Alcohol, Other Drugs, and Health: Current Evidence

JULY–AUGUST 2015

INTERVENTIONS & ASSESSMENTS

Referral to Treatment (the "RT" in "SBIRT") Does Not Lead to Treatment

It is widely assumed that although brief intervention may be inadequate, patients with substance use disorders identified by screening can be helped by referring them to treatment. Researchers did a systematic review and meta-analysis of the efficacy of brief alcohol intervention for increasing alcohol-related care (treatment). Most of the 13 randomized controlled trials in 5 countries (general medical outpatient and hospital and emergency care settings) studied brief advice or motivational interviewing that could have led to referral; 8 studies specified a referral intervention.

- Treatment receipt was not associated with drinking outcomes (examined in only 2 trials).
- Only one study found an effect on receipt of treatment—the intervention was a letter mailed to patients advising them to make an appointment.
- Ten studies had sufficient data for meta-analysis and one was excluded due to high risk of bias; there was no effect on receipt of treatment (relative risk, 1.08, 95% confidence interval 0.91–1.29).

Comments: Clinicians know that advising patients to seek substance use disorder treatment rarely leads to them receiving it. It is a tall order for a brief intervention to take a patient who is not seeking help from screening all the way to entering treatment. Now we have data that RT (the referral to treatment component of screening, brief intervention, and RT [SBIRT]) doesn't work for unhealthy alcohol use. It is possible, though unlikely, that improved referral strategies will be the solution. In general health settings, we need better ways to manage patients with screen-identified unhealthy alcohol use who could benefit from treatment.

Richard Saitz, MD, MPH

Reference: Glass JE, Hamilton AM, Powell BJ, et al. Specialty substance use disorder services following brief alcohol intervention: a meta-analysis of randomized controlled trials. *Addiction*. 2015;110(9):1404–1415.

No Impact of Brief Alcohol Interventions Delivered by Community Pharmacists

Pharmacists can play an important role in promoting health, including delivering alcohol screening and brief intervention. Researchers conducted a randomized controlled trial with follow-up at 3 months in 16 community pharmacies in the UK. Participants were 407 adult pharmacy customers with Alcohol Use Identification Test (AUDIT) scores of 8–19 randomized to a 10-minute brief intervention, or a leaflet-only control condition. The intervention was delivered by the pharmacists, who received a half-day of training. Follow-up was 80% at 3 months.

- The AUDIT score, the study's primary outcome, did not differ between the groups (between-group difference, -0.57 points [95% confidence interval (CI) (-1.59; 0.45)]), and did not change between baseline and follow-up. The proportion of people with an AUDIT score of ≥ 8 at follow-up did not differ between groups either (with control as reference, odds ratio, 0.87 [95% CI 0.50; 1.51]).
- For secondary outcomes:
  - ◊ Even though there was a decrease over time, there was no significant difference between groups on the AUDIT consumption subscale.

(continued page 2)

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No Impact of Brief Alcohol Interventions Delivered by Community Pharmacists (continued from page 1)

- ◊ There was no significant difference on the AUDIT problems subscale between groups.
- ◊ There was a difference between groups on the AUDIT dependence subscale (difference, -0.51 points), but it was in favor of the control group.
- ◊ Compared with the intervention group, general health-related quality of life was worse in the intervention group at follow-up.

Comments: This well-designed study tested an intervention that required minimal training for pharmacists. It found no evidence of efficacy and even found some worse (secondary) outcomes in the intervention group. Future studies should focus on evaluating the feasibility and efficacy of a more complex and more intensive intervention.

Nicolas A. Bertholet, MD, MSc

Reference: Dhital R, Norman I, Whittlesea C, et al. The effectiveness of brief alcohol interventions delivered by community pharmacists: randomized controlled trial. *Addiction*. 2015 [Epub ahead of print]. doi: 10.1111/add.12994.

Is Alcohol Screening, Brief Intervention, and Referral to Treatment More Cost-Effective in the Emergency Department than Primary Care?

Although there are concerns about effective implementation, alcohol screening, brief intervention, and referral to treatment (SBIRT) is recommended in the US by a number of national organizations, including the Substance Abuse and Mental Health Services Administration (SAMHSA). Researchers used data from 9835 participants with positive alcohol screens in the SAMHSA programs to model the cost-effectiveness of alcohol SBIRT delivered in the emergency department (ED) versus primary care (PC). The researchers constructed a decision analytic tree model and used standard methods and a variety of data sources to estimate costs and effectiveness.

- For the ED setting, per patient, SBIRT cost $12.81, decreased social costs by $544.55, and increased utility by 0.013.
- For the PC setting, per patient, SBIRT cost $21.44, decreased social costs by $239.39, and increased utility by 0.008.
- In probabilistic sensitivity analyses, ED was the more cost-effective setting for SBIRT except when the payer is not willing to pay more than $1500 per full utility gained.

Comments: This analysis suggests that social costs decrease and health utility increases with SBIRT in both ED and PC settings. However, I am not sure how to interpret the findings of the ED versus PC comparison in regards to clinical and resource allocation decision-making. Although many patients with unhealthy alcohol use are seen in both ED and PC settings, many others are seen in only one or the other over long time frames. From a resource allocation perspective, a more useful analysis would have been to compare alcohol SBIRT to usual care (no SBIRT), separately, in the 2 clinical settings. In addition, the findings assume efficacy of SBIRT in both settings but systematic reviews find consistent evidence for efficacy in PC (at least for hazardous use), but mixed evidence for the ED.

Kevin L. Kraemer, MD, MSc

Reference: Barbosa C, Cowell A, Bray J, Aldridge A. The cost-effectiveness of alcohol screening, brief intervention, and referral to treatment (SBIRT) in emergency and outpatient medical settings. *J Subst Abuse Treat*. 2015;53:1–8.

Computer-Delivered Alcohol Screening and Brief Intervention Shows Promise Among Pregnant Women

Tablet computers offer the potential to improve alcohol screening and brief intervention (SBI) implementation in busy clinical settings, such as prenatal clinics. Researchers conducted a small pilot randomized trial to assess computer-delivered alcohol SBI in pregnant women, 28 weeks gestation or less, with a positive alcohol screen.* Eligible women were randomized to: 1) a 20-minute, highly interactive, tailored alcohol intervention via tablet computer, followed by 3 tailored mailings over the remainder of pregnancy; or 2) a 20-minute, moderately interactive, control intervention focused on infant nutrition. The outcomes were feasibility and acceptability of the intervention, 90-day abstinence, and healthy birth (combination of live birth, normal birth weight, no neonatal intensive care needed).

- Of 524 pregnant women screened, 48 were enrolled and randomized (81% African American, 54% aged 18–25 years, 25% with *DSM-IV* alcohol abuse or dependence).
- Women in the intervention group were satisfied with the helpfulness, ease of use, and respectfulness of the intervention (scores 4.7–5.0 on a 5-point Likert scale).
- Compared with controls, the intervention group reported more abstinence at 90 days (90% versus 74%) and had a higher rate of healthy births (83% versus 61%), but neither difference was statistically significant.

Comments: This intervention appeared to be very acceptable to pregnant women and has the potential to overcome some of the barriers to alcohol SBI in prenatal settings. However, as the authors discuss, this pilot study was not powered for efficacy. A fuller assessment of the intervention's impact on prenatal alcohol use and birth outcomes will await a larger, adequately powered trial.

Kevin L. Kraemer, MD, MSc

*Positive T-ACE screener (≥ 2 affirmative answers to the following: "Tolerance: How many drinks does it take to make you feel high? Have people annoyed you by criticizing your drinking? Have you ever felt you ought to cut down on your drinking? Eye-opener: Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?"), plus drinking weekly or more often over past 4 weeks of pregnancy, OR ≥ 4 drinks at least monthly during year before pregnancy.

Reference: Ondersma SJ, Beatty JR, Svikis DS, et al. Computer-delivered screening and brief intervention for alcohol use in pregnancy: a pilot randomized trial. *Alcohol Clin Exp Res*. 2015;39(7):1219–1226.

HEALTH OUTCOMES

Continuing Methadone Treatment During Incarceration Results in More Treatment Re-Engagement, Less Opioid Use, and Less Injection Drug Use After Release from Jail or Prison

Most US correctional facilities discontinue opioid agonist treatment for people with opioid use disorder when they are incarcerated. Researchers randomized 283 Rhode Island inmates who wanted to continue methadone throughout incarceration to receive either continued methadone treatment or undergo standard forced withdrawal. The main outcome was re-engagement with a methadone clinic after release. Secondary outcomes included self-reported opioid use, injection drug use, reincarceration, and adverse events. Since withdrawal in RI jail and prison is tapered over several weeks, some patients in the forced withdrawal group were released while still receiving methadone.

- 96% of participants in the continued methadone group returned to a community methadone clinic within 1 month of release, compared with 78% in the withdrawal group. 100% of those receiving methadone at the time of release returned to a methadone clinic within 1 month of release, compared with 48% of those not receiving methadone.
- Participants in the continued methadone group were less likely than those in the forced withdrawal group to have opioid use (8% versus 18%) and injection drug use (17% versus 32%).
- There were no significant differences in re-incarceration or serious adverse events between groups.

Comments: This study provides strong evidence that continuing methadone treatment during incarceration among people with opioid use disorder increases the likelihood of re-engagement with methadone treatment after release, and decreases opioid and injection drug use.

Jamie K. Lim, BSc† and Alexander Y. Walley, MD, MSc

† MD candidate, Boston University School of Medicine

Reference: Rich JD, McKenzie M, Larney S, et al. Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail: a randomised, open-label trial. *Lancet*. 2015;386(9991):350–359.

"Doctor Shoppers" Travel Long Distances, Over State Lines to Fill Overlapping Prescriptions for Attention-Deficit/Hyperactivity Disorder Medications

"Doctor shopping" (obtaining overlapping prescriptions from different prescribers and pharmacies) is one way people obtain stimulants prescribed for attention-deficit/hyperactivity disorder (ADHD) for non-medical use. Prescription monitoring programs (PMP) help guard against this behavior, but they are state-based and generally do not provide information on prescriptions filled in other states. Researchers used a large prescription database (covering 65% of retail dispensing) to identify people who filled prescriptions for medications used to treat ADHD (a number of stimulants and clonidine) at multiple pharmacies.

- A total of 4.4 million individuals filled at least 1 ADHD medication over a yearlong period.
- "Shopping," defined as filling overlapping ADHD prescriptions from more than 1 prescriber and more than 2 pharmacies, occurred in 15,996 subjects (0.45%). "Heavy shopping" (≥ 5 shopping episodes over 18 months) occurred in 2,134 subjects (0.05%).
- While only 4% of non-shoppers had ADHD prescriptions filled in more than 1 state, this behavior was observed in 28% of shoppers and 43% of heavy shoppers. Shoppers travelled a median of 92 miles to fill prescriptions, heavy shoppers 333 miles, and non-shoppers 0.2 miles.
- Shoppers and heavy shoppers were more likely to pay in cash for at least 1 ADHD prescription (27%) than non-shoppers (14%).

Comments: This study provides a glimpse into the lengths that a small subset of the population will go to obtain ADHD medications for non-medical use. State-based PMPs need to share information across state borders, and pharmacies should be wary of individuals travelling long distances and over state lines to fill controlled substance prescriptions. Another potential measure would be to provide prescribers with information from large databases like this one.

Darius A. Rastegar, MD

Reference: Cepeda MS, Fife D, Berwaerts J, et al. Doctor shopping for medications used in the treatment of attention deficit hyperactivity disorder: shoppers often pay cash and cross state lines. *Am J Drug Alcohol Abuse*. 2015;41(3):226–229.

Abuse-Deterrent Formulations: Not All They're Cracked Up To Be?

An abuse-deterrent formulation (ADF) of sustained-release oxycodone hydrochloride (sold as OxyContin) was introduced in 2010 to curtail its widespread non-medical use. Initially, this introduction correlated with a sharp decrease in reported rates of non-medical use, which ultimately plateaued over time. The current analysis of data from the Survey of Key Informants' Patients Program examined the residual rates of non-medical use of reformulated oxycodone hydrochloride. Patients entering drug treatment with a diagnosis of opioid use disorder primarily misusing prescription opioids or heroin were included in the survey study (N=10,784); 2% of the sample (n=244) was interviewed to add context and expand on the structured survey.

- The ADF was associated with a significant reduction in past-month non-medical use of sustained release oxycodone formulations from 45% before introduction to 26% after introduction. This reduction was associated with an increased reports of using other opioids, particularly heroin.
- Up to 4 years after reformulation, 25–30% of participants still endorsed past-month non-medical use of sustained release oxycodone.
- Among 88 interviewed participants who endorsed non-medical use of oxycodone hydrochloride pre- and post-reformulation, 3 themes emerged to explain residual misuse: transition from non-oral routes to oral routes of use; successful efforts to tamper with the ADF mechanism; and exclusive use of the oral route of administration despite the formulation.

Comments: Although ADFs of prescription opioids have the potential to curtail non-medical use, their effectiveness is not absolute and some unintended consequences may emerge, such as migration to heroin use. Efforts to address the prescription opioid epidemic in this country should not focus solely on creation of formulations that may decrease but not eliminate non-medical use, but also ensuring appropriate prescribing of opioid analgesics and a more comprehensive, public health approach to the problem.

Jeanette M. Tetrault, MD

Reference: Cicero TJ and Ellis MS. Abuse-deterrent formulations and the prescription opioid abuse epidemic in the United States: lessons learned from OxyContin. *JAMA Psychiatry*. 2015;72(5):424–430.

Why Are the Harmful Effects of Alcohol Consumption Greater Among People with Low Socioeconomic Status?

This systematic review investigated the relationship between socioeconomic status (SES) and risk of mortality or morbidity for a number of alcohol-attributable conditions. It summarized data from 31 case-control or cohort studies (published in English) relating an overall measure of the effects of low SES (variously defined) to the risk of cancers related to alcohol, as well as to liver disease, hypertension, stroke, epilepsy, cardiac arrhythmias, and pancreatitis.

- Participants with low SES had a greater risk than those with high SES of developing head and neck cancer and stroke associated with alcohol consumption.
- There was a tendency for lower risk of breast cancer among women with low SES, but differences were not significant when adjusted for known confounders.
- Data were insufficient to specify the effects of SES on other alcohol-attributable diseases.

Comments: Theories to explain why people with low SES may experience more adverse effects from alcohol use include: 1) different drinking patterns, with higher rates of heavy episodic drinking among people with low SES; 2) clustering of lifestyle factors associated with poor health; and 3) decreased access to health care. In some studies, even though the reported total alcohol intake of people with low and high SES may be similar, the latter may be more likely to drink "moderate" amounts of alcohol on a regular basis, while people with low SES are more likely to have a few days of heavy consumption per week. There may also be differences according to the type of alcoholic beverage consumed, which was not considered in this study.

R. Curtis Ellison, MD

Reference: Jones L, Bates G, McCoy E, Bellis MA. Relationship between alcohol-attributable disease and socioeconomic status, and the role of alcohol consumption in this relationship: a systematic review and meta-analysis. *BMC Public Health*. 2015;15:400.

HIV AND HCV

Opioid Agonist Treatment Improves Antiretroviral Medication Adherence Among People with Injection Drug Use and HIV

Injection drug use (IDU) is one of the major risk factors for HIV infection. Antiretroviral therapy (ART) reduces HIV morbidity, mortality, and transmission, but requires lifelong adherence to daily medications. Opioid agonist treatment (OAT) with methadone or buprenorphine may help improve adherence to HIV treatment. Researchers used a population-based database in British Columbia, Canada to investigate the association of OAT with ART adherence among a cohort of individuals with HIV and a history of IDU.

- Of 12,349 participants in the cohort, 2928 (24%) had a history of IDU; 1852 were included in the study with 39,375 person-months of follow up.
- OAT was associated with an unadjusted odds ratio (OR) of 1.54 for ≥ 95% ART medication refill adherence. The adjusted OR was 1.96.

Comments: This study confirms prior observations of a positive effect of OAT on ART adherence. Other studies have shown that linking OAT with medical care facilitates both. There is an opportunity to improve HIV (and substance use disorder) outcomes by integrating OAT into HIV treatment; this should become a standard of care.

Darius A. Rastegar, MD

Reference: Nosyk B, Min JE, Colley G, et al. The causal effect of opioid substitution treatment on HAART medication refill adherence. *AIDS*. 2015;29(8):965–973.

HIV-infected Patients Receiving Methadone are More Likely to Adhere to Antiretroviral Treatment when Provided Higher Methadone Doses

Methadone maintenance treatment has been associated with improved adherence to antiretroviral therapy (ART) for HIV-infected individuals with opioid use disorder. Researchers tracked a cohort of 297 HIV-infected individuals receiving methadone maintenance to investigate the dose-response relationship between methadone dose and ART adherence. The primary exposure was high-dose methadone (≥ 100 mg) and the primary outcome was optimal (≥ 95%) ART adherence. ART adherence rates were determined based on pharmacy refill data.

- Patients receiving ≥ 100 mg/day of methadone had increased rates of optimal ART adherence (adjusted odd ratio [aOR], 1.38), compared with those receiving less.

(continued page 6)

HIV-Infected Patients Receiving Methadone are More Likely to Adhere to Antiretroviral Treatment when Provided Higher Methadone Doses

(continued from page 5)

- When stratified by methadone dose, there was an association between increasing dose and the proportion of optimally adherent participants (aOR, 1.06 per 20 mg/day increase).

Comments: This study demonstrates a dose-response relationship between methadone dose and ART adherence among patients receiving methadone. To improve outcomes in the care of HIV-infected individuals with opioid use disorder, providers should ensure adequate and effective methadone dosing.

Jamie K. Lim, BSc† and Alexander Y. Walley, MD, MSc
† MD candidate, Boston University School of Medicine

Reference: Lappalainen L, Nolan S, Dobrer S, et al. Dose-response relationship between methadone dose and adherence to antiretroviral therapy among HIV-positive persons who use illicit opioids. *Addiction*. 2015;110(8):1330–1339.

Brief Intervention May Reduce Consumption in some HIV-Infected Women with Hazardous Alcohol Use

Hazardous alcohol use occurs in as many as a quarter of HIV-infected women, and is associated with suboptimal antiretroviral therapy (ART) adherence and high-risk sexual behaviors. Researchers enrolled 148 women with hazardous alcohol use* from an HIV primary care clinic. Participants were randomized to receive either 2 sessions of alcohol brief intervention (BI) 1 month apart, or usual clinic care.

- Over the prior 90 days, the BI group had an average of 34 drinking days, 25 days of heavy episodic drinking, and a mean number of 10 drinks per drinking day. Numbers for the control group were similar.
- BI was associated with a decrease in the number of drinking days, but only for women whose number of drinking days fell between the 28th and 90th percentiles. Similar results were seen for the number of heavy drinking days. BI was also associated with a decrease in unprotected vaginal sex, compared with controls.
- The BI group did not experience a reduction in the mean number of drinks per drinking day, or in secondary outcomes including liver enzymes, ART adherence, virologic suppression, and appointment attendance.

* Defined as an average of ≥ 8 drinks in a week or ≥ 4 drinks on an occasion at least twice in the last 6 months, or a TWEAK score of ≥ 2 (5-question tool: Tolerance, Worried, Eye-opener, Amnesia, Cut down).

Comments: This intervention was not effective for the participants who drank the most, for those who drank least, or for clinical outcomes (e.g. virological suppression) despite the fact that it was adapted from a previously-published intervention and included content specific to HIV-infected women, adherence, and sexual risk. It did appear, however to reduce unprotected sex. This study is limited, as are many, by the reliance on self-report to determine alcohol consumption—participants in the intervention may have been more likely than those in the control group to report a reduction in alcohol consumption. Clearly we need to know more about how best to address unhealthy alcohol use in women with HIV infection.

Jessica S. Merlin, MD, MBA

Reference: Chander G, Hutton HE, Lau B, et al. Brief intervention decreases drinking frequency in HIV-infected, heavy drinking women: results of a randomized controlled trial. *J Acquir Immune Defic Syndr*. 2015 [Epub ahead of print]. PMID: 25967270.

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The major journals regularly reviewed for the newsletter include:

Addiction
Addiction Science & Clinical Practice
Addictive Behaviors
AIDS
Alcohol
Alcohol & Alcoholism
Alcoholism: Clinical & Experimental Research
American Journal of Drug & Alcohol Abuse
American Journal of Epidemiology
American Journal of Medicine
American Journal of Preventive Medicine
American Journal of Psychiatry
American Journal of Public Health
American Journal on Addictions
Annals of Internal Medicine
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Hepatology
Journal of Addiction Medicine
Journal of Addictive Diseases
Journal of AIDS
Journal of Behavioral Health Services & Research
Journal of General Internal Medicine
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
Preventive Medicine
Psychiatric Services
Substance Abuse
Substance Use & Misuse

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

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HCV Partly Explains the Increased Mortality among HIV-Infected Individuals with Injection Drug Use as an HIV Transmission Factor

HIV-infected patients with injection drug use (IDU) as a transmission factor have increased mortality even with access to antiretroviral treatment (ART). The purpose of this study was to determine whether the association between IDU as a transmission factor and mortality in this population was explained by increased prevalence of hepatitis C infection (HCV). The authors analyzed data from 16 centers in the Antiretroviral Therapy Cohort Collaboration, an international collaboration of cohort studies examining HIV-infected individuals initiating ART. Of 32,703 patients, 3374 reported IDU, 4630 had evidence of HCV infection, and 1116 died.

- There was an increased risk of mortality among patients reporting IDU as a transmission factor compared with those not (adjusted hazard ratio [aHR], 2.71), and among patients with HCV compared with those without (aHR, 2.65).
- The effect of IDU was attenuated after adjustment for HCV (aHR, 1.57), while the converse (attenuation of HCV effect by IDU) was less substantial (aHR, 2.04).
- CNS and respiratory mortality was less attenuated and violent mortality was not attenuated with adjustment for HCV.

Comments: HCV infection explains some of the association between history of IDU transmission risk and mortality in an analysis of a large cohort of HIV-infected individuals initiating ART. This study does not include measures of active IDU and does not include a measure of overdose-specific mortality. This is a timely discussion as the landscape of HCV treatment is shifting to more effective, and costly, direct-acting antivirals that may have the potential to impact the observed mortality difference.

Jeanette M. Tetrault, MD

Reference: May MT, Justice AC, Birnie K, et al. Injection drug use and hepatitis C as risk factors for mortality in HIV-infected individuals: the Antiretroviral Therapy Cohort Collaboration. *J Acquir Immune Defic Syndr*. 2015;69(3):348–354.

Continuing Medical Education (CME) Accreditation Statements

Sponsored by Boston University School of Medicine

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Boston University School of Medicine and Boston Medical Center. Boston University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians. Boston University School of Medicine designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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

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