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# Alcohol, Other Drugs, and Health: Current Evidence

MAY - JUNE 2020

## INTERVENTIONS & ASSESSMENTS

### Alcohol Abstinence to Treat Atrial Fibrillation

Both alcohol withdrawal and heavy drinking can trigger atrial fibrillation, but it is not known whether abstinence would reduce the occurrence of atrial fibrillation among people who drink regularly. Investigators studied 140 patients (85% male) with paroxysmal or persistent atrial fibrillation who were drinking an average of 17 drinks\* per week and were willing to consider abstinence. Participants in normal sinus rhythm were randomized to either encouragement to abstain (with monthly communication to assess adherence and provide positive reinforcement), or to continue their usual alcohol consumption. Patients with alcohol use disorder were excluded from the trial.

- The 70 patients in the abstinence group reduced their drinking to a mean of 2 drinks per week; 61% achieved abstinence and 76% drank  $\leq 2$  drinks per week. In the control group, drinking declined to 13 drinks per week.
- After two initial weeks in which outcomes were not assessed, atrial fibrillation recurred in 53% of the abstinence group and 73% of the control group. Median time in atrial fibrillation was 0.5% and 1.2%, respectively.

\* US standard drink = 12 g alcohol.

*Comments:* Abstinence may be difficult to achieve for those with alcohol use disorder and an inability to stop drinking despite wanting to do so. But for those without alcohol use disorder who are willing to abstain, have a reason (atrial fibrillation) to abstain, and are encouraged to abstain, they can do so and reap the benefits of less atrial fibrillation.

Richard Saitz, MD, MPH

*Reference:* Voskoboinik A, Kalman JM, De Silva A, et al. Alcohol abstinence in drinkers with atrial fibrillation. *N Engl J Med.* 2020;328:20–28.

### A Brief Motivational Intervention in a Trauma Center Did Not Have an Impact on Illicit Substance Use

Alcohol and illicit substance use are associated with traumatic injuries. Trauma center treatment for such injuries may be an opportunity to intervene and reduce further substance use. This study included adults admitted with a traumatic injury to a level I trauma center in Texas who had illicit substance use in the last 30 days, measured by self-report or urine drug screen. Participants were randomized to 1 of 3 groups: brief advice (BA), a brief motivational intervention (BMI), or BMI plus telephone booster 4 weeks later (BMI+B). BMI was delivered by trained research staff in a single 30–45 minute face-to-face session. Researchers assessed the mean percentage of days of self-reported abstinence from use of all substances (excluding alcohol) at baseline, 3, 6, 9, and 12 months.

(continued page 2)

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## A Brief Motivational Intervention in a Trauma Center Did Not Have an Impact on Illicit Substance Use (continued from page 1)

- During the study period, 5127 admissions were screened; 777 patients met study criteria, 416 agreed to participate, and 395 were included. Of these, 89% completed the 12-month follow-up.
- Cannabis was the most prevalent substance (88%), followed by cocaine (28%), sedatives (15%), non-medically used prescription opioids (11%), and methamphetamine (9%).
- All 3 groups reported reductions from baseline in the use of all substances (except alcohol) at all follow-up points, but there were no significant differences between groups.

*Comments:* This is another study that has failed to find a significant impact of brief intervention on illicit substance use among individuals identified through screening in a health care setting. It is possible that screening and brief advice have some effect, but the more intensive interventions tested so far do not provide additional benefit.

Darius A. Rastegar, MD

*Reference:* Field CA, Von Sternberg K, Velasquez MM. Randomized trial of screening and brief intervention to reduce injury and substance abuse in an urban level I trauma center. *Drug Alcohol Depend.* 2020;208:107792.

## Mirtazapine Reduces Methamphetamine Use Among Cisgender Men and Transgender Women Who Have Sex With Men

Methamphetamine use disorder is increasing in prevalence in the US, but unfortunately there are no FDA-approved medications for treating it. Mirtazapine, a mixed monoamine agonist-antagonist that increases norepinephrine, serotonin, and dopamine, showed promise in a prior 12-week trial among men who have sex with men. This study was a double-blind, placebo-controlled randomized trial of 24 weeks of mirtazapine (30 mg once daily), or placebo, among 120 cisgender men and transgender women with methamphetamine use disorder who have sex with men.

- Compared with those receiving placebo, participants receiving mirtazapine had 25% fewer methamphetamine-positive urine samples at 24 weeks, an effect that persisted at 36 weeks (risk ratio, 0.73).
- 18% of participants receiving mirtazapine and 8% receiving placebo achieved abstinence over the final 2 weeks of treatment, but the difference between groups was non-significant.
- Adherence to study medication was low; at week 24, participants took 28% of mirtazapine doses and 39% of placebo doses.

*Comments:* This is the second RCT to demonstrate benefit of mirtazapine in reducing methamphetamine use among cisgender men or transgender women who have sex with men. Many individuals with methamphetamine use disorder have comorbid sleep or mood disorders, and mirtazapine is effective for these indications. Given the dearth of treatment options and the overall safety profile of mirtazapine, it may be reasonable to consider off-label use of mirtazapine in patients with methamphetamine use disorder, especially for those with comorbid sleep disturbance or mood disorder, while we await additional studies in other populations.

Marc R. Larochelle, MD, MPH

*Reference:* Coffin PO, Santos GM, Hern J, et al. Effects of mirtazapine for methamphetamine use disorder among cisgender men and transgender women who have sex with men: a placebo-controlled randomized clinical trial. *JAMA Psychiatry.* 2020;77(3):246–255.

## HEALTH OUTCOMES

### Higher Buprenorphine Doses May Prevent Return to Use in Patients With Opioid Use Disorder

Data suggest that many patients treated for opioid use disorder (OUD) with buprenorphine may receive lower doses than recommended. Using data from German health insurance claims, researchers assessed the impact of buprenorphine dosage on risk of return to opioid use.\* Each patient with OUD identified in 2011 and 2012 and receiving buprenorphine (n=364) was followed for 4 years or until death. Buprenorphine dosage groups were: <6 mg/day (n=133), 6–<8 mg/day (n=40), 8–<10 mg/day (n=65), 10–<12 mg/day (n=27), 12–<16 mg/day (n=33), and ≥16 mg/day (n=66).

- Overall, 74% of the patients were male and the mean age was 34 years. The mean buprenorphine dose was 12.2 mg/day.
- 166 patients returned to opioid use during the study period.
- Patients receiving the lowest buprenorphine doses had the highest risk of return to use (64%).
- In analyses adjusted for age, gender, comorbidities, co-medication, fixed or variable dosing, up-dosing,

and take-home/office-based prescription, there was a protective effect of higher buprenorphine doses on the risk of return to use:

- Compared with patients receiving the lowest doses (<6 mg/day), the odds ratios (ORs) of return to use for each dose level were: 0.40 at 6–<8 mg/day, 0.28 at 8–<10, 0.26 at 10–<12, 0.40 at 12–<16, and 0.18 at ≥16.

\* Defined as either no opioid agonist treatment for >3 months and returning to opioid agonist treatment thereafter, or hospital stays with acute opioid intoxication.

*Comments:* This study found that higher buprenorphine doses were associated with a diminished risk of return to opioid use among people with OUD, highlighting the importance of adequate buprenorphine dosage in the treatment of this population.

Nicolas Bertholet, MD, MSc

*Reference:* Reimer J, Vogelmann T, Trümper D, Scherbaum N. Impact of buprenorphine dosage on the occurrence of relapses in patients with opioid dependence. *Eur Addict Res.* 2020;26(2):77–84.

### Opioid Agonist Treatment Rarely Used or Started During Opioid-related Hospitalizations

With increasing opioid-related hospitalizations in the US, how often is opioid agonist therapy (OAT) initiated or used for withdrawal management during admission? This retrospective cohort study examined the frequency of OAT receipt among 12,407 patients with opioid use disorder (OUD) during hospitalization in 109 Veterans Health Administration hospitals in 2017. Multi-level regression was used to determine patient and hospital-level characteristics associated with receiving OAT.

- Patients with OUD received OAT in only 15% of admissions.
- Hospitals varied widely in delivery of OAT, ranging from 0 to 43% of qualified admissions; large and medium-sized hospitals were more likely to provide OAT than small hospitals.
- Nearly 90% of patients were not receiving OAT at the time of admission; of these, only 2% initiated OAT and were linked to care following hospitalization.

- Patient-level characteristics associated with OAT receipt included: male gender, admission diagnosis related to OUD or OUD-related infection, OAT receipt prior to admission, and absence of a co-occurring substance use disorder diagnosis.

*Comments:* Hospitalization is a missed opportunity to initiate OAT among patients who are not receiving OUD treatment at the time of admission. Failure to continue previously prescribed OAT or manage withdrawal symptoms with OAT could also cause harm—for example, if patients leave the hospital against medical advice. Increasing appropriate OAT prescribing should be a goal for all health care systems, which may necessitate specific guidelines, provider education, and efforts to reduce stigma.

Aaron D. Fox, MD

*Reference:* Priest KC, Lovejoy TI, Englander H, et al. Opioid agonist therapy during hospitalization within the Veterans Health Administration: a pragmatic retrospective cohort analysis. *J Gen Intern Med.* 2020 [Epub ahead of print]. doi: 10.1007/s11606-020-05815-0.

## Heavy Episodic Drinking in High School is Associated With Heavy Drinking and DWI in Young Adulthood

While overall rates of alcohol use among US high school students have decreased over recent decades, rates of heavy episodic drinking remain high. This study examined the association between high school heavy episodic drinking\* and health risks in young adulthood using data from a nationally representative longitudinal study of tenth graders (N=2785), which followed them for 7 years.

- Heavy episodic drinking in high school was associated with the following outcomes at the first follow-up in young adulthood (4 years post-baseline):
  - Driving while impaired (DWI; adjusted odds ratio [aOR], 5.7).
  - Riding with an impaired driver (aOR, 4.2).
  - Drinking to black-out (aOR, 2.7).
  - Risky driving (aOR, 1.9).\*\*

- Parental monitoring and support for not using alcohol provided some protection against DWI, riding with an impaired driver, and black-out.

\* Defined as consuming 5–9 standard drinks in a day for males; 4–7 for females.

\*\* Measured via 21 questions from the validated Checkpoints Risky Driving Scale.

*Comments:* The typical trajectory of alcohol use during the high school years is one of increasing frequency and intensity, and teens who report heavy drinking in high school report riskier alcohol use as young adults, compared with peers who do not. Parenting skills may help to “bend the trajectory” of alcohol use among high school students and prevent risky behavior into adulthood.

Sharon Levy, MD, MPH

*Reference:* Vaca FE, Li K, Luk JW, et al. Longitudinal associations of 12th-grade binge drinking with risky driving and high-risk drinking. *Pediatrics*. 2020;145(2).

## HIV & HCV

### Opioid Agonist Treatment is Associated With Viral Suppression Among Women With HIV and Opioid Use Disorder

The goal of antiretroviral treatment (ART) is suppression of HIV. Previous studies have found lower rates of suppression among women, particularly those with illicit drug use. This study examined data from a cohort of people living with HIV and illicit drug use\* in Vancouver, Canada. The authors sought to investigate the association between receiving opioid agonist treatment (OAT), which was presumed to be evidence of opioid use disorder (OUD), and viral rebound among women with HIV who achieved viral suppression on ART.

- There were 185 women included from the cohort who achieved viral suppression; of these, 62 (34%) experienced at least one viral rebound event (defined as a viral load >1,000 copies/mL).
- In multivariable analyses, stimulant use was associated with an increased risk of viral rebound (adjusted hazard ratio [aHR], 2.35).

- The only protective factor was receiving OAT (aHR, 0.46), but the effect was attenuated when adherence was factored in (aHR, 0.57).

\* In this study classified as injection drug use, heroin use, and stimulant use in the last 6 months.

*Comments:* This study adds to the growing evidence of the benefits of OAT for OUD on the treatment of other chronic medical conditions. These results support the integration of OAT into regular medical care, especially for individuals with HIV infection, where adherence to treatment is vitally important.

Darius A. Rastegar, MD

*Reference:* Adams JW, Marshall BDL, Mohd Salleh NA, et al. Receipt of opioid agonist treatment halves the risk of HIV-1 RNA viral load rebound through improved ART adherence for HIV-infected women who use illicit drugs. *Drug Alcohol Depend*. 2020;206:107670.

## PRESCRIPTION DRUGS & PAIN

### Does Requiring Prescribers to Check Prescription Drug Monitoring Programs Increase Opioid-related Deaths?

Prescription drug monitoring programs (PDMPs) track controlled substance prescriptions, and they have been shown to reduce opioid prescribing when providers are required to access them program prior to prescribing opioids. To study whether the use of PDMPs is associated with prescription opioid or heroin-related deaths, researchers used Multiple Correspondence Analysis, a novel modeling tool, to create a single continuous measure of PDMP regulatory strength from multiple separate PDMP features.

- No association was found between PDMP regulatory strength and prescription opioid or heroin-related deaths.
- When the continuous measure of PDMP regulatory strength was replaced with a single dichotomous variable defining the requirement that prescribers

access the PDMP prior to prescribing, a positive association was found between that requirement and both prescription opioid and heroin-related death rates.

*Comments:* PDMPs have been promoted as important tools for identifying individuals who attempt to obtain prescription opioids from multiple providers or pharmacies. This study provides mixed evidence that the regulatory strength of PDMPs is associated with increased opioid-related overdose deaths. While the requirement that providers access the PDMP prior to prescribing opioids may be particularly salient, the difficulty of asserting causal inference in such observational studies is significant.

Joseph Merrill, MD, MPH

*Reference:* Meadowcroft D, Whitacre B. Do prescription drug monitoring programs encourage prescription—or illicit—opioid abuse? *Subst Abus.* 2019 [Epub ahead of print]. doi: 10.1080/08897077.2019.1695707.

### Complex Relationship Between Pain and Alcohol Consumption

The relationship between alcohol use and pain is complex and our understanding of it is incomplete. In this study, researchers assessed the bi-directionality of effects (alcohol consumption to pain, and pain to consumption) over time, and the possible moderation by gender and alcohol use disorder (AUD) symptoms.\* Using data from the 2001 and 2004 waves of the US National Epidemiological Survey on Alcohol and Related Conditions (NESARC), researchers found...

- In general, higher levels of baseline alcohol consumption were associated with lower levels of pain interference\*\* at follow-up.
- However, among men with  $\geq 2$  AUD symptoms, higher levels of alcohol consumption were associated with higher levels of pain interference.
- Higher levels of baseline pain were associated with lower levels of alcohol consumption at follow-up. No moderating effects were found for this association.

\* Measured via the *DSM-IV* version of the Alcohol Use Disorder and Associated Disability Interview Schedule.

\*\* Determined by 1 item from the Medical Outcomes Study 12-item Short-Form Health Survey, which asks participants the extent to which their engagement in daily activities was impacted by pain in the past 4 weeks, with response options ranging from (1) "not at all" to (5) "extremely."

*Comments:* Various mechanisms are likely at play within the bi-directional relationship between pain and alcohol consumption. The association between increased symptoms of AUD and higher levels of pain interference in men comes as no surprise since AUD may cause neurological dysregulations and increased sensitivity of stress systems.

Nicolas Bertholet, MD, MSc

*Reference:* Yeung EW, Lee MR, McDowell Y, et al. The association between alcohol consumption and pain interference in a nationally representative sample: the moderating roles of gender and alcohol use disorder symptomatology. *Alcohol Clin Exp Res.* 2020;44(3):645–659.

### Alcohol and Opioid Use Disorder in Hospitalized Patients

Two reviews on this topic appear in *Medical Clinics of North America: Update in Hospital Medicine* (2020).

Chernyavsky S, Dharapak P, Hui J, et al. Alcohol and the Hospitalized Patient. *Med Clin North Am.* 2020;104(4):681–694.

Herscher M, Fine M, Navalurkar R, Hirt L, Wang L. Diagnosis and Management of Opioid Use Disorder in Hospitalized Patients. *Med Clin North Am.* 2020;104(4):695–708.





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### Contact Information:

*Alcohol, Other Drugs, and Health: Current Evidence*  
Boston University School of  
Medicine/Boston Medical Center  
801 Massachusetts Ave., 2nd floor  
Boston, MA 02118  
[aodhce@bu.edu](mailto:aodhce@bu.edu)