Alcohol, Other Drugs, and Health: Current Evidence

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TABLE OF CONTENTS

Health Outcomes

Alcohol Use Disorders: Chronic or Not?

Interviews of a representative sample of 43,093 U.S. adults provide new information on the usual course of alcohol use disorders (abuse or dependence).

- Approximately 5% of adults had past-year abuse while 4% had past-year dependence. Lifetime prevalences were 18% and 13%, respectively.
- Of those with lifetime alcohol dependence, only 24% reported ever having received alcohol treatment, even though treatment was defined broadly and included (but was not limited to) participation in 12-step programs, care in an emergency department, and assistance by clergy or other professionals.
- The mean age of onset of an alcohol use disorder was 22 years.
- Most patients with lifetime abuse or dependence had only 1 episode (72%). Those with more than 1 episode had a mean of 5 episodes. The mean duration of the longest episode was about 3 years for abuse and 4 years for dependence.

Comments: This nationally representative survey tells us that alcohol use disorders begin in young adulthood and usually go untreated. They are characterized by recurrence for relatively few patients (though patients with recurring episodes are the ones that physicians are most likely to encounter and remember). More commonly, alcohol use disorders consist of 1 symptomatic episode, even when not treated, lasting up to several years.

Richard Saitz, MD, MPH

Reference: Hasin DS, et al. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States. *Arch Gen Psychiatry.* 2007;64(7):830–842.

Risk Factors for Nonfatal Drug Overdose

Fatal overdose is the leading cause of death among drug users, and nonfatal overdose causes medical complications. To identify risk factors for nonfatal overdose, researchers surveyed 772 street-recruited drug users in New York City who had been injecting drugs for at least 1 year and injected heroin in the last 2 months.

One of 6 subjects had a nonfatal overdose in the 6 months before study entry. In analyses adjusted for potential confounders, the following were significantly associated with an increased risk of nonfatal overdose in the last 6 months:

- an overdose more than 6 months before study entry (odds ratio [OR], 28.6)
- younger age (e.g., OR, 7.2 for subjects 18–24 versus those 45 and older)
- cocaine use in the last 6 months (OR, 2.1)
- serious withdrawal symptoms in the last 2 months (OR, 2.7)
- alcohol use in the last 6 months (OR, 1.9)

(continued on page 2)

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Risk Factors for Nonfatal Drug Overdose (continued from page 1)

Comments: This cross-sectional study confirms findings from previous studies reporting that nonfatal overdoses often recur in drug users and are positively associated with alcohol use, cocaine use, and periods of abstinence. Clinicians should target both drug users with previous overdoses and polysubstance users for overdose prevention efforts.

Alexander Y. Walley, MD

Reference: Coffin PO, et al. Identifying injection drug users at risk of nonfatal overdose. *Acad Emerg Med*. 2007;14(7):616–623.

The Effects of Alcohol Use on Blood Pressure: Does Gender Matter?

In this study, researchers assessed whether the effects of alcohol use on blood pressure differ by gender. They examined data from 2650 subjects who had participated in a national health and nutrition study and reported consuming about ≥1 drinks per day in the past year.

- Twenty-one percent of subjects had hypertension.
- Systolic blood pressure was significantly higher in men who drank ≥3 drinks per day than in men who drank 1 drink per day (e.g., about 125 mm Hg with 1 drink, 128 mm Hg with 3 drinks, and 131 mm Hg with ≥4 drinks per day). Results were similar for diastolic blood pressure.
- Alcohol use did not significantly affect blood pressure in women.

Comments: The results of this study should be interpreted with caution. The analyses were limited to subjects who consumed about ≥1 drink per day, a group representing a small proportion of the U.S. population. Further, no information on people who drank less or who abstained was provided. Thus, the author's statement that "alcohol intake of up to 2 drinks per day has no effect on blood pressure" cannot be supported. Similarly, while blood pressure did not differ among women who drank 1 drink per day and those who drank more, a significant difference might have been observed at a lower threshold: it is possible that women who consumed <1 drink per day had higher blood pressure than those who abstained, but this was not tested.

R. Curtis Ellison, MD

Reference: McFarlane SI, et al. Alcohol consumption and blood pressure in the adult US population: assessment of gender-related effects. *J Hypertens*. 2007;25(5):965–970.

What Predicts Harmful Alcohol Use After Liver Transplantation?

Patients should not drink alcohol after liver transplantation for alcoholic liver disease. To identify risk factors for alcohol use after liver transplantation, researchers analyzed pre- and post-transplantation data from 387 patients (76% male, average age 51 years) who underwent the procedure in Switzerland or France.

- During an average follow-up of 61 months after transplantation, 12% of patients had harmful alcohol use (about >3.5 drinks of alcohol per day plus alcohol-related physical or mental consequences).

(continued on page 3)

What Predicts Harmful Alcohol Use After Liver Transplantation? (continued from page 2)

- In adjusted analyses, the following 3 factors were significantly associated with harmful alcohol use after transplantation:
    - a score of >3 on the High-Risk Alcoholism Relapse scale,* used to assess pre-transplantation alcohol use (odds ratio [OR], 10.7)
    - psychiatric comorbidity (OR, 7.8)
    - pre-transplantation abstinence from alcohol for ≤6 months (OR, 3.3)
- Harmful alcohol use after transplantation occurred in 5% of patients with none of the above factors, in 18% with 1 factor, in 64% with 2 factors, and in 100% with all 3 factors.

Comments: This study found that pre-transplantation alcohol use, inpatient alcohol treatment, and psychiatric factors are associated with relapse to harmful alcohol use after liver transplantation for alcoholic liver disease. The outcome measure for this study required not only a fairly high daily intake of alcohol but also alcohol-related physical or mental harm. Thus, it is not clear how many patients in the "nonrelapse" group were drinking at unhealthy levels, despite recommendations to abstain after transplantation.

Kevin L. Kraemer, MD, MSc

*A scale from 0 to 6 points (total) based on 3 parameters: 1) duration of heavy drinking (0 points for <11 years, 1 point for 11-25 years, and 2 points for >25 years); 2) daily drinks (0 points for <9 drinks per day, 1 point for 9-17 drinks per day, and 2 points for >17 drinks per day); and 3) prior inpatient treatment for alcoholism (0 points for 0 treatments, 1 point for 1 treatment, and 2 points for >1 treatment)

Reference: De Gottardi A, et al. A simple score for predicting alcohol relapse after liver transplantation: results from 387 patients over 15 years. *Arch Intern Med.* 2007;167(11):1183–1188.

Estimating the Impact of Alcohol Use on Survival Among Veterans With HIV

The adverse impact of alcohol use on adherence to antiretroviral therapy (ART) has been repeatedly demonstrated. Alcohol's effects on survival among individuals with HIV, however, is not clear. Investigators estimated these effects by using a computer simulation model of HIV that incorporated data on drinking and ART adherence from an observational study of 2702 male veterans.

- Any drinking (versus no drinking) diminished survival (median time until death).
- As frequency of drinking increased, survival decreased (e.g., drinking 1–4 drinks one or more times per week reduced survival by more than one year; drinking 1–4 drinks daily reduced survival by 3 years).
- Heavier drinking had the greatest impact on survival (e.g., drinking ≥5 drinks one or more times per week reduced median survival by more than 2 years; drinking ≥5 drinks daily reduced survival by 6 years).

Comments: An association between mortality and heavier alcohol use among people taking ART is credible and supported in this model. But, the finding of diminished survival with consumption of lesser amounts is unexpected. As these findings are derived from a simulation model based on data from one observational cohort of veterans taking ART, generalization beyond the examined cohort requires caution.

Jeffrey H. Samet, MD, MA, MPH

Reference: Braithwaite RS, et al. Estimating the impact of alcohol consumption on survival for HIV+ individuals. *AIDS Care*. 2007;19(4):459–466.

Disclosure – Dr. Samet is a consultant to the Veterans Aging Cohort Study, which produced data that was used in the above study.

Divorce: Grounds for Substance Use Screening

Half of first marriages in the U.S. end in divorce. To estimate the extent to which substance use during marriage contributes to divorce rates among young adults, researchers studied 454 individuals in California and Oregon who had married by age 23 and completed periodic surveys as part of a longitudinal study.

- Twenty-two percent had divorced by age 29.
- In unadjusted analyses, greater frequencies of past-year alcohol intoxication (odds ratio, [OR], 1.3) and marijuana use (OR, 1.2), as well as any past-year hard drug use (OR, 1.8; borderline significance), predicted divorce by age 29.
- In analyses adjusted for potential confounders, however, only frequency of alcohol intoxication was significantly associated with divorce (OR, 1.2).

(continued on page 4)

Divorce: Grounds for Substance Use Screening (continued from page 3)

Comments: Greater frequency of alcohol intoxication at age 23 predicted marital dissolution by age 29. Frequent substance use has many adverse effects on marital relationships, including partner violence, legal problems, job loss, and sexual dysfunction. A social or family history of divorce or marital problems should cue all clinicians to ask carefully about substance use disorders (although universal screening is preferable). Also, clinicians should consider discussing the risk of marital discord and divorce when talking about heavy drinking with young married people.

Peter D. Friedmann, MD, MPH

References: Collins RL, et al. The role of substance use in young adult divorce. *Addiction*. 2007;102(5):786–794.

Drinking May Lower Postprandial Glycemia

Moderate drinking has been associated with a lower risk of type 2 diabetes. One possible explanation for this lower risk is that drinking may reduce postprandial glycemia.

Researchers in Australia assessed the association between postprandial glycemia and drinking beer, white wine, or gin under 3 conditions: without a meal, with a carbohydrate meal, and 1 hour before a carbohydrate meal. Subjects, who included 38 healthy college students (10 in the first condition, 10 in the second, and 18 in the third), had fingertip blood samples taken at baseline and at regular intervals over 2–3 hours.

Fasting glucose concentrations did not significantly differ among subjects. Mean glucose scores (which summarized glucose response over a 2–3 hour period) were significantly lower for

- isoenergetic portions of beer (58), wine (7), and gin (10) than for bread (100, an arbitrary reference score);
- meals consumed with 2 typical glasses of wine (63) or gin (80), but not beer, than meals consumed with water (100);
- meals preceded by 1 hour with about 2 drinks of beer (67), wine (75), or gin (78) than meals preceded with water (100).

Comments: This study in healthy subjects demonstrated that drinking approximately 2 drinks of beer, wine, or gin with, or within an hour before, a high-carbohydrate meal limited the rise in glucose that occurs after carbohydrate ingestion. Since higher glucose levels are associated with higher risk of diabetes and coronary heart disease, the demonstrated decrease in postprandial glycemia may be another mechanism by which moderate alcohol consumption lowers the risk of chronic diseases.

R. Curtis Ellison, MD

Reference: Brand-Miller JC, et al. Effect of alcoholic beverages on postprandial glycemia and insulinemia in lean, young, healthy adults. *Am J Clin Nutr.* 2007;85 (6):1545–1551.

Assessments and Interventions

Does Methadone Treatment Change Alcohol Consumption?

Patients receiving methadone treatment have a high prevalence of unhealthy alcohol use. The impact of such treatment on alcohol consumption, however, is not clearly understood. Therefore, researchers conducted a systematic review and summarized the findings of 15 relevant studies.

- Nine studies found no change in alcohol consumption after initiation of or during methadone treatment. Three studies found an increase in alcohol consumption, while another 3 reported a decrease.
- The studies that found no change or a decrease in alcohol consumption included 3 randomized controlled trials and 7 prospective cohorts. These were stronger methodologically than the studies that found an increase in alcohol consumption, which were all retrospective and subject to recall bias.

Comments: Alcohol consumption does not appear to change after initiation of methadone treatment. Regardless, to help prevent additional morbidity, clinicians should conduct screening and offer appropriate treatment for unhealthy alcohol use for all patients receiving methadone. To ensure this occurs, methadone treatment programs should develop cost-effective mechanisms for alcohol screening and intervention.

Julia H. Arnsten, MD, MPH

Reference: Srivastava A, et al. The effect of methadone maintenance treatment on alcohol consumption: a systematic review. *J Subst Abuse Treat.* 2007;doi: 10.1016/ j.jsat.2007.04.001.

Antiretroviral Medication Affects Dose of Methadone

Pharmacokinetic interactions between antiretrovirals and methadone can potentially affect levels of either medication and lead to over- and/or underdosing. These researchers evaluated the average change in methadone dose that occurred with co-administration of nevirapine, efavirenz, ritonavir-boosted lopinavir, or atazanavir in 120 patients in a directly observed therapy program. All patients also had Hepatitis C.

- For patients on nevirapine, the median change in methadone dose in the 3 months after baseline (initiation of highly active antiretroviral therapy [HAART]) was 20 mg/d ($P< 0.001$), with 32 (86%) of 37 patients requiring daily dose increases.
- For patients on efavirenz, the median change in methadone dose from baseline was 7.5 mg/d ($P=0.004$), with 11 (61%) of 18 patients requiring daily increases.
- For patients on ritonavir-boosted lopinavir or atazanavir, the median change from baseline was 0 for both ($P=0.56$ and 0.95, respectively).
- The HIV virus was suppressed to fewer than 400 copies/mL in 67%–76% of patients, with no difference based on antiretroviral regimen ($P=0.89$).

Comments: Clinicians providing either methadone or antiretrovirals to patients should be mindful of the potential interactions between these medications. Interactions can alter methadone levels, which can lead to sedation (from increased levels) or withdrawal (from decreased levels). Depending on the specific case, the dose of methadone will need to be increased, decreased, or maintained. Notably, there were significant variations in methadone dose requirements between individual patients. These data support close clinical observation of and medication adjustment in patients receiving methadone and HAART.

David A. Fiellin, MD

Reference: Tossonian HK, et al. Methadone dosing strategies in HIV-infected injection drug users enrolled in a directly observed therapy program. *J Acquir Immune Defic Syndr*. 2007;45(3):324–327.

Do Mortality Rates Differ by Type of Pharmacotherapy for Opioid Dependence?

The risk of death from overdose associated with induction, maintenance, or discontinuation of an opioid pharmacotherapy may depend on the opioid's mechanism of action. For example, methadone (full agonist) treatment may pose the greatest risk during treatment induction, whereas oral naltrexone (an antagonist) may be riskiest immediately after treatment is discontinued because of diminished opioid tolerance. In this study, Australian researchers analyzed coroner's reports and various prescription data sources to estimate mortality rates possibly associated with these pharmacotherapies.

- From 2000 to 2003, 1 buprenorphine-*, 32 oral naltrexone-, and 282 methadone-related deaths occurred.
- The overall mortality rate associated with methadone was significantly lower than the rate associated with oral naltrexone (2.7 vs. 10.1 per 1000 treatment episodes).
- The mortality rate associated with methadone treatment was 3.0 per 100 person years during the first week of treatment versus 0.34 per 100 person years during the remainder of treatment.
- The mortality rate associated with oral naltrexone treatment was 1 per 100 person years during treatment versus 22.1 per 100 person years in the 2 weeks after treatment was discontinued.

Comments: Although the methods used permit only crude estimates and specific causes of death were not addressed, these findings heighten concerns about the possible increased risk of opioid overdose shortly after oral naltrexone treatment is discontinued. More rigorous studies are needed to refine the estimates presented here, to define risks and benefits of other (e.g., depot) preparations of naltrexone in treating opioid dependence, and to develop treatment protocols to further enhance the safety profiles of specific opioid pharmacotherapies.

Marc N. Gourevitch, MD, MPH

*The low number of buprenorphine-associated deaths precluded their meaningful analysis.

Reference: Gibson AE, et al. Mortality related to pharmacotherapies for opioid dependence: a comparative analysis of coronial records. *Drug Alcohol Rev.* 2007;26 (4):405–410.

A Simplified Method to Assess Alcohol Use Disorders

One of the challenges with alcohol screening in primary care settings is the lack of a brief assessment to determine whether abuse or dependence is present in screen-positive patients. In this study, researchers developed a simple assessment with data from the cases (1522 injured patients) of a case-control study. They validated the assessment with data from the controls (1124 noninjured patients) from the same study, a primary care sample

(continued on page 6)

A Simplified Method to Assess Alcohol Use Disorders (continued from page 5)

(n=623), and a nationally representative sample of U.S. adults (n=26,946).

- Among subjects in the developmental sample, 2 criteria*—recurrent drinking in physically hazardous situations and drinking more or for longer than intended—had a sensitivity of 96% and a specificity of 85% for current alcohol use disorders.
- Among all subjects in the 3 validation samples, the criteria had a sensitivity of 72% to 94% and a specificity of 80% to 95%.
- Among screen-positive** subjects in the 3 validation samples, the criteria had a sensitivity of 77% to 95% and a specificity of 62% to 86%.

Comments: Clinicians must be able to quickly and accurately assess the presence of an alcohol use disorder if alcohol screening and intervention strategies are to be effective. Although the 2 criteria had reasonable sensitivity and specificity for alcohol use disorders in this retrospective study, it is not clear how the relevant questions should be worded for use in primary care settings or how they would perform outside the context of a large diagnostic questionnaire. As the researchers mention, the items should be tested prospectively in practice settings.

Kevin L. Kraemer, MD, MSc

*Based on positive responses to 3 questions from the Diagnostic Interview Schedule and 4 questions from the Alcohol Use Disorder and Associated Disabilities Interview Schedule
**Defined in the case-control and primary care studies as >4 in 1 day for women (>5 for men) over the past 3 months; defined in the national survey as ≥5 in a day in the past 12 months

Reference: Vinson DC, et al. Simplifying alcohol assessment: two questions to identify alcohol use disorders. *Alcohol Clin Exp Res*. 2007;31(8):1392–1398.

Who Receives and Remains in Office-Based Buprenorphine Treatment?

Buprenorphine treatment for opioid dependence has been provided in office-based settings in the United States for several years now. Data on patients receiving buprenorphine in these settings, however, are lacking. Therefore, researchers analyzed data from a medical record review of 86 patients receiving office-based buprenorphine treatment from 6 physicians in New York City.

- One-half of patients were misusing a prescription opioid at intake, 35% were using heroin, and 9% were using both. The remaining subjects were either transferring from other treatment, had cravings, or had fear of relapse.
- Almost 50% reported misusing non-opioid drugs (e.g., cocaine, marijuana) at intake.
- Sixty-three percent of patients received prescriptions for at least 1 psychiatric medication during buprenorphine treatment.
- The median time in treatment was 8 months (range <1 to 30 months).
- According to the last entry in the medical record, 24% were misusing any substance and 8% were misusing opioids. Fifty-eight percent were still receiving buprenorphine (52% from the index physician).
- Factors associated with retention in buprenorphine treatment with the index physician included full-time employment or other forms of support, stable housing, and prescription opioid (versus heroin) misuse at intake. Psychiatric disorders or substance misuse during treatment did not affect retention.

Comments: This is one of a growing number of descriptive studies of unselected patients receiving office-based buprenorphine treatment. It demonstrates that successful buprenorphine treatment can be achieved in office-based settings. To ensure successful treatment in these patients who often have psychiatric comorbidity, strong referral networks and access to consultation for complex cases are desirable.

Julia H. Arnsten, MD, MPH

Reference: Magura S, et al. Outcomes of buprenorphine maintenance in office-based practice. *J Addict Dis.* 2007;26 (2):13–23.

Health Plans' Requirements for Mental Health and Substance Use Screening

Most health plans cover some treatment for mental health and substance use disorders, but a minority of people who need these services receive them. Limited requirements for screening and identification of these disorders partially explain this treatment gap.

To estimate the extent of health plans' requirements for mental health and substance use screening in primary care, researchers analyzed data from a nationally representative survey of health plans in 1999 (n=434 health plans, 92% response rate) and 2003 (n=368, 83% response rate).

(continued on page 7)

Health Plans' Requirements (continued from page 6)

- The proportion of health plans with a screening requirement for mental health or substance use disorders* did not significantly change from 1999 (32%) to 2003 (34%).
- Among plans with a screening requirement, there was a significant increase in the proportion that required alcohol screening (from 33% in 1999 to 78% in 2003) and drug screening (from 8% to 78%).

Comments: Health plan mandates and reimbursement for substance use screening would encourage primary care physicians to take a greater role in identifying, managing, and referring patients with substance use disorders. The finding that only one-third of health insurance products in 1999 and 2003 required screening for mental health or substance use disorders highlights missed opportunities to improve detection and intervention. Although tracking adherence to such a requirement might be challenging to insurers, the recent addition of procedure codes for substance use screening and brief intervention promises to provide a mechanism for reimbursement and monitoring in the future.

Peter D. Friedmann, MD, MPH

*Use of a general health screening questionnaire including mental health, alcohol, or drug items and/or a screening questionnaire focused on mental health, alcohol, or drug problems

Reference: Horgan CM, et al. Health plan requirements for mental health and substance use screening in primary care. *J Gen Intern Med*. 2007; 22(7):930–936.

HAART and Drug Treatment May Improve Survival in People With HIV Who Inject Drugs

Highly active antiretroviral therapy (HAART) and methadone treatment have led to significant improvements in survival for people with HIV and opioid dependence, respectively. It is not clear, however, whether HIV infection and HAART influence the length of survival among people with injection drug use (IDU) who receive drug treatment.

This observational study from Spain examined survival among 1181 people with IDU (59% with HIV) who had been admitted to a substance abuse treatment program before or after 1997 (the era of established methadone programs and HAART). One-third of subjects with HIV had received HAART.

- Survival was shortest in people with IDU and HIV admitted to drug treatment before 1997. However, survival has improved substantially since 1997, when HAART was introduced.
- Survival since 1997 in people with IDU and HIV was similar to that in people with IDU but not HIV.

Comments: This study supports the benefit of both HAART and drug treatment on survival in people with IDU and HIV. The longer survival in patients who did not receive HAART may be partially attributable to access to drug treatment, prophylaxis for opportunistic infections, and ongoing clinical care. The increase in survival, even in patients with HIV who did not receive HAART, is encouraging. Yet, it reminds us of the challenge in providing state-of-the-art care to patients with substance use disorders and HIV.

David A. Fiellin, MD

Reference: Muga R, et al. Survival of HIV-infected injection drug users (IDUs) in the highly active antiretroviral therapy era, relative to sex- and age-specific survival of HIV-uninfected IDUs. *CID*. 2007;45(3):370–376.

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