Alcohol, Other Drugs, and Health: Current Evidence

NOVEMBER-DECEMBER 2018

TABLE OF CONTENTS

Visit our website:
www.aodhealth.org

INTERVENTIONS & ASSESSMENTS

Medication for Opioid Use Disorder After Opioid Overdose Is Associated With Reduced Mortality

Non-fatal opioid overdose is a major risk factor for fatal overdose and medication for opioid use disorder (MOUD) may reduce that risk. This study used data from multiple Massachusetts administrative systems (2011-2015) to create a retrospective cohort of overdose survivors (N=17,568), document the risk of subsequent fatal overdose, and assess the association between the receipt of MOUD and mortality. Criteria defining the index non-fatal overdose were validated, and for the main analysis, deaths occurring in the last month of MOUD and the month after MOUD were attributed to the medication.

- In the 12 months prior to the index overdose, 26% of individuals had any MOUD; 41% were prescribed opioids, 28% were prescribed benzodiazepines, and 22% had a detoxification admission.
- For the 12 months after the index overdose, the all-cause death rate was 4.7 per 100 patient-years and the opioid-related death rate was 2.1 per 100 patient-years. Seventeen percent of cases received buprenorphine for a median of 4 months, 11% received methadone for a median of 5 months, and 6% received naltrexone for a median of 1 month.
- Compared with no MOUD, the adjusted hazard ratio for all-cause mortality was 0.47 for methadone, 0.63 for buprenorphine, and 1.44 (but non-significant) for naltrexone. Similar hazard ratios were found for opioid-related mortality. In a secondary analysis in which deaths were only attributable to MOUD during the month MOUD was received, there was a two-thirds reduction in death.

Comments: Survivors of opioid overdose who receive medical attention have extremely high one-year mortality, and although methadone and buprenorphine are both strongly associated with reduced risk of death, less than one-third of patients received any MOUD in the year following non-fatal overdose. Selection bias is unlikely to account for such a striking reduction in mortality. Data were limited for naltrexone, with fewer cases treated, very short treatment duration, and no association with reduced mortality. Addressing the opioid crisis will require changes in systems of care to increase engagement and retention of high-risk groups in MOUD treatment.

Joseph Merrill, MD, MPH

Reference: Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. *Ann Intern Med*. 2018;169(3):137–145.

Few Patients Receiving Buprenorphine Taper Off; Most of Those Who Do Return to Treatment

Office-based buprenorphine is an effective treatment for opioid use disorder; the current standard of care is to continue it indefinitely. Some patients express a desire to eventually taper off; others experience external pressures to do so. However, data are scant on the frequency and success of tapering off. In this single-site, retrospective cohort study, researchers reviewed 12 years of office-based addiction treatment data including 1308 patients with a median follow-up of 316 days to determine the proportion who tapered off of buprenorphine, describe their characteristics, and determine the proportion that returned.

(continued page 2)

Alcohol, Other Drugs, and Health: Current Evidence **is a project of the Boston Medical Center produced in cooperation with the Boston University Schools of Medicine and Public Health. Initially supported by a grant from the National Institute on Alcohol Abuse and Alcoholism, the newsletter is currently supported by grant no. R25-DA013582 from the National Institute on Drug Abuse (NIDA). The content is solely the responsibility of the authors and does not necessarily represent the official views of NIDA or the National Institutes of Health.**

Few Patients Receiving Buprenorphine Taper Off; Most of Those Who Do Return to Treatment (continued from page 1)

- During the full follow-up period of 2361 days, 48 patients tapered off of buprenorphine. Using Kaplan-Meier proportion estimates, which account for censored participants (those lost to follow-up or at end of the study), 15% tapered off of buprenorphine.
- Patients who underwent a supervised taper were engaged in treatment longer (median 774 days versus 433 days), had lower prescribed dosages (45% prescribed <4 mg/day versus 19%), and were more likely to be employed or a student (52% versus 24%), compared with those who underwent an unsupervised taper.
- Most of the patients (61%) who tapered off of buprenorphine returned to treatment. Most of them (77%) had undergone an unsupervised taper.

Comments: This study shows that a small proportion of patients receiving buprenorphine taper off and most return to treatment. This supports treating opioid use disorder as a chronic condition and continuing with treatment indefinitely without placing arbitrary time limits or end-points.

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

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

Reference: Weinstein ZM, Gryczynski G, Cheng DM, et al. Tapering off and returning to buprenorphine maintenance in a primary care Office Based Addiction Treatment (OBAT) program. *Drug Alcohol Depend*. 2018;189:166–171.

Don't Forget the Children: Opioid Use Disorder Treatment Among US Adults Living With Children

Adults with opioid use disorder (OUD) living with children have unique treatment needs. This secondary data analysis of the 2010–2014 National Survey on Drug Use and Health explored among US adults living with children 1) the prevalence and correlates of OUD; 2) the proportion who seek treatment; and 3) the proportion who perceive a need for treatment and barriers to seeking treatment. The comparison group was adults without children.

- 820,000 adults with OUD live with at least one child.
- 28% reported receiving any past-year substance use treatment, which is similar to adults not living with a child (30%).
- Of adults living with children, 15% perceived an unmet treatment need.
- Among adults who perceived an unmet treatment need, those who lived with a child were more likely to report that access barriers prevented them from receiving care, such as not being able to find the right kind of program (adjusted odds ratio [aOR], 2.9), and stigma (aOR, 4.1).

Comments: Similar to those without children, most adults with OUD living with children are not receiving OUD treatment. Treatment programs need to take into account the unique needs of adults living with children, including onsite childcare and extended hours, as well as focusing on efforts to decrease stigma as it relates to children and families.

Jeanette M. Tetrault, MD

Reference: Feder KA, Mojtabai R, Musci RJ, Letourneau EJ. US adults with opioid use disorder living with children: treatment use and barriers to care. *J Subst Abuse Treat*. 2018;93:31–37.

HEALTH OUTCOMES

Dementia Risk With Low Amounts of Alcohol

Observational studies of the health effects of alcohol have many methodological challenges. Investigators attempted to address one by examining midlife drinking and dementia risk over 23 years. Of 10,308 adults studied prospectively, 1221 were excluded due to death, cardiometabolic disease, or missing data on alcohol (all of which could be related to dementia); 397 cases of dementia were detected in medical records codes.

- In analyses adjusted for socioeconomic status, health behaviors, and comorbidity, the hazard ratio for dementia was 1.45 for drinking <0.7 drinks in a week compared with 0.7–10 in a week, and 1.18 for every 5-drink increase over 10 in a week (1 drink=14g of alcohol, standard in the US).

Comments: Drinking nothing or less than three-quarters of a drink in a week, or >10 drinks in a week was associated with dementia. These associations may not be causal—other factors associated with alcohol use and dementia may be responsible for the risk. This study translated self-reported measures into weekly averages and did not measure heavy episodes (common among people who drink). Furthermore, most people categorized as "abstinent" drank as recently as one week prior. These decisions raise questions about the ability to interpret and attribute differences in dementia to abstinence or drinking low amounts. Clearly one cannot rely on such observational studies to dose a carcinogen with a narrow therapeutic index to achieve or avoid any health outcome. And if the inflection point for increasing dementia risk is 10 drinks in a week then most guidelines are too liberal.

Richard Saitz, MD, MPH

Reference: Sabia S, Fayosse A, Dumurgier J, et al. Alcohol consumption and risk of dementia: 23-year follow-up of Whitehall II cohort study. *BMJ*. 2018;362:k2927.

"Moderate" Drinking Associated With Progression of Non-alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) is common, but it is unknown how drinking low amounts of alcohol affects it. Investigators studied a prospective cohort of 58,927 Korean adults with NAFLD (identified from among ~350,000 people, a prevalence of 17%), followed for about 8 years. Participants had fatty liver by ultrasound but drank <20g of alcohol a day (30g/day for men), did not have hepatitis B or C or other known liver disease, were not taking medications known to cause fatty liver, and did not have an intermediate or higher probability of fibrosis based on non-invasive markers of liver fibrosis.* Light and "moderate" drinking, respectively, were defined as 1 to <10g/day and 10 to <20g/day for women, and 1 to <10g/day and 10 to <30g/day for men.

- "Moderate" drinking was associated with progression of the FIB-4* (hazard ratio [HR], 1.3) and worsening of the APRI* (HR, 1.1). Both light and "moderate" drinking were associated with worsening of the NFS (HR, 1.1 and 1.3, respectively).*

*FIB-4 (fibrosis-4 score, calculated based on age, asparate and alanine aminotransferase levels, and platelet count), APRI (aspartate aminotransferase to platelet ratio index), NFS (NAFLD fibrosis score).

Comments: The label "moderate" is a misnomer given that alcohol is a carcinogen at low doses; there are numerous studies identifying health risks at low doses and calling into question the existence of any health benefits. Low amounts of alcohol appear to be associated with liver disease progression in NAFLD. These findings raise questions about whether to identify people with NAFLD, a very common condition, to more appropriately advise them regarding alcohol risks.

Richard Saitz, MD, MPH

Reference: Chang Y, Cho YK, Kim Y, et al. Non-heavy drinking and worsening of non-invasive fibrosis markers in non-alcoholic fatty liver disease: a cohort study. *Hepatology*. 2018 [Epub ahead of print]. doi: 10.1002/hep.30170.

Same-Day Cannabis and Alcohol Use

Cannabis use frequently co-occurs with alcohol use. Researchers collected daily use data in 127 veterans (94% male) who reported at least one day of co-use over the past 180 days.

- Participants reported using cannabis on 40% of the days, alcohol on 28%, and both on 9%.
- They also reported cigarette use on 45% of the days and use of other drugs on 6% of the days.
- Prevalence of cannabis use disorder (CUD) and alcohol use disorder (AUD) were 37% and 40%, respectively; 15% of participants had both.
- Multilevel modeling analyses found that on days of

(continued page 4)

Same-Day Cannabis and Alcohol Use (continued from page 3)

cannabis use, participants were more likely to drink and to drink more (odds ratio [OR], 1.61 for 1–4 drinks for men or 1–3 drinks for women on that day, compared with no drinking; OR, 2.34 for heavy drinking [defined as ≥5 drinks for men, ≥4 drinks for women], compared with less drinking).
- Among participants with AUD (with or without CUD), cannabis use was associated with heavy drinking.
- In contrast, among people with CUD alone, cannabis use was associated with less heavy drinking.

Comments: In this almost exclusively male sample of veterans who used cannabis and alcohol on the same day, cannabis use was associated with heavy drinking, especially among people with AUD or co-occurring AUD and CUD. Results should be replicated in more diverse populations, notably women.

Nicolas Bertholet, MD, MSc

Reference: Metrik J, Gunn RL, Jackson KM, et al. Daily patterns of marijuana and alcohol co-use among individuals with alcohol and cannabis use disorders. *Alcohol Clin Exp Res*. 2018;42 (6):1096–1104.

Adolescent Emergency Department Visits Related to Cannabis Use Are Rising in Colorado

This study examined the impact of legalizing marijuana in Colorado (in 2009 for medical and 2014 for recreational use) on adolescent emergency department/urgent care (ED/UC) visits. Researchers reviewed International Classification of Diseases (ICD) codes and urine drug screens for patients aged 13–20 presenting to a Colorado children's hospital emergency department.

- In total, 4202 cannabis-related visits were identified; a psychiatric diagnosis was made in 71%.
- The rate of cannabis-related visits increased from 2 per 1000 visits in 2009 to 5 per 1000 in 2015, while the rate of cannabis-related behavioral health evaluations increased from 1 per 1000 visits in 2009 to 3 per 1000 in 2015.

Comments: To date, the impact of marijuana policy change on youth has not been fully determined and epidemiological studies have yielded mixed results. There is a well-documented relationship between chronic cannabis use during adolescence and increased risk of developing a mental health disorder. This study shines a light on the relationship between adolescent cannabis use and acute mental health problems. While the observational design and the changing laws preclude determination of causality, the findings serve as a provocative reminder that more research is needed to fully evaluate the impact of policy changes on public health, and particularly on adolescent mental health.

Sharon Levy, MD, MPH

Reference: Wang, GS, Davies SD, Halmo LS, et al. Impact of marijuana legalization in Colorado on adolescent emergency and urgent care visits. *J Adolesc Health*. 2018;63(2):239–241.

Cannabis Smoking Is Associated With Cough, Wheezing, and Dyspnea

Many Americans smoke marijuana and rates are increasing, raising concerns about potential effects on pulmonary health. Researchers conducted a systematic review and meta-analysis to examine the association between marijuana use and pulmonary health. They found 22 studies (10 prospective cohort and 12 cross-sectional) that met their inclusion criteria.

- In a pooled analysis of cross-sectional studies with low or moderate risk of bias, current marijuana smoking was associated with cough (odds ratio [OR], 4.4), chronic sputum production (OR, 3.4), wheezing (OR, 2.8), and dyspnea (OR, 1.6). The strength of the evidence was graded "low."
- Analysis of data on pulmonary function and development of chronic obstructive lung disease failed to show a significant association. The strength of the evidence was graded "insufficient."

Comments: This study suggests that marijuana smoking is associated with adverse pulmonary symptoms. It may also have a deleterious effect on pulmonary function, but longer and larger studies are needed to assess this.

Darius A. Rastegar, MD

Reference: Ghasemiesfe M, Ravi D, Vali M, et al. Marijuana use, respiratory symptoms, and pulmonary function: a systematic review and meta-analysis. *Ann Intern Med*. 2018;169:106–115.

HIV AND HCV

Prescription Opioid Use and Virologic Failure Among People Living With HIV

People living with HIV (PLWH) experience an increased burden of chronic pain and have high rates of prescription opioid use, including long-term opioid therapy (LTOT). The relationship between prescription opioid use, chronic pain and LTOT on HIV treatment outcomes was examined in two cohort studies of PLWH. Flores et al. evaluated the association between appearance of a prescription for an opioid in the electronic medical record and virologic failure (defined as HIV RNA ≥ 200 copies/mL) among a cohort of 1907 PLWH receiving HIV medical care in Texas.

- The median age was 45 years; 76% were male, 62% were Hispanic, 56% were men who have sex with men, 83% were prescribed anti-retroviral therapy (ART), and 33% had HIV RNA >200 copies/mL.
- While no current illicit drug use was reported by 58% of study participants, such data was missing for 34% of patients.
- 26% of study participants had an opioid prescription.
- An opioid prescription was associated with virologic failure (adjusted odds ratio [aOR], 1.34).

Merlin et al. evaluated the association between chronic pain and LTOT (defined as >90 consecutive days of an opioid prescription in the medical record) and HIV treatment outcomes, including retention in primary care and virologic failure (defined as HIV RNA >1000 copies/mL) among 2334 individuals receiving medical care at 5 HIV primary care clinics.

- Participants were predominantly male, white, middle aged, and 12% had HIV RNA >1000 copies/mL.
- Among all cohort participants, 25% reported chronic pain and 15% were prescribed LTOT.
- Among participants not receiving LTOT, chronic pain was associated with virologic failure (aOR,1.97).
- Among participants with chronic pain, LTOT was associated with lower rates of virologic failure (aOR, 0.56).

Comments: These studies offer seemingly contradictory findings. But there were substantial differences between both cohorts making a comparison difficult. And data on illicit/non-medical use of opioids was limited and neither study accounted for ART adherence to ART. Despite these significant limitations, it seems clear that caution is warranted when prescribing opioids but that some patients receive benefit.

Jeffrey Morgan, MA† & Seonaid Nolan, MD
†Contributing Editorial Intern and Research Coordinator, BC Centre on Substance Use

References: Flores J, Liang Y, Ketchum NS, et al. Prescription opioid use is associated with virologic failure in people living with HIV. *AIDS Behav*. 2018;22:1323–1328.

Merlin JS, Long D, Becker WC, et al. Brief report: the association of chronic pain and long-term opioid therapy with HIV treatment outcomes. *J Acquir Immune Defic Syndr*. 2018;79:1:77–82.

ADDICTION SCIENCE & CLINICAL PRACTICE

Call for Papers

Addiction Science & Clinical Practice (*ASCP*), founded in 2002 by the National Institute on Drug Abuse (NIDA) and now published by leading open-access publisher BioMed Central, is seeking submissions of the following article types:
Original Research • Reviews • Systematic Reviews and Meta-Analyses
Study Protocols • Case Studies • Case Reports

Editor-in-Chief
Jeffrey H. Samet, MD, MA, MPH

About the journal: *ASCP* provides a forum for clinically relevant research and perspectives that contribute to improving the quality of care for people with unhealthy alcohol, tobacco, or other drug use and addictive behaviors across a spectrum of clinical settings.
For more information or to submit manuscripts online, visit **www.ascpjournal.org**

18th Annual Chief Resident Immersion Training (CRIT) Program in Addiction Medicine

Accepting applications through **January 25, 2019**
www.bumc.bu.edu/crit

What: This is a four-day immersion training for internal and family medicine incoming chief residents on state-of-the-art methods to diagnose, manage, and teach about addiction medicine. Additional spaces are available for faculty mentors of chief residents as well as junior faculty members.
When: April 28 - May 1, 2019
Where: Wylie Inn and Conference Center, Beverly, MA
Cost: The grant supports up to 15 full chief resident scholarships that cover tuition, travel and accommodations. Faculty mentors and junior faculty are responsible for covering their travel and accommodations.
Sponsors: National Institute on Drug Abuse (NIDA) and Boston University School of Medicine.
For more information or to apply: Visit www.bumc.bu.edu/crit or contact Marlene Lira (marlene.lira@bmc.org, 617-414-6924)

8th Annual Fellow Immersion Training (FIT) Program in Addiction Medicine

Accepting applications through **January 25, 2019**
www.bumc.bu.edu/fit

What: The Fellow Immersion Training (FIT) program is a four-day intensive, immersion training that equips incoming and current clinical subspecialty fellows (e.g., Infectious Disease, Pain, Gastroenterology) with state-of-the-art skills and content to integrate addiction medicine into research and clinical care.
When: April 28 - May 1, 2019
Where: Wylie Inn and Conference Center, Beverly, MA
Cost: There is no tuition for fellows. Accommodations and travel for fellows are funded.
Sponsors: National Institute on Drug Abuse (NIDA) and Boston University School of Medicine.
For more information or to apply: Visit www.bumc.bu.edu/fit, or contact Kristina King (kristina.king@bmc.org, 617-414-6632).

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 University School of Medicine/Boston Medical Center
801 Massachusetts Ave., 2nd floor
Boston, MA 02118
aodhce@bu.edu