Alcohol, Other Drugs, and Health: Current Evidence

SEPTEMBER-OCTOBER 2022

TABLE OF CONTENTS

Visit our website:
www.aodhealth.org

INTERVENTIONS & ASSESSMENTS

Low-threshold Methadone Bridge Clinic Facilitates Linkage to Treatment for Opioid Use Disorder

In the US, federal regulations restrict the outpatient administration of methadone for opioid use disorder to licensed opioid treatment programs (OTPs). To relieve acute withdrawal while arranging a referral to an OTP, the regulations permit non-OTP-affiliated clinicians to administer methadone for up to 72 hours as a bridge to treatment, 1 day at a time. Clinicians at Boston Medical Center developed a walk-in methadone bridge clinic using this "72-hour rule" to address barriers in access to methadone.

- 142 patients received a mean of 2.1 days of emergency opioid withdrawal treatment during the evaluation period; 85% had fentanyl-positive urine drug test results.
- For de novo methadone initiation (n=139), the mean day 1 methadone dose was 28.4 mg, day 2 was 37 mg, and day 3 was 43 mg.
- 105 out of 121 (87%) referrals resulted in successful OTP linkage.
- At one month, 58% of total referrals (70 of 121) were retained in care at the referred OTP.

Comments: This study demonstrates that emergency methadone withdrawal treatment and OTP linkage in an outpatient bridge clinic is feasible and facilitates access to methadone. This model may be of particular use during care transitions, such as exiting the criminal justice system or discharge from a hospital. As of March 2022, the Drug Enforcement Agency is allowing non-OTP prescribers to request an exemption to dispense a 3-day supply of methadone. The added flexibility for dispensing a 3-day supply provides an opportunity for expansion of these types of services.

Lea Selitsky, MD, MPH* & Darius A. Rastegar, MD

* Contributing editorial intern and addiction medicine fellow, Johns Hopkins Medicine

Reference: Taylor JL, Laks J, Christine PJ, et al. Bridge clinic implementation of "72-hour rule" methadone for opioid withdrawal management: impact on opioid treatment program linkage and retention in care. *Drug Alcohol Depend*. 2022;236:109497.

Effectiveness and Adverse Events of Medications for Alcohol Use Disorder

Medications for the treatment of alcohol use disorder (AUD) can be effective and are underutilized, but there are limited data on the relative efficacy or adverse reactions among these medications, particularly for those that are newer or have been studied less.* Researchers conducted a meta-analysis of placebo-controlled randomized trials with durations of ≥4 weeks that examined outcomes of total abstinence, reduced heavy drinking,** and leaving studies due to adverse events. The meta-analysis included 156 trials with 27,334 participants.

(continued page 2)

Alcohol, Other Drugs, and Health: Current Evidence **is a project of the Grayken Center for Addiction at Boston Medical Center, produced in cooperation with Boston University. Initially supported by a grant from the National Institute on Alcohol Abuse and Alcoholism, the newsletter was supported by grant no. R25-DA013582 (PI: Jeffrey Samet) from the National Institute on Drug Abuse (NIDA) until July 2022. The content is solely the responsibility of the authors and does not necessarily represent the official views of Boston Medical Center, NIDA, or the National Institutes of Health.**

Effectiveness and Adverse Events of Medications for Alcohol Use Disorder

(continued from page 1)

- For abstinence, the following medications were more effective than placebo: gamma hydroxybutyrate (relative risk [RR], 1.96), baclofen (RR, 1.93), disulfiram (RR, 1.77), extended-release naltrexone (RR, 1.64), topiramate (RR, 1.41), acamprosate (RR, 1.33), and oral naltrexone (RR, 1.19).
- For heavy drinking, the following medications were more effective than placebo: disulfiram (RR, 0.19), baclofen (RR, 0.57), acamprosate (RR, 0.78), and oral naltrexone (RR, 0.81).
- Of the medications that were effective for reducing heavy drinking, disulfiram (RR, 2.45) and oral naltrexone (RR, 1.47) caused more participants to leave studies due to adverse effects than placebo.

* In the US, the Food and Drug Administration (FDA)-approved medications for AUD are disulfiram, naltrexone, and acamprosate.
** Defined as consumption on 1 occasion of ≥5 standard drinks for men, ≥4 or more drinks for women.

Comments: This study finds that a range of medications are effective for the treatment of AUD. Remarkably, several medications that are not FDA-approved for AUD outperformed approved medications in the two drinking outcomes. Of the medications, only baclofen and acamprosate reduced both drinking outcomes and didn't have adverse effects leading to study withdrawal. The side-by-side comparison of efficacy and adverse events using uniform study inclusion criteria may facilitate clinical decision-making and increase the use of these medications.

Timothy S. Naimi, MD, MPH

Reference: Bahji A, Bach P, Danilewitz M et al. Pharmacotherapies for adults with alcohol use disorders: A systematic review and network meta-analysis. *J Addict Med*. 2022;10.1097/ADM.0000000000000992.

Implementation of Screening and Brief Intervention Had an Effect on Unhealthy Alcohol Use in a Large Integrated Health System

Many individuals' drinking exceeds recommended limits without meeting criteria for alcohol use disorder (AUD). Guidelines recommend screening, brief intervention and referral to treatment (SBIRT) for individuals with unhealthy alcohol use, based on clinical trials showing efficacy. The effectiveness in real-world implementation of alcohol brief intervention (ABI) is less clear. Researchers at Kaiser Permanente Northern California investigated the effectiveness of an ABI initiative that included medical assistants administering a single-question screening for all adult patients at least annually.

- Over a 4-year period, 312,056 patients who screened positive, were continuously enrolled in the year prior and age ≤85 were included in this study.
- Of these eligible patients, 48% received an ABI. At 12 months, those who received the ABI had greater reductions in heavy drinking days (mean difference, -0.26), drinking days in a week (-0.05), and drinks in a week (-0.16). Improvements were not seen among those with an AUD diagnosis prior to screening.
- Patients who received an ABI were not more likely to receive specialty AUD treatment (either outpatient visits or pharmacotherapy), but those who did had significantly better drinking outcomes.

(continued page 3)

Implementation of Screening and Brief Intervention Had an Effect on Unhealthy Alcohol Use in a Large Integrated Health System (continued from page 2)

Comments: This study shows that a single-question screening had a modest effect on subsequent drinking among those with unhealthy alcohol use (but not AUD). This is consistent with prior studies showing efficacy for unhealth alcohol use but not AUD. The intervention did not seem to have an effect on referral to treatment. Primary care clinicians are increasingly burdened with a long list of recommended screening measures (along with other expectations); it is unclear to what extent this intervention should be a priority.

Darius A. Rastegar, MD

Reference: Chi FW, Parthasarathy S, Palzes VA, et al. Alcohol brief intervention, specialty treatment and drinking outcomes at 12 months: results from a systematic alcohol screening and brief intervention initiative in adult primary care. *Drug Alcohol Depend.* 2022;235:109458.

Barriers to and Facilitators of Integrating Routine Screening for Opioid Use Disorder into Primary Care

As part of a clinical trial of integrated care for co-occurring opioid use disorder (OUD) and mental health conditions, investigators studied the implementation of routine OUD screening in 10 primary care clinics across the US. Clinics received training and coaching to use the National Institute on Drug Abuse-modified Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) instrument and independently established workflows, target populations, and screening frequency. Evaluation used ethnographic observation and interviews with clinic staff members to determine barriers to and facilitators of implementation.

- Choosing who to screen (all patients versus targeted populations) and how frequently to screen was challenging for clinics, while implementing universal screening (i.e., every patient, every visit) aided implementation.
- Other challenges included: clinic staff turnover, difficulty with the instrument, discomfort with screening, and discouragement from low screening yield.
- Clinicians were uncertain about how to document and respond to positive screens for OUD.
- Clinic policies that were previously established to promote opioid safety may have contributed to stigma and limited disclosure of unhealthy opioid use.

Comments: For OUD screening to succeed, primary care patients must trust that disclosing unhealthy opioid use will enhance, not compromise, their care. The US Preventive Services Task Force recommends screening all adults 18 years or older by asking questions about unhealthy drug use. While the evidence for screening and brief intervention for unhealthy drug use is weak, evidence-based OUD treatment can be delivered in primary care, which provides sufficient rationale to screen. Creating brief, simple and universal screening procedures should enhance OUD screening implementation, but clinics should also be prepared to deliver OUD care, which includes patient-centered policies and staff training to combat stigma toward OUD.

Aaron D. Fox, MD

Reference: Austin EJ, Briggs ES, Ferro L, et al. Integrating routine screening for opioid use disorder into primary care settings: experiences from a national cohort of clinics. *J Gen Intern Med.* 2022;1–9.

Multilevel Community and Primary Care Team Intervention Increased Buprenorphine Uptake in Rural Communities

Buprenorphine is a highly effective yet underutilized medication for opioid use disorder (OUD). Well-documented barriers extend beyond clinicians' need to obtain a waiver to prescribe buprenorphine and include practice environment and supports. This implementation study targeted both the community—to improve understanding of OUD and its treatments—as well as training for practice teams on buprenorphine delivery in primary care. Forty-two rural primary care practices in Colorado enrolled in the practice training.

- On a 23-item implementation checklist for provision of buprenorphine in primary care, the mean number of items present increased from 4.7 to 13 per practice after the intervention.
- After the intervention, 23% of practices reported at least one buprenorphine induction compared with 9% of practices prior to the intervention.
- Using Prescription Drug Monitoring Program data, the number of individuals receiving buprenorphine increased 87% in counties with participating practices, compared with a 65% increase in other counties in the state.

Comments: These data show promise for an intervention targeting community members and primary care clinicians; practices can improve clinicians' readiness to prescribe and patients' receipt of buprenorphine. Improving the reach of buprenorphine should include efforts beyond increasing the number of clinicians eligible to prescribe it.

Marc R. Larochelle, MD, MPH

Reference: Zittleman L, Curcija K, Nease DE Jr, et al. Increasing capacity for treatment of opioid use disorder in rural primary care practices. *Ann Fam Med.* 2022;20:18–23.

HEALTH OUTCOMES

Menthol Use is Associated With Greater Smoking Frequency Among US Youth

Menthol is added to nicotine products to make them less aversive. While sweet and fruity cigarette and vape flavors were banned in 2009, menthol was not. This study used data from the Population Assessment of Tobacco and Health Study (N=1096 youth who smoke cigarettes, aged 12–14 at baseline) to assess associations between menthol flavored products, frequency of use, and nicotine dependence.*

- Among youth who smoked, those with menthol product use smoked an average of 3.1 additional days per month, were more likely to smoke frequently (adjusted rate ratio [aRR], 1.59), and had higher nicotine dependence scores, compared with peers who smoked non-menthol products.
- Compared with youth who continued menthol product use, those who switched to non-menthol products smoked 3.6 fewer days per month, had a 47% lower risk of frequent smoking (aRR, 0.68), and had 3% lower nicotine dependence scores.

* Assessed via the Wisconsin Inventory of Smoking Dependence Motives framework.

Comments: In addition to a minty taste and smell, menthol has cooling and painkilling effects, which may facilitate deeper inhalation. Menthol also slows nicotine metabolism, resulting in greater nicotine exposure. All of these factors combine to increase the risk of nicotine use disorder among people with menthol product use. The tobacco industry aggressively lobbied to prevent the FDA from banning menthol flavored products in 2009. In April 2021, the Biden administration proposed a federal menthol ban; this is now open for public commentary.

Sharon Levy, MD

Reference: Leas EC, Benmarhnia T, Strong DR, Pierce JP. Use of menthol cigarettes, smoking frequency, and nicotine dependence among US youth. *JAMA Netw Open*. 2022 Jun 1;5 (6):e2217144.

Close Emergency Department Follow-up After Opioid-related Visit Modestly Associated with Reduced Incident Overdose

Opioid-related emergency department (ED) visits represent a potential opportunity to engage patients in needed addiction care, especially if close follow-up for ongoing care can be arranged. Follow-up for opioid use disorder (OUD) care within 7 days of an ED visit has been proposed as an indicator of quality for addiction care. This study used data from 11 US state Medicaid programs to describe the association between ED follow-up within 7 days and subsequent hospital treatment of opioid overdose in a population with relatively high rates of OUD-related ED visits.

- Of the 114,945 patients in 11 states who experienced an ED visit that included an OUD-related diagnosis (including overdose) from 2016–2018, 16% had a follow-up visit within 7 days, with substantial variability across states (7% to 22%).
- Patients with a timely follow-up visit were more likely to be female and non-Hispanic White, less likely to have had an overdose or other substance use disorder diagnosis at the time of the ED visit, and much more likely to have been receiving medication for OUD (MOUD) prior to the ED visit.
- In multivariable analyses, having a follow-up visit within 7 days was associated with a lower likelihood of overdose within 6 months of the ED visit (hazard ratio, 0.91). However, results varied across states and only 2 states had statistically significant results.

Comments: Follow-up rates within 7 days after an OUD-related ED visit were very low in this 11-state Medicaid population, indicating substantial gaps in care. The high variability in follow-up rates across states, and the modest and variable associations between 7-day follow-up and overdose make it likely that unmeasured confounders were present in these analyses. Policymakers and health plans may be better served by quality measures of timely receipt of MOUD following OUD-related ED visits.

Joseph Merrill, MD, MPH

Reference: Medicaid Outcomes Distributed Research Network. Follow-up after ED visits for opioid use disorder: do they reduce future overdoses? *J Subst Abuse Treat*. 2022;142:108807.

Tobacco Smoking Reduction or Cessation Associated With Improved Alcohol Use Disorder Treatment Outcomes

In this systematic review, researchers summarized the evidence on the effect of tobacco smoking on the treatment of alcohol use disorder (AUD). Included studies (N=43) were conducted among ≥40 participants (n=10,296) who had AUD with or without tobacco smoking, with no other substance use disorders or co-morbid psychiatric disorders.

- Among patients receiving cognitive behavioral therapy for AUD (15 studies, 5542 participants), increased or continued tobacco smoking was associated with worse drinking outcomes in 10 studies, and no effect in 4 studies. One study showed a negative association.
- Among patients receiving AUD pharmacotherapy (15 studies, 2966 participants), smoking was associated with a 1.5–2.3 times higher risk of return to alcohol use in 6 studies. In 6 studies there was no difference in AUD outcomes between people with or without smoking. In one study results were mixed; 3 studies showed a negative association.
- In summary, 16 of 30 studies on behavioral or pharmacological AUD treatment showed that smoking reduction or cessation was associated with better drinking outcomes (lower rates of return to use, less drinking), whereas 4 studies showed the opposite.
- For smoking cessation treatment (13 studies, 1849 participants), 7 studies showed a positive effect of treatment on smoking. Only one study showed a reduction of both smoking and drinking, with a significant association between both (odds ratio, 1.6).

Comments: Current evidence suggests that positive AUD treatment outcomes are facilitated by tobacco smoking reduction or cessation. It should be noted that while smoking may trigger alcohol consumption, alcohol use may also promote smoking. Clinicians should inform patients of the potential benefit of reducing smoking for AUD treatment outcomes and offer support for smoking reduction or cessation.

Nicolas Bertholet, MD, MSc

Reference: van Amsterdam J, van den Brink W. Smoking as an outcome moderator in the treatment of alcohol use disorders. *Alcohol Alcohol*. 2022;agac027.

Visit

www.aodhealth.org

to view the newsletter online, sign up for a free subscription, and access additional features including downloadable training presentations and much more!

The major journals regularly reviewed for the newsletter include:

Addiction
Addiction Science & Clinical Practice
Addictive Behaviors
AIDS
Alcohol
Alcohol & Alcoholism
Alcoholism: Clinical & Experimental Research
American Journal of Drug & Alcohol Abuse
American Journal of Epidemiology
American Journal of Medicine
American Journal of Preventive Medicine
American Journal of Psychiatry
American Journal of Public Health
American Journal on Addictions
Annals of Internal Medicine
Archives of General Psychiatry
Archives of Internal Medicine
British Medical Journal
Drug & Alcohol Dependence
Epidemiology
European Addiction Research
European Journal of Public Health
European Psychiatry
Gastroenterology
Hepatology
Journal of Addiction Medicine
Journal of Addictive Diseases
Journal of AIDS
Journal of Behavioral Health Services & Research
Journal of General Internal Medicine
Journal of Hepatology
Journal of Infectious Diseases
Journal of Studies on Alcohol
Journal of Substance Abuse Treatment
Journal of the American Medical Association
Journal of Viral Hepatitis
Lancet
New England Journal of Medicine
Preventive Medicine
Psychiatric Services
Substance Abuse
Substance Use & Misuse

Many others periodically reviewed (see www.aodhealth.org).

Contact Information:

Alcohol, Other Drugs, and Health: Current Evidence
Boston Medical Center
801 Massachusetts Ave., 2nd floor
Boston, MA 02118
aodhce@bu.edu