Alcohol, Other Drugs, and Health: Current Evidence

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BEHIND THE EVIDENCE

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

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INTERVENTIONS & ASSESSMENTS

Psychostimulant Medications for Amphetamine-type Stimulant Use Disorder May Reduce Cravings and Use

High-quality evidence supporting the efficacy of prescription psychostimulants (PPs) for treating amphetamine-type stimulant use disorder (ATSUD) is lacking. Researchers performed a systematic review and meta-analysis of randomized placebo-controlled trials (10 studies with 561 participants), assessing the effect of PPs (methylphenidate, dextroamphetamine, and lisdexamphetamine) on ATSUD treatment retention, adverse events, early-stage ATS craving (<4 weeks treatment), end-point ATS craving (≥4 weeks treatment), withdrawal severity, and depression severity.

- The primary analyses showed no significant difference in early-stage ATS craving among participants receiving PPs versus placebo, but a modest reduction in end-point craving among those receiving PPs (standardized mean difference, -0.29).
- When studies with a high risk of bias were removed from the analyses, participants in the PP group also reduced ATS use as measured by urine drug testing, compared with placebo (relative risk [RR], 0.8).
- Subgroup analyses showed improved treatment retention among participants who received high-dose PPs (>162mg methylphenidate or 75mg dextroamphetamine; RR, 2.31), and who were enrolled in trials that had a longer period of treatment (>20 weeks; RR, 1.83).
- The subgroup of participants receiving PPs who had ATSUD and attention-deficit/hyperactivity disorder (ADHD) experienced reduced depressive symptom severity, compared with those receiving placebo (RR, -7.30).
- There was no significant difference between groups in adverse events or participants leaving the study.

Comments: In the absence of established pharmacotherapy for ATSUD, clinicians should consider the use of PPs. This study suggests that these medications may have a modest effect on cravings among patients with ATSUD, without increasing adverse events. Longer treatment duration, administering higher doses, and the provision of PPs for individuals with concurrent ADHD and ATSUD, may provide additional benefit.

Brigid Adviento, MD, MPH* & Darius A. Rastegar, MD

* 2023–24 Rich Saitz Editorial Intern & Addiction Medicine Fellow, University of Iowa Hospitals and Clinics

Reference: Sharafi H, Bakouni H, McAnulty C, et al. Prescription psychostimulants for the treatment of amphetamine-type stimulant use disorder: a systematic review and meta-analysis of randomized placebo-controlled trials. *Addiction*. 2024;119(2):211–224.

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HEALTH OUTCOMES

Telehealth Buprenorphine Initiation is Associated With Improved Treatment Retention for Individuals With Opioid Use Disorder

In the US, telehealth services were expanded during the COVID-19 pandemic to include prescribing buprenorphine for opioid use disorder (OUD). Two studies used large insurance databases to analyze the association between telehealth buprenorphine initiation and treatment retention and nonfatal overdose. Nguyen et al. performed a cross-sectional study using Medicare Advantage claims from March 2020 to November 2021, and compared in-person (n=9934) and telehealth (n=3314) buprenorphine initiation after balancing group covariates with propensity score matching. Hammerslag et al. performed a retrospective cohort study to compare in-person and telehealth buprenorphine initiations using Medicaid claims data from Kentucky and Ohio from November 2019 to December 2020 (n= 41,266).

- In Nguyen et al., the telehealth group was more likely to be ≥65 years of age, from a rural community, from the Midwest or South, have higher median household income, and lower comorbidity index. After propensity matching, in-person and telehealth groups were similar across all covariates except for comorbidity index, which continued to be lower in the telehealth group.
- In Hammerslag et al., the telehealth buprenorphine group was less likely to include Non-Hispanic Black individuals, and more likely to include individuals with a mental health diagnosis.
- Telehealth initiation was associated with improved treatment retention in both Nguyen et al. (odds ratio [OR], 1.37 for receiving a second buprenorphine refill after initiation) and Hammerslag et al. (Kentucky adjusted OR [aOR], 1.13 and Ohio aOR, 1.19 for continuous retention at least 90 days after initiation).
- Telehealth initiation of buprenorphine was significantly associated with reduced nonfatal opioid overdose in Nguyen et al. (adjusted incidence rate ratio, 0.64), but not in Hammerslag et al.

Comments: These analyses support the expansion of telehealth for treatment of OUD and suggest that telehealth initiation of buprenorphine is at least as effective as in-person initiation and may even lead to better outcomes. The observed improvements may be due to the population differences in those offered telehealth vs in-person initiation. They may also be explained by improved treatment engagement due to more accessible appointments to titrate buprenorphine to an effective dose.

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References: Nguyen B, Zhao C, Bailly E, Chi W. Telehealth initiation of buprenorphine for opioid use disorder: patient characteristics and outcomes. *J Gen Intern Med*. 2023 [Epub ahead of print]. doi:10.1007/s11606-023-08383-1.

Hammerslag LR, Mack A, Chandler RK, et al. Telemedicine buprenorphine initiation and retention in opioid use disorder treatment for Medicaid enrollees. *JAMA Netw Open*. 2023;6(10):e2336914.

Did Telehealth Expansion in the US During the COVID-19 Pandemic Improve Access to Substance Use Treatment and Outcomes?

In the US, changes in telehealth regulations during the COVID-19 pandemic expanded the provision of substance use disorder (SUD) treatment by telehealth. Two recent studies examined the role of telehealth in the delivery of addiction treatment over this period. Gainer and colleagues conducted a retrospective analysis of 544 patients receiving telehealth (video and telephone) and/or in-person treatment for any SUD from October 2020 to June 2022 at a community addiction clinic in Ohio. They compared risks of treatment discontinuation and factors associated with continued treatment engagement ("defined as at least one treatment visit within 14 days of the diagnostic evaluation, and completing at least two additional treatment visits within 34 days of the initiation date") between patients receiving telehealth and those receiving in-person care.

- Half of the patients (n=271) utilized multiple treatment modalities (telehealth with video, telephone, and in-person) in varying combinations.
- Most patients (85 percent) receiving telehealth services also received in-person care during the study period; 43 percent utilized in-person care only.
- There was lower risk of treatment discontinuation among individuals who received telehealth with video in their initial 14 days of treatment, compared with patients who received only in-person appointments (odds ratio [OR], 0.64).
- Patients had greater odds of treatment engagement with telehealth with video (OR, 5.40) and audio-only telehealth (OR, 2.12), compared with in-person only care.
- Continued engagement was associated with higher visit frequency in the first 14 days of treatment.

Focusing on opioid use disorder (OUD), Hailu and colleagues used a commercial insurance and Medicare Advantage claims database to examine telehealth adoption and OUD treatment characteristics. They compared changes in OUD treatment before and after the onset of the COVID-19 pandemic among clinicians with varying levels of telehealth utilization: low, medium, and high.

- After the onset of the pandemic, there was increased utilization of telehealth for OUD care; however, overall patient visits for OUD care did not change.
- There was no change in patient volume, or medication for OUD initiation, refills, or days' supply prescribed.
- There was no change in significant OUD-related clinical events such as overdose, admissions to inpatient detoxification or treatment, or injection-related infections.

Comments: Taken together, these studies suggest that telehealth is an important component of the addiction care system. By providing additional opportunities for connections with a clinician, telehealth may help improve treatment continuation, especially when utilized early in SUD care. Among commercially insured patients, the use of telehealth did not significantly change how prescribers provided medications for OUD, and there was no increase in opioid-related adverse events. There is a need for additional research to evaluate the impact of telehealth on addiction treatment access—particularly among Medicaid recipients and people who are uninsured—and whether or how telehealth could address inequities in addiction treatment access and engagement.

Elizabeth A. Samuels, MD, MPH, MHS

References: Gainer DM, Wong C, Embree JA, et al. Effects of telehealth on dropout and retention in care among treatment-seeking individuals with substance use disorder: a retrospective cohort study. *Subst Use Misuse*. 2023, 54(4);481–490.

Hailu R, Mehrotra A, Huskamp HA, Busch AB, Barnett ML. Telemedicine use and quality of opioid use disorder treatment in the US during the COVID-19 pandemic. *JAMA Netw Open*. 3;6(1):e2252381.

Cocaine or Methamphetamine Use Early in Opioid Use Disorder Treatment May Negatively Affect Treatment Outcomes

For people with opioid use disorder (OUD), the non-medical use of other substances may negatively impact treatment outcomes. Researchers investigated the association between patients' response to medications for OUD (MOUD) and the non-medical use of non-opioid substances in the four weeks prior to MOUD initiation and in the initial four weeks of MOUD receipt. They combined data from three clinical trials (N=2199 participants) and tested three MOUDs: methadone, buprenorphine, and extended-release naltrexone. Return to use was defined as four consecutive opioid-positive or missing urine drug tests between treatment weeks four and 12.

- The non-medical use of non-opioid substances prior to treatment entry was not associated with subsequent non-medical opioid use.

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Cocaine or Methamphetamine Use Early in Opioid Use Disorder Treatment May Negatively Affect Treatment Outcomes *(continued from page 3)*

- Cocaine and methamphetamine use in the first 4 weeks of MOUD receipt was associated with an increased odds of subsequent non-medical opioid use (odds ratio [OR], 1.4 for cocaine and 1.7 for methamphetamine). Other non-opioid substance use early in treatment was not associated with subsequent non-medical opioid use.

Comments: In this study, non-opioid substance use prior to MOUD initiation did not seem to have an effect on OUD treatment outcomes, but the use of methamphetamine or cocaine in the early stages of treatment was associated with a higher risk of return to non-medical opioid use. Efforts targeting the non-medical use of stimulants in the early stages of OUD treatment may improve outcomes.

Hassaan Yousufi, MD* & Darius A. Rastegar, MD

* Contributing Editorial Intern & Johns Hopkins Addiction Medicine Fellow

Reference: Castillo F, Hu MC, Liu Y, et al. Risks of returning to opioid use at treatment entry and early in opioid use disorder treatment: role of non-opioid substances. *Drug Alcohol Depend*. 2023;251:110926.

Policies Removing or Reducing Criminal Penalties for Drug Possession in Two US States Not Associated With Increased Rates of Overdose Fatality

This study examined drug overdose deaths before and after 2021 policy changes that removed or reduced criminal penalties for drug possession in two US states, Oregon and Washington. Investigators compared observed and expected fatal drug overdose rates for one year post-policy change using a synthetic control method. They estimated expected fatal drug overdose rates from the synthetic controls, which were subsets of data from the other US states modeled to fit pre-policy change trends in each state and the counterfactual conditions that would have been expected had these policy changes not occurred.

- In both states, the absolute difference in observed versus expected monthly fatal drug overdose rate post-policy change was not significant (0.268 per 100,000 state population in Oregon; 0.112 per 100,000 state population in Washington).
- A sensitivity analysis that used an interrupted time series approach instead of the synthetic control method similarly found no significant change in monthly fatal drug overdose rates.

Comments: This study provides preliminary evidence that drug decriminalization in two US states was not significantly associated with increases in fatal drug overdose rates; however, additional analyses including longer periods of time post-policy change are warranted. This study included data through March 2022, but provisional data from July 2022 to July 2023 demonstrates substantially larger increases in overdose deaths in Washington and Oregon compared with US other states. Additional well-controlled studies are needed to assess the impact of drug decriminalization on overdose deaths.

Aaron D. Fox, MD

Reference: Joshi S, Rivera BD, Cerdá M, et al. One-year association of drug possession law change with fatal drug overdose in Oregon and Washington. *JAMA Psychiatry*. 2023;80(12):1277–1283.

HIV & HCV

Drug Consumption Rooms Associated With Reduced Injection Equipment Sharing Among People Who Inject Drugs in France

Drug consumption rooms (DCRs) are part of a continuum of harm reduction strategies for people who use drugs. DCRs are available in limited jurisdictions due to legal and regulatory barriers, and concerns that they promote risky substance use. Available data suggest that DCRs may reduce drug use behaviors associated with the risk of injection-related infections and engage people in treatment. However, most studies of DCRs have lacked robust control groups. This controlled cohort study enrolled 665 people who inject drugs across four sites in France: two DCRs in Strasbourg and Paris, and two harm reduction programs in Bordeaux and Marseille, where no DCRs existed. The outcomes were injection equipment sharing, HCV testing, and opioid agonist treatment engagement at 12-month follow-up, adjusting for significant correlates.

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Drug Consumption Rooms Associated With Reduced Injection Equipment Sharing Among People Who Inject Drugs in France

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- Self-reported sharing of injection equipment was 1 percent for participants exposed to DCRs, compared with 10 percent for those not exposed.
- Participation in DCRs did not impact HCV testing or receipt of opioid agonist treatment.

Comments: These data suggest that DCRs may reduce injection-related infection risk behaviors among people who inject drugs, compared with standard harm reduction programs in France. The results add to literature supporting the benefits of DCRs as part of a comprehensive public health approach to reduce the harms of injection drug use.

Marc R. Larochelle, MD, MPH

Reference: Lalanne L, Roux P, Donadille C, et al. Drug consumption rooms are effective to reduce at-risk practices associated with HIV/HCV infections among people who inject drugs: Results from the COSINUS cohort study. *Addiction*. 2024;119(1):180–199.

Visit our website to hear an author interview on this study in the latest episode of our podcast, "Behind the Evidence."

PRESCRIPTION DRUGS & PAIN

For Men With Smoking Prior to Surgery, Perioperative Nicotine Replacement Reduced Pain Sensitivity and Need for Opioid Analgesics

Smoking tobacco increases the risk of postoperative complications, and smoking cessation is encouraged (and sometimes required) prior to surgery. For patients who are unable to stop smoking prior to surgery, enforced abstinence from nicotine in the perioperative period may cause hyperalgesia. In this study, 101 men who smoked at least 10 cigarettes per day and were admitted for abdominal surgery were randomly assigned to a placebo patch or nicotine patch (NRT) at a dose of 21mg for those smoking ≤20 cigarettes per day and 42mg for those smoking >20 cigarettes per day. The primary outcomes were pre-operative pain thresholds (measured by electrical and mechanical stimulation), and post-operative analgesic dose (measured as morphine equivalent [ME] per kg).

- Pre-operative pain thresholds were higher in the NRT group, compared with placebo.
- Post-operative pain scores were significantly lower in the NRT group.
- Post-operative analgesic dose was significantly lower in the NRT group, compared with placebo (median ME, 1.8 mg/kg versus 2.2 mg/kg).
- There was no significant difference between groups in post-operative nausea or sedation.

Comments: This study suggests that providing nicotine replacement therapy in the perioperative period may improve pain sensitivity and reduce the need for opioid analgesic medications among people who smoke.

Darius A. Rastegar, MD

Reference: Zhu C, Bi Y, Wei K, et al. Effect of perioperative high-dose transdermal nicotine patch on pain sensitivity among male abstinent tobacco smokers undergoing abdominal surgery: a randomized controlled pilot study. *Addiction*. 2023:118:1579–1585.

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Patients With Chronic Pain Report Mostly Positive Experiences Transitioning to Buprenorphine From Long-Term Opioid Therapy, With Important Caveats

The risks of full agonist long-term opioid therapy for chronic pain—and those of tapering off of these medications—make a transition from full agonists to buprenorphine an attractive and potentially safer option for some patients. This study in two US Department of Veterans Affairs pain care sites used qualitative semi-structured interviews with 19 patients currently prescribed buprenorphine to understand the experiences of patients with chronic pain who transitioned to buprenorphine after being prescribed full-agonist opioid therapy for at least one year.

- Most patients found buprenorphine equally or less effective for pain than full agonist opioid medications, but improved overall function and fewer side effects made most feel that buprenorphine was a better choice for them.
- Patients with opioid-related harm or openness to new approaches to pain management were more satisfied than the single patient who felt coerced to switch.
- The transition period was generally uncomplicated, but some patients recalled increased pain and short-term side effects during buprenorphine initiation and dose-finding.
- Transparent, patient-centered, non-judgmental provider communication and education about the transition to buprenorphine at least partially eased patient concerns.
- In marked contrast with other patients, all three Black patients in the study reported difficulty accessing any type of pain medication, being denied opioid pain medication prior to finding buprenorphine as an option, and stigma from some medical providers.

Comments: While this study documents mostly positive patient narratives about their transition to buprenorphine from full agonist opioid medications for chronic pain, the inclusion of only patients currently prescribed buprenorphine risks missing additional negative narratives. Given the complexity and stigma surrounding chronic pain management with opioids, especially in the context of structural racism, the importance of non-judgmental communication and emphasis on patient-centered outcomes cannot be overemphasized.

Joseph Merrill, MD, MPH

Reference: Edmond SN, Wesolowicz DM, Snow JL, et al. Qualitative analysis of patient perspectives of buprenorphine after transitioning from long-term, full-agonist opioid therapy among veterans with chronic pain. *J Pain*. 2024;25(1):132–141.

Listen to the first episode of Season 2 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.

S2 Episode 1 features an interview with **Dr Marie Jauffret-Roustide** on the article, "Drug consumption rooms are effective to reduce at-risk practices associated with HIV/HCV infections among people who inject drugs: Results from the COSINUS cohort study" that is summarized in this issue of *AODH*.

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