Alcohol, Other Drugs, and Health: Current Evidence

MAY-JUNE 2022

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INTERVENTIONS & ASSESSMENTS

Low-threshold Opioid Agonist Therapy Is a Safe Option

Low-threshold access to opioid agonist therapy (OAT) may increase the number of people benefiting from treatment. This study assessed the impact of low-threshold OAT (outpatient initiation of methadone or buprenorphine without prerequisite referral or abstinence from non-medical substance use, no urine testing) on treatment retention, non-medical opioid use, and safety (non-fatal and fatal intoxications, all-cause mortality) compared with the Norway standard intervention (treatment initiation with methadone or buprenorphine with referral and abstinence from non-medical substance use confirmed by urine testing).

- 128 patients receiving low-threshold OAT were included and compared with the 7900 patients in the Norway national reference cohort.
- Treatment retention rates were 95% and 92% in the low-threshold and reference cohort, respectively. Illicit opioid use rates were 7% and 10%.
- The rates of non-fatal intoxication were 7% and 6% in the low-threshold and reference cohort, respectively, and all-cause mortality was 1% and 1.3%.
- Healthcare utilization increased (incident rate ratios >3) for in- and outpatient care among both groups.

Comments: This study gives indications that in Norway—a country with a high coverage of OAT—a low-threshold access model of OAT appears at least as safe as the standard provision of OAT, with similar retention rates and non-medical opioid use rates. OAT was associated with an increase in healthcare utilization indicating that patients had better access to care than before OAT initiation.

Nicolas Bertholet, MD, MSc

Reference: Chalabianloo F, Ohldieck C, Haaland ØA, et al. Effectiveness and safety of low-threshold opioid-agonist treatment in hard-to-reach populations with opioid dependence. *Eur Addict Res*. 2022;28(3):199–209.

Mindfulness-based Intervention Shows Promise for Treating Comorbid Unhealthy Opioid Use and Pain

Large-scale studies of non-pharmacologic treatments such as mindfulness for individuals with both chronic pain and opioid use disorder (OUD) have been lacking. This randomized controlled study examined the effects of Mindfulness-Oriented Recovery Enhancement* (MORE; n=129) on pain and opioid use outcomes among individuals with "opioid misuse"** who were receiving opioid treatment for pain. A control group received group supportive psychotherapy (n=121). Participants were followed for 9 months.

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Mindfulness-based Intervention Shows Promise for Treating Comorbid Unhealthy Opioid Use and Pain (continued from page 1)

- Most participants were white (87%), had mean duration of chronic pain of >14 years, and had a daily mean morphine-equivalent (MME) opioid dose of 101 mg.
- Attrition was similar to other studies; 37% of participants had discontinued by 9 months.
- Compared with the control group, individuals randomized to MORE had lower odds of "opioid misuse" (odds ratio, 2.06), less pain severity (between-group effect, 0.49), less pain-related functional interference (between-group effect, 1.07), and greater reduction in total daily MME (between-group effect, 0.15 log mg).

* A manualized, group therapy intervention using a combination of mindfulness training, cognitive behavioral therapy, and principles from positive psychology.
** Defined as having a score higher than the validated cutoff (≥9 points) for "opioid misuse" on the Current Opioid Misuse Measure.

Comments: MORE shows promise as a non-pharmacologic treatment for individuals with both chronic pain and unhealthy opioid use, although this study was limited in the diversity of its participants and had high attrition. Studies like this demonstrate that non-pharmacologic treatments can be effective, but they require time and resources that may not be available in all settings.

Melissa B. Weimer, DO, MCR

Reference: Garland EL, Hanley AW, Nakamura Y, et al. Mindfulness-oriented recovery enhancement vs supportive group therapy for co-occurring opioid misuse and chronic pain in primary care: a randomized clinical trial. *JAMA Intern Med.* 2022;182(4):407–417.

HEALTH OUTCOMES

E-cigarette Use Associated With Lung Disease in Young Adults

E-cigarette use has become popular with youth, and the health risks of these products have not been fully elucidated. This nationally representative, population-based, longitudinal study examined the association between respiratory symptoms and the use of e-cigarettes and combustible cigarettes among young adults aged 18–24 with no prior history of respiratory disease (N=6378).

- There were no differences in the rates of reported respiratory symptoms between people who used combustible cigarettes, e-cigarettes, or both; all were more likely to report respiratory symptoms than those without use of either.
- Compared with people who never used combustible or e-cigarettes, people with e-cigarette use were more likely to report wheezing in the chest (adjusted odds ratio [aOR], 2.23) and wheezing during exercise (aOR, 2.41).

Comments: E-cigarettes have been promoted as a harm-reduction strategy for people with combustible cigarette use and marketed as safer because the exposure to "harmful or potentially harmful chemicals" (HPHC), as defined by the Food and Drug Administration, is much lower than from combustible cigarettes. This research adds to a growing evidence base that e-cigarette use causes exposure to chemicals that injure lung tissue, even though they are not defined as HPHCs. The public should be aware that although there may be a harm-reduction role for e-cigarettes for people with combustible cigarette use, they present a serious health risk for adolescents and people who do not have combustible cigarette use.

Sharon Levy, MD

Reference: Xie W, Tackett AP, Berlowitz JB, et al. Association of electronic cigarette use with respiratory symptom development among US young adults. *Am J Respir Crit Care Med*. 2022;10.1164/rccm.202107-1718OC.

Alcohol Use Associated With Poor Blood Pressure, Even After Controlling for Other Risk Factors

Alcohol use is positively associated with blood pressure, and is a risk factor for poor blood pressure control among people with established hypertension. However, the mechanism by which alcohol use is related to worse blood pressure control has not been fully characterized. Researchers assessed the potential mediating roles of several behavior-related risk factors that are associated with poor blood pressure control among 1835 persons with hypertension (51% women, 58% Black) participating in the longitudinal Coronary Artery Risk Development in Young Adults cohort study (2005–2016).

- Each additional drink per day of average consumption was associated with 0.71 mmHg higher systolic blood pressure (95% confidence interval [CI], 0.40, 1.03) and 0.36 mmHg higher diastolic blood pressure (95% CI, 0.16, 0.56).
- After adjusting for average daily alcohol consumption, heavy episodic drinking (defined as consuming ≥5 drinks at least once in the last 30 days) was not independently associated with blood pressure.
- The alcohol-blood pressure relationship was not mediated by smoking, physical inactivity, unhealthy diet, or poor medication adherence.

Comments: In this cohort, the relationship between increased alcohol use and higher blood pressure among individuals with hypertension was not mediated by common associated behavior-related risk factors, supporting a primary direct effect of alcohol on blood pressure. Addressing alcohol use is an important component of managing patients with hypertension.

Timothy S. Naimi, MD, MPH

Reference: Phillips AZ, Kiefe CI, Lewis CE, et al. Alcohol use and blood pressure among adults with hypertension: the mediating roles of health behaviors. *J Gen Intern Med*. 2022 [Epub ahead of print]. doi: 10.1007/s11606-021-07375-3.

Medications for Opioid Use Disorder Reduce the Risk of Repeat Overdose

Opioid overdose is a common and serious complication of opioid use disorder (OUD) and individuals who experience an overdose are at higher risk for another. In this study, researchers used New Jersey Medicaid data from 2014 to 2019 to evaluate associations between receipt of medications for OUD (MOUD; methadone, buprenorphine, and naltrexone) and repeat overdose.

- There were 4898 enrollees aged 12–64 years who experienced an initial opioid overdose requiring medical intervention and who had not received MOUD in the 180 days prior to the index event.
- The overall rate of repeat overdose within 12 months of the index overdose was 20%; one in five of these occurred within 30 days. Only 22% of people who experienced an overdose received MOUD in the follow-up period.
- Among individuals who received MOUD at any time during the follow-up period, 11% experienced a repeat overdose, compared with 22% of those who did not receive MOUD (hazard ratio, 0.35).

Comments: This study reinforces the benefits of MOUD for prevention of overdose and shows that we need to do a better job of linking individuals who experience overdose with evidence-based care. Not offering these medications during emergency department encounters for overdose is a missed opportunity for a life-saving intervention. The percentage of overdose survivors who receive MOUD within 30 days should be a publicly available quality of care metric.

Darius A. Rastegar, MD

Reference: Crystal S, Nowels M, Samples H, et al. Opioid overdose survivors: medications for opioid use disorder and risk of repeat overdose in Medicaid patients. *Drug Alcohol Depend*. 2022;232:109269.

Providing Buprenorphine During Incarceration Reduces Re-engagement With the Criminal-legal System

Incarcerated individuals with opioid use disorder (OUD) are at high risk for adverse outcomes after release. Previous studies have found improved outcomes associated with provision of medications for OUD (MOUD), but primarily examined the effects of methadone and naltrexone in urban settings. Researchers compared two adjacent rural Massachusetts counties, one of which (Franklin) offered buprenorphine to incarcerated individuals with OUD, while the other (Hampshire) did not.

- During the 2015–2019 study period, there were 469 adults with OUD released from jail in Franklin County and 272 from Hampshire.
- During the study period, 93% of individuals with OUD received MOUD while incarcerated in Franklin; most (86%) received buprenorphine. None of the individuals with OUD incarcerated at Hampshire received MOUD.

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Providing Buprenorphine During Incarceration Reduces Re-engagement With the Criminal-legal System (continued from page 3)

- Re-engagement with the criminal-legal system overall (i.e., re-incarceration, arraignment, or probation violation) was lower among individuals incarcerated at Franklin compared with Hampshire (48% versus 63%, respectively; adjusted odds ratio [aOR], 0.51), as was re-incarceration specifically (21% versus 39%; aOR, 0.37).

Comments: This study suggests that providing buprenorphine and other MOUD during incarceration reduces re-engagement with the criminal-legal system, adding to the many benefits of MOUD for people with OUD. Incarceration is an opportunity to engage individuals with OUD in treatment; MOUD should be the standard of care.

Darius A. Rastegar, MD

Reference: Evans EA, Wilson D, Friedmann PD. Recidivism and mortality after in-jail buprenorphine treatment for opioid use disorder. Drug Alcohol Depend. 2022;231:109254.

PRESCRIPTION DRUGS & PAIN

Provision of Naloxone with Opioid Analgesic Prescriptions Not Associated with Increased Opioid-related Risk Behaviors

Concerns that possessing naloxone could promote riskier opioid use may prevent clinicians and pharmacists from prescribing or dispensing naloxone along with opioid analgesics. Investigators randomized 7 pharmacies within a safety-net health system to implement a naloxone co-dispensing intervention, which included patient education and new screening and naloxone dispensing workflows, or to continue standard protocols, which included standing orders for naloxone. Outcomes were assessed among patients (N=768) filling long-term opioid prescriptions and a subset of participants (n=335) who completed surveys and urine drug testing to assess risk behaviors for unhealthy opioid use.

- Patients using intervention pharmacies were significantly more likely to receive naloxone (52% versus 14%; adjusted risk ratio [aRR], 3.38).
- The proportion of participants in each group that reported ≥1 opioid-related risk behaviors at 8 months follow-up did not significantly differ (38% versus 35%; aRR, 1.07).
- Risky drinking, tobacco use, other drug use, and opioid-related overdoses were not significantly different between groups.

Comments: Theories about "risk compensation" have been used as an argument against many effective health interventions, such as syringe services programs or HIV pre-exposure prophylaxis. This study shows that simple changes to pharmacy workflows and staff trainings resulted in large increases in naloxone dispensing without detectable differences in patients' opioid-related risk behaviors. Greater naloxone distribution is urgently needed.

Aaron D. Fox, MD

Reference: Binswanger IA, Rinehart D, Mueller SR, et al. Naloxone co-dispensing with opioids: a cluster randomized pragmatic trial. *J Gen Intern Med*. 2022;10.1007/s11606-021-07356-6.

Medical Cannabis Card Ownership May Increase Cannabis Use Disorder Symptoms and Improve Sleep

The use of cannabis for medicinal purposes is widespread in the US, yet little evidence is available on the effects of medical cannabis card acquisition. This study sought to evaluate the short-term effects of obtaining a medical cannabis card among adults seeking relief from chronic pain, insomnia, anxiety, or depression symptoms. In a single-site trial, participants randomized to wait 12 weeks before acquiring a medical cannabis card (n=81, 84% of those randomized) were compared with the subset of participants randomized to immediate card acquisition who successfully obtained a card (n=105, 61% of those randomized).

- Compared with the delayed card acquisition group, the immediate card acquisition group had more cannabis use disorder (CUD) symptoms (mean difference [MD], 0.28); fewer insomnia symptoms (MD, -2.90); and reported no significant changes in pain severity or symptoms of anxiety or depression.

Medical Cannabis Card Ownership May Increase Cannabis Use Disorder Symptoms and Improve Sleep (continued from page 4)

- More participants in the immediate card acquisition group developed (mostly mild) CUD (17%), compared with those in the delayed card acquisition group (9%; adjusted odds ratio, 2.88), particularly among participants with a chief concern of anxiety or depressive symptoms.
- Multiple sensitivity analyses, including those attempting to control for the lack of an intention-to-treat analysis, documented similar results.

Comments: This study provides some of the best, if limited, evidence of the effects of medical cannabis card acquisition on a range of commonly targeted symptoms. While generally mild, the increased incidence of CUD among those acquiring cards—especially among those with anxiety or depression—is potentially concerning, while possible improvements in sleep begs further investigation. These findings are relevant to discussions with patients interested in using cannabis for its potential medicinal benefits.

Joseph Merrill, MD, MPH

Reference: Gilman JM, Schuster RM, Potter KW, et al. Effect of medical marijuana card ownership on pain, insomnia, and affective disorder symptoms in adults: a randomized clinical trial. *JAMA Netw Open*. 2022;5(3):e222106.

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