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Alcohol, Other Drugs, and Health: Current Evidence

MARCH - APRIL 2020

INTERVENTIONS & ASSESSMENTS

Are Alcoholics Anonymous and Other 12-step Programs Effective for Alcohol Use Disorder?

A recent Cochrane Library systematic review included randomized trials, quasi-experimental studies, and non-randomized trials to assess the effectiveness of Alcoholics Anonymous (AA) and twelve-step facilitation (TSF) for alcohol use disorder. TSF is therapist-provided, formal, manual-guided behavioral counseling that is designed to encourage and supplement AA attendance. Twenty-seven studies (1 purely economic, 16 randomized) with 10,565 participants were included and the risk of selection bias was substantial, high, or unclear in most.

- A comparison of TSF with other clinical interventions combined 2 studies. One study (n=1726) compared TSF with motivational enhancement therapy and cognitive behavioral therapy; the other (n=210) compared network support (supporting AA involvement) with case management. The relative risk for abstinence at 12 months was 1.2 favoring TSF/network support compared with case management or the other psychotherapies (42% versus 35% of participants achieved abstinence, respectively).
 - ◊ One other trial described as very low quality (n=121 patients with severe mental illness) compared TSF with another psychosocial treatment and found 1.8 fewer drinks per drinking day favoring TSF.
- Three studies were identified that compared therapist-provided manualized behavioral counseling covering AA-relevant topics with lower intensity coverage and found 16% more days abstinent in one (n=95) and a relative risk of 1.2 for abstinence favoring higher intensity therapy in 2 others (n=659).
- The review identified one more study (n=307) that compared standard AA referral with more intensive encouragement to attend AA; the relative risk for abstinence was 1.3 favoring encouragement to attend AA.

Comments: Despite appearing to be a report of AA effectiveness in over 10,000 people in comparative studies, the report's main findings of effectiveness come from modest effects on secondary outcomes in studies with substantial risk of bias in just over 3000 people. More importantly, the studies tested manualized psychotherapy provided in conjunction with or supporting AA attendance or intensive referral to AA, not AA itself. The findings are not inconsistent with the idea that AA can help some people with alcohol use disorder, but they are not solid evidence for substantial effectiveness.

Richard Saitz, MD, MPH

Reference: Kelly JF, Humphreys K, Ferri M. Alcoholics Anonymous and other 12-step programs for alcohol use disorder. *Cochrane Database Syst Rev.* 2020;3:CD012880.

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Buprenorphine-naloxone Does Not Result in an Increased Incidence of Neonatal Opioid Withdrawal Syndrome Compared With Buprenorphine Alone

The standard of care for treating pregnant women with opioid use disorder (OUD) is opioid agonist treatment. The MOTHER study (2010) showed that buprenorphine was non-inferior—and for some outcomes superior—to methadone for the treatment of OUD in pregnancy, but it has long been thought that combination buprenorphine-naloxone (in contrast with buprenorphine alone) was not to be used in pregnant patients. This retrospective cohort study compared maternal and neonatal outcomes among pregnant women with OUD treated in a comprehensive perinatal program with buprenorphine alone (n=108) or the buprenorphine-naloxone combination (n=85). The primary outcome was incidence of neonatal abstinence syndrome (now referred to as neonatal opioid withdrawal) syndrome.

- The rate of neonatal abstinence syndrome was significantly higher among infants exposed in utero to buprenorphine (55%) versus buprenorphine-naloxone (35%).
- Combination buprenorphine-naloxone was associated with a reduced odds of neonatal abstinence syndrome (odds ratio, 0.45). However, after adjusting for clinical factors this association was no longer present.

Comments: This single-site retrospective cohort study of pregnant women with opioid use disorder suggests that buprenorphine-naloxone may be appropriate for treatment of OUD in this population. Larger, controlled trials should be performed to confirm these findings.

Jeanette M. Tetrault, MD

Reference: Mullins N et al. Buprenorphine and naloxone versus buprenorphine for opioid use disorder in pregnancy: a cohort study. *J Addict Med.* 2019 [Epub ahead of print]. doi: 10.1097/ADM.0000000000000562.

HEALTH OUTCOMES

Medical Cannabis Dispensary Density Associated With Cannabis Use Among Young Adults

Cannabis is increasingly available in many US states through medical cannabis dispensaries, which, together with their signage, may have an effect on cannabis use among near-by youth. This study used data from 2016–2017 interviews of a cohort of 1887 young adults (aged 18–22) in southern California. Researchers investigated the association between density of dispensaries with cannabis use and positive expectancies,* taking into account neighborhood socio-economic status.

- The average number of dispensaries within 4 miles of respondents' homes was 19; 84% of homes had ≥10 dispensaries within 4 miles.
- Higher dispensary density within 4 miles was associated with greater past-month cannabis use and more positive cannabis expectancies, compared with lower dispensary density.
- The effect of dispensaries with signage on positive cannabis expectancies was more than 6 times as large as the effect of total dispensary count.

* Measured as "the mean of four positive expectancy items (e.g. using marijuana relaxes you, helps you get away from your problems; lets you have more fun; makes sex more enjoyable) rated 1 = strongly disagree to 4 = strongly agree."

(continued page 3)

Medical Cannabis Dispensary Density Associated With Cannabis Use Among Young Adults

(continued from page 2)

Comments: Medical cannabis dispensaries may lead to more positive views and use of cannabis among local youth by creating perceptions of less harm and increased acceptability. Dispensary density and signage are two potential targets of regulation to consider to help reduce the possible harms associated with these outlets.

Darius A. Rastegar, MD

Reference: Shih RA, Rodriguez A, Parast L, et al. Associations between young adult marijuana outcomes and availability of medical marijuana dispensaries and storefront signage. *Addiction*. 2019;114:2162–2170.

Rates of Smoked Tobacco Use Decline While Cannabis Use Increases Among US Young Adults

This study analyzed data on smoked tobacco (i.e., cigarette and cigar) and cannabis use, examining exclusive (use of only one of these substances) and dual use from a US national survey of 18–22 year olds conducted 2002–2016.

- Over the course of the study, past-year exclusive smoked tobacco use decreased significantly from 23% in 2002 to 12% in 2016 among young adults in college, and from 34% to 18% among those not enrolled in college.
- Past-year exclusive cannabis use increased significantly from 6% in 2002 to 15% in 2016 among young adults in college, and from 5% to 11% among those not enrolled in college.
- Compared with those in college, young adults not enrolled in college had a significantly higher prevalence of smoked tobacco and dual tobacco/cannabis

use; those enrolled in college had a significantly higher prevalence of exclusive cannabis use.

Comments: After many decades of public health efforts, smoked tobacco use among young adults has decreased in general, although it is declining more slowly among young adults not enrolled in college, underscoring the challenges of reversing substance use epidemics. Rates of cannabis use are on the rise among young adults; this pattern is likely influenced by its legalization in several states, medicalization—which portrays cannabis as benign or even healthful—and an overall decreasing perception among the US public of its risks. These increasing rates are concerning because they may portend a new epidemic.

Sharon Levy, MD

Reference: Odani S, Soura BD, Tynan MA, et al. Tobacco and marijuana use among US college and noncollege young adults, 2002–2016. *Pediatrics*. 2019;144(6) e20191372.

Rapid Access to an Addiction Medicine Clinic Has the Potential to Decrease Emergency Department Visits for Alcohol-related Issues

Unhealthy alcohol use accounts for a significant proportion of emergency department (ED) visits and readmissions; providing timely access to addiction care could reduce them. A team in Ontario, Canada developed the rapid-access Alcohol Medical Intervention Clinic (AMIC), and evaluated its impact and acceptability. Patients presenting to the ED who experienced alcohol withdrawal, were at risk of alcohol withdrawal, or for whom alcohol was considered a major clinical concern were referred to the AMIC by the ED provider (98% ED physicians).

- 411 patients were referred and 248 presented to the AMIC (60%); of these, 194 consented to be included in the final sample in the study.
- On average, patients attended the AMIC within 7 days of referral. More than one-third presented within 1 day.

- Patients in the AMIC had an 82% reduction in ED visits in the 30-day period after initial presentation, compared with the 30 days prior.
- Compared with the 12 months prior to the implementation of AMIC, there was a reduction in the total number of alcohol-related ED admissions in the 12 months following AMIC implementation (32% versus 29%), and a 10% reduction in the total number of alcohol-related 30-day ED revisits (2.1% versus 1.9%).
- Patient satisfaction was high.

Comments: Providing rapid access to addiction care can help reduce ED admissions while offering access to specialized care. In this study, a significant proportion of patients were willing to attend when referred by ED clinicians. These changes must be interpreted with caution due to the absence of a control group.

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Rapid Access to an Addiction Medicine Clinic Has the Potential to Decrease Emergency Department Visits for Alcohol-related Issues (continued from page 3)

Nevertheless, the reduction observed in the total number of alcohol-related ED admissions after the implementation of the AMIC clinic supports the hypothesis that it had an effect on ED admissions.

Nicolas Bertholet, MD, MSc

Reference: Corace K, Willows M, Schubert N, et al. Alcohol Medical Intervention Clinic: a rapid access addiction medicine model reduces emergency department visits. *J Addict Med.* 2020;14(2):163–171.

Injection Drug Use-Related Infective Endocarditis is Increasing and Associated With Poor Patient Outcomes

The incidence of hospitalizations related to opioid use disorder (OUD) and medical complications such as injection drug use-related infective endocarditis (IDU-IE) have been increasing over the last twenty years. This large retrospective cohort study of patients hospitalized in Pennsylvania for infective endocarditis sought to describe the hospital length of stay, hospital charges, and insurance status of patients with IDU-IE versus non-IDU-IE.

- Over a 4-year period, 17,224 patients were hospitalized for infective endocarditis; of these, 1921 (11%) had IDU-IE.
- Total hospital admissions for infective endocarditis increased, but IDU-IE admissions increased by 238%, compared with 7% for non-IDU-IE admissions.
- Patients with IDU-IE were more likely to have Medicaid insurance, have higher hospital charges, and less likely

to complete the recommended hospital course (i.e., leave against medical advice), compared with patients with non-IDU-IE.

Comments: This study shows dramatic increases in rates of IDU-IE in Pennsylvania, mirroring national trends. The high rates of patients leaving the hospital without treatment suggests that current systems are not adequately equipped to provide essential, evidence-based medication treatments such as buprenorphine and methadone for this complex patient population. A limitation of this study is that it did not confirm substance route of administration and identified patients' substance use via ICD-10 codes, which likely underestimates the extent of the problem.

Melissa Weimer, DO, MCR

Reference: Meisner JA, Anesi J, Chen X, Grande D. Changes in infective endocarditis admissions in Pennsylvania during the opioid epidemic. *Clin Infect Dis.* 2019. pii: ciz1038.

Approximately One in Five Adults With Opioid Use Disorder in Six Large US Healthcare Systems Receive Buprenorphine

The US is in the midst of an opioid use disorder (OUD) and overdose crisis. The current need for treatment far exceeds the capacity of specialty programs. Many individuals with OUD can be treated in a primary care setting with buprenorphine and naltrexone. This study described the prevalence of OUD and receipt of these medications in six large US healthcare systems over a three-year period (2013–2016).

- Of the 1.4 million primary care patients age ≥ 18 in the study sample—most with commercial or employer-based insurance—13,942 (1%) had a documented diagnosis of OUD.
- Patients with OUD were more likely to be younger, male, and to have state-subsidized insurance.
- Among people with documented OUD, 21% received buprenorphine and 1% received extended-release naltrexone.

- A number of factors were associated with being less likely to receive buprenorphine, including older age, black race, Hispanic ethnicity, and not being commercially insured.

Comments: The FDA approval of sublingual buprenorphine for the treatment of OUD 18 years ago provided an opportunity for US primary care physicians to deliver evidence-based treatment to their patients with OUD. This study shows that we still have a long way to go. As with many other effective treatments for substance use disorder, concerning disparities exist.

Darius A. Rastegar, MD

Reference: Lapham G, Boudreau DM, Johnson EA, et al. Prevalence and treatment of opioid use disorders among primary care patients in six health systems. *Drug Alcohol Depend.* 2020;207:107732.

HIV & HCV

Medications for Alcohol Use Disorder Remain Underutilized, Especially Among People Living With HIV

Medications for alcohol use disorder (MAUD) are highly effective, yet they remain underutilized, particularly among people living with HIV (PLWH). Using 17 years of data from the US Veterans Aging Cohort Study, researchers examined predictors of MAUD initiation and retention among people with and without HIV who have alcohol use disorder (AUD). Initiation was defined as receipt of naltrexone (oral and injectable), acamprosate, or disulfiram within 30 days of diagnosis of AUD.* Retention was defined as filling the medication >80% of the days over six months.

- In the cohort of 163,339 individuals, 20% of PLWH had at least one AUD diagnosis compared with 22% of people without HIV.
- Out of the total population of people with AUD (n=35,027), 359 (1%) initiated MAUD and 49 (0.14%) were retained in treatment.
- The prevalence of MAUD initiation was lower among PLWH than among people without HIV (adjusted odds ratio, 0.66).

- Naltrexone was the most commonly prescribed MAUD, but its initiation was more common in people without HIV, compared with PLWH.
- Overall, older age and black race were associated with decreased odds of initiation of MAUD.

* Adding topiramate as an MAUD did not substantially change the results.

Comments: Despite MAUD being available for almost 70 years, people with AUD have minimal access to these highly effective medications; among the few who do access them, retention is extremely low. This study shows that other factors such as race and age may contribute to this gap, regardless of HIV status. Unlike most medications for opioid use disorder, MAUD are not controlled substances and do not require special licensure. Education for all healthcare professionals is overdue to increase access.

Melissa Weimer, DO, MCR

Reference: Oldfield B, McGinnis K, Edelman EJ, et al. Predictors of initiation of and retention on medications for alcohol use disorder among people living with and without HIV. *J Subst Abuse Treat.* 2020;109:14–22.

PRESCRIPTION DRUGS & PAIN

Factors Associated With Co-prescription of Naloxone With Opioid Medications

The US Centers for Disease Control's 2016 Guideline for Prescribing Opioids for Chronic Pain recommends that clinicians consider co-prescribing naloxone when they prescribe opioids to patients with known opioid overdose risks factors.* This retrospective observational study used a national insurance claims database to determine patient-level factors associated with receiving naloxone co-prescribed with an opioid, and changes in co-prescribing prevalence over the study period (2014–2017).

- Among 4.3 million adult patients with continuous insurance coverage who filled an opioid prescription, 3980 were co-prescribed naloxone.
- Compared with patients receiving <50 mg of morphine equivalents (MME) daily, patients receiving high-dose opioids (≥90 MME) had nearly four times greater odds of receiving naloxone co-prescriptions (adjusted odds ratio [aOR], 3.94).
- Naloxone co-prescription was also associated with receiving a concurrent benzodiazepine prescription (aOR, 1.27) and having opioid use disorder (aOR, 1.56).

- Prior opioid overdose was NOT associated with naloxone co-prescription.
- The prevalence of naloxone co-prescribing increased over the study period, but remained <2% among patients with overdose risk factors.

* Defined as people with: a prior opioid overdose, opioid use disorder, co-prescription of a benzodiazepine, or a prescription for high-dose opioid medication.

Comments: This study highlights missed opportunities to get naloxone into the hands of people who are at risk for opioid overdose. Community-based overdose education and naloxone distribution programs are another important source of naloxone; however, clinicians should be discussing the risk of overdose with patients to whom they prescribe opioids, and co-prescribing naloxone can be a strategy for mitigating risk.

Aaron D. Fox, MD

Reference: Lin LA, Brummett CM, Waljee JF, et al. Association of opioid overdose risk factors and naloxone prescribing in US adults. *J Gen Intern Med.* 2020;35(2):420–427.



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