Alcohol and Health: Current Evidence

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TABLE OF CONTENTS

ALCOHOL AND HEALTH OUTCOMES

Don't Blame Substance Use for Mood and Anxiety Disorders

Mood and anxiety disorders produce symptoms similar to those of substance intoxication and withdrawal, and therefore may be difficult to diagnose among patients who use substances. To tease out mood and anxiety disorders that are substance-induced from those that are independent of use, researchers analyzed data from a nationally representative survey of 43,093 adults in the United States.

- The 12-month prevalences of independent mood and anxiety disorders were 9.2% and 11.1%, respectively.
- Less than 1% of adults with a mood or anxiety disorder had episodes that were substance-induced (i.e., episodes that began after withdrawal or intoxication, and either were not associated with at least 1 month of abstinence or did not persist for more than 1 month after the cessation of withdrawal or intoxication).
- Independent mood and anxiety disorders were strongly and consistently associated with substance dependence (odds ratios from 2.2 to 13.9), and less consistently associated with substance abuse (odds ratios from 0.8 to 4.2).

Comments: This study suggests that most mood and anxiety disorders—despite being associated with substance dependence—are independent of substance intoxication and withdrawal. This finding challenges the assumption that mood and anxiety symptoms will resolve with abstinence from substance use. The implication, for which there is growing empirical support, is that mood and anxiety disorders in patients with substance use disorders, especially substance dependence, should be treated early and comprehensively.

Peter Friedmann, MD, MPH

Reference: Grant BF, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry.* 2004;61(8):807–816.

Reducing Mortality: Is Wine or Beer Better?

The lower risk of mortality from coronary artery disease in Mediterranean countries is often attributed to wine drinking. To examine whether wine or other alcohol consumption reduces the risk of death across a range of blood pressure levels, researchers conducted a prospective cohort study in France using questionnaire and medical exam data from 36,583 healthy men aged 30–59 who were followed for 13–21 years. Analyses were adjusted for potential confounders (e.g., age, smoking).

For 3 of 4 quartiles of systolic blood pressure (means 116 mm Hg, 139 mm Hg, and 158 mm Hg, but not mean 129 mm Hg), moderate wine drinkers (those who consumed <60 g of alcohol from wine per day and no beer) had a significantly lower risk of death from all causes (relative risks, RR, from 0.63 to 0.77) than did abstainers. Those who consumed both beer and wine, and those who consumed >=60 g of alcohol from wine per day did not experience a significant reduction in risk of death from all causes.

Comments: This is a very large study with excellent ascertainment of cause of death among men in eastern France where both beer and wine are commonly consumed, and lifestyle characteristics of wine drinkers and beer drinkers are similar. Although wine's alcohol content may lead to increases in blood pressure, some of its polyphenols or other non-alcoholic components may help protect against death. Such protection is lost when drinkers consume greater amounts of wine or when some of their alcohol intake is from beer.

R. Curtis Ellison, MD

Reference: Renaud SC, et al. Moderate wine drinkers have lower hypertension-related mortality: a prospective cohort study in French men. *Am J Clin Nutr.* 2004;80(3):621–625.

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Effects of Alcohol on Restenosis After PTCA and Stenting

Alcohol intake can reduce the risk of coronary artery disease through various possible mechanisms (e.g., influencing the coagulation cascade, affecting lipids). In a retrospective cohort study, researchers examined whether intake could lower risk of restenosis in men with coronary artery disease treated with percutaneous transluminal coronary angioplasty (PTCA) and stent implantation. They examined 225 men (with 346 stents among them) who underwent these procedures and had another angiogram 6 months later. Most consumed <350 g of alcohol per week (less than approximately 3 drinks a day).

- Men who consumed 50 g–700 g of alcohol per week, compared with those who drank <50 g per week, had significantly less coronary restenosis (34% versus 49%) and repeat angioplasty (23% versus 43%) per treated arterial segment. They also had a lower mean loss of the coronary artery luminal diameter (1.1 mm versus 1.5 mm).
- In multivariable analyses adjusted for various demographic, behavioral, and clinical factors, alcohol consumption was independently and significantly associated with restenosis (odds ratio, OR, 0.5), repeat angioplasty (OR 0.4), and loss of the luminal diameter (p=0.005).

Comments: These results, which support previous animal and human research, strongly suggest that moderate alcohol intake protects against restenosis in patients undergoing angioplasty and stenting. Similar studies of patients undergoing angioplasty are needed to determine if alcohol's apparent protection against restenosis remains with the implantation of drug-eluting stents (which were not used in this study).

R. Curtis Ellison, MD

Reference: Niroomand F, et al. Influence of alcohol consumption on restenosis rate after percutaneous transluminal coronary angioplasty and stent implantation. *Heart.* 2004;90(10):1189–1193.

Alcohol Consumption and Breast Cancer Risk

Findings on the relationship between alcohol and breast cancer risk have been inconsistent, and the effect of specific types of alcohol on this risk has not been adequately studied. Using questionnaire data from 13,074 Danish women aged 20–91 years (473 cases of breast cancer), researchers sought to clarify the effect of the type and amount of alcohol intake on breast cancer risk. Results from analyses adjusted for relevant confounders (e.g., age, hormone replacement therapy, parity) include the following:

- Total alcohol intake did not significantly affect the risk of breast cancer in the sample as a whole (both premenopausal and postmenopausal women).
- Premenopausal women who drank >27 drinks of any type of alcohol per week had a significantly greater risk (relative risk, RR, 3.5) compared with light drinkers (who consumed 1–6 drinks per week). Risk did not differ by type of alcohol.
- While their risk was not significantly impacted by total intake of all types of alcohol, women aged 70 or older who drank >6 drinks of spirits per week had a significantly greater risk (RR 2.4) compared with those who consumed <1 drink of spirits per week.

Comments: Previous studies on the relationship between alcohol and breast cancer have produced inconsistent results possibly because they may have not accounted for menopausal status (a risk for premenopausal women) or type of alcoholic beverage consumed (spirits as a risk for the elderly). Until these complex relationships are sorted out, it appears that breast cancer risk is just one more reason to advise against heavy drinking.

Joseph Conigliaro, MD, MPH

Reference: Petri AL, et al. Alcohol intake, type of beverage, and risk of breast cancer in pre- and postmenopausal women. *Alcohol Clin Exp Res.* 2004;28(7):1084–1090.

The Relationship Between Alcohol Intake and Cognitive Function

Studies examining alcohol's impact on cognitive impairment have produced varying results. To clarify the relationships between midlife alcohol consumption, and mild cognitive impairment and dementia in old age, researchers from Finland randomly selected subjects from a population-based study in the 1970s and re-examined them in 1998. Of these 1018 men and women aged 65–79 years, 61 developed mild cognitive impairment (based on various diagnostic criteria) and 48 were diagnosed with dementia. Analyses were adjusted for potential confounders (e.g., age, sex, body mass index, other cardiovascular risk factors).

- The relationship between alcohol frequency at baseline and subsequent mild cognitive impairment was U-shaped: non-drinkers and frequent drinkers (those who consumed alcohol several times per month) had significantly higher risk of cognitive impairment (relative risks, RRs, 2.2 and 2.6, respectively) than did infrequent drinkers.
- Alcohol frequency was significantly related to dementia only among carriers of the apolipoprotein E4 allele. Carriers who were infrequent or frequent drinkers had a higher risk (RRs 2.3 and 3.6, respectively) than did non-carriers who did not drink.

Comments: Unfortunately, this study suffers from very small numbers (e.g., totals of only 14–17 subjects with dementia in each alcohol category) and inadequate estimates of alcohol use (e.g., no data on amount consumed). Further, frequent drinkers—68% of whom drank only 1–2 times per month—were defined quite differently in this study than in others. Nonetheless, the results do suggest that apolipoprotein E4 status modifies alcohol's influence on dementia. Beyond that, better studies are needed to elucidate the relationship between moderate drinking and cognitive health.

R. Curtis Ellison, MD

Reference: Anttila T, et al. Alcohol drinking in middle age and subsequent risk of mild cognitive impairment and dementia in old age: a prospective population based study. *BMJ.* 2004;329(7465):539.

Alcohol's Impact on Heart Failure After MI

While patients with myocardial infarction (MI) may benefit from alcohol consumption (e.g., protection against coronary artery disease progression), they might also be more vulnerable to alcohol's cardiotoxic effects. This study aimed to assess the influence of alcohol intake on the development of symptomatic heart failure (hospitalization for heart failure or need for an angiotensin-converting enzyme inhibitor) in 2231 patients with a left ventricular ejection fraction <40% following MI. Three weeks prior to MI, 32% of these patients consumed 1–10 drinks per week while 11% consumed >10; two weeks after MI, 15% consumed 1–10 drinks per week while 1% consumed >10.

In analyses adjusted for various demographic, behavioral, and clinical factors, drinking before or after MI did not significantly affect risk of heart failure. However, despite this lack of statistical significance, hazard ratios for those consuming >10 drinks per week before MI indicated greater risk of all the cardiovascular outcomes examined (e.g., heart failure, total mortality, cardiovascular mortality).

Comments: Unlike most previous studies, this study did not find reductions in heart failure and death from moderate drinking among patients with MI and left ventricular dysfunction. However, because only 1% of those studied consumed >10 drinks per week, there were too few patients to test for either benefits or adverse consequences of drinking. The true balance of benefits and risks of alcohol use following MI remains unclear from observational studies and may be clarified only through clinical trials.

R. Curtis Ellison, MD

Reference: Aguilar D, et al. Alcohol consumption and prognosis in patients with left ventricular systolic dysfunction after a myocardial infarction. *J Am Coll Cardiol.* 2004;43(11):2015–2021.

INTERVENTIONS

Practice Guidelines for Managing Alcohol Withdrawal Delirium

Alcohol withdrawal delirium can cause serious morbidity and mortality if not treated appropriately. To inform clinical practice, researchers conducted a structured review and meta-analysis (including 9 prospective controlled trials) and developed evidence-based guidelines for managing alcohol withdrawal delirium.

Compared with neuroleptics, sedative-hypnotics were more effective at decreasing mortality (in 2 trials that had any deaths), and at shortening the duration of delirium (in 3 of 4 trials). In 2 studies reporting the time required to control agitation, intravenous diazepam was better than paraldehyde per rectum in 1, but intramuscular diazepam was no different from oral barbital in the other.

Based on these findings and review of other data, the researchers recommended the following:

- providing comprehensive monitoring and supportive care;
- using parenteral, rapid-acting sedative-hypnotics (preferably benzodiazepines due to their more favorable therapeutic/toxic index) to achieve light sedation;
- considering pentobarbital or propofol if agitation is not controlled with initial large doses of benzodiazepines (based on case reports); and
- considering neuroleptics only when the patient has continued agitation, disturbed thinking, or perceptual disturbances despite sedative-hypnotic treatment.

Comments: The practice guidelines outlined in this paper are very practical and reasonable. Although the studies examined are limited (the 9 trials were all published before 1979, 5 of the 9 included fewer than 20 subjects per treatment group, and conclusions about mortality were based on only 9 deaths), the evidence and years of clinical experience with these drugs support the use of sedative-hypnotics, primarily benzodiazepines, for alcohol withdrawal delirium.

Kevin L. Kraemer, MD, MSc

Reference: Mayo-Smith MF, et al. Management of alcohol withdrawal delirium: an evidence-based practice guideline. *Arch Intern Med*. 2004;164(13):1405–1412.

Effectiveness of a Depot Formulation of Naltrexone in Treating Alcohol Dependence

Naltrexone's efficacy in treating alcohol dependence is limited by patient non-adherence. To examine the safety and efficacy of an injectable, depot (sustained-release) formulation of naltrexone, researchers randomized 315 patients with alcohol dependence to receive 5 sessions of motivational enhancement therapy plus monthly naltrexone or placebo injections for 3 months.

- Patients in the naltrexone group, compared with those in the placebo group, had improvements in the time to heavy-drinking (medians 11 days versus 6 days, p=0.05) and γ-glutamyl transpeptidase levels (47 units per liter versus 63 units per liter, p=0.10).
- Patients receiving naltrexone also had a significantly longer time to their first-drinking day (medians 5 days versus 3 days), had more days abstinent (means 53 days versus 46 days), and were more likely to achieve total (3-month) abstinence (18% versus 10%).
- There were few major differences in the adverse reactions experienced by both groups, though patients in the naltrexone group were significantly more likely to report >=1 injection site reactions.

Comments: This study suggests that a depot formulation of naltrexone is safe and efficacious in treating alcohol dependence. Given its advantages (e.g., no need to take a daily dose), injectable naltrexone may be a useful option when non-adherence hinders an adequate response to oral therapy. At the time of this report, however, the depot formulation is not available for clinical use in the United States.

Joseph Conigliaro, MD, MPH

Reference: Kranzler HR, et al. Naltrexone depot for treatment of alcohol dependence: a multicenter, randomized, placebo-controlled clinical trial. *Alcohol Clin Exp Res.* 2004;28(7);1051–1059.

Addressing Risky Alcohol Use with Other Behavioral Risk Factors

Brief counseling is efficacious for addressing individual behavioral risk factors such as smoking and risky drinking. However, its efficacy in addressing *multiple* risk factors in a patient remains unclear. Researchers summarized 6 systematic reviews (focused primarily on cardiovascular disease and diabetes interventions) to examine the evidence for addressing multiple behavioral risk factors, including risky alcohol use, in primary care settings.

- Of secondary prevention trials for hypertension, 1 of 3 that targeted risky drinking led to a reduction in alcohol use; the only primary prevention study that was identified did not significantly affect use.
- One study of general practices in Britain tested nurse counseling and follow-up for smoking, diet, exercise, and alcohol consumption. The intervention lowered

(continued on page 5)

Addressing Risky Alcohol Use with Other Behavioral Risk Factors *(continued from page 4)*

cholesterol, blood pressure, and body mass index but had no effect on smoking or risky alcohol use.

Comments: As any primary care physician can attest, most patients have more than one health risk behavior. While evidence supports the use of interventions for individual risk factors, the efficacy and value of using an integrated approach to address multiple risk factors, including risky drinking, has yet to be clearly demonstrated. Nonetheless, the authors of this review suggest that, for now, primary care clinicians should address multiple risks with brief behavioral counseling (the 5A's: Assess, Advise, Agree on goals, Assist in developing a plan, Arrange follow-up); system supports such as computer-decision tools; clinician reminders to screen or intervene; staff training; multidisciplinary nurse-led teams; and referrals.

Richard Saitz, MD, MPH

Reference: Goldstein MG, et al. Multiple behavioral risk factor interventions in primary care: summary of research evidence. *Am J Prev Med.* 2004;27(2S):61–79.

Are Physicians Screening for Multiple Behavioral Risk Behaviors?

The United States Preventive Services Task Force recommends that primary care physicians screen all their patients for many health risk behaviors, including risky drinking. To ascertain the prevalence of 4 risk factors (i.e., physical inactivity, overweight, cigarette smoking, and risky drinking) and physicians' screening for related risk behaviors, researchers analyzed data from the 1998 National Health Interview Survey of 16,818 adults who had a routine checkup in the past year.

- Most (52%) of the respondents reported having >1 risk factor; 70% reported physical inactivity, 55% overweight, 20% smoking, and 8% risky drinking (average weekly consumption of >14 drinks for men and >9 drinks for women, or >=5 drinks in 1 day on 12 or more occasions).
- Twenty-nine percent reported receiving no screening in the past year, 12% reported being screened for 1 risk behavior, and 59% reported being screened for >=2 risk behaviors.
- Those who were screened were more likely to be asked about physical activity (54%) and tobacco use (53%) than about diet (48%) or alcohol use (45%).
- Women, the elderly, and those with lower levels of income and education reported being screened for fewer of their risk behaviors.

Comments: Screening for multiple risk behaviors in primary care should become the norm. The authors accurately conclude, however, that while primary care physicians can perform such screening, systems are required to support this and other efforts to accomplish effective health behavior change.

Jeffrey Samet, MD, MA, MPH

Reference: Coups EJ, et al. Physician screening for multiple behavioral health risk factors. *Am J Prev Med.* 2004;27(2S):34–41.

Alcohol Screening and Brief Intervention Training in Primary Care

Studies indicate alcohol screening and brief intervention (SBI) are effective in primary care settings but challenging to introduce into actual practice. In this study, researchers evaluated a 3-hour training (based on the literature and the National Institute on Alcohol Abuse and Alcoholism's *Physicians' Guide to Helping Patients with Alcohol Problems*) aimed at assisting implementation of SBI in primary care. Forty-four physicians and 41 clinical non-physicians (nurses, counselors, and physician assistants) from 10 practices across the United States, as well as 88 medical students, were trained. Results of pre-tests and post-tests and comparisons with 5 clinical practices that served as controls include the following:

- Knowledge regarding SBI increased significantly among all trainees.
- Confidence in screening patients increased significantly in physicians and medical students whereas confidence in conducting brief interventions increased significantly only in medical students.
- Physicians and non-physicians perceived significantly fewer obstacles to implementing brief interventions while only non-physicians perceived fewer barriers to screening.
- Trained providers reported significantly higher use of alcohol screening tests and management of patients for drinking than did untrained providers.
- The proportion of at-risk drinkers reporting (3 months after their office visit) that their providers talked to them about alcohol use was greater in the trained practices than in the untrained practices (47% versus 22%).

Comments: This training program increased provider knowledge, provider self-report of SBI, and patient report of discussions with their providers about alcohol use. These positive findings can be attributed in part to key features of the program—its systems approach and adaptability to fit within the existing practice and administrative structure of each clinical site.

Kevin L. Kraemer, MD, MSc

Reference: Babor TF, et al. Training medical providers to conduct alcohol screening and brief interventions. *Substance Abuse.* 2004;25(1):17–26.

SPECIAL POPULATIONS

Adolescent Substance Use and Later Alcohol and Drug Dependence

In cross-sectional surveys, early use of alcohol has been associated with an increased risk of alcohol use disorders in adulthood. But questions remain about whether early use plays a causal role in this risk. To assess the impact of substance use in early adolescence, researchers surveyed boys entering middle school in Miami-Dade County and then interviewed a random sample of these boys (942) approximately 7–10 years later (mean age of 20 years at follow-up).

- Both experimenters (1–9 lifetime drinks; no more than 1 lifetime use of illicit drugs) and regular users (alcohol use on >=10 occasions; illicit drug use on >6 occasions) during early adolescence were significantly more likely than abstainers to meet criteria for alcohol abuse (odds ratios, ORs, 1.7 and 2.5, respectively), alcohol dependence (ORs 2.3 and 3.7, respectively), and any substance use disorder (ORs 2.1 and 4.1, respectively) as adults.
- African Americans had the lowest prevalence of substance use during early adolescence. However, African Americans who were early users had significantly higher odds, than did whites or Hispanics, of having a substance use disorder in adulthood.
- Early substance users were also significantly more likely to have a psychiatric disorder in adulthood.

Comments: These prospectively collected data suggest that early substance use is associated with later abuse and dependence. However, they do not definitively answer whether early use is a marker for the risk, or a cause, of a later problem. The study also suggests that an ethnic group with a lower prevalence of early substance use is not necessarily protected from the development of dependence.

Richard Saitz, MD, MPH

Reference: Gil AG, et al. Associations between early-adolescent substance use and subsequent young-adult substance use disorders and psychiatric disorders among a multiethnic male sample in South Florida. *Am J Pub Health.* 2004;94(9):1603–1609.

Adolescent Health Behaviors Predict Adult Behaviors and Consequences

Two cohort studies in Finland examined how adolescent tobacco and alcohol use influence both adult use of these substances and related consequences.

In one study of 903 students followed from age 15 through 28, adolescent drinking predicted adult drinking. Further, both early alcohol and tobacco use predicted later smoking. The prevalence of smoking at age 28 among those who had not smoked at age 15 was significantly greater for those who had drunk, compared with those who had not drunk, during adolescence (27% vs. 18%).

The other study included a population-based sample of 10,943 people whose data from a questionnaire on substance use was gathered at age 14 and then linked to national crime and hospital registries covering the subsequent 17–18 years. Analyses were adjusted for social class, family type (two-parent or single-parent), school performance, and other substance use.

- Men who had been occasionally or often intoxicated at age 14, compared with those who had never been intoxicated, were significantly more likely as adults to have a driving-while-intoxicated (DWI) offense (odds ratios, ORs, 1.7 and 2.9, respectively) and to be treated in a hospital for addiction (ORs 2.5 and 7.5, respectively).
- Early smoking was also significantly associated with later DWI and hospital addiction treatment among men (OR 1.5 for experimental and 4.3 for daily use and DWI; OR 4.5 for daily use and hospitalization).
- Women who had been often intoxicated at age 14 were more likely to have a later DWI offense (OR 7.4, p=0.09). All other findings for women were non-significant.

Comments: These studies suggest that adolescent risk behaviors continue into adulthood, and that one risk behavior can lead to other risk behaviors and to serious consequences later in life. These findings highlight the importance of preventing alcohol and tobacco use in adolescence to avoid serious problems—including tobacco dependence, driving while intoxicated, and addiction—in adulthood.

Richard Saitz, MD, MPH

References: Paavola M et al. Smoking, alcohol use, and physical activity: a 13-year longitudinal study ranging from adolescence into adulthood. *J Adol Health*. 2004;35(3):238–244; Riala K, et al. Teenage smoking and substance use as predictors of severe alcohol problems in late adolescence and in young adulthood. *J Adol Health*. 2004;35(3):245–254.

Use of Youth Substance Abuse Treatment Versus the Justice System: Race is a Factor

Racial and ethnic disparities exist among youth who become involved with the juvenile justice system. Whether disparities exist in youth access to substance abuse treatment is less clear. To examine possible disparities in treatment use and how they may relate to justice system involvement, researchers assessed 420 adolescents aged 13–18 years who had received services from at least one public service sector (e.g., substance abuse treatment, social services, juvenile justice) and met DSM-IV criteria for substance abuse and/or dependence in the past year.

- Non-whites were much less likely than whites to have received outpatient substance abuse treatment during the past year (odds ratio, OR, 0.4).
- They were also much more likely to be involved in the juvenile justice system than to have received specialty alcohol or drug treatment (OR 10.2).

Comments: Non-white adolescents in the public system, compared with white adolescents, receive less appropriate care for substance abuse and dependence. They are much less likely to receive outpatient addiction treatment services and more likely to be involved in the justice system where their health needs may not be adequately addressed. As suggested by the authors, all adolescents— regardless of where they come into contact with the public service system— should be assessed for addictions and linked with treatment as appropriate.

Rosanne T. Guerriero, MPH

Reference: Aarons GA, et al. Race/ethnic disparity and correlates of substance abuse service utilization and juvenile justice involvement among adolescents with substance use disorders. *Journal of Ethnicity in Substance Abuse*. 2004;3(1):47–64.

Geography, Sociodemographic Factors, and the Risk of Substance Use Disorders

Few studies have compared the sociodemographic factors associated with drug use among people in urban, rural, and metropolitan areas. To examine whether residence in these areas modifies the relationship between sociodemographic factors and substance use disorders, researchers employed a nationally representative survey of 8098 adults in the United States aged 15–54 years.

- African Americans were significantly protected against substance use disorders in rural (odds ratios, OR, from 0.2 to 0.3) and urban (ORs from 0.2 to 0.3), but not metropolitan, areas.
- Workers in services (ORs from 2.2 to 4.4) and craft (ORs from 2.3 to 3.7) occupations, compared with those not in the labor force, were significantly more likely to have a substance use disorder in most geographic areas (borderline significant increased odds of drug abuse and dependence for rural service workers).
- Metropolitan residents in all occupations (compared with those not in the labor force) and people with no health insurance in all geographic areas (compared with those with private insurance) were also significantly more likely to have a substance use disorder.

Comments: This study suggests that geographic context and occupation type may impact risk of substance use disorders for some people. The relationship between these two variables is complex (certain occupations increased odds regardless of geographic context, while residents in one geographic area had higher odds regardless of occupation). However, the relationship between geography, insurance status, and the likelihood of a substance use disorder appears clear—those without health insurance had higher odds no matter where they lived.

Peter Friedmann, MD, MPH

Reference: Diala CC, et al. Gender, occupational, and socioeconomic correlates of alcohol and drug abuse among U.S. rural, metropolitan, and urban residents. *Am J Drug Alcohol Abuse.* 2004;30(2):409–428.

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