in the mid-30s: findings from the Victorian Adolescent Health Cohort Study. *Addiction.* 2025;120(12):2448–2464.

## Nicotine-containing E-cigarette Cessation Unaffected by Cannabis Co-use Among Youth

Laboratory research suggests that nicotine and tetrahydrocannabinol (THC) may enhance one another’s rewarding and dependence-related effects, raising concerns that cannabis use could interfere with nicotine cessation attempts. To clarify these relationships clinically among youth with nicotine-containing e-cigarette use, investigators conducted a secondary analysis of a single-site randomized controlled trial involving 261 participants aged 16–25 years. Participants were assigned to: 1) varenicline plus counseling; or 2) placebo plus counseling; or 3) enhanced usual care. At 12 weeks, nicotine-containing e-cigarette abstinence was assessed via self-report and verified with salivary cotinine testing. Investigators evaluated whether cannabis use frequency or cannabis use disorder (CUD) symptom severity affected

nicotine cessation outcomes, and whether cannabis use moderated treatment effects of varenicline on nicotine vaping cessation.

- At baseline, 28 percent of participants reported no past-month cannabis use, 38 percent reported cannabis use more than 0 days and less than 4 days per week, and 30 percent reported cannabis use 4–7 days per week.
- Cannabis use frequency was not significantly associated with nicotine abstinence, nor did it affect varenicline’s effectiveness for nicotine cessation.
- CUD symptom severity was not associated with nicotine abstinence, nor did it affect varenicline’s effectiveness for nicotine vaping cessation.

*(continued page 4)*

## Nicotine-containing E-cigarette Cessation Unaffected by Cannabis Co-use Among Youth *(continued from page 3)*

*Comments:* These findings indicate that cannabis and nicotine co-use does not hinder nicotine cessation among youth, nor does it reduce the therapeutic benefits of varenicline. These results support offering patients standard nicotine cessation treatments—including varenicline—regardless of cannabis use.

Susan L. Calcaterra, MD, MPH, MS

*Reference:* Gilman JM, Cather C, Reeder HT, et al. Cannabis use and nicotine vaping cessation outcomes: a secondary analysis of a randomized clinical trial. *JAMA Netw Open.* 2025;8(12):e2547799.

## Weekly Drug Testing is Associated With Modestly Improved Treatment Retention Among People Receiving Medications for Opioid Use Disorder

Urine drug testing (UDT) is routinely used alongside the provision of medications for opioid use disorder (MOUD) to monitor for nonmedical use of other substances and diversion. However, there is little evidence to guide us on how frequently to use this test. Researchers in British Columbia, Canada used data from a cohort of 30,898 adults with OUD who initiated methadone or buprenorphine to investigate the association of UDT frequency with MOUD retention and all-cause mortality.

- The study included 18,988 individuals who started methadone, and 11,910 who started buprenorphine; approximately 40 percent of all patients discontinued MOUD within one month of initiation.
- Weekly UDT was associated with a 5 percent decrease in the risk of MOUD discontinuation in the first year of treatment when compared with no testing. There was no significant difference in risk of MOUD discontinuation between less frequent and no testing.

- There was no significant association between UDT frequency and mortality.

*Comments:* This study suggests that UDT does not have a large impact on MOUD retention or mortality; it cannot tell us if it mitigates diversion. The modest improvement in retention with weekly UDT could be due to the information that UDT provides, or simply because these patients may have had more frequent contact with care. It should be noted that in British Columbia, methadone and buprenorphine are prescribed through primary care and dispensed at pharmacies; these findings may not apply to other settings.

Darius A. Rastegar, MD

*Reference:* Kurz M, Guerra-Alejos BC, Min JE, et al. Comparative effectiveness of urine drug testing scheduled alongside opioid agonist treatment; emulation of a population-based target trial in British Columbia, Canada. *Addiction.* 2025;120(12):2435–2447.

## PRESCRIPTION DRUGS & PAIN

### Abrupt Opioid Medication Dose Reductions Associated With Increased Mental Health and Substance Use-related Emergency Visits, While Modest Dose Reductions Are Not

Clinical guidelines have recommended limiting opioid medication doses for patients receiving long-term opioid therapy for chronic non-cancer pain. However, some studies have raised concerns about the safety of rapid or large dose reductions. This case-crossover study used linked primary care and hospital data from Victoria, Australia to examine whether changes in prescribed opioid dose were associated with subsequent mental health or substance use-related emergency department (ED) presentations. Adults with at least four opioid prescriptions in the prior year who later experienced a qualifying ED visit were included, allowing each individual to serve as their own control.

- Among 1458 individuals, 76 percent experienced an opioid dose reduction >25 percent in the 30 days preceding their ED visit.
- Compared with periods in which no opioid medications were prescribed, abrupt dose reductions (i.e., >25 percent) were associated with higher odds of mental health or substance use-related ED presentations (adjusted odds ratio [aOR], 1.78).
- Complete opioid medication discontinuation was also associated with increased risk of ED presentation (aOR, 2.04).

*(continued page 5)*

## Abrupt Opioid Medication Dose Reductions Associated With Increased Mental Health and Substance Use-related Emergency Visits, While Modest Dose Reductions Are Not *(continued from page 4)*

- In contrast, modest dose reductions (10–25 percent) were associated with a lower risk of ED presentation (aOR, 0.15). Stable or increased opioid dosing was associated with the lowest risk of ED presentation (aOR, 0.01).
- Findings were consistent across multiple control periods within individuals, strengthening causal inference and supporting a dose-response relationship.

*Comments:* This study underscores a critical distinction between intentional, patient-centered opioid de-prescribing and abrupt dose reduction. Large or rapid dose changes may destabilize patients, increasing psychological distress and acute care utilization rather

than improving safety. For clinicians, these results reinforce the importance of shared decision-making, close follow-up, and tapering plans that are responsive to patient stability rather than externally imposed targets. At a systems level, policies or performance metrics that incentivize rapid opioid dose reductions without adequate clinical support may inadvertently increase downstream morbidity and emergency care use.

John Fomeche, MD\* and Darius A. Rastegar, MD

\*2025–26 Rich Saitz Editorial Intern & Addiction Medicine Fellow, Yale University

*Reference:* Jung M, Xia T, Picco L, et al. Change in prescription opioid dose and the risk of mental health-related and substance use-related emergency department presentations: a case-crossover study. *Pain*. 2026;167(4):767–775.

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