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## ALCOHOL AND HEALTH OUTCOMES

### Safer Drinking Recommendations Should Vary by Sex and Age

Alcohol consumption has a U-shaped relationship with all-cause mortality; abstinence and heavy drinking increase risk. To quantify deaths attributable to and prevented by various levels of intake, researchers combined age- and sex-specific associations between alcohol consumption and mortality (from meta-analyses of observational studies) with population survey and national mortality data from England and Wales.

- Over the lifespan, mortality attributable to and prevented by alcohol consumption was relatively balanced, with 0.8% of all deaths in men prevented by use (95% confidence interval, CI, 0.2% to 1.3%) and 0.1% of all deaths in women attributable to use (95% CI, -0.3% to 0.4%).
- Deaths attributable to alcohol outweighed those prevented by use for men up to age 54 and for women up to age 64.
- Among men, those aged 16–24 years were at greatest risk of alcohol-related mortality (22% of deaths attributable to alcohol use), while those aged 75–85 years were most likely to benefit from consumption (3% of deaths prevented by use).
- Among women, those aged 35–44 years were at greatest risk (8% of deaths attributable to alcohol use), while those aged 85 and older were most likely to benefit (1% of deaths prevented by use).

Age	British Alcohol Units Per Week*	
	Men	Women
16-34	0	0
35-44	2	0
45-54	5	1
55-64	7	2
65-85+	8	3

\*A British alcohol unit is 9 g of alcohol. An American standard drink is 12 g of alcohol.

*Comments:* At least in England and Wales, mortality attributable to alcohol varies by age and sex. Recommendations of safest limits, which appear to be lower than the often cited "drink-a-day" for health, should vary as well. Abstinence is the safest choice for men up to age 34 and women up to age 44 because of their low risk of coronary heart disease and higher risk of alcohol-related traffic accidents. And although mortality benefits attributable to alcohol increase with age, a shift from abstinence to moderate consumption among elderly patients would only have a small effect on overall mortality.

Peter Friedmann, MD, MPH

*Reference:* White IR, et al. Mortality in England and Wales attributable to any drinking, drinking above sensible limits and drinking above lowest-risk levels. *Addiction*. 2004;99(6):749–756.

### Alcohol and Serious Consequences: Risks Increase Even with "Moderate Intake"

Risks of alcohol consumption are generally associated with heavy drinking. To examine the associations between consumption (including moderate intake) and negative consequences, investigators conducted a meta-analysis of 156 observational studies including 116,702 people.

- Risk increased significantly for drinkers, compared with non-drinkers, beginning at an intake of 25 g (<2 standard drinks) per day for the following: cancers of the oral cavity and pharynx (relative risk, RR, 1.9), esopha-

gus (RR 1.4), larynx (RR 1.4), breast (RR 1.3), liver (RR 1.2), colon (RR 1.1), and rectum (RR 1.1); liver cirrhosis (RR 2.9); essential hypertension (RR 1.4); chronic pancreatitis (RR 1.3); and injuries and violence (RR 1.1).

- Risks began to rise with any drinking and increased further with higher intake.
- The risk of coronary heart disease decreased significantly at 25 g per day (RR 0.8) and 50 g per day (RR 0.9), and increased at 100 g per day (RR 1.1).

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Boston Medical Center

## Alcohol and Serious Consequences (continued from page 1)

- The risk of hemorrhagic stroke increased significantly at 50 g per day (RR 1.8) and 100 g per day (RR 4.7); the risk of ischemic stroke increased at 100 g per day (RR 4.4).

*Comments:* This study contributes to our understanding of the risks and benefits of moderate drinking. However, the relative risks do not tell us whether risks of specific diseases outweigh overall health benefits of consumption, and 25 g may be greater

than amounts typically considered as moderate (e.g., 1 drink per day). Further, these results could reflect methodological limitations of the statistical models used. Nonetheless, the data raise concern about the risks associated with moderate drinking.

Richard Saitz, MD, MPH

*Reference:* Corrao G, et al. A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med.* 2004;38(5):613–619.

## Alcohol and the Risk of Ischemic and Hemorrhagic Stroke

Alcohol consumption has been linked to increased risk of hemorrhagic stroke and decreased risk of ischemic stroke. This study examined these associations in 19,544 Japanese men, aged 40–59 years, who were followed for 11 years. Results from analyses adjusted for potential confounders (e.g., age, smoking, diabetes, hypertension) include the following:

- Of 694 incident strokes, approximately one-half were hemorrhagic (compared with <20% in the United States).
- Compared with occasional drinking (1–3 days per month), consuming up to about 12 drinks (<150 g of alcohol) per week was associated with a significant decrease in risk (41%) of ischemic stroke, a borderline significant increase in risk (73%) of hemorrhagic stroke, and no excess risk of total stroke.
- Those who consumed greater amounts of alcohol experienced significant increases in risk of hemorrhagic stroke (approximately 2-fold) at all drinking

levels, but no significant differences in risk of ischemic stroke.

*Comments:* This study confirms findings from previous research—moderate alcohol consumption reduces risk of ischemic stroke. However, it found an increased risk of hemorrhagic stroke at amounts lower than previously reported in the United States (where increases are usually seen at >3–5 drinks per day). Because the greater prevalence of hemorrhagic stroke in Asia has a number of possible etiologies, it is unclear whether alcohol's impact on stroke will be the same in the United States as in Japan. Nonetheless, this study challenges the belief that only heavy drinking increases the risk of hemorrhagic stroke.

R. Curtis Ellison, MD

*Reference:* Iso H, et al. Alcohol consumption and risk of stroke among middle-aged men: the JPHC Study Cohort I. *Stroke.* 2004;35(5):1124–1129.

## Does Alcohol Intake Increase Colorectal Cancer Risk?

Alcohol intake may increase colorectal cancer risk. However, the magnitude of this risk and intake level at which it occurs are unknown. To examine the association between alcohol intake and colorectal cancer, researchers pooled primary data from 8 large prospective cohort studies in 5 countries that reported incident cases of colorectal cancer (4687) in a total of 489,979 men and women.

- Consuming  $\geq 45$  g of alcohol (roughly 3 standard drinks) per day, compared with

not drinking, significantly increased risk of colorectal cancer (relative risk, RR, 1.4). Consuming 30 g to <45 g per day also increased risk (RR 1.2) at a borderline level of significance.

- These results were consistent among men and women, by type of alcoholic beverage (i.e., beer, wine, liquor), and regardless of multivitamin use, folate and methionine intake, and smoking.

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## Does Alcohol Intake Increase Colorectal Cancer Risk? (continued from page 2)

- Those with a lower body mass index (BMI) who consumed alcohol had a higher risk of colorectal cancer.
- The effect of alcohol consumption, regardless of beverage type, was similar for all colon cancer sites.

*Comments:* The increased risk of colorectal cancer observed in this study is modest and occurs at a level of alcohol intake that is above the usual recommended threshold for low-risk drinking. Healthcare providers should be aware of these findings and

incorporate them into discussions with patients about the risks and benefits of alcohol consumption.

Kevin L. Kraemer, MD, MSc

*Reference:* Cho E, et al. Alcohol intake and colorectal cancer: a pooled analysis of 8 cohort studies. *Ann Intern Med.* 2004;140(8):603–613.

## Cognitive Effects of Moderate Alcohol Consumption

Several studies suggest that moderate drinking may reduce the risk of cognitive decline associated with aging and dementia, including Alzheimer disease. To assess the effect of alcohol on cognitive dysfunction (defined as scoring in the lowest quintile on tests of cognitive functioning), researchers evaluated approximately 11 years of follow-up data on 6033 men and women (aged 35–55 years at baseline and 46–68 when cognition was assessed) in the United Kingdom. Results from analyses adjusted for potential confounders (e.g., age, smoking, socioeconomic status, cholesterol and blood pressure levels) include the following:

- On most measures (tests of verbal and mathematical reasoning, verbal fluency, and verbal meaning), men who consumed >24 g of alcohol per week (over 3 standard drinks per day), compared with men who consumed <1 g per week, experienced significantly lower odds (odds ratios, ORs, from 0.5 to 0.6) of cognitive dysfunction (with borderline significant findings on the test of memory).
- Female drinkers experienced significantly lower odds of dys-

function on tests of verbal meaning (ORs from 0.3 to 0.6 at amounts ≤160 g per week) and on one measure of verbal fluency (OR 0.5 at 49–80 g per week).

- More frequent drinkers usually had the lowest odds of cognitive dysfunction on most measures. Lifetime abstaining men and women (compared with occasional and moderate drinkers) generally had higher odds.

*Comments:* This study is consistent with prior studies showing the possible benefits of moderate drinking on cognition in middle-aged adults. The mechanisms of protection against cognitive dysfunction are unknown, but may relate to decreased cerebral vascular disease and/or increased cerebral blood flow associated with moderate alcohol consumption.

R. Curtis Ellison, MD

*Reference:* Britton A, et al. Alcohol consumption and cognitive function in the Whitehall II Study. *Am J Epidemiol.* 2004;160(3):240–247.

## Alcohol Worsens HIV Treatment Adherence

Adherence to highly active antiretroviral therapy (HAART)—a treatment that has substantially reduced morbidity and mortality, and improved the quality of life of people infected with HIV—appears to decrease with alcohol use. To determine whether there is an amount of alcohol that does not affect adherence to HAART, researchers analyzed interview data from a prospective cohort of patients with HIV and a history of alcohol problems. Key findings from analyses adjusted for potential confounders (e.g., sex, race/ethnicity, age) include the following:

- Among the 267 subjects with HIV who were taking HAART (mostly male and ethnic minorities), 40% were currently drinking alcohol, with 16% consuming amounts associated with alcohol-related consequences in the general population (risky amounts: >14 drinks per week or >4 drinks per day for men; >7 drinks per week or >3 drinks per day for women).
- Alcohol use was the most significant predictor of non-

adherence (less than 100% of doses taken over the prior 3 days).

- Recent abstinence from alcohol was significantly associated with better adherence compared with both risky (odds ratio, OR, 3.6) and moderate (OR 3.0) amounts.

*Comments:* Alcohol use appears to be associated with decreased adherence to HAART. Commonly accepted low-risk drinking thresholds for the general population are not appropriate for patients with HIV and a history of alcohol problems; whether they are appropriate for patients with HIV alone remains unknown.

Joseph Conigliaro, MD, MPH

*Reference:* Samet JH, et al. Alcohol consumption and antiretroviral adherence among HIV-infected persons with alcohol problems. *Alcohol Clin Exp Res.* 2004;28(4):572–577.

## INTERVENTIONS

### Collaborative Care Reduces Alcohol Problems and PTSD in Trauma Patients

Of the 2.5 million Americans who sustain acute injuries that require hospitalization each year, approximately 20%–40% meet criteria for current or lifetime alcohol abuse or dependence, and 10%–40% will develop posttraumatic stress disorder (PTSD). This study assessed a multifaceted collaborative care intervention (delivered by a master's level case manager, a trauma support specialist, a psychiatrist, and a psychologist) to prevent or ameliorate these conditions among acutely injured trauma survivors.

Researchers randomly assigned 120 trauma center patients aged 18 or older (50% with alcohol abuse and/or dependence) to usual care (UC) or collaborative care (CC). Collaborative care combined usual trauma services with stepped care consisting of postinjury case management, motivational interviewing to reduce alcohol use, and pharmacotherapy and/or cognitive behavioral therapy for persistent PTSD. In the subsequent year, alcohol abuse/dependence decreased 24% on average in the CC group while increasing 13% in the

UC group (a significant difference). PTSD rates did not change in the CC group, but increased 6% in the UC group (also a significant difference).

*Comments:* This study suggests that early behavioral health intervention for injured survivors of trauma can be effectively delivered in trauma centers. Routine integration of mental health and substance abuse services into the acute management of individual or mass trauma appears to decrease alcohol consequences and even prevent PTSD, although studies of health-related quality of life and cost-effectiveness are warranted. Nonetheless, with a growing acceptance of alcohol screening and intervention by trauma surgeons, the time is right for the dissemination of effective collaborative care models.

Peter Friedmann, MD, MPH

*References:* Zatzick D, et al. A randomized effectiveness trial of stepped collaborative care for acutely injured trauma survivors. *Arch Gen Psychiat.* 2004;61(5):498–506.

### Naltrexone Underused to Treat Alcohol Dependence

A number of clinical trials have demonstrated naltrexone's efficacy in treating alcohol dependence. Practice guidelines suggest prescribing the drug for at least 3 months or longer, depending on need. To determine the frequency and duration of naltrexone use, researchers analyzed insurance claims of 1.5 million health plan members with prescription drug and behavioral health benefits, and assessed filled prescriptions for the drug from 2000 to 2002.

Less than 10% of plan members who received treatment for alcohol dependence received naltrexone. This proportion did not differ over the 3 years studied. Approximately one-half of the naltrexone prescriptions were supplied for 30

days or fewer.

*Comments:* Despite demonstrated efficacy, naltrexone is not being prescribed frequently, nor is it being prescribed for adequate courses of treatment. Efforts are needed to disseminate proven effective treatments for alcohol dependence, like naltrexone, into clinical practice.

Richard Saitz, MD, MPH

*Reference:* Harris KM, et al. Trends in naltrexone use among members of a large private health plan. *Psychiatr Serv.* 2004;55(3):221.

## SPECIAL POPULATIONS

## Anxiety, Sleep Disturbance, and Alcohol-Related Problems

Previous research has shown that people reporting sleep disturbances are at increased risk of depression, panic disorder, and possibly alcohol abuse. To examine whether sleep loss due to worry increases risk of developing alcohol-related problems, investigators analyzed interview data from a population-based sample of 1537 individuals in Baltimore in 1981 and again 12 years later.

In analyses adjusted for possible confounders (e.g., age, sex, race, education), the risk of developing an alcohol-related problem (defined as having any of the alcohol-related symptoms used to diagnose DSM-III-R abuse or dependence) was significantly higher among those who reported at baseline more-than-usual sleep loss due to worry, compared with those who reported no sleep disturbances. This increased risk was significant in subjects who reported at baseline both more-than-usual sleep loss due to worry and ever having an anxiety disorder (relative risk, RR, 3.8) or symptoms of

dysphoria (RR 2.7), but not significant in those without anxiety (RR 1.8) or dysphoria (RR 1.4). Simple insomnia (disturbed sleep that was not necessarily associated with worry) did not increase risk of subsequent alcohol-related problems.

*Comments:* This study suggests that patients with anxiety or mood symptoms who also report disturbed sleep due to worry may be at particular risk of developing alcohol-related problems. These patients may choose to self-medicate with alcohol at night to help relieve anxiety and induce sleep. The findings argue for increased attention to effective management of insomnia in patients with anxiety or other mood symptoms.

R. Curtis Ellison, MD

*Reference:* Crum RM, et al. Sleep disturbance and risk for alcohol-related problems. *Am J Psychiatry.* 2004;161(7):1197–1203.

## Alcohol and Aggression Experienced by College Women

Many studies have linked alcohol with sexual assault and rape on college campuses. To examine whether alcohol consumption is temporally related to victimization among college women, researchers interviewed 94 female college students in New York (using a validated calendar method) to determine daily alcohol intake and experiences of sexual and non-sexual aggression over a 6-week period.

Fourteen women (15%) experienced at least 1 incident of sexual aggression (ranging from unwanted contact to coerced sexual intercourse), while 19 (20%) experienced at least 1 incident of non-sexual aggression (physical violence such as being pushed, kicked, hit, or threatened with a knife). Women were significantly more likely to experience sexual aggression (odds ratio, OR, 9.0) and non-sexual aggression (OR 7.5) on days they had consumed  $\geq 5$  drinks than on days when they had abstained. They were also significantly more likely to experience sexual aggression (OR 3.2)

and non-sexual aggression (OR 2.9) on days they had consumed  $< 5$  drinks than on days they had abstained.

*Comments:* This small study provides further evidence that alcohol increases college women's risk of experiencing sexual and non-sexual aggression. Its findings support efforts on college campuses to teach female students the dangers of alcohol (especially heavier intake) and ways to adopt lower-risk drinking habits. These efforts must be coupled with initiatives that focus on perpetrators and address the role alcohol plays in their violent actions.

Rosanne T. Guerriero, MPH

*Reference:* Parks KA, et al. The temporal relationship between college women's alcohol consumption and victimization experiences. *Alcohol Clin Exp Res.* 2004;28(4):625–629.

## Alcohol Use and Racial and Ethnic Health Disparities

Certain minority groups, compared with other minority and non-minority groups, are more severely affected by alcohol use. Participants in a workshop on alcohol use and racial and ethnic health differences, sponsored by the National Institute on Alcohol Abuse and Alcoholism, concluded that interactions between alcohol, genes, and environment contribute to health disparities.

- Different populations exhibit genetic variations in alcohol-metabolizing enzymes, and these variations may contribute to differences in alcohol-related health outcomes.
- African Americans and Native Americans, compared with whites, have a greater incidence of fetal alcohol syndrome and fetal alcohol spectrum disorders, possibly due to genetic polymorphisms and nutrition.
- White Hispanic men have the highest mortality rate from cirrhosis.

- Mexican Americans have a gene allelic profile that may confer increased risk of alcohol dependence.
- African Americans, compared with whites, have a higher incidence of some cancers, which may be partly due to heavy drinking.

*Comments:* This paper confirms that our understanding of racial and ethnic disparities in alcohol-related health consequences is progressing, but we still have much to learn. Through better understanding, we may ultimately develop diagnostic, preventive, and therapeutic methods to decrease these disparities.

Kevin Kraemer, MD, MSc

*Reference:* Russo D, et al. Workshop on alcohol use and health disparities 2002: a call to arms. *Alcohol.* 2004;32(1):37–43.



## Using the AUDIT in a College Sample

Hazardous drinking is common among college students, and its early detection and intervention can prevent serious consequences. This study assessed the validity of the Alcohol Use Disorders Identification Test (AUDIT), a 10-item screening tool for hazardous use, alcohol abuse, and dependence, among college students by comparing it with well-established reference standards (a validated calendar method for consumption and a diagnostic interview).

Among a sample of 302 college students (61% female), the AUDIT performed best as a screen for hazardous drinking amounts with a cut-off of 6 having a sensitivity of 91% and specificity of 60%. Hazardous amounts were defined as follows: for men, 4 or more times when  $\geq 5$  drinks were consumed in 1 sitting, or  $\geq 57$  drinks over the past 28 days; and for women, 4 or more times when  $\geq 4$  drinks were consumed in 1 sitting, or  $\geq 29$  drinks over the past 28 days. The AUDIT performed less well in detecting current

alcohol abuse or dependence (sensitivity 78%, specificity 57%) and lifetime abuse or dependence (sensitivity 71%, specificity 61%).

*Comments:* Using well-established reference standards, the authors demonstrated that the AUDIT performs well as a screen for hazardous drinking amounts and less well for alcohol abuse or dependence in college students. Researchers should study ways to improve the sensitivity of the AUDIT in the college population, as they have in other groups. But for now, using a lower cut-off on the AUDIT than is standard for adults seems a reasonable approach to early identification of hazardous drinking in college students.

Joseph Conigliaro, MD, MPH

*Reference:* Kokotailo PK, et al. Validity of the Alcohol Use Disorders Identification Test in College Students. *Alcohol Clin Exp Res.* 2004;28(6):914-920.

## Adolescent Substance Abuse in the US and Australia

While the United States' national drug control policy advocates for reducing drug use, Australia's supports reducing the harms of use. To explore potential cross-national differences in the prevalence of, and risk and protective factors for, adolescent substance use that may be associated with these policies, researchers analyzed survey data from 40,845 adolescents in the United States (US) and Australia.

- More Australian youths reported regular cigarette and alcohol use than did US adolescents, whereas more US youths reported current marijuana use.
- Generally, risk and protective factors were similar in both the US and Australia. However, community norms, youth attitudes, and parental attitudes favorable to drug use were more common in Australia. Sensation seeking and possessing stronger social skills were more common in the US.
- Peer/individual risk and protective factors were more strongly related to substance use in the US; family factors protective against regular alcohol use

were also stronger in the US.

*Comments:* This study is an interesting initial effort to understand the implications of differing national drug control strategies on adolescent substance use. The US-supported abstinence strategy may heighten the risk of adolescent rebelliousness that may lead to substance use. In contrast, the harm-reduction model of Australia may contribute to more tolerant youth, parental, and community attitudes, which in turn may also increase use. However, these interpretations, which relate observed cross-national differences to policy differences, must be considered speculative (as the authors admit), but they are a useful first step.

Jeffrey Samet, MD, MA, MPH

*Reference:* Beyers JM, et al. A cross-national comparison of risk and protective factors for adolescent substance use: the United States and Australia. *J Adolesc Health.* 2004;35(1):3-16.

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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](mailto:ahce@bu.edu)