Alcohol, Other Drugs, and Health: Current Evidence

JULY-AUGUST 2007

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Health Outcomes

Unhealthy Alcohol Use and the Preventive Paradox

People who drink the heaviest amounts have the highest risk of harm from alcohol. People who consume less, however, accrue most of the harm because they, as a group, are much larger. To examine whether the distribution of alcohol-related problems, deaths, and hospital admissions supports this preventive paradox, researchers pooled data from 4 Finnish population surveys. They compared self-reported problems (n=5558) and alcohol-related hospital admissions and deaths (n=6726) in the 10% of the population who drank the most* with the 90% who drank less (excluding abstainers).

- The 90% of men consuming less experienced 70% of the self-reported problems, 70% of the alcohol-related hospitalizations, 64% of the alcohol-related deaths, and 64% of the premature life-years lost.
- The 90% of women consuming less experienced 64% of the self-reported problems, 60% of the alcohol-related hospitalizations, 93% of the alcohol-related deaths, and 98% of the premature life-years lost.
- Drinking ≥5 drinks, versus less, on an occasion in the past year was generally related to more harm.

Comments: The preventive paradox suggests efforts to reduce the population harms of alcohol use must reach the majority of drinkers rather than the smaller proportion of heavy drinkers. These findings support this paradox and NIAAA** recommendations to use the screening question, "How many times in the past year have you had 5 or more drinks in a day (4 or more for women)?" If screening and brief interventions can produce even modest reductions in heavy drinking episodes among otherwise nonproblem drinkers, the public's health will most likely benefit.

Peter D. Friedmann, MD, MPH

*At least 753 drinks per year for men and at least 213 drinks per year for women
**National Institute on Alcohol Abuse and Alcoholism

Reference: Poikolainen K, et al. Alcohol and the preventive paradox: serious harms and drinking patterns. *Addiction*. 2007;102 (4):571–578.

Death After Detox Among Patients Without Primary Care

Inpatient detoxification may provide an important opportunity for patients, particularly those without primary care, to receive additional interventions aimed at lowering their mortality risk. To help inform such interventions, researchers in Boston assessed the rate, causes, and predictors of death among 470 participants in a randomized controlled trial that examined efforts to link patients to primary care after detoxification.

- During a mean of 4 years after detoxification, 27 (6%) subjects died. The annual age-adjusted mortality rate was 1608 per 100,000 people, 4.4 times that of the Boston population.

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Alcohol, Other Drugs, and Health: Current Evidence **is a project of the Boston Medical Center, supported by the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism, and produced in cooperation with the Boston University Schools of Medicine and Public Health.**

Death After Detox (continued from page 1)

- Causes of death included poisoning (41% of 22 deaths with a known cause), trauma (14%), cardiovascular disease (14%), exposure to cold (9%), alcohol abuse (9%), diabetes (5%), lung cancer (5%), and intracerebral hemorrhage (5%).
- In adjusted analyses, mortality risk was significantly higher in subjects with heroin versus cocaine as their drug of choice (hazard ratio [HR], 6.9) and persistent homelessness (HR, 2.4). Risk was borderline significantly higher in subjects who had ever attempted suicide (HR, 2.1).
- Accessing primary care after detoxification did not affect mortality risk.

Comments: This study confirms an increased risk of mortality among substance users. Efforts, such as overdose prevention education, integrated housing services, and psychiatric care, that address the factors associated with this increased risk may improve the chance of survival after detoxification. This study was most likely underpowered to determine the impact of accessing primary care on mortality risk.

Alexander Y. Walley, MD

Reference: Saitz R, et al. Risk of mortality during four years after substance detoxification in urban adults. *J Urban Health*. 2007;84 (2):272–282.

Leading Causes of Premature Death in Heroin Users

Many studies on mortality in heroin users report traditional mortality data, which does not account for age at death. To examine causes of premature death and years of potential life lost (YPLL) among heroin users, researchers assessed 581 ethnically diverse men who had been admitted to a compulsory drug treatment program in California for heroin-dependent criminal offenders. Subjects were evaluated every 10 years over 33 years.

- During follow-up, 282 subjects (49%) died. Mean age was 25 years at study entry and 47 years at death. On average, YPLL before age 65 was 18 years per person.
- The leading causes of death were heroin overdose (17% of deaths), chronic liver disease (15%), cardiovascular disease (12%), cancer (11%), accidents (8%), and homicide (7%).
- The leading causes of YPLL were heroin overdose (22% of all YPLL), chronic liver disease (14%), accidents (10%), cardiovascular disease (9%), homicide (9%), and cancer (5%).
- YPLL for each cause of death examined was significantly and substantially higher among subjects in this study than among the U.S. population (e.g., 43 YPLL versus 12 YPLL from unintentional injuries, including overdoses and accidents).

Comments: This study's strength is its consideration of premature mortality among heroin users. The results revealed disparities between leading causes of death and YPLL among heroin users and extremely large discrepancies in YPLL between heroin users and the U.S. population. One conclusion from this study is that inadequate drug treatment capacity may be partly responsible for the higher number of premature deaths among persons with opioid dependence.

Julia H. Arnsten, MD, MPH

Reference: Smyth B, et al. Years of potential life lost among heroin addicts 33 years after treatment. *Prev Med*. 2007;44(4):369–374.

Drug Use Disorders: Onset, Mental Health Impairment, and Comorbidity

Drug use disorders (abuse and dependence) have substantial health and economic consequences. To comprehensively describe the epidemiology of these disorders, including their relationship with mental health impairment and psychiatric comorbidity, researchers at the National Institutes of Health studied data from a representative sample of 43,093 U.S. adults surveyed in 2001-2002. Major findings include the following:

- Two percent of adults have a current drug use disorder; the lifetime prevalence is 10%. Most have abuse, not dependence.
- Drug use disorders are more common in adults aged 18–29 years than in adults aged 30 or older. Onset peaks at age 19 and is rare after age 25.
- In analyses adjusted for demographics and psychiatric disorders, people with current drug use disorders had significantly more mental health impairment (as measured by the Short-Form Health Survey) than did people without these disorders. Dependence was associated with greater impairment.
- People with current drug use disorders also had significantly higher odds in adjusted analyses of having an alcohol use disorder (odds ratio [OR], 5.6), nicotine dependence (OR, 3.2), any mood disorder (OR, 1.8), and any personality disorder (OR, 2.2).

Comments: This detailed survey tells us that drug use disorders begin in youth and are associated with substantial mental health impairment and comorbidity. These observations suggest that prevention and treatment efforts should be stepped up and should address coexisting mental health issues.

Richard Saitz, MD, MPH

Reference: Compton WM, et al. Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry.* 2007;64(5):566–576.

Illicit Drug Use, Depression, and HIV Medication Use Among Women

Illicit drug use and depressive symptoms are common in patients with HIV, may affect use of highly active antiretroviral therapy (HAART), and are both treatable. Investigators studied 1710 HIV-positive women from 6 U.S. sites to evaluate the impact of self-reported depressive symptoms and use of illicit drugs (crack, cocaine, heroin, or amphetamines) on HAART use over 8 years. Analyses controlled for potential confounding variables, including virologic and immunologic measures.

- During the 6 months before baseline, 13% of subjects used crack, 7% used heroin, 7% used cocaine, and 4% used amphetamines.
- HAART use was significantly less likely among the following: subjects with illicit drug use but no depressive symptoms versus those with neither (odds ratio [OR], 0.8); subjects with *both* illicit drug use and depressive symptoms versus those with neither (OR, 0.5).
- Having depressive symptoms only did not significantly affect HAART use.

Comments: Illicit drug use alone and in combination with depressive symptoms is associated with decreased use of HAART. The association between illicit drug use and HAART use has been reported previously. However, the interaction between depression and illicit drug use that further decreases the odds of HAART use is notable. These findings may reflect clinician or patient behaviors or preferences and should be confirmed in male patients. Finally, because both drug use and depression are treatable, effective interventions that address these frequently comorbid conditions should help improve use of HAART.

David A. Fiellin, MD

Reference: Cook JA, et al. Illicit drug use, depression and their association with highly active antiretroviral therapy in HIV-positive women. *Drug Alcohol Depend*. 2007;89 (1):74–81.

Smoking, Drinking, and the Risk of Raynaud's Phenomenon

Studies examining the association between alcohol and tobacco use and primary Raynaud's phenomenon have yielded conflicting results. Using data from the community-based Framingham Heart Study Offspring Cohort, researchers assessed these possible associations in 1602 men and 1840 women who were white and had a mean age of about 62 years. Analyses were adjusted for key confounders (e.g., cardiovascular disease, body mass index).

- Approximately 6% of women and 4% of men had Raynaud's phenomenon.

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Smoking, Drinking, and the Risk of Raynaud's Phenomenon (continued from page 3)

- Regular smoking in the past 12 months, versus not smoking, was significantly associated with an increased risk of Raynaud's in men (odds ratio [OR], 2.6) but not in women.
- Moderate drinking, versus not drinking,* was significantly associated with a decreased risk in men (OR, 0.5) but not in women.
- However, drinking red wine (approximately 1 glass or more per week), versus no red-wine drinking, appeared to lower risk for both men (OR, 0.3) and women (OR, 0.6).
- Heavier drinking, versus not drinking, was significantly associated with increased risk in women (OR, 1.7) but not in men.

Comments: The major limitation of this epidemiological work is its generalizability because the cohort was white and middle-aged. Nevertheless, this study shows yet another harm of smoking and another possible benefit of moderate alcohol use in men. It also suggests that the impact of these behaviors on the risk of Raynaud's may be sex specific.

Jeffrey H. Samet, MD, MA, MPH

*Not drinking is about <2 drinks per week for both women and men; moderate drinking is ≥2 to ≤7 drinks per week for women and ≥2 to ≤14 drinks for men; heavier drinking is >7 drinks per week for women and >14 drinks for men.

Reference: Suter LG, et al. Smoking, alcohol consumption, and Raynaud's phenomenon in middle age. *Am J Med*. 2007;120(3):264–271.

Alcohol Use, Bone Density, and Hip Fractures in Older Adults

Moderate drinking has been consistently linked with higher bone mineral density but not hip fracture risk. Researchers in this study analyzed the impact of alcohol consumption on hip fracture risk using data from a study of 5865 adults aged 65 and older from 4 U.S. communities.

All participants had reported their alcohol use yearly and had their hospital records examined for hip fracture diagnoses. A subgroup of 1567 in 2 communities underwent a single scan to assess bone mineral density (BMD).

- During about 12 years of follow-up, 412 hip fractures occurred.
- In analyses adjusted for potential confounders (e.g., age, sex, weight), light-to-moderate drinkers had a lower risk of hip fracture than abstainers while heavy drinkers had a higher risk (e.g., hazard ratio [HR], 0.9 for 1–6 drinks per week, 1.3 for ≥14 drinks per week; *P* for trend=0.02).
- Results for men and women were similar.
- Among participants who underwent scans, BMD of both the total hip and femoral neck increased as consumption increased.

Comments: Among older adults, alcohol consumption has a U-shaped relationship with hip fracture risk but a graded positive relationship with bone mineral density of the hip. This suggests that the higher hip fracture risk among heavier drinkers may be due to unmeasured, non-BMD factors. For example, this study did not directly examine fall incidence, which may have been associated with both alcohol consumption and hip fracture risk.

Julia H. Arnsten, MD, MPH

Reference: Mukamal KJ, et al. Alcohol consumption, bone density, and hip fracture among older adults: the Cardiovascular Health Study. *Osteoporos Int*. 2007;18 (5):593–602.

Drug Use in Young Adulthood May Lead to a Decline in Health Later

Self-rated general health is highly correlated with important health outcomes, including mortality. Researchers investigated the association between self-reported drug use at baseline and self-rated general health 15 years later among 3124 subjects. At baseline, subjects were from 4 U.S. cities, aged 20–32 years, and reported "good" or "excellent" health.

- At baseline, 812 subjects had never used illicit drugs, 1554 had used drugs in the past but not currently, 503 used marijuana only, and 255 used hard drugs (cocaine, amphetamines, opiates).
- Hard drug use at baseline was significantly associated with health decline (report of "fair" or "poor" health) at follow-up (odds ratio [OR] in adjusted analyses, 1.8 versus no hard drug use).

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Drug Use in Young Adulthood May Lead to a Decline in Health Later (continued from page 4)

- Cigarette smoking independently predicted health decline (OR, 1.7) and weakened the apparent effect of hard drug use at baseline (OR, 1.2 and no longer statistically significant).
- Neither marijuana use at baseline nor past drug use was significantly associated with health decline at follow-up.

Comments: This cohort study demonstrates an association between drug use in young adulthood and a decline in self-reported health 15 years later. The investigators aptly noted that another addictive behavior, cigarette smoking, independently predicted health decline and may overshadow the effects of intermittent drug use. The study is limited by a lack of information on ongoing drug use behaviors over follow-up.

David A. Fiellin, MD

Reference: Kertesz SG, et al. Illicit drug use in young adults and subsequent decline in general health: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Drug Alcohol Depend.* 2007;88(2-3):224–233.

Wine Drinkers May Have Better Health Outcomes

While animal experiments show that polyphenols in wine, rather than alcohol in general, may protect against the development of atherosclerosis, thrombosis, and other disorders, data from human studies are inconsistent. In this study, researchers evaluated the effects of alcoholic beverage preference (the beverage subjects reported drinking the most often) on mortality and quality of life in old age among 2468 Finnish men.

Subjects were businessmen or executives with a similar socioeconomic status and aged 40–55 years at baseline. Of those who drank and had a beverage preference, most preferred spirits (n=937). Preferences remained consistent throughout follow-up, and total alcohol consumption was not significantly different across the preference groups.

- During 29 years of follow-up, 814 men died.
- Men who preferred wine (n=251) or beer (n=694) had a lower mortality risk than men who preferred spirits (relative risks, 0.7 and 0.9, respectively) in analyses adjusted for cardiovascular risk factors and total alcohol consumption. Results were significant for wine drinkers only.
- Men who preferred wine also had significantly higher scores on the general health and mental health scales of a validated questionnaire used to determine health-related quality of life at follow-up.

Comments: Because subjects were from the same socioeconomic group, potential confounding from lifestyle factors was probably low. Also, wine drinkers still fared better than others when possible confounding by total alcohol intake and cardiovascular risk factors was addressed. Nevertheless, this is an observational study, and residual confounding by unmeasured lifestyle factors may have influenced the results.

R. Curtis Ellison, MD

Reference: Strandberg TE, et al. Alcoholic beverage preference, 29-year mortality, and quality of life in men in old age. *J Gerontology*. 2007;62A(2):213–218.

Risky Drinking Cut-offs for the Elderly Are Not Clear

Researchers in this retrospective study assessed drinking patterns and their health impact among elderly primary care patients. They analyzed data from 24,863 ethnically diverse patients, aged 65 to 103 years, from 6 VA medical centers, 2 hospital-based health care networks, and 3 community health centers.

- Most subjects (70%) abstained in the past year; 22% drank moderately (1–7 drinks per week), 4% drank risky amounts (8–14 drinks per week), and 5% drank heavily (>14 drinks per week) or reported heavy drinking episodes (≥4 drinks in 1 day).
- Depression or anxiety symptoms were significantly more common among abstainers (odds ratio [OR] in adjusted analyses, 1.4), heavy drinkers (OR, 1.8), and heavy drinkers with heavy drinking episodes (OR, 1.7) than among moderate drinkers.
- Poor social support was significantly more common among abstainers (OR, 1.5) and heavy drinkers (OR, 2.0) than among moderate drinkers, while fair/poor health was reported more frequently by abstainers (OR, 1.8) and heavy drinkers with heavy drinking episodes (OR, 1.3).
- Risky drinkers and moderate drinkers did not significantly differ on the 3 outcomes measured.

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Risky Drinking Cut-offs for the Elderly Are Not Clear (continued from page 5)

Comments: While these findings support those of a recent study* that indicated similar disability and mortality outcomes in elders who drank ≤1 or ≤2 drinks per day, they conflict with others (e.g., a 10-year prospective study**). The present study did not examine medical outcomes or mortality. Also, it grouped ex-drinkers with abstainers, which makes the poorer outcomes in "nondrinkers" not surprising but does not affect the main comparisons between moderate and risky drinkers. Further research is needed to clarify risky drinking cut-offs in the elderly.

R. Curtis Ellison, MD

*Lang I, et al. *J Am Geriatr Soc*. 2007;55(1):49–57
**Moos RH, et al. Am J Public Health. 2004;94(11):1985–1991
(These articles were summarized in the May-June 2007 issue and March-April 2005 issue, respectively, of Alcohol, Other Drugs, and Health).

Reference: Kirchner JE, et al. Alcohol consumption among older adults in primary care. *J Gen Intern Med*. 2007;22(1):92–97.

Assessments and Interventions

Why Don't Primary Care Clinicians Screen Teens for Substance Abuse?

Screening rates for substance abuse in teens are poor in primary care settings. To assess possible reasons for this lack of screening, researchers conducted focus groups with a total of 38 clinicians (13 physicians, 10 nurses, 8 social workers, 6 nurse practitioners or physician assistants, and 1 psychologist) at 6 primary care sites. Each of the 6 focus groups identified and ranked barriers to screening teens.

The most common barriers to screening included the following (listed in order of perceived importance):

- lack of time
- insufficient training to assist teens who screen positive
- competing medical problems faced by teens
- lack of treatment resources for substance abuse
- a "tenacious" parent of a teen who will not leave the exam room, hindering confidential discussions
- poor knowledge of screening tools

Comments: The barriers identified in this study will not surprise most primary care clinicians. Improvements in many areas, including training in screening and brief intervention, information technology, and decision-support systems, are needed to address these barriers and increase substance abuse screening and intervention in teens.

Kevin L. Kraemer, MD, MSc

Reference: Van Hook S, et al. The "Six T's": barriers to screening teens for substance abuse in primary care. *J Adoles Health*. 2007;40(5):456–461.

Buprenorphine Treatment in Less Specialized Settings: Can It Work?

Buprenorphine treatment outcomes are generally evaluated in resource-rich settings (e.g., with research staff) or in patients with some social support. The effectiveness of this treatment in everyday practice settings and among more destitute patients remains unclear. Two studies explored more generalizable approaches to buprenorphine treatment for opioid dependence.

Researchers in the Boston area assessed 99 patients receiving buprenorphine treatment in (1) a hospital-based primary care center with an on-site pharmacy but no on-site addiction counselor or (2) a neighborhood health center with an on-site addiction counselor but no on-site pharmacy.

At 6 months, 54% of patients were "sober" (determined by the treating physician and based on urine toxicology, self-reported drug use, and clinical assessment). Clinical outcomes did not differ across the treatment settings.

Other Boston researchers compared the effectiveness of buprenorphine in patients treated at a clinic for the homeless (n=44) and in housed patients treated at a general primary care setting (n=41). A nurse care manager was actively engaged in patients' care at both sites.

Although homeless patients had many more comorbidities than housed patients, treatment outcomes were similar between the groups:

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Buprenorphine Treatment in Less Specialized Settings: Can It Work? (continued from page 6)

- Twenty-one percent of homeless patients and 22% of housed patients "failed treatment."*
- Both groups had a median treatment retention of 9 months.
- Of those in treatment for 12 months, 4% of both groups used illicit opioids.
- Homelessness resolved for 36%, and employment rates increased in both groups.

Comments: The above findings support the effectiveness of extending office-based buprenorphine treatment into less specialized, low-intensity settings and to patients with only marginal social support. These feasibility and effectiveness studies should extend the reach of buprenorphine treatment for opioid dependence.

Marc N. Gourevitch, MD, MPH

*Eloped during treatment induction or were discharged because of either disruptive behavior or ongoing alcohol or other drug use while not adhering to intensified substance abuse treatment

References: Mintzer IL, et al. Treating opioid addiction with buprenorphine-naloxone in community-based primary care settings. *Ann Fam Med.* 2007;5(2):146–150; Alford DP, et al. Treating homeless opioid dependent patients with buprenorphine in an office-based setting. *J Gen Intern Med*. 2007;22(2):171–176.

Coordinated Treatment for Hepatitis C in Injection Drug Users

Since 2002, consensus guidelines have recommended coordinated care for treating chronic hepatitis C (HCV) among injection drug users (IDUs). This small, uncontrolled study evaluated one such model of care implemented by multidisciplinary teams across 6 infectious disease clinics and 11 drug treatment units in Italy.

IDUs in drug treatment who were anti-HCV positive were screened for chronic HCV, counseled about the disease, and referred to an infectious disease clinic for further evaluation. When indicated, patients received treatment (weekly injections of pegylated interferon and oral ribavirin twice per day) and were monitored on the drug treatment unit.

- Over approximately 1 year, 169 patients were referred to the clinics, but 69% were ineligible to receive treatment (e.g., 54 for normal ALT values, 14 for alcohol abuse). "Uncontrolled" psychiatric conditions were among the exclusions, but none were reported.
- Fifty-five percent of patients who received treatment had a sustained virological response (SVR): 35% of patients with genotypes 1 or 4 (the most common genotypes in IDUs in the United States) and 70% of patients with genotype 3.
- Treatment was discontinued in 19 (36%) patients for various reasons (e.g., side effects, relapse).

Comments: Effective models of coordinated care are greatly needed for IDUs given their high prevalence of both HCV and contraindications to treatment. This study's small and selective sample, the uncertain fate of patients with comorbid psychiatric conditions, and the impressive SVRs suggest the need for better controlled studies. Nonetheless, this report implies that coordinated hepatitis C and addiction treatment might be feasible in settings with universal health coverage.

Peter D. Friedmann, MD, MPH

Reference: Guadagnino V, et al. Effectiveness of a multidisciplinary standardized management model in the treatment of chronic hepatitis C in drug addicts engaged in detoxification programmes. *Addiction.* 2007;102(3):423–431

Should Smoking Prompt Screening for Unhealthy Alcohol Use?

Primary care clinicians are more likely to screen their patients for smoking than for drinking, despite the association between the two risk behaviors. To confirm this association and determine whether smoking status could be used to detect unhealthy alcohol use, researchers assessed 42,374 U.S. adults who had participated in a national survey on alcohol and related conditions.

- Risky drinking* was significantly more common in daily (odds ratio [OR], 3.2), occasional (OR, 5.3), and former (OR, 1.2) smokers than in subjects who never smoked.

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*Risky drinking: >14 drinks per week or ≥5 drinks per occasion for men; >7 drinks per week or ≥4 drinks per occasion for women

Should Smoking Prompt Screening? (continued from page 7)

- A diagnosis of alcohol abuse or dependence was also significantly more common in daily (OR, 3.5) and occasional (OR, 5.4) smokers than in subjects who never smoked.
- Current smoking (daily or occasional) had a sensitivity and specificity* of 43% and 82%, respectively, for risky drinking and 51% and 78%, respectively, for an alcohol diagnosis.
- Forty-one percent of subjects with risky drinking and 37% of subjects with an alcohol diagnosis never smoked.

Comments: The findings from this large, population-based sample suggest healthcare providers should suspect unhealthy alcohol use among current smokers. However, a broader screening strategy is still needed because approximately 40% of the unhealthy alcohol use in this sample occurred in never smokers.

Kevin L. Kraemer, MD, MSc

*Sensitivity is the proportion of patients with a condition that test positive for that condition; specificity is the proportion of patients without the condition who test negative.

Reference: McKee SA, et al. Smoking status as a clinical indicator for alcohol misuse in US adults. *Arch Intern Med*. 2007;167(7):716-–721.

Journal Alert

Annals of Epidemiology Reviews Risks and Benefits of Moderate Drinking

A supplement to the *Annals of Epidemiology* focuses on the risks and benefits of moderate drinking. It is based on discussions from an international symposium sponsored by at least one organization whose funding is derived primarily from companies that sell alcoholic beverages. The supplement includes review articles, analyses, and proceedings of discussions said to encourage the airing of controversies and disagreements.

Topics covered include the following:

- the role of healthy lifestyles in explaining observed benefits of alcohol on heart disease
- effects of moderate drinking on dementia, noncoronary heart diseases, cancer, liver disease, mental health, and mortality
- mechanisms of alcohol's effects on health
- intervention studies
- net effects of drinking on health
- social and cultural aspects of drinking
- messages about the risks and benefits of drinking for the general public
- implications for future research

Comments: Without randomized clinical trials, many questions regarding the potential benefits of moderate drinking will remain controversial. This publication, however, thoughtfully and clearly delineates some of the key areas of uncertainty in the current scientific literature.

Richard Saitz, MD, MPH

Reference: Ellison RC (Guest Editor). Health risks and benefits of moderate alcohol consumption: proceedings of an international symposium. *Ann Epidemiol.* 2007;17(5S).

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