Alcohol, Other Drugs, and Health: Current Evidence

NOVEMBER-DECEMBER 2023

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INTERVENTIONS & ASSESSMENTS

Trazodone Improves Subjective Sleep Quality Among Individuals With Opioid Use Disorder Receiving Buprenorphine

Sleep disturbances are common among individuals with opioid use disorder (OUD), but many medications prescribed for sleep are associated with significant risks and side effects. Trazodone is prescribed widely at low doses to help with sleep. This 6-week placebo-controlled trial in India evaluated the effect of trazodone among 100 adult men with OUD who were receiving buprenorphine and had sleep disturbance, defined as a score of ≥6 on the Pittsburgh Sleep Quality Index (PSQI). Participants were given trazadone 50 mg or placebo tablets and told they could take up to 3 tablets one hour before bedtime.

- The primary outcome measure was a PSQI of ≤5; 82% of participants assigned to trazodone achieved this outcome, compared with 18% of those receiving placebo.
- There was no significant difference between groups in daytime sleepiness, withdrawal, craving, depression, or anxiety scores.

Comments: The standard of care for insomnia is cognitive behavioral therapy. This study found that trazodone had short-term subjective benefits for individuals with OUD receiving buprenorphine, suggesting that it is a reasonable medication to treat insomnia in this population.

Darius A. Rastegar, MD

Reference: Goyal P, Kattula D, Rao R, et al. Trazodone for sleep disturbance in opioid dependence patients maintained on buprenorphine: a double blind, placebo-controlled trial. *Drug Alcohol Depend*. 2023;250:110891.

Single-item Screening Tool for Cannabis Use Disorder Opens Opportunities in Primary Care

Medical and nonmedical cannabis use—and cannabis use disorders (CUD)—have been increasing in the US, especially in states that have legalized its use. A brief, valid cannabis screen in primary care could facilitate the identification and treatment of unhealthy cannabis use. Two studies evaluated the real-world screening performance of a single-item cannabis screen* and characterized patterns of medical and nonmedical cannabis use and CUD in a single health system in a US state with legalized nonmedical cannabis use. To assess CUD and describe patterns of use among the 108,950 adults who completed routine cannabis screening in primary care, 5000 patients were randomly sampled and 1688 (34 percent) completed a detailed survey.

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Single-item Screening Tool for Cannabis Use Disorder Opens Opportunities in Primary Care (continued from page 1)

- In this sample (mean age 51 years, 56 percent women, 74 percent White, 65 percent commercially insured, 48 percent with ≥4 years of college), 93 percent had no CUD, 5 percent had mild CUD, and 2 percent had moderate-to-severe CUD.
- Performance of the single-item screening response of monthly or more cannabis use was excellent, with sensitivity of 71 percent and specificity of 92 percent for any CUD, and sensitivity of 96 percent and specificity of 89 percent for moderate-to-severe CUD.
- Among respondents with any cannabis use…
  - the prevalence of CUD was 21 percent and moderate-to-severe CUD was 7 percent.
  - 42 percent reported medical cannabis use only, 25 percent reported nonmedical use only, and 33 percent reported both reasons for use.
- While the prevalence of any CUD did not differ depending on reasons for use, the prevalence of moderate-to-severe CUD was higher among people with nonmedical use (7 percent) or among those with both reasons for use (8 percent), compared with those with medical use only (1 percent).

* The single-item screen, embedded in a routine annual 7-item behavioral health questionnaire, asked: "How often in the past year have you used marijuana?" The response options were: "never," "less than monthly," "monthly," "weekly," or "daily or almost daily."

Comments: In this relatively high-resource population in a state that legalized nonmedical cannabis use, a single-item cannabis screen embedded in usual care showed excellent screening performance, providing an opportunity to identify CUD in primary care. Assessing reasons for cannabis use may be helpful in identifying people with nonmedical use who are more likely to have moderate-to-severe CUD, and those with medical cannabis use who may benefit from a discussion of the risks and limited medical benefits of cannabis, as well as safer alternatives. While prior studies have not shown brief interventions based on screening for non-prescribed substance use in primary care to be effective, this targeted cannabis screening opens new opportunities.

Joseph Merrill, MD, MPH

References: Matson TE, Lapham GT, Bobb JF, et al. Validity of the Single-Item Screen-Cannabis (SIS-C) for cannabis use disorder screening in routine care. *JAMA Netw Open*. 2022;5(11):e2239772.

Lapham GT, Matson TE, Bobb JF, et al. Prevalence of cannabis use disorder and reasons for use among adults in a US state where recreational cannabis use is legal. *JAMA Netw Open*. 2023;6(8):e2328934.

Emergency Department Administration of Medications for Opioid Use Disorder Varies by Patient Clinical Presentation

Researchers conducted a mixed methods study to examine variability in the provision of medications for opioid use disorder (buprenorphine and methadone; MOUD) and naloxone prescribing among patients presenting to three US emergency departments (EDs) with one of three conditions: opioid overdose, opioid withdrawal, or other OUD-related concerns. Researchers then conducted focus groups with providers to gain insights into treatment variability in these different clinical scenarios.

- There were 1339 OUD-related visits during the study period: 265 visits for overdose (20 percent), 123 for opioid withdrawal (9 percent), and 951 for other OUD-related conditions (71 percent).

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Emergency Department Administration of Medications for Opioid Use Disorder Varies by Patient Clinical Presentation (continued from page 2)

- Overall, 23 percent of patients received MOUD during or after their ED visit, most commonly buprenorphine. MOUD provision was least common among people treated after an overdose (6 percent), and most common among patients experiencing opioid withdrawal (69 percent).
- Naloxone was prescribed in less than one-third of visits (31 percent), most commonly after a visit for overdose (45 percent of overdose visits).
- There were 28 focus group participants (physicians and nurses) who highlighted different opportunities and challenges delivering care for the three patient groups:
  - Key factors identified for successful treatment initiation included perceived patient receptivity, provider confidence, and patient clinical readiness.
  - Participants felt most comfortable starting buprenorphine in patients presenting with opioid withdrawal. However, lack of adequate treatment of withdrawal symptoms during the ED visit, and severity of these symptoms, could impact whether someone was started on MOUD.
  - Patients' mistrust in the medical system, and clinician uncertainty about OUD treatment were seen as significant contributors to missed opportunities to initiate treatment and/or link people to care and services.
  - Participants felt uncertainly and a lack of preparedness about treating patients with chronic pain.

Comments: Overall, this study found significant variability in ED MOUD and naloxone provision to patients with various OUD clinical presentations. They also found clinician-reported variability in clinician confidence, patient readiness, and clinician-perceived patient receptivity to OUD treatment across all clinical scenarios. Incorporating tailored ED guidance for various clinical presentations of OUD may improve clinician comfort and knowledge, and close treatment gaps.

Elizabeth A. Samuels, MD, MPH, MHS

Reference: Faude S, Delgado MK, Perrone J, et al. Variability in opioid use disorder clinical presentations and treatment in the emergency department: A mixed-methods study. *Am J Emerg Med*. 2023;66:53–60.

Is Phenobarbital an Effective Treatment for Alcohol Withdrawal Syndrome in the Emergency Department?

Alcohol withdrawal syndrome (AWS) is a potentially life-threatening condition commonly treated in the emergency department (ED). Phenobarbital may be used alone or in combination with benzodiazepines to treat AWS. Its long half-life, self-tapering quality, GABAergic properties—and the fact that it reduces glutamate (AMPA) receptor activity—suggest that it may be useful to treat AWS in the ED. Researchers conducted a systematic review of studies examining the administration of phenobarbital to treat moderate-to-severe AWS in the ED.

- Overall, there was limited literature examining the administration of phenobarbital to treat AWS (i.e., 7 articles that assessed a total of 1034 patients) in the ED. Research was of heterogeneous quality; small in size; used variable medication dosages and combinations; had a variety of comparison groups; and had significant risk of bias.
- Retrospective cohort (n=3) and chart review (n=2) studies had small sample sizes, but showed possible decreased repeat ED visits among patients with AWS discharged after treatment with phenobarbital alone or in combination with lorazepam.
- The 2 randomized controlled trials were small in size and heterogeneous. One was placebo controlled and showed a reduction in intensive care unit (ICU) admissions and length of stay. The other was a comparison of phenobarbital with relatively lower doses of lorazepam and showed no difference in admissions or ED length of stay.
- Some studies showed that administration of phenobarbital in combination with benzodiazepines was found to be benzodiazepine-sparing and associated with reduced ICU, ED, and hospital lengths of stay.

Comments: Studies examining the administration of phenobarbital in the ED are generally small in size and of mixed-to-low quality. Current preliminary direct evidence supports the use of phenobarbital to treat AWS in the ED and that it may reduce ICU admissions. Further studies are needed to examine its safety, symptom improvement, dosing strategies, and its administration in combination with benzodiazepines.

Elizabeth A. Samuels, MD, MPH, MHS

Reference: Punia K, Scott W, Manuja K, et al. Phenobarbital for alcohol withdrawal management in the emergency department: A systematic review of direct evidence for the SAEM GRACE initiative. *Acad Emerg Med*. 2023 [Epub ahead of print]. doi: 10.1111/acem.14788.

HEALTH OUTCOMES

Racial and Ethnic Bias Contribute to Provider Diagnosis of Alcohol Use Disorder in Veteran Populations

In the US, Black and Hispanic veterans are more likely than White veterans to be diagnosed with alcohol use disorder (AUD) by Veterans Health Administration (VHA) healthcare providers. Researchers analyzed data from >700,000 veterans to examine racial and ethnic differences in the association between self-reported alcohol consumption and provider-generated AUD diagnosis. Alcohol consumption was measured via the Alcohol Use Disorders Identification Test (AUDIT-C), with a possible score range of 0–12 (higher scores indicating a greater likelihood of AUD).

- Among the 638,204 men, for any given AUDIT-C score, Black veterans were more likely to receive an AUD diagnosis compared with White veterans. In general, for a given AUDIT-C score, Hispanic veterans were less likely than Black veterans and more likely than White veterans to receive an AUD diagnosis.
- Among the 61,808 women, Black veterans were more likely than Hispanic or White veterans to receive an AUD diagnosis at almost every alcohol consumption level, with significant differences noted for AUDIT-C scores of 2, 4, 5, 6, and 7.

Comments: These results suggest that for a given level of reported alcohol consumption, VHA healthcare providers are more likely to diagnose a Black or Hispanic person with AUD than a White person. Identifying the causes of this bias and mitigating them are important next steps for improving diagnosis—and subsequent treatment—for persons with AUD.

Carrie Mintz, MD

Reference: Vickers-Smith R, Justice AC, Becker WC, et al. Racial and ethnic bias in the diagnosis of alcohol use disorder in veterans. *Am J Psychiatry*. 2023;180(6):426–436.

In Two US Cities, Cannabis Decriminalization and Legalization Reduce—but Do Not Eliminate—Racial Disparities in Cannabis-associated Arrests

"War on drugs" policies in the US have been associated with aggressive enforcement in minority communities and inequitable drug-related arrests. One of the rationales for the decriminalization and legalization of cannabis is to reduce these disparities and the harms they cause to minority communities. This study looked at the impact of cannabis decriminalization in Washington, DC and legalization in Los Angeles, California on cannabis-associated arrests and disparities between White and Black individuals.

- In Washington, DC, prior to cannabis decriminalization, there were 84 cannabis-associated arrests per 100,000 Black people compared with 5 per 100,000 White people, an absolute difference of 80 and a Black/White ratio of 18.
- After decriminalization, there were 19 arrests per 100,000 Black people compared with 2 per 100,000 White people, an absolute difference of 18 and a Black/White ratio of 12.
- In Los Angeles, prior to cannabis legalization, there were 56 cannabis-associated arrests per 100,000 Black people compared with 7 per 100,000 White people, an absolute difference of 50 and a Black/White ratio of 8.
- After legalization, there were 20 arrests per 100,000 Black people compared with 3 per 100,000 White people, an absolute difference of 17 and a Black/White ratio of 7.
- After decriminalization and legalization, there was an increase in arrests for public consumption in both cities, with a Black/White ratio of 9 in Washington, DC and 7 in Los Angeles.

Comments: This study shows that decriminalization and legalization of cannabis reduced, but did not eliminate, disparities in cannabis-associated arrests in two US cities. Overall, the impact of these changes is positive, but the structural issues that lead to these disparities remain.

Darius A. Rastegar, MD

Reference: Joshi S, Doonan SM, Pamplin JR 2nd. A tale of two cities: racialized arrests following decriminalization and recreational legalization of cannabis. *Drug Alcohol Depend.* 2023;249:109911.

Cannabidiol Vaping is Popular Among High School Students, Particularly Those With E-cigarette Use

Youth vaping via e-cigarettes and other devices is common in the US, and the use of one substance is often a risk factor for the use of others. This study used the nationally representative 2022 National Youth Tobacco Survey of middle and high school students (N=28,291) to examine the associations between e-cigarette use and cannabidiol (CBD) vaping.

- 7 percent of respondents had vaped CBD in their lifetime; 6% were unsure whether or not they had ever vaped CBD.
- CBD vaping was more common in older (high school versus middle school) and sexual minority students, and was similar across genders, races, and ethnicities.
- 21 percent of respondents with current e-cigarette use and only 1 percent of respondents who did not have e-cigarette use reported current CBD vaping.

Comments: Vaping is a relatively new mode of substance delivery that has become popular with adolescents within the last decade. While the initial attention to high levels of youth e-cigarette use in the late 2010s has passed, this article is a reminder that the introduction of youth-friendly vaping products forever changed the ways in which adolescents use substances, and that e-cigarette use may serve as a gateway to, or marker of, other substance use. Substantial evidence suggests that vaping can result in higher and quicker concentrations of drugs in the brain than smoking. While CBD is not psychoactive, cannabinoids play a major role in guiding brain development. The impact of high-intensity CBD use during adolescence on long-term brain development is unknown, but it is an area of significant concern.

Sharon Levy, MD, MPH

Reference: Dai HD, Subramanian R, Mahroke A, Wang M. Prevalence and factors associated with vaping cannabidiol among US adolescents. *JAMA Netw Open*. 2023;6(8):e2329167.

PRESCRIPTION DRUGS & PAIN

Multicomponent Intervention to Reduce Opioid Pain Medication Dosage May Be Effective Among People Interested in Tapering or Cessation

This multicenter, randomized clinical trial tested whether a multicomponent, group-based, self-management intervention could help adults with chronic, non-cancer pain prescribed high doses of opioid medications (N=608; median daily dosage of ~45 morphine milligram equivalent [MME]) reduce their opioid dose and improve pain-related disability. The intervention included 3 day-long group sessions, individual consultation with a nurse, and an individualized opioid tapering plan, while the comparison group received usual care. Both groups received a self-help booklet and relaxation CD. Researchers assessed participants' opioid use, pain interference, pain intensity, withdrawal, depression, anxiety, and quality of life at 4, 8, and 12 months.

- At 12 months, compared with those receiving usual care, more intervention group participants completely discontinued opioid medications (7 versus 29 percent, respectively), and reduced opioid medication dosage by more than half from their baseline dose (27 versus 57 percent).

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Multicomponent Intervention to Reduce Opioid Pain Medication Dosage May Be Effective Among People Interested in Tapering or Cessation (continued from page 5)

- 42 of 90 participants who fully discontinued opioid medications were receiving <30 MME at baseline.
- Pain scores were not significantly different between groups at any follow-up time-point.
- There were very serious adverse events (experienced by 8 percent of patients in the intervention group, and 5 percent in the control group); one participant in the intervention arm was hospitalized due to a suicide attempt.

Comments: This study provides more evidence that patients receiving high doses of opioid medications for chronic, non-cancer pain who want to taper or stop their medication can do so with education and support. However, clinicians must not extrapolate findings to patients who choose not to taper opioid medications. Due to the association between opioid medication dose and the risk of overdose or developing substance use disorder, voluntary tapers could also improve these outcomes. Importantly, worsening mental health and suicidality remain concerns during and following opioid medication tapers.

Aaron D. Fox, MD

Reference: Sandhu HK, Booth K, Furlan AD, et al. Reducing opioid use for chronic pain with a group-based intervention: a randomized clinical trial. *JAMA*. 2023;329(20):1745–1756.

Listen to Episode 5 of our podcast, "**Behind the Evidence**," supported by the Grayken Center for Addiction at Boston Medical Center.

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.

Episode 5 features an interview with **Dr Sumeet Singh-Tan, DO** on her article, "Addiction consult service and inpatient outcomes among patients with alcohol use disorder," that was recently summarized in *AODH*.

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