Alcohol, Other Drugs, and Health: Current Evidence

MAY-JUNE 2019

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INTERVENTIONS & ASSESSMENTS

Receipt of Medication for Opioid Use Disorder While Incarcerated Improves Post-release Treatment Outcomes

Compared with the general population, the prevalence of opioid use disorder (OUD) is high among criminal justice-involved populations. Without treatment, individuals are at increased risk for overdose and recidivism post-release. Individual studies have demonstrated the efficacy of medication for OUD (MOUD; i.e., methadone, buprenorphine, and naltrexone) for incarcerated individuals, but no quantitative summary of this research currently exists. Researchers conducted the first meta-analysis on the effectiveness of MOUD in correctional settings with respect to post-release substance use treatment engagement, opioid use, criminal behavior/recidivism, and health risk behaviors.

- Only methadone had a sufficient number of studies (n=18) to meta-analyze.
- Data from randomized controlled trials (RCTs) involving 807 inmates demonstrated that methadone provided during incarceration was significantly associated with post-release: community treatment engagement (odds ratio [OR], 8.69), reduction in illicit opioid use (OR, 0.22), and reduction in injection drug use (OR, 0.26), but not with recidivism (OR, 0.93).
- Individual buprenorphine or naltrexone studies showed these medications to be either superior to methadone or placebo, or as effective as methadone in reducing illicit opioid use post-release.

Comments: Though limited by heterogeneity and a small number of RCTs, these results demonstrate that MOUD increases community treatment engagement and reduces illicit opioid use and injection drug use in the post-release period. Future research should accurately test for moderation by methadone dose, continuation versus induction, or type of correctional facility. Studies demonstrating the efficacy of buprenorphine or naltrexone treatment among incarcerated individuals are also needed.

Seonaid Nolan, MD

Reference: Moore KE, Roberts W, Reid HH, et al. Effectiveness of medication assisted treatment for opioid use in prison and jail settings: a meta-analysis and systematic review. *J Subst Abuse Treat.* 2019;99:32–43.

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HEALTH OUTCOMES

Purported Protective Effects of Alcohol Largely Non-causal

Based on decades of studies that have found associations between self-reported alcohol use at a point in time and disease in follow-up many years later, it has almost become dogma that consuming low amounts of alcohol is protective against cardiovascular disease. But higher-quality studies suggest that these effects are attributable to study methodology, not alcohol. Another large study (n=512,715 Chinese adults, 10 years of follow-up) confirms this conclusion. Some 160,000 participants were genotyped for variants involved in alcohol metabolism and participated in a Mendelian randomization study.

- Conventional epidemiological analyses adjusted for demographics and smoking found "U-shaped" curves for stroke and coronary heart disease, with nadirs for people who reported drinking occasionally and those drinking 100 g ethanol in a week on average (about 7 US standard drinks).
- In the genotypic analyses, there was a linear association between genotype-predicted mean alcohol consumption and stroke risk (with alcohol accounting for 8% of all ischemic strokes and 16% of all intracerebral hemorrhages in men), and no association (protective or harmful) with coronary heart disease.
- Of note, both self-reported alcohol and genotype-predicted means were associated linearly with known alcohol effects (systolic blood pressure, HDL cholesterol, and gamma-glutamyl transferase).

Comments: No study is perfect, nor can a single study answer a question definitively. But we now have several Mendelian randomization studies and several high-quality meta-analyses that have minimized confounding and biases and suggest that the previously observed associations between consumption of low amounts of alcohol and cardiovascular outcomes are not cause and effect.

Richard Saitz, MD, MPH

Reference: Millwood IY, Walters RG, Mei XW, et al. Conventional and genetic evidence on alcohol and vascular disease aetiology: a prospective study of 500 000 men and women in China. *Lancet*. 2019;393(10183):1831–1842.

Drinking Patterns During Pregnancy and Birth Outcomes

Alcohol use during pregnancy causes both physical and neurodevelopmental problems in children. The relationship between the amount and timing of alcohol consumption and impact on the fetus is poorly understood. In this study, a cohort of women were surveyed about alcohol use twice during pregnancy. Authors used a cluster analysis to identify 5 distinct trajectories of prenatal alcohol exposure (PAE), varying from none to high sustained PAE.*

- Only high sustained PAE (compared with none) was associated with fetal growth retardation; high sustained PAE was also associated with neurodevelopmental deficits at 6 and 12 months.
- "Moderate"-to-high PAE with reduction early in gestation and low-to-moderate sustained PAE were also both associated with neurodevelopmental deficits at 6 and 12 months.
- Low-to-"moderate" PAE with discontinuation was not associated with neurodevelopmental deficits in infancy.

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Drinking Patterns During Pregnancy and Birth Outcomes (continued from page 2)

* Defined as: minimal to no PAE throughout gestation (mean oz per day = 0), low-to-"moderate" PAE with discontinuation early in gestation (mean oz per day = 0.05), low-to-"moderate" PAE sustained across gestation (mean oz per day = 0.31), "moderate"-to-high PAE with reduction early in gestation (mean oz per day = 0.26), and high PAE sustained across gestation (mean oz per day = 1.58).

Comments: Fetal alcohol syndrome has long been recognized as a constellation of growth deficits, dysmorphology, and neurodevelopmental delays. More recently, a broader spectrum of fetal alcohol effects has been recognized with alcohol-related neurodevelopmental delay the most common. The findings of this study underscore alcohol's potential toxicity even at lower levels of exposure. While there may well be a dose level effect, there is no known "safe" level of alcohol consumption during pregnancy.

Sharon Levy, MD, MPH

Reference: Bandoli G, Coles CD, Kable JA, et al. Patterns of prenatal alcohol use that predict infant growth and development. *Pediatrics*. 2019;143(2): e20182399.

Alcohol Consumption and the Risk of Chronic Kidney Disease

Epidemiological studies have found inconsistent results on whether "moderate" consumers of alcohol are at a lower risk of developing chronic kidney disease (CKD). The present analyses are from the Atherosclerosis Risk in Communities Study, a large, prospective, population-based, multi-cultural study. It reports the relation of varying levels of alcohol consumption at baseline—compared with abstinence—to the incidence of CKD (the diagnosis required both a low glomerular filtration rate (GFR), and a decrease in GFR from previous levels) over 24 years of follow-up. Of 12,692 participants aged 45-64 years, 3664 participants developed CKD during follow-up; 25% of participants in their analyses were lifetime abstainers, and analyses included adjustment for known risk factors for CKD.

- In comparison with lifetime abstainers, participants reporting all levels of alcohol consumption showed a significant decrease in the risk of incident CKD.
  - For those reporting ≤1 drink in a week, the decrease was 12%, with the greatest decrease in risk (29%) for participants reporting that they consumed 8–14 drinks in a week. For those reporting ≥15 drinks in a week, the decrease in risk was 23%.

Comments: Among the strengths of the study are the very large number of participants who developed CKD during follow-up and the use of a clear definition for diagnosing the disease. However, only baseline alcohol intake was used as the exposure and type of beverage or pattern of drinking could not be assessed. The results of this study are consistent with findings of some earlier research showing a protective effect of "moderate" drinking on the risk of kidney disease. While mechanisms are not clear, effects on renal vessels that are similar to those described for coronary and cerebrovascular arteries could play a role if the findings represent causality.

R. Curtis Ellison, MD

Reference: Hu EA, Lazo M, Rosenberg SD, et al. Alcohol consumption and incident kidney disease: results from the Atherosclerosis Risk in Communities Study. *J Ren Nut.* 2019 [Epub ahead of print]. doi: 10.1053/j.jrn.2019.01.011.

Cannabis Use Is Associated With Suicide Attempts in Adolescents From Low- and Middle-Income Countries

Cannabis use may be associated with suicide among adolescents. To assess this association, researchers used data from 86,254 adolescents from 21 low- and middle-income countries that participated in the Global School-Based Student Health Survey. Associations between either having used cannabis at least once over the past 30 days, and lifetime use of cannabis, and at least one suicide attempt over the past 12 months were assessed, adjusting for age, gender, food insecurity, alcohol use, amphetamine use, smoking, and anxiety-induced insomnia.

- The mean age was 14 years and 49% of the participants were female.
- Age- and gender-adjusted prevalence of past 30-day and lifetime cannabis use were 3% and 4%, respectively.
- The prevalence of any past 12-month suicide attempt was 10%.
- In the adjusted model, cannabis use was associated with suicide attempts: odds ratios for a suicide attempt over the past 12 months were 2.03 for participants with past 30-day cannabis use and 2.30 for those with lifetime cannabis use.
- There was no evidence that the associations differed by sex.

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Cannabis Use Is Associated With Suicide Attempts in Adolescents From Low- and Middle-Income Countries

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Comments: This cross-sectional study showed an association between cannabis use and suicide attempts among adolescents living in low- and middle-income countries. Causality should be assessed in prospective studies and should include not only suicide attempts but also completed suicides.

Nicolas Bertholet, MD, MSc

Reference: Carvalho AF, Stubbs B, Vancampfort D, et al. Cannabis use and suicide attempts among 86,254 adolescents aged 12 -15 years from 21 low- and middle-income countries. *Eur Psychiatry*. 2019;56:8–13.

Higher National Cannabis Potency Is Associated With Progression to Cannabis Use Disorder Symptoms

Over the last few decades, there has been an increase in cannabis potency and use in the United States. Researchers used data from the Michigan Longitudinal Study to determine whether higher average potency levels at initiation of cannabis use were associated with progression to regular use, daily use, and cannabis use disorder (CUD) symptoms. Cannabis potency was obtained from analysis of cannabis confiscated by the US Drug Enforcement Agency and reported as an annual average.

- The average potency of cannabis (%THC) increased from 4% to 12% between 1994 and 2012.
- Potency was not associated with progression to first use or to regular cannabis use.
- After adjusting for sex, regular use, and birth year, potency was associated with progression to first CUD symptoms (hazard ratio [HR], 1.4). For every 1% increase in cannabis potency, there was a 1.4 times increased risk of progression to CUD symptom onset.
- Progression to first CUD symptoms was associated with regular cannabis use (HR, 4.1) and daily cannabis use (HR, 3.14).

Comments: This study suggests that cannabis potency may be associated with CUD symptom progression. Study limitations included the use of a national measure of potency, which cannot account for local or individual cannabis potency differences. Nonetheless, this should raise concerns about potential harms. The increasing legalization of cannabis in the US should be viewed as an opportunity to potentially regulate potency to limit harms while this is studied further.

Jarratt Pytell, MD† & Darius A. Rastegar, MD

† Contributing editorial intern and Addiction Medicine Fellow, Johns Hopkins Medicine

Reference: Arterberry BJ, Treloar Padovano H, Foster KT, et al. Higher average potency across the United States is associated with progression to first cannabis use disorder symptom. *Drug Alcohol Depend.* 2019;195:186–192.

PRESCRIPTION DRUGS & PAIN

Driving Under the Influence of Medical Cannabis: How Common Is It?

Driving under the influence of cannabis (DUIC) has been shown to be associated with increased risk of motor vehicle crashes in some studies, while others have shown no association. Little is known about the prevalence of driving under the influence of medical cannabis. The authors of this study sought to determine the prevalence and correlates of DUIC among 790 adults with chronic pain seeking medical cannabis certification or re-certification. The mean age was 46 years; 52% were male, and 81% were white.

- Overall, 56% reported driving within 2 hours of cannabis use, 53% reported DUIC while "a little high," and 22% reported DUIC while "very high."
- Greater quantity of cannabis consumed and heavy episodic drinking were associated with driving within 2 hours of use, while a little high, and while very high.

Comments: Patients with chronic pain certified for medical cannabis use were 5–10 times more likely than the general population age 16 and over to report DUIC. Although these data are limited by retrospective self-report and lack of validated survey methodology, they do suggest the need for more research to understand personal and public health implications of driving risk among patients with medical cannabis certification.

Jeanette M. Tetrault, MD

Reference: Bonar EE, Cranford JA, Arterberry BJ, et al. Driving under the influence of cannabis among medical cannabis patients with chronic pain. *Drug Alcohol Depend*. 2019;195:193–197.

Adolescents and Young Adults Receiving Dental Opioid Prescriptions May Experience Continued Opioid Use and OUD

Wisdom tooth extraction is a rite of passage for many adolescents and young adults that is often accompanied by a prescription for an opioid analgesic. Exposure to opioids can lead to continued use and development of opioid use disorder (OUD). Researchers used data from a commercial insurance database to investigate the associations between receiving an opioid prescription after a dental encounter and continued opioid use (defined as receiving another prescription 90–365 days after the index prescription) and health care encounters for OUD within 365 days.

- Among patients aged 16–25 who had continuous coverage for one year (754,000 individuals), 97,462 (13%) received an opioid prescription; of these, 29,791 received their first opioid prescription from a dental clinician (31% of those who received an opioid).
- Of those who received an opioid, 7% received another prescription for an opioid 90–365 days later, compared with 0.1% of an opioid-nonexposed comparison cohort.
- Of those who received an opioid, 6% had at least one subsequent health care encounter associated with OUD within a year, compared with 0.4% in the opioid-nonexposed cohort.
- The quantity of opioid prescribed (more or less than 20 pills) was not associated with persistent use or subsequent OUD.

Comments: This study adds to a growing body of evidence demonstrating that even short-term exposure to prescription opioids can lead to persistent use and OUD in those susceptible. Guidelines recommending prescribing smaller quantities of opioids may not reduce these risks. Given that there is no evidence that opioids are more effective than nonsteroidal anti-inflammatory drugs for analgesia after minor procedures, they should not be routinely prescribed, especially to those at a vulnerable younger age.

Darius A. Rastegar, MD

Reference: Schroeder AR, Dehghan M, Newman TB, et al. Association of opioid prescriptions from dental clinicians for US adolescents and young adults with subsequent opioid use and abuse. *JAMA Intern Med*. 2019;179(2):145–152.

ADDICTION SCIENCE & CLINICAL PRACTICE

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