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Alcohol, Other Drugs, and Health: Current Evidence

MARCH–APRIL 2014

INTERVENTIONS & ASSESSMENTS

Gabapentin Can Decrease Heavy Drinking and Increase Abstinence for Patients with Alcohol Dependence

Existing pharmacotherapies for alcohol use disorders have modest efficacy and there are few choices. Researchers tested gabapentin, 900 mg and 1800 mg three times a day, versus placebo, in a randomized trial. The 150 adults had alcohol dependence, were abstinent for at least 3 days, did not use other drugs or have significant comorbidity, and were recruited by advertisements. Primary outcomes were ascertained for 97% of participants.

- At 12 weeks, there was a linear dose effect, and abstinence (17% versus 4%) and no heavy drinking (45% versus 23%) were more common in the 1800 mg dose group, although 95% confidence intervals for these effects overlapped with the lower dose and with effects in the placebo group.
- Findings beyond consumption (such as sleep outcomes) were difficult to

interpret because of substantial loss to follow-up.

Comments: This trial appears to provide proof of the concept that gabapentin can reduce consumption among people with alcohol dependence (corresponding in *DSM-5* to moderate to severe alcohol use disorder). Although many clinicians may be eager to have another treatment option, careful subject selection (not in a general medical setting), the abuse potential of gabapentin, and the overlapping confidence intervals across the study groups suggest that widespread use of the treatment for dependence should await a larger effectiveness trial.

Richard Saitz, MD, MPH

Reference: Mason BJ, Quello S, Goodell V, et al. Gabapentin treatment for alcohol dependence: a randomized clinical trial. *JAMA Intern Med.* 2014;174(1):70–77.

Cannabis Use in Adolescents: Efficacy of a Prevention-Focused Brief Intervention in Primary Care

In the U.S., rates of illicit cannabis use typically increase during adolescence. Primary care visits may be a good opportunity to provide prevention-focused brief interventions (BI) for cannabis use in this population. In this trial, adolescents aged 12–18 (n=714) who reported no lifetime use of cannabis were randomized to a motivational interview-based prevention BI with a therapist, an animated interactive computer-based prevention BI, or to a control group (brochure). Both interventions provided cannabis and alcohol norms for age and gender and explored goals and values, reasons for avoiding use, and risky scenarios (with a focus on refusal skills).

- Compared with controls, participants who received the computer BI report-

ed lower rates of any cannabis use over 12 months (17% versus 24%) and lower frequency of use at 3 and 6 months.

- There were no significant differences between controls and participants who received the therapist BI in rate or frequency of cannabis use.
- With respect to the use of other drugs at 3 months, differences in favor of the interventions were observed between controls and those who received the computer BI or the therapist BI. For alcohol use at 6 months and delinquency at 3 months, differences were observed between controls and those who received the therapist BI.

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Now an
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See page 6

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Cannabis Use in Adolescents: Efficacy of a Prevention-Focused Brief Intervention in Primary Care (continued from page 1)

Comments: This is the first trial of a primary prevention-focused brief intervention in primary care for self-reported illicit cannabis use in adolescents. The effects were small and dissipated over time, but a computer-based BI appears to be a promising approach for prevention. Questions remain about the optimal content of the BI and whether repeating these interventions over time

may increase or prolong their efficacy, and whether intervention effects could be confirmed with biological measures of use.

Nicolas Bertholet, MD, MSc

Reference: Walton MA, Resko S, Barry KL, et al. A randomized controlled trial testing the efficacy of a brief cannabis universal prevention program among adolescents in primary care. *Addiction*. 2014;109(5):786–797.

Single Screening Questions Can be Used to Assess for Substance Dependence in Primary Care

Single screening questions (SSQs) can help identify individuals with unhealthy alcohol or other drug use, but their utility in providing more information about severity is less clear. In this study, 303 primary care patients were asked SSQs followed by the Alcohol Use Disorders Identification Test–Consumption (AUDIT-C), the Drug Abuse Screening Test (DAST-10), and lastly the Composite International Diagnostic Interview (CIDI), to establish a diagnosis of alcohol or other drug dependence. The SSQs were: “How many times in the past year have you had X or more drinks in a day?” and “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”

- The alcohol SSQ had a sensitivity of 88% and specificity of 84% for dependence and performed better than the AUDIT-C.
- The SSQ for other drugs had a sensitivity of 97% and specificity of

79% for dependence; this was similar to the performance of the DAST.

- The optimal cutoffs for dependence were 8 or more times for alcohol and 3 or more times for other drugs in the past year.

Comments: This study shows that SSQs can be an effective tool in primary care for identifying alcohol and drug dependence, not just at-risk use. Like longer screening tools, they can provide an initial severity assessment that should be confirmed with more extensive interviews. One caution, however, is that participants in the study were interviewed anonymously by research staff and these questions may not perform as well when used by clinicians who record the results in medical records.

Darius A. Rastegar, MD

Reference: Saitz R, Cheng D, Allensworth-Davies D, et al. The ability of single screening questions for unhealthy alcohol and other drug use to identify substance dependence in primary care. *J Stud Alcohol Drugs*. 2014;75(1):153–157.

HEALTH OUTCOMES

Most Adults with Heavy Episodic Drinking in the U.S. Have Never Talked with a Health Professional About Their Alcohol Use

The U.S. Preventive Services Task Force and other health organizations recommend screening and brief intervention for unhealthy alcohol use, but it is not known how often patients speak with their health professionals about their consumption. Researchers examined

data from 166,753 participants in the 2011 Behavioral Risk Factor Surveillance System (BRFSS) nationally representative survey of U.S. adults. Specifically, they analyzed responses to the question: “Has a doctor or other health professional ever talked with you about alcohol use?”

(continued page 3)

Most Adults with Heavy Episodic Drinking in the U.S. Have Never Talked with a Health Professional About Their Alcohol Use (continued from page 2)

- 52% of respondents reported current alcohol use and 13% reported heavy episodic drinking.*
- Among all respondents, only about 16% (17% for people with current alcohol use; 14% for abstainers) reported ever discussing alcohol use with a health professional.
- Among people with current heavy episodic drinking, only 25% reported ever discussing alcohol use with a health professional (ranging from 24% for those with 1–2 episodes of heavy episodic drinking in the past month to 35% for those with ≥ 10 episodes in the past month).

* Defined as ≥ 4 standard drinks (women) or ≥ 5 drinks (men) on ≥ 1 occasions in the last 30 days.

Comments: This report suggests that a large majority of U.S. adults—even those with heavy episodic drinking—have never spoken with a health professional about their alcohol use. Although the study was limited by reliance on self-report, uncertainty about whether respondents underwent alcohol screening, and a 50% response rate, it suggests a large implementation gap.

Kevin L. Kraemer, MD, MSc

Reference: McKnight-Eily LR, Liu Y, Brewer RD, et al. Vital signs: communication between health professionals and their patients about alcohol use – 44 states and the District of Columbia, 2011. *MMWR Morb Mortal Wkly Rep.* 2014;63(1):16–22.

Low-Dose Opioids May be Safe in Patients with Severe Chronic Obstructive Pulmonary Disease on Long-Term Oxygen Therapy

Opioid and benzodiazepine medications have the potential to decrease some symptoms in patients with severe chronic obstructive pulmonary disease (COPD), but their safety in this population is unclear. Researchers analyzed national prospective data from 2249 Swedish adults (≥ 45 years of age; 59% women) who initiated long-term oxygen therapy for COPD. Exposure to opioids and benzodiazepines was extracted from a national medication registry and defined as ≥ 1 prescriptions in the 91 days before initiation of oxygen therapy.

- In the 91 days before study entry, 23% of participants had exposure to opioids, 24% to benzodiazepines, and 9% to both.
- 50% of participants died during a median 1.1 years of follow-up.
- Participants who were prescribed higher doses of opioids (>30 mg morphine equivalents in a day) had higher mortality, but those prescribed lower doses (≤ 30 mg) did not.

- Participants exposed to benzodiazepines had higher mortality, but there was no definite dose-response.
- Participants who were prescribed high concurrent doses of opioids and benzodiazepines had higher mortality, but those prescribed low concurrent doses did not.

Comments: This study suggests that low-dose opioids may be safe to prescribe for breathlessness in patients with severe COPD on oxygen therapy. Unfortunately, the indication for opioid and/or benzodiazepine therapy was not obtainable from the data registry. It is not known how many participants were in hospice or terminal care, circumstances under which the prescription of opioids and benzodiazepines for symptom relief and comfort generally outweighs concern about mortality risk.

Kevin L. Kraemer, MD, MSc

Reference: Ekström MP, Bornefalk-Hermansson A, Abernethy AP, Currow DC. Safety of benzodiazepines and opioids in very severe respiratory disease: national prospective study. *BMJ.* 2014;348:g445.

Most Alcohol Use Disorders Remit, but Unhealthy Drinking Often Persists

People with alcohol use disorders (AUDs) commonly remit, but subsequent rates of unhealthy drinking among this population remain uncertain. This prospective cohort study identified 198 adults in the Netherlands with DSM-5 AUDs and followed them for 3 years to examine changes in drinking patterns.

- At baseline, 69% of participants had a mild AUD (2–3 DSM-5 criteria); 17% had a moderate AUD (4–5 criteria); and 25% had a severe AUD (≥ 6 criteria).
- AUD persisted among 30% of the 115 participants assessed at the 3-year follow-up.
- Adults aged 18–24 years at baseline had a 7-fold higher

risk of AUD persistence than those aged 25–44 years. More weekly drinks (odds ratio [OR], 1.03 per drink) and a co-occurring anxiety disorder (OR 4.6) were also associated with increased AUD persistence.

- Among individuals whose AUD remitted at 3 years, 55% drank at lower-risk levels (≤ 7 standard drinks per week for women, ≤ 14 for men), 36% drank above those limits, and 9% abstained.
- The mean change in number of weekly drinks was associated with AUD persistency: +9.6 for those with AUD persistence and -5.5 for those who remitted.

(continued page 4)

Most Alcohol Use Disorders Remit, but Unhealthy Drinking Often Persists (continued from page 3)

Comments: Most adults with AUDs (70%) remit within three years, but over 90% of those in remission continue to drink and over one-third continue to drink at unhealthy levels. Given the ongoing risk of relapse associated with continued drinking, this study suggests a need for ongoing monitoring and maintenance care among patients with a history of an AUD even after 3 years of remission. Primary care physicians should assess alcohol consumption and consequences among

such patients at periodic visits, and deliver brief counseling emphasizing that abstinence remains the safest option.

Peter D. Friedmann, MD

Reference: Tuithof M, Ten Have M, van den Brink W, et al. Predicting persistency of DSM-5 alcohol use disorder and examining drinking patterns of recently remitted individuals: a prospective general population study. *Addiction*. 2013;108(12):2091–2099.

Midlife Alcohol Consumption and Cognitive Decline

Some researchers suggest that lower-risk alcohol use may be associated with better cognitive function, but the impact of alcohol use on cognitive aging trajectories is not well known. This study examined the association between midlife alcohol use (assessed 3 times over a 10-year period) and cognitive decline (3 waves of cognitive assessment in the next 10-year period) in 5054 men and 2099 women (mean age=56), measuring global cognitive function, executive function, and memory.

- Men with an average daily consumption of ≥ 36 g of alcohol showed a significantly faster decline on all cognitive measures compared with those with an average daily consumption of 0.1–19.9 g. The effect size was comparable to 2.4 extra years of decline for global cognitive function, 1.5 for executive function, and 5.7 for memory. There were no differences observed between 10-year abstainers, those who ceased alcohol use within the last 10 years, those with occasional alcohol use, those with an average daily consumption of 20–35.9 g, and those with an average daily consumption of 0.1–19.9 g.

- In women, 10-year abstainers showed a faster decline in global cognitive function and executive function compared with those with an average daily consumption of 0.1–9.9 g. There were no other statistically significant differences between groups.

Note: Analyses were adjusted for age, ethnicity, education, occupation, marital status, smoking history, physical activity level, time since first cognitive evaluation, and interaction between each covariate and time.

Comments: In men, heavy alcohol use in midlife appears to be harmful to cognitive function, and no benefit was found for light to moderate use. Among women, abstainers showed a faster cognitive decline, but the number of abstainers was small and residual confounding is likely. No differences were observed among women with alcohol use, even though some results suggested that those with heavier use might experience a faster cognitive decline.

Nicolas Bertholet, MD, MSc

Reference: Sabia S, Elbaz A, Britton A, et al. Alcohol consumption and cognitive decline in early old age. *Neurology*. 2014;28;82(4):332–339.

Effects of Alcohol Consumption on the Risk of Gout

A recent meta-analysis assessed the effects of alcohol consumption on the risk of developing gout. A total of 12 articles with 17 studies involving 42,924 cases met the inclusion criteria.

- Pooled relative risk (RR) for light alcohol consumption (defined as ≤ 1 drink in a day) versus abstinence or occasional consumption was 1.16.
- Moderate (>1 to <3 drinks in a day) and heavy consumption (≥ 3 drinks in a day) had RRs of 1.58 and 2.64, respectively.
- Essentially all of the studies reviewed showed an increase in risk of gout for heavy drinking.

Comments: Considerable research has shown that alcohol intake, especially heavier drinking, increases serum uric acid levels and the risk of gout. Further, it

has been shown that, among patients with gout, the risk of an attack is higher during the two days after alcohol consumption, especially among patients with gout who do not have good control of their hyperuricemia with allopurinol or other medications. The authors point out that they were unable to evaluate the effects of different beverage types; some previous analyses suggest that the risk is lower for the consumption of wine than it is for other beverages containing alcohol, especially beer. The analytic methodology in this paper was appropriate, and the data suggest that even light drinking is associated with a modest increase in the risk of gout.

R. Curtis Ellison, MD

Reference: Wang M, Jiang X, Wu W, Zhang D. A meta-analysis of alcohol consumption and the risk of gout. *Clin Rheumatol*. 2013;32:1641–1648.

Factors Associated with of Receiving Buprenorphine Treatment for Opioid Use Disorders

Buprenorphine provides an alternative to methadone for patients with opioid use disorders, but few studies have focused on patient determinants of buprenorphine treatment. This retrospective cohort analysis studied data from 4030 individuals with an opioid use disorder who sought treatment in a large U.S. managed-care organization. Patients called a centralized triage program where licensed mental health professionals performed a telephone assessment and subsequently referred them to an appointment with a group-model or contracted-network provider.

- Overall, 17% (n=702) of patients received treatment with buprenorphine.
- The mean age of individuals receiving buprenorphine treatment compared with an alternative therapy was 32 versus 34 years and 42% of both samples were female. Individuals who received treatment with buprenorphine were less likely to be enrolled in a commercial health plan (61% versus 73%) or Medicaid (1.3% versus 2.9%).
- Younger age, residing in a metropolitan area, having Drug Addiction Treatment Act 2000-waivered physicians in the area, and having a point-of-service health

plan were associated with receipt of treatment with buprenorphine.

- Having a co-occurring alcohol or non-opioid drug dependency decreased the likelihood of receiving treatment with buprenorphine by 52% and 98%, respectively. Having a comorbid drug-induced mental disorder or chronic pain diagnosis increased the likelihood of receiving treatment with buprenorphine by 221% and 82%, respectively.

Comments: This study highlights the importance of structural and patient factors associated with receiving treatment with buprenorphine in the U.S. Studies that include other factors such as medication cost, whether waived physicians are actually prescribing treatment, patient preferences, and prior treatment attempts would shed further light on structural and patient-level factors associated with the type of treatment patients receive for opioid use disorders.

Jeanette M. Tetrault, MD

Reference: Murphy SM, Fishman PA, McPherson S, et al. Determinants of buprenorphine treatment for opioid dependence. *J Subst Abuse Treat.* 2014;46(3):315–319.

HIV AND HCV

Patients Value Programs that Integrate Medical and Substance Use Treatment

The FAST PATH program was developed at Boston Medical Center to enhance the treatment of alcohol and other drug dependence. It was based at an infectious disease clinic serving an HIV-infected population and a primary care clinic where patients at risk for HIV were enrolled. Each patient received care from a multidisciplinary team consisting of a physician, a nurse, and an addiction counselor case manager. Services included: medication treatment with buprenorphine for opioid dependence, HIV risk-reduction counseling, individual and group counseling, and referral to additional substance use disorder services. Participants were interviewed 6 months after enrollment and a subset participated in focus groups. Qualitative analytic methods were used to identify key themes.

- Integration of care was generally viewed positively, although some participants expressed reservations about having to stop seeing their regular primary care practitioner in order to access the other services.
- Buprenorphine treatment was an important motivator for many of the patients to participate in this program.

- Program structure received mixed reviews. Some did not like attending mandatory counseling sessions, while others felt that having structure was helpful.
- Counseling and education also received mixed reviews. Some liked the structured learning, while participants almost universally felt that the HIV risk-reduction counseling was not helpful.

Comments: This study provides patient perspectives that largely reinforce the findings of previous studies: 1) integration of substance use disorder services with primary care is feasible and valued by those who need these services; 2) buprenorphine is a well-received tool for the treatment of opioid use disorders; and 3) additional counseling and education are not universally valued.

Darius A. Rastegar, MD

Reference: Drainoni ML, Farrell C, Sorensen-Alawad A, et al. Patient perspectives of an integrated program of medical care and substance use treatment. *AIDS Patient Care STDS.* 2014;28(2):71–81.

Barriers and Facilitators for HCV Treatment Engagement within Integrated Care Delivery Models

Uptake of hepatitis C (HCV) treatment among patients with opioid use disorders tends to be low. This qualitative investigation explored the barriers and facilitators affecting the delivery and uptake of HCV care and treatment within opioid treatment programs. Patients, healthcare professionals, and peer workers from the centers were recruited for in-depth, semi-structured interviews. Patient participants were separated into three groups: those without engagement in HCV care; those who were assessed for HCV care but did not follow through with further care or treatment; and those who were actively engaged in HCV care and treatment.

- Overall, 76 interviews were completed; 56 were with patients and 19 were with staff.
- Differences emerged between the patient groups. Among those who never engaged in HCV care, barriers included the participants' perception that they were physically well and asymptomatic, other life priorities, and concern about side effects of treatment. Patients who engaged in care were motivated by close contacts becoming sick, wanting to live longer, and hearing positive stories of treatment.
- Presence of an engaged clinician and treatment accessibility facilitated patients' engagement in this integrated care model.

Comments: This investigation supports previous reports that integrated care delivery models of HCV treatment within opioid agonist treatment settings improve engagement in HCV care. Increasing education and outreach and the development of more tolerable treatment regimens show promise for improving HCV treatment engagement among patients with opioid use disorder.

Jeanette M. Tetrault, MD

Reference: Treloar C, Rance J, Dore GJ, Grebely J. Barriers and facilitators for assessment and treatment of hepatitis C virus infection in the opioid substitution treatment setting: insights from the ETHOS study. *J Viral Hepat.* 2013 [Epub ahead of print]. doi: 10.1111/jvh.12183.

Correlates of Crack or Injection Drug Use Cessation among Canadians Coinfected with HIV and Hepatitis C

Crack and injection drug use are associated with worse treatment outcomes for both HIV and hepatitis C (HCV) infection and cessation facilitates better HIV and HCV care. Canadian researchers examined data from a cohort of 521 patients with HIV and HCV co-infection as well as crack and injection drug use to find factors associated with substance use cessation. The median follow-up time was 3 years.

- 69% of the cohort ceased drug use during follow-up.
- Having a fixed address (adjusted odds ratio [aOR], 1.73) and smoking crack without injecting (aOR, 3.10) were positively associated with cessation.
- Living alone (aOR, 0.47), current tobacco use (aOR, 0.41), hazardous alcohol consumption (aOR, 0.67), snorting drugs (aOR, 0.52), and cumulative episodes of addiction treatment (aOR, 0.88) were negatively associated with cessation.
- Age, education, duration of HIV infection, and care adherence were not associated with cessation.

Comments: Among patients coinfecting with HIV and HCV, crack and injection drug use cessation is common, but less likely to occur in patients living alone, with unstable housing, or those with the use of multiple substances (e.g., tobacco, alcohol, or other drugs). For patients with multiple treatment attempts, strategies for more effective treatment engagement may improve outcomes.

Alexander Y. Walley, MD, MSc

Reference: Cox J, Maurais E, Hu L, et al. Correlates of drug use cessation among participants in the Canadian HIV-HCV Co-infection Cohort. *Drug Alcohol Depend.* 2014;137:121-128.

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The major journals regularly reviewed for the newsletter include:

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Addiction Science & Clinical Practice
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AIDS
Alcohol
Alcohol & Alcoholism
Alcoologie et Addictologie
Alcoholism: Clinical & Experimental Research
American Journal of Drug & Alcohol Abuse
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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
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Many others periodically reviewed (see www.aodhealth.org).

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Target Audience

The target audience is generalist clinicians, many of whom have received limited training on detecting and treating substance abuse.

Educational Needs Addressed

Primary-care clinicians often miss the diagnosis of alcohol or drug problems and cannot stay abreast of the current substance-abuse literature in the context of a busy practice. Because of the effects of alcohol and drugs on adherence to care plans and physician-patient relationships, patients with alcohol or drug problems may receive suboptimal treatment for other conditions. Further, physicians sometimes perceive alcohol or drug dependence as less treatable than other medical conditions, and thus delegate responsibilities for screening and intervention to others. At the root of the screening and treatment gap is the inadequate provision of substance-abuse education in medical schools and mental-health fields. The newsletter addresses this not only by research dissemination but by providing free downloadable teaching tools for use by educators.

Educational Objectives

At the conclusion of this program, participants will be able to state the latest research findings on alcohol, illicit drugs, and health; incorporate the latest research findings on alcohol, illicit drugs, and health into their clinical practices, when appropriate; and recognize the importance of addressing alcohol and drug problems in primary care settings. In sum, the purpose of the newsletter is to raise the status of alcohol and drug problems in both academic and clinical culture to promote evidence-based screening and treatment and ultimately improve patient care.

Disclosure Statement

Boston University School of Medicine asks all individuals involved in the development and presentation of Continuing Medical Education/Continuing Education (CME/CE) activities to disclose all relationships with commercial interests. This information is disclosed to activity participants. Boston University School of Medicine has procedures to resolve apparent conflicts of interest. In addition, faculty members are asked to disclose when any unapproved use of pharmaceuticals and devices is being discussed.

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Alcohol, Other Drugs, and Health: Current Evidence

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