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

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Alcohol, Other Drugs, and Health: Current Evidence

JANUARY-FEBRUARY 2023

INTERVENTIONS & ASSESSMENTS

Are American Adults Receiving Recommended Alcohol Screening at Primary Care Visits?

The US Preventive Services Task Force (USPSTF) recommends screening all adults for unhealthy alcohol use during primary care visits. Investigators used nationally representative survey data (N=19,213 primary care visits) to estimate the percentage of visits in which a validated alcohol screening questionnaire was administered, and whether practitioners documented providing counseling or education on alcohol use (or referral for these services). Investigators also examined patient and visit characteristics that predicted alcohol screening receipt.

- Alcohol screening with a validated questionnaire was documented in 2.6% of visits.
- Patients' sex, race/ethnicity, age group, or length of appointment time were not associated with screening receipt.
- Receiving care from one's assigned primary care physician, being a new patient to the practice, or having chronic medical conditions were associated with screening receipt.
- Alcohol counseling or referral was documented in 0.8% of visits.

Comments: Investigators note that more than three-quarters of adult participants in other national surveys report that a medical professional had asked them about alcohol consumption recently; however, the USPSTF recommends screening with structured validated questionnaires, which occurred with very low frequency in this national study. The Alcohol Use Disorders Identification Test (AUDIT), AUDIT-C, and the NIAAA Single Alcohol Screening Question are straightforward to use and screen for the full spectrum of unhealthy alcohol use (risky drinking and alcohol use disorders). Because brief interventions (i.e., 10-15 minutes of focused counseling on reducing alcohol use) lead to clinically meaningful reductions in alcohol consumption, higher rates of screening and counseling or referral could substantially reduce alcohol-related morbidity and mortality.

Aaron D. Fox, MD

Reference: Chatterton B, Agnoli A, Schwarz EB, Fenton JJ. Alcohol screening during US primary care visits, 2014–2016. *J Gen Intern Med*. 2022;37(15):3848–3852.

Psilocybin Plus Psychotherapy Associated With Reductions in Drinking Among Adults With Alcohol Use Disorder

There is growing interest in the prescribing of psychedelic medications to treat substance use disorder. Researchers conducted a double-blind, placebo-controlled, randomized trial of psilocybin compared with placebo (diphenhydramine) among 93 people aged 25–65 with alcohol use disorder and ≥4 heavy drinking days in the 30 days prior to enrollment. Medication was administered in weeks 4 and 8 of the study; both groups received 12 sessions of psychotherapy during the first 12 weeks of the study.

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Psilocybin Plus Psychotherapy Associated With Reductions in Drinking Among Adults With Alcohol Use Disorder (continued from page 1)

- Approximately 90% of participants correctly guessed their treatment group.
- In the 32 weeks after the first medication dose, the psilocybin group reported 10% heavy drinking days versus 24% in the placebo group.
- Compared with the placebo group, participants receiving psilocybin had significantly lower mean drinks per day (mean difference, 1.09 drinks), higher rates of abstinence, and greater reductions in WHO risk scores. Differences in drinking days were non-significant.
- Although there were more adverse events in the psilocybin group (e.g., headache), there were only 3 serious adverse events, all of which were in the placebo group.

Comments: Treatment with psilocybin and psychotherapy resulted in substantial reductions in most drinking measures compared with a diphenhydramine control, with no serious adverse events associated with psilocybin. Most participants could guess their treatment group, suggesting a possible source of bias in the results. Additional research should clarify the effects of psilocybin independent of psychotherapy, the duration of effects over longer follow-up periods, and explore effects among higher-risk populations.

Timothy S. Naimi, MD, MPH

Reference: Bogenschutz MP, Ross S, Bhatt S, et al. Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry*. 2022;79(10): 953–962.

HEALTH OUTCOMES

Premature Mortality Due to Overdose Rising Among US Adolescents

Years of life lost (YLL) is an epidemiologic tool that measures premature mortality. Researchers used nationally representative data to examine US trends in YLL due to unintentional overdose 2016–2020 among adolescents aged 10–19.

- YLL due to unintentional overdose remained stable 2016–2019, and then more than doubled 2019–2020.
- Illicitly manufactured fentanyl and synthetic opioids other than methadone were involved in 81% of unintentional overdoses in 2020.

Comments: In the US, mortality from unintentional overdose is rising faster among adolescents than in any other age group, even as rates of unhealthy substance use (except for cannabis) are dropping. Adolescents are prone to impulsivity and risk-taking and are developmentally disposed to seek large neurological reward—all characteristics that promote substance use in this age group. Many adolescents who die of an unintentional overdose are victims of the increasingly contaminated illicit drug supply and do not have opioid use disorder. Novel strategies are needed to protect this group.

Sharon Levy, MD

Reference: Hermans SP, Samiec J, Golec A, et al. Years of life lost to unintentional drug overdose rapidly rising in the adolescent population, 2016–2020. *J Adol Health*. 2022;S1054-139X(22)00542-0.

Increased Risk of Death Following Compulsory Substance Use Treatment

In Sweden, individuals may be legally coerced into treatment for substance use disorder if they are not interested in entering treatment voluntarily, and they are deemed to be at risk of harming themselves or their families, or causing "irreparable damage to their futures." Researchers examined 2000–2017 data on individuals who completed 6 months of compulsory treatment (the maximum duration; N=7929) and had a "regular" discharge (i.e., not deceased or discharged to jail, prison, or hospital) to determine mortality rates in the year following treatment discharge. During the study period, treatment programs did not offer medications for opioid use disorder.

- During a follow-up period of 6945 person-years, 494 individuals who received compulsory treatment died—a mortality rate of 7 per 100 person-years—substantially higher than age and sex-matched rates.
- Mortality rates were highest during the first 2 weeks after discharge, with a rate of 14 per 100 person-years versus 4 per 100 person-years for the remainder of the year.
- For deaths from "external causes" (including overdose and suicide), there was a hazard ratio of 2.6 during the first 2 weeks compared with the following 2 weeks.

Comments: While compulsory treatment is ostensibly intended to help individuals at high risk of harming themselves or others, this study suggests that it can be harmful, particularly if focused on abstinence as a goal. These results support a move away from coercive program-centered models of care toward voluntary patient-centered models focused on health promotion and harm reduction.

Darius A. Rastegar, MD

Reference: Ledberg A, Reitan T. Increased risk of death immediately after discharge from compulsory care for substance abuse. *Drug Alcohol Depend*. 2022;236:109492.

Receipt of Prescription Stimulant Medications after Drug-Related Poisoning Associated with Mixed Outcomes in Buprenorphine Treatment

Patients with opioid use disorder (OUD) have high rates of attention-deficit/hyperactivity disorder, as well as increasing rates of co-occurring stimulant use disorder, especially methamphetamine use disorder. Clinicians treating OUD must weigh the potential risks and benefits of prescribing stimulant medications to patients receiving buprenorphine for OUD. This retrospective recurrent-event cohort study used administrative claims data (2006–2016) to investigate the association between days with stimulant prescription and both drug-related poisonings and buprenorphine treatment retention in patients who had already experienced a drug-related poisoning.

- Among 22,946 individuals who were prescribed buprenorphine and experienced a drug-related poisoning, stimulant treatment days were associated with a 19% increased odds of subsequent drug-related poisoning (odds ratio [OR], 1.19), compared with no stimulant treatment.
- Stimulant treatment days were associated with 36% decreased odds of attrition from buprenorphine treatment (OR, 0.64).
- Buprenorphine treatment days were associated with a 38% decreased odds of drug-related poisoning (OR, 0.62).

Comments: The modest increase in per-day risk of drug-related poisoning associated with stimulant medication prescription was offset by the association between stimulant prescription and improved buprenorphine retention, which protects against overdose. Given the benefits of buprenorphine retention beyond overdose prevention, these data are reassuring that treatment with stimulant medications is not likely to increase risk substantially in patients receiving buprenorphine, although clinicians and patients should weigh both risks and benefits of this medication combination.

Joseph Merrill, MD, MPH

Reference: Mintz CM, Xu KY, Presnall NJ, et al. Analysis of stimulant prescriptions and drug-related poisoning risk among persons receiving buprenorphine treatment for opioid use disorder. *JAMA Netw Open*. 2022;5(5):e2211634.

Which Buprenorphine Taper Characteristics Are Associated with Subsequent Overdose Risk?

This retrospective cohort study assessed the association of buprenorphine taper characteristics* with opioid overdose in Ontario, Canada. Participants were 5774 adults with opioid use disorder treated with buprenorphine for ≥60 days who subsequently underwent a buprenorphine taper and were followed for ≤18 months after buprenorphine discontinuation.

- Lower rates of overdose death were observed among people with:
  - ◊ ≥1 year of buprenorphine receipt, compared with people with <1 year (7 versus 10 overdoses per 100 person-years, respectively; adjusted hazard ratio [aHR], 0.69).
  - ◊ Lower versus higher taper rates:
    – Patients tapered at the rate of 2 mg per month had 7 overdoses per 100 person years; those tapered >2–4 mg per month had 11 overdoses per 100 person-years; and patients tapered >4 mg per month had 17 overdoses per 100 person-years.

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Which Buprenorphine Taper Characteristics Are Associated with Subsequent Overdose Risk?

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  - 2 mg per month versus >4 mg per month, aHR, 0.65; >2–4mg per month versus >4 mg per month, aHR, 0.69.
  - ◊ A smaller proportion of days with dose decreases (1.75 percent days with dose decreases versus >3.50% of days, 6 versus 14 overdoses per 100 person-years, respectively; aHR, 0.64).
- Overall duration of taper was not associated with risk of overdose.

* Taper characteristics included: time to initiation of taper, rate of taper, the proportion of days when the prescribed buprenorphine dose was decreasing, and the duration of the taper.

Comments: Buprenorphine is highly protective against overdose; patients should be encouraged to continue receiving this medication for as long as they need. Patients who want to taper off of buprenorphine should be advised of the risks. This study showed that overall taper duration was not associated with differences in overdose risk, but higher rates of dose reductions, and tapers with a higher proportion of days with dose decreases were associated with increased risk of overdose. If a patient is stopping buprenorphine treatment, risk of opioid overdose may be decreased by waiting until they have had a year of treatment, and tapering at a slower rate with fewer days with a dose decrease.

Elizabeth A. Samuels, MD

Reference: Bozinoff N, Men S, Kurdyak P, et al. Prescribing characteristics associated with opioid overdose following buprenorphine taper. *JAMA Netw Open*. 2022;5(9):e2234168.

How Does Social Support Affect Recovery from Opioid Use Disorder?

The aim of this study was to better understand the role of social networks in maintaining recovery from opioid use disorder (OUD). Researchers completed longitudinal surveys (2 surveys, 3 months apart) with 106 adults receiving medications for OUD in Delaware who planned to disclose their substance use, treatment, or recovery to a person in their life. Surveys assessed the degree of social support provided, and closeness to—and history of shared substance use with—the person to whom they disclosed.

- Participants who disclosed to someone with whom they felt close had increased commitment to recovery. This was stronger among individuals whose close contacts provided higher social support.
- Disclosure to someone with whom participants had previously used substances was associated with decreased commitment to recovery.

Comments: Social networks and relationships can influence recovery. This study demonstrates that disclosing substance use, treatment, or recovery to a highly supportive and close person—without a shared substance use history—may be beneficial to recovery.

Elizabeth A. Samuels, MD, MPH, MHS

Reference: Brousseau NM, Karpyn A, Laurenceau JP, et al. The impacts of social support and relationship characteristics on commitment to sobriety among people in opioid use disorder recovery. *J Stud Alcohol Drugs*. 2022 Sep;83(5):646–652.

HIV & HCV

Is Injection Drug Use Associated with HCV Reinfection Among People Receiving Medications for Opioid Use Disorder?

Treatment of hepatitis C virus (HCV) with elbasvir–grazoprevir is safe and effective in people with injection drug use (IDU) who are receiving medications for opioid use disorder (MOUD; methadone, buprenorphine, or buprenorphine–naloxone). However, the likelihood of HCV reinfection in this population—and whether continued IDU following HCV treatment completion affects this likelihood—are not well understood. Researchers examined a cohort of adults with HCV receiving MOUD who completed elbasvir–grazoprevir treatment to examine the rate of HCV reinfection over a 3-year period. Participants were recruited from 13 countries, including the US.

- Among the 286 participants (604 person-years) included in analyses, the rate of HCV reinfection was 1.7 per 100-person years. Among participants who reported IDU in the last month (n=91; 212 person-years), the reinfection rate was higher (1.9 per 100 person-years).
- Risk for HCV reinfection was highest within 6 months of HCV treatment completion.
- More than 50 percent of participants had urine drug tests positive for substances other than MOUD, and approximately 20 percent reported IDU throughout the study period.

(continued page 5)

Is Injection Drug Use Associated with HCV Reinfection Among People Receiving Medications for Opioid Use Disorder?

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Comments: Among people who completed elbasvir–grazoprevir treatment for HCV, and received MOUD, HCV reinfection rates were low overall, despite the relatively high prevalence of continued IDU among participants. Risk of HCV reinfection was highest within 6 months of HCV treatment completion, suggesting that this period may be key for optimizing MOUD and ensuring access to needle and syringe services programs for people who complete HCV treatment and have IDU.

Carrie Mintz, MD

Reference: Grebely J, Dore GJ, Altice, FL et al. Reinfection and risk behaviors after treatment of hepatitis C virus infection in persons receiving opioid agonist therapy: a cohort study. *Ann Intern Med*. 2022;175(9):1221–1229.

PRESCRIPTION DRUGS & PAIN

State Opioid Prescribing Limits Are Not Associated With Reduced Prescribing or Overdose

The rise in opioid prescribing and overdose that began in the US in the 1990s has led to a number of interventions to discourage and limit opioid prescribing, including state laws that "cap" or limit dose and/or duration of initial opioid prescriptions. This study used 2013–19 administrative insurance claims from commercial and Medicare Advantage plans to investigate the association between state cap laws and opioid prescribing and overdose.

- Between 2017 and 2019, 32 states implemented a cap law; 16 states (plus the District of Columbia) did not. Two states that implemented laws before 2017 were not included. The characteristics of the 2 cohorts prior to implementation, including opioid prescribing and overdose rates, were similar.
- State opioid cap laws were not associated with any of the opioid prescribing outcomes, including proportion of persons receiving a prescription and the volume, duration, or dosage of the prescriptions.
- State opioid cap laws were not associated with opioid overdose outcomes overall, or with prescription or non-medical opioid overdose rates.

Comments: This study suggests that state cap laws do not have a significant impact on opioid prescribing or overdose. This is probably because these laws were implemented in the context of growing awareness of harms, and implementation of other measures and efforts to limit prescribing. While well-intended, these laws create additional administrative burdens for clinicians and pharmacies without proven value.

Darius A. Rastegar, MD

Reference: Tormohlen KN, McCourt AD, Schmid I, et al. State prescribing cap laws' association with opioid analgesic prescribing and opioid overdose. *Drug Alcohol Depend*. 2022;240:109626.

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Is an Opioid-sparing Pain Management Protocol Comparable to Standard Care Following Certain Orthopedic Surgeries?

In North America, patients undergoing orthopedic and other surgeries frequently receive prescriptions for more opioid analgesics than guidelines recommend for the postoperative period. Investigators examined an opioid-sparing postoperative pain protocol that included patient education, non-steroidal anti-inflammatory drugs, acetaminophen, and a limited amount of opioid analgesic to be used as a rescue medication. Adult patients (N=200) undergoing outpatient arthroscopic shoulder or knee surgery were randomized to the opioid-sparing protocol or standard care, and followed for 6 weeks postoperatively to assess opioid consumption, pain, patient satisfaction, opioid prescriptions, and adverse events.

- Participants had a mean age of 43; most participated in moderate or vigorous physical activity prior to their injury, and few had co-morbid chronic health conditions.
- The intervention group took far fewer opioid medications—measured in oral morphine equivalents—than the standard care group (median, 0 mg versus 40 mg, respectively), and were prescribed fewer opioid medications than the standard care group (mean, 40 mg versus 341 mg).
- There were no significant differences between groups in patient satisfaction or daily pain scores over the first 14 post-operative days, and no difference in requests for additional opioids after discharge.

Comments: By administering patient education and non-opioid analgesics, investigators achieved good post-operative pain management for healthy adults undergoing arthroscopic orthopedic surgeries. These simple and effective measures for post-operative management should be adopted more broadly. However, the implications for the opioid overdose crisis, which is currently being driven by illicitly manufactured fentanyl, should not be overstated. Practitioners and health systems must commit to improving diagnosis and treatment of opioid use disorder in addition to reducing opioid prescribing.

Aaron D. Fox, MD

Reference: NO PAin Investigators, Gazendam A, Ekhtiari S, et al. Effect of a postoperative multimodal opioid-sparing protocol vs standard opioid prescribing on postoperative opioid consumption after knee or shoulder arthroscopy: a randomized clinical trial. *JAMA*. 2022;328(13):1326–1335.

NEW PODCAST: "BEHIND THE EVIDENCE"

The editors of *Alcohol, Other Drugs, and Health: Current Evidence* are pleased to announce the launch of a new podcast, "**Behind the Evidence**," which is 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 1 features an interview with Jessica Taylor, MD (Boston Medical Center/ Boston University Chobanian & Avedisian School of Medicine) on her recent research and work on a low-threshold methadone bridge clinic and linkage to opioid use disorder treatment, described in a recent publication that was summarized in the September-October 2022 issue of *AOD Health*.

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