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Alcohol, Other Drugs, and Health: Current Evidence

MAY - JUNE 2021

INTERVENTIONS & ASSESSMENTS

Cohort of People With Non-Medical Opioid Use Did Not Substitute Cannabis for Opioids

Studies reporting an association between medical cannabis laws and decreased rates of opioid-related overdose have raised the question of whether individuals at risk of opioid-related overdose substitute cannabis for non-prescription opioids, thereby reducing their overdose risk. This exploratory study used a within-person analysis to examine the association between cannabis use and non-medical opioid use in a cohort of 211 adults with non-medical opioid use (mean age 43 years, 64% male, 41% white, 78% unmarried, 80% unemployed, 67% moderate-to-severe opioid use disorder [OUD], 50% at least moderate pain over last 30 days).

- Participants completed daily interactive voice response questions about cannabis and opioid use for a 90-day period, with a 70% completion rate.
- Participants reported opioid use without cannabis on 15% of days on average, cannabis use without opioids on 15% of days, both cannabis and opioid use on 7% of days, and neither cannabis nor opioid use on 63% of days.
- The adjusted odds of non-medical opioid use was 1.86 on days when cannabis was used, compared with days when cannabis was not used.
- Results did not differ for patients with and without moderate-to-severe pain, and were consistent across gender and OUD severity.

Comments: This study failed to find evidence of substitution of cannabis for non-medical opioids in a cohort at risk for opioid-related overdose. While the study findings are exploratory, they are consistent with growing evidence that goes against the hypothesis that cannabis is being substituted for opioids and is associated with reduced opioid complications.

Joseph Merrill, MD, MPH

Reference: Gorfinkel LR, Stohl M, Greenstein E, et al. Is cannabis being used as a substitute for non-medical opioids by adults with problem substance use in the United States? A within-person analysis. *Addiction*. 2021;116(5):1113–1121.

Gaps in Screening and Treatment of Opioid Use Disorder and Related Infections in Carceral Settings

The US is experiencing a syndemic of substance use disorders and associated infections (e.g., HIV and viral hepatitis). There is a high prevalence of these conditions in correctional settings, where rates of screening and treatment for both opioid use disorder (OUD) and chronic infections remain low. Researchers reviewed the evidence regarding the screening and treatment of OUD and associated chronic infections in US correctional settings, identifying existing challenges and making suggestions for improvement.

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Gaps in Screening and Treatment of Opioid Use Disorder and Related Infections in Carceral Settings (continued from page 1)

- HIV and viral hepatitis screening in correctional settings is not universal. Implementation of universal screening may be a way to improve the identification of HIV and viral hepatitis infections.
- Many prisons or jails cannot afford to offer HIV and HCV medications, so the availability of treatment varies between institutions. Novel approaches are needed to source medications for a reasonable cost, via either competitive contract bidding, or bulk purchase across institutions.
- Medication for OUD (MOUD) is unavailable in most jails and prisons, despite the known benefits. Use of long-acting injectable MOUD (i.e., extended-release buprenorphine) may address the reasons often cited for not offering daily dose methadone or buprenorphine in these settings (e.g., diversion, overdose risk, need for regular dose adjustments, etc.).
- Integration of telemedicine in correctional settings should be considered to improve access to specialty service consultations (e.g., infectious diseases and addiction medicine).

Comments: Despite the high prevalence of OUD and chronic infections in correctional settings, screening and treatment rates for both conditions remain low. Implementing broader screening, nuanced approaches to procuring medications, more widespread use of long-acting medications for the treatment of HIV and OUD, and expanding access to specialty care may improve the management of these conditions.

Piper Dickhout, BSc† and Seonaid Nolan, MD

† Contributing Editorial Intern

Reference: Krsak M, Montague BT, Trowbridge P, et al. Opioid use and chronic infections: the value of addressing the syndemic in correctional settings via telemedicine guidance and broader use of long-acting medications. *J Infect Dis.* 2020;222(Suppl 5):S486–S493.

Internet-based Cognitive Behavioral Therapy (CBT) for Alcohol Use Disorder Is Not Inferior to Face-to-face CBT for Reducing Alcohol Consumption

Cognitive behavioral therapy (CBT) has been shown to be effective for treating alcohol use disorder (AUD), but most individuals with AUD do not receive treatment. Previous studies have indicated that internet-based CBT is also effective, but less is known about how it compares with face-to-face treatment. Researchers in Sweden recruited 301 treatment-seeking individuals with AUD through a website to compare alcohol consumption 3 and 6 months after receipt of 5 face-to-face CBT modules, or 5 internet-based CBT modules. They excluded individuals at risk for severe withdrawal or suicide and those requiring medication for AUD or with a mental illness requiring separate treatment.

- Attrition was not significantly different between the 2 groups: 33% at 3 months and 43% at 6 months.
- The face-to-face group completed more modules (4.2) than the internet group (3.7).
- The primary outcome measure—difference between groups in alcohol consumption during the previous week at 6-month follow-up—was non-inferior. Both groups had a decline in self-reported drinks from approximately 24 to 12 drinks in the past week.

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Internet-based Cognitive Behavioral Therapy (CBT) for Alcohol Use Disorder Is Not Inferior to Face-to-face CBT for Reducing Alcohol Consumption (continued from page 2)

Comments: This study suggests that internet-based CBT is a good option for individuals with AUD who are seeking treatment and are interested in this approach. This has the potential to expand access to treatment for AUD. Further research is needed on matching individu-

als to the treatment approach that works best for them.

Darius A. Rastegar, MD

Reference: Johansson M, Sinadinovic K, Gajecski M, et al. Internet-based therapy versus face-to-face therapy for alcohol use disorder, a randomized controlled non-inferiority trial. *Addiction*. 2021;116(5):1088–1100.

HEALTH OUTCOMES

Incarceration Is Associated With Subsequent Overdose-related Death

Drug overdose is a growing cause of mortality in North America. Previous studies have found that recent incarceration is associated with an increased risk of overdose compared with the general population. Researchers used data from British Columbia health insurance and incarceration records to examine the association between incarceration during the 5-year period of 2010-2014 and subsequent overdose-related death over the 3-year period of 2015-2017.

- Of the 765,690 people in the cohort, 5743 were incarcerated during the initial 5-year period. Those who were incarcerated were younger, more likely to be male, to have substance use disorder (SUD), and to live in more materially deprived neighborhoods.
- During the 3-year follow-up period, 634 people died from drug overdose. In unadjusted analyses, those

who had prior incarceration were 41 times more likely to die from drug overdose than those who did not.

- After adjusting for individual and neighborhood characteristics, the hazard ratio was substantially reduced but still elevated at 4; SUD alone accounted for 84% of the reduction.

Comments: Although the mechanism of this association is not clear, this study suggests that overdose-related death should be added to the list of harms of incarceration on individuals and communities. We need to explore alternatives to incarceration and, at a minimum, incarceration should be used as opportunity to engage individuals with SUD in treatment.

Darius A. Rastegar, MD

Reference: Gan WQ, Kinner SA, Nicholls TL, et al. Risk of overdose-related death for people with a history of incarceration. *Addiction*. 2021;116(6):1460–1471.

The Impact of Alcohol Use on Liver Diseases

Mortality from liver disease has increased over the last decade in the US. Alcohol is a known cause, but its use also contributes to the development or progression of other types of liver disease, complicating efforts to quantify the overall impact of alcohol use on liver disease. Researchers developed causal and statistical models based on a narrative review of the literature to assess the relationships between alcohol use and the development or progression of various liver diseases in the US in 2017, including through alcohol's interactions with other relevant behavior-related risk factors.

- Alcohol use caused 54,500 incident cases of liver cirrhosis, of which approximately 35% were from diseases other than alcohol-associated cirrhosis.
- Through interaction with behavioral risk factors, alcohol use accounted for the progression to cirrho-

sis of 10,400 cases of obesity-related liver disease and 7700 cases of hepatitis C virus.

- Alcohol use caused 47,300 total deaths from liver disease, including 6600 from liver cancer.

Comments: Accounting for alcohol's role in liver diseases that are exacerbated by alcohol consumption or caused by alcohol-associated risk factors yields substantially higher estimates of morbidity and mortality than those based on diseases for which alcohol is the original or principal cause. This has important implications for public health surveillance, and serves as a reminder to clinicians about the role of alcohol in a wide range of liver diseases.

Timothy S. Naimi, MD, MPH

Reference: Rehm J, Patra J, Brennan A, et al. The role of alcohol use in the aetiology and progression of liver disease: A narrative review and a quantification. *Drug Alcohol Rev*. 2021;10.1111/dar.13286.

Childhood Depression and Nicotine Use Associated With Unhealthy Opioid Use in Young Adulthood

Rates of opioid overdose are rising among US young adults. Researchers sought to explore childhood antecedents of: non-medical (prescription) opioid use, frequent (weekly or more) non-medical opioid use, and heroin use via a longitudinal survey conducted between 1993 and 2015. They assessed 1252 participants (25% American Indian, 75% white, non-Hispanic) in North Carolina, recruited at age 9.

- By age 30, 9% of participants had had weekly non-medical opioid use and 7% had used heroin.
- Cannabis use was associated with any non-medical opioid use, but not frequent non-medical opioid or heroin use.
- Depression and tobacco use were associated with frequent non-medical opioid and heroin use.

- Neither anxiety, ADHD, nor alcohol use were associated with non-medical opioid or heroin use.

Comments: Addiction is a chronic disorder that typically begins in the teen years; adolescence is an ideal time to identify and intervene in order to prevent addiction. This longitudinal study identified modifiable antecedents of opioid use disorder, including depression and tobacco use. Screening for and treating these conditions during childhood may yield health benefits above and beyond addressing those caused by the primary condition.

Sharon Levy, MD

Reference: Shanahan L, Hill SN, Bechtiger L, et al. Prevalence and childhood precursors of opioid use in the early decades of life. *JAMA Pediatr.* 2021;175(3):276–285.

HIV & HCV

Alcohol Use Has a Detrimental Impact on Liver Disease Among Patients With HCV

This systematic review and a meta-analysis evaluated the relationship between alcohol use and liver disease progression among people with HCV infection. Researchers evaluated 33 longitudinal and case-control studies reporting on biological outcomes (the majority were case-control studies). They excluded studies reporting solely on liver cancer and liver transplants.

- There was a dose-dependent, exponential relationship between level of alcohol use and progression of liver disease (incidence of cirrhosis): the higher the daily alcohol intake, the greater the probability of liver cirrhosis in patients with HCV.
- Every daily drink containing 12g of alcohol increased the risk of cirrhosis by 11%.

Comments: Alcohol use plays a significant and detrimental role in liver disease progression among people with HCV. The conclusions of this systematic review rely heavily on case-control studies; results could be impacted by limitations of the included studies such as recall bias, and biases related to self-report. Nevertheless, it is important to keep raising awareness on the links between alcohol use and HCV complications.

Nicolas Bertholet, MD, MSc

Reference: Llamosas-Falcón L, Shield KD, Gelovany M, et al. Impact of alcohol on the progression of HCV-related liver disease: A systematic review and meta-analysis. *J Hepatol.* 2021;S0168-8278(21)00253-1.

PRESCRIPTION DRUGS & PAIN

Despite Guidelines, Few Patients Prescribed Long-term Opioid Therapy Also Receive Naloxone

US guidelines recommend prescribing naloxone, an opioid antagonist that reverses opioid overdose, to patients prescribed long-term opioid therapy (LTOT). This retrospective study used pharmacy claims data to examine how frequently naloxone was co-prescribed with LTOT and whether individual or community characteristics were associated with co-prescribing. A large database from US commercial

pharmacies included 6 million LTOT treatment episodes (defined as filling opioid prescriptions for ≥ 90 days) among 5 million unique individuals in 2017–2018. Individual and community characteristics included age, sex, high-dose LTOT (≥ 90 milligrams morphine equivalent daily), benzodiazepine co-prescribing, insurance type, prescriber specialty, and county-level urbanicity, overdose rate, and poverty.

(continued page 5)

Despite Guidelines, Few Patients Prescribed Long-term Opioid Therapy Also Receive Naloxone (continued from page 4)

- Overall, naloxone was co-prescribed in only 2.3% of LTOT treatment episodes.
- Naloxone co-prescribing was associated with receiving high-dose opioid prescriptions (adjusted odds ratio [aOR], 3.19) and benzodiazepine medications (aOR, 1.12), although co-prescribing remained uncommon during these treatment episodes (7.3% and 3.5%, respectively).
- Co-prescribing was higher when Medicare or Medicaid was the payer (aOR, 1.48 and 1.87, respectively), versus other insurance or cash payment (aOR, 0.81 and 0.77, respectively).
- Naloxone co-prescribing increased with age up the 46–55 year range, but then was lower in older age groups.
- Co-prescribing was more common in LTOT treatment episodes from counties with high (versus low) overdose rates and urban (versus rural) counties.

Comments: Many patients who should receive naloxone from pharmacies do not. Community-based naloxone distribution programs remain critically important, but clinicians who prescribe LTOT also need to do their part. Avoiding known risks, such as prescribing LTOT in high doses or with benzodiazepines, is one step; prescribing naloxone, which is safe and simple to administer, could also prevent accidental opioid overdose deaths. Measures that may help increase co-prescribing include electronic prompts when prescribing, automatic dispensing of naloxone with opioid prescriptions and reducing cost barriers.

Aaron D. Fox, MD

Reference: Stein BD, Smart R, Jones CM, et al. Individual and community factors associated with naloxone co-prescribing among long-term opioid patients: a retrospective analysis. *J Gen Intern Med.* 2021;10.1007/s11606-020-06577-5.

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