# Alcohol and Health: Current Evidence

#### **NOV-DEC 2005**

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# ALCOHOL AND HEALTH OUTCOMES

#### The Perils of Weekend and Holiday Partying

To determine whether popular drinking occasions (e.g., holidays, weekends) are associated with an increased risk of intoxication-related deaths, researchers in Finland analyzed data from a national death registry and a drinking habits survey of 15–69 year-olds. Of the 373,000 deaths that occurred in the study population from 1987 to 2001, 28,622 (8%) were related to alcohol intoxication.

- The risk of intoxication-related death was significantly greater on both the eve and day of holidays than on other days (mortality rate ratios\* for all festivals combined between 1.7 and 2.0).
- The risk of intoxication-related death, as well as blood alcohol concentrations and volume of alcohol consumed, was significantly greater on weekends than on weekdays (mortality rate ratios between approximately 1.1 and 1.6).
- The risk of death from other causes was only slightly elevated on the eve and day of holidays (mortality rate ratios between

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1.03 and 1.08) and not significantly different on the weekends.

*Comments*: Intoxication is more common on weekends and holidays. This study confirms that the risk of intoxication-related death is also greater during these times. Heavy drinking on special occasions (e.g., "just on weekends") is not benign. These findings should be shared with people who think it is.

Rosanne Guerriero, MPH Richard Saitz, MD, MPH

\*Observed number of intoxication-related deaths divided by the expected number of intoxicationrelated deaths; the expected number was the total observed number of intoxication-related deaths during the study timeframe divided by 365.25

Reference: Mäkelä P, et al. Temporal variation in deaths related to alcohol intoxication and drinking. Int J Epidemiol. 2005;34(4):765–771.

#### Cannabinoids, GABA-Benzodiazepine Receptors, and Alcoholism

Twin and other genetic studies have clearly demonstrated that biology contributes substantially to the risk of alcohol dependence. Two recent studies, which add to this evidence, identified a link between central nervous system mechanisms and alcoholism.

In one study, researchers administered the intravenous benzodiazepine midazolam to 11 men with alcohol dependence who were abstinent at enrollment and to 10 men without dependence who drank.

- Neither GABA\*-benzodiazepine receptor occupancy (measured by positron emission tomography) nor the plasma concentration of midazolam differed significantly between the groups.
- However, sleep time after the midazolam infusion (which was measured by electroencephalography and reflects GABA-benzodiazepine receptor function) was significantly lower in men with alcohol dependence (16 versus 34 minutes).

In the second study, two strains of mice were given a choice between ethanol and water. CBI knockout mice (mice bred to have no cannabinoid CBI receptors) drank significantly less ethanol than did wild-type mice (who have these receptors).

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\*Gamma-aminobutyric acid

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#### Cannabinoids (continued from page 1)

*Comments*: The first study implies that men with alcohol dependence have significantly different GABA-benzodiazepine receptor function, which could explain the need for more alcohol to achieve effects. The mouse study found that receptors that play a role in marijuana intoxication and dependence, and obesity are also associated with alcohol intake. Both studies suggest possible etiologies for alcohol dependence and potential targets for alcoholism treatment.

Richard Saitz, MD, MPH

#### Alcohol's Role in Fall-Related Injuries in Younger and Older Adults

Falls can cause substantial morbidity and mortality. To study possible contributions of alcohol and benzodiazepines to falls in adults of all ages, investigators in Austria assessed use of these substances in 1611 injury patients seen in the emergency department of (and later admitted to) a trauma surgery hospital.

- Thirty-eight percent (615) of patients were injured in a fall.
- Men with falls were significantly more likely than women with falls to test positive for alcohol (40% versus 8%), benzodiazepines (9% versus 3%), or both (3% versus 0.3%).
- Patients aged 18–70 years with falls were significantly more likely than those over 70 with falls to test positive for alcohol.
- In an age-matched sample including all patients with injuries, those with falls were significantly more likely than those with other injury causes to test positive

administration and ethanol conditioned place preference are reduced in mice lacking cannabinoid CB1 receptors. *Behav Brain Res.* 2005;164(2):206–213.

References: Lingford-Hughes AR, et al.

GABA-benzodiazepine receptor function

study. Psychopharm. 2005;180(4):595-606;

in alcohol dependence: a combined 11C-

flumazenil PET and pharmacodynamic

Thanos PK, et al. Ethanol self-

for alcohol (50% versus 21% for men; 19% versus 3% for women).

 Use of benzodiazepines alone or with alcohol did not significantly differ between those with falls and those with other injury causes.

*Comments:* Alcohol and, less commonly, benzodiazepines appear to contribute substantially to serious injuries due to falls. Falls are usually viewed as an older-adult problem. However, alcohol's involvement in falls among younger adults in this study emphasizes that further attention should be given to this concern in adults of all ages.

Richard Saitz, MD, MPH

Reference: Kurzthaler I, et al. Alcohol and benzodiazepines in falls: an epidemiological view. *Drug Alcohol Depend*. 2005;79 (2):225–230.

#### Abstainers and Coronary Heart Disease: Are Unknown Risk Factors to Blame?

Epidemiological studies have found that coronary heart disease (CHD) is much less common in light drinkers than in abstainers. To examine whether unknown risk factors might explain this finding, researchers in Finland compared 1161 life-long abstainers with 27,311 light drinkers (those who drank <6 drinks per week). Analyses were adjusted for potential confounders (e.g., sex, age, income).

Of the 16 potential CHD risk factors examined, only low body mass index (BMI) and low leisure-time physical activity were *more* prevalent among abstainers than among light drinkers (odds ratio [OR] 1.3 for BMI <20 versus 20–24.9; OR 1.3 for the lowest amount of exercise versus the highest amount).

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#### Abstainers and Coronary Heart Disease (continued from page 3)

• Five of the risk factors (smoking, insomnia, anxiety, low reward for work effort, and adverse life events) were less prevalent among abstainers (ORs ranging from 0.2 to 0.8).

*Comments*: To exclude alcohol use as the reason for less CHD in light drinkers, an unknown risk factor would have to be much more prevalent in abstainers than in light drinkers. None of the 16 CHD risk factors examined in this study met this criterion. Nonetheless, the possibility of a multifactorial or other unknown explanation remains possible.

It should be noted that these findings differ from those of a

Does Drinking Affect Pneumoconiosis?

Drinking adversely affects a range of comorbid illnesses. Little is known, however, about its impact on pneumoconiosis. Researchers recruited 300 Chinese patients with pneumoconiosis from a community-based case registry and examined the prevalence and effects of alcohol consumption on healthrelated quality (HRQOL) and lung function (defined as predicted forced expiratory volume in 1 second [FEV1%]).

- Seventy-two percent reported being abstinent in the past year. Among the drinkers, 88% consumed <7 drinks per week, and none drank >21 drinks per week.
- Drinkers were younger and had less concurrent medical illness than did nondrinkers.
- Drinkers also had significantly better HRQOL and FEV1%, though findings for the latter were of borderline significance when analyses adjusted for potential confounders

recent American study, probably because nondrinkers in this Finnish cohort were *lifetime* abstainers rather than previous drinkers who may have quit due to poor health. Given the abundance of observational studies on moderate drinking, only a well-designed randomized controlled trial could provide more definitive evidence. Peter Friedmann, MD, MPH

Reference: Poikolainen K, et al. Alcohol and coronary heart disease risk-is there an unknown confounder? *Addiction*. 2005;100(8):1150-1157.

(e.g., age, concurrent medical illness).

*Comments*: In this cross-sectional evaluation, few Chinese patients with pneumoconiosis consumed any alcohol, and few of the drinkers drank heavily. Drinkers had better HRQOL and (potentially) lung function than did non-drinkers, perhaps because healthier people chose to drink. The impact of heavy drinking on people with pneumoconiosis remains unknown.

Joseph Conigliaro, MD, MPH

Reference: Tang WK, et al. Alcohol consumption, lung function, and quality of life in pneumoconiosis. *Alcohol Clin Exp Res.* 2005;29(7):1230–1236.

# Alcohol Consumption and Subclinical Carotid Atherosclerosis

While many studies have linked alcohol intake with vascular diseases, few have examined its association with subclinical atherosclerosis. In this study, researchers assessed whether alcohol intake could decrease carotid intima-media thickness (IMT, a marker for atherosclerosis severity) in 1230 male and 1190 female participants of a health study in northeastern Germany.

- In analyses adjusted for age, diabetes, systolic blood pressure, smoking status, lifestyle patterns, and education, the relationship between IMT and alcohol intake in men was J-shaped. Men who drank between 5 and 6 drinks per day had the lowest mean IMT.
- This relationship became borderline significant when analyses adjusted for either HDL or fibrinogen, and became nonsignificant when analyses adjusted for both.
- Alcohol intake did not significantly affect IMT in women.

*Comments:* The results of this study add to the conflicting picture of alcohol's effects on subclinical atherosclerosis, whether estimated by carotid IMT or by calcified plaque in the coronary arteries. While this study found a beneficial effect on IMT from high levels of alcohol intake in men, many other studies have shown little or no effect. These findings suggest that cardiovascular events prevented by moderate drinking may be due more to factors affecting clotting and endothelial function than to atherosclerosis. R. Curtis Ellison, MD

*Reference:* Schminke U, et al. Association between alcohol consumption and subclinical carotid atherosclerosis. The Study of Health in Pomerania. *Stroke.* 2005;36(8):1746–1752.

# INTERVENTIONS

#### The Cost-Effectiveness of Alcohol Interventions

Healthcare systems and funding agencies often use costeffectiveness data to make resource-allocation decisions about which treatment options to offer patients. Two recent reviews illustrated different approaches to cost-effectiveness analysis as applied to alcohol interventions.

In the first study, researchers used computer simulation models and published data from alcohol intervention trials to estimate the incremental cost-effectiveness (CE) ratio (i.e., dollars\* needed for each quality-adjusted life-year [QALY] gained) of several approaches to treating problem drinking and alcohol dependence.

- Various brief interventions for problem drinking yielded CE ratios of \$62 to \$505 per QALY (compared with no intervention).
- Motivation enhancement therapy (MET), which focuses on motivation and commitment to change, yielded CE ratios of \$1613 to \$2531 per QALY (compared with an initial assessment, feedback, and education).
- Naltrexone plus counseling for severe alcohol dependence yielded a CE ratio of \$9750 per QALY (compared with placebo plus counseling).

In the second study, researchers performed a cost-effectiveness analysis within a randomized clinical trial of MET (n=347) versus social behavior and network therapy (n=261) for alcohol problems. They collected data on treatment costs,\*\* health and societal resources use, and QALYs.

#### Can Folate Block Some of Alcohol's Potential Harms?

Two recent studies examined whether folate intake moderates alcohol's effects on health outcomes. In the first study, researchers from Australia followed 17,447 women (aged 40–69 years at recruitment) for 9–13 years to assess whether folate affected breast cancer risk among moderate drinkers. During follow-up, 537 invasive breast cancers were diagnosed (according to a cancer registry).

- In analyses adjusted for potential confounders (e.g., total calorie intake), women who consumed an average of >=3 drinks per day at baseline had a nonsignificantly higher hazard of breast cancer than did abstainers\* (hazard ratio [HR] 1.4).
- Folate intake was not directly associated with risk of breast cancer. However, a high folate intake mitigated the

- The more expensive social behavior and network therapy yielded the same number of QALYs as did MET.
- Social behavior and network therapy cost \$331 on average and yielded a net reduction in resource use of \$1195 whereas MET cost \$193 on average and yielded a net reduction of \$888.

*Comments*: In the first study, the CE ratios for most interventions examined were well below what purchasers of healthcare commonly pay to treat other diseases (e.g., \$50,000 to \$100,000 per QALY). In the second study, the social behavior and network therapy program was more expensive, but no more effective, than was MET. Regardless, both therapies saved about 5 times as much in health and societal resources use as they cost to deliver. Kevin L. Kraemer, MD, MSc

\*For purposes of this summary, 2003 Australian dollars were converted to 2003 US dollars using historical exchange rates. \*\*For purposes of this summary, 2001 UK pounds were converted to 2001 US dollars using historical exchange rates.

References: Mortimer D, et al. Economic evaluation of interventions for problem drinking and alcohol dependence: cost per QALY estimates. *Alcohol Alcohol.* 2005;40(6):549–555; UKATT Research Team. Cost effectiveness of treatment for alcohol problems: findings of the randomized UK alcohol treatment trial (UKATT). *BMJ.* 2005;331(7516):544.

risk associated with drinking. The hazard ratio of breast cancer associated with drinking >=3 drinks per day (compared with abstaining) was

- 2.0 for women with a daily folate intake of 200 µg;
- 0.8 (a nonsignificant difference) for those with a daily intake of 400 µg.

In the second study, researchers conducted a crosssectional analysis of 988 women to assess the relationship between alcohol, folate, and homocysteine (which, when elevated, raises the risk of heart disease). Analyses were also adjusted for potential confounders.

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#### Can Folate Block Some of Alcohol's Potential Harms? (continued from page 4)

- Of women with the lowest folate intake (<288 µg of folate per day), those who consumed approximately >=1 drink per day had significantly higher homocysteine levels than did lighter drinkers and nondrinkers.
- The opposite was true for those with the highest folate intake (>720 µg of folate per day): among these women, those who drank >=1 drink per day had significantly *lower* homocysteine levels than did lighter drinkers and non-drinkers.

*Comments:* These studies support previous evidence of folate's potentially important role in reducing risk of certain health outcomes in moderate drinkers. It appears that women who drink alcohol and also consume sufficient levels of folate may

### Predicting Alcohol Withdrawal in Medical Inpatients

Although alcohol dependence is common in medical inpatients, it often remains undetected. As a result, patients may suffer serious consequences of withdrawal during their hospital stays. Researchers in the United Kingdom assessed whether the AU-DIT\* and/or blood testing (GGT, AST, ALT, MCV)\*\* could predict risk of withdrawal in 874 medical inpatients aged 16 or older.

- Of the 98 patients who scored >=8 on the AUDIT (a positive test for an alcohol use disorder), 17 experienced clinically significant withdrawal symptoms.
- All patients with withdrawal had an AUDIT score of >=8 (sensitivity 100%).
- All but I patient with withdrawal had abnormal blood test results.
- Most patients without withdrawal had a normal AUDIT score (specificity 91%).
- Although a positive AUDIT score plus any 2 abnormal blood tests had a sensitivity of 94% and a specificity of 98%, fewer than half of patients with this combination had withdrawal.

#### Written Advice for Emergency Care Patients: Does It Work?

Emergency care clinicians need pragmatic and effective methods to screen for and address risky drinking. In this study, Swedish researchers assessed whether emergency care patients may benefit from simple written advice about safer drinking. During the first half of the study, they screened 771 emergency care patients for risky drinking\*; for the remaining half, they screened another 563 and provided written advice (without counseling). Researchers assessed alcohol measures at baseline and 6 months later (approximately 50% follow-up rate).

- Approximately 23% of patients drank risky amounts at baseline.
- The proportion of risky drinkers with heavy drinking epi-

have no increased risk of breast cancer and have lower homocysteine levels.

R. Curtis Ellison, MD

\*Those who never consumed at least 12 drinks in a year

References: Baglietto L, et al. Does dietary folate intake modify effect of alcohol consumption on breast cancer risk? Prospective cohort study. *BMJ*. 2005;331(7502):807; Chiuve SE, et al. Alcohol intake and methylenetetrahydrofolate reductase polymorphism modify the relation of folate intake to plasma homocysteine. *Am J Clin Nutr.* 2005;82(1):155–162.

*Comments:* Drawing firm conclusions based on a small sample is risky. Nonetheless, given that the AUDIT identifies alcohol dependence, it is not surprising that it can also predict alcohol withdrawal. However, most patients with dependence will not have significant withdrawal symptoms. Adding blood tests improves detection of those at risk of withdrawal but may predict only 50%, at best, of withdrawal cases. Therefore, alcohol screening in the hospital is mainly useful for ruling out risk of withdrawal and identifying patients who might be ready for alcohol-dependence treatment.

Richard Saitz, MD, MPH

\*Alcohol Use Disorders Identification Test \*\*Gamma glutamyltransferase, aspartate aminotransferase, alanine aminotransferase, and mean corpuscular volume

Reference: Dolman JM, et al. Combining the AUDIT questionnaire and biochemical markers to assess alcohol use and risk of alcohol withdrawal in medical inpatients. *Alcohol Alcohol*. 2005;40(6):515–519.

sodes<sup>\*\*</sup> decreased significantly from baseline to follow-up in both groups (from 92% to 68% of those receiving written advice; from 94% to 59% of those receiving screening only).

 Among patients receiving written advice, the proportion of risky drinkers ready to change their drinking significantly increased (from 8% at baseline to 23% at follow-up).

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\*Determined by the AUDIT-C and defined as heavy episodic drinking (see below) and/or approximately >=6 drinks for women and >=9 drinks for men per week

\*\*>=6 standard drinks at one occasion at least once per month

#### Written Advice for Emergency Care Patients (continued from page 5)

*Comments*: This study showed that written advice does little to reduce risky drinking. The authors' contention that screening alone may have reduced the likelihood of heavy drinking episodes is suspect for several reasons (e.g., nonrandomized study design, limited follow-up). Further, fewer subjects may have had heavy drinking episodes because of their injury, not because they received alcohol screening. The search for an efficient alcohol intervention in the busy emergency setting still requires attention.

Jeffrey Samet, MD, MA, MPH

Reference: Nordqvist C, et al. Can screening and simple written advice reduce excessive alcohol consumption among emergency care Patients? *Alcohol Alcohol.* 2005;40(5):401– 408.

## SPECIAL POPULATIONS

#### Elders with Alcohol Dependence Receive Less Aftercare

Previous literature suggests that older patients with alcohol dependence respond as well as or better than younger patients to formal treatment. To contrast treatment outcomes between these groups, researchers studied a cohort of 1358 older and middle-aged patients who entered inpatient rehabilitation for alcohol dependence.

- At baseline, elderly patients had significantly worse physical health, better mental health, and less severe alcohol use than did middle-aged patients.
- Similar proportions of elderly and middle-aged patients completed at least 25 days of inpatient rehabilitation (78% and 83%, respectively) and were abstinent in the month after treatment (~85%).
- However, elderly patients were significantly less likely in the month after treatment to engage in aftercare (odds ratio [OR] 0.6), contact a sponsor (OR 0.5), or report a much- or somewhat-improved quality of life (OR 0.4).

*Comments*: Although older patients with alcohol dependence respond well to intensive inpatient treatment, this study found they are almost half as likely as middle-aged patients to receive formal or informal aftercare. The chronic relapsing nature of alcohol dependence suggests the need for ongoing care, and the authors propose that patient management via technology (e.g., telephone, Internet) might fill this gap. Since older patients have significant physical health problems for which they commonly seek medical attention, generalist clinicians have a potential role in the long-term monitoring and management of alcohol dependence among the elderly.

Peter Friedmann, MD, MPH

Reference: Oslin DW, et al. Treatment outcomes for alcohol dependence among middle-aged and older adults. *Addict Behav.* 2005;30(7):1431–1436.

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