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NOVEMBER–DECEMBER 2012

INTERVENTIONS & ASSESSMENTS

Implementation of Alcohol Screening and Brief Intervention Leads to Less Reduction in Risky Use: A Cautionary Tale

Controlled clinical trials have found efficacy for alcohol screening and brief intervention (ASBI), but dissemination of the practice has been difficult. Researchers in the Netherlands conducted a randomized trial of ASBI implementation in 70 general practices including 6318 patients, 712 of whom had nondependent risky drinking.* Intervention-group practices received ASBI training, reminder cards, practice guidelines, a feedback report, facilitated linkage with a local addiction treatment program, outreach visits, mailings and posters for patients, and personalized feedback for patients. Control-group practices were mailed practice guidelines and patient letters only.

- At 2 years, patients in intervention practices were significantly less likely than patients in control practices to be abstinent or to have low-risk drinking (Alcohol Use Disorders Identification

*Alcohol Use Disorders Identification Test scores of 8–19.

Test [AUDIT] scores <8) (36% versus 47%, respectively). They were also significantly more likely to be drinking hazardous amounts (AUDIT scores 8–15) (59% versus 47%, respectively).

Comments: Despite efficacy in controlled trials, few clinical practices have implemented ASBI. As a result, large-scale implementation efforts have been undertaken. This trial of a substantial effort to implement ASBI (much more substantial than is likely widely feasible) found that patients in practices exposed to such efforts actually had increased, not decreased, alcohol risks. It appears that getting ASBI to work in the real world remains elusive, and results of such efforts may not be benign.

Richard Saitz MD, MPH

Reference: Hilbink M, Voerman G, van Beurden I, et al. A randomized controlled trial of a tailored primary care program to reverse excessive alcohol consumption. *J Am Board Fam Med.* 2012;25(5):712–722.

Acamprosate Was Not Effective for Treating Alcohol Dependence in a Family Medicine Setting

Acamprosate can support abstinence in alcohol-dependent patients; however, most prior research was conducted in specialty settings, and its efficacy in primary care remains uncertain. In this 12-week study, researchers randomized 100 recently detoxified alcohol-dependent adults in 2 family medicine settings to 666 mg acamprosate 3 times daily or to placebo. The age range of participants was 21–65 years; 62% were men, and 91% were white. Each arm received brief behavioral interventions for 5 sessions (30 minutes in the first session, 20 minutes in each remaining session) delivered via workbook

by the family physician. The outcomes were percent days abstinent and percent heavy drinking days* assessed by validated calendar-based interviews at weeks 0, 2, 6, and 12.

- Medication adherence was high.
- Both study arms reported 21% days abstinent at week 0 and about 55% days abstinent at weeks 2, 6, and 12. Similarly, study arms did not differ in percent heavy drinking days during follow-up.

*Heavy drinking days defined in this study as ≥ 5 drinks per day for men and ≥ 4 per day for women.

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Acamprosate for Dependence Not Effective in Family Care (continued from page 1)

- Participants with an initial goal of abstinence did better on both outcomes than those with an initial goal of alcohol reduction, but there was no difference in the effect of abstinence by study arm.
- Diarrhea was the main adverse effect of acamprosate.

Comments: Acamprosate was ineffective in these family medicine settings. The finding of no significant difference is not likely due to inadequate power, because the percent days abstinent in each study arm were nearly identical. Because 90% of participants were recruited through advertising, it was not clear how many had a prior relationship with the clinic or the physician who delivered the behav-

ioral intervention, which may have affected the outcome. Acamprosate trials in the US have been largely negative, whereas European studies have been positive; this is another negative US trial. Getting acamprosate to have efficacy in any setting in the US may have more to do with how patients undergo detoxification or with other unknown patient selection factors.

Kevin L. Kraemer, MD, MSc

Reference: Berger L, Fisher M, Brondino M, et al. Efficacy of acamprosate for alcohol dependence in a family medicine setting in the United States: a randomized, double-blind, placebo-controlled study. *Alcohol Clin Exp Res*. November 7, 2012 [E-pub ahead of print]. doi: 10.1111/acer.12010

For People Who Drink Heavily, Alcohol Consumption Decreases after a Health-Care Visit without Brief Intervention

In many studies of alcohol brief intervention (BI), the effects of BI delivered at what are thought to be “teachable moments” are dwarfed by the decreases in consumption seen in both intervention and control groups. Investigators followed general-practice outpatients and general hospital inpatients identified by screening as having unhealthy alcohol use* for 12 months. These patients were BI randomized trial participants who were in the control groups and thus did not receive the intervention.

- At 1 year, half (or fewer) were either abstinent or drinking <30 g alcohol per day for men or <20 g per day for women. Lower risk consumption was more common in inpatients (50%) than in outpatients (26%).
- Receipt of alcohol-related treatment or advice during the year (18–29% received some form of treatment) was not associated with changes in consumption at follow-up.

Comments: The authors summarize their

*Drinking risky amounts (20/30 g alcohol daily) or meeting DSM-IV criteria for abuse or dependence.

results succinctly: “treatment is a window of opportunity for self-change.” Unhealthy alcohol use improves after a health-care visit—which may be a “learnable moment,” even when there has been no alcohol counseling. This makes sense, because patients themselves may connect their visit with their alcohol use and change their drinking as a result. It is also possible that patients changed as a result of screening or coincidentally. Regardless of the cause, the observed improvement means as many as half of patients won’t benefit from BI, since they will improve on their own. It also suggests that research should identify which patients are less likely to change spontaneously, and thus might benefit from counseling. A “learnable moment” may have even greater impact than a “teachable moment.”

Richard Saitz MD, MPH

Reference: Bischof G, Freyer-Adam J, Meyer C, et al. Changes in drinking behavior among control group participants in early intervention studies targeting unhealthy alcohol use recruited in general hospitals and general practices. *Drug Alcohol Depend*. 2012;125(1–2):81–88.

Effectiveness and Feasibility of Extended-Release Naltrexone plus Medical Management in Primary Care: 15-Month Results

Extended-release naltrexone (XR-NTX) is safe and effective for the treatment of alcohol dependence and offers treatment-adherence advantages given its depot formation. The feasibility of implementing XR-NTX plus medical management into primary care practices was established in a previous 12-week observational study (http://www.bu.edu/aodhealth/issues/issue_may10/tetrault_lee.html), but data regarding feasibility and efficacy past 24 weeks of treatment have been lacking. In this study, the authors investigated treatment retention, adverse-event rates, and enrollment in ancillary alcohol treatment (including 12-step programs) among patients enrolled in the extension phase of the initial study. Of 65 patients enrolled, 40 completed the first 12 weeks of treatment, and 19 continued on to the extension phase (median duration of treatment, 38 weeks [range, 16–72 weeks]; median total XR-NTX injections, 8).

- No study-related adverse events were noted in the extension phase.

- Ancillary alcohol treatment was endorsed by 11 of the 19 patients (58%).
- Past 30-day self-reported drinking was 0.2 drinks per day versus 6 drinks per day at baseline; the rate of abstinent days was 82% versus 38%, and the rate of heavy drinking days was 11% versus 61%.

Comments: Long-term combination treatment with XR-NTX and medical management is feasible in primary care practice. Although efficacy is suggested in this observational single-arm study, experimental studies are needed to lend further support to implementation of XR-NTX in primary care practice.

Jeanette M. Tetrault, MD

Reference: Lee JD, Grossman E, Huben L, et al. Extended-release naltrexone plus medical management alcohol treatment in primary care: findings at 15 months. *J Subst Abuse Treat.* 2012;43(4):458–462.

Meta-Analysis: Behavioral Counseling Interventions for Nondependent Unhealthy Alcohol Use Decrease Drinking in Adult Primary Care Patients

To help the US Preventive Services Task Force update its guidelines, researchers searched for English-language controlled trials published between 1985 and 2012 that evaluated behavioral counseling interventions for unhealthy alcohol use identified by screening in primary care settings. Twenty-three trials met eligibility criteria. Interventions were usually multicontact and included brief advice/feedback, motivational interviews, and cognitive strategies delivered in very brief, brief, or extended formats.

- Compared with controls, adults receiving behavioral counseling interventions:
 - decreased their weekly alcohol consumption more (mean difference, 3.6 fewer drinks per week), were more likely to drink lower risk amounts (mean risk difference, 11%), and were less likely to report heavy drinking* episodes (mean risk difference, 12%) at 12 months. Brief (<15 minutes each) multicontact interventions had the best supporting evidence.
 - had fewer hospital inpatient days (low strength of evidence) but no difference in emergency department (ED) visits, legal problems, mortality, or quality of life.

*Defined across studies as ≥ 5 drinks per occasion for men and ≥ 4 drinks for women.

- Compared with controls, young adults/college students receiving behavioral counseling interventions decreased their consumption and had fewer motor vehicle crashes, ED visits, and academic consequences.
- Evidence was not sufficient to make conclusions about other groups (e.g., pregnant women, adolescents, older adults).

Comments: This well-done systematic review supports behavioral counseling interventions for primary care patients who screen positive for nondependent unhealthy alcohol use. The main observed benefit was for intermediate outcomes such as alcohol consumption. However, response to initial or repeated interventions over time could lead to reductions in “hard” outcomes such as mortality, alcohol-related trauma, and liver disease. The results do not apply to patients with alcohol dependence, since most of the included trials excluded such patients.

Kevin L. Kraemer, MD, MSc

Reference: Jonas DE, Garbutt JC, Amick HR, et al. Behavioral counseling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2012; 157(9):645–654.

Systematic Review: Adding Psychosocial Support to Routine Counseling in Opioid Agonist Treatment Does Not Provide Additional Benefits

Opioid agonist treatment (OAT) in the form of methadone or buprenorphine has become a standard treatment for opioid dependence and has been shown to be effective. Evidence of the effectiveness of additional psychosocial in-

terventions is less clear. This systematic review, which included 35 studies with 4319 participants, looked at 13

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Psychosocial Support: No Additional Benefit to Patients Receiving OAT (continued from page 3)

different psychosocial interventions combined with OAT. Most of the studies (24) looked at behavioral interventions; 7 assessed counseling interventions. When comparing the effectiveness of OAT plus psychosocial interventions with OAT alone:

- investigators found no significant difference in treatment retention (relative risk [RR], 1.02), opioid abstinence during treatment (RR, 1.19), or any of the following measures: compliance, psychiatric symptoms, depression, or abstinence at the end of treatment.

Comments: Although this review failed to find benefit from the addition of specific psychosocial interventions to OAT,

it is important to keep in mind that most of these studies were performed in methadone maintenance programs where standard treatment included routine counseling. Moreover, studies evaluated a wide range of treatments with different goals; it is possible some of the psychosocial interventions may have benefited patients in other ways than those assessed in this meta-analysis.

Darius A. Rastegar, MD

Reference: Amato L, Minozzi S, Davoli M, et al. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. *Cochrane Database Syst Rev.* 2011;(10):CD004147.

Brief Intervention for Patients Admitted to Emergency Services for Acute Alcohol Intoxication (AAI) May Decrease AAI Readmission Rates

Emergency department (ED) visits for acute alcohol intoxication (AAI) are common. Using a pre-post study design, the authors compared 1-year AAI readmission rates among patients who received intensive care management* (ICM) in the ED (n=106) and those who received standard care (n=97).** The intervention component of ICM lasted 10–15 minutes and was carried out twice within a 30-minute interval, with the second intervention including referral to treatment. Subjects were enrolled 24 hours a day over a 1-month period. Eighty percent were identified as needing emergency treatment by ambulance personnel or police. There were no differences between ICM and standard-care control groups in baseline GGT and CDT levels.

- In the ICM group, 71% of subjects received the brief intervention, and 59% were referred to outpatient treatment or specialized hospitalization.

*Delivery of staff training and setup of ICM care protocols in the ED plus a behavioral intervention based on FRAMES (Feedback, Responsibility, Advice, Menu, Empathy, Self-efficacy) provided by a specialized addiction-medicine liaison.

**Medical care for AAI or withdrawal only.

- In the control group, 43% of subjects were referred to outpatient treatment or specialized hospitalization.
- The AAI readmission rate was lower in the ICM group than in the control group (32% versus 59%).
- Assignment to outpatient treatment or hospitalization was associated with less readmission for AAI in the ICM group but not in the control group.

Comments: This naturalistic study offers evidence that a liaison team specially trained to implement alcohol brief intervention and treatment within the ED may decrease readmission among patients presenting with acute intoxication. Randomized trials are needed to confirm efficacy. Intoxicated patients remained hospitalized until the next morning in this study, since interventions were conducted between 8 a.m. and 11 a.m. This may seem an encumbrance for ED staff but has the potential to positively impact readmissions—an even more significant burden for the ED.

Nicolas Bertholet, MD

Reference: Schwan R, Di Patritio P, Albuissou E, et al. Usefulness of brief intervention for patients admitted to emergency services for acute alcohol intoxication. *Eur J Emerg Med.* 2012;19(6):384–388.

HEALTH OUTCOMES

Is “Moderate” Alcohol Consumption Associated with an Increased Risk of Atrial Fibrillation in Patients with Cardiovascular Disease?

Previous research in the general population has suggested an increased risk of atrial fibrillation (AF) in people who drink heavily. Results on the association with lower drinking amounts have not been consistent. This study analyzed the association between alcohol consumption and AF in subjects diagnosed with coronary heart disease, stroke, diabetes, or other manifestations of cardiovascular disease (CVD) based on patient data from 2 large antihypertensive

-drug treatment trials (N=30,433). Median follow-up was 56 months.

- Subjects who drank “moderate” amounts* had a higher (continued on page 5)

*Defined in this study as 1–21 drinks per week for men and 1–14 drinks per week for women (1 drink = 12–15 g alcohol).

“Moderate” Drinking and Atrial Fibrillation Risk (continued from page 4)

risk of AF than those who drank light amounts,** although the risk of death during follow-up was lower for those who drank moderately (9.9%) compared with those who drank lightly (12.5%).

- Excluding subjects with heavy episodic drinking (>5 drinks per single occasion or per day on average), the risk of AF was 13% higher in subjects who drank moderately compared with those who drank lightly.

Comments: Although the multiple analyses in this paper were done appropriately, the wide range chosen for moderate drinking, which exceeds US guidelines, likely leads to an overestimate of AF risk associated with moderate drinking. Another concern is the possibility of “collider bias” in

**Less than 1 drink per week (reference category).

the estimates; i.e., given that moderate alcohol consumption is associated with a lower risk of both CVD and diabetes, it can be assumed that subjects in this study who developed CVD despite consuming alcohol had other risk factors that overcame any potential protection afforded by drinking. Unless adjusted for, these other risk factors could affect the subsequent course of subjects following the onset of CVD, including the development of AF. Thus, the association between “moderate” alcohol consumption and atrial fibrillation after someone has developed CVD remains unclear.

R. Curtis Ellison, MD

Reference: Liang Y, Mente A, Yusuf S, et al. Alcohol consumption and the risk of incident atrial fibrillation among people with cardiovascular disease. *CMAJ*. 2012;184(16):E857–E866.

HIV & HCV

HIV Infection Incidence Is Reduced 54% in People with Injection Drug Use Who Receive Opioid Agonist Treatment

Cohort studies have demonstrated that opioid-dependent people with injection drug use who receive opioid agonist treatment (OAT) have lower HIV infection rates than those not receiving OAT. Researchers conducted a meta-analysis to quantify the association between OAT receipt and HIV incidence. Data from 12 published and 3 unpublished prospective studies that measured HIV incidence and OAT exposure were included in the study, 9 of which were sufficiently similar to include in the main meta-analysis. Overall, 819 incident HIV infections over 23,608 person years were included.

- Opioid agonist treatment was associated with a 54% reduction in HIV incidence (rate ratio [RR], 0.46).
- The benefit was consistent, although it diminished when the meta-analysis was limited to 6 studies that allowed adjustment for confounders (RR, 0.60) or to 5 studies that had less bias (RR, 0.61).

- The benefit did not vary by geographical region, study site, provision of incentives, gender, or ethnicity.
- In the 4 studies that measured it, detoxification with methadone was associated with an increased risk of HIV transmission compared with no treatment or OAT (RR, 1.54).

Comments: This meta-analysis provides strong support for OAT as a key public health tool to reduce HIV incidence in people with opioid dependence who inject drugs. People undergoing methadone detoxification should be offered HIV risk-reduction interventions to address higher HIV incidence.

Alexander Y. Walley, MD, MSc

Reference: MacArthur GJ, Minozzi S, Martin N, et al. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. *BMJ*. 2012;345:e5945.

Injectable Extended-Release Naltrexone Is Not Associated with Liver Enzyme Elevation in Patients with HCV, HIV

Injectable extended-release naltrexone (XR-NTX) is approved for treatment of opioid and alcohol dependence. Patients with drug and alcohol problems are more likely to have HCV and/or HIV infection, which may place them at greater risk for XR-NTX hepatotoxicity. This secondary analysis of data from a randomized controlled trial assessed the safety and efficacy of XR-NTX for treatment of opioid dependence in a sample of Russian adults without decompensated liver disease* (N=250). The prevalence of HCV and HIV in the sample was high (89% and 42%,

respectively). Participants (88% men, 100% white) were followed for 6 months and underwent liver chemistry tests for ALT, AST, and GGT at monthly visits. Longitudinal analysis of the frequency with which patients had liver enzyme elevations >3 times the upper limit of normal (ULN) was conducted using generalized estimating equations. At 6 months,

- ALT was elevated >3 times ULN in 20% of XR-NTX patients versus 13% of placebo patients (p=0.88).

*Patients were excluded if they had evidence of ascites, jaundice, encephalopathy, esophageal varices, or baseline AST/ALT >3 times ULN.

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Extended-Release Naltrexone Is Not Associated with Liver-Enzyme Elevation (continued from page 5)

- AST was elevated in 14% of XR-NTX patients versus 11% of placebo patients ($p=0.71$).
- GGT was elevated in 23% of XR-NTX patients versus 21% of placebo patients ($p=0.81$).
- elevations were not more common in patients with HIV than in those with HCV.

Comments: In this sample of opioid-dependent patients—the majority with HCV infection and more than a third co-infected with HIV—treatment with XR-NTX was not significantly associated with elevation of liver enzymes. A limitation is the modest sample size, which should lead to cautious interpretation of results (particularly since slightly

more elevations were observed in the XR-NTX group for each liver enzyme). Also, there was no comparison of the effect of XR-NTX on liver enzymes among participants with and without HCV. Nevertheless, results suggest XR-NTX is not strongly associated with hepatotoxicity, even among persons with HCV and HIV.

Judith Tsui, MD, MPH

Reference: Mitchell MC, Memisoglu A, Silverman BL. Hepatic safety of injectable extended-release naltrexone in patients with chronic hepatitis C and HIV infection. *J Stud Alcohol Drugs.* 2012;73(6):991–997.

Alcohol Use Does Not Affect CD4 T-cell Count Response after Antiretroviral Therapy Initiation

Alcohol can cause immune suppression in individuals with HIV. Among HIV-infected individuals not receiving antiretroviral therapy (ART), heavy alcohol use lowers CD4 T-cell counts compared with no alcohol use. Using data from the Johns Hopkins Clinical Cohort, the authors sought to determine the longitudinal effect of quantity and frequency of alcohol use on CD4 T-cell response to ART, the differential effect of alcohol on CD4 T-cell count response in people who achieved viral suppression compared with those who did not, and the effect of alcohol on immune function, stratified by sex. Out of roughly 6000 patients enrolled in the cohort, 1107 participants reported alcohol use via computer-assisted self-interview within 6 months of ART initiation, had their CD4 T-cells measured, and were not virologically suppressed at the time of the interview. Sixty percent had a baseline CD4 T-cell count <200 cells/mm³. Among patients who used alcohol ($n=440$), the median number of drinks per day was 2 (interquartile range, 1–4).

- No differences were noted in CD4 T-cell counts among patients who used alcohol, irrespective of drinking quantity or frequency, gender, or virologic suppression.
- Among those without suppressed viral load, there was no change in CD4 T-cell count by quantity or frequency of alcohol use.

Comments: These data suggest the benefits of ART initiation outweigh potential risks of ongoing alcohol use in HIV-infected men and women who meet criteria for HIV treatment. Validation of these findings in other patient samples will lend further support to ART treatment initiation despite alcohol use.

Jeanette M. Tetrault MD

Reference: Kowalski S, Colantuoni E, Lau B, et al. Alcohol consumption and CD4 T-cell count response among persons initiating antiretroviral therapy. *J AIDS.* 2012;61(4):455–461.

Behavioral Activation May Reduce HIV Sexual Risk Behaviors among Methamphetamine-Using Men Who Have Sex with Men

Methamphetamine use is associated with high-risk sexual behavior among men who have sex with men (MSM). Researchers recruited 16 HIV-negative adult MSM who reported engaging in unprotected sex while using methamphetamine in the past 3 months. All subjects received 10 counseling sessions: an orientation, 2 sessions to enhance information-motivation-behavioral skills associated with sexual risk reduction, 6 sessions of behavioral activation* with risk-reduction counseling, and 1 session focused on relapse prevention. Subjects were assessed at baseline and at 3 and 6 months. The primary outcome measure was number of unprotected anal intercourse episodes in the past 3 months.

- Subjects reported a mean of 5.93 unprotected anal intercourse episodes in the past 3 months at baseline; this declined to 1.07 after 3 months and to 0.86 after 6 months. Episodes of unprotected anal intercourse while using methamphetamine declined from 4.43 at baseline

to 0.86 and 0.14 at 3 and 6 months, respectively.

- Subjects reported a mean of 3.33 episodes of methamphetamine use in the past 3 months at baseline; this declined to 1.19 at 3 months and to 0.69 at 6 months.
- There was a significant reduction in depression scores after the intervention and at 6 months.

Comments: This study presents a labor-intensive but promising approach to facilitating positive behavioral change in a high-risk group. It is not clear what components of the intervention were most effective and whether a shorter intervention would have similar effects. Moreover, it is not clear how durable these effects will be. The next step is to compare behavioral activation with standard behavioral counseling to assess its effectiveness.

Darius A. Rastegar, MD

Reference: Mimiaga MJ, Reisner SL, Pantalone DW, et al. A pilot trial of integrated behavioral activation and sexual risk reduction counseling for HIV-uninfected men who have sex with men abusing crystal methamphetamine. *AIDS Patient Care STDS.* 2012;26(11):681–693.

*A type of behavioral therapy that focuses on helping patients re-engage in life's activities and find enjoyment in previously enjoyed activities without drug use.

ETHICAL CONDUCT OF ALCOHOL AND OTHER DRUG RESEARCH: FEATURE ARTICLE

Paying Participants to Take Part in Addiction Research: Ethical Considerations

Mary-Tara Roth, RN, MSN, MPH

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In many settings, research studies pay participants to help with recruitment, increase compliance with protocol requirements, and improve retention.¹⁻³ The amount of payment depends on a range of factors. Is the study recruiting healthy individuals who do not have the condition under investigation, or individuals who may receive medical benefit from participation? What are the potential risks of participation? How much inconvenience is expected due to the number and length of study visits?

Reasons for Concern about Payments

Payment amounts are likely to depend on the particular aspects of the study population. For example, in addiction research, participants may be more likely to be poor, disenfranchised, and lacking a stable or sufficient income, and to have fewer social resources and support than the general population. Ethical concerns about paying individuals to take part in a study, especially one that may pose greater than minimal risk, are heightened for such populations.⁴ The main ethical concern, applicable to any study population, centers on whether participants take part in a study because of the payment, even when participation would not be in their best interest. In people with drug addiction, there are additional concerns about whether monetary or other payment might motivate more drug use or relapse, since cash or transferable goods on hand might be used to procure the drug of abuse.

These concerns relate to the possibility that informed consent would not be voluntary, and thus would not be valid. Human-subjects research regulations and ethical guidelines state that consent should be sought only when subjects have received sufficient information to consider the risks and benefits of participation, and that they decide to take part without the presence of coercion or undue influence.⁵ Thus, payment to research participants should be evaluated to ensure that it doesn't increase potential for coercion or undue influence, which would threaten the validity of informed consent. The terms "coercion" and "undue influence" are sometimes used interchangeably; however, coercion is the threat of removing benefits to which someone is entitled to get him or her to participate. Undue influence is providing an attractive incentive to participate. Depending on the study and the study population, paying research participants could be seen as exerting undue influence, particularly when it leads to study participation that is not in an individual's best interest.⁶ Coercion is easier to spot: "Take part in this study, or you won't be able to get care at the free clinic anymore." Undue influence, however, may be more subtle and depend on other contextual factors: "Take part in this study and receive \$100." Researchers must determine at what point \$100 could be considered undue influence.

Payment for taking part in research studies can encompass several types of transactions. While it often involves money, other forms of payment, such as course credit and in-kind payments, are used as well.^{3,7,8} Payment of some sort is not unusual⁹; however, some advocate for limitations, believing either that any inducement for participating in research adds to the difficulty subjects have in assessing risk, or that research should be an altruistic, socially responsible, humanitarian activity.¹⁰⁻¹²

Payment to Participants and the Belmont Principles

The 3 ethical principles of the Belmont Report¹³ provide the philosophical underpinnings of US human-subjects protection regulations. Assessing the ethics of payment to participants under these principles can help us understand the issues. Beneficence, the first principle, speaks to risks and benefits of a study: risks should be minimized, while benefits to the subject and society are maximized. A study may be judged as too risky for subjects based on the science, design, or level of monitoring. Since payment to research subjects should not be considered a "benefit"¹⁴ (i.e., a study is not more "beneficent" because it pays more), such payment must not be seen as offsetting the risks of the study. As such, the ethical concept of beneficence is usually not considered in assessing payment of participants.

The second principle, respect for persons, speaks to autonomy—the idea that an individual who is competent can make decisions on his or her own, and that the decision to take part in research is voluntary. The consent process supports this principle, ensuring that all the information about the purpose, risks, and benefits of study participation have been related so potential subjects can make a fully informed decision. The question of whether payment affects a person's ability to make a good decision comes up here, and we can quickly see the complexities involved. Will a \$25 dollar payment at each study visit to account for 2 hours of time and transportation reimbursement sway an individual to participate at increased risk to himself? What if that amount is \$40 per visit . . . or \$80? How does the picture change if a potential participant is destitute and needs cash to buy food? In this case, could any payment amount have the potential for undue influence? On the other hand, is restricting payment because of this possibility rightfully protective of a vulnerable population subject to exploitation or, instead, paternalistic and disrespectful?

Last, the principle of justice speaks to equitable selection of research participants. Research that presents potential benefits should be accessible to all, and risks of research should not be endured only by those who happen to be more easily accessible to the researcher. A payment that is

Paying Participants to Take Part in Addiction Research (continued from page 8)

sufficient to attract people who have to take time off from work to participate may be extremely attractive to a person who is homeless, who may not fully assess the potential risks (undue influence). On the other hand, reducing the payment for the same study would likely limit the people who enroll to those who are not employed.

Does Payment for Research Participation Lead to Use of Drugs of Addiction?

Some experts consider addiction to hold too great a power over people, so that provision of cash, or even in-kind payment that could be transferred to cash, would be used to buy drugs.^{15,16} In response to such concerns, the market has provided possible solutions. One example is a credit card for people recovering from drug use (www.nextstepcard.com).¹⁷ This card limits the types of purchases that can be made, such as not allowing purchases at bars or liquor stores. The user also cannot use it to make ATM withdrawals or receive cash back when making purchases.

However, there growing empirical evidence that payment for research participation does not promote the purchase of drugs or lead to relapse. Dempsey¹⁸ found that participants receiving \$150–\$300 either in cash or money order did not affect cocaine use the day of, or after, discharge. Festinger et al.¹⁹ randomly assigned participants to receive different amounts of cash or gift card payments. Neither the type of payment nor the amount (up to \$70) had a significant effect on rates of new drug use. A subsequent study²⁰ that tested higher payment amounts (up to \$160) had similar findings. Vandrey et al.²¹ found that receipt of \$100 checks did not increase subsequent rates of cocaine use compared with controls among participants in a contingency management program. Although more research in this area is needed, these studies call into question the commonly held assumption that a person with drug addiction who is given a sum of money will be driven by his addiction to use that money to buy drugs.

The IRB and Assessment of Payment

The amount that the study proposes to pay participants will be judged by an Institutional Review Board (IRB). Among other criteria, IRB members must determine whether risks to subjects are minimized and reasonable, that informed consent is properly obtained, and that selection of subjects is equitable.²² Although payment to subjects affects each of the aforementioned criteria, there are general guidelines (but no specific directives) in the regulations as to what amount is appropriate. One survey found that IRB members often struggle to determine at what point undue influence could occur in a study, and that their decisions are often based on members' own perceptions rather than objective assessment.²³

Understanding the ethical issues and being well-versed in the current empirical evidence surrounding compensation for participation in addiction research can help researchers justify

to the IRB whether payment to subjects in a given study is appropriate, and if so, what amount, type, and disbursement schedule is ethically sound. A well-considered and ethically justified approach will always fare better in IRB review and promote ethical conduct of the study for participants.

Conclusion

The choice to take part in a research study can be complex and based on multiple factors, including intrinsic personal beliefs and external influences. The possibility for undue influence exists in many research studies and is not always in the form of monetary payment (think, for example, of a new treatment for a severe disease with limited alternative options). For any population, when undue influence is a possibility, the consent process should underscore the potential risks and ensure that all subjects understand those risks and appreciate what they mean in relation to their own situations. People can make bad decisions about spending their money, and this possibility, of course, is not limited to people who use drugs. Although more research is needed (and there is a great opportunity for researchers in the addiction field to do this research, even in the context of ongoing studies), current evidence suggests that monetary payment does not make addiction-research participants more likely to buy and use drugs. Addiction researchers must navigate the potentially complex ethical gray area between allowing autonomous individuals to make their own decisions about study participation and providing protections to those who may have limited autonomy.

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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

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