Alcohol, Other Drugs, and Health: Current Evidence

JULY-AUGUST 2020

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INTERVENTIONS & ASSESSMENTS

Ninety-five Percent of Adolescents With Diagnosed Opioid Use Disorder Are Not Prescribed Recommended Treatment

Few adolescents diagnosed with opioid use disorder (OUD) are prescribed the recommended medications for OUD (MOUD). This study used data from the Ohio Medicaid program to examine adolescents' (N=626,508; aged 12–18 years) receipt of MOUD (buprenorphine and/or naltrexone) within 3 months of an OUD diagnosis.

- Overall, 5% of adolescents with an OUD diagnosis received MOUD; those aged 16–18 were more likely to receive a prescription for MOUD than adolescents aged 12–15 (6% versus 1%, respectively).
- Most adolescents with OUD had a health care appointment within 3 months of the OUD diagnosis; 49% had a general medical appointment, 40% had an emergency department visit, and 28% had a behavioral health appointment.
- Around 10% of adolescents with OUD received a prescription for an opioid pain medication within 3 months of their diagnosis.

Comments: This study confirms that very few adolescents diagnosed with OUD receive the standard-of-care treatment, and adds a new insight: the low levels of MOUD receipt are NOT due to lack of interaction with the medical system. The finding that youth with OUD were nearly twice as likely to receive an opioid pain medication as they were to be prescribed MOUD indicates that the healthcare system is not adequately prepared to manage substance use disorders, despite the availability of effective treatment.

Sharon Levy, MD, MPH

Reference: Chavez LJ, Bonny AE, Bradley KA, et al. Medication treatment and healthcare use among adolescents with opioid use disorder in Ohio. *J Adolesc Health*. 2020;67(1):33–39.

Although Not Evidence-based, the USPSTF Recommends Screening Adults for Drug Use

Previously, the US Preventive Services Task Force (USPSTF) has found the evidence to be insufficient to recommend screening for unhealthy drug use,* although US health agencies have sponsored such screening programs. The USPSTF recently published a new recommendation.

- "The USPSTF recommends screening by asking questions about unhealthy drug use in adults 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred." This is a grade B recommendation, which means that "the USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial."

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Although Not Evidence-based, the USPSTF Recommends Screening Adults for Drug Use (continued from page 1)

- The USPSTF also concluded that that "the current evidence is insufficient to assess the balance of benefits and harms of screening" adolescents.
- The evidence review found that brief screening tools are valid, and treatment for drug use disorder (e.g., pharmacotherapy for opioid use disorder) has efficacy in people who seek it.
- However, among those identified by screening, brief counseling lacked efficacy for reducing drug use or increasing treatment entry.

* Defined as "the use of substances (not including alcohol or tobacco products) that are illegally obtained or the nonmedical use of prescription psychoactive medications."

Comments: The USPSTF's recommendation represents a stunning departure from its decades of strict reliance on evidence of a preventive service's efficacy. Clearly there are reasons to identify unhealthy drug use: to diagnose and treat symptoms that could be caused by use; to prescribe medications; to better know one's patient; and to demonstrate to patients, clinicians, and policy-makers that drug use is a medical issue. But clinicians should be aware of the potential risks of documenting illegal behavior in the medical record (e.g., in some states, drug use by pregnant women is deemed criminal child abuse), and they should not expect patients to reduce their use or link to specialized care as a result of their brief advice.

Richard Saitz, MD, MPH.

References: US Preventive Services Task Force. Screening for unhealthy drug use: US Preventive Services Task Force recommendation statement. *JAMA*. 2020;323(22):2301–2309.
Patnode CD, Perdue LA, Rushkin M, et al. Screening for unhealthy drug use: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2020;323(22):2310–2328.
Saitz R. Screening for unhealthy drug use: neither an unreasonable idea nor an evidence-based practice. *JAMA*. 2020;323(22):2263–2265.
Bradley KA, Lapham GT, Lee AK. Screening for drug use in primary care: practical implications of the new USPSTF recommendation. *JAMA Intern Med*. 2020 [Epub ahead of print]. doi:10.1001/jamainternmed.2019.7335.

Gabapentin as a Treatment for Alcohol Use Disorder and Alcohol Withdrawal Symptoms

Pharmacological options for treatment of alcohol use disorder (AUD) are limited. Gabapentin may improve alcohol withdrawal symptoms through its hypothesized action on GABA and glutamate activity. In this randomized trial, researchers assessed the effects of gabapentin on alcohol consumption over 16 weeks among 96 people with AUD and withdrawal symptoms* who were abstinent at baseline (those with acute withdrawal symptoms** were excluded). Participants were randomized to receive gabapentin (up to 1200 mg/day) or placebo. All also received 9 brief educational and supportive sessions.

- At follow-up, 27% of participants receiving gabapentin had no heavy drinking days, compared with 9% of participants receiving placebo. There were also more people with total abstinence in the gabapentin group (18%), compared with placebo (4%).
- In secondary analyses, gabapentin showed an effect only among participants with high alcohol withdrawal symptoms, compared with those with low withdrawal symptoms (based on median split of alcohol withdrawal symptoms at baseline).
- Participants in the gabapentin group reported more dizziness compared with the placebo group.
- Overall, 30% of participants in the gabapentin group and 39% in the placebo group did not complete treatment, although they were included in the final analysis.

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Gabapentin as a Treatment for Alcohol Use Disorder and Alcohol Withdrawal Symptoms (continued from page 2)

* Measured via the modified Alcohol Withdrawal Symptoms Checklist (AWSC).
** Defined as a Clinical Institute Withdrawal Assessment for Alcohol–Revised (CIWA-Ar) score of ≥10.

Comments: This study provides evidence that gabapentin may be useful to treat AUD among people with significant alcohol withdrawal symptoms, but these results should be replicated since people with acute withdrawal symptoms were excluded. Potential efficacy should be balanced with the risk of misuse and the risk for overdose death among people who use other drugs.

Nicolas Bertholet, MD, MSc

Reference: Anton RF, Latham P, Voronin K, et al. Efficacy of gabapentin for the treatment of alcohol use disorder in patients with alcohol withdrawal symptoms: a randomized clinical trial. *JAMA Intern Med*. 2020;180(5):1–9.

HEALTH OUTCOMES

Vast Majority of US Adults Experiencing Nonfatal Opioid Overdose Do Not Receive Treatment

In the US, few people who could benefit from opioid use disorder (OUD) treatment receive it, including those who experience nonfatal opioid overdoses. This study used 5 years of claims data for 6451 commercially insured adults who were treated for opioid overdose in an emergency department to investigate OUD treatment receipt within 90 days of the overdose. OUD treatment receipt was defined as receiving buprenorphine or naltrexone, or inpatient or outpatient treatment encounters. Methadone was not covered by insurance for these patients during the study period, so it was not included.

- 17% of patients received OUD treatment within 90 days post-overdose.
- The majority of patients (n=5769) had not received OUD treatment in the 90 days before their overdose, and only 11% of these patients received OUD treatment in the 90 days post-overdose.
- Patients with prescription opioid overdoses were less likely to receive OUD treatment than those with heroin overdoses.
- In stratified analyses examining patients who were not receiving OUD treatment in the 90 days before their overdose, Black, Hispanic, female, and younger patients were less likely to receive OUD treatment than white, male, and older patients.

Comments: Despite study limitations, including an inability to determine patients' access to methadone, these data demonstrate that even commercially insured patients rarely receive OUD treatment following an overdose. Initiating buprenorphine in the emergency department is feasible and effective, and other interventions are needed to facilitate treatment entry following an overdose. However, a better understanding why people do not enter treatment following an overdose is most critical for designing patient-centered treatment and harm-reduction interventions that could reduce overdose deaths.

Aaron D. Fox, MD

Reference: Kilaru AS, Xiong A, Lowenstein M, et al. Incidence of treatment for opioid use disorder following nonfatal overdose in commercially insured patients. *JAMA Netw Open*. 2020;3(5):e205852.

Non-prescribed Buprenorphine Use Among People With Opioid Use Disorder is Primarily Therapeutic and Reduces the Risk of Overdose

Buprenorphine is an effective treatment for opioid use disorder (OUD) and reduces the risk of overdose, but many people with OUD in the US do not have access to it and there are concerns about diversion. Previous studies have indicated that reasons for non-prescribed buprenorphine use (NPBU) among individuals with OUD are generally consistent with therapeutic goals. Researchers in Ohio recruited a cohort of 356 individuals with OUD and self-reported NPBU to investigate motivations for NPBU and the association between NPBU and self-reported overdose.

- Based on qualitative interviews of 65 participants, a number of motivations for NPBU were identified:
  - Avoiding the demands of formal treatment (e.g., attending meetings).
  - "Geographic cure" (doing a self-taper in another locality).
  - As a path to formal treatment (avoiding the wait).
  - Desire for autonomy and self-determination (having ownership over the recovery process).

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Non-prescribed Buprenorphine Use Among People With Opioid Use Disorder is Primarily Therapeutic and Reduces the Risk of Overdose (continued from page 3)

- In a separate analysis of the entire cohort, 28% of participants reported experiencing an overdose in the past 6 months.
  - Higher mean percentage of days of NPBU in the past 6 months was associated with a decreased risk of overdose in both unadjusted (odds ratio [OR], 0.82) and adjusted analyses (adjusted OR [aOR], 0.81), with a linear trend of lower overdose risk with increasing NPBU.
  - Factors associated with an increased risk of overdose included prior overdose (aOR, 2.19) and injection drug use (aOR, 2.49).

Comments: These studies show that individuals with OUD are generally using non-prescribed buprenorphine for appropriate reasons and that diversion of buprenorphine has some benefits. This highlights the need for accessible, flexible, patient-centered treatment. Moreover, efforts to criminalize and clamp down on buprenorphine diversion are likely to do more harm than good.

Darius A. Rastegar, MD

References: Silverstein SM, Daniulaityte R, Miller SC, et al. On my own terms: motivations for self-treating opioid-use disorder with non-prescribed buprenorphine. *Drug Alcohol Depend*. 2020;210:107958.
Carlson RG, Daniulaityte R, Silverstein SM, et al. Unintentional drug overdose: is more frequent use of non-prescribed buprenorphine associated with lower risk of overdose? *Int J Drug Policy*. 2020;79:102722.

Benzodiazepines and Alcohol Are Often Involved in Opioid Overdose Deaths

Opioid overdose is a growing cause of death in the US. The risk of fatal overdose from opioids is increased by the concomitant use of other sedating drugs such as benzodiazepines and alcohol. Researchers used data from a National Vital Statistics System database of all opioid-related poisoning deaths from 1999 to 2017 to characterize alcohol and benzodiazepine co-involvement. They also looked at correlations of alcohol co-involvement in opioid-related deaths with state-level heavy episodic drinking prevalence,* and of benzodiazepine co-involvement in opioid-related deaths with state-level benzodiazepine prescribing.**

- From 1999 to 2017, there were 399,230 reported poisoning deaths involving opioids; 66% of fatalities were men, and 51% were aged 35–54.
- Alcohol co-involvement in opioid-related deaths increased from 12% in 1999 to 15% in 2017; in the same period, benzodiazepine co-involvement in opioid-related deaths increased from 9% in to 21%.
- Across states, heavy episodic drinking was positively correlated with alcohol co-involvement in opioid-related deaths, and benzodiazepine prescribing was likewise positively correlated with benzodiazepine co-involvement in opioid-related deaths.

* Defined as ≥5 standard drinks for men and ≥4 for women on 1 occasion in the last month. Data from 2015–2017 Behavioral Risk Factor Surveillance System.
** Data from 2012 (most recent available).

Comments: This study shows that alcohol and benzodiazepines are often involved in opioid overdose deaths. Given the limitations of death reports, this data likely underestimates the prevalence. Nevertheless, this study underscores the importance of avoiding the co-prescribing of opioids and benzodiazepines, as well as addressing unhealthy alcohol use among individuals who use opioids (prescribed and non-prescribed).

Darius A. Rastegar, MD

Reference: Tori ME, Larochelle MR, Naimi TS. Alcohol or benzodiazepine co-involvement with opioid overdose deaths in the United States, 1999–2017. *JAMA Netw Open*. 2020;3

Link Between Cannabis Use and Alcohol Consequences Among College Students

Cannabis use may have an impact on negative outcomes of alcohol consumption, but longitudinal data is lacking. Using data from a cohort study of 997 US college students (evaluated 4 times/year during their first 3 years of college), researchers assessed associations between cannabis use changes and negative alcohol consequences.*

- Changes in cannabis use were not associated with the overall number of alcohol consequences (after accounting for changes in alcohol use).
- However, when alcohol consequences were analyzed separately by type of consequence, increases in cannabis use were associated with an increase in alcohol-related risky behaviors, physical dependence symptoms, and lack of self-care.
- Sex was not a moderator in these associations.

* Measured with the Young Adult Alcohol Consequences Questionnaire (YAACQ), comprising 48 items grouped in 8 domains: blackout/hangover consequences, social/interpersonal consequences, impaired control, risky behaviors, academic/occupational consequences, self-perception consequences, self-care consequences, and physical dependence.

Comments: These results suggest that, among college students, increased cannabis use has a detrimental effect on some consequences of alcohol use that can be considered more severe (e.g., physical dependence symptoms). Providers should consider incorporating discussions about cannabis use into alcohol use harm-reduction strategies in this population.

Nicolas Bertholet, MD, MSc

Reference: Wardell JD, Egerton GA, Read JP. Does cannabis use predict more severe types of alcohol consequences? Longitudinal associations in a 3-year study of college students. *Alcohol Clin Exp Res*. 2020;44(5):1141–1150.

PRESCRIPTION DRUGS & PAIN

Opioid Prescribing Interventions to Decrease Opioid Use Disorder and Overdose Likely Miss at-risk Patients

Recent clinical guidelines in the US have cautioned against the prescription of high-dose opioid medications (>90mg morphine equivalent dose [MED] per day), particularly for chronic pain, and many clinicians have adjusted their practice accordingly. This cross-sectional study of commercially insured adults (N=227,038) with a new diagnosis of opioid use disorder (OUD) or opioid overdose examined patterns of opioid prescribing in the 12 months prior to diagnosis.

- 51% of patients in the study had a diagnosis of chronic pain.
- 35% of patients with incident OUD or opioid overdose were not prescribed an opioid in the year before their diagnosis.
- From 2006–2016, the proportion of patients not receiving a prescription opioid in the year before their OUD or opioid overdose diagnosis increased by 86%.
- Among the 65% of patients who received an opioid prescription prior to their diagnosis of OUD or opioid overdose, most were prescribed >20mg MED per day; only 13% were prescribed high-dose opioid medications (>150mg MED per day).

Comments: This study highlights the limitations of opioid prescription-focused interventions to prevent the development of OUD and opioid overdose, but confirms that even patients who are prescribed lower doses of opioid medications can be at risk. Although opioid prescriptions have reduced overall in the US since 2006, opioid overdoses remain high due to fentanyl contamination of the US drug supply and ongoing barriers to OUD treatment. Without a systematic approach to addressing OUD and opioid overdose, interventions that focus on prescription opioids alone will continue to fall short.

Melissa Weimer, DO, MCR

Reference: Wei YJ, Chen C, Fillingim R, et al. Trends in prescription opioid use and dose trajectories before opioid use disorder or overdose in US adults from 2006 to 2016: A cross-sectional study. *PLoS Med*. 2019;16(11):e1002941.

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