Type of Alcohol Consumed and Mortality from All Causes, Coronary Heart Disease, and Cancer

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Background: **Although the J-shaped relation between alcohol intake and mortality has been reproduced in many large cohort studies, the question of whether the effects of beer, wine, and spirits differ remains controversial.**

Objective: **To examine the relation between intake of different types of alcohol and death from all causes, coronary heart disease, and cancer.**

Design: **Pooled cohort studies in which intake of beer, wine, and spirits; smoking status; educational level; physical activity; and body mass index were assessed at baseline.**

Setting: **Copenhagen, Denmark.**

Participants: **13 064 men and 11 459 women 20 to 98 years of age.**

Measurements: **Number of deaths and time to death from all causes, coronary heart disease, and cancer during follow-up.**

Results: **During 257 859 person-years of follow-up, 4833 participants died. J-shaped relations were found between total alcohol intake and mortality at various levels of wine intake. Compared with nondrinkers, light drinkers who avoided wine had a relative risk for death from all causes of 0.90 (95% CI, 0.82 to 0.99) and those who drank wine had a relative risk of 0.66 (CI, 0.55 to 0.77). Heavy drinkers who avoided wine were at higher risk for death from all causes than were heavy drinkers who included wine in their alcohol intake. Wine drinkers had significantly lower mortality from both coronary heart disease and cancer than did non–wine drinkers ($P = 0.007$ and $P = 0.004$, respectively).**

Conclusion: **Wine intake may have a beneficial effect on all-cause mortality that is additive to that of alcohol. This effect may be attributable to a reduction in death from both coronary heart disease and cancer.**

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Several population studies from different countries have shown a J-shaped relation between intake of alcohol and mortality from all causes (1–6). Studies comparing different countries have found a strong inverse relation between incidence rates of coronary heart disease and wine consumption but a weak or nonexistent relation for consumption of beer or spirits (7–9). The findings that different types of alcoholic beverages have different effects on mortality are indirectly supported by several clinical and experimental studies (10–12). In contrast, prospective studies have shown that beer (13), spirits (14), and wine (15) may have protective effects. However, most of these investigations were based on populations with one predominant type of alcohol consumption; this precluded valid comparison of the effects of the three different types of alcohol. We sought to analyze the effect of intake of different types of alcohol on mortality from all causes, coronary heart disease, and cancer in several large Danish cohort studies.

Methods

The Copenhagen Centre for Prospective Population Studies is based on three study samples: that of the Copenhagen City Heart Study; that of the Copenhagen County Centre of Preventive Medicine (the former Glostrup Population Studies), which includes six cohorts; and that of the Copenhagen Male Study (16–18). The study samples of the Copenhagen City Heart Study, initiated in 1976, and the Copenhagen County Centre of Preventive Medicine, initiated in 1964, were randomly selected within age strata from the populations residing in defined areas in greater Copenhagen. For the Copenhagen Male Study, initiated in 1971, employees of 14 large companies in Copenhagen were invited to participate. The mean participation rate in all studies was 80% (range, 69% to 88%). The combined study sample comprises 13 064 men and 11 459 women for whom information on alcohol intake and lifestyle-related variables, described below, was complete.

Alcohol Intake

Participants of the Copenhagen City Heart Study and the studies in the Copenhagen County Centre of Preventive Medicine were asked about their current average weekly intake of beer, wine, and spirits. In the Copenhagen Male Study, participants were asked about their average

daily intake of beer, wine, and spirits on weekdays (Monday through Thursday) and weekends (Friday through Sunday); these reports were combined to estimate weekly alcohol consumption. Persons in our study who did not drink alcohol because they were receiving disulfiram or other medication were excluded from the analysis.

One bottle of beer contains 11.6 g of alcohol, and 12 g is an approximate average for one serving of wine or spirits. We grouped participants into five categories on the basis of total intake of alcohol: less than 1 drink/wk (nondrinkers), 1 to 7 drinks/wk, 8 to 21 drinks/wk, 22 to 35 drinks/wk, and more than 35 drinks/wk. Intake of beer, wine, and spirits was categorized similarly; however, because of the frequency of end point data, "more than 21 drinks/wk" is the highest intake category for the individual types of beverages.

Smoking Status

Participants reported whether they were never-smokers, former smokers, or current smokers. Current smokers reported grams of tobacco smoked per day in the form of cigarettes (1 g/d), small cigars (3 g/d), cigars (5 g/d), and pipe tobacco (50 g/package). Five groups were defined: never-smokers, former smokers, smokers of 1 to 14 g of tobacco daily, smokers of 15 to 24 g of tobacco daily, and smokers of more than 24 g of tobacco daily.

Education

Participants reported the number of years that they attended school. Three groups were defined: fewer than 8 years, 8 to 11 years, and 12 or more years of school education.

Physical Activity

Participants reported whether they were physically active during leisure time. Four groups were defined: sedentary (<2 h/wk), light activity (2 to 4 h/wk), moderate activity (>4 h/wk, noncompetitive) and heavy activity (>4 h/wk, competitive).

Body Mass Index

Body weight and height were measured while the participant was wearing light clothes and no shoes. Body mass index was calculated as weight in kg divided by height in meters squared. Five categories of body mass index were defined: less than 20.0 kg/m^2, 20.0 to 24.9 kg/m^2, 25.0 to 29.9 kg/m^2, 30.0 to 34.9 kg/m^2, and 35.0 kg/m^2 or more.

Changes in Lifestyle-Related Variables

When participants were re-examined during follow-up, the newly obtained values for alcohol intake, smoking status, physical activity, and body mass index were used to replace the old values in the statistical analyses. Observation time and vital status were included in the modeling accordingly.

Follow-up

Participants were followed from date of entry into the study to date of death, loss to follow-up, emigration, or end of follow-up, whichever came first. The vital status of populations was followed by using each participant's unique identification number in the national Central Person Register until 9 January 1995. Fewer than 1% of the participants were lost to follow-up. Causes of death were obtained from the National Board of Health and were defined by using codes from International Classifications of Diseases, Eighth Revision (codes 410.0 to 414.0 for coronary heart disease and codes 140.0 to 209.0 for cancer). According to a previous study, the reported diagnoses for these grouped codes have proven to be sufficiently valid (20).

Statistical Analysis

We performed Poisson regression (21) by using SAS/STAT software (22) to estimate the effect of alcohol intake on the risk for death. These models generate estimates of relative risk that are adjusted for confounders. Each model included the following potential confounders as categorical variables: age, cohort study, sex, education, body mass index, physical activity, and smoking status. Owing to collinearity, it was impossible to include both the amount by type of beverage (beer, wine, or spirits) consumed and total alcohol intake in the same regression. We therefore estimated the influence of alcohol according to number of drinks consumed per week (0, 1 to 7, 8 to 21, 22 to 35, >35) in three regressions: 1) total alcohol consumption in drinks per week, without considering beverage type; 2) alcohol consumption in drinks of each beverage per week, without considering the total intake; and 3) percentage of total alcohol intake consumed as wine (0%, 1% to 30%, >30%).

Effects that were insignificant according to the likelihood ratio test (5% level) were removed by backward elimination. A term indicating interaction between total alcohol intake and percentage alcohol consumed as beer, wine,

Table 1. **Baseline Characteristics of the Study Participants**

Characteristic	Nondrinkers	Non–Wine Drinkers	Drinkers with Wine as 1% to 30% of Total Alcohol Intake	Drinkers with Wine as >30% of Total Alcohol Intake
Participants, *n*	5910	5767	3754	9092
Mean age ± SD, *y*	57 ± 13	57 ± 12	51 ± 13	51 ± 13
Men, %	28	74	82	45
Current smoker, %	50	67	61	51
Highest educational level, %	6	6	14	18
Physically active, %	26	30	36	31
Mean sex-weighted body mass index, kg/m^2	26	26	25	25
Mean total alcohol intake, *drinks/wk*				
1–7 drinks/wk	–	3.6	5.5	3.7
8–21 drinks/wk	–	13.3	13.7	12.8
22–35 drinks/wk	–	28.2	27.1	27.6
>35 drinks/wk	–	55.4	49.5	50.8
Proportion of wine relative to total alcohol intake, %				
1–7 drinks/wk	–	0	22	69
8–21 drinks/wk	–	0	19	58
22–35 drinks/wk	–	0	15	54
>35 drinks/wk	–	0	14	56

or spirits was included in the analyses to assess whether the effects of beer, wine, and spirits differed at different levels of total alcohol intake; no such effects were identified, as judged from the fit of the model. Likewise, no interaction was found between sex and intake of different types of beverage in terms of mortality.

Results

A total of 4275 women and 1635 men drank less than 1 drink per week; 64 women and 1032 men drank 35 or more drinks per week. Of 13 613 participants who drank alcohol, 12 846 (69%) included wine in their intake (**Table 1**). During 257 859 person-years of follow-up, 4833 participants died; of these, 1075 died of coronary heart disease and 1552 died of cancer.

Baseline Characteristics

Compared with participants who drank alcohol but no wine, those for whom wine made up more than 30% of their total alcohol intake were more likely to be women and have a higher educational level but were less likely to be smokers (**Table 1**). Participants for whom wine made up more than 30% of their alcohol intake were similar to those who drank no alcohol in terms of smoking habits, body mass index, and physical activity. Across categories of total alcohol intake, mean alcohol intake within the different categories of wine drinking was similar; for example, among participants who drank 8 to 21 drinks/wk, those who drank no wine, those who drank 1% to 30% wine, and those who drank more than 30% wine had a mean alcohol intake of 13.3, 13.7, and 12.8 drinks/wk, respectively. However, among light drinkers (1 to 7 drinks/wk), those who drank 1% to 30% of their alcohol as wine had a slightly higher mean intake than did those who avoided wine and those who drank more than 30% of their alcohol intake as wine. Thus, assessment of the effects of wine intake may not be subject to residual confounding by total alcohol intake when controlled for as specified.

Total Alcohol Intake and Mortality

We found J-shaped relations between total alcohol intake and all-cause mortality in the three substudies. Pooled analyses also revealed J-shaped relations (**Table 2**). When nondrinkers were used as the reference group (relative risk, 1.00), intake of 1 to 7 drinks per week carried a relative risk of 0.82 (95% CI, 0.76 to 0.88) and intake of more than 35 drinks per week carried a relative risk of 1.10 (CI, 0.95 to 1.26). Alcohol intake was negatively related to death from coronary heart disease and positively related to death from cancer (**Table 2**).

Intake of Beer, Wine, and Spirits and Mortality

Light to moderate intake of beer or spirits had a small effect on death from all causes (**Table 2**). This finding contrasted with the effect of wine intake on mortality: Participants who drank 8 to 21 glasses of wine per week had a relative risk for death from all causes of 0.76 (CI, 0.67 to 0.86).

Intake of fewer than 22 drinks of beer, wine, and spirits per week all carried lower risk for death from coronary heart disease; the reduction in risk was of the same magnitude for beer and wine drinking but was smaller and not statistically significant for spirits drinking. Furthermore, light to moderate drinkers of wine had a lower risk for death from cancer than those who did not drink wine, an association that was not found for beer and spirits drinkers (**Table 2**).

Wine Intake and All-Cause Mortality

We estimated three J-shaped risk functions between total alcohol intake and mortality, adjusted for age, sex, smoking status, educational level, physical activity, and body mass index (**Figure 1**). Compared with nondrinkers, light drinkers who avoided wine had a relative risk for death from all causes of 0.90 (CI, 0.82 to 0.99) and light drinkers who drank wine had a relative risk of 0.66 (CI, 0.55 to 0.77). Compared with light drinkers who avoided wine, light drinkers for whom wine made up 30% or less of their total alcohol intake and those for whom wine made up more than 30% of their total alcohol intake had lower risk for all-cause mortality (relative risks, 0.67 [CI, 0.53 to 0.84] and 0.83 [CI, 0.74 to 93]).

At all levels of alcohol intake, wine drinkers were at significantly lower risk than non–wine drinkers for all-cause mortality ($P < 0.001$). The risk functions for the two strata of wine drinking did not differ significantly ($P = 0.15$).

Death from Coronary Heart Disease, according to Total Alcohol Intake, in Wine Drinkers and Non–Wine Drinkers

Wine drinkers had a lower risk for death from coronary heart disease than did non–wine drinkers at all levels of total alcohol intake. Compared with nondrinkers, light drinkers who avoided wine had a relative risk for death from coronary heart disease of 0.76 (CI, 0.63 to 0.92) and those who drank wine had a risk of 0.58 (CI, 0.47 to 0.72) (**Figure 2**, *top*).

Death from Cancer, according to Total Alcohol Intake, in Wine Drinkers and Non–Wine Drinkers

In both wine drinkers and non–wine drinkers, risk for death from cancer increased as total alcohol intake increased. At all levels of alcohol intake, non–wine drinkers

Table 2. **Relative Risk for Death with Regard to Total Alcohol Intake and Intake of Beer, Wine, and Spirits**

Alcohol Intake	Relative Risk for Death (95% CI)		
	All Causes	Coronary Heart Disease	Cancer
Total*			
0 drinks/wk	1.00 (referent)	1.00 (referent)	1.00 (referent)
1–7 drinks/wk	0.82 (0.76–0.88)	0.68 (0.58–0.79)	1.02 (0.87–1.17)
8–21 drinks/wk	0.82 (0.75–0.89)	0.61 (0.52–0.72)	1.05 (0.90–1.21)
22–35 drinks/wk	1.00 (0.89–1.12)	0.67 (0.52–0.86)	1.35 (1.10–1.65)
>35 drinks/wk	1.10 (0.95–1.26)	0.51 (0.35–0.73)	1.36 (1.06–1.75)
Beer†			
0 drinks/wk	1.00 (referent)	1.00 (referent)	1.00 (referent)
1–7 drinks/wk	0.90 (0.83–0.97)	0.78 (0.67–0.91)	1.05 (0.92–1.19)
8–21 drinks/wk	0.99 (0.90–1.09)	0.63 (0.52–0.77)	1.32 (1.12–1.55)
>21 drinks/wk	1.31 (1.15–1.49)	0.78 (0.58–1.05)	1.46 (1.16–1.84)
Wine†			
0 drinks/wk	1.00 (referent)	1.00 (referent)	1.00 (referent)
1–7 drinks/wk	0.80 (0.74–0.86)	0.74 (0.63–0.86)	0.86 (0.76–0.97)
8–21 drinks/wk	0.76 (0.67–0.86)	0.64 (0.48–0.84)	0.78 (0.64–0.96)
>21 drinks/wk	0.90 (0.66–1.23)	0.75 (0.39–1.45)	0.87 (0.51–1.48)
Spirits†			
0 drinks/wk	1.00 (referent)	1.00 (referent)	1.00 (referent)
1–7 drinks/wk	0.94 (0.87–1.01)	0.97 (0.83–1.12)	0.95 (0.84–1.08)
8–21 drinks/wk	1.02 (0.90–1.15)	0.78 (0.59–1.03)	1.13 (0.93–1.38)
>21 drinks/wk	1.42 (1.06–1.91)	1.12 (0.55–2.28)	1.81 (1.14–2.89)

* Adjusted for age, sex, smoking habits, educational level, physical activity, and body mass index.
† Adjusted for other types of alcohol, age, sex, smoking habits, educational level, physical activity, and body mass index. Because of the frequency of end point data, ">21 drinks/wk" is the highest intake category for the individual types of beverages.

had a higher risk for death from cancer than did wine drinkers (**Figure 2**, *bottom*). Compared with nondrinkers, those who drank 22 to 35 drinks/wk but avoided wine had a risk of 1.63 (CI, 1.23 to 2.16) and those who drank more than 35 drinks/wk (heavy drinkers) had a risk of 1.52 (CI, 1.07 to 2.17). Participants who drank 22 to 35 drinks/wk and those who drank more than 35 drinks/wk, including wine, had relative risks for cancer of 1.24 (CI, 0.97 to 1.57) and 1.31 (CI, 0.96 to 1.79), respectively (**Figure 2**, *bottom*).

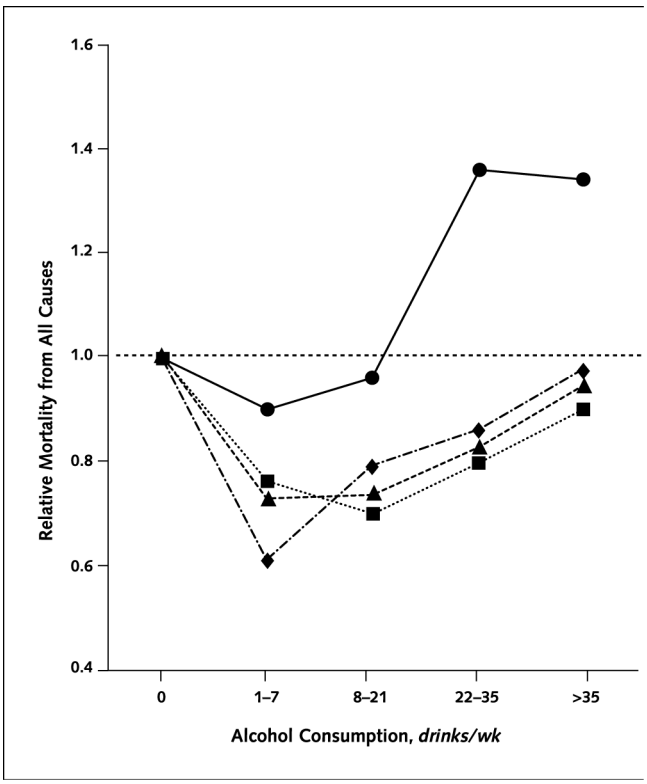
Effects of Sex and Educational Level

At all levels of alcohol intake, both men and women who drank wine had lower all-cause mortality than did those who drank no wine. Educational level seemed to have no modifying effect on this relation.

Drinking Pattern

In the Copenhagen Male Study, it appeared that more participants drank both moderately and heavily during weekends compared with weekdays. No major beverage-specific differences in the weekend pattern of alcohol consumption were detected. On weekdays, however, beer drinking predominated—39% of participants had light (1 to 2 drinks/d) intake of beer, 16% had light intake of wine, and 15% had light intake of spirits (**Table 3**).

Figure 1. **Relative risk for death from all causes in relation to total alcohol intake.**



Data pertain to non–wine drinkers (*circles*), wine drinkers (*triangles*), drinkers for whom wine made up 1% to 30% of their total alcohol intake (*diamonds*), and drinkers for whom wine made up more than 30% wine of their total alcohol intake (*squares*). Relative risk is set at 1.00 among nondrinkers (<1 drink/wk). Estimates were adjusted for age, sex, educational level, smoking status, physical activity, and body mass index.

Discussion

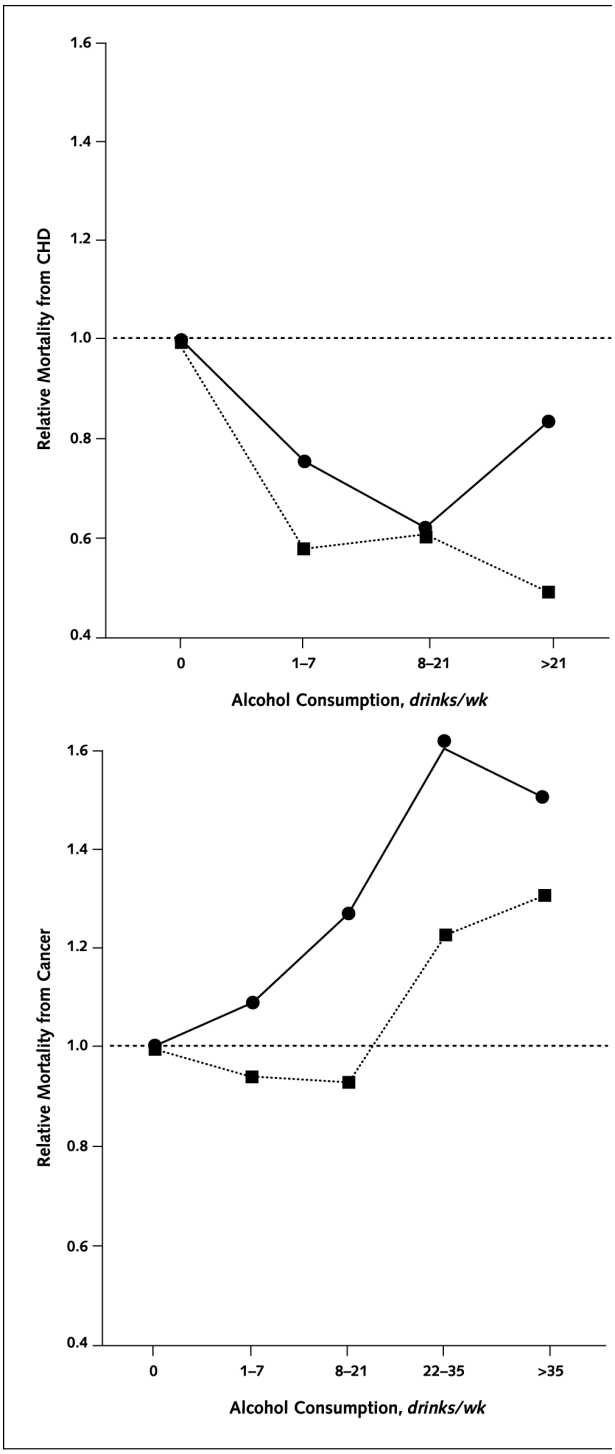
In this prospective, population-based analysis, we found a significant decrease in all-cause mortality among wine drinkers compared with non–wine drinkers at all levels of alcohol intake.

The beneficial effects of light to moderate alcohol intake on coronary heart disease risk factors, such as platelet aggregation and high-density lipoprotein cholesterol level, have been described in previous studies (23–25). Population studies have described a J-shaped relation between alcohol intake and death from cardiovascular disease and from all causes (26, 27). Studies of populations whose members predominantly drank one of three types of alcoholic beverages found that the predominant beverage had the apparently strongest and most significant association with risk for death or morbidity from coronary heart disease (13, 15, 27–29).

Cross-sectional comparisons at the population aggregate level have shown a strong inverse relation between wine intake and incidence of coronary heart disease but no such relation for other types of alcoholic beverages (7–9). This type of study, however, is inadequate to determine a causal relationship because exposure–disease relationships cannot be compared at the individual level and because information on temporal separation of cause and effect is lacking. However, the results of these studies as well as our study are supported by clinical and experimental studies suggesting that such substances as flavonoids and antioxidants, which are found in wine but not in beer or spirits, have a beneficial effect on risk for coronary heart disease (30).

Our observation of a significant decrease in all-cause mortality in wine drinkers, independent of total alcohol intake, may be confounded by genetic, psychosocial, or lifestyle-related factors. In our study, 67% of non–wine drinkers and 54% of wine drinkers were current smokers.

Figure 2. **Relative risk for death from coronary heart disease (*CHD*) (*top*) and cancer (*bottom*) in relation to intake of total alcohol.**



Data refer to non–wine drinkers (*circles*) and wine drinkers (*squares*). Relative risk is set at 1.00 among nondrinkers (<1 drink/wk). Estimates were adjusted for age, sex, educational level, smoking status, physical activity, and body mass index.

In addition, a larger proportion of wine drinkers were of higher social class, as indicated by educational level (**Table 1**). Therefore, we carefully controlled for these two factors in all our analyses. However, no data on participants' dietary habits were available. Wine intake may be associated with consumption of a presumably healthy Mediterranean diet (31, 32). This diet includes fruits and vegetables, which were found to have a weak protective effect against coronary heart disease in 6 of 10 cohort studies (33). In a review, Block and colleagues (34) found a strong protective effect of intake of fruits and vegetables against cancer. To explain the effect of wine drinking observed in our study, this diet, apart from being closely associated with wine intake, would have to have had a strong effect on all-cause mortality. Most of the dietary studies that we cite controlled for alcohol intake but not specifically for wine intake; this implies that the effects of diet may be attributed to confounding by an effect of wine. Several of these factors, which we controlled for in this study, may be associated with dietary habits. This is especially likely for educational level (32), a factor that we found had only a small influence on the relation between wine intake and mortality.

An alternative explanation for our findings may be a confounding effect of drinking pattern. A study from Australia suggested that only persons who had a small but regular alcohol intake were at lower risk for major coronary events, whereas those who had infrequent intake experienced no beneficial effect (35). In our study, wine drinkers may have had a small but regular intake compared with beer drinkers, whose drinking patterns may more closely resemble binging; such a difference in drinking pattern could explain our findings. However, in the cohort from the Copenhagen Male Study, only minor differences were observed in drinking patterns among wine, beer, and spirits drinkers. In this cohort, it seemed that beer drinkers had more regular drinking patterns than did wine and spirits drinkers. This finding is in agreement with the results of a recent large cross-sectional study from Denmark (36). Therefore, drinking pattern is not a strong confounder of our results.

The higher mortality among non–wine drinkers compared with light drinkers may be due to development of illnesses that led them to stop drinking. On the other hand, large cohort studies of the relation between total alcohol intake and cause-specific mortality have found that higher mortality among nondrinkers is attributable to coronary heart disease only, which may contradict this sugges-

tion. Furthermore, it seems unlikely that differences in presence of disease at baseline would be responsible for the differences between wine drinkers and non–wine drinkers in a given category of alcohol intake.

Is it alcohol or another substance, or alcohol and another substance, that in low doses produces a beneficial effect on all-cause mortality? A recent review by Rimm and colleagues (37) showed that the J-shaped relation between alcohol intake and coronary heart disease mortality persisted in populations with very different drinking patterns, such as wine drinkers in Italy and beer drinkers in Hawaii. Therefore, the beneficial effect, especially the lower risk for coronary heart disease among drinkers of small doses of ethanol, is a consistent finding.

To determine whether a small dose of alcohol together with another substance is associated with lower mortality, it is necessary to study populations with substantial intake of all three types of beverages in homogenous settings and with homogenous drinking patterns. The few studies that have investigated mortality in populations with mixed drinking patterns have all suggested an additional beneficial effect of wine compared with other beverages (19, 38, 39). However, several studies had methodologic limitations. The sample in Rosenberg and associates' case–control study was small (39). The study by Klatsky and coworkers (38) assessed mortality only among persons who had a clear preference for different types of alcoholic beverages and had no well-defined reference group. The results of the Copenhagen City Heart Study (19) were questionable because of the choice of reference group and because the relative risks in the upper end of the range of moderate alcohol intake were unreliable (40). In our study, which included three times as many deaths as all previous studies combined (37), we assessed mortality among persons with different levels of wine intake as well as different levels of alcohol intake, from nondrinkers to heavy drinkers.

The finding of a J-shaped relation between alcohol intake and mortality at all levels of wine intake agrees with the conclusions of Rimm and associates (37). It is also in agreement with the studies of the relation between beer, spirits, and mortality (4, 13). Furthermore, this finding agrees with study results on the effect of rice wine (which is considered a source of ethanol but not of other components present in grape wine) and mortality (6).

The two risk functions for drinkers for whom wine made up 1% to 30% of their total alcohol intake and those for whom wine made up more than 30% of their total alcohol intake did not differ significantly. This finding indicates the absence of a detectable dose-dependent effect of wine on all-cause mortality. Thus, there may be an unrecognized lifestyle factor strongly related to mortality, other than those already controlled for, that distinguishes wine drinkers from non–wine drinkers. Another speculative explanation is that a threshold effect may be associated with wine drinking at a low intake. Our data do not allow us to conduct valid dose-dependent analysis in this lower range of wine drinking, but a mean wine intake of 22% in the lowest category of total alcohol intake suggests that wine intake in that group in our study was not negligible (**Table 1**).

Whereas intake of beer and spirits seemed to be associated with a dose-dependent increase in risk for death from cancer, the increase in this risk among wine drinkers began at a higher intake and became significant only among heavy drinkers (**Figure 2**, *bottom*). This finding is supported by those of Jang and colleagues (42), who noted that resveratrol from grapes inhibits initiation, promotion, and progression of cancer. It is further supported by the results of our recent study of the relation between beer, wine, and spirits and cancer of the upper digestive tract (41), although these cancers are rare.

Table 3. **Distribution of Participants in the Copenhagen Male Study (n = 3244) according to Alcohol Intake on Weekdays and Weekends**

Alcohol Intake*	Participants Who Drank Alcoholic Beverages	
	Weekdays	Weekend
	n (%)	
Beer		
0 drinks/d	1653 (51)	943 (29)
1–2 drinks/d	1258 (39)	1779 (55)
3–5 drinks/d	288 (9)	424 (13)
≥6 drinks/d	45 (1)	98 (3)
Wine		
0 drinks/d	2632 (81)	1505 (46)
1–2 drinks/d	518 (16)	1360 (42)
3–5 drinks/d	88 (3)	338 (10)
≥6 drinks/d	6 (0.1)	41 (0.1)
Spirits		
0 drinks/d	2715 (84)	1555 (48)
1–2 drinks/d	486 (15)	1468 (45)
3–5 drinks/d	43 (0.1)	207 (6)
≥6 drinks/d	0	14 (0.4)

* Measured by day rather than by week to highlight the differences between alcohol consumption on weekdays and weekends.

Our finding that risk for death is significantly lower among drinkers of wine than among persons who do not drink wine, independent of level of alcohol intake, suggests that wine may contain one or several substances that add to the beneficial effect of intake of a small amount of ethanol.

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References

1. **Fuchs CS, Stampfer MJ, Colditz GA, Giovannucci EL, Manson JE, Kawachi I, et al.** Alcohol consumption and mortality among women. N Engl J Med. 1995;332:1245-50.
2. **Doll R, Peto R, Hall E, Wheatley K, Gray R.** Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. BMJ. 1994;309:911-8.
3. **Grønbæk M, Deis A, Sørensen TI, Becker U, Borch-Johnsen K, Müller P, et al.** Influence of sex, age, body mass index, and smoking on alcohol and mortality. BMJ. 1994;308:302-6.
4. **Farchi G, Fidanza F, Mariotti S, Menotti A.** Alcohol and mortality in the Italian rural cohorts of the Seven Countries Study. Int J Epidemiol. 1992;21:74-81.
5. **Klatsky AL, Armstrong MA, Friedman GD.** Alcohol and mortality. Ann Intern Med. 1992;117:646-54.
6. **Yuan JM, Ross RK, Gao YT, Henderson BE, Yu MC.** Follow up study of moderate alcohol intake and mortality among middle aged men in Shanghai, China. BMJ. 1997;314:18-23
7. **St. Leger AS, Cochrane AL, Moore F.** Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine. Lancet. 1979;1:1017-20.
8. **Criqui MH, Rigel BL.** Does diet or alcohol explain the French paradox? Lancet. 1994;344:1719-23.
9. **Renaud S, de Lorgeril M.** Wine, alcohol, platelets, and the French paradox for coronary heart disease. Lancet. 1992;339:1523-6.
10. **Hertog MG, Kromhout D, Aravanis C, Blackburn H, Buzina R, Fidanza F, et al.** Flavonoid intake and long-term risk of coronary heart disease and cancer in the Seven Countries Study. Arch Intern Med. 1995; 155:381-6.
11. **Ruf JC, Berger JL, Renaud S.** Platelet rebound effect of alcohol withdrawal and wine drinking in rats. Relation to tannins and lipid peroxidation. Arterioscler Thromb Vasc Biol. 1995;15:140-4.
12. **Frankel EN, Kanner J, German JB, Parks E, Kinsella JE.** Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. Lancet. 1993;341:454-7.
13. **Keil U, Chambless LE, Döring A, Filipiak B, Stieber J.** The relation of alcohol intake to coronary heart disease and all-cause mortality in a beer-drinking population. Epidemiology. 1997;8:150-6.
14. **Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, et al.** Prospective study of alcohol consumption and risk of coronary disease in men. Lancet. 1991;338:464-8.
15. **Stampfer MJ, Golditz GA, Willett WC, Speizer FE, Hennekens CH.** A prospective study of moderate alcohol consumption and the risk of coronary disease and stroke in women. N Engl J Med. 1988;319:267-73.
16. **Appleyard M, Hansen AT, Schnohr P, Jensen G, Nyboe J.** Østerbroundersøgelsen. The Copenhagen City Heart Study. A book of tables with data from the first examination (1976-78) and a five year follow-up (1981-83). The Copenhagen City Heart Study Group. Scand J Soc Med Suppl. 1989;41:1-160.
17. **Hein HO, Sørensen H, Suadicani P, Gyntelberg F.** Alcohol consumption, Lewis phenotypes, and risk of ischaemic heart disease. Lancet. 1993; 341:392-6.
18. **Heitmann BL.** The influence of fatness, weight change, slimming history and other lifestyle variables on diet reporting in Danish men and women aged 35-65 years. Int J Obes Relat Metab Disord. 1993;17:329-36.

19. **Grønbæk M, Deis A, Sørensen TI, Becker U, Schnohr P, Jensen G.** Mortality associated with moderate intake of wine, beer, or spirits. BMJ. 1995;310:1165-9.
20. **Mabeck CE, Wichmann B.** [Causes of death and death certificates. An evaluation of the diagnosis in 373 death certificates]. Ugeskr Laeger. 1980; 142:257-61.
21. **McCullagh P, Nelder JA.** Generalized Linear Models. New York: Chapman and Hall; 1983.
22. SAS/STAT software: the GENMOD procedure, release 6.09. Cary, NC: SAS Institute; 1993.
23. **Suh I, Shaten J, Cutler JA, Kuller LH.** Alcohol use and mortality from coronary heart disease: the role of high-density lipoprotein cholesterol. The Multiple Risk Factor Intervention Trial Research Group. Ann Intern Med. 1992;116:881-7.
24. **Diehl AK, Fuller JH, Mattock MB, Salter AM, el-Gohari R, Keen H.** The relationship of high density lipoprotein subfractions to alcohol consumption, other lifestyle factors, and coronary heart disease. Atherosclerosis. 1988;69:145-53.
25. **Renaud SC, Beswick AD, Fehily AM, Sharp DS, Elwood PC.** Alcohol and platelet aggregation: the Caerphilly Prospective Heart Disease Study. Am J Clin Nutr. 1992;55:1012-7.
26. **Poikolainen K.** Alcohol and mortality: a review. J Clin Epidemiol. 1995;48:455-65.
27. **Kittner SJ, Garcia-Palmieri MR, Costas R Jr, Cruz-Vidal M, Abbott RD, Havlik RJ.** Alcohol and coronary heart disease in Puerto Rico. Am J Epidemiol. 1983;117:538-50.
28. **Rimm EB, Chan J, Stampfer MJ, Colditz GA, Willett W.** Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men. BMJ. 1995;310:555-9.
29. **Yano K, Rhoads GG, Kagan A.** Coffee, alcohol and risk of coronary heart disease among Japanese men living in Hawaii. N Engl J Med. 1977; 297:405-9.
30. **Hertog MG, Feskens EJ, Hollman PC, Katan MK, Kromhout D.** Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. Lancet. 1993;342:1007-11.
31. **Rimm EB, Ellison RC.** Alcohol in the Mediterranean diet. Am J Clin Nutr. 1995;61:1378S-1382S.
32. **Tjønneland A, Grønbæk M, Stripp C, Overvad K.** Wine intake and diet in a random sample of 48763 Danish men and women. Am J Clin Nutr. 1999;69:49-54.
33. **Ness AR, Powles JW.** Fruit and vegetables, and cardiovascular disease: a review. Int J Epidemiol. 1997;26:1-13.
34. **Block G, Patterson B, Subar A.** Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence. Nutr Cancer. 1992;18:1-29.
35. **McElduff P, Dobson AJ.** How much alcohol and how often? Population based case-control study of alcohol consumption and risk of a major coronary event. BMJ. 1997;314:1159-64.
36. **Grønbæk M, Tjønneland A, Johansen D, Stripp C, Overvad K.** Type of alcohol and drinking pattern in 56,970 Danish men and women. Eur J Clin Nutr. 2000;54:174-6.
37. **Rimm EB, Klatsky A, Grobbee D, Stampfer MJ.** Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine, or spirits? BMJ. 1996;312:731-6.
38. **Klatsky AL, Armstrong MA.** Alcoholic beverage choice and risk of coronary artery disease mortality: do red wine drinkers fare best? Am J Cardiol. 1993;71:467-9.
39. **Rosenberg L, Slone D, Shapiro S, Kaufman DW, Miettinen OS, Stolley PD.** Alcoholic beverages and myocardial infarction in young women. Am J Public Health. 1981;71:82-5.
40. **Wilson V, Gregson D, Smyth E.** Mortality associated with wines, beers, and spirits. Inappropriate groups were used to calculate relative risk [Letter]. BMJ. 1995;311:1166.
41. **Jang M, Cai L, Udeani GO, Slowing KV, Thomas CF, Beecher CW, et al.** Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. Science. 1997;275:218-20.