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Alcohol and Health: Current Evidence

JULY-AUGUST 2005

ALCOHOL AND HEALTH OUTCOMES

Risky Drinking Limits: National Recommendations Make Sense

Some clinicians question the drinking limits* defined by national guidelines. They are uncertain whether exceeding these limits, even slightly, causes serious health consequences. To examine the association between exceeding drinking limits and alcohol abuse and dependence (which include a range of health consequences), researchers analyzed data from a nationally representative sample of 26,946 adult drinkers.

- Approximately 37% of subjects who exceeded daily limits about once per week had current alcohol dependence and/or abuse.
- As the frequency of exceeding daily limits increased, the prevalence of dependence increased (from 0.4% among those who never exceeded daily limits to 41% among those who exceeded these limits daily or almost daily).
- Exceeding weekly limits significantly increased the prevalence of dependence among drinkers who *never exceeded daily limits* (2% of those who exceeded weekly but not daily limits versus 0.3% of those who exceeded neither limit); or *exceeded daily limits >=2 times per month* (e.g., 27% of those who exceeded weekly plus daily limits twice per week versus 9% of those who exceeded the daily, but not the weekly, limits).

Comments: The more frequently one exceeds daily drinking limits, the greater the risk of consequences. However, recommended drinking limits—like other measures in medicine (e.g., blood pressure)—do not provide a clear threshold above which health consequences will develop. Nonetheless, this study, like others, supports national drinking recommendations, showing that drinking more than the recommended limits is associated with substantial health consequences.

Richard Saitz, MD, MPH
Rosanne T. Guerriero, MPH

*Daily limits defined as <=4 drinks for men, <=3 drinks for women; weekly limits defined as <=14 drinks for men, <=7 drinks for women

Reference: Dawson DA, et al. Quantifying the risks associated with exceeding recommended drinking limits. *Alcohol Clin Exp Res.* 2005;29(5):902–908.

Cautions in Interpreting the Cardiovascular Effects of Moderate Drinking

Moderate drinking has been linked to lower risks of cardiovascular disease (CVD) and death. These potential benefits, however, may be explained by more CVD risk factors in nondrinkers (i.e., confounders). To explore this possibility, investigators at the Centers for Disease Control studied 235,730 adult nondrinkers* and moderate drinkers** who had participated in a nationally representative telephone survey (54% response rate).

- Most (27 of 30) characteristics associated with CVD were significantly more common in nondrinkers than in moderate drinkers.
- Nondrinkers were older; less likely to be white, married, educated, and physically active; and less likely to have a high income, health insurance, a personal doctor, a flu shot, and cholesterol or colorectal cancer screenings.
- Nondrinkers were also more likely to have diabetes, hypertension, obesity, high cholesterol, asthma, poor dental health, arthritis, and poor health status.
- Smoking and male sex were the only CVD risk factors more common in moderate drinkers.

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Cautions in Interpreting Cardiovascular Effects (continued from page 1)

Comments: Many epidemiological studies of moderate drinking have adjusted for certain confounders but have either ignored others (e.g., psychosocial risks) or not accounted for the interactions between confounders (e.g., diabetes and lack of health insurance). Although this study examined the prevalence of possible confounders and found that most CVD risk factors were more common in nondrinkers, it did not directly test whether these confounders explained the relationship between alcohol and CVD. A prominent alcohol epidemiologist recently wrote that confounders may largely—or entirely—explain the observed cardiovascular benefits of moderate drinking. Only a large-scale, randomized trial can determine whether alcohol decreases CVD. In the meantime, I agree with the American Heart Association's statement that "there is little current justification to recommend alcohol as a cardioprotective strategy."

Richard Saitz, MD, MPH

*Abstinent for the past 30 days
**<=2 standard drinks per day for men, <=1 for women

References: Naimi TS, et al. Cardiovascular risk factors and confounders among nondrinking and moderate drinking U.S. adults. *Am J Prev Med.* 2005;28(4):369–373; Wannamethee SG. Alcohol and mortality: diminishing returns for benefits of alcohol. *Int J Epidemiol.* 2005;34(1):205–206; Goldberg IJ, et al. Wine and your heart: a science advisory for healthcare professionals from the Nutrition Committee, Council on Epidemiology and Prevention, and Council on Cardiovascular Nursing of the American Heart Association. *Circulation.* 2001;103(3):472–475.

Changes in Alcohol Intake and Subsequent Health Outcomes

To assess how changes in drinking over time may impact coronary heart disease (CHD), stroke, and all-cause mortality, investigators analyzed data from 6544 middle-aged, healthy British men who had participated in a 20-year prospective study on cardiovascular health. During follow-up, 922 men died from CHD or had a nonfatal myocardial infarction, 352 had a stroke, and 1552 died from all causes.

- The relationship between alcohol intake at study entry and the risks of CHD, stroke, and all-cause mortality was generally U-shaped, with the lowest risk for subjects who consumed 1–2 drinks per day or 1–6 drinks per day only on the weekends.
- In analyses that averaged consumption during follow-up (to account for intake over time), the benefits of lighter drinking and the risks of heavier drinking increased. Further, the risks of nondrinking decreased.

Comments: It is laudable to try to account for drinking, and changes in drinking, over time when assessing how alcohol use influences health outcomes. However, the results of this study are difficult to interpret for two major reasons. First, by using one value of "average" intake, investigators cannot accurately assess the effects of changes in drinking over time. Second, grouping subjects who drank small amounts regularly without bingeing with subjects who were weekend bingers is problematic. Researchers should be encouraged to study changes in alcohol intake over time, using appropriate methods, so we can better understand the effects of alcohol on CHD, stroke, and mortality.

R. Curtis Ellison, MD

Reference: Emberson JR, et al. Alcohol intake in middle age and risk of cardiovascular disease and mortality: accounting for intake variation over time. *Am J Epidemiol.* 2005;161(9):856–863.

Alcohol Increases the Urge to Smoke

Many studies have shown a positive association between cigarette smoking and alcohol drinking. To examine this association more closely, researchers assessed the urge to smoke in 16 heavy drinkers/light smokers* who all drank the following (one beverage per test session): a placebo beverage (with 1% ethanol for taste), a low dose of alcohol (approximately 2 drinks), and a high dose of alcohol (approximately 4 drinks). Subjects refrained from smoking 2 hours before and throughout the test sessions. They reported their urges to smoke at baseline and after consuming the drinks.

- Both the high and low doses of alcohol, compared with placebo, significantly increased the urge to smoke for stimulation. The high dose of alcohol produced the greatest increases.
- The high and low doses of alcohol, compared with placebo, produced similar, but nonsignificant, increases in the urge to smoke to relieve negative mood and withdrawal.
- Baseline smoking levels did not significantly affect the results.

Comments: In this experiment, alcohol use produced dose-dependent increases in the urge to smoke in heavy-drinking, cigarette-deprived light smokers. Urge increases were stronger for positive reinforcing effects (stimulation) than for negative reinforcing effects (to relieve negative mood and withdrawal). Given these results, clinicians should consider advising alcohol abstinence when helping patients to stop smoking.

Joseph Conigliaro, MD, MPH

*Those without alcohol dependence who consumed 10–40 drinks per week with at least 1 weekly binge (>=5 drinks per occasion for men, >=4 for women) and smoked at least 3 times per week but <12 cigarettes per smoking day

Reference: King AC, et al. Alcohol dose-dependent increases in smoking urge in light smokers. *Alcohol Clin Exp Res.* 2005;29(4):547–552.

INTERVENTIONS

Screening for Unhealthy Alcohol Use with 1 or 2 Questions

Simplifying strategies to screen for unhealthy alcohol use (i.e., consumption of risky amounts or an alcohol use disorder) remains a formidable task. One desired outcome of simplification efforts is a briefer screening test. To compare the performances of some brief tests to detect unhealthy alcohol use, investigators screened 1537 emergency department patients with an acute injury, 1151 emergency patients with a medical illness, and 1112 randomly selected people who were contacted by telephone.

Researchers asked each subject a question about alcohol consumption in a day ("When was the last time you had more than X drinks in 1 day?" with X being 5 for men and 4 for women); a question about average consumption per occasion; and a standard question about drinking frequency. Diagnostic interviews determined the presence of an alcohol use disorder and validated calendar methods determined drinking amounts.

The question about consumption in a day, when answered "in the past 3 months," performed the best. Its respective sensitivities and specificities were 85% and 70% in men and 82% and 77% in women. Findings were similar when screening was conducted in person or by telephone.

Comments: This study suggests that asking one straightforward question can identify unhealthy alcohol use, providing yet more evidence of the utility of very brief alcohol screening tests. Further, the efficacy of screening by phone may allow the collection of some alcohol-related data before the clinician-patient encounter.

Jeffrey Samet, MD, MA, MPH

Reference: Canagasaby A, et al. Screening for hazardous or harmful drinking using one or two quantity-frequency questions. *Alcohol Alcohol.* 2005;40(3):208–213.

Talking with Patients Resistant to Changing Their Drinking

When talking with patients about alcohol, physicians may encounter "reactance," patient resistance to relinquishing control in interpersonal situations. Signs of this resistance include arguing, changing the subject, and generally responding negatively. To understand how clinicians should approach resistant patients, researchers observed counseling sessions of adults with alcohol dependence who had participated in a randomized trial of 3 standardized psychosocial therapies (that turned out to be equally effective). Researchers tested the relation between what clinicians said and drinking outcomes in 141 patients 1 year after treatment.

- Among resistant patients, clinician directiveness—characterized by closed-ended questions, interpretation, confrontation, topic initiation, education, and advice giving—was significantly associated with fewer abstinent days and more drinks per drinking day.
- However, among patients with low resistance, directiveness did not significantly affect drinking outcomes.

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Talking with Patients Resistant to Changing Their Drinking (continued from page 3)

Comments: This study suggests that when patients appear to resist changing their drinking, clinicians should avoid the natural tendency to give information and advice. What should we do when talking with resistant patients in general health care settings? Although not addressed directly by this research, prior studies of motivational interviewing suggest that we should encourage patients to talk about what they find most important and then should spend most of our time listening and demonstrating that we have heard them.

Richard Saitz, MD, MPH

Reference: Karno MP, et al. Less directiveness by therapists improves drinking outcomes of reactant clients in alcoholism treatment. *J Consult Clin Psychol.* 2005;73(2):262–267.

Monthly Injectable Naltrexone Is Efficacious for Treating Alcohol Dependence

Medications have moderate efficacy for treating alcohol dependence. However, adherence is a great challenge in patients with alcoholism. Researchers tested a new polylactideco-glycolide-based, long-acting formulation of naltrexone in a multicenter randomized trial of 624 patients with alcohol dependence and >=2 heavy drinking episodes* per week in the month before screening. Subjects were assigned to receive injections of either naltrexone (380 mg or 190 mg) or placebo every 4 weeks for 6 months. They were also provided with supportive therapy sessions that included feedback on addiction-related consequences.

- Nausea, fatigue, decreased appetite, dizziness, injection site pain, and discontinuation of injections due to adverse effects were significantly more common in the higher-dose naltrexone group than in the placebo group. Results appeared similar for the lower-dose group.
- The rate of heavy drinking decreased significantly in the higher-dose group and at a borderline significant level in the lower-dose group (hazard ratios 0.8 for both compared with placebo).
- Subgroup analyses indicated that heavy drinking decreased only in men and having abstinence as a treatment goal did not affect the results (though naltrexone's efficacy was greatest in the 8% who had abstained for 7 days before study entry).

Comments: This trial is particularly important among studies of pharmacotherapy for alcohol dependence. It not only highlights the potential advantages of a medication that poses fewer challenges to good adherence, but also did not require patients to stop drinking to enroll. Injectable naltrexone will likely become an attractive adjunct to supportive therapy for people who seek treatment for alcohol dependence.

Richard Saitz, MD, MPH

*>=5 drinks for men or >=4 drinks for women

Reference: Garbutt JC, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence. A randomized controlled trial. *JAMA*. 2005;293(13):1617–1625.

Computerized Brief Intervention Decreases Drinking and Consequences

Time and labor constraints on clinicians have spurred the search for innovative methods to deliver personalized feedback on unhealthy drinking behavior. One such innovation is computer-based brief intervention (BI). To assess the efficacy of computer-based BI to reduce unhealthy alcohol use, researchers conducted a randomized trial of 61 problem drinkers (AUDIT* >=8) who were not in alcohol treatment and were recruited through newspaper advertising. Subjects were assigned to receive a computer-based BI** either shortly after study entry (i.e., intervention group) or at least 4 weeks after entry (i.e., control group).

- At baseline, both groups averaged about 5.6 drinks per day.
- At 4 weeks, the intervention group had significantly greater reductions in their average drinks per day than did the control group (changes from baseline of -3 drinks and -1.5 drinks, respectively). This reduction persisted for the intervention group at 12 months.
- The intervention group also significantly improved from baseline on a number of other drinking measures (e.g., alcohol consequences, readiness to change).

Comments: It seems inevitable that computers will play an ever-larger role in clinical assessment, intervention, and monitoring for a whole host of disorders. This study adds to a growing body of research that supports the effectiveness of individualized, nonthreatening feedback—whether by a human or machine—about drinking.

Peter Friedmann, MD, MPH

*Alcohol Use Disorders Identification Test
**An online version is available at www.drinkerscheckup.com

Reference: Hester RK, et al. The Drinker's Check-up: 12-month outcomes of a controlled clinical trial of a stand-alone software program for problem drinkers. *J Subst Abuse Treat.* 2005;28:159–169.

SPECIAL POPULATIONS

Cost Savings from Alcohol Intervention for Trauma Patients

Brief alcohol interventions for injured patients in emergency departments and inpatient trauma services can decrease future alcohol intake and repeat injuries. To estimate the cost effectiveness of broadly implementing alcohol screening and intervention for these patients, researchers used published data and a decision-analysis model that simulated cost-benefit scenarios under a variety of conditions. Findings from the model include the following:

- Twenty-seven percent of injured adults treated in an emergency department (representing 5.5 million visits per year in the United States) would be candidates for an alcohol intervention.
- Under baseline model assumptions (e.g., for implementation costs, injury rates), each $1 spent on alcohol screening and intervention for trauma patients would save $3.81 in future direct healthcare costs. This corresponds to a net cost savings of $89 per patient screened or $1.82 billion in direct healthcare costs each year.
- When model assumptions were allowed to vary, screening and intervention remained cost saving in 92% of simulations.

Comments: The consistent finding of cost savings over a wide range of conditions lessens concerns raised by the uncertainties in the researchers' baseline assumptions (e.g., high efficacy of intervention, low cost of screening) and decision-analysis model (e.g., lack of consideration for false-positive and false-negative screening results). This well-done analysis lends support to broader implementation and funding for alcohol screening and intervention efforts in emergency departments and trauma services.

Kevin L. Kraemer, MD, MSc

Reference: Gentilello LM, et al. Alcohol interventions for trauma patients treated in emergency departments and hospitals: a cost-benefit analysis. *Ann Surg*. 2005;241(4):541–550.

Early Drinking Increases Later Risky Behaviors in Urban Youth

Early alcohol use can contribute to later sexual and alcohol-related risk behaviors. To examine this association among urban youth—a group with a high prevalence of sexual risk behaviors—researchers surveyed 1034 African American and Hispanic students from Brooklyn. Subjects completed questionnaires in the 7th grade and then again in the 10th grade. Analyses were adjusted for some potential confounders (e.g., age, ethnicity, early sexual initiation).

- In the 7th grade, approximately 25% of students reported ever drinking alcohol; 9% reported drinking in the past month.
- In the 10th grade, prevalence of use greatly increased: 63% reported ever drinking alcohol and 29% reported drinking in the past month.
- Students who had drunk in the 7th grade (versus those who had abstained) were more likely in the 10th grade to report alcohol use, binge drinking, drunkenness, and having an alcohol or drug problem. They were also more likely to report a greater number of sexual partners, unprotected sex, pregnancy, and being drunk or high during sex. Female students who had drunk during the 7th grade were also more likely in the 10th grade to report having had sex.

Comments: Although these analyses were not adjusted for psychosocial risk factors, the results confirm the dangers of early alcohol use. The high prevalence of drinking in 7th graders suggests that screening and prevention programs must begin well before the teenage years. These programs should emphasize alcohol's influence on risky sexual behaviors and related consequences, including exposure to HIV and other sexually transmitted diseases.

Joseph Conigliaro, MD, MPH

Reference: Stueve A, et al. Early alcohol initiation and subsequent sexual and alcohol risk behaviors among urban youths. *Am J Pub Health*. 2005;95(5):887–893.

Drinking May Increase Coronary Calcification in Blacks and Binge Drinkers

Moderate drinking may improve cardiovascular health, possibly by protecting against atherosclerosis. To examine this further, researchers assessed alcohol consumption, coronary heart disease risk factors, and coronary calcification (a marker for atherosclerosis) in 3037 adults during 15 years of follow-up. Subjects were aged 33–45 years at follow-up; 55% were women and 45% were black.

- As alcohol intake increased (from 0 to >=14 drinks per week), HDL cholesterol and blood pressure levels increased while mean C-reactive protein and fibrinogen levels decreased.
- The prevalence of coronary calcification (calcium scores >0 on computed tomography scanning) also increased as drinking increased (8% of those who abstained to 19% of those who drank >=14 drinks per week; *P* for trend <0.001). However, this trend remained significant only in blacks when analyses were stratified by race.
- Coronary calcification occurred more frequently in binge drinkers than in nonbinge drinkers (odds ratio 2.1).
- Adjusting analyses for coronary risk factors did not significantly affect the results.

Comments: This study found that alcohol use does not protect against—but increases—coronary calcification, though increases may be limited to blacks and occur primarily among binge drinkers. Unfortunately, the results are based on a very small number of cases (due to the young age of the cohort) and a definition of coronary calcification that is an inadequate marker for coronary disease. In any case, this and other studies suggest that moderate drinking's reported protection against heart attack may result more from its effects on coagulation than its effects on atherosclerosis.

R. Curtis Ellison, MD

Reference: Pletcher MJ, et al. Alcohol consumption, binge drinking, and early coronary calcification: findings from the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Epidemiol.* 2005;161(5):423–433.

Inherited Differences in Metabolism Influence Risk of Alcohol Dependence

About 50% of a person's risk for alcohol dependence is determined by genetics. Emerging research suggests that this propensity toward dependence may result from inherited differences in metabolism.

Chai and colleagues genotyped 24 Korean men with the early-onset, familial form of alcoholism (Type II), 48 with late-onset alcoholism (Type I), and 38 healthy controls. They found that

- high-active forms of the alcohol dehydrogenases ADH2 and ADH3, which convert ethanol to acetate and acetaldehyde (a toxin that causes flushing and other unpleasant symptoms) were significantly more common in healthy controls and men with late-onset alcoholism than in men with early-onset familial alcoholism;
- active forms of aldehyde dehydrogenase ALDH2, which clears the toxin acetaldehyde, were significantly less common in healthy controls than in men with either type of alcoholism.

Guindalini et al genotyped 92 patients with alcoholism and 92 healthy subjects. They found that the healthy subjects were significantly more likely to have 2 alleles associated with more active (and protective) forms of the alcohol dehydrogenase ADH4 than were patients with alcoholism.

Comments: A metabolic predisposition to produce and accumulate acetaldehyde is protective against alcohol dependence, and these studies have isolated specific genetic targets. After further verification in larger samples, these findings hold great promise for genetic testing and targeted prevention, medication development, and even genetic therapy.

Peter Friedmann, MD, MPH

References: Chai YG, et al. Alcohol and aldehyde dehydrogenase polymorphisms in men with type I and type II alcoholism. *Am J Psychiatry.* 2005;162(5):1003–1005; Guindalini C, et al. Association of genetic variants of alcohol dehydrogenase 4 with alcohol dependence in Brazilian patients. *Am J Psychiatry.* 2005;162(5):1005–1007.

Does Brief Intervention Reduce Drinking in Pregnant Women?

Alcohol use by pregnant women can cause birth defects, developmental disorders, and mental retardation in the exposed fetus. To test if brief intervention reduces prenatal alcohol use, researchers randomized 304 pregnant women—all of whom scored positive on the T-ACE* questionnaire and were drinking (or at risk for drinking**)—to either usual care or a 25-minute brief intervention. On average, women in both groups drank 20% of days and 1.8 drinks per drinking day prior to pregnancy and 5% of days and 1.6 drinks per drinking day at enrollment.

- Both the intervention and usual care groups decreased drinking, from enrollment to delivery, to 2% of days and 0.5 drinks per day (no significant differences between groups).
- Brief intervention was significantly more effective than was usual care at reducing drinking frequency in women who drank more often at baseline.
- Among these heavier-drinking women, those who had a partner participate in the intervention had greater reductions in drinking frequency than did those without partner involvement.

Comments: Although this study did not find an overall effect of brief intervention on prenatal alcohol use, it does highlight that pregnancy can strongly motivate women to change their drinking. Most women substantially decreased their drinking after learning of their pregnancies. The additional decreases in both groups after enrollment suggest that screening and assessment should be routinely performed. Further, targeted interventions deserve further study given that heavier-drinking women responded best to the intervention, especially when their partners were involved.

Kevin L. Kraemer, MD, MSc

*Tolerance, *Annoyed*, *Cut down*, *Eye-opener
**Any alcohol use in the 3 months before study enrollment while pregnant, consumption of at least 1 drink per day in the 6 months before study enrollment, or drinking during a previous pregnancy

Reference: Chang G, et al. Brief intervention for prenatal alcohol use: a randomized trial. *Obstet Gynecol.* 2005;105(1):991–998.

New resource for clinicians…

Helping Patients with Alcohol Problems

A free web-based curriculum on screening and brief intervention for alcohol problems

www.mdalcoholtraining.org

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Contact Information:

Alcohol and Health: Current Evidence
Boston University School of Medicine/
Boston Medical Center
91 East Concord Street, Suite 200
Boston, MA 02118
ahce@bu.edu