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Alcohol, Other Drugs, and Health: Current Evidence

SEPTEMBER–OCTOBER 2014

INTERVENTIONS & ASSESSMENTS

Screening for Unhealthy Alcohol Use: Some Patients Don't Want Their Clinician to Know

Routine screening for unhealthy alcohol use is recommended in primary care settings, but the utility of annual repeat screening is uncertain. This study included 18,493 Veterans Administration outpatients who had 1 to 4 prior negative annual in-person AUDIT-C clinical screens and completed both a clinical AUDIT-C screen and an AUDIT-C screen on a confidential mailed survey (that was not shared with the clinician) the following year. Test characteristics of the clinical screen were compared with the mailed survey response.

- Ten percent of those with a prior negative clinical screen reported unhealthy alcohol use on the mailed survey.
- Among those with unhealthy drinking on the mailed screen, agreement of the clinical screen dropped from 41% among those with only 1 prior negative screen, to 33% among those with 2, 26% among those with 3, and 17% among those with 4 prior negative clinical screens.
- Among those without unhealthy drinking on the mailed screen, agreement was consistently high (98%).

Comments: Many of us have seen patients who repeatedly deny unhealthy alcohol use despite evidence to the contrary. This study found that having clinicians repeat the same questions at annual visits did not change these patients' responses. Although the authors focus on the diminishing sensitivity of the AUDIT-C as an annual in-person screen, the responses to the AUDIT-C on the mailed survey suggest that many of these patients have insight about their drinking behavior and are more likely to respond truthfully by mail knowing that information is not shared with their clinician. The reasons these patients withhold truthful responses from their clinicians merits further investigation, because even if we develop alternative ways to detect their unhealthy alcohol use it will be difficult to address their problem in the absence of trust in their providers.

Peter D. Friedmann, MD

Reference: Lapham GT, Rubinsky AD, Williams EC, et al. Decreasing sensitivity of clinical alcohol screening with the AUDIT-C after repeated negative screens in VA clinics. *Drug Alcohol Depend.* 2014;142:209–215.

Ear Acupuncture and Acupressure Modestly Efficacious for Smoking Cessation

Ear acupuncture (EAP) and related treatments are used for smoking cessation but trials have found variable effectiveness, perhaps because treatments and comparisons have also varied widely. Investigators in a systematic review (including Chinese databases) summarized 25 studies of EAP and ear acupressure (EAPR) compared with: sham, placebo, no intervention, body acupuncture, and medical or behavioral treatments. The main report is limited to the 12 most valid comparisons; participant number

ranged from 23 to 396 in each study.

- There were no differences in smoking cessation between EAP/R and other active treatments.
- EAP/R increased cessation compared with inactive treatments. The quit rate in 6-week to 3-month follow-up studies for EAP/R was 16% versus 10% in controls; rates were 12% and 6% respectively at 6 months. Only 1 study

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Ear Acupuncture and Acupressure Modestly Efficacious for Smoking Cessation (continued from page 1)

- assessed 12-month effects (and did show efficacy).
- Adverse effects included sore ears, bruising, facial swelling, headache, dizziness, nausea and vomiting, and tape allergy (EAPR).

Comments: This review highlights how varied interventions and comparisons can be, making determinations about effectiveness difficult. In addition, there was little study of long-term efficacy. The authors also noted that more studies would be useful to compare acu-

puncture and related treatments with pharmacotherapies. These treatments seem to be reasonable options but comparative effectiveness studies would help clinicians and patients choose among the many options to support smoking cessation.

Richard Saitz, MD, MPH

Reference: Di YM, May BH, Zhang AL, et al. A meta-analysis of ear-acupuncture, ear-acupressure and auriculotherapy for cigarette smoking cessation. *Drug Alcohol Depend.* 2014;142:14–23.

Initiating Buprenorphine Treatment During Hospitalization Improves Engagement in Care and Reduces Illicit Opioid Use

Individuals with substance use disorders (SUD) are at risk for medical problems leading to hospitalization. To determine whether hospitalization may provide an opportunity to engage this population in long-term SUD treatment, researchers randomized 139 hospitalized patients with opioid dependence to receive a 5-day buprenorphine taper ($n = 67$) or buprenorphine induction with linkage to an outpatient opioid agonist treatment (OAT) program with buprenorphine ($n = 72$). Participants were interviewed at 1, 3, and 6 months after enrollment; approximately 60% followed up at each interval.

- Fifty-two participants (72%) randomized to linkage entered the OAT program within 6 months, compared with 8 (12%) of those assigned to detoxification.
- At 6-month follow-up, 12 participants (17%) randomized to linkage were enrolled in the OAT program, compared with 2 (3%) randomized to detoxification.
- Compared with controls, participants randomized to linkage were more likely to report no illicit opi-

oid use in the past 30 days at each interval (38% versus 9%) and reported fewer days of illicit opioid use in the past 30 days (mean of 8 versus 14).

Comments: This study demonstrates that initiating buprenorphine treatment during hospitalization improves engagement in care and reduces illicit opioid use, although the effect was modest. Retention was poorer than what is usually observed, probably because this is a high-risk and vulnerable population that was not necessarily seeking care. Implementing programs like this would require the development of systems to identify and link patients with care, as well as incentives for hospitals and outpatient programs. Making outpatient treatment more accessible may achieve the same goal.

Darius A. Rastegar, MD

Reference: Liebschutz JM, Crooks D, Herman D, et al. Buprenorphine treatment for hospitalized, opioid-dependent patients: a randomized clinical trial. *JAMA Intern Med.* 2014;174(8):1369–1376.

Brief Intervention for Unhealthy Alcohol Use in Dental Practice May Benefit People with Heavy Drinking

An annual visit to a dental provider offers an opportunity to screen and counsel adults about alcohol consumption. This controlled trial tested the efficacy of a brief intervention for unhealthy alcohol use in 13 dental practices that were randomized to deliver an intervention or to a control condition. Participants were eligible if they reported weekly risky drinking (>14 drinks in a week for men or >7 drinks in a week for women) OR 1 or more episodes of heavy drinking over the past 30 days (≥ 5 drinks in an occasion for men, ≥ 4 for women). Once included in the study, participants were categorized in three weekly drinking categories: ≤ 6 , 7 to 12, and >13 drinks in a week. The intervention was delivered by dental hygienists trained in motivational interviewing techniques and included normative feedback and specific feedback with regard to the risk of oral cancer. Participants were followed-up at 3 and 6 months. Participants randomized to receive the intervention who did not receive it ($n = 67$) were excluded from the analyses.

- The study found decreases in the number of drinks consumed in a week in both the intervention and control groups at 3 and 6 months. Specifically, in subgroup analyses, this decrease was significant only among people with heavy weekly

drinking (average consumption of ≥ 13 drinks in a week).

- At 6 months, among people with heavy weekly drinking, the intervention group showed continued decrease in consumption, with a 43% decrease from baseline, compared with a 21% decrease from baseline in the control group.
- There were no significant differences between groups among people with “moderate” (7–12 drinks in a week) and light (≤ 6 drinks in a week) weekly drinking at baseline.

Comments: This study provides encouraging results for the efficacy of brief intervention in the dental setting, but some important limitations call for replication. The recruitment of dental practices and participants was lower than expected, leading to limited power and a small number of participants. In addition, the authors did not conduct intention to treat analyses. The small number of invited practices that agreed to participate (13 out of 387) suggests that implementation might be problematic in dental practice.

Nicholas Bertholet, MD, MSc

Reference: Neff JA, Kelley ML, Walters ST, et al. Effectiveness of a screening and brief intervention protocol for heavy drinkers in dental practice: A cluster-randomized trial. *J Health Psychol.* 2014 [Epub ahead of print]. doi: 10.1177/1359105313516660.

HEALTH OUTCOMES

States Allowing Medical Marijuana May Have Lower Mortality From Opioid Analgesic Overdose

Although chronic or severe pain is a common indication for medical marijuana in some states, it is not known whether opioid analgesic mortality has decreased in the 23 states that have adopted medical marijuana laws. Researchers compared opioid analgesic overdose mortality rates from 1999 to 2010 between states with and without medical marijuana laws. They developed multivariable regression models with time-varying implementation of medical marijuana laws as the main independent variable and adjusted for state-specific prescription opioid control policies and unemployment rate.

- Age-adjusted opioid analgesic overdose mortality rates increased from 1999 to 2010 in states with and without medical marijuana laws, but were higher in states with such laws.
- In adjusted analyses, opioid analgesic overdose mortality decreased by 25% in states with medical marijuana laws compared with states without laws. Similar results were seen in analyses restrict-

ed to outcomes of non-suicide overdose deaths and heroin overdose deaths.

- State-specific analyses did not indicate a significant difference in opioid analgesic overdose mortality before and after implementation of medical marijuana laws.

Comments: The results of this analysis are very intriguing, but do not demonstrate a causative association. Many opioid analgesic overdoses occur in individuals who are not receiving treatment for pain. Medical marijuana could potentially lead to decreased opioid overdose mortality by serving as an adjuvant analgesic or anxiolytic/intoxicant when taken instead of prescription and non-prescription opioids. Prospective studies are needed to determine the utility of medical marijuana policies in decreasing harm from opioid analgesics.

Kevin L. Kraemer, MD, MSc

Reference: Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. *JAMA Intern Med.* 2014; 174(10):1668–1673.

Abstinence is Associated with Improved Quality of Life Among People in Recovery from Alcohol Use Disorders

Alcohol use disorder (AUD) treatment programs typically pursue abstinence as a goal. However, reduction in drinking may be a reasonable objective for some people, particularly if it leads to an improvement in quality of life (QOL). Researchers used data from the What Is Recovery? study, a survey of a national sample of US adults who described themselves as being in recovery, examining QOL among 5380 abstinent and non-abstinent participants who considered themselves to be in recovery from AUD.

- The majority of those in recovery were abstaining from alcohol use (90%). Those not abstaining were significantly more likely to be female, younger, unemployed, without formal treatment or Alcoholics Anonymous exposure, without a lifetime DSM-IV dependence diagnosis, and had fewer lifetime DSM-IV dependence symptoms.
- On multivariable analysis, the strongest factors related to non-abstinent recovery were fewer DSM-IV dependence symptoms and younger age. The odds of abstinence increased linearly with the length of

time in recovery.

- Abstainers reported a higher QOL than non-abstainers. On multivariable analysis, the strongest correlates of higher QOL were abstinence, longer length of time in recovery, and being married.

Comments: The main limitation of the study is that it cannot inform us about how an abstinence goal affects the likelihood of achieving recovery since it included no people who are not in recovery. Furthermore, the association between abstinence and QOL may not be causal. Nonetheless, this study suggests that achieving abstinence is probably best for most people with an AUD. Some younger individuals try non-abstinence-based recovery, but most end up transitioning to abstinence over time.

Darius A. Rastegar, MD

Reference: Subbaraman MS, Witbrodt J. Differences between abstinent and non-abstinent individuals in recovery from alcohol use disorders. *Addict Behav.* 2014;39:1730–1735.

Marijuana Use Is Associated with Decreased Abstinence from Heavy Alcohol and Other Drug Use in Individuals with Substance Use Disorders

Although marijuana use is common among people with substance use disorders, it is not known whether and how marijuana use should be managed during alcohol and other drug treatment. In this study, researchers conducted a secondary analysis of prospective data from 535 people with DSM-IV alcohol and/or other drug dependence (mean age 38 years, 73% male, 46% white) in a randomized trial of chronic disease management. Adjusted regression models were used to estimate the association of marijuana use (30-day use assessed at baseline, 3 months, and 6 months) with abstinence from heavy alcohol* and drug use** at the subsequent assessment (3, 6, or 12 months).

- At study entry, 17% of participants had alcohol dependence, 26% had drug dependence, and 57% had both.
- 35%, 34%, and 43% reported abstinence from heavy alcohol use and other drug use at 3, 6, and 12 months.
- In adjusted analyses, marijuana use was associated with a 27% reduced odds of abstinence from heavy alcohol use and other drug use.

- In post hoc analyses, greater frequency of marijuana use was associated with decreased abstinence from heavy alcohol use and other drug use.

* Heavy alcohol use defined as ≥ 4 standard drinks for women and ≥ 5 standard drinks for men on an occasion at least once in prior 30 days.

** Drug use defined as any use of cocaine, amphetamines, heroin, and non-medical use of other opioids.

Comments: The mechanisms for this finding are not known. Marijuana use may compromise decision-making, activate brain pathways also influenced by alcohol and other drugs, and nudge individuals into social settings where alcohol and other drugs are available. Although the study does not prove that marijuana cessation counseling will lead to better alcohol and other drug treatment outcomes, I agree with the authors that marijuana use should be identified and addressed in individuals with alcohol and other drug dependence.

Kevin L. Kraemer, MD, MSc

Reference: Mojarrad M, Samet JH, Cheng DM, et al. Marijuana use and achievement of abstinence from alcohol and other drugs among people with substance dependence: a prospective cohort study. *Drug Alcohol Depend.* 2014;142:91–97.

Buprenorphine Treatment Non-Adherence Associated with Psychiatric Comorbidity and Other Substance Use

In an effort to improve treatment outcomes and minimize adverse events (e.g., accidental overdose, use of other substances), the authors of this study sought to identify factors associated with buprenorphine treatment non-adherence among a sample of patients receiving buprenorphine at a single Veterans Association hospital over a 7-year period. At this site, patients enrolled in buprenorphine treatment are instructed to return to the clinic within 24 hours for a pill count if they are called through the random “call-back” program. Patients were deemed to be compliant if they had a correct pill count at the time of the call-back and a positive urine drug screen (UDS) for buprenorphine/norbuprenorphine.

- Of 209 eligible patients receiving buprenorphine during the study period, only 69 patients were included in the analysis as the other 140 did not have the opportunity to participate in a call-back (e.g., discharged, tapered); 35% (n = 24) of patients were considered non-compliant.

- Factors associated with buprenorphine non-adherence by linear regression analysis were: UDS positive for marijuana or benzodiazepines, smoking cigarettes, and having a psychiatric comorbidity.
- Other factors, including treatment retention, were not associated with medication non-adherence.

Comments: This study suggests that some patients receiving buprenorphine treatment who smoke cigarettes, have psychiatric comorbidity, or use marijuana or benzodiazepines may be at increased risk for treatment non-adherence. However, these data come from a single site and only include only a small proportion of the patients who were engaged in the call-back program; these factors limit generalizability.

Jeanette M. Tetrault, MD

Reference: Fareed A, Eilender P, Ketchen B, et al. Factors affecting noncompliance with buprenorphine maintenance treatment. *J Addict Med.* 2014;8(5):345–350.

Association of Alcohol Intake with the Risk of Different Types of Breast Cancer

To determine associations between alcohol consumption and the risk of breast cancer, this study examined data from a clinical trial of enhanced screening for prostate, lung, colorectal, and ovarian cancer. During a follow-up period averaging about 9 years, a total of 1905 women were diagnosed with invasive breast cancer.

- There was an increase in breast cancer risk associated with alcohol intake for estrogen and progesterone-positive (ER+/PR+) tumors, but not for other histologic types of breast cancer.
- The increased risk was predominantly seen among PR+ cancers (< ½ drink in a week [relative risk (RR), 1.15] and ½ – < 1 drink in a week [RR, 1.25]). There was no evidence of an increase in risk from alcohol consumption for women with ER+/PR- tumors.

Comments: The analyses for this study were well done, although details about alcohol consumption were limited, folate levels were not assessed, the associations might be explained by factors other than alcohol (especially since such low doses might not plausibly increase risk), and the results might not generalize to a lower socioeconomic status population. But the main advance this study provides is the suggestion that alcohol’s effects on the development of breast cancer may differ by type of breast cancer. These findings might lead to a greater understanding of how to better prevent such cancers.

R. Curtis Ellison, MD

Reference: Falk RT, Maas P, Schairer C, et al. Alcohol and risk of breast cancer in postmenopausal women: an analysis of etiological heterogeneity by multiple tumor characteristics. *Am J Epidemiol.* 2014;180(7):705–717.

HIV AND HCV

HIV Medication Adherence Is Not Improved by Prescription Opioid Pain Medication, Worse Among People With Nonmedical Use of Prescription Opioids

Pain, prescribed opioid pain medication, and nonmedical use of prescription opioids use are common in people with HIV infection. Researchers conducted a prospective cohort study among 258 people with HIV to determine whether pain severity was associated with worse anti-retroviral therapy (ART) adherence, whether taking opioids for pain as prescribed was associated with better ART adherence, and the association between nonmedical use of prescription opioids and ART adherence.

- Over the last week, 48% of participants reported severe pain and 34% reported moderate pain; opioid medication for pain was prescribed to 53% of the cohort.
- Nonmedical use of prescription opioids was reported by 21% of participants.
- Severe pain was associated with worse ART adherence

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HIV Medication Adherence Is Not Improved by Prescription Opioid Pain Medication, Worse Among People With Nonmedical Use of Prescription Opioids (continued from page 5)

in unadjusted analyses (odds ratio [OR], 1.37), but not in analyses adjusted for homelessness severity, self-rated health, depression, illicit substance use, and non-medical use of prescription opioids.

- Receiving prescribed opioid medication for pain was not associated with worse adherence in unadjusted (OR, 1.40) or adjusted analyses.
- Nonmedical use of prescription opioids was associated with worse adherence in unadjusted (OR, 1.70) and adjusted (OR, 1.47) analyses.

Comments: This study confirms that nonmedical use of prescription opioids, like other unhealthy substance use, is asso-

ciated with worse ART adherence. It does not confirm that treating pain with opioids improves ART adherence. Determining which patients with HIV infection and pain benefit from prescribed opioids more than they are harmed remains a clinical dilemma that warrants further prospective research into identifying modifiable risk factors and treatment approaches.

Alexander Y. Walley, MD, MSc

Reference: Jeevanjee S, Penko J, Guzman D, et al. Opioid analgesic misuse is associated with incomplete antiretroviral adherence in a cohort of HIV-infected indigent adults in San Francisco. *AIDS Behav.* 2014;18(7):1352–1358.

Motivational Enhancement Therapy Increases Alcohol Abstinence in Patients with HCV and Alcohol Use Disorders

To determine whether motivational enhancement therapy (MET) can reduce alcohol use among patients with hepatitis C (HCV) and alcohol use disorders, this clinical trial randomized 139 of these patients to MET (n = 70), or to general health education sessions (n = 69) for 3 months, with follow-up 3 months later. Study clinicians were mainly psychologists who delivered the MET or health education in 4 30–45 minute sessions. The follow-up rate exceeded 84%; intent to treat analysis was performed.

- MET increased the percentage of days abstinent from baseline (35%) to follow-up (73%), which was significantly greater than the change (35% to 59%) in the control group.
- Drinks per week dropped in both groups and did not differ.
- Secondary outcomes—including heavy drinking days, 30-day abstinence, carbohydrate-deficient transferrin

(CDT), and antiviral treatment initiation—did not differ across the groups.

Comments: MET appeared to increase the proportion of self-reported abstinent days, although objective measures like CDT did not differ, making it possible that reporting effects (e.g., social desirability in the MET group) may explain the findings. It is also unclear whether a 13 percentage-point increase in abstinent days would have a meaningful effect on the natural history of HCV. Alcohol use was a relative contraindication to pegylated interferon and ribavirin treatment for HCV. It remains to be seen whether it will remain a barrier to HCV treatment in the new era of highly efficacious and well-tolerated direct antiviral agents.

Peter D. Friedmann, MD

Reference: Dieperink E, Fuller B, Isenhardt C, et al. Efficacy of motivational enhancement therapy on alcohol use disorders in patients with chronic hepatitis C: a randomized controlled trial. *Addiction.* 2014;109(11):1869–1877.

Among People with HIV, Cigarette Smoking is Associated with Poor Antiretroviral Therapy Adherence and a Detectable Viral Load

Cigarette smoking is highly prevalent among individuals with HIV; studies have suggested a correlation between smoking and suboptimal antiretroviral therapy (ART) adherence, virologic failure independent of adherence, and mortality. Researchers used data from a primary care-based randomized controlled trial of an ART adherence intervention for patients with depression to investigate the effects of smoking on HIV outcomes in terms of health care utilization and alcohol and substance use. Fifty-seven percent of participants identified as currently smoking.

- As in prior studies, smoking was strongly associated with suboptimal ART adherence and having a detectable viral load.

- Patients who smoked attended fewer outpatient medical visits and viewed health as less important in overall quality of life.
- Individuals with unhealthy alcohol use, marijuana, cocaine, and heroin use were more likely to smoke (odds ratios, 2.87–4.75). Participants with and without smoking did not differ with respect to their low-risk use of alcohol, non-medical use of prescription opioids, or sedative use.

Comments: The authors of this study suggest that individuals who smoke may be less concerned with their health and are therefore likely to underutilize primary care, leading to higher inpatient admission rates and mortality. They also hypothesize (continued page 7)

Among People with HIV, Cigarette Smoking is Associated with Poor Antiretroviral Therapy Adherence and a Detectable Viral Load (continued from page 6)

that concurrent illicit substance use could lead to poor ART adherence and ultimately virologic failure. Studies using more advanced epidemiologic techniques are required to establish these causal relationships. Additionally, smoking status may be a marker for other unhealthy substance use; interventions to address smoking and other substances together should be considered. As patients

who smoked underutilized primary care, community-based interventions may be optimal.

Jessica S. Merlin, MD, MBA

Reference: O'Cleirigh C, Valentine SE, Pinkston M, et al. The unique challenges facing HIV-positive patients who smoke cigarettes: HIV viremia, ART adherence, engagement in HIV care, and concurrent substance use. *AIDS Behav.* 2014 [Epub ahead of print]. PMID: 24770984.

HCV-Related Knowledge is Associated with Willingness to Undergo HCV Treatment Among Patients Receiving Methadone

With the rapidly changing landscape of hepatitis C (HCV) treatment, developing an understanding of factors affecting the likelihood of treatment engagement is imperative, especially among patients receiving methadone maintenance treatment. This investigation is part of a larger project testing the feasibility of an HCV care delivery model within an opioid treatment program. Between November 2012 and February 2013, patients receiving methadone maintenance at a single site in New York City (total population: 550–600 patients) were approached to complete a survey. Of these, 320 completed the 30-item survey regarding HCV-related knowledge and willingness to undergo HCV treatment.

- The mean age of respondents was 53 ± 9 years; 60% were male. The mean duration of methadone maintenance treatment was 7 ± 6.7 years; HCV seropositivity was self-reported by 46% of participants.
- Seventy-eight percent of patients expressed willingness to engage in HCV education and treatment.
- Younger patients, those willing to attend an HCV-

related educational activity, and those with higher HCV-related knowledge were more accepting of treatment. Fear of side effects was the most commonly reported barrier to treatment acceptance.

Comments: Patients in this study with a higher level of HCV-related knowledge were more accepting of HCV treatment. These findings underscore the importance of public health efforts to dispel myths about HCV natural history and treatment, especially current interferon-free treatment regimens. Studies investigating factors associated with treatment engagement among patients with HCV seroconfirmation would inform future educational initiatives and will need to take into consideration the ever-changing landscape of HCV treatment options.

Jeanette M. Tetrault, MD

Reference: Zeremski M, Dimova RB, Zavala R, et al. Hepatitis C virus-related knowledge and willingness to receive treatment among patients on methadone maintenance. *J Addict Med.* 2014;8(4):249–257.

FEATURE ARTICLE: ETHICAL CONDUCT OF ALCOHOL AND OTHER DRUG RESEARCH

Ethical Considerations in the Conduct of Alcohol Administration Studies Enrolling People with Alcohol Use Disorders

Sylvia Baedorf Kassis, MPH

Project Manager, Neurological Clinical Research Institute, Department of Neurology, Massachusetts General Hospital, Boston, MA, USA
Instructor, Master of Science in Clinical Investigation (MSCI) Program, Boston University School of Medicine, Division of Graduate Medical Sciences, Boston, MA, USA

Alcohol use disorders are associated with significant health and social consequences; their study has become a national research priority, but not without controversy. The National Institute on Alcohol Abuse and Alcoholism supports research involving the administration of alcohol to human subjects as a critical experimental approach to addressing the etiology, treatment, and prevention of alcohol use disorders.¹ Studies examining the effects of alcohol have the potential to increase understanding of the factors that influence alcohol consumption and unhealthy

use, as well as potentially mitigate these effects.² Some studies, however, may raise ethical concerns, especially when considering the strength of the hypothesis being tested, study design, cohort selected, study risk profile, and validity of the informed consent process. While there is a wide range of research involving the administration of alcohol that could be discussed in relation to the aforementioned topics—including studies of healthy college

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Ethical Considerations in the Conduct of Alcohol Administration Studies Enrolling People with Alcohol Use Disorders (continued from page 7)

students³ and the administration of ethanol to prevent alcohol withdrawal syndrome⁴—the primary focus of this article will be on addressing the ethical issues surrounding one of the more controversial types of alcohol administration studies: enrolling people who engage in heavy drinking and/or those with an alcohol use disorder.

Since the first systematic review of the physiologic effects of alcohol was published in the 1950s, there has been a long tradition of scientific research based on the administration of alcohol to human subjects that has advanced understanding of alcohol's effects in areas such as aggression, information processing, and perceptions of risk-taking.^{5,6} Further, several treatment approaches have been investigated via the administration of alcohol to alcoholics.⁶ Despite this rich history of research experience in the field, and in light of past research abuses, it is not uncommon to find ethics boards taking a more protectionist stance when reviewing alcohol administration studies. Thus, it is helpful when considering such research to anticipate the major ethical questions that may be raised and to be prepared with thoughtful, well-reasoned responses that address the potential concerns.

Ethical Considerations

The importance of the hypothesis being tested

When developing the study idea, a careful review of the literature and a well-articulated rationale for how the proposed study will further understanding of the issue and expand the knowledge base are crucial. The more controversial the subject area, the more important it is for researchers to be able to describe the data that exists, the ways in which they are insufficient, and how the research study posits to fill a gap in the literature. While not at all unique in the research approval process, in the case of alcohol administration studies enrolling people with unhealthy alcohol use, this kind of justification is essential to alleviating the concerns of ethics boards that might question the societal value of the research question under investigation.

The appropriateness of the study design

The process by which the study question will be answered warrants a complete explanation so that the methodology being used to assess the hypothesis is robust and scientifically valid.⁶ The involvement of biostatisticians and other design experts who are familiar with alcohol administration studies is essential to ensuring the soundest methodological approaches are selected and any limitations to the proposed procedures addressed completely.

The enrollment of only the most suitable subject population

Closely related to the validity of the hypothesis and study design is the need for a full justification of the subject pop-

ulation to be recruited into the study. While in research ethics there is always a consideration of the Belmont Principle of Justice in the enrollment of study participants, studies that have the potential to include individuals considered particularly vulnerable and in need of protection frequently undergo a more careful review. To this end, it behooves investigators to develop study inclusion and exclusion criteria that carefully weigh out the potential consequences of research participation. In general, for alcohol administration studies among those with unhealthy alcohol use, the participants should be those not in, or seeking treatment or working on quitting drinking as exposure in those people could thwart their efforts. These participants are likely to continue drinking, no more or no less, after alcohol is administered as part of a study protocol.

A complete assessment of potential risks and benefits

To justify alcohol administration studies in people who may have an alcohol use disorder, the risks to individual participants must be weighed against the potential benefits to themselves and society. While the assumption has been that the administration of alcohol in a study population is detrimental to wellbeing and sobriety, almost all of the studies that have evaluated research participants following exposure to alcohol have failed to identify adverse effects on subsequent drinking behavior and psychosocial adjustment.⁶ So, the question becomes: Can we place individuals at possible risk in order to answer a question that may not benefit them directly, but could impact our understanding of alcohol dependence and/or therapeutic options moving forward?

It should also be noted that some research participants have reported personal benefit from their participation in these studies, including heightened self-esteem, acknowledgement of denial, and access to free treatment. While these are certainly valid feelings, the fact that most research is designed not to benefit the individual, but to answer a specific research question and contribute to generalizable knowledge, must be reiterated to the participant during the consent process and over the course of the study. That noted, studies involving alcohol administration to people with heavy drinking or alcohol use disorders should all offer participants help with their drinking at the conclusion of the study.

A well-conducted, well-documented, and informed consent process

Tucker and Vuchinich (2000) describe obtaining informed consent from people with unhealthy alcohol use within the disease model that generally asserts (erroneously, according to the authors) alcohol use disorders are *prima facie* evidence that an individual's decision-making capacity is impaired. In contrast to the aforementioned view, these authors report that a proper research context that emphasizes environmental influences on behavior, as opposed to stable

(continued page 9)

Ethical Considerations in the Conduct of Alcohol Administration Studies Enrolling People with Alcohol Use Disorders (continued from page 8)

biological or personality dispositions, allows for non-coercive informed consent.⁷ They go on to argue that these views, while well understood in certain segments of the alcohol research community, are not necessarily accepted by other scientists, professionals, and lay persons who may sit on ethics boards.

Thus, when considering alcohol consumption studies enrolling people with heavy drinking and/or alcohol use disorders, ethics boards will likely ask to review a detailed description of the consent process. Further, because some may question the ability of this population to give fully informed consent, they will expect the principal investigator to be able to address how the research team will ensure valid consent is obtained and coercion is avoided.

Conclusion

There is no question that research studies involving the administration of alcohol to human subjects have their place in the study of alcohol use disorders. It is essential, however, before undertaking such a research endeavor, to consider the results of relevant past studies and ensure ethical principles have been adhered to in the study design, selection of participants, assessment of risks and benefits, and in the informed consent process.

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Many others periodically reviewed (see www.aodhealth.org).

Contact Information:

Alcohol, Other Drugs, and Health: Current Evidence
 Boston University School of Medicine/Boston Medical Center
 801 Massachusetts Ave., 2nd floor
 Boston, MA 02118
aodhce@bu.edu



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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.

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Course Faculty

Richard Saitz, MD, MPH, FASAM, FACP

Course Director

Professor of Community Health Sciences and Medicine

Chair, Department of Community Health Sciences

Boston University Schools of Public Health & Medicine

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David A. Fiellin, MD

Professor of Medicine

Yale University School of Medicine

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Nicolas Bertholet, MD, MSc

Department of Medicine and Public Health

Lausanne University, Switzerland

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R. Curtis Ellison, MD

Professor of Medicine and Public Health

Boston University School of Medicine

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Peter D. Friedmann, MD, MPH

Professor of Medicine and Community Health

Warren Alpert Medical School of Brown University

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Kevin L. Kraemer, MD, MSc

Professor of Medicine and Clinical and Translational Science

University of Pittsburgh Schools of Medicine

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Hillary Kunins, MD, MPH, MS

New York City Department of Health and Mental Hygiene, and

Professor of Clinical Medicine, Psychiatry & Behavioral Sciences

Albert Einstein College of Medicine

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Jessica S. Merlin MD, MBA

Assistant Professor

Department of Medicine

Division of Infectious Diseases

Division of Gerontology, Geriatrics, and Palliative Care

University of Alabama at Birmingham

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Darius A. Rastegar, MD

Associate Professor of Medicine

Johns Hopkins School of Medicine

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Jeffrey H. Samet, MD, MA, MPH

Professor of Medicine and Community Health Sciences

Boston University Schools of Medicine and Public Health

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Jeanette M. Tetrault, MD

Assistant Professor of Medicine (General Medicine)

Yale University School of Medicine

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Alexander Y. Walley, MD, MSc

Assistant Professor of Medicine

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Katherine Calver, PhD

Managing Editor

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CME Program Manager

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