Alcohol, Other Drugs, and Health: Current Evidence

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TABLE OF CONTENTS

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INTERVENTIONS & ASSESSMENTS

Social Worker-led Inpatient Navigation Reduced Hospital Readmissions and Improved Substance Use Disorder Treatment Engagement

Hospitalized patients with substance use disorder (SUD) are at high risk for hospital readmission and emergency department use. Addiction consult services have emerged to improve inpatient management of SUD-related care and increase linkage to SUD treatment upon discharge. However, engagement of hospitalized individuals can be challenging and length of stay may be short. This single-site randomized controlled trial tested whether adding a patient navigator who engaged individuals during hospitalization and followed them for up to 90 days reduced readmissions and improved SUD treatment rates compared with treatment as usual that included an addiction consult service.

- Compared with treatment as usual, navigation reduced 12-month inpatient admission rates from 8 to 6 per 1000 person-days and emergency department visits from 28 to 18 per 1000 person-days.
- Community SUD treatment initiation within 3 months was higher among patients receiving navigation (50%), compared with treatment as usual (35%).
- Navigation was provided by masters-level social workers with an average caseload of 13 patients per week.

Comments: Hospitalization is often a missed—if challenging—opportunity to engage and link individuals with SUD to community treatment. This randomized controlled trial demonstrated that patient navigators improved SUD treatment engagement and reduced care utilization. Further work is needed to understand the reproducibility, scalability, and sustainability of this intervention.

Marc R. Larochelle, MD, MPH

Reference: Gryczynski J, Nordeck CD, Welsh C, et al. Preventing hospital readmission for patients with comorbid substance use disorder: a randomized trial. *Ann Intern Med*. 2021;174(7):899–909.

The Benefits of Extended-release Naltrexone Paired with Psychosocial Interventions for Alcohol Use Disorder

Oral naltrexone has been shown to reduce alcohol consumption and craving in individuals with alcohol use disorder (AUD), yet evidence regarding the efficacy of the extended-release injectable formulation (XR-naltrexone) is limited. Researchers conducted a systematic review and meta-analysis of 7 randomized controlled trials evaluating 1500 adults with AUD receiving XR-naltrexone (150–400 mg) for 2–6 months or placebo, plus some form of behavioral therapy. The primary outcome was the pooled weighted mean difference (WMD) in drinking days and heavy drinking days per month.

(continued page 2)

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The Benefits of Extended-release Naltrexone Paired with Psychosocial Interventions for Alcohol Use Disorder (continued from page 1)

- Compared with patients who received placebo, those who received XR-naltrexone had 2 fewer drinking days and 1.2 fewer heavy drinking days per month.
- Longer treatment duration (>3 months) resulted in 1.9 fewer heavy drinking days per month (WMD, −1.9; 95% CI = −3.2, −0.5; P = 0.01),* compared with treatment duration of <3 months.
- Compared with patients in studies requiring abstinence prior to treatment initiation, patients in studies that did not require lead-in abstinence had 2 fewer heavy drinking days per month (WMD, -2.0; 95% CI = −3.52, −0.48; P = 0.01).*

*Overlap of 95% CIs between subgroups indicate potential lack of statistical significance. However, researchers maintain clinical significance of findings.

Comments: With a modest reduction in drinking days and heavy drinking days per month compared with psychosocial interventions and placebo alone, the results of this meta-analysis suggest that XR-naltrexone may have some efficacy for AUD treatment, especially with longer treatment duration. Further research is needed to determine the long-term efficacy of XR-naltrexone, its effects among an actively drinking population, and how it compares (e.g., efficacy and cost) with oral naltrexone.

Jonah Hamilton† and Seonaid Nolan, MD

† Contributing editorial intern and Research Coordinator, British Columbia Centre on Substance Use.

Reference: Murphy CE 4th, Wang RC, Montoy JC, et al. Effect of extended-release naltrexone on alcohol consumption: a systematic review and meta-analysis. *Addiction*. 2021;10.1111/add.15572.

HEALTH OUTCOMES

Shorter Wait-times Associated With Improved Post-hospital Discharge Linkage to Opioid Use Disorder Treatment

Buprenorphine and methadone are effective treatments for opioid use disorder (OUD), but most individuals with OUD do not receive them. Hospitalization is an opportunity to initiate treatment, but many patients do not link with care after hospital discharge. Researchers used data from patients admitted to Boston Medical Center who were started on buprenorphine to investigate the association between the wait-time for follow-up appointments and linkage with OUD care.

- The study included adults with OUD who were started on buprenorphine during hospitalization and provided with a follow-up appointment at 1 of 2 affiliated clinics.
- Of 142 patients, 77 (55%) arrived at their follow-up appointment; 56 (39%) had an appointment 0–1 days after discharge from the hospital, and the remainder (61%) had an appointment 2 or more days after discharge.
- Patients with a follow up 0–1 days after discharge were more likely to arrive at their appointment than those with an appointment 2 or more days after discharge (63% versus 42%, respectively).
- In multivariable analyses, having a follow-up appointment 0–1 days after discharge was associated with improved odds of arriving at the appointment (odds ratio, 2.6).

(continued page 3)

Shorter Wait-times Associated With Improved Post-hospital Discharge Linkage to Opioid Use Disorder Treatment (continued from page 2)

Comments: We need to do more to improve engagement and retention in evidence-based treatments for OUD. This study suggests that providing a follow-up appointment within a day after hospital discharge is one tool to accomplish this.

Darius A. Rastegar, MD

Reference: Roy PJ, Price R, Choi S, et al. Shorter outpatient wait-times for buprenorphine are associated with linkage to care post-hospital discharge. *Drug Alcohol Depend*. 2021;224:108703.

Paternal Alcohol Consumption Linked With Fetal Anomalies

Paternal alcohol consumption can cause genetic and epigenetic sperm abnormalities. This study used a national database collected during a preconception health examination that was offered in all 31 provinces in China 2010–2012 (N=529,090). The team evaluated the association between paternal alcohol consumption prior to conception and the risk of birth defects, controlling for confounders, including maternal alcohol consumption and paternal smoking.

- Paternal alcohol consumption was reported by 31% of couples and 3.3% reported maternal consumption.
- Couples that reported paternal alcohol consumption had a 35% increased risk of having a baby with a birth defect (odds ratio, 1.35).

Comments: This study suggests that paternal alcohol use prior to conception increases the risk of birth defects; the authors recommend further study to elucidate the highest risk consumption patterns. Parenting is often a strong motivation to make behavioral changes; these findings may provide young men a reason to evaluate their alcohol consumption and seek treatment if needed.

Sharon Levy, MD

Reference: Zhou Q, Song L, Chen J, et al. Association of preconception paternal alcohol consumption with increased fetal birth defect risk. *JAMA Pediatr*. 2021;175(7):742–743.

Is Involvement With the US Criminal Justice System Associated With Morbidity, Including Substance Use Disorders, Among Older Adults?

During the era of mass incarceration in the US, exposure to the criminal justice system has increasingly been recognized as a risk factor for negative health outcomes. This study of adults aged ≥50 examined whether recent "criminal justice involvement" (defined as self-reported arrest, parole, or probation in the past year) was associated with self-reported mental illness, substance use disorders, and medical multi-morbidity (i.e., having ≥2 chronic conditions). Data were derived from the 2015–2018 National Survey of Drug Use and Health (N=34,898).

- Overall, 1.2% of the sample reported recent criminal justice involvement.
- A greater percentage of individuals with (versus without) recent criminal justice involvement reported having any substance use disorder (35% versus 4%) and moderate or serious mental illness (21% versus 6%), but not medical multi-morbidity (24% versus 26%).
- In analyses adjusting for age, gender, race/ethnicity, marital status, education, income, and health insurance status, having all 3 conditions (mental illness, substance use disorder, and medical multi-morbidity) was strongly associated with recent criminal justice involvement (adjusted odds ratio, 8.56).
- Individuals with recent arrest had greater odds of reporting mental illness or multi-morbidity than those on parole or probation.

Comments: Substance use disorder prevalence tends to decrease with age, but this study demonstrates a high prevalence among middle-aged and older adults with recent criminal justice involvement. These self-reported data were not ideal to study medical multi-morbidity, however, because people without reliable access to medical care may be unaware of medical comorbidities. Future studies should move beyond descriptive analyses to examine whether criminal justice involvement can be causally linked to these conditions, and to identify interventions that best address them among this highly marginalized population.

Aaron D. Fox, MD

Reference: Han BH, Williams BA, Palamar JJ. Medical multimorbidity, mental illness, and substance use disorder among middle-aged and older justice-involved adults in the USA, 2015–2018. *J Gen Intern Med*. 2021;36(5):1258–1263.

THC Concentration in Cannabis Increased Worldwide Between 1970 and 2017

Delta-9-tetrahydrocannabinol (THC) is the major psychoactive component of cannabis. Higher potency of THC is associated with intoxication, anxiety, and cognitive impairment during use; long-term exposure has been associated with psychotic disorders and cannabis use disorder. Cannabidiol (CBD), a cannabinoid that is not psychoactive, may moderate some of these effects. Previous studies have demonstrated an increase in THC concentration in certain countries over limited time intervals. In this study, the authors conducted a systematic review of studies that reported mean THC or CBD concentrations over at least 3 annual time points.

- Twelve eligible studies were included. These collected samples from 1970 to 2017 in the US, UK, Netherlands, France, Denmark, Italy, and New Zealand.
- Ten of these studies used non-random sampling (e.g., law enforcement seizures). Otherwise, they were judged to have a low risk of bias.
- THC concentration in herbal cannabis rose annually by 0.29%.
- THC concentration in cannabis resin rose annually by 0.57%.
- CBD concentration in herbal cannabis and cannabis resin was unchanged.

Comments: Cannabis has become steadily more potent over the past 5 decades. This study quantifies these changes from an international perspective and is the first meta-analysis to describe CBD concentrations in addition to THC. Increased potency will likely lead to more adverse outcomes among people who use cannabis. Its legalization is an opportunity to regulate potency and potentially mitigate harms.

Ashish Thakrar, MD† and Darius A. Rastegar, MD

† Contributing editorial intern and addiction medicine fellow, Johns Hopkins Bayview Medical Center

Reference: Freeman TP, Craft S, Wilson J, et al. Changes in delta-9-tetrahydrocannbinol (THC) and cannabidiol (CBD) concentrations in cannabis over time: systematic review and meta-analysis. *Addiction*. 2021;116:1000–1010.

Machine-learning Algorithm Predicts Future Mortality Following Non-fatal Opioid Overdose

This retrospective cohort study used 2014–2016 Pennsylvania Medicaid data to develop a predictive model for all-cause mortality following non-fatal opioid overdose through applied machine learning. The algorithm used 348 predictors for 9686 individuals, including variables at the individual level (socio-demographics, health status, and health service utilization) and community level (e.g., poverty level, suicide rate) from the 180 days that preceded an index overdose. The main outcome was all-cause mortality within 180 days after the index overdose.

- Overall, 346 (3.6%) individuals died within 180 days after an index overdose.
- Those in the highest-risk group (≥98th percentile of risk) had a 180-day mortality rate of 20%; in the lowest -risk group (<25th percentile), the mortality rate was 1.5%.*
- When sensitivity and specificity were balanced, the algorithm's negative and positive predictive values were 98% and 6.5%, respectively.
- Receiving medications for opioid use disorder or risk-mitigation interventions (naloxone, urine drug testing, substance use disorder counseling) after overdose were associated with lower mortality.
- Several community-level variables, such as county-level poverty or suicide rates, were important predictors of mortality.

* Individuals were stratified into 6 subgroups "at similar risk according to the risk scores (i.e., the individual's estimated probability of death) generated by the validated machine learning algorithm."

Comments: Having a score at the time of non-fatal opioid overdose to estimate future mortality risk could be useful for clinicians, health insurers, or government agencies. However, this algorithm used all-cause mortality as an outcome, which may have placed more emphasis on age and disability as predictors than if overdose mortality was used as the outcome. Even without a risk score, this study reinforces the importance of prescribing naloxone as well as identifying and treating opioid use disorder at the time of an overdose.

Aaron D. Fox, MD

Reference: Guo J, Lo-Ciganic WH, Yang Q, et al. Predicting mortality risk after a hospital or emergency department visit for nonfatal opioid overdose. *J Gen Intern Med*. 2021;36(4):908–915.

PRESCRIPTION DRUGS & PAIN

Risks Associated With Prescription Opioid Dose Decrease or Discontinuation

Data suggest that discontinuation of prescription opioid medication after long-term high-dose opioid therapy may be associated with adverse outcomes, including overdose and suicide. Researchers used Oregon Medicaid data linked with prescription drug monitoring program and vital statistics data to characterize risks associated with opioid prescribing patterns after an episode of high-dose opioid prescribing (N=14,596).

- Subsequent opioid prescribing patterns were: abrupt opioid medication discontinuation without >50% dose reduction (29% of episodes); opioid discontinuation after >50% dose reduction (11%); opioid continuation with >50% dose reduction (44%); and stable or increasing opioid dose (16%).
- Compared with stable or increasing dose, the risk of suicide was higher with discontinuation, whether it was abrupt (adjusted hazard ratio [aHR], 3.63) or with dose reduction (aHR, 4.47).
- Compared with stable or increasing dose, the risk of overdose was lower with abrupt discontinuation or dose reduction and discontinuation (aHR, 0.62 and 0.36, respectively).

Comments: This study provides observational data identifying adverse events associated with different patterns of opioid prescribing after receipt of long-term high-dose opioid therapy. For methodologic reasons, this study did not include patients receiving a truly stable opioid dose. These data highlight the need for risk assessment and mitigation for all patients receiving high-dose opioid medications for chronic pain.

Joseph Merrill, MD, MPH

Reference: Hallvik SE, El Ibrahimi S, Johnston K, et al. Patient outcomes following opioid dose reduction among patients with chronic opioid therapy. *Pain*. 2021;10.1097/j.pain.0000000000002298.

Call for Papers

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