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Alcohol, Other Drugs, and Health: Current Evidence

MARCH - APRIL 2018

INTERVENTIONS & ASSESSMENTS

Early Access to Buprenorphine During Pregnancy Is Associated With Postpartum Treatment Retention

Among women with opioid use disorder, treatment with buprenorphine—compared with methadone—is associated with longer gestation, decreased preterm birth, and improved fetal outcomes including greater birth weight and head circumference. However, factors associated with postpartum treatment retention are unclear. Researchers conducted a retrospective chart review of all maternal and infant records for women prescribed buprenorphine during pregnancy within a family medicine residency program in rural Maine over an 8-year time period (2007–2015) to examine 6 and 12-month treatment retention. Women were excluded from the analysis if pregnancy was terminated, if buprenorphine treatment was terminated or the woman was transferred to buprenorphine treatment during pregnancy, or if the woman or infant required transfer to a tertiary care facility.

- A total of 190 maternal-infant dyads were included; >95% of women were low-income and had Medicaid as primary or secondary insurer; >95% were Caucasian.
- At 12 months postpartum, women were more likely to be retained in buprenorphine treatment if they entered treatment early in pregnancy (defined as either at the time of conception or prior to 13 weeks gestation).
- Illicit substance use (including opioids, cocaine, and benzodiazepines) during the third trimester of pregnancy was associated with poorer treatment retention at both 6 and 12 months postpartum.

Comments: This study adds to the growing body of literature recommending early access to care for all people with opioid use disorder, but especially women of childbearing age.

Jeanette M. Tetrault, MD

Reference: O'Connor AB, Uhler B, O'Brien LM, and Knuppel K. Predictors of treatment retention in postpartum women prescribed buprenorphine during pregnancy. *J Subst Abuse Treat.* 2018;86:26–29.

HEALTH OUTCOMES

Living in a Household With Someone Receiving Prescription Opioids Is Associated With Initiation of Prescription Opioid Use

Opioid prescribing has increased dramatically in the US over the past few decades and has paralleled an increase in prescription opioid use disorders and overdose. Prescription opioid use may spread through families and other networks. Researchers used a commercial insurance database to investigate the association between being prescribed an opioid for the first time and being in a household with someone who is prescribed opioids. Households with individuals prescribed non-steroidal anti-inflammatory (NSAID) medications were used as a comparison.

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Living in a Household With Someone Receiving Prescription Opioids Is Associated With Initiation of Prescription Opioid Use (continued from page 1)

- The study included 12.7 million individuals in 5.9 million “opioid households” and 6.4 million in 3 million “NSAID households.”
- The unadjusted 1-year risk of being prescribed an opioid for the first time was 11.68% in an opioid household and 10.60% in an NSAID household. The adjusted risk was 11.83% for opioid households and 11.11% for NSAID households, an absolute difference of 0.71%.

Comments: This study suggests that the likelihood of being prescribed an opioid for the first time increases with household exposure. While the absolute increase seems modest (1 in 140), when applied to millions of households, this translates to tens of thousands of people. Moreover, this analysis only captures those who initiated opioid use through prescription; there are many more who are taking household members’ opioids without a prescription.

Darius A. Rastegar, MD

Reference: Seamans MJ, Carey TS, Westreich DJ, et al. Association of household opioid availability and prescription opioid initiation among household members. *JAMA Intern Med.* 2018;178:102–109.

E-cigarette and Other Smokeless Product Use Is Associated With Cigarette Smoking Initiation Among Adolescents

Rates of standard tobacco (cigarette) smoking among adolescents plummeted over the past 20 years, but more recently rates have stabilized and the use of non-cigarette products has increased. In this longitudinal survey of more than 10,000 youth aged 12–17, researchers examined whether use of smokeless tobacco products by non-smokers predicted cigarette initiation.

- 4.6% of non-smokers initiated cigarette smoking in the one-year observation period, and 2.1% reported past 30-day cigarette smoking.
- In adjusted models, odds of past 30-day cigarette smoking at follow-up was approximately twice as high among baseline cigarette non-smokers that used e-cigarettes, hookah, or other tobacco products, compared with those who had not.
- Youth who used more than one non-cigarette product at baseline had 3.8 greater odds of past 30-day cigarette smoking at follow-up, compared with those who had no tobacco product use at baseline.

Comments: E-cigarettes, hookah, and similar products are often promoted as harm reduction for cigarette smokers. This study demonstrates that use of any nicotine-based product by adolescents is associated with cigarette smoking initiation; this risk should be considered among the public health harms of these products. Efforts to regulate these products using strategies known to reduce youth cigarette use should be applied broadly to nicotine-containing non-cigarette products.

Sharon Levy, MD, MPH

Reference: Watkins SL, Glantz SA, Chaffee BW. Association of noncigarette tobacco product use with future cigarette smoking among youth in the Population Assessment of Tobacco and Health (PATH) study, 2013-2015. *JAMA Pediatr.* 2018;172(2):181–187.

Factors Associated with the Persistence of Risky Drinking Over Time

Alcohol use is often not constant over time. Similarly, patterns of alcohol use can change. To identify predictors of persistence and change in risky alcohol use patterns, researchers used a representative sample of the Finnish population aged ≥ 30 years, surveyed in 2000 and 2011. Participants reported baseline risky drinking (defined as consuming ≥ 21 drinks [8g of ethanol each] in a week for men, ≥ 14 for women), without a diagnosis of *DSM-IV* alcohol abuse or dependence. Persistent risky drinking was defined as reporting risky drinking at baseline and at follow-up.

- At baseline, 11% of the participants had risky drinking.
- The overall rate of persistent risky drinking was 49% and it predominantly occurred among men (71%).
- Factors associated with persistent risky drinking were: male gender (adjusted odds ratio [aOR], 1.68), higher education (aOR, 1.36), and smoking (aOR, 1.91).
- Risky drinking was less likely to persist among individuals aged ≥ 60 when compared with those aged 30–44 (aOR, 0.22).

The Effects of Alcohol Consumption on Obesity

The public has long been concerned about the association between alcohol consumption and weight gain, as all alcoholic beverages contain calories. This study described the effects on changes in weight associated with changes in alcohol intake over repeated 4-year periods among a large cohort of male health professionals who were followed for 24 years.

- Compared with non-drinkers, participants who consumed alcoholic beverages had increases in weight, mostly < 0.5 pound over a 4-year period; these differences were significant for regular beer and liquor, but not for wine or light beer.
- The largest increases in weight (around 0.6 pounds) were observed among people increasing their alcohol intake by an average of ≥ 2 drinks/day.

- Economic activity, living alone, presence of psychiatric disorder, presence of chronic disease, psychological distress, depressive symptoms, age at first drink, and family history of alcohol disorders were not predictive of persistent risky drinking in multivariable analyses.

Comments: This study points to important factors associated with the persistence of risky drinking that could help clinicians identify those in need of intervention. It underscores the relative stability over time of risky drinking, and to the importance of smoking status in the persistence of risky drinking. The possible synergistic role of risky drinking and smoking calls for combined actions.

Nicolas Bertholet, MD, MSc

Reference: Härkönen J, Aalto M, Suvisaari J, et al. Predictors of persistence of risky drinking in adults: an 11-year follow-up study. *Eur Addict Res.* 2017;23(5):231–237.

- Participants decreasing their alcohol intake by 1-2 drinks/day over the 4-year period experienced a decrease in weight of around ≤ 0.5 pounds.

Comments: This is a very well-done analysis; adjustments were made for known potential confounders associated with changes in weight and appropriate sensitivity analyses were done. The study indicates that calories from alcohol are metabolized similarly to those from other foods and do have some effect on weight change.

R. Curtis Ellison, MD

Reference: Downer MK, Bertoina ML, Mukamal KJ, et al. Change in alcohol intake in relation to weight change in a cohort of US men with 24 years of follow-up. *Obesity.* 2017;25:1988–1996.

HIV AND HCV

Syringe Services Program Implemented During an HIV Outbreak Leads to Reductions in HIV Risk Behaviors

In 2014 a county in southern Indiana experienced the largest HIV outbreak in a rural setting in the United States. Investigators utilized a mixed-methods approach to describe injection-related HIV risk behaviors before and after implementation of an emergency syringe services program (SSP) in Scott County among persons who inject drugs (PWID) between April and August 2015.

- 148 participants (62% of all SSP clients) had > 2 SSP visits (> 7 days apart) and were included in the analysis.
- Participants were predominantly male (56%), non-Hispanic white (98%), and had a median age of 34 years.

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Syringe Services Program Implemented During an HIV Outbreak Leads to Reductions in HIV Risk Behaviors

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- Over a median of 10 weeks, participants reported significant reductions in:
 - syringe sharing to inject (18% to 2%) and divide drugs (19% to 4%).
 - sharing other injection equipment (24% to 5%).
 - number of uses of the same syringe (2 to 1).
- Qualitative study participants described access to sterile syringes and safer injection education through the SSP as explanatory factors for these reductions.

Comments: Although this was the first example of an SSP implemented emergently to control an outbreak of HIV

among PWID in a rural setting in the US, its findings, which demonstrate a rapid reduction in injection-related HIV risk behaviors, are consistent with those reported by SSPs implemented in non-outbreak settings. These findings underscore the need for harm reduction interventions for PWID that include access to syringes and sterile injection equipment as well as comprehensive HIV prevention services.

Seonaid Nolan, MD

Reference: Patel MR, Foote C, Duwve J, et al. Reduction of injection-related risk behaviors after emergency implementation of a syringe services program during an HIV outbreak. *J Acquir Immune Defic Syndr.* 2018;77(4):373–382.

Unhealthy Alcohol Use Is Not Associated With CD4 Count Change Among People With HIV Who Are Not Receiving Antiretroviral Therapy

Unhealthy alcohol use has been associated with poor HIV outcomes, at least partially due to its effect on HIV treatment adherence. Less is known about its impact on individuals who are not receiving antiretroviral treatment (ART); it is possible that alcohol may have direct effects on immune function. Researchers investigated the association between CD4 count changes and unhealthy alcohol use* among individuals with HIV in Uganda who did not meet WHO or local eligibility criteria for ART.

- The study included 446 participants, of whom 43% met criteria for unhealthy alcohol use. The median CD4 cell count at baseline was 550 cells/mm³ and the median duration of follow-up was 12.4 months.

- Unhealthy alcohol use was not associated with an increased rate of CD4 cell count decline in unadjusted or adjusted analyses.

* Defined as 3-month Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) score of ≥ 3 for women and ≥ 4 for men, or phosphatidylethanol (an alcohol biomarker) ≥ 50 ng/ml.

Comments: This study suggests that unhealthy alcohol use does not have a direct impact on short-term CD4 cell count changes; however, it has been shown to be associated with other harms, including decreased ART adherence, increased HIV transmission, and poor clinical outcomes.

Darius A. Rastegar, MD

Reference: Hahn JA, Cheng DM, Emenyonu NI, et al. Alcohol use and disease progression in an antiretroviral naïve cohort. *J Acquir Immune Defic Syndr.* 2018;77(5):492–501.

Alcohol Use Disorder Contributes to Decompensated Cirrhosis Among Individuals With Chronic Hepatitis C

Direct-acting antivirals (DAAs) hold considerable promise for eliminating the global burden of hepatitis C (HCV) infection and chronic liver disease. The relative contribution of alcohol use to HCV-related decompensated cirrhosis is unclear, and restriction of DAA access on the basis of ongoing alcohol use persists in many settings. Researchers evaluated the contribution of alcohol-related diagnoses—defined as non-liver-related hospitalization due to alcohol use and labeled alcohol use disorder (AUD)—to population-level diagnosis of decompensated cirrhosis among people with HCV (defined by presence of antibody). HCV diagnosis notifications from British Columbia (BC), Canada; New South Wales (NSW), Australia; and Scotland from 1995

through 2011, 2012, and 2013, respectively, were linked to hospital admission data between 2001 and 2012, 2013, and 2014, respectively. Age-standardized decompensated cirrhosis incidence was determined and associated factors, including AUD-associated population attributable fractions (PAF), were computed.

- 4.6%, 3.7%, and 4.3% of people with HCV in BC, NSW, and Scotland, respectively, had decompensated cirrhosis diagnosis and 28%, 32%, and 50% of those with decompensated cirrhosis had AUD based on the authors' definition.
- Age-standardized decompensated cirrhosis rates were higher in people with AUD in NSW and Scotland.

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Alcohol Use Disorder Contributes to Decompensated Cirrhosis Among Individuals With Chronic Hepatitis C

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- The PAFs of decompensated cirrhosis related to AUD were 13%, 25%, and 40%, respectively.

Comments: Although the definitions for HCV infection, AUD, and decompensated cirrhosis diagnoses were not standardized and perhaps lack clinical correlation, these data suggest a strong contribution of AUD to decompensated cirrhosis among patients with HCV. The results

suggest the need for tailored interventions to include DAA access for all patients with HCV linked to specialized treatment for those with alcohol-related diagnoses.

Jeanette M. Tetrault, MD

Reference: Alavi M, Janjua NZ, Chong M, et al. The contribution of alcohol use disorder to decompensated cirrhosis among people with hepatitis C: An international study. *Journal of Hepatology*. 2018;68(3):393–401.

PRESCRIPTION DRUGS & PAIN

People With Injection Drug Use and Pain Are More Likely to Report Nonmedical Prescription Opioid Use

Nonmedical prescription opioid use (NMPOU) is associated with high morbidity and mortality. People who inject drugs (PWID) have a high burden of chronic pain, but there is a dearth of data identifying a relationship between dimensions of physical pain and their association with NMPOU. This analysis used cross-sectional interview data from 706 PWID in San Francisco, California.

- 48% of participants reported past 24-hour physical pain
- 48% reported past 24-hour pain interference with general activity, physical ability, or mood.
- 15% reported past 24-hour NMPOU.
- Past 24-hour pain level above median was associated with increased odds of past 24-hour NMPOU (adjusted odds ratio [aOR], 2.15).
- Past 24-hour pain interference above median across

several domains was similarly associated with increased odds of past 24-hour NMPOU.

Comments: These cross-sectional data do not distinguish between whether the observed association between past 24-hour pain and NMPOU is causal. Importantly, these data highlight the high burden of recent pain among PWID. Furthermore, they suggest that the development of interventions to address NMPOU may benefit from understanding and targeting the motivation for use (e.g., untreated pain, euphoric effects, or minimizing withdrawal symptoms).

Marc R. Larochelle, MD, MPH

Reference: Dahman D, Kral AH, Wenger L, et al. Physical pain is common and associated with nonmedical prescription opioid use among people who inject drugs. *Subst Abuse Treat Prev Policy*. 2017;12:29.

No Change in Pain or Depression Outcomes After Implementation of Clinic-based Opioid Dose Reduction and Risk Mitigation Strategies

Clinic-level interventions aiming to reduce opioid dose and mitigate risks of long-term opioid therapy could have adverse effects on pain, function, and depression symptoms. Researchers conducted telephone interviews among patients receiving long-term opioid therapy at primary care clinics conducting dose reduction and risk mitigation interventions (n=935), compared with patients in clinics without such interventions (n=653).

- Response rates were 40% (intervention group) and 28% (control).
- The average age was 62 and two-thirds of patients had a mental health disorder diagnosis; patients in intervention clinics had lower opioid doses compared with controls (mean daily morphine-equivalent dose 47 mg versus 74 mg, respectively).

- After controlling for patient characteristics and co-morbidity and weighted for non-response, there were no significant differences in pain scores between intervention and control clinic patients, or in items related to pain intensity, interference in activities, or enjoyment of life.
- Depression scores (PHQ-8, range 0–24) were lower in intervention clinic patients, but the difference was not clinically significant. There were no significant differences in patient reported opioid-related pain relief or side effects.

Comments: While significantly limited by a low response rate and non-randomized observational design, this study found no evidence that clinic-level dose reduction and risk mitigation strategies were associated with clinically meaningful changes in chronic

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No Change in Pain or Depression Outcomes After Implementation of Clinic-based Opioid Dose Reduction and Risk Mitigation Strategies

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pain outcomes or depression symptoms. These data support efforts to implement opioid prescribing guidelines such as those from the Centers for Disease Control and Prevention.

Joseph Merrill, MD, MPH

Reference: Thakral M, Walker RL, Saunders K, et al. Comparing pain and depressive symptoms of chronic opioid therapy patients receiving dose reduction and risk mitigation initiatives with usual care. *J Pain*. 2018;19(1):111–120.

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