Alcohol and Health: Current Evidence

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Alcohol and Health Outcomes

Moderate Drinking Lowers MI Risk in Men With Healthy Lifestyles

Some researchers suggest that moderate drinkers have a lower risk of myocardial infarction (MI) because of healthy lifestyles and not alcohol use. To assess this possibility, researchers examined MI, drinking, and healthy lifestyle factors in men—selected from the 51,529 participants of the Health Professionals Follow-up Study—who were free of cardiovascular disease, most cancers, and diabetes at study entry. Healthy lifestyle factors included a body mass index of <25; moderate-to-vigorous activity for >=30 minutes per day; abstinence from smoking; and a healthy diet.*

- Regardless of drinking, men with more healthy lifestyle factors had much lower rates of MI during 16 years of follow-up.

Approximate Rates of MI per 100,000 Person Years

# of Healthy Lifestyle Factors	Non-drinkers	Drinkers of ≈1-2 drinks/day
0-1	575	400
4	275	100

- Among 8867 men with all 4 healthy lifestyle factors (106 with MI), those who drank approximately one half to 2 drinks per day had a significantly lower MI risk than did nondrinkers (relative risks in fully adjusted analyses ranged from 0.3 to 0.5).

Comments: This study illustrates that rates of MI decrease markedly as the number of healthy lifestyle factors increases. Still, regardless of other factors, moderate alcohol use lowers rates further. These results tend to refute the hypothesis that the lower risk of coronary heart disease among moderate drinkers is due to their associated healthy lifestyle habits and not their alcohol consumption.

R. Curtis Ellison, MD

*Determined by a food questionnaire and healthy eating index; defined as an index score in the top 50% of participant scores

Reference: Mukamal KJ, et al. Alcohol consumption and risk for coronary heart disease in men with healthy lifestyles. *Arch Intern Med.* 2006;166(19):2145–2150.

Drinking Increases the Risk of Sunburn

Alcohol consumption may increase the risk of basal cell carcinoma and melanoma, although data are inconclusive. In this study, a researcher explored whether drinking may increase the risk of sunburn—a known risk factor for skin cancer. He examined data from 299,658 respondents (response rate 77%) to the 2004 Behavioral Risk Factor Surveillance System, a national telephone survey.

- One third of adults reported sunburn (red skin for more than 12 hours) in the past year.
- Respondents with a heavy drinking episode (>=5 drinks on an occasion in the past month) were more likely than those without a heavy drinking episode to report sunburn (52% vs. 30%, a significant difference in adjusted analyses).

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Drinking Increases the Risk of Sunburn (continued from page 1)

- Respondents who usually drank <1 to >=3 standard drinks per day in the past month also had an increased prevalence of sunburn. Their risk generally increased as the amounts they consumed increased (odds ratios comparing drinkers with nondrinkers ranged from 1.2 to 1.4 in analyses adjusted for demographic and behavioral factors).
- An estimated 18% of all sunburns were attributable to alcohol use.

Comments: Because the findings are from a cross-sectional survey, they should be confirmed in other studies. But, it is certainly plausible that excess sun exposure can be added to the list of risky behaviors associated with alcohol.

Richard Saitz, MD, MPH

Reference: Mukamal KJ. Alcohol consumption and self-reported sunburn: a cross-sectional, population-based survey. *J Am Acad Dermatol.* 2006;55(4):584–589.

Randomized Trial Shows Patients With Diabetes and MI Benefit From Red Wine

Observational studies suggest that moderate alcohol consumption reduces myocardial infarction (MI) risk in most populations, including patients with diabetes. Clinical trial data, however, are lacking.

In this randomized trial, 131 subjects with diabetes who had recently suffered an initial MI were advised to consume a Mediterranean-type diet and either drink 4 ounces of red wine daily or abstain. At baseline and 12 months later (n=115), researchers measured cardiac function and markers of inflammation and oxidative stress (none of which differed between the groups at baseline).

- At follow-up, markers of both inflammation (i.e., C-reactive protein, tumor necrosis factor-α, interleukin-6, and interleukin-18) and oxidative stress (i.e., nitrotyrosine) were significantly lower in the intervention group than in the control group.
- Cardiac function was also better in the intervention group (i.e., lower myocardial performance index and higher transmitral Doppler flow, pulmonary venous flow, and ejection fraction).
- Changes in concentrations of nitrotyrosine, C-reactive protein, tumor necrosis factor-α, and interleukin-6 were positively related to changes in the cardiac function markers.
- Weight loss and diet did not differ between the groups.

Comments: This study found that, over 1 year, many measures of inflammation and ventricular function in subjects with diabetes and a recent MI were better in those advised to drink red wine daily than in those advised to abstain. While this was an unblinded trial without detailed compliance data, indirect evidence (e.g., food diaries) suggests that most subjects followed the advice given. Further, weight loss and diet were not different between the groups, implying that the changes seen were likely related to wine consumption.

R. Curtis Ellison, MD

Reference: Marfella R, et al. Effect of moderate red wine intake on cardiac prognosis after recent acute myocardial infarction of subjects with Type 2 diabetes mellitus. *Diabet Med.* 2006;23(9):974–981.

Cabernet Sauvignon Reduces Brain Amyloid Deposits in Mice

According to observational data, moderate wine consumption may reduce the risk of dementia, including Alzheimer's disease (AD). To examine this possibility, researchers assessed cognitive function and neuropathology inTg2576 mice, which are bred to model human AD, after the mice randomly received Cabernet Sauvignon, ethanol, or only water each day for 7 months. Mice received the Cabernet Sauvignon or ethanol in their drinking water and consumed the human equivalent of approximately 1–2 drinks per day.

At 7 months, food and fluid intake and body weight did not differ among the Tg2576 mice. Compared with Tg2576 mice who received ethanol or water, Tg2576 mice who received Cabernet Sauvignon had

- better cognitive function (measured by a maze behavioral test);
- fewer indicators of AD-type neuropathology (i.e., lower concentration of amyloid beta–protein [Aβ] peptides and less amyloid plaque burden);
- greater non-amyloidogenic processing of amyloid precursor protein, which helps prevent Aβ peptide generation.*

Results did not significantly differ among Tg2576 mice who received ethanol or water.

Comments: This study suggests that the polyphenols in Cabernet Sauvignon, but not ethanol, attenuated AD-type cognitive deterioration by modulating AD-amyloid neuropathology in the brains of mice bred to model the disease in humans. These results, along with findings from some epidemiological studies, support the premise that moderate wine consumption may decrease the risk of Alzheimer's disease.

R. Curtis Ellison, MD

*From analyses that compared only the Cabernet Sauvignon and ethanol groups

Reference: Wang J, et al. Moderate consumption of Cabernet Sauvignon attenuates Aβ neuropathology in a mouse model of Alzheimer's disease. *FASEB J.* 2006;20(13):2313–2320.

Early-Onset Alcohol Dependence Is More Severe

Early age of drinking onset (e.g., before age 14 years) is known to increase the risk of developing alcohol dependence. Researchers analyzed data from a national interview survey to determine how age of onset of alcohol dependence affects the disease's course.

- Among 4778 persons who ever had alcohol dependence, approximately 79% developed the disease before age 30 years (e.g., 15% before age 18 years, 69% before age 25 years).
- In analyses adjusted for potential confounders, people who first had dependence before age 25 years were less likely than those who developed dependence at age 30 or older to ever seek help.
- However, those with an earlier onset had more episodes of dependence, episodes lasting >1 year, and dependence symptoms.

Comments: These findings are important because they suggest that early drinking increases the risk of dependence *and* that early-onset dependence is more severe than later-onset dependence. Clearly, prevention and even treatment efforts should reach people at a young age, when most cases of alcohol dependence develop.

Richard Saitz, MD, MPH

Reference: Hingson RW, et al. Age of alcohol-dependence onset: associations with severity of dependence and seeking treatment. *Pediatrics.* 2006;118(3):755–763.

Heavy Drinking May Quicken HIV Progression

Unhealthy alcohol use and human immunodeficiency virus (HIV) are both prevalent conditions and frequently co-exist. The relationship between unhealthy alcohol use and HIV disease progression, however, is poorly understood.

To explore this relationship, researchers randomized 32 male rhesus macaques to receive, on 4 consecutive days per week for the entire study, either a sucrose solution or an ethanol solution (enough to achieve a plasma concentration of 50 to 60 mM). After 3 months, 16 of the macaques (8 in the ethanol group and 8 in the sucrose group) were inoculated with simian immunodeficiency virus (SIV).

- The ethanol and sucrose groups did not differ on serum chemistries or blood counts before SIV inoculation.
- Neither ethanol treatment nor SIV inoculation significantly affected body weight, serum chemistries, or blood counts, including CD4 cell counts.
- Of the macaques with SIV, plasma viral load was significantly higher in the ethanol group (448±28 copies/mL) than in the sucrose group (362±22copies/mL) 30 to 120 days after inoculation.

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Heavy Drinking May Quicken HIV Progression (continued from page 3)

- SIV disease progression, characterized by conditions such as persistent anorexia and opportunistic infection, was much quicker in the ethanol group (median survival of 374 days) than in the sucrose group (median survival of 900 days).

Comments: This study in an animal model of HIV disease suggests that heavy alcohol use among people infected with HIV would increase viral load and accelerate disease progression. These results support the practice of identifying and addressing unhealthy alcohol use in patients with HIV.

Joseph Conigliaro, MD, MPH

Reference: Bagby GJ, et al. Chronic binge ethanol consumption accelerates progression of Simian Immunodeficiency Virus Disease. *Alcohol Clin Exp Res.* 2006;30(10):1781–1790.

As Per Capita Alcohol Consumption Increases, So Does Sickness Absence

Heavy drinking is associated with an increased risk of many illnesses. In this study, researchers examined the relationship between alcohol use and job absence due to sickness from 1935 to 2002 in Sweden. They linked population-level data on alcohol sales to health insurance and workforce survey data. Analyses controlled for unemployment and wages over time.

- For men, a one-liter increase in per capita alcohol consumption was associated with an estimated 11% to 21% increase in sickness absence.
- From 1998 to 2002, the rate of sickness absence in men increased by 76%. Alcohol consumption accounted for 6% of this increase (according to projected estimates).
- For women, alcohol consumption was not significantly related to sickness absence.

Comments: The relationship between population-level alcohol use and harms (such as accidents and cirrhosis) is well established. The current study documents another harm, sickness absence. Among alcohol's adverse effects on productivity and workplace performance, absenteeism is likely the "tip of the iceberg." For this reason, alcohol consumption, even after hours, by workers should be a legitimate concern of clinicians who practice in employee health settings or are involved with workplace prevention initiatives and employee assistance programs.

Peter D. Friedmann, MD, MPH

Reference: Norström T. Per capita alcohol consumption and sickness absence. *Addiction.* 2006;101(10):1421–1427.

Assessments and Interventions

Brief Intervention in Primary Care: Does It Really Work in Practice?

Although the efficacy of brief intervention (BI) for unhealthy alcohol use in primary care patients is established, important implementation questions remain (e.g., who should deliver a BI?; how effective is BI in general clinical practice?). To address these issues, researchers evaluated BI among a randomly selected sample of adult risky drinkers* in 15 clinics within 5 managed care organizations.

Clinics were randomly assigned to provide 1 of the following: BI by licensed practitioner (MD, NP); BI by mid-level professional (nurse); or no BI. Follow-up was completed by 1329 subjects (of 2923) at 3 months and 737 at 12 months.

- At 3 months, patients who received BI as well as those who did not had significant decreases in consumption from baseline.
- A greater proportion of intervention than control patients decreased consumption by >=1 drinks per week (60% vs. 53%).
- Decreases and differences between groups persisted at the 12-month follow-up.
- Provider type (licensed or mid-level) did not significantly affect the results.
- The estimated cost of BI ranged between $2.82 and $4.16.

Comments: This effectiveness study had substantial loss to follow-up. Still, its findings suggest that BI can be implemented at a defined cost in managed-care primary care settings and may produce modest decreases in alcohol consumption, whether delivered by a physician, nurse practitioner, or nurse. No cost-effectiveness outcomes were described despite the article's title.

Jeffrey Samet, MD, MA, MPH

*Assessed with adapted versions of the first 3 questions of the Alcohol Use Disorders Identification Test (AUDIT); defined as AUDIT scores of >=7 for women or older men and >=8 for younger men

Reference: Babor TF, et al. Brief interventions for at-risk drinking: patient outcomes and cost-effectiveness in managed care organizations. *Alcohol Alcohol.* 2006;41(6):624–631.

Can Treatment or AA Lower Mortality Risk in People With Alcohol Use Disorders?

The risk of death is higher in people with alcohol use disorders (AUDs) than in those without. To determine whether professional treatment or participation in Alcoholics Anonymous (AA) could decrease this risk, researchers assessed rates and predictors of mortality over 16 years in 628 patients (53% men; 81% white) who sought help for their AUDs for the first time at study entry.

During follow-up, 121 patients died. The overall death rate was 22% for men and 17% for women. Sixty-eight percent of patients with a known cause of death died from an alcohol-related condition. In analyses adjusted for baseline characteristics, death rates were significantly lower for subjects with the following 1 year after study entry:

- No drinking-related problems or dependence symptoms
- Remission (i.e., abstinence or no heavy drinking or drinking-related problems)
- Shorter length (<3 weeks) of inpatient care combined with remission or no drinking-related problems
- Longer length (>8 weeks) of outpatient care combined with no drinking-related problems
- Longer length (>4 months) of AA participation, particularly when combined with any positive drinking outcome (e.g., remission)

Comments: This study suggests that longer duration of outpatient care and AA participation—but not inpatient care—can help prevent death in patients with AUDs. Clinicians should aggressively engage patients with AUDs for whom initial inpatient therapy is insufficient to continue outpatient treatment and AA.

Joseph Conigliaro, MD, MPH

Reference: Timko C, et al. Predictors of 16-year mortality among individuals initiating help-seeking for an alcoholic use disorder. *Alcohol Clin Exp Res.* 2006;30(10):1711–1720.

Naltrexone With Compliance Therapy Is No Better Than Placebo for Alcoholism

The COMBINE Study recently showed that naltrexone, but not acamprosate, with medical management has modest efficacy in treating alcohol dependence. In a similar study conducted at 3 treatment centers across Australia, researchers randomized 169 subjects with alcohol dependence to receive naltrexone (50 mg per day), acamprosate (1998 mg per day), or placebo for 12 weeks. All subjects were offered 4 to 6 sessions of compliance therapy (CT);* 118 (70%) completed the study.

- Neither naltrexone/CT nor acamprosate/CT was significantly more effective than placebo/CT at extending the time to first drink, delaying a return to heavy drinking,** increasing days abstinent, or decreasing consumption, dependence severity, or craving.
- These null results remained even among the 94 subjects who completed the study with 80% compliance.
- Naltrexone was significantly associated with a longer time to heavy drinking among subjects with, at baseline, minimal depressive symptoms (25 and 35 days longer than with placebo or acamprosate, respectively) or low severity of alcohol dependence (42 days longer than with acamprosate).

Comments: This study's findings suggest that naltrexone might have limited utility in settings (such as typical primary care practices) that cannot deliver the 9 sessions of fairly intensive medical management used in the COMBINE study. Nonetheless, naltrexone might prove useful, if validated in future studies, among patients with low levels of depressive symptoms or dependence.

Peter D. Friedmann, MD, MPH

*A brief intervention provided by psychologists and other clinical staff that addressed potential barriers to treatment compliance, such as ambivalence and misperceptions about medication
**>=6 drinks for men, >=4 drinks for women

Reference: Morley KC, et al. Naltrexone versus acamprosate in the treatment of alcohol dependence: a multi-centre, randomized, double-blind, placebo-controlled trial. *Addiction.* 2006;101(10):1451–1462.

Combined Carbamazepine and Tiapride for Alcohol Withdrawal

Combined treatment with the antiepileptic carbamazepine and the dopamine antagonist tiapride may be effective for mild-to-moderate alcohol withdrawal. In this retrospective descriptive study, researchers reviewed medical records at 5 psychiatric hospitals and identified 540 patients admitted for alcohol detoxification and treated with the combination of carbamazepine and tiapride.

Treatment dosage and frequency varied (e.g., average of 543 mg carbamazepine and 796 mg tiapride on day 1; 680 mg and 1035 mg, respectively, on day 2; and tapered doses through day 10). Twenty-eight percent of subjects ended treatment prematurely.

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Combined Carbamazepine and Tiapride (continued from page 5)

- Nineteen percent of subjects had prior alcohol withdrawal delirium, and 28% had a prior alcohol withdrawal seizure.
- During treatment, 2% had delirium, and 1% had seizure. Eight percent experienced medication side effects, whereas 2% showed no improvement.
- Scores on the Clinical Institute Withdrawal Scale – Alcohol, used to assess withdrawal, averaged 12.3 (moderate withdrawal) on day 1 of treatment and gradually decreased to 2.6 on day 9.

Comments: In this study, the incidences of alcohol withdrawal delirium and seizure were relatively low, even though a substantial minority of patients reported having had these complications previously. However, whether the low occurrence of complications was due to combined carbamazepine and tiapride cannot be ascertained from this study because of the lack of a control group and uncertainty about how patients were selected to receive the therapy. Randomized trials are necessary to determine if combining carbamazepine and tiapride is superior or even equally efficacious to standard benzodiazepine therapy.

Kevin L. Kraemer, MD, MSc

Reference: Soyka M, et al. Treatment of alcohol withdrawal syndrome with a combination of tiapride/carbamazepine: results of a pooled analysis in 540 patients. *Eur Arch Psychiatry Clin Neurosci.* 2006;256(7):395–401.

Special Populations

Does Alcohol Increase Risk of Attempted Suicide and Suicidal Ideation in Black Adults?

Risk factors for attempted suicide and suicidal ideation among black adults are not well understood. To identify possible risk factors, researchers conducted a household survey of 5181 black adults in the United States between 2001 and 2003. Respondents completed a full diagnostic interview for psychiatric diagnoses and reported lifetime suicide attempts, ideation, and planning.

- Four percent reported ever having attempted suicide, while 12% reported past suicidal ideation. Of those with past suicidal ideation, 35% had made a suicide plan.
- In analyses adjusted for potential confounders (e.g., age, sex, birth cohort, other psychiatric diagnoses), blacks with alcohol abuse or alcohol dependence had significantly higher risks of attempted suicide (odds ratios [ORs] 4.8 and 5.7, respectively) and suicidal ideation (ORs 3.3 and 4.0, respectively) than did blacks without alcohol diagnoses.
- Eighteen other psychiatric diagnoses were also associated with higher risks of attempted suicide and suicidal ideation. Risks increased with each additional psychiatric diagnosis.

Comments: The finding of higher risks of attempted suicide and suicidal ideation among blacks with alcohol abuse and/or alcohol dependence is consistent with research on alcohol and suicide in other populations. However, because this paper did not focus only on alcohol diagnoses, it did not report on higher-risk subgroups of blacks with alcohol diagnoses or on the effect of alcohol treatment. Nevertheless, this research underscores the need to carefully assess suicidal ideation and plans among blacks with alcohol abuse and/or dependence.

Kevin L. Kraemer, MD, MSc

Reference: Joe S, et al. Prevalence of and risk factors for lifetime suicide attempts among blacks in the United States. *JAMA*. 2006;296(1):2112–2123.

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