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ALCOHOL AND HEALTH OUTCOMES

Does Alcohol Consumption Increase the Risk of Ischemic Stroke?

Prior studies of the association between alcohol consumption and ischemic stroke have produced inconsistent results and have limitations. To address these issues, researchers assessed alcohol intake and prevalence of incident ischemic stroke (412 cases identified) in 38,156 male health professionals, aged 40–75 years, over a 14-year period.

- In analyses adjusted for potential confounders, the risk of ischemic stroke among drinkers versus that of nondrinkers increased as alcohol consumption increased (relative risk [RR] 1.0 for <1 drink per day, RR 1.3 for 1–2 drinks per day, and RR 1.4 for >2 drinks per day, $P=0.01$ for trend). These findings were not significant when analyses were adjusted for hypertension.
- In analyses adjusted for beverage type, the risk of ischemic stroke decreased with increasing red wine use, compared with no red wine use ($P=0.02$ for trend). This finding was not significant when analyses also adjusted for hypertension. Other

beverage types did not significantly affect risk.

- The risk of ischemic stroke was lowest, though not statistically significant, in people who consumed 1–2 drinks on 3–4 days each week (RR 0.7 compared with those who abstained).

Comments: Although this study reported some benefit from red wine use, its clearest finding was the increase in risk of ischemic stroke with increasing alcohol consumption, starting at 1–2 drinks per day. The complexities associated with beverage type and pattern of use, as indicated in these findings, highlight the challenge in making recommendations about safer drinking.

Kevin L. Kraemer, MD, MSc

Reference: Mukamal KJ, et al. Alcohol and risk for ischemic stroke in men: the role of drinking patterns and usual beverage. *Ann Intern Med.* 2005;142(1):11–19.

Alcohol May Increase Oral Mucosal Transmission of HIV

The HIV virus can infect oral mucosal cells. A number of variables determine the likelihood of infection, such as viral load and host defense mechanisms. To examine whether alcohol weakens these defenses and facilitates transmission, researchers measured the effects of various concentrations of ethanol (0%–4%) on the efficiency of infection of oral epithelial cells with HIV.

Primary oral epithelial cells (POEs) treated with 4% ethanol—similar to the concentration of alcohol found in most beers—had a 3- to 6-fold higher susceptibility of infection (i.e., more

cell colonies infected) than did POEs not exposed to ethanol. In addition, treated POEs had increased HIV RNA levels.

Comments: This in vitro study suggests that alcohol may play a role in oral HIV transmission. These results from the laboratory may prove useful when counseling patients about the risks of oral sex.

Joseph Conigliaro, MD, MPH

Reference: Zheng J, et al. Ethanol stimulation of HIV infection of oral epithelial cells. *JAIDS.* 2004;37(4):1445–1453.

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Alcohol Intake, Survival, and Quality of Life

To determine the relationship between mid-life alcohol consumption and later quality of life and mortality, researchers in Finland collected clinical and questionnaire data from 1808 healthy male executives (aged 40–55 years at baseline) and reassessed them at various intervals over 29 years.

- A significantly greater proportion of heavy drinkers (consumed >349 g of alcohol per week) than moderate drinkers (consumed 1–349 g per week) or nondrinkers died (38%, 25%, and 27%, respectively).
- In analyses adjusted for age, smoking, cholesterol, and glucose levels, heavy drinkers (compared with moderate drinkers) had a borderline significant increased risk of death from all causes (hazard ratio [HR] 1.3) and a significantly greater risk of noncardiovascular, noncancer, and nonviolent deaths (HR 2.8).
- Alcohol consumption was not significantly associated with quality of life (determined by the RAND 36, a validated survey measure) at follow-up among survivors. However, it was

worse among heavy drinkers in adjusted analyses that accounted for deaths during follow-up.

- Nondrinkers did not differ significantly from moderate drinkers on mortality or quality of life.

Comments: While the poorer outcomes experienced by heavy drinkers are not surprising, the lack of differences between nondrinkers and moderate drinkers in this population of high socioeconomic status is notable. Unfortunately, this study has several substantial limitations, including not adequately adjusting for potential confounders and defining moderate drinking broadly (e.g., included amounts often considered as heavy drinking). Nonetheless, future studies investigating how social factors, like socioeconomic status, may influence drinking outcomes should be encouraged.

R. Curtis Ellison, MD

Reference: Strandberg AY, et al. Alcohol consumption, 29-y total mortality, and quality of life in men. *Am J Clin Nutr.* 2004;80(5):1366–1371.

Does Alcohol Consumption Decrease the Risk of Coronary Artery Calcification?

Decreased coronary atherosclerosis is one possible mechanism to explain the lower rates of coronary artery disease (CAD) outcomes observed in light-to-moderate drinkers. To study this further, researchers measured coronary artery calcification (using electron beam computed tomography) and alcohol consumption in 1795 adults aged 55 and older without known CAD.

In analyses controlling for various cardiovascular risk factors, the odds of extensive coronary calcification (calcium score of ≥ 400 , a score associated with proven CAD) were significantly lower in people who consumed the following:

- <1 drink per day (odds ratio [OR] 0.5) or 1–2 drinks per day (OR 0.4) compared with those who did not drink
- <1 drink of wine per day (OR 0.7) or 1–2 drinks of wine per day (OR 0.5) compared with those who did not drink wine
- <1 drink of liquor per day (OR 0.6)

compared with those who did not drink liquor

Results did not differ between men and women.

Comments: According to this study, light-to-moderate alcohol consumption decreases odds of extensive coronary calcification in a population of asymptomatic adults. This finding suggests a lower burden of coronary atherosclerosis in light-to-moderate drinkers and is consistent with current public health recommendations on lower-risk drinking. The influence of longitudinal changes in drinking patterns and of heavy drinking on coronary calcification was not ascertained.

Kevin L. Kraemer, MD, MSc

Reference: Vlienthart R, et al. Alcohol consumption and coronary calcification in a general population. *Arch Int Med.* 2004;164(21):2355–2360.

INTERVENTIONS

Disulfiram or Naltrexone for Alcohol Dependence?

Both disulfiram and naltrexone have proven efficacy for treating alcohol dependence. However, few studies have compared these treatments. In an open-label trial, researchers in India randomized 100 men with alcohol dependence to receive either naltrexone (50 mg per day) or disulfiram (250 mg per day). All patients had a family member accompany them to follow-up appointments, received weekly supportive psychotherapy and, when symptomatic, were prescribed sertraline for depression and zolpidem for insomnia.

Follow-up at 1 year was 97%. Compared with the naltrexone group, patients in the disulfiram group had significantly more days abstinent (means 306 days versus 243 days), longer time to relapse (defined as drinking approximately ≥ 3 –4 standard drinks in 24 hours; means 119 days versus 63 days), and lower serum gamma-glutamyltransferase levels (means 85 U/L versus 107 U/L).

Patients in the naltrexone group had less craving.

Comments: The primary limitations of this study were the lack of blinding and the lack of a placebo control group. In addition, generalizability of the results may be limited to patients with substantial social support. Nonetheless, this study suggests that disulfiram, at least in some cases, may have advantages over naltrexone for the treatment of alcohol dependence.

Richard Saitz, MD, MPH

Reference: De Sousa A, et al. A one-year pragmatic trial of naltrexone versus disulfiram in the treatment of alcohol dependence. *Alcohol Alcohol*. 2004;39(6):528–531.

Talking About Alcohol in Primary Care: Do Patients Find It Useful?

Alcohol screening and brief interventions in primary care are efficacious but not optimally delivered in clinical practice. To examine the prevalence and perceived usefulness of alcohol use discussions in primary care, researchers in Finland surveyed 1203 patients (representing a 60% response rate) of 14 general practitioners at 2 health centers. Upon leaving an appointment with their physicians, patients completed a questionnaire that assessed the occurrence, duration, content, and usefulness of an alcohol use discussion during their visits.

- Discussions with physicians about alcohol were rare (only 12% of patients reported having one), brief (89% were <5 minutes), and most often included inquiries about quantities consumed and information about alcohol's harms.
- A great majority of patients (81%) felt that the discussions were useful, a finding similar among both heavy drinkers (who were identified by the Alcohol Use Disorders Identification Test) and non-heavy drinkers.

Comments: Alcohol use discussions are uncommon in primary care but apparently perceived as useful by a large proportion of patients (even after considering this study's limited survey response rate and the possible bias introduced by such selective discussion). These findings, if replicated in other countries, support efforts to improve implementation of alcohol discussions in primary care and assuage concerns that talking about alcohol engenders patient dissatisfaction with their physicians.

Jeffrey Samet, MD, MPH

Reference: Aalto M, et al. Usefulness, length and content of alcohol-related discussions in primary health care: the exit poll survey. *Alcohol Alcohol*. 2004;39(6):532–535.

Brief Alcohol Intervention: Prolonged Benefits?

To examine whether brief intervention (BI) provides benefits beyond 1 year, investigators in Norway reassessed 247 adults who, in 1986, had been drinking at least 2–3 times per week, had elevated serum gamma-glutamyltransferase (GGT) levels, and had entered a randomized trial of BI. During the trial, these participants received either minimal intervention (a 10-minute discussion of possible reasons for elevated GGT); more extensive intervention (15 minutes of counseling regarding decreasing drinking

and monthly visits until GGT levels normalized); or no intervention (though controls eventually received BI at 1-year follow-up). In this more recent study, investigators compared these participants with a new control group of subjects who, in 1986, also had been drinking at least 2–3 times per week but had GGT levels slightly below those required for inclusion in the original trial.

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Brief Alcohol Intervention: Prolonged Benefits? (continued from page 3)

Nine years after the original trial (70% follow-up), those who had received BI, including members of the original control group, had significant decreases in GGT levels (compared with levels at trial entry). These decreases significantly differed from the increases seen in the new control group.

Comments: These results are informative, particularly in the absence of a clinical trial of BI with a decade of follow-up. The better outcomes among drinkers with high GGT levels than among those with lower levels suggests that the intervention played a

role. This is the third (of 4) controlled studies in the literature to show long-term benefits. Brief intervention for risky drinking may be more effective than previously thought.

Richard Saitz, MD, MPH

Reference: Nilssen O. Long-term effect of brief intervention in at-risk alcohol drinkers: a 9-year follow-up study. *Alcohol Alcohol*. 2004;39(6):548–551.

Primary Medical Care Improves Addictive Problems

Addiction treatment and primary care commonly remain unlinked, despite potential benefits from their integration. To assess whether receipt of primary care improves addiction severity among adults with addictions, researchers studied a prospective cohort of 391 patients in a detoxification program who had previously participated in a randomized trial of linked primary care.

In analyses adjusted for potential confounders, receipt of ≥ 2 primary care visits over 2 years, compared with fewer or no visits, was significantly associated with the following:

- lower odds of drug use or alcohol use to intoxication (odds ratio 0.5)
- lower alcohol severity (determined by the Addiction Severity Index) among patients with alcohol as their first or second drug of choice
- lower drug severity among patients with heroin or cocaine as their first or second drug of choice
- decreased substance-related problems (determined by the InDUC-2R questionnaire)

Receipt of primary care was not significantly associated with receipt of substance abuse treatment.

Comments: Receipt of primary medical care by adults with addictions was associated with reduced addictive problems over a 2-year period. Because the exposures were measured simultaneously with the outcomes, an alternative interpretation—that people with improved addictive problems seek primary care—is possible. Nonetheless, this study adds to the growing literature indicating that efforts to link addiction specialty care with primary medical care are worthwhile.

Peter Friedmann, MD, MPH

Reference: Saitz R, et al. Primary medical care and reductions in addiction severity: a prospective cohort study. *Addiction*. 2005;100(1):70–78.

SPECIAL POPULATIONS

Older Adults Often Exceed Alcohol Consumption Limits

Guidelines for “safe” alcohol use among older adults recommend daily limits (no more than 2 drinks for men and 1 drink for women), weekly limits (no more than 14 drinks for men and 7 drinks for women) or a combination (no more than 1 drink per day, 7 drinks per week, or 3 drinks per drinking session, regardless of sex). The proportion of older adults who actually exceed each of these limits (i.e., engage in risky drinking) and experience associated alcohol-related problems is unknown. To explore these issues, researchers surveyed 1291 non-abstinent, community-dwelling older adults at baseline and 10 years later.

- The prevalence of risky drinking differed across guidelines, ranging from 23% to 50% among women and from 29% to 45% among men.

- Both men and women who exceeded consumption limits were more likely to have alcohol-related problems (e.g., difficulties with relationships and functioning) both at study entry and follow-up. These problems were more prevalent in men.
- Both men and women reduced consumption after 10 years.
- The limit of no more than 7 drinks per week/3 drinks per day offered the best combination of sensitivity and specificity in predicting alcohol-related problems in both men and women. At this cut-off, 16% of women and 34% of men had alcohol use problems at follow-up.

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Older Adults Often Exceed Alcohol Consumption Limits (continued from page 4)

Comments: This study supports the use of national guidelines for risky and less risky drinking that do not differ by sex. Physicians should counsel patients to avoid exceeding these limits and can provide data from this study as one reason to do so (to avoid the risk of subsequent alcohol-related problems).

Joseph Conigliaro, MD, MPH

Reference: Moos RH, et al. High-risk alcohol consumption and late-life alcohol use problems. *Am J Public Health.* 2004;94(11):1985–1991.

Moderate Alcohol Intake and Cognitive Decline in Elderly Women

To examine the effects of moderate alcohol intake on cognitive function, researchers evaluated 12,480 participants (aged 70–81 years) in the Nurses' Health Study and reassessed them 2 years later (approximately 90% follow-up). They used tests of memory, fluency, and attention to determine cognitive impairment (defined as the lowest 10% of scores) and decline (defined as the highest 10% of score decreases).

- In analyses adjusted for potential confounders, moderate drinkers (consumed 1.0–14.9 g of alcohol per day) had significantly lower risks of cognitive impairment and decline on tests of general cognition and verbal memory than did nondrinkers (relative risks 0.8–0.9).
- Consuming 15–30 g of alcohol per day, beverage type, and ApoE genotype were not significantly associated with cognitive function.

Comments: This is a well-conducted study of stable drinkers

(those recently changing their intake and ex-drinkers were excluded) that used valid measures of cognitive function. As an editorialist points out, however, the study is limited by its observational design: it is plausible that moderate drinking produces cognitive benefits, or that women in good health choose to drink moderately. Further, assessing cognitive function twice may not be adequate to determine the change in function over time. Nevertheless, these findings echo those from many previous studies and support the need for continued efforts to elucidate the effects of alcohol intake among older adults.

R. Curtis Ellison, MD

References: Stampfer MJ, et al. Effects of moderate alcohol consumption on cognitive function in women. *NEJM.* 2005;352(3):245–253; Evans DA, et al. Alcohol consumption and cognition. *NEJM.* 2005;352(3):289–290.

Adolescent Drinking Portends Early Adult Harms

Many people view teenage drinking as a stage adolescents will “mature out of,” despite the teen prevalence of binge drinking (up to one-third) and alcohol use disorders (up to 5%). Two recent prospective studies followed mid-adolescents into young adulthood to examine the relationships between teen drinking and later alcohol use disorders and psychosocial problems.

Bonomo et al assessed 1943 Australian teens, 1601 of whom were followed through age 20. They found that 5% of those who drank during adolescence met criteria for alcohol dependence by age 20 and that dependence was more likely among those who, as teens, had engaged in the following (analyses adjusted for sex, marital status, and parental alcohol use):

- frequent drinking (≥ 3 days in the past week; odds ratio [OR] 3.1 compared with teens who had not drunk frequently)

- antisocial behavior (≥ 2 incidents of property damage, interpersonal violence, or theft in the previous 6 months; OR 2.4 compared with teens without antisocial behavior)

Wells et al studied 953 New Zealand mid-adolescents and controlled for 32 potential confounders, including mental health disorders, socioeconomic status, family background, other drug use, risk taking, and other behavioral measures. They found that heavier drinking at age 16 independently predicted the following:

- alcohol dependence at ages 16 through 21, but not ages 21 through 25
- continued heavier drinking at ages 16 through 25
- greater numbers of sexual partners and violent offenses at ages 16 through 25

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Adolescent Drinking Portends Early Adult Harms (continued from page 5)

Comments: Drinking in mid-adolescence is not a “phase,” but a marker for alcohol problems, HIV risk behaviors, and violence over the ensuing decade. Statistical control for various behavioral and familial factors lessened the association between early drinking and later dependence, suggesting that the former may be a harbinger—but not a sole cause—of dependence during adulthood. Nonetheless, unambiguous education and feedback about these potential harms should be part and parcel of counseling and prevention efforts for

adolescents and young adults.

Peter Friedmann, MD, MPH

References: Bonomo YA, et al. Teenage drinking and the onset of alcohol dependence: a cohort study over seven years. *Addiction*. 2005;99(12):1520–1528; Wells JE, et al. Drinking patterns in mid-adolescence and psychosocial outcomes in late adolescence and early adulthood. *Addiction*. 2005;99(12):1529–1541.

Alcohol, Adolescents, and Brain Damage

The high prevalence and significant consequences of alcohol use among adolescents and college students are well known. To summarize the neurologic and neurocognitive effects of underage drinking, researchers systematically reviewed the literature and found the following:

- Underage drinking substantially increases risk of developing an alcohol use disorder in adulthood.
- Adolescents and young adults are more susceptible to the negative cognitive effects of alcohol than are adults.
- Alcohol use can cause a host of immediate neurological consequences (e.g., blackouts, hangovers, overdose with respiratory arrest and death), cognitive dysfunction (e.g., memory, language, learning, and visuospatial problems), and sleep disturbance. These problems, along with mood disorders often associated with alcohol use, can impair intellectual development and academic performance—impacting adolescents even after they become adults.
- Alcohol use, which impairs motor skills and judgment, can contribute to

motor vehicle crashes (and related injuries and death), other unintentional injuries, risky sexual behaviors, assault, suicide attempts, drowning, and other drug use among adolescents and young adults.

Comments: These well-documented, serious short- and long-term consequences underscore the danger of dismissing underage drinking as a normal “rite of passage” (e.g., “kids will be kids”). As stated by the authors, underage drinking must be addressed with a combination of individual strategies (e.g., identifying and counseling at-risk youth, parental education) and environmental efforts (e.g., curbing advertising and availability).

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

Reference: Zeigler DW, et al. The neurocognitive effects of alcohol on adolescents and college students. *Prev Med*. 2005;40(1):23–32.

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