

# Selected April, May and June, 2009 Articles by Howard Maccabee M.D. Ph.D

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## Long-term wine consumption is related to cardiovascular mortality and life expectancy independently of moderate alcohol intake: the Zutphen Study

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ABSTRACT

Background: Light to moderate alcohol intake lowers the risk of cardiovascular mortality, but whether this protective effect can be attributed to a specific type of beverage remains unclear. Moreover, little is known about the effects of long-term alcohol intake on life expectancy.

**Methods:** The impact of long-term alcohol intake and types of alcoholic beverages consumed on cardiovascular mortality and life expectancy at age 50 was investigated in the Zutphen Study, a cohort of 1373 men born between 1900 and 1920 and examined repeatedly between 1960 and 2000. Hazard ratios (HRs) for total alcohol intake and alcohol from wine, beer and spirits were obtained from time-dependent Cox regression models. Life expectancy at age 50 was calculated from areas under survival curves.

**Results:** Long-term light alcohol intake, that is (20 g per day, compared with no alcohol, was strongly and inversely associated with cerebrovascular (HR 0.43, 95% CI 0.26 to 0.70), total cardiovascular (HR 0.70, 95% CI 0.55 to 0.89) and all-cause mortality (HR 0.75, 95% CI 0.63 to 0.91). Independent of total alcohol intake, long term wine consumption of, on average, less than half a glass per day was strongly and inversely associated with coronary heart disease (HR 0.61, 95% CI 0.41 to 0.89), total cardiovascular (HR 0.68, 95% CI 0.53 to 0.86) and all-cause mortality (HR 0.73, 95% CI 0.62 to 0.87). These results could not be explained by differences in socioeconomic status. Life expectancy was about 5 years longer in men who consumed wine compared with those who did not use alcoholic beverages.

**Conclusion:** Long-term light alcohol intake lowered cardiovascular and all-cause mortality risk and increased life expectancy. Light wine consumption was associated with 5 years longer life expectancy; however, more studies are needed to verify this result.

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# Functional Limitations, Socioeconomic Status, and All-Cause Mortality in Moderate Alcohol Drinkers

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## KEYWORDS

alcohol o function o socioeconomic status o risk adjustment

## ABSTRACT

**OBJECTIVES:** To determine whether the survival benefit associated with moderate alcohol use remains after accounting for nontraditional risk factors such as socioeconomic status (SES) and functional limitations.

**DESIGN:** Prospective cohort.

**SETTING:** The Health and Retirement Study (HRS), a nationally representative study of U.S. adults aged 55 and older.

**PARTICIPANTS:** Twelve thousand five hundred nineteen participants were enrolled in the 2002 wave of the HRS.

MEASUREMENTS: Participants were asked about their alcohol use, functional limitations (activities of daily living, instrumental activities of daily living, and mobility), SES (education, income, and wealth), psychosocial factors (depressive symptoms, social support, and the importance of religion), age, sex, race and ethnicity, smoking, obesity, and comorbidities. Death by December 31, 2006, was the outcome measure.

RESULTS: Moderate drinkers (1 drink/d) had a markedly more-favorable risk factor profile, with higher SES and fewer functional limitations. After adjusting for demographic factors, moderate drinking (vs no drinking) was strongly associated with less mortality (odds ratio (OR)=0.50, 95% confidence interval (CI)=0.40-0.62). When traditional risk factors (smoking, obesity, and comorbidities) were also adjusted for, the protective effect was slightly attenuated (OR=0.57, 95% CI=0.46-0.72). When all risk factors including functional status and SES were adjusted for, the protective effect was markedly attenuated but still statistically significant (OR=0.72, 95% CI=0.57-0.91).

CONCLUSION: Moderate drinkers have better risk factor profiles than nondrinkers, including higher SES and fewer functional limitations. Although these factors explain much of the survival advantage associated with moderate alcohol use, moderate drinkers maintain their survival advantage even after adjustment for these factors.

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# A Combined Healthy Lifestyle Score and Risk of Pancreatic Cancer in a Large Cohort Study

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Arch Intern Med. 2009;169(8):764-770. 4-27-09

Background Smoking, alcohol use, diet, body mass index (calculated as weight in kilograms divided by height in meters squared), and physical activity have been studied independently in relation to pancreatic cancer. We generated a healthy lifestyle score to investigate their joint effect on risk of pancreatic cancer.

Methods In the prospective National Institutes of Health-AARP Diet and Health Study, a total of 450 416 participants aged 50 to 71 years completed the baseline food frequency questionnaire (1995-1996) eliciting diet and lifestyle information and were followed up through December 31, 2003. We identified 1057 eligible incident pancreatic cancer cases. Participants were scored on 5 modifiable lifestyle factors as unhealthy (0 points) or healthy (1 point) on the basis of current epidemiologic evidence. Participants received 1 point for each respective lifestyle factor: nonsmoking, limited alcohol use, adherence to the Mediterranean dietary pattern, body mass index ( $\geq 18$  and  $<25$ ), or regular physical activity. A combined score (0-5 points) was calculated by summing the scores of the 5 factors. Cox proportional hazards regression models were used to estimate relative risk (95% confidence interval) for pancreatic cancer.

Results Compared with the lowest combined score (0 points), the highest score (5 points) was associated with a 58% reduction in risk of developing pancreatic cancer in all participants (relative risk, 0.42; 95% confidence interval, 0.26-0.66;  $P_{\text{trend}} < .001$ ). Scores of less than 5 points were associated with 27% of pancreatic cancer cases in our population.

Conclusion Findings from this large study suggest that having a high score, as opposed to a low score, on an index combining 5 modifiable lifestyle factors substantially reduces the risk of developing pancreatic cancer.

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## Ethanol intake and the risk of pancreatic cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC).

Rohrmann S, Linseisen J, Vrieling A, Boffetta P, Stolzenberg-Solomon RZ, Lowenfels AB, Jensen MK, Overvad K, Olsen A, Tjønneland A, Boutron-Ruault MC, Clavel-Chapelon F, Fagherazzi G, Misirli G, Lagiou P, Trichopoulou A, Kaaks R, Bergmann MM, Boeing H, Bingham S, Khaw KT, Allen N, Roddam A, Palli D, Pala V, Panico S, Tumino R, Vineis P, Peeters PH, Hjartaker A, Lund E, Redondo Cornejo ML, Agudo A, Arriola L, Sánchez MJ, Tormo MJ, Barricarte Gurrea A, Lindkvist B, Manjer J, Johansson I, Ye W, Slimani N, Duell EJ, Jenab M, Michaud DS, Mouw T, Riboli E, Bueno-de-Mesquita HB

**OBJECTIVE:** To examine the association of baseline and lifetime ethanol intake with cancer of the pancreas in the European Prospective Investigation into Cancer and Nutrition (EPIC). **METHODS:** Included in this analysis were 478,400 subjects, of whom detailed information on the intake of alcoholic beverages at baseline and over lifetime was collected between 1992 and 2000. During a median follow-up time of 8.9 years, 555 non-endocrine pancreatic cancer cases were observed. Multivariate Cox proportional hazard models were used to examine the association of ethanol intake at recruitment and average lifetime ethanol intake and pancreatic cancer adjusting for smoking, height, weight, and history of diabetes. **RESULTS:** Overall, neither ethanol intake at recruitment (relative risk (RR) = 0.94, 95% confidence interval (CI) 0.69-1.27 comparing 30+ g/d vs. 0.1-4.9 g/d) nor average lifetime ethanol intake (RR = 0.95, 95% CI 0.65-1.39) was associated with pancreatic cancer risk. High lifetime ethanol intake from spirits/liquor at recruitment tended to be associated with a higher risk (RR = 1.40, 95% CI 0.93-2.10 comparing 10+ g/d vs. 0.1-4.9 g/d), but no associations were observed for wine and beer consumption. **CONCLUSION:** These results suggest no association of alcohol consumption with the risk of pancreatic cancer.

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## Long-term wine consumption is related to cardiovascular mortality and life expectancy independently of

# moderate alcohol intake: the Zutphen Study

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Background: Light to moderate alcohol intake lowers the risk of cardiovascular mortality, but whether this protective effect can be attributed to a specific type of beverage remains unclear. Moreover, little is known about the effects of long-term alcohol intake on life expectancy.

Methods: The impact of long-term alcohol intake and types of alcoholic beverages consumed on cardiovascular mortality and life expectancy at age 50 was investigated in the Zutphen Study, a cohort of 1373 men born between 1900 and 1920 and examined repeatedly between 1960 and 2000. Hazard ratios (HRs) for total alcohol intake and alcohol from wine, beer and spirits were obtained from time-dependent Cox regression models. Life expectancy at age 50 was calculated from areas under survival curves.

Results: Long-term light alcohol intake, that is 20 g per day, compared with no alcohol, was strongly and inversely associated with cerebrovascular (HR 0.43, 95% CI 0.26 to 0.70), total cardiovascular (HR 0.70, 95% CI 0.55 to 0.89) and all-cause mortality (HR 0.75, 95% CI 0.63 to 0.91). Independent of total alcohol intake, long-term wine consumption of, on average, less than half a glass per day was strongly and inversely associated with coronary heart disease (HR 0.61, 95% CI 0.41 to 0.89), total cardiovascular (HR 0.68, 95% CI 0.53 to 0.86) and all-cause mortality (HR 0.73, 95% CI 0.62 to 0.87). These results could not be explained by differences in socioeconomic status. Life expectancy was about 5 years longer in men who consumed wine compared with those who did not use alcoholic beverages.

Conclusion: Long-term light alcohol intake lowered cardiovascular and all-cause mortality risk and increased life expectancy. Light wine consumption was associated with 5 years longer life expectancy; however, more studies are needed to verify this result

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## Effects of beer, wine, and liquor intakes on bone mineral density in older men and women

May 2009

The authors state that moderate intake of alcohol has been reported to have beneficial effects on bone. However, different classes of alcoholic beverages have not been investigated. Their objective was to determine the association between intake of total alcohol or individual alcoholic beverages and bone mineral density (BMD). Adjusting for potential confounding factors, the authors examined alcohol

intakes and BMD at 3 hip sites and the lumbar spine in 1,182 men and in 1,289 postmenopausal and 248 premenopausal women in the population-based Framingham Offspring cohort (age: 29-86 y). Men were predominantly beer drinkers and women were predominantly wine drinkers. Results showed that compared with nondrinkers, hip BMD was greater (3.4-4.5%) in men consuming 1-2 drinks/day of total alcohol or beer, whereas hip and spine BMD were significantly greater (5.0-8.3%) in postmenopausal women consuming > 2 drinks/d of total alcohol or wine. Intake of > 2 drinks/d of liquor in men was associated with significantly lower (3.0-5.2%) hip and spine BMD than was intake of 1-2 drinks/d of liquor in men. After adjustment for silicon intake, all intergroup differences for beer were no longer significant; differences for other alcohol sources remained significant. Power was low for premenopausal women, and the associations were not significant. The authors conclude that moderate consumption of alcohol may be beneficial to bone in men and postmenopausal women. However, in men, high liquor intakes (> 2 drinks/d) may be associated with lower BMD. The tendency toward stronger associations between BMD and beer or wine, relative to liquor, suggests that constituents other than ethanol may contribute to bone health. Silicon appears to mediate the association of beer, but not that of wine or liquor, with BMD. Other components need further investigation.

Professor R Curtis Ellison comments: A number of previous studies have suggested that moderate alcohol intake may improve bone mineral density (BMD) and lower the risks of fractures in the elderly. Results from this well-done study support such findings. Further, while polyphenols in wine have been thought to provide additional health benefits, this study suggests that silicon present in beer may be an important factor associated with its improvement in BMD. For the three hip sites studied, male subjects reporting a total alcohol intake of 1-2 drinks/d had the highest BMD; men reporting > 2 drinks/d of liquor (but not beer or wine) had poorer bone density. For women, the highest levels of BMD were among those reporting > 2 drinks/day, but the average intake within this category was not given.

In an accompanying editorial 'Alcohol and recommendations for bone health: should we still exercise caution?' (Am J Clin Nutr 2009;89:999-1000), Helen M. Macdonald states that while most studies support improved bone health from moderate alcohol intake, the greater effects in women from >2 drinks/day in the present study should not be taken to indicate that drinking guidelines for women need to be increased. Further, servings today are often larger than in the past -- there is more alcohol in a 'typical drink' -- which would argue against recommending that women drink more drinks per day.

A meta-analysis by Berg et al (Association between alcohol consumption and both osteoporotic fracture and bone density. Am J Med 2008;121:406-418). involving the review of 33 previous studies, supports a reduced risk of hip fracture and higher bone density among men and women who consume small to moderate amounts of alcohol (in comparison with non-drinkers). There is probably a "J-shaped" curve, with increased risk of fractures among heavier drinkers.

Source: Tucker KL, Jugdaohsingh R, Powell JJ, Qiao N, Hannan MT, Sripanyakorn S, Cupples LA, Kiel DP. Am J Clin Nutr 2009;89:1188-1196.

<http://www.nutrition.org/media/publications/ajcnApril309.pdf>

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## Wine drinkers have reduced risk of gullet cancer

May 2009

Drinking a glass of wine a day could reduce the risk of Barrett's Esophagus (BE) - a precursor to oesophageal cancer by 56%, a new study has concluded of gullet cancer



The type of alcohol that people drink and their social background appears to be linked to the risk of developing BE, which occurs when heartburn or acid reflux permanently damages the oesophageal lining. The study found that, compared to the general population, people with BE have a 30 to 125-fold increased risk of developing oesophageal adenocarcinoma (EAC), which is the fastest growing cancer in the US.

The study included 953 men and women in Northern California between 2002 and 2005. Results suggest that people who drank one or more glasses of red or white wine a day had 56% reduced risk of BE, but the protective effect of wine did not increase with higher consumption.

One theory as to why wine reduces the risk of BE and oesophageal cancer is that the antioxidants neutralise the oxidative damage caused by gastro-oesophageal reflux disease, a risk factor for BE. Another theory is that wine drinkers typically consume food with their wine, reducing the potentially damaging effect of alcohol on oesophageal tissue.

The incidence of EAC has increased by more than 500% in the last three decades. The rate of increase is most predominant among Caucasian males, which the authors say suggests that environmental or lifestyle factors may play important roles. It said that stratification by beverage type showed an inverse association for wine drinkers compared to non-drinkers. In addition, education status was significantly inversely associated with the risk of BE. Those who preferred wine were more likely to have college degrees and regularly take vitamin supplements than those who preferred beer or liquor.

The study concluded that there were "associations between alcohol types, socioeconomic status, and the risk of Barrett's oesophagus". But it said: "Although choice of alcoholic beverages was associated with several factors, multiple adjustments (including for gastro-oesophageal reflux disease or GERD) did not eliminate the association between alcohol and Barrett's oesophagus."

The research findings were echoed by two other studies published in the same issue of Gastroenterology. Australian researchers found that people who drank wine were at a lower risk of EAC and Irish researchers found that people who drank wine were at a lower risk for oesophagitis, an irritation of the oesophagus that follows chronic heartburn and often precedes BE and cancer.

Source: "Alcohol Types and Sociodemographic Characteristics as Risk Factors for Barrett's Esophagus" Ai Kubo, T. R. Levin, G. Block, G. J. Rumore, C. P. Quesenberry Jr, P. Buffler, D. A. Corley. Gastroenterology, March 2009, Volume 136, Issue 3, Pages 806-815

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## Moderate drinking stimulates endorphin release

May 2009 endorphin release

New animal research finds that light to moderate drinking releases pleasure-causing endorphins in the brain, but the same is not true of heavy drinking.

Researchers at McGill University in Montreal found that low to moderate alcohol consumption affected the release of beta-endorphins in the midbrain/ventral tegmental area (VTA) of lab rats' brains.

"We found that low to moderate but not high doses of alcohol increase the release of beta-endorphin in the VTA, one of the brain regions shown to be important for mediating the rewarding effect of alcohol," said researcher Christina Gianoulakis. "This supports a role of beta-endorphin in mediating some of the rewarding effects of alcohol. However, the same doses of alcohol that increase beta-endorphin release in

the VTA have no significant effect on the release of enkephalins and dynorphins, the other two families of endogenous opioid peptides we examined."

Heavy drinking, on the other hand "is known to induce sedative and hypnotic effects, and often increase rather than decrease anxiety," Gianoulakis noted.

Source: The study appears in the March 2009 issue of the journal *Alcoholism: Clinical and Experimental Research*.

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# One to two drinks daily may lower risk of cognitive decline in older adults

June 2009

Research by Dr. Kaycee Sink, an assistant professor of medicine in geriatrics at the Wake Forest University School of Medicine, in Winston-Salem and colleagues, suggests that moderate drinking can lower the risk of dementia in older people.

The study found that amongst cognitively normal adults, one to two alcoholic drinks a day is associated with a 37% decreased risk of dementia over six years. However, among study participants who had mild cognitive impairment at the start of the study, drinking moderately had no effect. And heavier drinking - two or more drinks a day - nearly doubled their risk of developing dementia during the six-year follow-up.

The authors looked at 3,069 men and women, average age 79, and followed them for six years. At the study start, 2,587 were evaluated as cognitively normal; 482 had mild cognitive impairment, which can progress to dementia. The researchers asked about alcohol intake, smoking, depression, social activity and other factors, and tested the participants' cognitive functioning at the end of the study. About 38% of the participants had one to seven drinks a week, while about 9% had eight to 14 drinks a week.

Sink concludes that "If you are cognitively normal, there is no reason you should avoid light to moderate use of alcohol, and it may be beneficial. But if you have memory problems, we would probably say any amount of alcohol may be hazardous for your cognitive functioning. If you already have some memory problems, drinking is not going to help prevent progression to dementia, and may accelerate your progression."

Exactly why and how alcohol seems to help preserve normal cognitive functioning isn't clear. It is thought that it may increase the release of a neurotransmitter, acetylcholine, which helps brain cells communicate with each other.

Dr. Denis Evans, Jesmer Professor of Internal Medicine at the Rush Institute for Healthy Aging at Rush University Medical Center, in Chicago comments that "the first finding in the new study -- the 37% reduction in dementia among cognitively healthy moderate drinkers -- "is a very substantial reduction and is consistent with other studies,"

In regard to the finding that those mildly impaired get no benefit or, if they drink more than moderately, increase their risk of dementia? "There may not have been enough participants to definitively find a link", Evans said.



Sink presented her findings at the American Geriatrics Society annual meeting, in Chicago in April.

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# BMC researchers find that single question can identify unhealthy alcohol use in patients

April 2009

Researchers at Boston Medical Center (BMC) have found that a single-screening question recommended by the National Institute of Alcohol Abuse and Alcoholism (NIAAA) accurately identifies unhealthy alcohol use in primary-care patients. This research supports the use of the brief screen in the primary-care setting.

Unhealthy alcohol use, the spectrum from risky consumption to alcohol use disorders, alcohol abuse and dependence, is prevalent but under-diagnosed in primary-care settings. Commonly used alcohol screening instruments are comprised of multiple questions, often do not cover the full spectrum of unhealthy use, and can be time consuming to administer. Consequently, many patients are not screened.

The NIAAA recommends a single-question screen for unhealthy alcohol use. The recommended question asks, "How many times in the past year have you had X or more drinks in a day?" (where X is 5 for men and 4 for women). The NIAAA recommended screening test had not previously been validated in the primary-care setting. BMC researchers attempted to validate this version of the screening question in a sample of primary-care patients.

Of the 286 study participants reviewed, unhealthy alcohol use was reported by 31% of participants. 6% consumed risky amounts but did not have alcohol-related problems or a disorder, 13% consumed risky amounts and had problems but no current disorder and 12% had a current alcohol use disorder. The single-question screen was 81.8% sensitive and 79.3% specific for the detection of unhealthy alcohol use. It was slightly more sensitive and less specific for the detection of a current alcohol use disorder.

Peter Smith, MD, attending physician in the section of General Internal Medicine at Boston Medical Center explained that single-question screening tests for unhealthy alcohol use may help to increase the frequency of screening in primary-care and brief intervention by primary-care physicians for those with unhealthy alcohol use reduces risky consumption among those without dependence and improves patient outcomes.

Source: The BMC study appears online in the Journal of General Internal Medicine.

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# Red or white wine have an equal effect on breast-cancer risk

A study funded by the National Cancer Institute to evaluate the effect of red and white wine on breast-cancer risk concludes that they have an equal effect on breast-cancer risk. The results of the study, led by researchers at Fred Hutchinson Cancer Research Center, were published in the March issue of *Cancer Epidemiology, Biomarkers and Prevention*.

Lead author Polly Newcomb, Ph.D., M.P.H., head of the Cancer Prevention Program in the Public Health Sciences Division at the Hutchinson Center stated that the research aimed to tease out red wine's effects on breast-cancer risk, as previous studies have found positive effects relating to heart disease and prostate cancer. Instead, Newcomb and colleagues found no compelling reason to choose red over white wine.

For the study, the researchers interviewed 6,327 women with breast cancer and 7,558 age-matched controls about their frequency of alcohol consumption (red wine, white wine, liquor and beer) and other breast-cancer risk factors, such as age at first pregnancy, family history of breast cancer and postmenopausal hormone use. The study participants, ages 20 to 69, were from Wisconsin, Massachusetts and New Hampshire. The frequency of alcohol consumption was similar in both groups, and equal proportions of women in both groups reported consuming red and white wine.

The researchers found that women who consumed 14 or more US drinks (14g) per week, regardless of the type (wine, liquor or beer), faced a 24% increase in breast cancer compared with non-drinkers.

Source: No Difference Between Red Wine or White Wine Consumption and Breast Cancer Risk Polly A. Newcomb, Hazel B. Nichols, Jeannette M. Beasley, Kathleen Egan, Linda Titus-Ernstoff, John M. Hampton, and Amy Trentham-Dietz *Cancer Epidemiol. Biomarkers Prev.* 2009 18: 1007-1010.