Alcohol, Other Drugs, and Health: Current Evidence

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INTERVENTIONS & ASSESSMENTS

Does Extended Release Buprenorphine Improve Treatment Retention Compared with Other Medications for Opioid Use Disorder?

Despite robust evidence of the efficacy of medications for opioid use disorder (MOUD), retention in treatment remains poor, with more than half of patients discontinuing pharmacotherapy in the first year. In 2017, the FDA approved monthly extended-release depot buprenorphine (XR-BUP), which may be more convenient for patients than daily sublingual buprenorphine. Researchers used a nationally representative data set of 27 million commercially insured individuals to describe rates of discontinuing XR-BUP compared with other MOUD during 2018.

- In this cohort, 14,358 individuals initiated MOUD: 12,171 (85%) received sublingual buprenorphine, 1173 (8%) extended-release naltrexone, 810 (6%) methadone, and 204 (1%) XR-BUP.
- Three months after initiation, the rates of treatment discontinuation were: 34% of patients receiving sublingual buprenorphine, 50% of those receiving XR-BUP, 58% of those receiving methadone, and 65% of those receiving extended-release naltrexone. The rate of discontinuation of XR-BUP was significantly higher than that of sublingual buprenorphine.
- Uptake of XR-BUP increased as the year progressed, and clinicians broadly adhered to dosing guidelines for XR-BUP (2 monthly doses of 300 mg followed by 100 mg doses).

Comments: Although these findings may not generalize to publicly insured or uninsured patients, they demonstrate that treatment retention remains a stubborn obstacle for people with OUD, despite the promise of XR-BUP. Future research will need to explore whether alternative dosing—such as providing higher doses of XR-BUP, or supplementing it with sublingual buprenorphine—improves retention.

Ashish Thakrar, MD* and Darius A. Rastegar, MD

* Contributing editorial intern and addiction medicine fellow, Johns Hopkins Bayview Medical Center

Reference: Morgan JR, Walley AY, Murphy SM, et al. Characterizing initiation, use, and discontinuation of extended-release buprenorphine in a nationally representative United States commercially insured cohort. *Drug Alcohol Depend*. 2021;225:108764.

Availability of Medications for Opioid Use Disorder Remains Strikingly Low in Specialty Addiction Treatment Programs

Medications for opioid use disorder (MOUD) are proven to treat opioid use disorder and reduce the risk of opioid overdose, but they are underutilized in the U.S. Specialty substance use disorder (SUD) treatment programs—including outpatient, intensive outpatient, and residential programs—have access to health care professionals with SUD treatment expertise and should offer a prime opportunity to initiate MOUD. This study

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Availability of Medications for Opioid Use Disorder Remains Strikingly Low in Specialty Addiction Treatment Programs (continued from page 1)

merged a national database of admissions to SUD treatment with state-level data on MOUD accessibility to estimate rates of MOUD availability among SUD treatment programs, and the likelihood that individuals with OUD admitted to these programs will receive MOUD.

- MOUD availability increased in all treatment facilities over time, although a minority of all programs offered MOUD.
- MOUD receipt among individuals with OUD increased from 2007 to 2018 in all treatment facilities.
- In 2018, MOUD receipt by individuals with OUD was lowest in residential treatment settings (11%) versus non-intensive outpatient treatment (40%).
- MOUD utilization gains were highest for individuals in the Northeast, non-White individuals, and those who live in Medicaid expansion states.

Comments: This study demonstrates that access to MOUD remains very low for patients with OUD, even among facilities and programs that receive state and federal funding to provide OUD treatment. Although MOUD availability has increased over the last 10 years, large barriers to access exist in the very programs that have the most resources to provide this care. Efforts to expand MOUD access need to target specialty addiction treatment programs.

Melissa Weimer, DO, MCR

Reference: Solomon KT, Bandara S, Reynolds IS, et al. Association between availability of medications for opioid use disorder in specialty treatment and use of medications among patients: a state-level trends analysis. *J Subst Abuse Treat.* 2021;132:108424.

HEALTH OUTCOMES

High-dose Benzodiazepines Associated With Non-fatal Drug Poisonings in Patients Receiving Buprenorphine

Benzodiazepine use has been associated with both benefit and harm among patients receiving buprenorphine for opioid use disorder (OUD). Using a nationally representative database of commercially insured patients, this case-crossover study—in which cases acted as their own controls—examined the relationships between receipt of benzodiazepine and Z-drugs (i.e., zolpidem, zaleplon, and eszopiclone) and non-fatal drug-related poisonings among patients receiving buprenorphine for OUD.

- Among the 23,036 people with OUD who were receiving buprenorphine and had a non-fatal drug-related poisoning, 51% received a benzodiazepine and 22% received a Z-drug.
- Short-acting benzodiazepines had slightly higher odds of poisoning than long-acting benzodiazepines (odds ratios [ORs], 1.86 and 1.68, respectively).
- Receipt of high-dose benzodiazepines or Z-drugs (>30 mg daily diazepam-equivalents) was associated with an increased risk of poisoning (OR, 1.64), compared with receipt of low-dose benzodiazepines or Z-drugs (≤30 mg daily diazepam -equivalents).
- Days of benzodiazepine or Z-drug treatment without buprenorphine were associated with an increased risk of poisoning (OR, 1.81), while days of benzodiazepine or Z-drug treatment with buprenorphine treatment were associated with a decreased risk (OR, 0.63).

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High-dose Benzodiazepines Associated With Non-fatal Drug Poisonings in Patients Receiving Buprenorphine

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Comments: In this study of patients with OUD, receipt of high-dose benzodiazepines or Z-drugs was associated with increased risk of non-fatal drug poisonings. Although avoidance of prescribing high-dose benzodiazepines concurrently with buprenorphine may reduce the risk of poisoning in some patients, clinicians should still weigh the risks and benefits with patients before benzodiazepine dose reduction or discontinuation.

Tae Woo (Ted) Park, MD

Reference: Xu KY, Borodovsky JT, Presnall N, et al. Association between benzodiazepine or z-drug prescriptions and drug-related poisonings among patients receiving buprenorphine maintenance: a case-crossover analysis. *Am J Psychiatry*. 2021;178(7):651–659.

Many Pharmacies in US Counties With High Opioid Overdose Rates Do Not Provide Buprenorphine

Buprenorphine is an effective treatment for opioid use disorder (OUD), but most individuals with OUD are not engaged in treatment. One of the potential barriers to treatment is access to buprenorphine at local pharmacies. Researchers investigated access by contacting 2 randomly selected pharmacies (one independent and one chain pharmacy) in each of 473 US counties with an opioid overdose rate over the national average, and inquired about the availability of buprenorphine.

- Of the 971 pharmacies contacted, 675 (73%) reported that they did dispense buprenorphine, 183 (20%) reported that they did not, and the remaining 63 (7%) would not disclose this over the phone.
- Independent pharmacies were significantly more likely to report being unable to dispense buprenorphine (25% versus 15% of chain pharmacies). Pharmacies in the South were more likely to deny buprenorphine dispensing than those in other regions (26% versus 11–18%).
- In analyses adjusted for potential confounders, pharmacy variables associated with not dispensing buprenorphine included being in the South compared with the Northeast (adjusted prevalence ratio [aPR], 2.1), and being independent (aPR, 1.6).

Comments: This study shows that lack of access to buprenorphine in pharmacies is another barrier to OUD treatment. The reasons for pharmacies not providing buprenorphine were not assessed in this study, but possibilities include heightened vigilance of opioid prescribing in general, and stigma towards individuals with OUD.

Darius A. Rastegar, MD

Reference: Kazerouni NJ, Irwin AN, Levander XA, et al. Pharmacy-related buprenorphine access barriers: an audit of pharmacies in counties with high opioid overdose burden. *Drug Alcohol Depend*. 2021;224:108729.

Escalating Alcohol Use During Adolescence Is Associated With Non-medical Opioid Use in Young Adulthood

Opioid use disorder is rare among adolescents, but the incidence increases as teens transition to adulthood. This study used longitudinal data to examine alcohol consumption trajectories as antecedents of non-medical opioid use (NMOU; use of heroin or non-medical use of prescription opioids) among a sample of 580 predominantly African-American youth in Baltimore. Researchers assessed participants' substance use annually from age 14 to 26.

- Six trajectories of alcohol consumption were identified;* 2 trajectories (adolescent increasing and adolescent limited) were defined by substantial increases in alcohol consumption ages 14–18.
- Unadjusted models found higher odds of NMOU only among individuals with the adolescent increasing and adolescent limited trajectories of alcohol consumption, compared with those with the abstaining trajectory of alcohol use.
- Models adjusted for potential confounders found significant increases in the odds of NMOU among individuals with the adolescent increasing alcohol consumption trajectory (adjusted odds ratio [aOR], 3.3). Male gender was associated with an increased odds of NMOU (aOR, 1.7), while non-white race was associated with a decreased odds (aOR, 0.5).

* Alcohol use trajectories in this cohort were described thus: Young adult increasing (21% of participants; rapid increase in alcohol consumption age ≥18); adult increasing (19%; very little consumption age <21, frequency increasing ages 21–26); abstaining (19%; little to no consumption ages 14–26); experimenting (15%; infrequent consumption beginning in adolescence, little or no consumption by age 26); adolescent increasing (15%; consumption initiated in adolescence with rapid increase); and adolescent limited (10%; consumption initiated in adolescence, but declined at age 18).

Comments: The developing adolescent brain is particularly susceptible to substance use disorders. This article adds to the evidence that early unhealthy substance use serves as a marker of future risk, and suggests a true gateway. Prevention and intervention efforts targeting alcohol use that begins and escalates during adolescence may have an impact on future NMOU.

Sharon Levy, MD

Reference: Thrul J, Reboussin BA, Rabinowitz JA, et al. Alcohol trajectories and subsequent risk for opioid misuse in a cohort of urban adolescents. *Subst Abus*. 2021 [Epub ahead of print]. doi:10.1080/08897077.2021.1890675.

Is Cannabis Legalization Associated with an Increase in Cannabis-related Motor Vehicle Crash Fatalities?

Cannabis use is a risk factor for motor vehicle crash (MVC) fatalities, but the degree of a driver's intoxication varies by tetrahydrocannabinol (THC) level. However, cannabis testing does not assess THC levels in most US states, and testing rates among MVC decedents vary among states and over time, which may bias estimates of cannabis involvement. Researchers assessed cannabis involvement and THC levels among fatally injured drivers in Washington State before and after the legalization of non-medical ("recreational") cannabis use, with and without imputation of missing cannabis testing data among the roughly half of decedents who were not tested.

- Using data from all MVC decedent drivers based on observed and imputed values, the prevalence of cannabis involvement in MVC fatalities was 9% prior to legalization and 19% after.
- In adjusted analyses, the proportion of decedent drivers with high THC levels (>10 ng/mL) increased nearly 5-fold after legalization.
- Although cannabis testing rates increased during the study period, findings were generally similar when restricted to those with completed cannabis testing.

Comments: This study is one of the first to impute cannabis involvement in MVC fatalities among decedents without testing, and to measure and impute THC levels (rather than simply the presence or absence of THC). Legalization of non-medical cannabis use in Washington State was associated with increases in cannabis involvement in MVC fatalities, including at levels clearly associated with impairment. These results add to literature suggesting that legalizing cannabis may increase MVC fatalities, and highlights the need to better characterize and mitigate those risks.

Timothy S. Naimi, MD, MPH

Reference: Tefft B, Arnold LS. Estimating cannabis involvement in fatal crashes in Washington State before and after recreational cannabis legalization using multiple imputation of missing values. *Am J Epidemiol*. 2021 [Epub ahead of print]. doi:10.1093/aje/kwab184

HIV/HCV

Patients Receiving Methadone More Likely to Undergo Hepatitis C Screening Among Medicaid-insured New Yorkers With Opioid Use Disorder

Rates of hepatitis C virus (HCV) infection have more than doubled over the last decade in the US. Injection drug use is the primary risk factor for HCV; thus, it is important to screen people with opioid use disorder (OUD) for it. The US Centers for Disease Control and Prevention recommend one-time HCV screening in all adults and periodic testing while risk factors persist. However, few studies have reported the prevalence of HCV screening in people with OUD. This cross-sectional study examined the association between receipt of different types of OUD treatment and HCV screening in 2014 among patients with New York State Medicaid diagnosed with OUD.

- Of the 79,764 patients identified with OUD, 48% received medications for opioid use disorder (MOUD) and 32% received non-pharmacologic OUD treatment.
- Compared with patients receiving no OUD treatment, patients receiving methadone were most likely to be screened for HCV (32%), followed by patients receiving naltrexone (21%), patients receiving buprenorphine (16%), and patients receiving non-pharmacologic treatment (17%).

Comments: A minority of this cohort of patients with OUD were screened for HCV in 2014, despite federal recommendations. However, these data suggest that engagement in OUD treatment, particularly MOUD, is associated with increased rates of HCV screening. Moreover, the higher rates of screening in patients receiving methadone, which is only dispensed via regulated opioid treatment programs, suggest that federal and state policy can have a significant impact on HCV screening.

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Reference: Choi S, Healy S, Shapoval L, et al. Hepatitis C virus screening among Medicaid-insured individuals with opioid use disorder across substance use disorder treatment settings. *Subst Use Misuse*. 2021;56(2):258–263.

PRESCRIPTION DRUGS & PAIN

Urine Drug Testing Among People Prescribed Opioid Medications for Chronic Pain: Useful Tool or Blunt Instrument?

Guidelines recommend using urine drug testing (UDT) to monitor patients prescribed opioid medications for chronic pain; however, interpreting results can be challenging. This study used UDT results and clinical data from a multisite trial that sought to improve clinicians' adherence to opioid prescribing guidelines. Adult patients (N=638) who received long-term opioid therapy for chronic pain were included. Two physicians with expertise in pain and addiction determined whether UDT results were *concerning* for unhealthy substance use or diversion (i.e., selling, trading, or giving away prescribed medication), *uncertain*, or *not concerning*.

- Most patients were 45–64 years old; 60% had mental health-related diagnoses, and 17% had a substance use disorder diagnosis.
- Overall, 37% of patients had ≥1 *concerning* UDT result. In 24% of these patients, it was due to non-detection of a prescribed substance; in 23% of these patients, it was due to detection of a non-prescribed substance (most commonly cocaine or benzodiazepines).
- Having a *concerning* UDT result was associated with younger age (18–34 years old versus >65; adjusted odds ratio [aOR], 4.8), mental health-related diagnoses (aOR, 1.6), and substance use disorder diagnoses (aOR, 2.3).
- 35% of patients had ≥1 *uncertain* UDT result.

Comments: In this study, UDT frequently produced concerning results that would affect management decisions. For example, detection of a non-prescribed benzodiazepine would indicate an elevated overdose risk. However, there was also substantial uncertainty regarding results even among expert adjudicators. UDT results are only one piece of clinical data that should influence prescribing decisions and misinterpretation could lead to harms (e.g., involuntary opioid tapering is associated with elevated overdose risk). Clinicians need skills to interpret UDT results, humility to recognize uncertainty, and a strategy for responding to unexpected results in patient-centered ways.

Aaron D. Fox, MD

Reference: Larochelle MR, Cruz R, Kosakowski S, et al. Do urine drug tests reveal substance misuse among patients prescribed opioids for chronic pain? *J Gen Intern Med*. 2021;10.1007/s11606-021-07095-8.

Call for Papers

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