

Appendix F

Bibliography of Abstracts

Alcohol Risk and Chronic Disease – 2006 Campaign

Bibliography of Abstracts

Cancer

Bagnardi, V.; Blangiardo, M.; La Vecchia, C.; Corrao, G. (2001). Alcohol consumption and the risk of cancer: a meta-analysis. Alcohol Research and Health, 25(1):263-270.

Alcohol consumption has been linked to an increased risk for various types of cancer. A combined analysis of more than 200 studies assessing the link between alcohol and various types of cancer (i.e., a meta-analysis) sought to investigate this association in more detail. This meta analysis found that alcohol most strongly increased the risks for cancers of the oral cavity, pharynx, esophagus, and larynx. Statistically significant increases in risk also existed for cancers of the stomach, colon, rectum, liver, female breast, and ovaries. Several mechanisms have been postulated through which alcohol may contribute to an increased risk of cancer. Concurrent tobacco use, which is common among drinkers, enhances alcohol's effects on the risk for cancers of the upper digestive and respiratory tract. The analysis did not identify a threshold level of alcohol consumption below which no increased risk for cancer was evident. Section headings in this article include: (1) Methods used for the meta-analysis, (2) Limitations and strengths of the meta-analysis, (3) Mechanisms of alcohol-related carcinogenesis, (4) effects of combined alcohol and tobacco use, and (5) Risks associated with different types of alcoholic beverages.

Brown, L.M., Hoover, R., Silverman, D., Baris, D., Hayes, R., Swanson, G. M., Schoenberg, J., Greenberg, R., Liff, J., Schwartz, A., Dosemeci, M., Pottern, L., Fraumeni, J. F. Jr. (2001). Excess incidence of squamous cell esophageal cancer among US Black men: role of social class and other risk factors. American Journal of Epidemiology, 153(2):114-22.

Data from a population-based case-control study were used to evaluate the relation between social class factors and squamous cell esophageal cancer and the extent to which alcohol, tobacco, diet, and low income contribute to the higher incidence among Black men than among White men in the United States. A total of 347 male cases (119 White, 228 Black) and 1,354 male controls (743 White, 611 Black) were selected from three US geographic areas (Atlanta, Georgia, Detroit, Michigan, and New Jersey). Cases were residents of the study areas aged 30-79 years who had been diagnosed with histologically confirmed esophageal cancer between 1986 and 1989. The adjusted odds ratios for subjects with annual incomes less than \$10,000 versus incomes of \$25,000 or more were 4.3 (95% confidence interval: 2.1, 8.7) for Whites and 8.0 (95% confidence interval: 4.3, 15.0) for Blacks. The combination of all four major risk factors-low income, moderate/heavy alcohol intake, tobacco use, and infrequent consumption of raw fruits and vegetables-accounted for almost all of the squamous cell esophageal cancers in Whites (98%) and Blacks (99%) and for 99% of the excess incidence among Black men. Thus, lifestyle modifications, especially a lowered intake of alcoholic beverages, would markedly decrease the incidence of squamous cell esophageal cancer in both racial groups and would narrow the racial disparity in risk. Further studies on the determinants of social class may help to identify a new set of exposures for this tumor that are amenable to intervention.

Cancer Care Ontario. (2005). Alcohol use increases cancer risk (Dec. 2005) Retrieved from http://www.cancercare.on.ca/index_cancerfactsalcoholuse+cancerrisk.htm

Alcohol consumption has been established as a convincing risk factor for cancers of the mouth, pharynx, larynx, esophagus, liver and breast, and a probable risk factor for cancers of the colon and rectum. In at least some of these cancers, alcohol and tobacco use together increase risk to a higher level than if the risks from the two were added together.

The amount consumed, rather than the type of alcohol (beer, wine, or spirits), appears to influence the risk of cancer. For liver cancer, it is heavy and persistent use that causes damage. Risk of the other cancers linked to alcohol consumption increases slightly with even low or moderate consumption, and rises with the amount consumed.

Because there is evidence that moderate alcohol use also has beneficial health effects, safe drinking guidelines developed in Canada recognize the need for balance. (Moderate use, for example, appears to reduce overall mortality, but not cancer-related mortality.)

The guidelines recommend no more than two drinks a day, with a weekly maximum of nine drinks for women and 14 for men. Persons with a family history of cancer are encouraged to drink less. In Ontario, 70% of men and 86% of women aged 19 and older report that they either drink alcohol in accordance with these guidelines, or don't drink at all.

Castellsague, X., Munoz, N., De Stefani, E., Vitoria, C. G., Quintana, M. J., Castelletto, R., Rolon, P. A. (2000). Smoking and drinking cessation and risk of esophageal cancer (Spain). Cancer Causes & Control, 11(9):813-8.

OBJECTIVES: To explore the effectiveness of alcohol drinking and tobacco smoking cessation in reducing esophageal cancer risk, taking into account the key characteristics of each habit and the simultaneous exposure to both habits. **METHODS:** Data from a series of five hospital-based case-control studies of incident squamous-cell carcinoma of the esophagus conducted by the International Agency for Research on Cancer (IARC, Lyon, France) in high-risk areas in South America were combined and analyzed by multivariate logistic regression procedures. A total of 2063 men (655 case patients and 1408 control subjects) were included in the pooled analysis. **RESULTS:** For either habit, the risk of esophageal cancer decreased rapidly, strongly and significantly with longer periods of abstinence. The risk reduction was statistically significant regardless of the intensity and duration of each habit and the type of tobacco or alcoholic drink consumed. For subjects exposed to both risk factors, the protective effect of quitting both habits appeared to be synergistic, reaching, after only five to nine years of simultaneous cessation of both exposures, a 70% risk reduction, a reduction that clearly overlapped with the risk intervals of both never-smokers and never-drinkers. The risk benefit of merely quitting alcohol drinking was delayed (>10 years of cessation) unless it was also accompanied by a few years of smoking cessation. **CONCLUSIONS:** Our findings solidly demonstrate for the first time the effectiveness of smoking and drinking cessation in reducing esophageal cancer risk. For the large proportion of subjects in the general population exposed to both risk factors, our results further emphasize the importance of smoking cessation to effectively reduce cancer risk.

Castellsague, X., Munoz, N., De Stefani, E., Vitoria, C. G., Castelletto, R., Rolon, P. A., Quintana, M. J. (1999). Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in men and women. International Journal of Cancer, 82(5):657-64.

To estimate the independent and joint effects of tobacco smoking and alcohol drinking, we analyzed data from a series of 5 hospital-based case-control studies of squamous-cell carcinoma of the esophagus conducted in high-risk areas in South America. A total of 830 case subjects and 1779 control subjects were included in the pooled analysis. All

exposure characteristics of amount, duration, cessation and type of alcohol and tobacco consumed were strongly related to esophageal-cancer risk in both sexes. Women had the same exposure profile as men, but the magnitudes of the associations were lower than were those among men. Black-tobacco smoking was associated with a 2-fold increased risk as compared with the smoking of blond or mixed tobacco. Quitting either of the 2 habits significantly reduced esophageal-cancer risk. Alcohol and tobacco alone were strongly related to the risk of esophageal cancer, even in the absence of the other exposure. A history of simultaneous exposure to cigarette smoking and alcohol drinking had a strong multiplicative effect on risk. Concomitant exposure to heavy alcohol drinking and black-tobacco smoking identified the group with the highest risk for developing esophageal cancer (odds ratio = 107). A synergistic interaction was found between the 2 habits, particularly in women and in moderately exposed men. Moderate cigarette smoking without drinking and moderate alcohol drinking without smoking had a negligible effect on esophageal-cancer risk. However, simultaneous exposure to the same moderate amounts increased the risk 12- to 19-fold in men and in women respectively. The overall public-health implications of these findings are obvious for a tumor that depends on preventive strategies for its control. Copyright 1999 Wiley-Liss, Inc.

Castellsague, X.; Quintana, M.J.; Munoz, N.; De Stefani, E.; Victora, C.G.; Castelletto, R.; Rolon, P.A. (1999). Smoking and drinking habits' characteristics and risk of esophageal cancer in men and women. European Journal of Cancer, 35(S2):S31.

Data from five case-control studies of squamous cell carcinoma of the esophagus conducted in high-risk areas in South America were combined for meta-analysis using multivariate logistic regression. The studies used the same research protocol and data collection procedures. A total of 830 cases and 1,779 controls were included in the analysis. In both men and women, esophageal cancer risk was strongly related to alcohol and cigarette consumption and cessation. Women and men had the same exposure profile, but the magnitudes of the associations among women were somewhat lower than were those among men. The exposure characteristics that most strongly influenced the risk of esophageal cancer were: average daily alcohol consumption, years of cigarette smoking, type of tobacco smoked, and time since quitting either habit. The relative risk for black tobacco smoking was about two times higher than that for blond tobacco smoking, and a synergistic interaction with number of cigarettes smoked was found. Strong inverse dose-response relationships were identified with time since quitting either habit. Risk reduction after cessation was consistently observed regardless of the previous duration and intensity of the habit and the type of tobacco or alcoholic beverage consumed.

Castellsague, X.; Munoz, N.; De Stefani, E.; Victora, C.G.; Castelletto, R.; Rolon, P.A. (1999). Simultaneous exposure to tobacco and alcohol consumption and esophageal cancer risk. European Journal of Cancer, 35(S2):S31.

Data from five case-control studies of squamous cell carcinoma of the esophagus conducted in high risk areas in South America were combined for meta-analysis using multivariate logistic regression. A total of 830 cases and 1,779 control subjects were included. A history of simultaneous exposure to cigarette smoking and alcohol intake had a strong dose-related, multiplicative effect on esophageal cancer risk. A synergistic interaction was found between smoking and alcohol among women. Among men the synergistic interaction was detected only among moderately exposed subjects. Alcohol and tobacco alone were strongly related to the risk of esophageal cancer. Moderate cigarette smoking without drinking and moderate alcohol drinking without smoking had little or no effect on esophageal cancer risk. However, the simultaneous exposure to the same moderate amounts increased the risk 13-fold in men and 19-fold in women. The subgroup with the highest risk of esophageal cancer were those who combined heavy alcohol drinking with black tobacco smoking, which was associated with a 107-fold

increase in risk. The highest risk reduction was observed when both habits were stopped. Quitting cigarette smoking was associated with a subsequent risk reduction for both current and ex-alcohol drinkers. The risk reduction effects associated with alcohol consumption cessation were modest and long-term unless there was a few years of concomitant cigarette smoking cessation. Priority should be given to smoking prevention and cessation programs.

Corrao, G., Bagnardi, V., Zambon, A., Arico, S. (1999). Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis. Addiction, 94(10):1551-73.

OBJECTIVE: To compare the strength of the evidence provided by the epidemiological literature on the association between alcohol consumption and the risk of six cancers (oral cavity, oesophagus, colorectum, liver, larynx, breast), hypertension, cerebrovascular diseases, gastric and duodenal ulcer, liver cirrhosis and other chronic liver diseases, pancreatitis and injuries and adverse effects. METHODS: A search of the epidemiological literature from 1966 to 1998 was performed by several bibliographic databases. Meta-regression models were fitted considering fixed and random models and linear and non-linear effects of alcohol intake on the risk of each condition. The effects of some characteristics of the studies including an index of their quality were considered as putative sources of heterogeneity of the estimates. Publication bias was also investigated by asymmetry of funnel plots. RESULTS: Of the 397 initially reviewed studies, 200 were selected for meta-analysis. Since qualitative characteristics of the studies were often significant sources of heterogeneity among them, the estimates of the pooled dose-response slopes were based only on the 123 studies with higher quality score and/or reporting adjusted estimates of relative risks. Higher alcohol-related risks were found for liver cirrhosis, neoplasms of the upper respiratory and digestive tracts, haemorrhagic stroke and injuries and adverse effects. Weaker but significant associations were found for colorectum, liver and breast cancers, essential hypertension and chronic pancreatitis. For all these conditions, low intakes, corresponding to daily consumption of two drinks or two glasses of wine (25 g/day), have shown significant risks. Ischaemic stroke and gastric and duodenal ulcer seem independent of alcohol intake. The area in which the study was performed, the study's design and the outcome variable differently affected the slopes. CONCLUSIONS: The small number of sufficiently reliable studies, the strong indications of heterogeneity across them and the suspicion of publication bias suggest that there is a great need for well-conducted epidemiological studies performed in several countries, to examine the dose-response relationship between alcohol intake and the risk of several alcohol-related conditions, as well as the role of drinking pattern in determining the risk.

Coups, E. J., Ostroff, J. S. (2005). A population-based estimate of the prevalence of behavioral risk factors among adult cancer survivors and noncancer controls. Preventive Medicine, 40(6):702-11.

BACKGROUND: Behavioral risk factors have significant biomedical and psychosocial effects for cancer survivors. Representative data on the prevalence of a wide range of behavioral risk factors among cancer survivors are lacking. METHODS: We used data from the 2000 National Health Interview Survey to examine the prevalence of smoking, physical inactivity, dietary risk factors, being overweight, risky alcohol use, and sun protection behaviors among a sample of 32,346 adults, 1646 of whom were cancer survivors. RESULTS: With the exception of smoking, there were few differences in age-stratified behavioral risk factor prevalences between cancer survivors and noncancer controls. Among the cancer survivors, there were few differences in behavioral risk factor prevalence rates for survivors of different cancers. Exceptions included a high rate of current smoking for cervical and uterine cancer survivors. The prevalences of physical inactivity, dietary risk factors, and being overweight were relatively high across cancer

types, whereas the prevalence of risky drinking was particularly low. CONCLUSIONS: This study provides benchmark estimates of the prevalence of multiple cancer-related behavioral risk factors among U.S. cancer survivors. The results reveal considerable opportunities for behavioral risk factor interventions among cancer survivors. We discuss implications of the results and outline directions for future research.

Hanaoka, T., Tsugane, S., Ando, N., Ishida, K., Kakegawa, T., Isono, K., Takiyama, W., Takagi, I., Ide, H., Watanabe, H. (1994). Alcohol consumption and risk of esophageal cancer in Japan: a case-control study in seven hospitals. Japanese Journal of Clinical Oncology, 24(5):241-6.

In a multi-center case-control study, we evaluated the risk of esophageal cancer in the Japanese population. All patients and controls were inpatients in the surgical departments of seven hospitals nationwide. Patients eligible for the study were those newly diagnosed as having primary esophageal cancer. One control per case was selected from among patients admitted to the same hospital, and 141 male pairs were analyzed using logistic regression analysis. The results showed dose-response relation between the risk of esophageal cancer and both the quantity (g/week) and frequency (times/week) of alcohol drinking (P value for trend = 0.0001). Although a statistically significant risk increase was shown among moderate to heavy smokers (15 < or = cigarette/day < 25) (odds ratio, 4.35:95% confidence interval, 1.81-10.49), the dose-response for cigarette smoking was unclear (P value for trend = 0.07). No combined effect of alcohol drinking and cigarette smoking was found. A frequent intake of fruit was associated with a decreased risk (P value for trend = 0.02). After adjustment for alcohol consumption, cigarette smoking and fruit intake were found not to be associated with the risk, whereas a preference for high-temperature food and drink showed a statistically significant positive association (P value for trend = 0.02). Drinkers who consumed shochu most frequently showed a three-fold increased risk over that for beer consumers, although the association disappeared after adjusting for the amount of alcohol consumed. The present results confirm alcohol intake and a preference for high-temperature food to be associated with an increased risk of esophageal cancer and show the amount of alcohol consumed, rather than the type of alcoholic beverage, to be the main risk determinant.

Hendriks, H.F.J. (2002). Report of the 30th International Medical Advisory Board Conference held in Brussels, Belgium, 13-16 October 2002. Alcohol Research, 7(6):239-240.

Several papers presented at the 30th International Medical Advisory Board Conference held in Brussels, Belgium, 13-16-Oct-2002, are summarized. The session on alcohol and vascular disease was followed by sessions on approaches to treatment and the education of medical professionals. The treatment session included findings from a meta-analysis of 15 randomized controlled trials of acamprosate (acetyl homotaurinate) in 11 European countries (N > 4,400). Clear positive effects of acamprosate were found, including more days of abstinence and increased abstinence rates. The session on alcohol and the liver included a presentation on the epidemiology of alcoholic liver disease (ALD). The Dionysos study has shown that there is a threshold for ALD at 30 g alcohol/day in both sexes. Genetic factors appear to be involved in ALD, and viral infection and obesity both add to the risk. The session on alcohol and cancer included an overview of the relation between alcohol use and cancer. Among lifestyle factors relevant to cancer, alcohol plays a modest role with an attributable risk of 4%-6% compared to 30% for smoking, and 20%-50% for diet. Alcohol is associated with cancers of the mouth, esophagus, and breast and with colorectal cancer. The session on alcohol and driving examined the effects of lowering the legal blood alcohol limit from 0.08% to 0.05% in Denmark. The final session was on alcohol and young people. The number of drinking

occasions and the frequency of intoxication are increasing in northern Europe but not in southern Europe.

Inoue, M., Tsugane, S., JPHC Study Group. (2005). Impact of alcohol drinking on total cancer risk: data from a large-scale population-based cohort study in Japan. British Journal of Cancer, 92(1):182-7.

We conducted a cohort study of alcohol consumption and total cancer incidence and mortality in 73,281 subjects (35,007 men and 38,274 women) aged 40-59 years old at baseline over a 10-year follow-up period. During 1990-2001, a total of 3403 cases of newly diagnosed cancer and 1208 cancer deaths were identified. In men, the lowest risk of developing cancer was observed among occasional drinkers, and a linear positive association with increased ethanol intake was noted (hazard ratio 1.18 for 1-149 g per week, 1.17 for 150-299 g per week, 1.43 for 300-449 g per week, 1.61 for > or = 450 g per week, P for trend < 0.001). The positive relation was similar for cancer incidence and mortality, but was more striking among current smokers and alcohol-related cancers. Relatively few women were regular drinkers. Our results suggest that increased ethanol intake linearly elevates the risk of cancer, and that nearly 13% of cancers among males in this study were due to heavy drinking (> or = 300 g per week of ethanol), to which smoking substantially contributed. The simultaneous reduction of smoking is therefore important for reducing the effect of alcohol on cancer risk.

Kato, H., Yoshikawa, M., Miyazaki, T., Nakajima, M., Fukai, Y., Tajima, K., Masuda, N., Tsukada, K., Fukuda, T., Nakajima, T., Kuwano, H. (2001). Expression of p53 protein related to smoking and alcoholic beverage drinking habits in patients with esophageal cancers. Cancer Letters, 167(1):65-72.

In esophageal squamous cell carcinoma (SCC), we used immunohistochemical analysis to further elucidate the correlation of p53 protein expression with clinicopathological factors, as well as with risk factors, such as tobacco smoking, alcohol consumption and a family history of cancer, using odds ratios (ORs). The expression of p53 protein was demonstrated in 55.1% of 89 esophageal SCC cases examined by immunohistochemistry. The expression of p53 protein did not correlate with gender, age, histological grading, lymph node metastasis, or TNM stage. The prevalence of p53 expression was significantly higher in patients with multiple primary esophageal cancers (P<0.05). p53 expression did not correlate with prognosis in univariate survival analysis. The esophageal SCC in either smokers or alcohol users was 4.67-5.83 times more likely to express p53 protein, while the likelihood of p53 expression in patients who use both tobacco and alcohol was more than 14.0 times. However, a significant association was not found between p53 expression and a family history of cancer, this having an OR as low as 1.85. The expression of p53 protein did not correlate with clinicopathological factors and prognosis in univariate and multivariate survival analyses. In contrast, tobacco smoking and alcohol consumption were shown to be strongly associated with p53 mutations in esophageal carcinogenesis.

Pedersen, A., Johansen, C., Gronbaek, M. (2004) Relations between amount and type of alcohol and colon and rectal cancer in a Danish population based cohort study. Comment in: Gut. 2004 Jan;53(1):155-6; PMID: 14684595 Gut. 52(6):861-7, 2003 Jun.

BACKGROUND: There may be a weak association between total alcohol intake and colorectal cancer but the effect of different types of alcohol and effect on colon subsites have not been investigated satisfactorily. AIMS: To investigate the relationship between amount and type of alcohol and the risk of colon and rectal cancer. SUBJECTS: A population based cohort study with baseline assessment of weekly intake of beer, wine, and spirits, smoking habits, body mass index, educational level, and leisure time physical activity in Copenhagen, Denmark. The study included a random sample of 15 491 men

and 13 641 women, aged 23-95 years. Incident cases of colorectal cancer were identified in the nationwide Danish Cancer Register. RESULTS: During a mean follow up of 14.7 years, we observed 411 colon cancers and 202 rectal cancers. We observed a dose-response relationship between alcohol and rectal cancer. Drinkers of more than 41 drinks a week had a relative risk of rectal cancer of 2.2 (95% confidence limits 1.0-4.6) compared with non-drinkers. Drinkers of more than 14 drinks of beer and spirits a week, but not wine, had a risk of 3.5 (1.8-6.9) of rectal cancer compared with non-drinkers, while those who drank the same amount of alcohol but including more than 30% of wine had a risk of 1.8 (1.0-3.2) of rectal cancer. No relation between alcohol and colon cancer was found when investigating the effects of total alcohol, beer, wine, and spirits, and percentage of wine of total alcohol intake. CONCLUSION: Alcohol intake is associated with a significantly increased risk of rectal cancer but the risk seems to be reduced when wine is included in the alcohol intake.

Sakata, K., Hoshiyama, Y., Morioka, S., Hashimoto, T., Takeshita, T., Tamakoshi, A. (2005) JACC Study Group. Smoking, alcohol drinking and esophageal cancer: findings from the JACC Study. Journal of Epidemiology, 15 Suppl 2:S212-9.

BACKGROUND: Using a large-scale cohort of about 110,000 people established in 45 areas throughout Japan from 1988 through 1990, the study attempted to uncover the joint effects of combined smoking and alcohol intake on esophageal cancer mortality. METHODS: A cohort established from 1988 through 1990 included 46,465 men and 64,327 women aged 40 years and older and younger than 80. The number of female smokers and drinkers was low, and women were excluded from the analysis for that reason. In addition, 308 people with histories of malignant neoplasm, and 3,579 with unclear smoking and drinking data were also excluded, resulting in 42,578 people available for analysis. A follow-up of these individuals was conducted until 1999. Cox proportional hazards model was used for the analysis. RESULTS: The joint effects of number of cigarettes and amount of alcohol consumed per day were compared with non-smokers and non-drinkers or those consuming less than one unit of alcohol per day. An increased synergistic esophageal cancer mortality risk (3.88) for both smoking and drinking was observed for those smoking 20 cigarettes or less per day and drinking one unit of alcohol or more but less than three units per day, with the risk rising (6.30) for those smoking at least 21 cigarettes and drinking at least three units of alcohol per day. Even in non-smokers with increased alcohol consumption, and in non-drinkers or those drinking at most one drink per day with increased smoking, no increased risk was observed. CONCLUSIONS: In this cohort study of a Japanese population, increased esophageal cancer mortality risk was observed only when both factors of alcohol and tobacco intake were present simultaneously.

Su, L., J., Arab, L. (2004) Alcohol consumption and risk of colon cancer: evidence from the National Health and Nutrition Examination Survey I: epidemiologic follow-up study. Nutrition & Cancer, 50(2):111-9.

The epidemiologic findings on the relationship between alcohol consumption and colon cancer are inconsistent. The National Health and Nutrition Examination Survey (NHANES) I Epidemiologic Follow-Up Study (NHEFS) included a prospective cohort population representative of the general U.S. population, which had not been fully utilized for examining the risk between colon cancer and alcohol drinking. The NHEFS consisted of 10,220 participants prospectively followed over a decade. Alcohol consumption, amount and type of beverage, and drinking patterns at baseline were considered in examination of the effect of alcohol consumption on the risk of colon cancer. The consumption of one or more alcoholic beverages a day at baseline was associated with approximately a 70% greater risk of colon cancer [relative risk (RR)=1.69; 95% confidence interval (CI)=1.03, 2.79], with a strong positive dose-response relationship (P=0.04). This association appeared to be exclusively related to daily drinking of one or

more drinks of liquor (RR=2.48; 95% CI=1.66, 4.53). Additionally, more than a 70% increased risk of colon cancer was observed for more than 34 yr of alcohol drinking history compared with nondrinkers (RR=1.73; 95% CI=1.08, 2.78). Overall, alcohol consumption was significantly associated with increased risk of colon cancer. The most important factor for colon cancer seems to be liquor consumption.

Wang, X. D. Retinoids and alcohol-related carcinogenesis. (2003) [Review] *Journal of Nutrition*, 133(1):287S-290S.

Chronic and excessive alcohol intake is associated with an increased incidence of a variety of cancers (e.g., liver, oral cavity, esophagus, colorectal and breast). Long-term alcohol intake results in impaired nutritional status of retinoic acid (RA), the most active derivative of vitamin A, which may provide a promoting environment for tumor formation. Recent studies demonstrate that chronic alcohol-induced hepatocellular proliferation, which may convert hepatocytes from a state of resistance to a carcinogen to a state of high susceptibility, is due to alcohol-impaired RA metabolism and signaling and crosstalk with the Jun N-terminal kinases-dependent signaling pathway. Further, the restoration of hepatic RA homeostasis by treatment with either RA supplementation or inhibitors of RA catabolism can suppress alcohol-induced hepatocyte hyperproliferation and restore alcohol-deregulated apoptosis, thereby reducing the risk of alcohol-promoted hepatocellular carcinogenesis. These studies indicate the importance of RA actions in the prevention and/or treatment of alcohol-related carcinogenic process in the liver and other organs.

Xu, Y., Ross, M. C., Ryan, R., Wang, B. (2005). Cancer risk factors among Southeast Asian American residents of the U.S. Central Gulf Coast. *Public Health Nursing*, 22(2):119-29.

This study profiles aggregate-specific cancer risk factors of Southeast Asian Americans residing along the Central Gulf Coast in the United States. An investigator-designed cross-sectional survey was conducted with 332 volunteer Southeast Asian community residents aged 18 years and above. Aggregate-specific cancer risk factors include high prevalence of hepatitis, high smoking and drinking rates in men, extended ultraviolet light exposure without protection, low colorectal and prostate cancer screening rates, and knowledge deficits of cancer and cancer screenings. Based on the study findings, progress toward the targets of the Alabama Comprehensive Cancer Control Plan: 2001-2005 is evaluated and compared to available national data. Implications for public health nursing practice and future research are also addressed. In particular, the study findings underscore the importance of developing culturally tailored interventions to reduce cancer risk factors in this underserved Asian American population.

Yang, C., X., Wang, H., Y., Wang, Z., M., Du, H., Z., Tao, D. M., Mu, X. Y., Chen, H., G., Lei, Y., Matsuo, K., Tajima, K. (2005). Risk factors for esophageal cancer: a case-control study in South-western China. *Asian Pacific Journal of Cancer Prevention*, 6(1):48-53.

Esophageal cancer is a crucial cancer in China. Yanting in Sichuan Province was a key area with highest esophageal cancer mortality in China, but little evidence on esophageal cancer risk factors has been reported for this area and the etiology remains unclear. To clarify risk factors, a 1:1 matched case-control study was conducted. Totals of 185 eligible esophageal cancer patients and 185 healthy residents matched for sex and age were recruited. Conditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for possible risk/protective factors. All ORs were adjusted by family history of esophageal cancer and occupation, and then further adjusted by other possible confounding factors. Our results showed that smoking and alcohol drinking were risk factors for esophageal cancer with dose-response. The ORs

(95% CI) compared with never smokers and drinkers were 4.06 (1.55-10.6) and 2.49 (1.06-5.85), respectively. The OR was further increased to 8.86 (95% CI, 3.82-20.5) for both smoking and drinking in combination. Eating food rapidly (OR=5.84, 95% CI, 2.05-16.7), drinking shallow ground water (OR=4.18, 95% CI, 1.30-13.4) and frequent intake of pickled vegetables (OR=2.12, 95% CI, 1.00-4.49) appeared to increase the risk, while frequent intake of fresh fruit (OR=0.42, 95% CI, 0.19-0.89), fresh vegetables (OR= 0.62, 95% CI, 0.32-1.17) and eggs (OR=0.59, 95% CI, 0.25-1.39) decreased the risk. In conclusion, smoking and alcohol drinking are common in Yanting and main contributors to esophageal cancer. Consumption of fresh fruit and eggs are not common and high consumption of these two foods as well as fresh vegetables may decrease the risk of esophageal cancer in this area. In addition, drinking shallow ground water and eating food rapidly, as well as frequent intake of pickled vegetables, are also factors increasing the risk.

Yang, C., X., Matsuo, K., Ito, H., Hirose, K., Wakai, K., Saito, T., Shinoda, M., Hatooka S., Mizutani, K., Tajima, K. (2005) Esophageal cancer risk by ALDH2 and ADH2 polymorphisms and alcohol consumption: exploration of gene-environment and gene-gene interactions. Asian Pacific Journal of Cancer Prevention, 6(3):256-62.

Alcohol drinking is a major risk factor for esophageal cancer in Japan and its impact may be modulated by levels of ALDH2, ADH2 and CYP2E1, three representative alcohol-metabolizing enzymes which display genetic polymorphisms altering individual alcohol-oxidizing capacity and drinking behavior. To assess the actual influence of ADH2 Arg47His, ALDH2 Glu487Lys and CYP2E1 variant c2 allele polymorphisms on esophageal cancer risk with conjunction with alcoholic consumption, the present 1:3 matched case-control study was conducted. The 165 histologically diagnosed Japanese esophageal cancer cases were here compared with 495 randomly selected controls, matched with respect to sex and age. Conditional logistic regression was used to calculate Odds Ratios (ORs) and 95% confidence intervals (95% CI). Significant gene-environment interactions between alcohol drinking and both ADH2 and ALDH2 were observed regarding esophageal cancer risk. The ADH2 Arg47His polymorphism showed moderately increased risk (OR for Arg/His and Arg/Arg relative to His/His: 2.01 (1.39-2.90)). In the ALDH2 case, comparing the Glu/Lys with the Glu/Glu genotype, ORs were markedly increased to 9.64 (3.23-28.8) and 95.4 (28.7-317) from 1.88 (0.42-8.37) and 4.62 (0.93-23.1) for moderate drinking and heavy drinking, respectively. No significant alteration in risk was observed with the CYP2E1 polymorphism. In conclusion, the present study revealed a significant gene-environment interaction between alcohol drinking and the ALDH2 polymorphism regarding esophageal cancer risk among a general population in Japan, providing concrete evidence of a role for acetaldehyde in neoplastic development. Interactions between ALDH2 and ADH2 need further clarification.

Breast Cancer

Chen, W., Y., Colditz, G., A., Rosner, B., Hankinson, S. E., Hunter, D. J., Manson, J. E., Stampfer, M. J., Willett, W. C., Speizer, F. E. (2002). Use of postmenopausal hormones, alcohol, and risk for invasive breast cancer. Annals of Internal Medicine, 137(10):798-804.

BACKGROUND: Physiologic evidence suggests that use of alcohol increases the risk for breast cancer through a hormonal mechanism, but the relationship among breast cancer, alcohol, and postmenopausal hormones (PMH) remains unclear. OBJECTIVE: To examine the relation between concurrent use of alcohol and PMH and invasive breast cancer. DESIGN: Prospective cohort study SETTING: Nurses' Health Study. PARTICIPANTS: 44 187 postmenopausal women. MEASUREMENTS: Self-reported data on PMH use and breast cancer obtained from biennial questionnaires completed from 1980 to 1994 and average alcohol consumption in 1980, 1984, 1986, and 1990. RESULTS: 1722 women developed invasive breast cancer. Risk for breast cancer was elevated in women who currently used PMH for 5 or more years and did not drink alcohol (relative risk, 1.32 [95% CI, 1.05 to 1.66]) and those who never used PMH but drank 20 or more g (1.5 to 2 drinks) of alcohol daily (relative risk, 1.28 [CI, 0.97 to 1.69]). Current users of PMH for 5 or more years who consumed 20 or more g of alcohol daily had a relative risk for breast cancer nearly twice (1.99 [CI, 1.42 to 2.79]) that of nondrinking nonusers of PMH. A hypothetical postmenopausal woman whose lifetime risk for breast cancer is 4% could increase her risk to 8% with 5 or more years of current PMH use and consumption of more than one alcoholic drink daily. CONCLUSIONS: Both alcohol consumption and PMH use were associated with an increased incidence of breast cancer. Women who are currently taking PMH may want to consider the added risks of regular alcohol consumption.

Collaborative Group on Hormonal Factors in Breast Cancer Alcohol, tobacco and breast cancer: Collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. (2002). British Journal of Cancer, 87(11):1234-1245.

This investigation analyzed data on 53,515 women with invasive breast cancer and 95,067 controls from 53 studies comprising over 80% of the relevant information on alcohol and tobacco consumption and breast cancer. Relative risks (RRs) of breast cancer were estimated after stratifying by study, age, parity, and women's age when first child was born, and consumption of alcohol and tobacco. The average consumption of alcohol reported by controls from developed countries was 6.0 g/day and was greater in ever-smokers (8.4 g/day) than never-smokers (5.0 g/day). Compared with women who reported drinking no alcohol, the RR of breast cancer was 1.32 for an intake of 35-44 g/day and 1.46 for 45 or more g/day. The RR of breast cancer increased by 7.1% for each additional 10 g/day intake in both ever-smokers and never-smokers. By contrast, the relationship between smoking and breast cancer was substantially confounded by the effect of alcohol. When analyses were limited to 22,255 women with breast cancer and 40,832 controls who reported drinking no alcohol, smoking was not associated with breast cancer. If the observed relationship for alcohol is causal, these results suggest that about 4% of the breast cancers in developed countries are attributable to alcohol. It is concluded that smoking has little or no independent effect on the risk of developing breast cancer, and that the effect of alcohol on breast cancer needs to be interpreted in the context of its beneficial effects (in moderation) and its harmful effects on other organs.

Dorgan, J. F., Baer, D. J., Albert, P. S., Judd, J. T., Brown, E. D., Corle, D. K., Campbell, W. S., Hartman, T. J., Tejpar, A. A., Clevidence, B. A., Giffen, C. A., Chandler, D. W., Stanczyk, F. Z., Taylor, P. R. (2001). Serum hormones and the alcohol-breast cancer association in postmenopausal women. Journal of the National Cancer Institute, 93(9):710-715.

BACKGROUND: Alcohol ingestion is associated with an increased risk of breast cancer in most epidemiologic studies. Results, however, are heterogeneous at lower levels of alcohol intake, and a biologic mechanism for the association has not been clearly identified. To determine whether alcohol consumption by postmenopausal women elevates serum levels of hormones associated with an increased risk of breast cancer, we performed a controlled feeding study. **METHODS:** Participants were 51 healthy postmenopausal women not using hormone replacement therapy. Each participant rotated through three 8-week dietary periods in which she consumed 15 or 30 g of alcohol per day or an alcohol-free placebo beverage. The order of assignment to the three alcohol levels was random. During the dietary periods, all food and beverages were supplied by the study, and energy intake was adjusted to keep body weight constant. Levels of estradiol, estrone, estrone sulfate, testosterone, androstenedione, progesterone, dehydroepiandrosterone (DHEA), DHEA sulfate (DHEAS), and androstenediol were measured by radioimmunoassays in serum collected at the end of each dietary period. All statistical tests are two-sided. **RESULTS:** When women consumed 15 or 30 g of alcohol per day, respectively, estrone sulfate concentrations increased by 7.5% (95% confidence interval [CI] = -0.3% to 15.9%; $P = .06$) and 10.7% (95% CI = 2.7% to 19.3%; $P = .009$) and DHEAS concentrations increased by 5.1% (95% CI = 1.4% to 9.0%; $P = .008$) and 7.5% (95% CI = 3.7% to 11.5%; $P < .001$) relative to levels when women consumed placebo. None of the other hormones measured changed statistically significantly when women consumed alcohol. **CONCLUSIONS:** Results suggest a possible mechanism by which consumption of one or two alcoholic drinks per day by postmenopausal women could increase their risk of breast cancer

Ellison, R. C., Zhang, Y., McLennan, C. E., Rothman, K. J. (2001). Exploring the relation of alcohol consumption to risk of breast cancer. American Journal of Epidemiology, 154(8):740-747.

There are lingering questions regarding the relation between alcohol consumption and breast cancer risk in women. Using a meta-analysis of epidemiologic studies carried out through 1999, this study examined the dose-response relation and whether effect estimates differed according to various study characteristics. In general, there was a monotonic increase in the relative risk of breast cancer with alcohol consumption, but the magnitude of the effect was small; in comparison with nondrinkers, women averaging 12 grams per day of alcohol consumption (approximately one typical drink) had a relative risk of 1.10 (95 percent confidence interval [CI]: 1.06, 1.14). Estimates of relative risk were 7 percent greater in hospital-based case-control studies than in cohort studies or community-based case-control studies, 3 percent greater in studies published before 1990 than in studies published later, and 5 percent greater in studies conducted outside of the United States than in studies within the United States. The findings of five US cohort studies published since 1990 yielded a relative risk of 1.06 (95 percent CI: 1.00, 1.11) for consumers of 12 grams per day, as compared with nondrinkers. Cohort studies with less than 10 years of follow-up gave estimates 11 percent higher than cohort studies with longer follow-up periods. No meaningful difference was seen by menopausal status or type of beverage consumed.

Feigelson, H. S., Calle, E. E., Robertson, A. S., Wingo, P. A., Thun, M. J. (2001). Alcohol consumption increases the risk of fatal breast cancer (United States). Cancer Causes & Control. 12(10):895-902.

OBJECTIVE: To investigate the hypothesis that alcohol consumption increases the risk of breast cancer mortality. **METHODS:** We examined breast cancer mortality in relation to self-reported alcohol consumption in women from the American Cancer Society Cancer Prevention Study (CPS)-II. After 14 years of follow-up, 1,442 eligible breast cancer deaths were observed among 242,010 women. Cox proportional hazards models were constructed for total alcohol consumption and for beer, wine, and liquor separately. **RESULTS:** Total alcohol consumption was associated with increased risk of fatal breast cancer among post- but not pre- or perimenopausal women. Even less than one drink/day was associated with up to a 30% increase in breast cancer mortality among postmenopausal women compared to non-drinkers (RR = 1.3, 95% CI: 1.1-1.6 for women drinking 0.26-<1 drink/day). When examined separately, consumption of beer, wine, and liquor each increased the risk of breast cancer among postmenopausal women. We found no evidence that alcohol consumption was more deleterious among women at high risk for breast cancer compared to average-risk women. **CONCLUSION:** This study adds to the evidence that postmenopausal women can reduce their risk of breast cancer by avoiding or minimizing their use of alcohol.

Horn-Ross, P. L., Canchola, A. J., West, D. W., Stewart, S. L., Bernstein, L., Deapen, D., Pinder, R., Ross R. K., Anton-Culver, H., Peel, D., Ziogas, A., Reynolds, P., Wright, W. (2004). Patterns of alcohol consumption and breast cancer risk in the California Teachers Study cohort. Cancer Epidemiology, Biomarkers & Prevention, 13(3):405-11.

Alcohol consumption of approximately two drinks or more per day has been associated with elevated breast cancer risk in the California Teachers Study cohort as well as in many other populations. The objective of this analysis is to examine effects of age at drinking and drinking patterns and to identify effect modifiers. Of the 103,460 at-risk cohort members, age <85, who resided in California and completed the baseline alcohol assessment, 1,742 were diagnosed with invasive breast cancer after joining the cohort and before January 2001. Incident breast cancers were identified through the California Cancer Registry and follow-up for death and confirmation of continued California residence used various sources. Multivariate Cox proportional hazards regression models were used to estimate relative risks (RRs). Elevated breast cancer risk was most evident for recent drinking [RR = 1.28, 95% confidence interval (CI): 1.06-1.54 for ≥ 20 g/day versus nondrinkers], with no clear pattern for consumption during earlier periods of life. This elevation in risk was 32% among postmenopausal women (95% CI: 1.06-1.63) and 21% among pre/perimenopausal women (95% CI: 0.76-1.92). Highest risks associated with heavy alcohol consumption were observed among postmenopausal women with a history of biopsy-diagnosed benign breast disease (RR = 1.97, 95% CI: 1.39-2.79 compared to nondrinkers without benign breast disease) or who had used combination hormone replacement therapy (HRT) (RR = 2.24, 95% CI: 1.59-3.14 compared to nondrinkers who never used HRT). Recent alcohol consumption equivalent to two or more drinks per day increases the risk of invasive breast cancer, with the greatest RRs observed among heavy drinkers who are also postmenopausal and have a history of benign breast disease or who use HRT.

Jain, M. G., Ferrenc, R. G., Rehm, J. T., Bondy, S. J., Rohan, T. E., Ashley, M. J., Cohe, J.E., Miller, A. B. (2000). Alcohol and breast cancer mortality in a cohort study. Breast Cancer Research & Treatment, 64(2):201-9.

Available epidemiological evidence indicates that alcohol intake is associated with a higher risk of developing breast cancer. Plausible biological pathways include its effect on levels of estrogens, cell membrane integrity and cell-to-cell communication, inhibition of DNA repair, and congener effect. The present study evaluated the impact of alcohol on mortality from breast cancer, an area with relatively few studies in the literature. The subjects were participants in a Canadian prospective cohort study, the National Breast

Screening Study (NBSS). Women were enrolled in the cohort from 1980 to 1985 to evaluate the efficacy of mammographic screening. Information on usual diet and alcohol intake at enrolment and other epidemiological variables was collected by means of a mailed, self-administered questionnaire. Mortality from breast cancer during follow-up to 31 December, 1993 was ascertained by record linkage to the Canadian Mortality Data Base maintained by Statistics Canada. During the follow-up period of 1980-1993 (average 10.3 years), 223 deaths from breast cancer were identified for this analysis. The hazard ratios for the risk of death from breast cancer increased with intakes of total alcohol of 10-20 g/day (1.039, 1.009-1.071) and > 20 g/day (1.063, 1.029-1.098). This increase was contributed largely by the intake of wine, a 15% increase in risk at intakes higher than 10 g/day of alcohol from wine. Alcohol from spirits was associated with a small decrease in risk of death (hazard ratio at 10g/day, 0.945, 0.915-0.976). The effect of alcohol from beer was not significant in the two categories studied. Although our results were statistically significant, the magnitude of the change in risk was small.

Key, T. J., Schatzkin, A., Willett, W. C., Allen, N. E., Spencer, E. A., Travis, R. C. (2004). Diet, nutrition and the prevention of cancer. [Review] Public Health Nutrition, 7(1A):187-200.

OBJECTIVE: To assess the epidemiological evidence on diet and cancer and make public health recommendations. DESIGN: Review of published studies, concentrating on recent systematic reviews, meta-analyses and large prospective studies. CONCLUSIONS AND RECOMMENDATIONS: Overweight/obesity increases the risk for cancers of the oesophagus (adenocarcinoma), colorectum, breast (postmenopausal), endometrium and kidney; body weight should be maintained in the body mass index range of 18.5-25 kg/m², and weight gain in adulthood avoided. Alcohol causes cancers of the oral cavity, pharynx, oesophagus and liver, and a small increase in the risk for breast cancer; if consumed, alcohol intake should not exceed 2 units/d. Aflatoxin in foods causes liver cancer, although its importance in the absence of hepatitis virus infections is not clear; exposure to aflatoxin in foods should be minimised. Chinese-style salted fish increases the risk for nasopharyngeal cancer, particularly if eaten during childhood, and should be eaten only in moderation. Fruits and vegetables probably reduce the risk for cancers of the oral cavity, oesophagus, stomach and colorectum, and diets should include at least 400 g/d of total fruits and vegetables. Preserved meat and red meat probably increase the risk for colorectal cancer; if eaten, consumption of these foods should be moderate. Salt preserved foods and high salt intake probably increase the risk for stomach cancer; overall consumption of salt preserved foods and salt should be moderate. Very hot drinks and foods probably increase the risk for cancers of the oral cavity, pharynx and oesophagus; drinks and foods should not be consumed when they are scalding hot. Physical activity, the main determinant of energy expenditure, reduces the risk for colorectal cancer and probably reduces the risk for breast cancer; regular physical activity should be taken.

Kinney, A. Y., Millikan, R. C., Lin, Y. H., Moorman, P. G., Newman, B. (2000). Alcohol consumption and breast cancer among black and white women in North Carolina (United States). Cancer Causes & Control, 11(4):345-57.

OBJECTIVE: The purpose of this study was to investigate the effects of alcohol consumption on breast cancer risk in black and white women. METHODS: We used data from the Carolina Breast Cancer Study, a population-based, case-control study of black and white women in North Carolina. Interviews were conducted with 890 cases and 841 controls frequency-matched on age and race. RESULTS: Overall, the prevalence of moderate to high levels of alcohol consumption was low. Compared with abstainers, the multivariate odds ratio for recent intake of one or two drinks per day was 1.4 (95% CI = 0.9-2.1) and two or more drinks a day was 1.0 (95% CI = 0.6-1.6); increasing

consumption was not associated with risk (p for trend = 0.6). The associations were similar, but somewhat weaker, for average lifetime consumption. Among women who consumed 91 g/week or more of alcohol, a nonsignificant increased risk of breast cancer was observed for women reporting binge drinking (OR = 1.5; 95% CI = 0.9-2.3), but not for those who consumed less than 91 g/week reporting binge drinking (OR = 1.0; 95% CI = 0.6-1.5). Odds ratios did not differ meaningfully by race, age, menopausal status, exogenous hormone use, or body mass index. CONCLUSIONS: These data provide little evidence for an association between alcohol consumption and risk of breast cancer among either black or white women.

Kropp, S., Becher, H., Nieters, A., Chang-Claude, J. (2001). Low-to-moderate alcohol consumption and breast cancer risk by age 50 years among women in Germany. American Journal of Epidemiology, 154(7):624-34.

Studies of the association between alcohol drinking and breast cancer show a tendency towards an increase in risk for high consumption levels but yield less consistent results for low-to-moderate levels, particularly among premenopausal women. In a population-based case-control study in Germany, the authors determined the effect of alcohol consumption at low-to-moderate levels on breast cancer risk among women up to age 50 years. The study included 706 case women whose breast cancer had been newly diagnosed in 1992-1995 and 1,381 residence- and age-matched controls. In multivariate conditional logistic regression analysis, the adjusted odds ratios for breast cancer were 0.71 (95% confidence interval (CI): 0.54, 0.91) for average ethanol intake of 1-5 g/day, 0.67 (95% CI: 0.50, 0.91) for intake of 6-11 g/day, 0.73 (95% CI: 0.51, 1.05) for 12-18 g/day, 1.10 (95% CI: 0.73, 1.65) for 19-30 g/day, and 1.94 (95% CI: 1.18, 3.20) for \geq 31 g/day. The association with high daily ethanol intake of \geq 19 g was modified by educational level, such that odds ratios were 3.7, 1.6, and 0.7 for women with low, moderate, and high levels of education, respectively. These data suggest that low-level consumption of alcohol does not increase breast cancer risk in premenopausal women.

Lenz, S. K., Goldberg, M. S., Labreche, F., Parent, M. E., Valois, M. F. (2002). Association between alcohol consumption and postmenopausal breast cancer: results of a case-control study in Montreal, Quebec, Canada. Cancer Causes & Control, 13(8):701-10.

OBJECTIVES: To determine the association between postmenopausal breast cancer and prior consumption of alcoholic beverages. METHODS: This case-control study, conducted in all Montreal hospitals between 1996 and 1997, included 556 postmenopausal women (age 50-75 years) who had a new histologically confirmed diagnosis of primary, malignant breast cancer. Control subjects (577) were selected from other histologically confirmed sites of cancer. A detailed history of alcohol consumption and other risk factors was obtained by interview. Indices reflecting alcohol consumption were developed and unconditional logistic regression was used to estimate adjusted odds ratios (OR) and 95% confidence intervals (CI). RESULTS: Current regular drinkers of any type of alcohol were at an increased risk of breast cancer (OR = 1.5; 95% CI 1.0-2.2). For all beverages considered, current regular drinkers showed higher risks than ever regular drinkers. The risk of breast cancer was highest among women who reported exclusive drinking of wine on a weekly or daily basis (e.g. current regular drinking: OR = 2.3; 95% CI 1.2-4.3). Women who started to drink wine on or before the age of 40 were at a 2.5 times increased risk (95% CI 1.4-4.4). CONCLUSIONS: Our findings provide further support for a positive association between the risk of postmenopausal breast cancer and alcohol consumption.

Lin, Y., Kikuchi, S., Tamakoshi, K., Wakai, K., Kondo, T., Niwa, Y., Yatsuya, H., Nishio, K., Suzuki, S., Tokudome, S., Yamamoto, A., Toyoshima, H., Tamakoshi, A. (2005).

Prospective study of alcohol consumption and breast cancer risk in Japanese women. International Journal of Cancer, 116(5):779-83.

Epidemiologic evidence is lacking for the association between alcohol consumption and the risk of breast cancer in Japanese women. We addressed this association in a prospective cohort study with an average follow-up of 7.6 years. At baseline (1988-1990), cohort participants completed a self-administered questionnaire that included alcohol use, reproductive history and hormone use. The women were followed up for breast cancer incidence through December 31, 1997. Cox proportional hazards models were used to calculate relative risks (RRs) and 95% confidence intervals (CIs) for breast cancer incidence and any association with alcohol consumption. During a follow-up of 271,412 person-years, we identified 151 women with breast cancer, of whom 45 were current drinkers and 11 drank ≥ 15 g of alcohol/day. After adjustment for age and other potential risk factors for breast cancer, the RR for current drinkers was 1.27 (95% CI 0.87-1.84) compared to nondrinkers. Average alcohol intake of < 15 g/day did not significantly increase the risk for breast cancer. However, risk was significantly increased for women who consumed ≥ 15 g/day of alcohol (RR = 2.93, 95% CI 1.55-5.54). Age at starting drinking and frequency of consumption per week were not significantly associated with breast cancer risk. Our cohort study demonstrated that Japanese women who consume at least a moderate amount of alcohol have an increased risk of breast cancer. (c) 2005 Wiley-Liss, Inc.

Mannisto, S., Virtanen, M., Kataja, V., Uusitupa, M., Pietinen, P. (2000). Lifetime alcohol consumption and breast cancer: a case-control study in Finland. Public Health Nutrition, 3(1):11-8.

OBJECTIVE: To study the association between lifetime alcohol consumption and the risk of breast cancer. DESIGN AND SETTING: A case-control study carried out in eastern Finland. Information about alcohol consumption was obtained by two methods: a self-administered food frequency questionnaire (FFQ) including alcohol consumption during the previous 12 months, and a lifetime alcohol consumption questionnaire (AQ) which was administered by the study nurse. SUBJECTS: The study consisted of 301 breast cancer cases (25-75 years old) and 443 population controls. RESULTS: The subjects reported higher current alcohol consumption in the AQ compared to the FFQ. According to the AQ, premenopausal cases consumed on average 28 g and controls 24 g alcohol week⁻¹; in postmenopausal women the values were 15 and 14 g, respectively. About 30% of premenopausal and 60% of postmenopausal women were classified as non-drinkers. The correlation for current alcohol consumption between the FFQ and the AQ was 0.80 in premenopausal women but only 0.40 in postmenopausal women. Current alcohol consumption seemed to influence the reporting of total lifetime alcohol consumption. Current alcohol consumption was not associated with the risk of breast cancer either in premenopausal or postmenopausal women; neither were associations found between alcohol consumption at age of first use, use before the age of 30, or total lifetime alcohol consumption and the risk of breast cancer. CONCLUSIONS: On average, one to three drinks per week did not increase the risk of breast cancer in this study. Consumption levels were, however, too low to exclude increased risk with high regular consumption. Further research is necessary on lifetime alcohol consumption.

Mattisson, I., Wirfalt, E., Wallstrom, P., Gullberg, B., Olsson, H., Berglund, G. (2004). High fat and alcohol intakes are risk factors of postmenopausal breast cancer: a prospective study from the Malmo diet and cancer cohort. International Journal of Cancer, 110(4):589-97.

Associations between intakes of relative fat, total alcohol and alcoholic beverages and risk of breast cancer were examined in a subsample of 11726 postmenopausal women from the MDC cohort. The MDC conducted baseline examinations from 1991 to 1996; the

end of follow-up was 31 December 2001. Data were obtained by an interview-based diet history method, a structured questionnaire, anthropometric measurements and national and regional cancer registries. During 89602 person-years of follow-up, 342 incident cases were documented. Cox regression analysis examined breast cancer risks adjusted for potential confounders. Two energy-adjustment approaches (i.e., adjusting for total energy vs. adjusting for nonalcohol energy) were used. High total alcohol intake was associated with a nonsignificantly elevated risk. High wine intake was associated with a significantly elevated breast cancer risk (relative risk = 2.12, 95% CI 1.24-3.60). There were significant trends of increased breast cancer risk across quintiles of relative fat intake. Mutual adjustment did not affect risk estimates for total alcohol or relative fat intakes. The specific energy-adjustment approach did not influence associations differentially. Copyright 2004 Wiley-Liss, Inc.

McTiernan, A. (2003). Behavioral risk factors in breast cancer: can risk be modified?. [Review] *Oncologist*, 8(4):326-34.

The International Agency for Research on Cancer estimates that 25% of breast cancer cases worldwide are due to overweight/obesity and a sedentary lifestyle. The preponderance of epidemiologic studies indicates that women who engage in 3-4 hours per week of moderate to vigorous levels of exercise have a 30%-40% lower risk for breast cancer than sedentary women. Women who are overweight or obese have a 50%-250% greater risk for postmenopausal breast cancer. Alcohol use, even at moderate levels (two drinks per day) increases risk for both premenopausal and postmenopausal breast cancer. Certain dietary patterns, such as high fat, low vegetables/fruits, low fiber, and high simple carbohydrates, may increase risk, but definitive data are lacking. These lifestyle factors are likely associated with breast cancer etiology through hormonal mechanisms. The worldwide trends of increasing overweight and obesity and decreasing physical activity may lead to an increasing incidence of breast cancer unless other means of risk reduction counteract these effects. Thus, adoption of lifestyle changes by individuals and populations may have a large impact on the future incidence of this disease.

Nichols, H. B., Trentham-Dietz, A., Love, R. R., Hampton, J. M., Hoang Anh, P. T., Allred, D. C., Mohsin, S. K., Newcomb, P. A. (2005). Differences in breast cancer risk factors by tumor marker subtypes among premenopausal Vietnamese and Chinese women. *Cancer Epidemiology, Biomarkers & Prevention*, 14(1):41-7.

We evaluated associations between reproductive and lifestyle risk factors with breast cancer tumor marker status in a case-control study. Cases were premenopausal women living in Vietnam and China who were eligible for a clinical trial of oophorectomy and tamoxifen as treatment for breast cancer (n = 682). Controls were nonrelative hospital visitors, matched on age to the cases (n = 649). Immunohistochemical analysis was used to identify the presence of estrogen receptor (ER) and progesterone receptor and the overexpression of HER-2/neu oncogene. Odds ratios (OR) and 95% confidence intervals (95% CI) were estimated using unconditional logistic regression, adjusted for known confounders. Overall, 280 (61%) tumor samples were ER positive and 176 (38%) were ER negative. HER-2/neu overexpression was detected in 161 (35%) samples, whereas 286 (26%) samples were HER-2/neu negative. We observed an inverse trend between increasing parity and decreasing breast cancer risk (P = 0.002). Women ages \geq 25 years at first birth had increased breast cancer risk compared with women ages $<$ 25 years at first birth (OR, 1.53; 95% CI, 1.20-1.95). Women who consumed alcohol had increased risk of breast cancer compared with women who did not (OR, 1.85; 95% CI, 1.32-2.61). Compared with controls, OR estimates for breast cancer by parity and age at first birth were significantly associated with ER and/or HER-2/neu tumor status by Wald test (P < 0.05). Family history, age at menarche, cumulative lactation, body mass index, and education were not significantly related to breast cancer risk. Our findings support

the hypothesis that some breast cancer risk factors differ by ER and HER-2/neu tumor marker subtypes.

Onland-Moret, N. C., Peeters, P. H., van der Schouw, Y. T., Grobbee, D. E., van Gils C, H. (2005). Alcohol and endogenous sex steroid levels in postmenopausal women: a cross-sectional study. Journal of Clinical Endocrinology & Metabolism, 90(3):1414-9.

Breast cancer risk increases with increased levels of alcohol consumption, potentially through an effect on sex hormone levels. In a cross-sectional study among Dutch participants (n = 17,357) of the European Prospective Investigation into Cancer and Nutrition conducted in Utrecht, The Netherlands (Prospect-EPIC), we investigated the relation between alcohol intake and estrogen and androgen levels. Alcohol intake was calculated from a food frequency questionnaire. Women were included if they were postmenopausal, had donated a blood sample, and did not use hormone replacement therapy or oral contraceptives at the time of blood donation (n = 1093). Women who consumed more than 25 g of alcohol per day had higher levels of estrone (P(trend) = 0.001), estradiol (P(trend) = 0.03), dehydroepiandrosterone sulfate (P(trend) = 0.18), and higher estrone/estradiol (P(trend) = 0.14) and estrone/androstenedione (P(trend) = 0.06) ratios, compared with nondrinkers. Levels of androstenedione, testosterone, and SHBG did not differ between women who consumed alcohol and nondrinkers. Furthermore, there were no differences in the free androgen index or estradiol to testosterone ratio. In conclusion, levels of estrogens and dehydroepiandrosterone sulfate are higher in women who consume more alcohol. This finding supports the hypothesis that alcohol use may increase breast cancer risk at least partially through an effect on sex steroid levels.

Petri, A, L., Tjonneland, A., Gamborg, M., Johansen, D., Hoidrup, S., Sorensen, T. I., Gronbaek, M. (2004). Alcohol intake, type of beverage, and risk of breast cancer in pre- and postmenopausal women. Alcoholism: Clinical & Experimental Research, 28(7):1084-90.

BACKGROUND: Most studies of the relation between alcohol consumption and breast cancer have shown a modestly increased risk, although the results are still conflicting. **METHODS:** The aim of this prospective population-based cohort study was to assess the influence of alcohol intake and type of beverage (beer, wine, or spirits) on breast cancer risk in relation to menopausal status. Among 13,074 women aged 20 to 91 years, we examined the relationship between breast cancer risk, total alcohol intake, and type of alcohol in relation to menopausal status. The women were classified as premenopausal or as postmenopausal at younger than 70 years or 70 years or more. **RESULTS:** During follow-up, 76 premenopausal and 397 postmenopausal women developed breast cancer. Premenopausal women who had an intake of more than 27 drinks per week had a relative risk of breast cancer of 3.49 (95% confidence limits, 1.36-8.99) compared with light drinkers (p = 0.011), whereas there were no differences in risk in the lower-intake categories. The increased risk of breast cancer among premenopausal women was independent of the type of alcohol. Postmenopausal women older than 70 years of age who had an intake of more than six drinks per week of spirits had a relative risk of breast cancer of 2.43 (95% confidence limits, 1.41-4.20) compared with women who consumed less than one drink of spirits per week (p = 0.0014). **CONCLUSIONS:** Total alcohol intake of more than 27 drinks per week increases breast cancer risk in premenopausal women independently of the type of alcohol. Among postmenopausal women, an intake of spirits of more than six drinks per week increases breast cancer risk.

Rohan, T. E., Jain, M., Howe, G.R., Miller, A. B. (2000). Alcohol consumption and risk of breast cancer: a cohort study. Cancer Causes & Control, 11(3):239-47.

OBJECTIVES: To study the association between alcohol consumption and breast cancer risk. **METHODS:** A case-cohort analysis was undertaken within the cohort of 56,837

women who were enrolled in the Canadian National Breast Screening Study (NBSS) and who completed a self-administered dietary questionnaire. (The NBSS is a randomized controlled trial of screening for breast cancer in women aged 40-59 at recruitment.) The cohort was recruited between 1980 and 1985, and during follow-up to the end of 1993 a total of 1469 women in the dietary cohort were diagnosed with biopsy-confirmed incident breast cancer. For comparative purposes a subcohort consisting of a random sample of 5681 women was selected from the full dietary cohort. After exclusions for various reasons the analyses were based on 1336 cases and 5238 noncases. RESULTS: When compared to nondrinkers the adjusted incidence rate ratios (95% confidence intervals) for those consuming > 0 and < or = 10 g of alcohol/day, > 10 and < or = 20 g/day, > 20 and < or = 30 g/day, > 30 and < or = 40 g/day, > 40 and < or = 50 g/day, and > 50 g/day were 1.01 (0.84-1.22), 1.16 (0.91-1.47), 1.27 (0.91-1.78), 0.77 (0.51-1.16), 1.00 (0.57-1.75), and 1.70 (0.97-2.98), respectively; the associated p value for the test for trend was 0.351. Similar findings were obtained when analyses were conducted separately in the screened and control arms of the NBSS, in premenopausal and postmenopausal women, for screen-detected and interval-detected breast cancer, and by levels of other breast cancer risk factors. CONCLUSIONS: The results of this study suggest that alcohol consumption might be associated with increased risk of breast cancer at relatively high levels of intake.

Santos, Silva, I. (2002) Alcohol, tobacco and breast cancer: should alcohol be condemned and tobacco acquitted? British Journal of Cancer, 87(11):1195-1196.

This editorial comments on a report in the current issue of the journal in which over 80% of the worldwide epidemiological information from 53 studies on alcohol, tobacco, and breast cancer risk in women was reanalyzed (Collaborative Group on Hormonal Factors in Breast Cancer. Alcohol, tobacco and breast cancer. British Journal of Cancer, 87:1234-1245, 2002). The reanalysis included 58,515 women with and 95,067 without breast cancer and showed that the relative risk of breast cancer increased by 7.1% for each additional 10 g/day (one drink/day) intake of alcohol. Compared with women reporting no alcohol drinking, the risk of developing breast cancer was 32% higher among those who reported drinking 35-44 g/day and 46% higher among those who reported consuming 45 g/day or more. The effect of alcohol was not confounded by smoking or by any other known risk factor for breast cancer. It was estimated that in developed countries the cumulative incidence of breast cancer by age 80 would be 8.8 per 100 women in nondrinkers and 9.4, 10.1, 10.8, 11.6, 12.4, and 13.3 per 100 women respectively among women consuming an average of 1, 2, 3, 4, 5, and 6 alcoholic drinks/day. In contrast, the relationship between smoking and breast cancer was substantially confounded by alcohol's effects, and no association was found between smoking and breast cancer when the analysis was restricted to non-drinkers. The author of the editorial argues, however, that it is premature to conclude that this matter is settled.

Spencer, Charmaine. Alcohol and Seniors. (2004). Public Health Agency of Canada. Retrieved from: <http://www.agingincanada.ca/index.htm>

Breast cancer is an important health concern among women as they age. Developing breast cancer can have a profound effect on women psychologically, physically and socially. It is also important from a national perspective: Canada has the second highest incidence of breast cancer in the world (trailing only the United States). It is estimated that in 2003 there will be over 21,000 new cases of breast cancer among women in Canada (Canadian Cancer Society). The provinces with the highest rates of new cases of breast cancer are Manitoba (116/ 100,000), Nova Scotia, (112), Quebec (110), Alberta (109), and PEI (107). (Canadian Cancer Society)

What is the Risk of Breast Cancer for Women in Canada?

According to Canadian Cancer Agency figures: Women have a lifetime probability of 11.4 % of developing breast cancer (or 1 in 8.8 women will develop it). While women tend to think of it as a middle age disease, the probability of developing breast cancer is higher

among women aged 60-69 and 70-79 than in younger women. See below for factors associated with breast cancer in women.

Does Drinking Affect the Risk of Developing Breast Cancer in Pre and Postmenopausal Women?

Yes, absolutely. There is association between the level of alcohol consumption and increased risk of breast cancer. Particularly, there is a significantly increased risk of breast cancer where the woman drinks more than two drinks daily over a period of years. (Stoll)

Women who drink moderately (<2 drinks a day) and who are on estrogen replacement therapy for five years are at greater risk a breast cancer. They have about double the risk of developing breast cancer of women who are only on the hormone replacement therapy or women who only drink alcohol (Chen et al.) For many years it was thought that it might be the smoking not drinking that was tied to breast cancer risk (and many drinkers are also smokers) However, more recent research says no. It is clearly the alcohol.

At What Level of Drinking, Does the Risk of Breast Cancer Increase?

A large study found that compared with women who reported drinking no alcohol, the relative risk of breast cancer was 1.32 for an intake of 35--44 g per day alcohol (in other words, drinking between 3 and 3.5 standard drinks a day), and 1.46 for those drinking more than 45 g per day alcohol. In other words, compared to women who are non drinkers, the relative risk is 32% for between 3 and 3.5 standard drinks a day, and 46% higher for more than slightly less than 4 standard drinks a day.

The relative risk of breast cancer increased by 7.1% for each additional 10 g per day intake of alcohol, i.e. for each extra unit or drink of alcohol consumed on a daily basis.

This increase was the same in smokers and women who had never smoked.

(Collaborative Group)

Stevens, R. G., Davis, S., Mirick, D. K., Kheifets, L., Kaune, W. (2000). Alcohol consumption and urinary concentration of 6-sulfatoxymelatonin in healthy women. Epidemiology, 11(6):660-5.

Consumption of alcoholic beverages may suppress circulating melatonin levels at night, possibly resulting in an increase in circulating estrogen. An increased estrogen burden could increase the risk of breast cancer. This study was designed to investigate whether alcohol consumption is associated with a decrease in nighttime melatonin levels in a group of healthy women. A total of 203 randomly selected healthy women between the ages of 20 and 74 years were recruited for a broader study of the effects of exposure to power-frequency magnetic fields on nocturnal levels of urinary 6-sulfatoxymelatonin. For the purposes of this analysis, data collection consisted of the following during two seasons of the year: (1) an in-person interview, (2) a daily activity diary, and (3) nocturnal urine collection for each of 3 consecutive nights. We found that the nocturnal urinary concentration of the primary metabolite of melatonin (6-sulfatoxymelatonin) decreased in a dose-dependent manner with increasing consumption of alcoholic beverages in the preceding 24-hour period, after taking into account the independent effects on melatonin of age, hours of darkness, use of medications that affect melatonin levels, and body mass index. A categorical analysis revealed no effect of one drink, but a 9% reduction with two drinks, a 15% reduction with three drinks, and a 17% reduction with four or more drinks. It remains unknown whether such a change could affect estrogen levels or breast cancer risk.

Stoll, B. A.(1999). Alcohol intake and late-stage promotion of breast cancer. [Review] European Journal of Cancer, 35(12):1653-8.

Breast cancer risk in women rises with increasing alcohol intake and is widely assumed to be mediated by increased oestrogen concentrations. However, observations that mechanisms and risk are likely to differ between pre- and postmenopausal women suggest that the postmenopausal disease in particular, may involve a promoting role for

concomitants of hyperinsulinaemia which is commonly associated with alcoholic cirrhosis of the liver. The MEDLINE database and ongoing studies were examined for clinical, epidemiological and laboratory data on; (a) alcohol-related increase in the incidence of breast cancer in relation to menopausal status, oestrogen concentrations and the oestrogen receptor (ER) status of the tumour; (b) activation of insulin-like growth factor 1 receptor (IGF1R) in mammary tissue by alcohol-related hyperinsulinaemia; (c) interaction between ER and IGF1R in breast cancer cell systems. Epidemiological association between alcohol intake and increased breast cancer risk is more clearly seen in postmenopausal than premenopausal women, and a significant risk is associated with intake of more than two drinks (over 30 g) daily over a period of years. Alcohol-related hyperinsulinaemia is reported to increase with increasing degrees of cirrhosis and damage to liver function. Laboratory evidence suggests that hyperinsulinaemia can stimulate expression of IGF1R in mammary tissue, and this protein is likely to have a crucial role in mitogenesis and transformation to an oestrogen-independent malignant phenotype. It is postulated that in women with a history of long-term intake of moderate quantities of alcohol, the concomitants of hyperinsulinaemia may help to stimulate progression in precancerous breast lesions in the years leading up to the menopause and may increase the risk of breast cancer manifesting after the menopause.

Terry, P., Suzuki, R., Hu, F. B., Wolk, A. (2001). A prospective study of major dietary patterns and the risk of breast cancer. Cancer Epidemiology, Biomarkers & Prevention, 10(12):1281-5.

Our aim was to study the broader eating patterns that potentially reflect many dietary exposures working together in their association with breast cancer risk. Using data from a prospective study of 61,463 women with an average follow-up of 9.6 years and 1,328 incident cases of breast cancer, we conducted a factor analysis to identify major dietary patterns. Proportional hazards regression was used to estimate hazard ratios. We found no association between the "Western" dietary pattern (characterized by such foods as red and processed meats, refined grains, fat, and sweets) or the "healthy" dietary pattern (fruit and vegetables, fish and poultry, low-fat dairy, and whole grains) and breast cancer risk. However, women who were in the highest category of the "drinker" dietary pattern (wine, beer, and spirits) had a moderately increased risk (rate ratio = 1.27; 95% confidence interval, 1.06-1.52; P for trend, 0.002). The positive association was somewhat weaker among women below 50 years of age, a finding not inconsistent with chance. Our results are in agreement with the majority of previous studies that show alcohol consumption moderately increases the risk of breast cancer, but our results do not support any association between breast cancer risk and the "Western" or "healthy" dietary patterns.

Tjonneland, A., Thomsen, B. L., Stripp, C., Christensen, J., Overvad, K., Mellemkaer, L., Gronbaek, M., Olsen, J. H. (2003). Alcohol intake, drinking patterns and risk of postmenopausal breast cancer in Denmark: a prospective cohort study. Cancer Causes & Control, 14(3):277-84.

OBJECTIVE: The available epidemiological evidence indicates that drinking alcohol per se is associated with breast cancer. However, it has not been investigated how the breast cancer risk for a given total alcohol consumption depends on the drinking frequency. METHODS: Within the prospective study on 'Diet, Cancer and Health', we examined the relationship between breast cancer, intake of total alcohol and frequency of drinking among 23,778 postmenopausal women, among whom 425 cases of breast cancer accrued during a median follow-up of 4.8 years. RESULTS: The dose-response relationship between total alcohol intake and breast cancer showed an increase in the rate ratio of 1.10 per 10 g/day (95% CI: 1.04-1.16) with no evidence for differences by type of alcohol beverage. No interaction was found between drinking frequency and total alcohol intake in the risk of breast cancer ($p = 0.40$). CONCLUSIONS: The present study

supports previous ones in showing a monotonic increase in the risk of breast cancer among postmenopausal women with increasing average daily intake of alcohol, and this relationship with alcohol intake did not depend on drinking frequency.

Tjønneland, A., Christensen, J., Thomsen, B.L., Olsen, A., Stripp, C., Overvad, K., Olsen, J.H., (2004). Lifetime alcohol consumption and postmenopausal breast cancer rate in Denmark: a prospective cohort study. Journal of Nutrition, 134(1):173-8.

Alcohol intake may be one of the few modifiable risk factors for breast cancer. In a prospective cohort of 29,875 women with 423 cases of breast cancer during 1993-2000, we examined the relationship between postmenopausal breast cancer incidence rate and alcohol consumption in different life periods. When alcohol intake during four age ranges, twenties, thirties, forties and fifties was evaluated, only the intake in the fifties increased the risk of breast cancer [rate ratio (RR)=1.12 (95% CI: 1.05-1.19)] per 10 g/d increase in alcohol intake. After adjustment for intake at study entry, this association was no longer present [RR=1.01 (95% CI: 0.91-1.13)]. The cumulative lifetime alcohol intake, adjusted for recent intake, showed no association with postmenopausal breast cancer risk. Recent alcohol intake, adjusted for the alcohol intake in the other life time periods, showed a significant association of RR=1.09 (95% CI: 1.00-1.18) per 10 g/d. There was no indication of a higher risk among women with early drinking start, nor did women who started to drink before their first birth have a higher risk than women who started to drink later in life. Our results suggest that baseline intake of alcohol is a more important determinant of postmenopausal breast cancer risk than earlier lifetime exposure.

Trentham-Dietz, A., Newcomb, P. A., Storer, B. E., Remington, P. L. (2000). Risk factors for carcinoma in situ of the breast. Cancer Epidemiology, Biomarkers & Prevention, 9(7):697-703.

As more women obtain screening mammograms regularly and at younger ages, the diagnosis of breast carcinoma in situ becomes more frequent. To examine whether risk factors for carcinoma in situ correspond with risk factors for invasive breast cancer, we analyzed data from a population-based case-control study conducted in 1988-1990. We identified newly diagnosed cases of carcinoma in situ (n = 301) and invasive breast cancer (n = 3789) in women 18-74 years of age from Wisconsin's statewide tumor registry. Cases and population controls (n = 3999) completed structured telephone interviews. Overall, associations with risk of carcinoma in situ in relation to many reproductive life-style risk factors were similar to those associated with risk of invasive disease. Women who reported a family history of breast cancer had a 2-fold elevated risk of carcinoma in situ (odds ratio, 2.67; 95% confidence interval, 2.00-3.57). Personal history of benign biopsied breast disease also increased risk of carcinoma in situ (odds ratio, 2.19; 95% confidence interval, 1.62-2.95). Subgroup analysis suggested that high vitamin A intake and high alcohol intake may be associated with risk of ductal but not lobular carcinoma in situ. These data support the presence of common risk factors between in situ and invasive breast cancer.

Yang, C., Hamajima, N., Iwata, H., Saito, T., Matsuo, K., Hirose, K., Inoue, M., Takezaki T., Tajima, K. (2002). A49T, V89L and TA repeat polymorphisms of steroid 5alpha-reductase type II and breast cancer risk in Japanese women. Breast Cancer Research, 4(4):R8, 2002.

BACKGROUND: Breast cancer is hormone related, as are cancers of the endometrium, ovary, and prostate. Several studies have suggested that higher extracellular levels of androgens are associated with breast cancer risk, while biological evidence indicates that androgens are protective. The codon 49 alanine to threonine substitution (A49T), codon 89 valine to leucine substitution (V89L) and TA repeat polymorphisms of the steroid 5alpha-reductase type II (SRD5A2) gene are considered functional with respect to

enzyme activity converting testosterone into dihydrotestosterone. To test the hypothesis that these three polymorphisms are associated with risk of breast cancer, a case-control study was conducted with patients of Aichi Cancer Center Hospital. METHODS: The cases were 237 patients histologically diagnosed with breast cancer, and the controls were 185 noncancer outpatients. DNA from peripheral blood was genotyped by PCR methods. RESULTS: The threonine allele of A49T was not found in our subjects. Compared with the V/V genotype of V89L, the L/L genotype was associated with a decreased risk (crude odds ratio [OR] = 0.61, 95% confidence interval [CI] = 0.36-1.05). This was also the case for the TA(9/9) genotype, with an OR of 0.58 (95% CI = 0.13-2.63) relative to TA(0/0). Among women with the TA(0/0) genotype, however, the OR for the L/L genotype was 0.46 (95% CI = 0.24-0.88) compared with the V/V genotype, and those with the V/V and TA(0/0) genotypes had the highest risk. The haplotype with the L and TA(9) repeat alleles was not found. CONCLUSION: This study is the first to our knowledge focusing on Japanese women, suggesting that SRD5A2 polymorphisms might have an association with breast cancer risk. Further large-sample studies will be required to confirm the association and to assess any interactions with environmental factors.

Cancer & Stroke

Trevisan, M., Schisterman, E., Mennotti, A., Farchi, G., Conti, S. (2001) Drinking pattern and mortality: the Italian Risk Factor and Life Expectancy pooling project. Annals of Epidemiology, 11(5):312-9.

PURPOSE: To analyze the relationship between an aspect of drinking pattern (i.e., drinking with or without meals) and risk of all-cause and specific-cause mortality. **METHODS:** The Risk Factors and Life Expectancy Study, is a pooling of a series of epidemiological studies conducted in Italy. Eight-thousand six-hundred and forty-seven men and 6521 women, age 30-59 at baseline, and free of cardiovascular disease, were followed for mortality from all causes, cardiovascular and noncardiovascular, during an average follow-up of 7 years. **RESULTS:** Drinkers of wine outside meals exhibited higher death rates from all causes, noncardiovascular diseases, and cancer, as compared to drinkers of wine with meals. This association was independent from the cardiovascular disease (CVD) risk factors measured at baseline and the amount of alcohol consumed and seemed to be stronger in women as compared to men. **CONCLUSIONS:** The present results indicate that drinking patterns may have important health implications, and attention should be given to this aspect of alcohol use and its relationship to health outcomes. The relationship between alcohol consumption and disease has been the focus of intensive scientific investigation (1-9). Most studies to date, however, have limitations. A major drawback is that limited information has been collected regarding the complex issue of alcohol consumption. In many studies, ascertainment of alcohol consumption frequently focused only on quantity of alcohol consumed without considering the many different components of alcohol consumption, particularly drinking pattern (10-12). It has been hypothesized, and preliminary data support the notion, that drinking pattern could have important influences on determining the health effects of alcohol (13,14). The present study examines the relationship between one aspect of drinking pattern (drinking wine outside meals) and mortality in a large cohort of men and women.

Stroke

American Heart Association. (2002). Alcohol, Wine and Cardiovascular Disease. American Heart Association. Retrieved from:

<http://www.americanheart.org/presenter.jhtml?identifier=4422> .

Are there cardiovascular risks associated with drinking alcohol?

Drinking too much alcohol can raise the levels of some fats in the blood (triglycerides) (tri-GLIS'er-idz). It can also lead to high blood pressure, heart failure and an increased calorie intake. (Consuming too many calories can lead to obesity and a higher risk of developing diabetes.) Excessive drinking and binge drinking can lead to stroke. Other serious problems include fetal alcohol syndrome, cardiomyopathy (kar"de-o-mi-OP'ah-the), cardiac arrhythmia (ah-RITH'me-ah) and sudden cardiac death.

AHA Recommendation

If you drink alcohol, do so in moderation. This means an average of one to two drinks per day for men and one drink per day for women. (A drink is one 12 oz. beer, 4 oz. of wine, 1.5 oz. of 80-proof spirits, or 1 oz. of 100-proof spirits.) Drinking more alcohol increases such dangers as alcoholism, high blood pressure, obesity, stroke, breast cancer, suicide and accidents. Also, it's not possible to predict in which people alcoholism will become a problem. Given these and other risks, the American Heart Association cautions people NOT to start drinking ... if they do not already drink alcohol. Consult your doctor on the benefits and risks of consuming alcohol in moderation.

What about red wine and heart disease?

Over the past several decades, many studies have been published in science journals about how drinking alcohol may be associated with reduced mortality due to heart disease in some populations. Some researchers have suggested that the benefit may be due to wine, especially red wine. Others are examining the potential benefits of components in red wine such as flavonoids (FLAV'oh-noidz) and other antioxidants (an"tih-OK'sih-dants) in reducing heart disease risk. Some of these components may be found in other foods such as grapes or red grape juice. the linkage reported in many of these studies may be due to other lifestyle factors rather than alcohol. Such factors may include increased physical activity, and a diet high in fruits and vegetables and lower in saturated fats No direct comparison trials have been done to determine the specific effect of wine or other alcohol on the risk of developing heart disease or stroke.

Are there potential benefits of drinking wine or other alcoholic beverages?

Research is being done to find out what the apparent benefits of drinking wine or alcohol in some populations may be due to, including the role of antioxidants, an increase in HDL ("good") cholesterol or anti-clotting properties. Clinical trials of other antioxidants such as vitamin E have not shown any cardio-protective effect. Also, even if they were protective, antioxidants can be obtained from many fruits and vegetables, including red grape juice. The best-known effect of alcohol is a small increase in HDL cholesterol. However, regular physical activity is another effective way to raise HDL cholesterol, and niacin can be prescribed to raise it to a greater degree. Alcohol or some substances such as resveratrol (res-VAIR'ah-trol) found in alcoholic beverages may prevent platelets in the blood from sticking together. That may reduce clot formation and reduce the risk of heart attack or stroke. (Aspirin may help reduce blood clotting in a similar way.) How alcohol or wine affects cardiovascular risk merits further research, but right now the American Heart Association does not recommend drinking wine or any other form of alcohol to gain these potential benefits. The AHA does recommend that to reduce your risk you should talk to your doctor about lowering your cholesterol and blood pressure, controlling your weight, getting enough exercise and following a healthy diet. There is no scientific proof that drinking wine or any other alcoholic beverage can replace these conventional measures.

Beilin, L. J., Puddey, I. B. (1992) Alcohol and hypertension. Clinical and experimental hypertension Part A, Theory and practice, 14(1-2):119-38.

The relationship between regular alcohol consumption and blood pressure elevation is now firmly established. Outstanding issues which will be discussed relate to the nature of the dose response curve, interactions between alcohol and other dietary and behavioural factors, mechanisms involved and the question of any protective influence of alcohol on atherosclerotic and ischaemic cardiovascular disease associated with hypertension. Alcohol is an important contributory to the prevalence of hypertension, and resistance to drug therapy in drinking communities. Heavy drinking and binge drinking increases the risk of stroke.

Brathen, G., Brodtkorb, E., Sand, T., Helde, G., Bovim, G. (2000). Weekday distribution of alcohol consumption in Norway: influence on the occurrence of epileptic seizures and stroke? European Journal of Neurology, 7(4):413-21.

Binge drinking at weekends is considered to be a predominant feature of alcohol consumption in the Nordic countries. Neurological diseases, such as seizures and stroke, have been reported to occur in temporal relation to alcohol intoxication and withdrawal. We wanted to investigate weekday variances in alcohol consumption in relation to the onset of neurological symptoms in these disorders. Consecutive patients admitted for epileptic seizures (n = 142) and ischemic strokes (n = 91) were included in the study. Control groups were consecutively hospitalized sciatica patients (n = 181), outpatients with epilepsy (n = 91), and healthy subjects (n = 254). The day-by-day alcohol intake during the 8 days prior to hospital admission was recorded. Seizures occurring in subjects with hazardous alcohol consumption, operationally defined by a score > or =8 in the Alcohol Use Disorders Identification Test (AUDIT-positive) were considered to be related to alcohol use. Binge drinkers were identified by an alcohol intake, on at least 1 of the last 3 days, of >or =6 standard units in men, or > or =4 standard units in women. Thirty-five percent of seizure patients were AUDIT-positive, in contrast to 18% and 16% of stroke and sciatica patients, and 12% and 13% of epilepsy outpatients and healthy controls. Twenty-three percent of seizure patients were binge drinkers whereas in the other groups, this proportion did not exceed 10%. In all groups, alcohol consumption peaked on Saturdays. More seizures occurred on Mondays compared to Saturdays, with a diminishing trend through the week. However, AUDIT-negative seizure patients, of which binge drinking occurred in only 5%, caused this difference. AUDIT-positive seizure patients had a higher and more evenly distributed alcohol intake through the week, and the occurrence of seizures in this group did not differ significantly between days of the week. Alcohol consumption peaked 2 days prior to the onset of withdrawal seizures. The weekend drinking pattern was confirmed for all the study groups. Hazardous alcohol consumption preceded every third acute seizure, but was found in only one of eight outpatients with epilepsy. AUDIT-negative patients caused a peak of seizure admissions on Mondays, compared to Saturdays, with a diminishing trend through the week.

Bulpitt, C. J. (2005). How many alcoholic drinks might benefit an older person with hypertension?. Journal of Hypertension, 23(11):1947-51.

Lowering alcohol intake reduces blood pressure and hence cardiovascular risk. However, abstainers have an increase in cardiovascular risk and the advice to reduce intake to low levels may not be sound. This review examines the effects of lowering alcohol consumption in terms of blood pressure and coronary heart disease (CHD). The relationship between both CHD and stroke and alcohol consumption, and the benefits and disadvantages of alcohol consumption in the general population, are discussed. Where available, the results of large meta-analyses are reported. It is concluded that the hypertensive patient over the age of 60 who drinks over 16 drinks per week should be advised to reduce his or her alcohol intake but a daily drink may be advisable and the patient should not stop drinking entirely. It is not suggested that the non-drinker should

start drinking, but most hypertensives are over the age of 60 when community studies suggest that drinking alcohol does more good than harm.

Berger, K., Ajani, U. A., Kase, C. S., Gaziano, J. M., Buring, J. E., Glynn, R. J., Hennekens, C. H. (2000). Light-to-moderate alcohol consumption and risk of stroke among U.S. male physicians. Comment in: New England Journal of Medicine, 341(21):1557-64.

BACKGROUND: Several studies have shown U- or J-shaped relations between alcohol consumption and the risk of stroke. We evaluated the effect of light-to-moderate alcohol intake on the risk of stroke, with separate analyses of ischemic stroke and hemorrhagic stroke. **METHODS:** Our analyses were based on a prospective cohort study of 22,071 male physicians, 40 to 84 years old, who were participating in the Physicians' Health Study. At base line, the participants reported that they had no history of stroke, transient ischemic attack, or myocardial infarction and were free of cancer. Alcohol intake, reported by 21,870 participants at base line, ranged from none or almost none to two or more drinks per day. **RESULTS:** During an average of 12.2 years of follow-up, 679 strokes were reported. As compared with participants who had less than one drink per week, those who drank more had a reduced overall risk of stroke (relative risk, 0.79; 95 percent confidence interval, 0.66 to 0.94) and a reduced risk of ischemic stroke (relative risk, 0.77; 95 percent confidence interval, 0.63 to 0.94). There was no statistically significant association between alcohol consumption and hemorrhagic stroke. The overall relative risks of stroke for the men who had one drink per week, two to four drinks per week, five or six drinks per week, or one or more drinks per day were 0.78 (95 percent confidence interval, 0.59 to 1.04), 0.75 (95 percent confidence interval, 0.58 to 0.96), 0.83 (95 percent confidence interval, 0.62 to 1.11), and 0.80 (95 percent confidence interval, 0.64 to 0.99), respectively, in an analysis in which we controlled for major risk factors for stroke. **CONCLUSIONS:** Light-to-moderate alcohol consumption reduced the overall risk of stroke and the risk of ischemic stroke in men. The benefit is apparent with as little as one drink per week. Greater consumption, up to one drink per day, does not increase the observed benefit.

Burns, J., Crozier, A., Lean, M. E. (2001). Alcohol consumption and mortality: is wine different from other alcoholic beverages?. [Review] Nutrition Metabolism & Cardiovascular Diseases, 11(4):249-58.

BACKGROUND: Alcohol has been an integral part of the diets of many cultures for thousands of years, and formed the basis of early antiseptics. However, many health professionals have been loath to recommend its moderate consumption. Fears of increased risks of cancers, strokes and coronary heart disease (CHD), as well as its role in accidents, violence, psychological and social decline (when consumed in excess) meant that alcohol was viewed as generally detrimental to health. Recent reports have examined some of these fears and suggest that the moderate consumption of alcoholic beverages, particularly red wine, may actually protect against the development of CHD. Evidence for the influence of alcoholic drinks on strokes and cancer is less clear. **OBJECTIVES:** This review discusses the chemical differences between red wine and other alcoholic beverages and their possible effects on the development of CHD, stroke and cancer. **DATA SYNTHESIS AND CONCLUSIONS:** Both clinical and experimental evidence suggest that red wine does indeed offer a greater protection to health than other alcoholic beverages. This protection has been attributed to grape-derived antioxidant polyphenolic compounds found particularly in red wine.

Daniel, S., Bereczki, D. (2004). Alcohol as a risk factor for hemorrhagic stroke. [Review] Ideggyogyaszati Szemle, 57(7-8):247-56.

PURPOSE: Whereas the protective effect of mild-to-moderate alcohol consumption against ischemic stroke has been well recognized, there is conflicting evidence regarding the link between alcohol consumption and hemorrhagic strokes. The aim of the present study is to summarize the results of case-control and cohort studies published on this issue. **METHODS:** Recent epidemiologic articles on the relationship between alcohol consumption and hemorrhagic stroke were identified by Medline searches limited to title words using the following search terms: "alcohol AND cerebrovascular dis*", "alcohol AND stroke", "alcohol AND cerebral hemorrhage" and "alcohol AND hemorrhagic stroke". **RESULTS:** Most case-control and cohort studies either reported only on total strokes or on a combined group of hemorrhagic strokes including intracerebral as well as subarachnoid hemorrhages. There was a consensus among reports that heavy alcohol consumption was associated with a higher risk of hemorrhagic strokes. Controversy remains regarding the effect of mild-to-moderate alcohol consumption: while some studies reported a protective effect, others found a dose-dependent linear relationship between the amount of alcohol consumed and the risk of hemorrhagic stroke. The differential effect of moderate alcohol consumption on hemorrhagic compared to ischemic strokes is mostly attributed to alcohol- and withdrawal-induced sudden elevations of blood pressure, and coagulation disorders. **CONCLUSIONS:** Heavy drinking should be considered as one of the risk factors for hemorrhagic stroke. In contrast to the protective effect of mild-to-moderate alcohol use against ischemic strokes, moderate drinking might result in an increased risk of hemorrhagic strokes.

Djousse, L., Ellison, R. C., Beiser, A., Scaramucci, A., D'Agostino, R. B., Wolf, P. A. (2002). Alcohol consumption and risk of ischemic stroke: the Framingham study. Comments in: Stroke, 33(4):890-1;and 33(4):907-12.

BACKGROUND AND PURPOSE: Stroke is a major cause of death in the United States. The association between alcohol consumption and ischemic stroke (IS) remains controversial. **METHODS:** We used data collected on participants in the Framingham Study to assess the association between total alcohol intake and type of alcoholic beverage and development of IS, overall and according to age. **RESULTS:** A total of 196 men and 245 women developed IS during three 10-year follow-up periods. In the categories of never drinkers, drinkers of 0.1 to 11, 12 to 23, and > or =24 g/d of ethanol (a "typical drink" is approximately 12 g of ethanol), and former drinkers of 0.1 to 11 and > or =12 g/d, crude incidence rates of IS were 6.5, 5.9, 4.9, 5.0, 6.7, and 17.8 cases per 1000 person-years, respectively, for men and 5.9, 4.1, 4.1, 4.3, 8.3, and 7.1, respectively, for women. Overall, compared with never drinkers in a multivariate Cox regression, current alcohol consumption was not related significantly to IS in either sex. Former drinking of > or =12 g/d of alcohol was associated with a 2.4 times higher risk of IS among men but not among women. When stratified by age, alcohol intake was associated with lower risk of IS among subjects aged 60 to 69 years. In beverage-specific analysis, only wine consumption was related to a decreased risk of IS. **CONCLUSIONS:** Our data showed no significant association between total alcohol and IS overall but showed a protective effect of alcohol among subjects aged 60 to 69 years.

Eidelman, R. S., Vignola, P., Hennekens, C. H. (2002). Alcohol consumption and coronary heart disease: a causal and protective factor. Seminars in Vascular Medicine, 2(3):253-6.

Although heavy alcohol consumption is one of the leading causes of preventable deaths, light to moderate consumption of alcohol is associated with a reduced risk of coronary heart disease and total mortality. These benefits have been found in both men and women who consume as little as one to six alcoholic beverages per week regardless of whether the source is wine, beer, or liquor. Further, apparent benefits include a reduced risk for the development of peripheral arterial disease, ischemic stroke, sudden cardiac death, and angina. Even small amounts of alcohol have been associated with increases

in blood pressure and increased risks of some cancers, especially breast. The difference between consuming light to moderate and heavy amounts of alcohol may mean the difference between preventing and causing premature death for all causes, especially coronary heart disease.

Emberson, J. R., Shaper, A. G., Wannamethee, S. G., Morris, R. W., Whincup, P. H. (2005). Alcohol intake in middle age and risk of cardiovascular disease and mortality: accounting for intake variation over time. *American Journal of Epidemiology*, 161(9):856-63.

Moderate alcohol consumption is associated with a decreased risk of cardiovascular disease. However, the impact of variation in alcohol intake over time on estimated risk relations has not been adequately addressed. In this study, 6,544 middle-aged British men without previous cardiovascular disease were followed for cardiovascular events and all-cause mortality over 20 years from 1978/1980 to 1998/2000. Alcohol intake was ascertained at regular points throughout the study. A total of 922 men had a major coronary event within 20 years, 352 men had a stroke, and 1,552 men died of all causes. Baseline alcohol intake displayed U-shaped relations with cardiovascular disease and all-cause mortality, with light drinkers having the lowest risks and nondrinkers and heavy drinkers having similarly high risks. However, the nature of these relations changed after adjustment for intake variation; risks associated with nondrinking were lowered, and risks associated with moderate and heavy drinking increased. Regular heavy drinkers had a 74% higher risk of a major coronary event, a 133% higher risk of stroke, and a 127% higher risk of all-cause mortality than did occasional drinkers (these estimates were 8%, 54%, and 44% before adjustment for intake variation). The findings suggest that considerable caution may be needed before any recommendations regarding acceptable limits of alcohol consumption are made.

Health Canada & The Canadian Coalition for High Blood Pressure Prevention and Control January 2000, National High Blood Pressure Prevention and Control Strategy Summary Report of the Expert Working Group, p. 4 Retrieved from:

http://www.phac-aspc.gc.ca/ccdpc-cpcmc/cvd-mcv/publications/nhbppcs_e.html

High blood pressure is one of the most common and important health problems facing Canadians. It is one of the main risk factors for heart disease, stroke, and kidney failure. Heart disease and stroke account for 37% of all deaths.

The mortality rates of heart disease and stroke have decreased in the past several years. This is probably due to a combination of factors including a decrease in smoking and salt consumption, and improved treatment. The aging of the population will lead to an increase in deaths due to these two diseases unless further prevention efforts are undertaken now.

The prevention and control of high blood pressure would have a major impact on health, quality of life, disability and death among Canadians. It would also reduce the need for health care expenditures for these diseases.

This report outlines a strategy to prevent and control high blood pressure. It is directed at policy makers at the local, provincial / territorial, and national level in both the health and non-health sectors. The strategy is based on current research and expertise. A multi-faceted, comprehensive approach is proposed because there is no one intervention that will accomplish the goal of improving the health of Canadians through high blood pressure prevention and control.

This report focuses on the general population. It does not address the unique needs of children, pregnant women or aboriginal peoples. Each of these groups need to be studied in their own right and, in particular, with the involvement of aboriginal people themselves.

Hillbom, M., Numminen, H., Juvela, S. (1999). Recent heavy drinking of alcohol and embolic stroke. Stroke, 30(11):2307-12.

BACKGROUND AND PURPOSE: Epidemiological evidence suggests that heavy alcohol consumption increases the risk for ischemic stroke, whereas light-to-moderate alcohol intake decreases the risk, but the role of different drinking patterns has remained unclear. We investigated recent light, moderate, and heavy alcohol drinking and former heavy drinking as risk factors for acute ischemic brain infarction by etiological subtype of stroke. **METHODS:** We compared 212 consecutive patients aged between 16 and 60 years, who were completely evaluated for the etiology of their ischemic stroke, with 274 control subjects admitted to the emergency unit of the same hospital. ORs, as estimates of multivariate relative risks (RRs), and 95% CIs after adjustment for possible confounding variables were calculated by logistic regression. The ORs were adjusted for age, sex, body mass index, hypertension, diabetes, hyperlipemia, current smoking, and history of migraine. **RESULTS:** Recent heavy drinking but not former heavy drinking was an independent risk factor for stroke (RR 1.82, 95% CI 1.08 to 3.05). Consumption of 151 to 300 g and >300 g alcohol within the week preceding the onset of stroke significantly increased the risk for cardioembolic and cryptogenic stroke. Consumption of >40 g alcohol within the preceding 24 hours increased the risk for cardiogenic embolism to the brain among those who had a high-risk source (RR 4.75, 95% CI 1.23 to 18.4), the risk for tandem embolism among those who had prominent large-artery atherosclerosis (RR 7.68, 95% CI 1.82 to 32.3), and the risk for cryptogenic stroke (RR 3.84, 95% CI 1.69 to 8.71). Light drinking did not increase the risk for stroke. **CONCLUSIONS:** We conclude that acute drinking of intoxicating amounts of alcohol may trigger the onset of embolic stroke among subjects who have a source of thrombus in the heart or the large arteries.

Iso, H., Baba, S., Mannami, T., Sasaki, S., Okada, K., Konishi, M., Tsugane, S. (2004). JPHC Study Group. Alcohol consumption and risk of stroke among middle-aged men: the JPHC Study Cohort I. Stroke, 35(5):1124-9.

BACKGROUND AND PURPOSE: The impact of light-to-moderate alcohol consumption on risk of stroke has not been well examined in a single study, although the effect is hypothesized to differ among stroke subtypes from meta-analyses. **METHODS:** A total of 19 544 men aged 40 to 59 years living in communities were followed-up from 1990 to 1992 to the end of 2001 in the Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Disease (JPHC Study). **RESULTS:** After 214 504 person-years of follow-up, 694 incident strokes were documented, of which 611 were confirmed by imaging studies or autopsy, including 219 intraparenchymal hemorrhages, 73 subarachnoid hemorrhages, and 319 ischemic strokes. Alcohol consumption was positively associated with age-adjusted risk of total stroke with a 68% excess risk among drinkers of > or =450 g ethanol per week compared with occasional drinkers. This excess risk was confined primarily to hemorrhagic stroke, which remained statistically significant even after controlling for hypertension and other cardiovascular risk factors (RR: 2.15; 95% CI: 1.22 to 3.79). There was a lower risk of ischemic stroke, more specifically lacunar infarction, a higher risk of hemorrhagic stroke, and no excess risk of total stroke among drinkers of 1 to 149 g ethanol per week compared with occasional drinkers; the respective multivariate RR (95% CI) was 0.59 (0.37 to 0.93), 0.43 (0.22 to 0.87), 1.73 (0.98 to 3.07), and 0.98 (0.71 to 1.36). **CONCLUSIONS:** We found differential effects of light-to-moderate alcohol consumption on risks of hemorrhagic and ischemic strokes among middle-aged men. Light-to-moderate alcohol consumption, ie, < or =2 drinks per day, does not raise the risk of total stroke.

Jousilahti, P., Rastenyte, D., Tuomilehto, J. (2000) Serum gamma-glutamyl transferase, self-reported alcohol drinking, and the risk of stroke. Comment in: Stroke, 31(8):1851-5.

BACKGROUND AND PURPOSE: There is still conflicting evidence regarding a link between alcohol drinking and the risk of stroke. In most prospective studies, the assessment of the alcohol drinking has been based on self-reporting, which may be unreliable. The aim of the present study was to examine the relationship between stroke and both the self-reported alcohol drinking and the serum gamma-glutamyl transferase (GGT) concentration, which was regarded as a biological marker of alcohol drinking. **METHODS:** A prospective cohort study of 14 874 Finnish men and women aged 25 to 64 years who participated in a cardiovascular risk-factor survey in 1982 or 1987. The following risk factors, determined at baseline, were included in data analyses: self-reported alcohol drinking, GGT, smoking, blood pressure, serum cholesterol, and body mass index. The cohorts were followed until the end of 1994. Stroke events were identified through the national death registry and hospital discharge Registry by computerized record linkage. **RESULTS:** Serum GGT concentration was associated with the risk of total and ischemic stroke in both genders. There was also a significant association among men between GGT and the risk of intracerebral hemorrhage and among women between GGT and the risk of subarachnoid hemorrhage. The relationships remained statistically significant also after adjustment for other risk factors. Self-reported alcohol drinking did not associate with any type of stroke. **CONCLUSIONS:** These results support the hypothesis that excessive alcohol drinking is related to an increased risk of stroke. Biological markers of alcohol drinking, such as serum GGT level, are useful for the assessment of risks related to alcohol drinking.

Kiyohara, Y., Kato, I., Iwamoto, H., Nakayama, K., Fujishima, M. (1995). The impact of alcohol and hypertension on stroke incidence in a general Japanese population: The Hisayama Study. *Stroke*, 26(3):368-372.

BACKGROUND AND PURPOSE: The relationship between alcohol intake and stroke has been inconsistent in previous studies. We examined the separate and combined effects of drinking habits and hypertension on stroke incidence in a prospective survey of a general Japanese population. **METHODS:** A total of 1621 stroke-free Hisayama residents aged 40 years or older were classified by their alcohol intake into nondrinkers, light drinkers (< 34 g of ethanol per day), and heavy drinkers (> or = 34 g of ethanol per day) and followed up prospectively for 26 years from 1961. **RESULTS:** During the follow-up period, cerebral infarction developed in 244 subjects and cerebral hemorrhage in 60. For men, the incidence of cerebral hemorrhage increased significantly with rising alcohol consumption. In contrast, the incidence of cerebral infarction was slightly lower in light drinkers than in nondrinkers, while it increased significantly in heavy drinkers compared with light drinkers. Female drinkers had a lower incidence of cerebral infarction but a slightly higher incidence of cerebral hemorrhage than nondrinkers, as did male light drinkers. Among the hypertensive subjects, the age- and sex-adjusted relative risk of cerebral hemorrhage was significantly elevated in heavy drinkers versus abstainers (3.13; 95% confidence interval [CI], 1.08 to 9.10), but the increase was not significant for light drinkers. In contrast, the relative risk did not significantly increase for normotensive light and heavy drinkers. Compared with hypertensive light drinkers, the relative risk of cerebral infarction significantly increased in hypertensive heavy drinkers (1.96; 95% CI, 1.08 to 3.57) but remained unchanged in normotensive heavy drinkers. Significant associations between alcohol intake and stroke were substantially the same even after controlling for other risk factors in multivariate analysis. **CONCLUSIONS:** Among hypertensive individuals, heavy alcohol consumption leads to a significant increase in the risk of cerebral hemorrhage, suggesting a synergistic effect of alcohol and hypertension, while light alcohol consumption significantly reduces the risk of cerebral infarction

Laatikainen, T., Manninen, L., Poikolainen, K., Vartiainen, E. (2003) Increased mortality related to heavy alcohol intake pattern. *Journal of Epidemiology & Community Health*, 57(5):379-84.

STUDY OBJECTIVE: Although moderate alcohol intake is related to decreased all cause and ischaemic heart disease mortality, intake of large amounts at a time may be harmful. **DESIGN:** A cohort study, average follow up time was 7.3 years. **SETTING:** Finland. **PARTICIPANTS:** General population sample of 5092 men, aged from 25 to 64 years, who had consumed alcohol during the 12 months before the baseline examination. **MAIN RESULTS:** The main outcome measure was death. After excluding cases with previous myocardial infarction at the baseline examination and after adjustment for age, education, smoking, and average alcohol intake in Cox proportional hazards model, subjects with heavy drinking pattern (six or more drinks at a time) still had higher mortality from all causes than drinkers without heavy drinking occasions (RR 1.57; 95% CI 1.17 to 2.10). Respective analyses showed increased risk also for ischaemic heart disease (1.77; 95% CI 1.01 to 3.08), external causes (2.90; 95% CI 1.47 to 5.72) and alcohol related causes of death (2.73; 95% CI 1.13 to 6.64). The last two risk ratios were not adjusted for smoking. Relative risk point estimates were approximately similar for drinkers with heavy drinking occasions irrespective of beverage type, although those for beer and wine did not reach significance, probably because of the small number of cases. The highest average alcohol intake was found among drinkers who consumed all three types of beverage. **CONCLUSIONS:** Consuming six or more drinks at a time is related to increased mortality among working age male drinkers. The authors found no clear evidence for beverage specific differences.

Maheswaran, R., Beevers, M., Beevers, D. G. (1992). Effectiveness of advice to reduce alcohol consumption in hypertensive patients. Hypertension, 19(1):79-84.

The relation between alcohol consumption and blood pressure is well recognized, and advice to reduce alcohol plays an important part in the management of hypertensive patients. We have evaluated the effectiveness of this advice in a randomized, controlled, single-blind clinical study. After a 2-week run-in period, hypertensive men regularly consuming more than 20 units/wk (1 unit = 10 g) of alcohol were randomly assigned either to the "advice" or control group and were seen at 2-week intervals over an 8-week study period. The outcome measures were: reported alcohol consumption (1-week retrospective diary), markers of alcohol consumption (serum gamma-glutamyl transpeptidase, aspartate aminotransferase, uric acid, mean corpuscular volume), and blood pressure (sitting and standing). Over 18 months, 67 men who drank more than 20 units/wk of alcohol were seen. Twenty-six either were excluded, refused to participate, or dropped out due to nonattendance. Forty-one patients completed the study. After intervention, reported alcohol consumption fell from 60 units/wk to around 30 units/wk in the advice group, whereas it remained between 50 and 60 units/wk in the control group (analysis of variance [ANOVA] $F = 7.1$, p less than 0.05). This was accompanied by falls in gamma-glutamyl transpeptidase (20.9%) and aspartate aminotransferase (18.1%), but no significant changes were seen in the control group. Standing diastolic blood pressure fell significantly in the advice group (from 101.5 mm Hg to 96.3 mm Hg) compared with the control group (ANOVA $F = 4.8$, p less than 0.05). The results suggest that advice to reduce alcohol consumption is a useful form of treatment for hypertensive patients who drink excessively.

Mukamal, K. J., Ascherio, A., Mittleman, M. A., Conigrave, K. M., Camargo, C. A. Jr., Kawachi, I., Stampfer, M. J., Willett, W. C., Rimm, E. B. (2005). Alcohol and risk for ischemic stroke in men: the role of drinking patterns and usual beverage. Annals of Internal Medicine, 142(1):11-9.

BACKGROUND: The association of light to moderate alcohol consumption with risk for ischemic stroke remains controversial, as do the roles of beverage type and drinking pattern. **OBJECTIVE:** To assess the association of drinking patterns and beverage type with risk for ischemic stroke among men. **DESIGN:** Prospective cohort study. **SETTING:** United States. **PARTICIPANTS:** 38 156 male health professionals who were free of

known cardiovascular disease or cancer at baseline in 1986. MEASUREMENTS: With a semi-quantitative food-frequency questionnaire, the authors individually ascertained consumption of regular and light beer, red and white wine, and liquor every 4 years. Alcohol consumption was categorized as light (0.1 to 9.9 g/d, or <1 drink daily), moderate (10.0 to 29.9 g/d, or 1 to 2 drinks daily), and heavier (> or =30.0 g/d, or > or =3 drinks daily). RESULTS: During a follow-up period of 14 years, 412 cases of incident ischemic stroke were documented. Compared with abstainers, light drinkers had a multivariate-adjusted relative risk of 0.99 (95% CI, 0.72 to 1.37), moderate drinkers had a multivariate-adjusted relative risk of 1.26 (CI, 0.90 to 1.76), and heavier drinkers had a multivariate-adjusted relative risk of 1.42 (CI, 0.97 to 2.09; P = 0.01 for trend). Consumption of 10.0 to 29.9 g of alcohol per day on 3 to 4 days per week appeared to be associated with the lowest risk (relative risk, 0.68 [CI, 0.44 to 1.05]). Red wine consumption was inversely associated with risk in a graded manner (P = 0.02 for trend), but other beverages were not. The apparently higher risk for ischemic stroke with heavier alcohol use appeared to be most pronounced for the embolic subtype. LIMITATIONS: This study had limited power to examine specific drinking patterns and heavy drinking and could not assess risk for hemorrhagic stroke. CONCLUSIONS: In this sample of male health professionals, light and moderate average alcohol use was generally not associated with an increased risk for ischemic stroke, although drinking pattern and beverage type modified this relation. Intake of more than 2 drinks per day may be associated with a higher risk for ischemic stroke.

Mukamal, K. J. (2004). Alcohol consumption and abnormalities of brain structure and vasculature. [Review] American Journal of Geriatric Cardiology, 13(1):22-8.

Research on how alcohol consumption influences the structure and blood supply of the brain has generally focused on two primary areas of interest: the atrophic effect of heavy drinking on brain structure and the effects of moderate and heavy drinking on the risk of stroke. Heavy alcohol consumption results in atrophy of gray and white matter, particularly in the frontal lobes, cerebellum, and limbic structures. Heavy drinking also raises the risk of ischemic and hemorrhagic stroke, while light drinking is associated with a lower risk of ischemic stroke. Recently, the author and his colleagues studied alcohol consumption and prevalence of subclinical abnormalities detected by magnetic resonance imaging of the brain among 3376 older adults enrolled in the Cardiovascular Health Study. They found that alcohol consumption was positively associated with measures of brain atrophy and inversely associated with subclinical infarcts in a dose-dependent manner. Alcohol consumption and white matter lesions had a U-shaped relationship, with the lowest prevalence among those who consumed 1-6 drinks per week. Further research is needed to determine how these associations interact to influence overall brain function.

Nelson, Brian D. (2005). Heavy Drinking Boosts Risk Of Heart Attack Deaths. Wisconsin Heart & Vascular Clinics, S.C. Retrieved from:

<http://www.whvc.org/matters/default.asp?dismode=article&artid=276>

This article describes a study in which data were collected from 1,835 patients in the hospital after suffering heart attacks who were asked how often they had three or more drinks in a one to two hour period. This was the time used to describe binge drinking. Among the patients, "binge drinkers had a 73 percent higher death rate after their heart attacks compared to non-binging patients" The study author reported, "Even taking into account their lifestyles, they [patients] had a higher risk of death. Surprisingly, those who binged, but did so less than once a week, had a death rate just as high - 1.93 times that of patients who did not binge. This suggests that even occasional binge drinking has risks, especially in people who have suffered a heart attack."

This study showed a high correlation between binge drinking and health problems and these risks were similar for all types of alcoholic drinks. The study author explained,

"People may be getting the message that a glass of wine a day may be good for you. But it is very important to realize that going beyond that one drink a day may totally eliminate any benefit that alcohol may confer."

Papadakis, J. A., Ganotakis, E. S., Mikhailidis, D. P. (2000). Beneficial effect of moderate alcohol consumption on vascular disease: myth or reality?. [Review] Journal of the Royal Society of Health, 120(1):11-5.

Moderate ethanol consumption (1-3 drinks/day on 5-6 days/week) has a favourable effect on vascular disease-related mortality and morbidity [especially ischaemic heart disease (IHD)]. This cardioprotective effect may be due to significant effects on cardiovascular risk factors such as high density cholesterol (HDL) concentration (HDL protects from IHD) and an inhibition of platelet aggregation (increased platelet aggregability predicts coronary events). In contrast, alcoholics and problem drinkers have an excess of IHD-related, and possibly stroke-related, mortality. Excessive alcohol intake may raise the blood pressure. Prolonged alcohol abuse can also result in alcoholic heart muscle disease. Alcohol is the major cause of non-ischaemic cardiomyopathy in Western society. Although there is a widespread belief that red wine protects more than other alcoholic beverages, several studies do not support this interpretation.

Pinder, R. M., Sandler, M. (2004). Alcohol, wine and mental health: focus on dementia and stroke. [Review] Journal of Psychopharmacology, 18(4):449-56.

The relative risks of coronary heart disease (CHD) and overall mortality are reduced by moderate consumption of alcoholic beverages, particularly wine, which has major implications for public health. It appears likely that this beneficial effect of alcohol will soon be extended to some mental disorders. Although data on psychosis and mood and anxiety disorders are currently lacking, it appears that the relative risks of developing ischaemic stroke and Alzheimer's or vascular dementia are also lowered by moderate alcohol consumption. Such findings are still tentative because of the inherent methodological problems involved in population-based epidemiological studies, and it is unclear whether the benefit can be ascribed to alcohol itself or to other constituents specific to wine such as polyphenols. Plausible biological mechanisms have been advanced for the protective effect of alcohol and wine against CHD, many of which will also play roles in their protective actions against cerebrovascular disease and dementia. The specific antioxidant properties of wine polyphenols may be particularly important in preventing Alzheimer's disease. Because of the substantially unpredictable risk of progression to problem drinking and alcohol abuse, the most sensible advice to the general public is that heavy drinkers should drink less or not at all, that abstainers should not be indiscriminately encouraged to begin drinking for health reasons, and that light to moderate drinkers need not change their drinking habits for health reasons, except in exceptional circumstances.

Puddey, I. B., Beilin, L. J., Vandongen, R. (1986). Effect of regular alcohol use on blood pressure control in treated hypertensive subjects: a controlled study. Clinical and experimental pharmacology & physiology, 13(4):315-8.

Forty-four males with treated essential hypertension and a moderate-to-heavy alcohol intake participated in a randomized controlled crossover trial of the effects of varying alcohol intake on blood pressure control. Usual antihypertensive therapy was maintained unchanged throughout. Self-reported alcohol consumption fell from 452 ml ethanol/week (s.e.m. = 29) during normal drinking habits to 64 ml/week (s.e.m. = 8) while drinking low alcohol content beer. Mean systolic and diastolic blood pressures were significantly lower during the last 2 weeks of reduced alcohol (supine 5.0 mmHg, s.e.m. = 1.4, and 3.0 mmHg, s.e.m. = 0.9, respectively; erect 5.9 mmHg, s.e.m. = 1.6, and 2.9 mmHg, s.e.m. = 1.0, respectively). Body weight was also lower (0.94 kg, s.e.m. = 0.25) at the conclusion

of the low alcohol intake period. Regression analysis suggested that reduction in alcohol intake contributed independently to the fall in both systolic and diastolic blood pressure, while weight change contributed independently to the fall in systolic blood pressure alone. It was concluded that curtailing moderate to heavy alcohol intake leads to improved blood pressure control in treated essential hypertensive males.

Reims, H. M., Kjeldsen, S. E., Brady, W. E., Dahlof, B., Devereux, R. B., Julius, S., Beevers, G., De Faire, U., Fyhrquist, F., Ibsen, H., Kristianson, K., Lederballe-Pedersen, O., Lindholm, L. H., Nieminen, M. S., Omvik, P., Oparil, S., Wedel, H. (2004). Alcohol consumption and cardiovascular risk in hypertensives with left ventricular hypertrophy: the LIFE study. Journal of Human Hypertension, 18(6):381-9.

The Losartan Intervention For End point reduction in hypertension (LIFE) study showed superiority of losartan over atenolol for reduction of composite risk of cardiovascular death, stroke, and myocardial infarction in hypertensives with left ventricular hypertrophy. We compared hazard ratios (HR) in 4287 and 685 participants who reported intakes of 1-7 and >8 drinks/week at baseline, respectively, with those in 4216 abstainers, adjusting for gender, age, smoking, exercise, and race. Within categories, clinical baseline characteristics, numbers randomized to losartan and atenolol, and blood pressure (BP) lowering were similar on the drug regimens. Overall BP control (<140/90 mmHg) at end of follow-up was similar in the categories. Composite end point rate was lower with 1-7 (24/1000 years; HR 0.87, P<0.05) and >8 drinks/week (26/1000 years; HR 0.80, NS) than in abstainers (27/1000 years). Myocardial infarction risk was reduced in both drinking categories (HR 0.76, P<0.05 and HR 0.29, P<0.001, respectively), while stroke risk tended to increase with >8 drinks/week (HR 1.21, NS). Composite risk was significantly reduced with losartan compared to atenolol only in abstainers (HR 0.81 95% confidence interval, CI (0.68, 0.96), P<0.05), while benefits for stroke risk reduction were similar among participants consuming 1-7 drinks/week (HR 0.73, P<0.05) and abstainers (HR 0.72, P<0.01). Despite different treatment benefits, alcohol-treatment interactions were nonsignificant. In conclusion, moderate alcohol consumption does not change the marked stroke risk reduction with losartan compared to atenolol in high-risk hypertensives. Alcohol reduces the risk of myocardial infarction, while the risk of stroke tends to increase with high intake.

Reynolds, K., Lewis, B., Nolen, J. D., Kinney, G. L., Sathya, B., He, J. (2003). Alcohol consumption and risk of stroke: a meta-analysis. JAMA, 289(5):579-88.

CONTEXT: Observational studies suggest that heavy alcohol consumption may increase the risk of stroke while moderate consumption may decrease the risk. OBJECTIVE: To examine the association between alcohol consumption and relative risk of stroke.

DATA SOURCES: Studies published in English-language journals were retrieved by searching MEDLINE (1966-April 2002) using Medical Subject Headings alcohol drinking, ethanol, cerebrovascular accident, cerebrovascular disorders, and intracranial embolism and thrombosis and the key word stroke; Dissertation Abstracts Online using the keywords stroke and alcohol; and bibliographies of retrieved articles. STUDY SELECTION: From 122 relevant retrieved reports, 35 observational studies (cohort or case control) in which total stroke, ischemic stroke, or hemorrhagic (intracerebral or total) stroke was an end point; the relative risk or relative odds and their variance (or data to calculate them) of stroke associated with alcohol consumption were reported; alcohol consumption was quantified; and abstainers served as the reference group. DATA EXTRACTION: Information on study design, participant characteristics, level of alcohol consumption, stroke outcome, control for potential confounding factors, and risk estimates was abstracted independently by 3 investigators using a standardized protocol. DATA SYNTHESIS: A random-effects model and meta-regression analysis were used to pool data from individual studies. Compared with abstainers, consumption of more than 60 g of alcohol per day was associated with an increased relative risk of total stroke, 1.64

(95% confidence interval [CI], 1.39-1.93); ischemic stroke, 1.69 (95% CI, 1.34-2.15); and hemorrhagic stroke, 2.18 (95% CI, 1.48-3.20), while consumption of less than 12 g/d was associated with a reduced relative risk of total stroke, 0.83 (95%, CI, 0.75-0.91) and ischemic stroke, 0.80 (95% CI, 0.67-0.96), and consumption of 12 to 24 g/d was associated with a reduced relative risk of ischemic stroke, 0.72 (95%, CI, 0.57-0.91). The meta -regression analysis revealed a significant nonlinear relationship between alcohol consumption and total and ischemic stroke and a linear relationship between alcohol consumption and hemorrhagic stroke. CONCLUSIONS: These results indicate that heavy alcohol consumption increases the relative risk of stroke while light or moderate alcohol consumption may be protective against total and ischemic stroke. Results of the study included the following:

“Compared with the reference group of abstainers, alcohol consumption of less than 12 g/d, or less than 1 drink per day based on US conversions, was significantly associated with a decreased relative risk of total stroke, while alcohol consumption of more than 60 g/d, or more than 5 drinks per day, was significantly associated with an increased relative risk of total stroke. The association between alcohol consumption and relative risk of ischemic stroke was J-shaped with the lowest risk among those consuming less than 12 g/d, or less than 1 drink per day, or 12 to 24 g/d, or 1 to 2 drinks per day, and the highest risk among those consuming more than 60 g/d, or more than 5 drinks per day. Relative risk of hemorrhagic stroke increased linearly with increasing alcohol consumption, and those consuming more than 60 g/d, or more than 5 drinks per day, had the highest relative risk.”

Schroder, H., Marrugat, J., Elosua, R., Covas, M. I. (2002). Tobacco and alcohol consumption: impact on other cardiovascular and cancer risk factors in a southern European Mediterranean population. British Journal of Nutrition, 88(3):273-81.

Tobacco and alcohol consumption are strongly related to other cardiovascular and cancer risk factors. The aim of the present study was to analyse the association of nutrient intake, blood lipid variables and leisure-time physical activity with tobacco and alcohol consumption status. Participants were recruited in a cross-sectional population-based survey, including cardiovascular risk factor measurements and evaluation of physical activity and diet intake in a Mediterranean population (n 1748). Multiple linear regression analysis, adjusted for several confounders, showed a direct association of saturated fatty acids (g and % total energy intake), dietary cholesterol intakes and serum triacylglycerol with smoking. An inverse association was observed for smoking and unsaturated fatty acids (% energy intake), vitamin C, alpha-tocopherol and beta-carotene intakes, leisure-time physical activity and HDL-cholesterol. These associations were not observed for alcohol drinking. After adjusting for the confounders earlier mentioned, low dietary intakes of vitamin C and dietary fibre were more likely in heavy-smokers as compared with non-smokers (odds ratio 1.74 (95 % CI 1.07, 2.73) and 1.94 (95 % CI 1.29, 2.92) of low vitamin C (<60 mg/d) and dietary fibre intakes (<10 g/d) respectively). Alcohol consumption was directly associated with HDL-cholesterol and triacylglycerol, and attenuated the effects of smoking on HDL-cholesterol. These results suggest that the dietary intake of fibre and several antioxidant components of the Mediterranean diet is reduced in smokers, who also show an adverse lipid profile. However, the worst triacylglycerol levels are associated with the combination of heavy smoking and heavy alcohol drinking. Moderate alcohol consumption was not associated with an unhealthy diet pattern or adverse lipid profile. The health benefits of the Mediterranean diet appear to be strongly counteracted by smoking.

Sesso, H. D., Stampfer, M. J., Rosner, B., Hennekens, C. H., Manson, J. E., Gaziano, J. M. (2000). Seven-year changes in alcohol consumption and subsequent risk of cardiovascular disease in men. Archives of internal medicine, 160(17):2605-12.

BACKGROUND: Few studies have examined whether changes in alcohol consumption influence future cardiovascular risk. **OBJECTIVE:** To examine whether 7-year changes in alcohol consumption are associated with the subsequent risk of cardiovascular disease (CVD). **METHODS:** We prospectively followed up 18,455 men aged 40 to 84 years from the Physicians' Health Study with no history of CVD or cancer. Alcohol consumption was reported on the baseline and the 7-year questionnaires; follow-up for this analysis began after the 7-year questionnaire (median follow-up, 5.8 years). There were 1091 CVD cases, including myocardial infarction, angina pectoris, revascularization, stroke, and CVD-related death. **RESULTS:** Among men initially consuming 1 drink per week or less (n=7360), those with moderate increases (> 1 to < 6 drinks per week) in alcohol consumption had a borderline significant (P=.05) 29% reduced risk of CVD compared with men with no changes (-1 to 1 drink per week). Among men initially consuming greater than 1 to 6 drinks per week (n=6612), those with moderate increases had a nonsignificant (P=.32) 15% decrease in CVD risk compared with men with no changes. Finally, among men initially consuming 1 drink per day or more (n=4483), those who increased intake had a 63% increased risk of CVD compared with men with no changes. **CONCLUSIONS:** These prospective data suggest that, among men with initially low alcohol consumption (< />=1 drink per week), a subsequent moderate increase in alcohol consumption may lower their CVD risk. The possible reduction in CVD risk from increasing alcohol intake did not extend to men initially consuming greater than 1 drink per week. Given the potential risks and benefits associated with alcohol consumption, physician counseling of patients must be individualized in the context of the primary prevention of CVD.

Srinivas, R. Pamidi (2003) Drinking Less Alcohol Lowers Blood Pressure, Clinical Trials Conclude *Wisconsin Heart & Vascular Clinics*, S.C. Retrieved from:
<http://www.whvc.org/matters/default.asp?dismode=article&artid=186>

In this article the author explains that some of the research suggests that alcohol may have some health benefits while other studies show that it can lead to serious illness. The earliest references to alcohol and high blood pressure were found in 1915. More recently studies have shown that as participants lowered their alcohol intake, their blood pressure dropped. Srinivas reports that "consuming three or more drinks of alcohol per day approximately doubles the risk of having high blood pressure." His advice is "People with known high blood pressure should limit their average maximum alcohol intake to one drink per day in women and two drinks per day in men. Women are generally smaller than men and have markedly less gastric alcohol dehydrogenase than men (meaning that more alcohol is absorbed in women). People who should not drink alcohol at all include pregnant women and anyone with a history of, or a potential risk for serious medical complications from alcohol."

Standridge, J. B., Zylstra, R. G., Adams, S. M. (2004). Alcohol consumption: an overview of benefits and risks. [Review] *Southern Medical Journal*, 97(7):664-72.

Published health benefits of regular light-to-moderate alcohol consumption include lower myocardial infarction rates, reduced heart failure rates, reduced risk of ischemic stroke, lower risk for dementia, decreased risk of diabetes and reduced risk of osteoporosis. Numerous complimentary biochemical changes have been identified that explain the beneficial effects of moderate alcohol consumption. Heavy alcohol consumption, however, can negatively affect neurologic, cardiac, gastrointestinal, hematologic, immune, psychiatric and musculoskeletal organ systems. Binge drinking is a significant problem even among moderate drinkers and is associated with particularly high social and economic costs. A cautious approach should be emphasized for those individuals who drink even small amounts of alcohol. Physicians can apply the research evidence describing the known risks and benefits of alcohol consumption when counseling their patients regarding alcohol consumption.

Xin, X., He, J., Frontini, M. G., Ogden, L. G., Motsamai, O. I., Whelton, P.K. (2001). Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension, 38(5):1112-7.

Alcohol drinking has been associated with increased blood pressure in epidemiological studies. We conducted a meta-analysis of randomized controlled trials to assess the effects of alcohol reduction on blood pressure. We included 15 randomized control trials (total of 2234 participants) published before June 1999 in which alcohol reduction was the only intervention difference between active and control treatment groups. Using a standard protocol, information on sample size, participant characteristics, study design, intervention methods, duration, and treatment results was abstracted independently by 3 investigators. By means of a fixed-effects model, findings from individual trials were pooled after results for each trial were weighted by the inverse of its variance. Overall, alcohol reduction was associated with a significant reduction in mean (95% confidence interval) systolic and diastolic blood pressures of -3.31 mm Hg (-2.52 to -4.10 mm Hg) and -2.04 mm Hg (-1.49 to -2.58 mm Hg), respectively. A dose-response relationship was observed between mean percentage of alcohol reduction and mean blood pressure reduction. Effects of intervention were enhanced in those with higher baseline blood pressure. Our study suggests that alcohol reduction should be recommended as an important component of lifestyle modification for the prevention and treatment of hypertension among heavy drinkers.

General Health Benefits

American Heart Association (2002) Alcohol, wine and cardiovascular disease. Retrieved from: <http://www.americanheart.org/presenter.jhtml?identifier=4422>

Are there cardiovascular risks associated with drinking alcohol?

Drinking too much alcohol can raise the levels of some fats in the blood (triglycerides) (tri-GLIS'er-idz). It can also lead to high blood pressure, heart failure and an increased calorie intake. (Consuming too many calories can lead to obesity and a higher risk of developing diabetes.) Excessive drinking and binge drinking can lead to stroke. Other serious problems include fetal alcohol syndrome, cardiomyopathy (kar"de-o-mi-OP'ah-the), cardiac arrhythmia (ah-RITH'me-ah) and sudden cardiac death.

AHA Recommendation

If you drink alcohol, do so in moderation. This means an average of one to two drinks per day for men and one drink per day for women. (A drink is one 12 oz. beer, 4 oz. of wine, 1.5 oz. of 80-proof spirits, or 1 oz. of 100-proof spirits.) Drinking more alcohol increases such dangers as alcoholism, high blood pressure, obesity, stroke, breast cancer, suicide and accidents. Also, it's not possible to predict in which people alcoholism will become a problem. Given these and other risks, the American Heart Association cautions people NOT to start drinking ... if they do not already drink alcohol. Consult your doctor on the benefits and risks of consuming alcohol in moderation.

What about red wine and heart disease?

Over the past several decades, many studies have been published in science journals about how drinking alcohol may be associated with reduced mortality due to heart disease in some populations. Some researchers have suggested that the benefit may be due to wine, especially red wine. Others are examining the potential benefits of components in red wine such as flavonoids (FLAV'oh-noidz) and other antioxidants (an"tih-OK'sih-dants) in reducing heart disease risk. Some of these components may be found in other foods such as grapes or red grape juice. The linkage reported in many of these studies may be due to other lifestyle factors rather than alcohol. Such factors may include increased physical activity, and a diet high in fruits and vegetables and lower in saturated fats. No direct comparison trials have been done to determine the specific effect of wine or other alcohol on the risk of developing heart disease or stroke.

Are there potential benefits of drinking wine or other alcoholic beverages?

Research is being done to find out what the apparent benefits of drinking wine or alcohol in some populations may be due to, including the role of antioxidants, an increase in HDL ("good") cholesterol or anti-clotting properties. Clinical trials of other antioxidants such as vitamin E have not shown any cardio-protective effect. Also, even if they were protective, antioxidants can be obtained from many fruits and vegetables, including red grape juice. The best-known effect of alcohol is a small increase in HDL cholesterol. However, regular physical activity is another effective way to raise HDL cholesterol, and niacin can be prescribed to raise it to a greater degree. Alcohol or some substances such as resveratrol (res-VAIR'ah-trol) found in alcoholic beverages may prevent platelets in the blood from sticking together. That may reduce clot formation and reduce the risk of heart attack or stroke. (Aspirin may help reduce blood clotting in a similar way.) How alcohol or wine affects cardiovascular risk merits further research, but right now the American Heart Association does not recommend drinking wine or any other form of alcohol to gain these potential benefits. The AHA does recommend that to reduce your risk you should talk to your doctor about lowering your cholesterol and blood pressure, controlling your weight, getting enough exercise and following a healthy diet. There is no scientific proof that drinking wine or any other alcoholic beverage can replace these conventional measures.

Ashley, M.J.; Ashley, M.J.; Rehm, J.; Walsh, G.; Single, E.; Room, R. (1999). Low-risk drinking guidelines: Scientific evidence. Canadian Journal of Public Health, 90(4):264-270.

In 1997 the Addiction Research Foundation of Ontario and Canadian Centre on Substance Abuse released updated guidelines for low-risk alcohol consumption. This paper presents the scientific rationale behind this statement. Important comprehensive overviews of the consequences of alcohol use were studied. Formal meta-analyses on morbidity and mortality were examined wherever possible. Individual elements from similar guidelines were investigated for their scientific foundation. Limited original analyses defined risk levels by average weekly consumption. The evidence reviewed demonstrated that placing limits on both daily intake and cumulative intake over the typical week is justified for the prevention of important causes of morbidity and mortality. Gender-specific limits on weekly consumption were also indicated. In these updated guidelines intended for primary prevention, days of abstinence are not necessarily recommended. Intoxication should be avoided and abstinence is sometimes advisable. Available evidence does not strongly favor one alcoholic beverage over another for cardiovascular health benefits. Copyright 1999 - Canadian Public Health Association

Cancer Care Ontario (2005) Alcohol use increases cancer risk. Retrieved from http://www.cancercare.on.ca/index_cancerfactsalcoholuse+cancerrisk.htm.

Alcohol consumption has been established as a convincing risk factor for cancers of the mouth, pharynx, larynx, esophagus, liver and breast, and a probable risk factor for cancers of the colon and rectum. In at least some of these cancers, alcohol and tobacco use together increase risk to a higher level than if the risks from the two were added together.

The amount consumed, rather than the type of alcohol (beer, wine, or spirits), appears to influence the risk of cancer. For liver cancer, it is heavy and persistent use that causes damage. Risk of the other cancers linked to alcohol consumption increases slightly with even low or moderate consumption, and rises with the amount consumed.

Because there is evidence that moderate alcohol use also has beneficial health effects, safe drinking guidelines developed in Canada recognize the need for balance. (Moderate use, for example, appears to reduce overall mortality, but not cancer-related mortality.)

The guidelines recommend no more than two drinks a day, with a weekly maximum of nine drinks for women and 14 for men. Persons with a family history of cancer are encouraged to drink less. In Ontario, 70% of men and 86% of women aged 19 and older report that they either drink alcohol in accordance with these guidelines, or don't drink at all.

Gronbaek, M., Johansen, D., Becker, U., Hein, H. O., Schnohr, P., Jensen, G., Vestbo, J., Sorensen, T. I. (2004). Changes in alcohol intake and mortality: a longitudinal population-based study. *Epidemiology*, 15(2):222-8.

BACKGROUND: Using alcohol intake at one point in time, numerous studies have shown a J- or U-shaped relation with all-cause mortality. Mortality is lowest among the light to moderate drinkers, with the risk of dying from coronary heart disease higher among nondrinkers and the risk of dying from cancer higher among heavy drinkers. We studied whether changes in individual alcohol intake result in corresponding changes in mortality.

METHODS: In a longitudinal study of 6644 men and 8010 women, age 25 to 98 years, who had attended at least 2 health surveys with a 5-year interval between them, we addressed the risk of death after combinations of changes in alcohol intake. **RESULTS:** Mortality after changes in alcohol intake was consistent with the mortality observed among those who reported stable drinking. Stable drinkers showed a U-shaped all-cause mortality, with relative risks of 1.29 (95% confidence interval [CI] = 1.13-1.48) for nondrinkers (< 1 drink per week) and 1.32 (1.15-1.53) for heavy drinkers (> 13 drinks per week) compared with light drinkers (1 to 6 drinks per week). For coronary heart disease mortality, stable nondrinkers had a relative risk of 1.32 (0.97-1.79) compared with stable light drinkers and those who had reduced their drinking from light to none increased their risk (1.40; 1.00-1.95), and those who had increased from nondrinking to light drinking

reduced their relative risk ratio (0.71; 0.44-1.14). Cancer mortality was increased in all groups of heavy drinkers. **CONCLUSION:** Persons with stable patterns of light and moderate alcohol intake had the lowest all-cause mortality. Individual changes in alcohol intake were followed by corresponding changes in mortality.

Heart and Stroke Foundation – 10 Ways to improve your health. (Healthy Living, Family Health) Retrieved from:

<http://ww2.heartandstroke.ca/Page.asp?PageID=33&ArticleID=4593&Src=living&From=SubCategory>

9. Think about your alcoholic consumption for 10 seconds. Research shows that drinking more than nine (for women) and 14 (for men) standard drinks of beer, wine or liquor a week increases the risk of heart disease and stroke. Choose other beverages instead – sparkling mineral water or low-sodium tomato juice makes for a delightful, heart-healthy change. [Read more about alcohol consumption here](#)

Lin, Y., Kikuchi, S., Tamakoshi, A., Wakai, K., Kawamura, T., Iso, H., Ogimoto, I., Yagyu, K., Obata, Y., Ishibashi, T. (2005). The JACC Study Group. Alcohol consumption and mortality among middle-aged and elderly Japanese men and women. Annals of Epidemiology, 15(8):590-7.

PURPOSE: We conducted a prospective cohort study to examine the association between alcohol intake and the risk of all-cause mortality among middle-aged and elderly Japanese men and women. **METHODS:** At baseline(1988-1990), a total of 110,792 Japanese men and women aged 40 to 79 years were asked to complete a questionnaire that included information on alcohol intake, and were followed up for all-cause mortality through December 31, 1999. Relative risks (95% confidence interval) were calculated using Cox proportional-hazards models. **RESULTS:** The risk of all-cause mortality was lowest among current drinkers with an alcohol intake of 0.1 to 22.9 g/d (RR, 0.80; 95% CI, 0.72-0.88 for men; and RR, 0.88; 95% CI, 0.77-1.00 for women). Excessive mortality associated with heavy drinking (> or = 69 g/d) was observed for cancer, cardiovascular disease and injuries and other external causes in men, while significantly reduced mortality with light drinking was seen for cancer in men and CVD in women. For men, the benefit associated with light alcohol consumption (< 23 g/d) was more apparent among nonsmokers than among smokers. **CONCLUSION:** Our prospective data show a 12% to 20% decreased risk of all-cause mortality in both Japanese men and women who consumed less than 23 g/d of alcohol (approximately 2 drinks), although heavy drinking increased that risk.

Ogborne, A. C., Smart, R.G., (2001). Public opinion on the health benefits of moderate drinking: results from a Canadian National Population Health Survey. Addiction, 96(4): 641-9.

Aims. To explore beliefs about the health benefits of drinking alcohol in the Canadian population. **Design.** Secondary analysis of data from a national population health survey. **Participants.** Canadians age 12 or older (weighted n = 72 375) in all provinces but Alberta excluding those living in remote regions, native reserves and armed forces bases. **Measures.** Responses to questions concerning the definition of moderate drinking and the belief that moderate drinking can be good for health. Self-reports of age, gender, province of residence, quantity and frequency of drinking, health problems and indicators of alcohol dependence. **Findings.** Fifty-seven per cent of respondents believed that moderate drinking has health benefits. Forty-seven per cent defined moderate drinking as drinking less than one drink a day and believed this to be good for health. Twelve per cent defined moderate drinking as one or more drinks a day and believed this is good for health. Belief in the health benefits of moderate drinking was more common among men, those age 45 or older, residents of Ontario and Quebec, more frequent drinkers and

those with ischaemic heart disease. Those who believed in the health benefits of at least one drink a day were more often males, older persons and frequent, heavy drinkers. Conclusions. Belief in the health benefits of moderate drinking is generally associated with a conservative definition of moderate drinking. However, some drinkers at risk for alcohol problems may be influenced to drink by the belief that this can have health benefits or use this belief as an excuse for drinking.

Meister, K. A., Whelan, E.M., Kava, R. (2000) The health effects of moderate alcohol intake in humans: an epidemiologic review. Critical Reviews in Clinical Laboratory Sciences, 37(3):261-96.

A large body of scientific evidence associates the moderate intake of alcohol with reduced mortality among middle-aged and older people in industrialized societies. This association is due largely to a reduced risk of death from coronary heart disease, which appears to outweigh any possible adverse effects of moderate drinking. The regular consumption of small amounts of alcohol is more healthful than the sporadic consumption of larger amounts. No beneficial effect of moderate drinking on mortality has been demonstrated in young adults (premenopausal women and men who have not reached their forties). It is theoretically possible that moderate drinking in young adulthood might reduce the risk of later heart disease; however, this has not been clearly demonstrated. For some individuals (e.g., those who cannot keep their drinking moderate, pregnant women, and those who are taking medications that may interact adversely with alcoholic beverages), the risks of alcohol consumption, even in moderation, outweigh any potential benefits. Because even small amounts of alcohol can impair judgment and coordination, no one should drink alcoholic beverages, even in moderation, before driving a motor vehicle or performing other activities that involve attention and skill.

Mukamal, K. J. & Rimm, E. B. (2001). Alcohol's effects on the risk for coronary heart disease. [Review] Alcohol Research & Health: the Journal of the National Institute on Alcohol Abuse & Alcoholism, 25(4):255-6.

Several studies have indicated that moderate drinkers have a lower risk of both nonfatal myocardial infarction and fatal heart disease than do abstainers. To determine whether alcohol truly prevents coronary heart disease or whether other factors may contribute to this observed relationship, researchers conducted a systematic literature review and a combined analysis (i.e., meta-analysis) of 42 published studies. This analysis found that consumption of up to two drinks per day can promote changes in the levels of molecules that reduce the risk of heart disease while also increasing the levels of certain molecules that promote heart disease. Alcohol also may affect the risk of heart disease by acting on other various other molecules involved in a variety of physiological processes related to heart disease. Finally, the relationship between alcohol consumption and heart disease may be modulated by genetic factors.

Pinder, R. M. & Sandler, M. (2004) Alcohol, wine and mental health: focus on dementia and stroke. [Review] Journal of Psychopharmacology, 18(4):449-56.

The relative risks of coronary heart disease (CHD) and overall mortality are reduced by moderate consumption of alcoholic beverages, particularly wine, which has major implications for public health. It appears likely that this beneficial effect of alcohol will soon be extended to some mental disorders. Although data on psychosis and mood and anxiety disorders are currently lacking, it appears that the relative risks of developing ischaemic stroke and Alzheimer's or vascular dementia are also lowered by moderate alcohol consumption. Such findings are still tentative because of the inherent methodological problems involved in population-based epidemiological studies, and it is unclear whether the benefit can be ascribed to alcohol itself or to other constituents specific to wine such as polyphenols. Plausible biological mechanisms have been

advanced for the protective effect of alcohol and wine against CHD, many of which will also play roles in their protective actions against cerebrovascular disease and dementia. The specific antioxidant properties of wine polyphenols may be particularly important in preventing Alzheimer's disease. Because of the substantially unpredictable risk of progression to problem drinking and alcohol abuse, the most sensible advice to the general public is that heavy drinkers should drink less or not at all, that abstainers should not be indiscriminately encouraged to begin drinking for health reasons, and that light to moderate drinkers need not change their drinking habits for health reasons, except in exceptional circumstances.

Reynolds, K., Lewis, B., Nolen, J. D., Kinney, G. L., Sathya, B., He, J. (2003). Alcohol consumption and risk of stroke: a meta-analysis.[erratum appears in JAMA. 2003 Jun 4;289(21):2798 JAMA, 289(5):579-88.

CONTEXT: Observational studies suggest that heavy alcohol consumption may increase the risk of stroke while moderate consumption may decrease the risk. OBJECTIVE: To examine the association between alcohol consumption and relative risk of stroke. DATA SOURCES: Studies published in English-language journals were retrieved by searching MEDLINE (1966-April 2002) using Medical Subject Headings alcohol drinking, ethanol, cerebrovascular accident, cerebrovascular disorders, and intracranial embolism and thrombosis and the key word stroke; Dissertation Abstracts Online using the keywords stroke and alcohol; and bibliographies of retrieved articles. STUDY SELECTION: From 122 relevant retrieved reports, 35 observational studies (cohort or case control) in which total stroke, ischemic stroke, or hemorrhagic (intracerebral or total) stroke was an end point; the relative risk or relative odds and their variance (or data to calculate them) of stroke associated with alcohol consumption were reported; alcohol consumption was quantified; and abstainers served as the reference group. DATA EXTRACTION: Information on study design, participant characteristics, level of alcohol consumption, stroke outcome, control for potential confounding factors, and risk estimates was abstracted independently by 3 investigators using a standardized protocol. DATA SYNTHESIS: A random-effects model and meta-regression analysis were used to pool data from individual studies. Compared with abstainers, consumption of more than 60 g of alcohol per day was associated with an increased relative risk of total stroke, 1.64 (95% confidence interval [CI], 1.39-1.93); ischemic stroke, 1.69 (95% CI, 1.34-2.15); and hemorrhagic stroke, 2.18 (95% CI, 1.48-3.20), while consumption of less than 12 g/d was associated with a reduced relative risk of total stroke, 0.83 (95% CI, 0.75-0.91) and ischemic stroke, 0.80 (95% CI, 0.67-0.96), and consumption of 12 to 24 g/d was associated with a reduced relative risk of ischemic stroke, 0.72 (95% CI, 0.57-0.91). The meta-regression analysis revealed a significant nonlinear relationship between alcohol consumption and total and ischemic stroke and a linear relationship between alcohol consumption and hemorrhagic stroke. CONCLUSIONS: These results indicate that heavy alcohol consumption increases the relative risk of stroke while light or moderate alcohol consumption may be protective against total and ischemic stroke. Results of the study included the following:

"Compared with the reference group of abstainers, alcohol consumption of less than 12 g/d, or less than 1 drink per day based on US conversions, was significantly associated with a decreased relative risk of total stroke, while alcohol consumption of more than 60 g/d, or more than 5 drinks per day, was significantly associated with an increased relative risk of total stroke. The association between alcohol consumption and relative risk of ischemic stroke was J-shaped with the lowest risk among those consuming less than 12 g/d, or less than 1 drink per day, or 12 to 24 g/d, or 1 to 2 drinks per day, and the highest risk among those consuming more than 60 g/d, or more than 5 drinks per day. Relative risk of hemorrhagic stroke increased linearly with increasing alcohol consumption, and those consuming more than 60 g/d, or more than 5 drinks per day had the highest relative risk."

Russell, M., Dorn, J., Freudenheim, J. L., Muti, P., Nochajski, T., Hovey, K. & Trevisan, M. (2004) Heavy, lifetime alcohol users may be toasting metabolic syndrome. American Heart Foundation. Retrieved from <http://www.americanheart.org/presenter.jhtml?identifier=3026064>

Total volume is the total number of drinks in a lifetime; frequency is the total lifetime drinking days; intensity is volume divided by frequency or drinks per drinking day, averaged over a lifetime. Researchers studied lifetime drinking patterns using a large population-based sample from northwestern New York state, developed and maintained by University of Buffalo researchers. The database provided healthy controls for case-control studies of chronic disease, with 2,817 individuals, 35 to 79 years old, who drank at least once a month for at least six months during their lifetime.

"Individuals who had an early peak of drinking behavior are at higher risk of metabolic syndrome compared to those who have initiated drinking later in life and maintained a low moderate level through life," said Fan. The early group peaked drinking at about age 20–30; then sharply dropped as they age. Among women, the former early-peak-drinkers have a 52 percent higher risk of metabolic syndrome than current low-level drinkers.

"A history of heavy, episodic drinking carries a greater risk of developing metabolic syndrome, regardless of gender," said Fan. "Young people who tend to become involved in episodic drinking rather than moderate drinking should be discouraged."

The researchers concluded that it is healthier to drink smaller amounts per drinking day than to drink more on fewer days, in line with current guidelines on moderate drinking.

"The drinking pattern of one drink per day is much healthier than seven drinks on a weekend," said Fan.

Standridge, J.B., Zylstra, R. G., Adams, S. M. (2004). Alcohol consumption: an overview of benefits and risks. [Review] *Southern Medical Journal*, 97(7):664-72.

Published health benefits of regular light-to-moderate alcohol consumption include lower myocardial infarction rates, reduced heart failure rates, reduced risk of ischemic stroke, lower risk for dementia, decreased risk of diabetes and reduced risk of osteoporosis. Numerous complimentary biochemical changes have been identified that explain the beneficial effects of moderate alcohol consumption. Heavy alcohol consumption, however, can negatively affect neurologic, cardiac, gastrointestinal, hematologic, immune, psychiatric and musculoskeletal organ systems. Binge drinking is a significant problem even among moderate drinkers and is associated with particularly high social and economic costs. A cautious approach should be emphasized for those individuals who drink even small amounts of alcohol. Physicians can apply the research evidence describing the known risks and benefits of alcohol consumption when counseling their patients regarding alcohol consumption.

Tom Blackwell. (2006). *Beer may hike lung cancer risk*. *National Post*, Published: Wednesday, April 12, 2006 Retrieve from:

<http://www.canada.com/topics/bodyandhealth/story.html?id=285912b6-8633-4c42-b718-88c834299c19&p=1>

Montreal study: 'It seems to point to a harmful effect of alcohol'

Beer drinking, even if it is relatively moderate, heightens the risk of contracting lung cancer, while imbibing a little wine can have the opposite effect, suggests a striking new Canadian study.

The findings by Montreal-based researchers add to a growing body of literature linking alcohol consumption and cancer, though the reason for that connection is still largely a mystery.

Previous studies had indicated some kind of relationship between alcohol and lung cancer.

But most of that research did not factor in the effect of smoking on the subjects, making the results controversial at best.

In the new Montreal study, the authors took some pains to adjust for the participants' smoking habits and believe they have more accurately depicted the actual impact of alcohol.

"I thought the study was quite provocative and interesting," said Norman Giesbrecht, a senior scientist at Ontario's Centre for Addiction and Mental Health after reading the paper, which was published this month in the journal *Cancer Causes and Control*.

"There are signals that alcohol is potentially a carcinogen at relatively low levels of consumption, and one does not have to be a fall-down, chronic, dependent drunk to experience some risk," Dr. Giesbrecht said.

The findings of the Montreal and other studies on alcohol and cancer are particularly significant given that rates of high-risk drinking have been climbing in some provinces recently, Dr. Giesbrecht said.

And the per-capita consumption of alcohol is going up across Canada, he added.

Andrea Benedetti, the paper's lead author and a biostatistician at McGill University's faculty of medicine, said there were some inconsistencies in the study's findings, but a clear message did emerge.

"It's another piece of evidence and it seems to point to a harmful effect of alcohol," Dr. Benedetti said in an interview.

Previous research has found a strong link between alcohol and cancers of the mouth, pharynx, esophagus and larynx. Increased risk has also been found with stomach, colon, rectum, liver, breast and ovary cancers.

There are only theories about why alcohol might be carcinogenic.

Animal studies have indicated that a component of ethanol can be carcinogenic, while another hypothesis suggests the oxidative effect of alcohol could damage DNA.

The latest study analysed results from two large surveys in Quebec.

The first, conducted in the 1980s, looked at 699 recently diagnosed male lung cancer patients and 507 randomly selected controls.

The second, carried out in the mid-1990s, involved 1,094 men and women with lung cancer and 1,468 controls.

In both surveys, questionnaires were used to collect information on food consumption, drinking, smoking and other factors.

The Montreal researchers used four different statistical techniques to try to filter out the effect of smoking on cancer risk in an effort to isolate the effects of drinking.

In the first study, drinking beer increased the lung cancer risk by 20% for those who downed up to six brews a week, and by 50% for those who drank seven or more, the researchers concluded.

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In the second study, beer consumption appeared harmful to men, as well, but not to those who regularly ate fruit and vegetables.

People in the later study who drank wine, though, saw their lung cancer risk drop, by 70% for women and 40% for men.

The protective effect of the wine may be a result of the composition of different types of alcohol, Dr. Benedetti observed.

She noted that other research suggests moderate quantities of red wine can help prevent some disease.

Differences in the lifestyles of beer versus wine drinkers could also be part of the equation, although the Montreal researchers tried to eliminate that factor by separating results according to income and education level.

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