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Light-to-Moderate Alcohol Consumption and Mortality in the Physicians' Health Study Enrollment Cohort

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OBJECTIVES This study examined the relationship between light-to-moderate alcohol consumption and cause-specific mortality.

BACKGROUND Previous studies suggest a J-shaped relation between alcohol and total mortality in men. A decrease in cardiovascular disease (CVD) mortality without a significant increase in other causes of mortality may explain the overall risk reduction at light-to-moderate levels.

METHODS We conducted a prospective cohort study of 89,299 U.S. men from the Physicians' Health Study enrollment cohort who were 40 to 84 years old in 1982 and free of known myocardial infarction, stroke, cancer or liver disease at baseline. Usual alcohol consumption was estimated by a limited food frequency questionnaire.

RESULTS There were 3,216 deaths over 5.5 years of follow-up. We observed a U-shaped relationship between alcohol consumption and total mortality. Compared with rarely/never drinkers, consumers of 1, 2 to 4 and 5 to 6 drinks per week and 1 drink per day had significant reductions in risk of death (multivariate relative risks [RRs] of 0.74, 0.77, 0.78 and 0.82, respectively) with no overall benefit or harm detected at the ≥2 drinks per day level (RR = 0.95; 95% confidence interval (CI), 0.79 to 1.14). The relationship with CVD mortality was inverse or L-shaped with apparent risk reductions even in the highest category of ≥2 drinks per day (RR = 0.76; 95% CI, 0.57 to 1.01). We found no clear harm or benefit for total or common site-specific cancers. For remaining other cancers, there was a nonsignificant 28% increased risk for those consuming ≥2 drinks per day.

CONCLUSIONS These data support a U-shaped relation between alcohol and total mortality among light-to-moderate drinking men. The U-shaped curve may reflect an inverse association for CVD mortality, no association for common site-specific cancers and a possible positive association for less common cancers. (J Am Coll Cardiol 2000;35:96–105) © 1999 by the American College of Cardiology

Previous research suggests a J-shaped relationship between the level of alcohol consumption and total mortality in men. There is little debate over the causal relationship between heavy alcohol intake and increased risk of mortality (1–5), particularly deaths from liver disease, cancers of the oropharynx and esophagus (6–12) and noncoronary cardiovascular disease (CVD) such as cardiomyopathy and hemorrhagic stroke (3,4,13,14). The reduction in total mortality at light-to-moderate levels appears to be due to a reduction in CVD, without significant increases in other causes of mortality (13–31). This reduction is primarily manifested through a reduction in death from coronary heart disease (CHD), a relationship which appears to be inverse or L-shaped (32).

While there is general agreement that the mortality curve is J-shaped, there is still some disagreement over its precise nadir. Together, the uncertainty of the nadir, the known risks from heavy alcohol consumption and a new public interest in the potential benefits of light-to-moderate consumption of alcohol make it even more important to know more accurately the range of light-to-moderate alcohol consumption where the benefits outweigh the risks.

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Abbreviations and Acronyms

CHD = coronary heart disease
CI = confidence interval
CVD = cardiovascular disease
MI = myocardial infarction
RR = relative risk

We therefore examined, prospectively, the relationship between light-to-moderate alcohol consumption and mortality in the Physicians' Health Study enrollment cohort of 89,299 apparently healthy men. We also examined the relationship of alcohol consumption and specific causes of death, including cardiovascular diseases and various cancers, in order to have a better understanding of the exact nature of risks and benefits associated with light-to-moderate alcohol consumption.

METHODS

Study population. The Physicians' Health Study is a randomized, double-blind, placebo-controlled trial testing two primary-prevention hypotheses: 1) whether 325 mg of aspirin taken every other day reduces mortality from CVD, and 2) whether 50 mg of beta carotene taken on alternate days decreases the incidence of cancer. Potentially eligible participants in the Physicians' Health Study were male physicians residing in the U.S. In 1982 and 1983, letters of invitation, informed consent forms and baseline questionnaires were mailed to the 261,248 eligible men who were listed on an American Medical Association mailing tape. By December 31, 1983, 112,528 physicians had responded to the initial enrollment questionnaire. Most of these individuals provided data on alcohol consumption, as well as other baseline characteristics prior to December 31, 1983. These analyses were confined to the 89,299 respondents age 40 to 84 years who provided alcohol data and had no prior history of myocardial infarction (MI), stroke, cancer or liver disease at baseline, including 21,876 randomized participants and 67,423 nonrandomized respondents.

Data collection. On the baseline questionnaire, physicians reported their age and cardiovascular risk factors, including cigarette smoking status (never, past, current—including number of cigarettes smoked daily), use of antihypertensive medication, systolic and diastolic blood pressure, history of cholesterol lowering medications, cholesterol level, frequency of vigorous exercise and personal history of angina pectoris or diabetes mellitus. Body-mass index (kg/m^2) was calculated using self-reported weight and height.

Study participants also gave information regarding usual alcohol intake in the previous year as part of a brief dietary questionnaire. Exposure was categorized by responses to the enrollment question, "How often do you usually consume alcoholic beverages (beer, wine, liquor)?" Response options were as follows: rarely/never, 1 to 3 times per month, 1 time per week, 2 to 4 times per week, 5 to 6 times per week, daily and $\geq$2 per day.

End points. In 1990, death certificates were obtained for the respondents who died before the end of 1989, using the National Death Index. The deaths were classified by trained nosologists using the first revision of the Ninth International Classification of Diseases in conjunction with the Automated Classification of Medical Entities Decision Tables to manually select underlying cause of death. Cause was assigned for the 3,216 deaths that accrued over the six year period among the 89,299 respondents used in this analysis. End points for this analysis included total death and death due to CVD, MI, stroke, other cardiovascular diseases, total cancer, colorectal cancer, prostate cancer, lung cancer, pancreatic cancer, hematologic (lymphoma/leukemia) cancer, other cancers, other (non-CVD, non-cancer) causes, liver disease, suicide and violence/accident. Sudden deaths were classified in the category of other CVD death.

Statistical analysis. We computed means or proportions of baseline risk factors for the reference group (rare and nondrinkers) and the six reported levels of drinking. Proportional hazards models were used to compute age-adjusted and multivariate-adjusted relative risks (RRs) for each intake category, as compared with the reference category, for total mortality as well as for each specific cause of death. The multivariate analyses were adjusted for age, cigarette smoking (never, past, current), reported diabetes, reported vigorous exercise and body-mass index (estimated by reported weight and height). Models that included reported history of angina and transient ischemic attacks to the multivariate models did not materially alter the results. We excluded hypertension (reported treatment or reported systolic blood pressure) and reported treatment for hypercholesterolemia because of the concern that they may be in the causal pathway. However, in alternative analyses we included these two risk factors, and results were not materially different from those observed for the full multivariate models. We tested for linear trend in RR across the seven alcohol consumption categories using an ordinal alcohol variable. We also tested for the presence of a nonlinear association by comparing log likelihoods of these linear models with log likelihoods from models with categorized alcohol consumption. For analyses of cause-specific deaths, deaths other than the cause-specific death of interest were censored at the time of death.

RESULTS

During a mean follow-up period of 5.46 years, 3,216 (3.6%) of the 89,299 male physicians died. Table 1 displays major causes of deaths as a percentage of the total deaths. Of the 3,216 total deaths, 1,450 (45.1%) died of CVD, including 514 (16.0%) from MI and 150 (4.7%) from stroke. All cancers accounted for 944 (29.4%) of the deaths, including

Table 1. Cause of Death Among the 89,299 Eligible Participants

Cause of Death	Number	% of Total Deaths
CVD	1,450	45.1
MI	514	16.0
Stroke	150	4.7
Other CVD	786	24.4
Cancer	944	29.4
Lung	207	6.4
Colon	112	3.5
Prostate	78	2.4
Pancreatic	85	2.6
Lymphoma/leukemia*	137	4.3
Other cancer†	325	10.1
Other	822	25.6
Liver	35	1.1
Violent, accident	189	5.9
Pulmonary	174	5.4
Suicide	122	3.8
Renal/genitourinary	36	1.1
Unknown	35	1.1
Miscellaneous	231	7.2
Total	3,216	100

*Lymphoma, 85 (2.6%); leukemia, 52 (1.6%); †other causes of cancer include: brain, 57 (1.8%); stomach, 33 (1.0%); bladder, 14 (0.4%); and melanoma, 18 (0.6%).

207 (6.4%) from lung cancer, 112 (3.5%) from colon cancer and 78 (2.4%) from cancer of the prostate. There were 822 (25.6%) other deaths (non-CVD, non-cancer) which included 35 (1.1%) deaths from liver disease; 311 (9.7%) from violent, accidental, or suicidal death; 441 (13.7%) from miscellaneous causes; and 35 (1.1%) from unknown causes.

Table 2 shows the baseline characteristics according to level of alcohol intake. Overall, it was a group of light-to-moderate alcohol consumers with 97% reported drinking <2 drinks per day. Over 28% drank 1 to 3 drinks per month or less, with 17% drinking rarely or never. Only 3% reported drinking ≥2 drinks per day (the highest drinking category). Compared with the reference group, those that consumed ≥1 drink per day tended to be older, smoke more, have higher total cholesterol and have an increased prevalence of hypertension. Nondrinkers had higher rates of diabetes.

Total mortality. When compared with the reference group of nondrinkers, we observed a statistically significant decrease in total mortality among light-to-moderate drinkers of <2 drinks per day after adjustment for age (Table 3). Results were not materially altered after multivariate adjustment. Figure 1A shows a U-shaped relationship between alcohol consumption and total mortality after multivariate adjustment (p for nonlinear association <0.001). The relationship between alcohol and cardiovascular, cancer and other deaths are shown in Figure 1B, 1C and 1D, respectively. There was no overall benefit or harm detected among those who consumed ≥2 drinks per day (RR = 0.95; 95% confidence interval [CI], 0.79 to 1.14).

Cardiovascular disease death. For the 1,450 deaths due to CVD, the relationship between light-to-moderate alcohol consumption and CVD mortality appeared to be inverse or L-shaped (Fig. 1B) with trends toward reduced risk apparent at 1 drink per week. As shown in Table 4, we observed

Table 2. Baseline Characteristics According to Level of Alcohol Consumption

	Number of Drinks						
	Rarely/Never	**1–3/Month**	**1/Week**	**2–4/Week**	**5–6/Week**	**1/Day**	**≥2/Day**
Number (%)	15,166 (17.0)	10,308 (11.5)	12,506 (14.0)	18,555 (20.8)	9,975 (11.2)	19,963 (22.4)	2,826 (3.2)
Age	56.0 ± 10.9*	53.2 ± 10.3	53.1 ± 10.1	53.2 ± 9.7	53.9 ± 9.6	57.6 ± 10.4	57.8 ± 10.2
Smoking (%)							
Never	61.4	53.4	52.0	46.5	41.1	33.6	26.1
Past	28.7	34.8	37.6	42.9	47.2	50.7	51.1
Current	9.9	11.8	10.4	10.7	11.8	15.7	22.8
Cholesterol							
History† (%)	7.7	8.5	8.0	7.7	7.9	9.1	11.9
mg/dl‡	207 ± 48	211 ± 47	211 ± 46	211 ± 45	212 ± 45	215 ± 47	219 ± 49
Hypertension (%)§	18.1	16.6	15.2	15.8	16.7	22.3	27.1
Body mass index							
kg/m^2	25.0 ± 3.4	25.1 ± 3.4	25.1 ± 3.2	25.0 ± 3.0	24.8 ± 2.9	24.8 ± 2.9	25.2 ± 3.2
>26.5¶ (%)	26.3	26.8	27.2	24.5	22.7	22.3	29.3
Exercise ≥1/week (%)	64.7	63.2	69.9	74.2	75.3	72.5	63.3
Angina (%)	3.5	2.8	2.8	2.6	2.5	3.6	3.6
Diabetes (%)	5.4	3.9	2.8	2.3	2.2	2.7	2.8

*For continuous variables means ± standard deviation are presented. †History of treatment for hypercholesterolemia (n = 76,846). ‡Reported plasma level (n = 33,238). §Self-reported systolic blood pressure ≥160 mm Hg, diastolic blood pressure ≥95 mm Hg or reported treatment for hypertension. ¶Highest quartile.

Table 3. RR of Total Mortality According to Level of Alcohol Consumption

	Number of Drinks						
	Rarely/Never	**1–3/Month**	**1/Week**	**2–4/Week**	**5–6/Week**	**1/Day**	**≥2/Day**
Age adjusted cases (n = 3216)	723	338	335	477	284	889	170
RR (95% CI)*	1.00 (Ref)	0.88 (0.78–1.01)	0.74 (0.65–0.84)	0.73 (0.65–0.82)	0.76 (0.67–0.88)	0.85 (0.77–0.94)	1.13 (0.96–1.34)
RF† adjusted cases (n = 2912)							
RR (95% CI)*	1.00 (Ref)	0.86 (0.75–0.99)	0.74 (0.65–0.85)	0.77 (0.68–0.87)	0.78 (0.67–0.90)	0.82 (0.74–0.92)	0.95 (0.79–1.14)

*p for nonlinear association < 0.05. †Adjusted for age and other coronary risk factors, including smoking, diabetes, exercise and body mass index.
CI = confidence interval; RF = risk factor; RR = relative risk.

a borderline or significant 19% to 26% reduction in cardiovascular death after adjustment for available risk factors among drinkers who consumed ≥1 drink per week (p for linear trend <0.001). Of the CVD deaths, 514 were attributed to MI. As for CVD deaths, the relationship between alcohol consumption and death from MI was L-shaped (Table 4) with significant reductions in risk of 32% to 47% among those who consumed ≥1 drink per week or more (p for linear trend <0.001). For stroke, we observed no significant increase or decrease in any category; however, there was a nonsignificant suggestion of reduced risk of fatal stroke among the light drinkers—monthly to 2 to 4 drinks per week (Table 4). Other causes of CVD death accounted for 786 of the total deaths. There was a nonsignificant trend across categories toward lower risk of other CVD death after multivariate adjustment (p = 0.12).

Cancer deaths. In total, 944 deaths due to various cancers accrued. The age-adjusted RR for total cancer death (Table 5) was significantly increased (RR = 1.53; 95% CI, 1.15 to 2.05) at the highest drinking level; however, a large proportion of the excess risk appeared to be due to confounding by smoking. When the relationship was adjusted for available potential confounders, excluding smoking, the RR was not materially altered (RR = 1.54; 95% CI, 1.14 to 2.08), but after further adjustment for smoking the RR was attenuated and not significant (RR = 1.18; 95% CI, 0.87 to 1.62). After multivariate adjustment, no significant increases or decreases in risk of lung, colon, prostate, pancreatic or hematologic (lymphoma or leukemia) were apparent in any drinking category. We observed an increase in the age-adjusted risk of lung cancer among those who consumed ≥2 drinks per day (RR = 2.53; 95% CI, 1.47 to 4.35) which was explained largely by smoking status (multivariate RR = 1.30; 95% CI, 0.72 to 2.34). Lung and prostate cancer tended to be lower among lighter drinkers and pancreatic cancer rates tended to be higher among those in the ≥2 drinks per day category, but none of these associations was statistically significant. There was no increased risk for the other cancers at intake <14 drinks per week after multivariate adjustment (Table 5). For the remaining group of less common cancers, an increased risk was suggested (RR = 1.28; 95% CI, 0.74 to 2.21) among those who drank ≥2 drinks per day. The test for linear trend, however, was not significant (p for trend = 0.92). This category included stomach, bladder, brain, esophageal and other less common cancers.

All other deaths. The remaining causes of mortality accounted for 822 deaths. There were significantly decreased risks of other (non-cancer and non-CVD) deaths among those who consumed <7 drinks per week (Table 6) (p for nonlinear association = 0.002). These deaths included violent/accidental, suicide, pulmonary, renal/genitourinary and gastrointestinal hemorrhage deaths. Alcohol intake was not significantly associated with the 189 violent or accidental deaths or with the 122 suicides in the age-adjusted or

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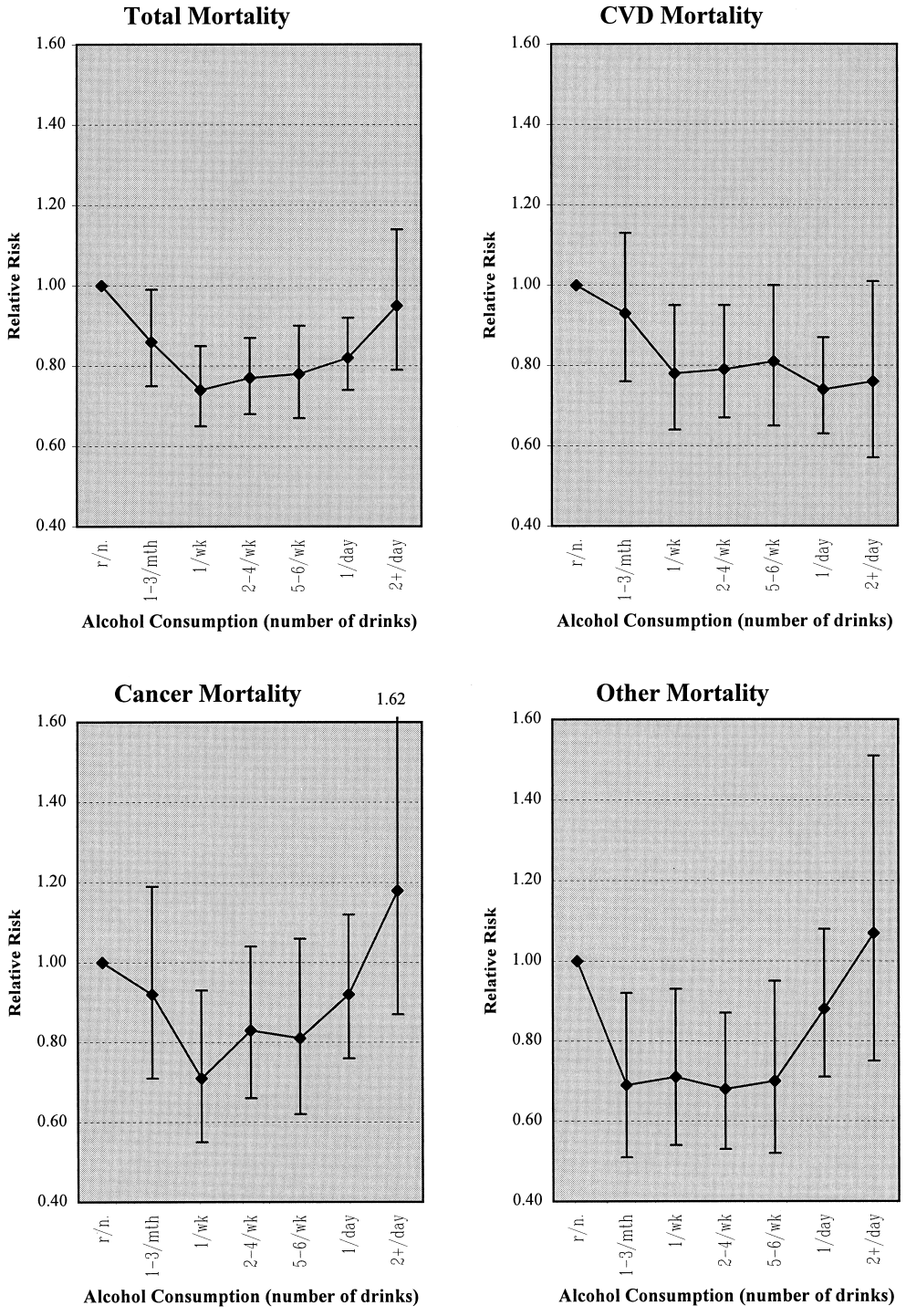

Figure 1. **A.** Relative risk of total mortality by alcohol consumption category after multivariate adjustment. **B.** Relative risk of CVD mortality by alcohol consumption category after multivariate adjustment. **C.** Relative risk of cancer mortality by alcohol consumption category after multivariate adjustment. **D.** Relative risk of other mortality by alcohol consumption category after multivariate adjustment.

multivariate models. While rates of violent death were slightly reduced and rates of suicide were slightly increased in the highest drinking category, these estimates were based on only seven violent deaths and suicides; thus confidence bounds were wide. Alcohol intake of 1 to 6 drinks per week had a nonsignificant inverse association with pulmonary death. Alcohol was not significantly associated with the 36 deaths attributed to renal/genitourinary causes or the 30

Table 4. RR (95% CI) of CVD Mortality According to Level of Alcohol Consumption

	Number of Drinks						
	Rarely/Never	**1–3/Month**	**1/Week**	**2–4/Week**	**5–6/Week**	**1/Day**	**≥2/Day**
Total CVD							
Age adjusted (n = 1450)*	1.00 (Ref)	0.95 (0.79–1.14)	0.78 (0.65–0.95)	0.75 (0.64–0.89)	0.76 (0.62–0.93)	0.77 (0.66–0.89)	0.92 (0.71–1.20)
RF† adjusted (n = 1328)*	1.00 (Ref)	0.93 (0.76–1.13)	0.78 (0.64–0.95)	0.79 (0.67–0.95)	0.81 (0.65–1.00)	0.74 (0.63–0.87)	0.76 (0.57–1.01)
MI							
Age adjusted (n = 514)*	1.00 (Ref)	0.82 (0.61–1.11)	0.68 (0.50–0.91)	0.62 (0.47–0.82)	0.57 (0.40–0.80)	0.50 (0.39–0.65)	0.70 (0.44–1.10)
RF† adjusted (n = 480)*	1.00 (Ref)	0.86 (0.63–1.16)	0.64 (0.47–0.89)	0.68 (0.51–0.91)	0.61 (0.42–0.88)	0.53 (0.41–0.69)	0.60 (0.36–0.98)
Stroke							
Age adjusted (n = 150)	1.00 (Ref)	1.09 (0.59–1.99)	0.70 (0.36–1.36)	0.62 (0.34–1.16)	1.02 (0.54–1.93)	1.30 (0.84–2.01)	0.96 (0.40–2.31)
RF† adjusted (n = 136)	1.00 (Ref)	0.95 (0.49–1.83)	0.62 (0.30–1.28)	0.59 (0.30–1.15)	1.10 (0.58–2.11)	1.21 (0.76–1.94)	0.84 (0.34–2.04)
Other CVD							
Age adjusted (n = 786)	1.00 (Ref)	1.03 (0.79–1.34)	0.89 (0.69–1.16)	0.89 (0.71–1.13)	0.89 (0.67–1.17)	0.91 (0.74–1.11)	1.12 (0.79–1.60)
RF† adjusted (n = 712)	1.00 (Ref)	0.99 (0.75–1.31)	0.93 (0.71–1.22)	0.94 (0.73–1.20)	0.94 (0.70–1.26)	0.84 (0.67–1.05)	0.89 (0.61–1.30)

*p for linear trend < 0.05. †Adjusted for age and other coronary risk factors, including smoking, diabetes, exercise and body mass index.
RF = risk factor.

deaths attributed to liver disease. However, there was a nonsignificant trend toward increased risk at both the 1 and ≥2 drinks per day categories.

DISCUSSION

In this prospective cohort study among 89,299 U.S. male physicians there was a U-shaped relationship between light-to-moderate alcohol intake and risk of total mortality with a decreased risk of total mortality of up to 26% among those who consumed 1 to <14 drinks per week. There was no significant overall increased risk of death among those who consumed ≥2 drinks per day in this cohort of moderate drinkers. The U-shaped mortality curve observed in this study among light-to-moderate drinkers is consistent with the previous studies (1–5, 31).

Alcohol and total mortality. The U-shaped relationship between alcohol and total mortality is the result of the summation of the disease-specific curves. The nadir of the curves results from lower risk of CVD death (and perhaps non-cancer and non-CVD causes of death) among lighter drinkers without any increased risk in cancer. At ≥2 drinks per day, the CVD benefits may begin to be offset by increasing risk of some of the less common cancers. The individual CVD, cancer and other death curves derived from this cohort may help predict the overall mortality curve for a given population by weighing each curve according to the cause specific mortality distribution and then combining the weighted curves into a single mortality curve.

The precise location of the nadir varies from study to study. Our results showed similar reductions in mortality between 1 and 7 drinks per week with a slightly greater reduction in all cause mortality at 1 drink per week. This is consistent with two recent studies, one in Danish adults and the other in British male physicians with nadirs between 1 to 6 drinks per week and 5 to 9 drinks per week, respectively (32, 33). However, the drinking level associated with the lowest total mortality varies widely from as low as 1 drink per week to 5 drinks per day (34, 35). The exact location of the nadir may vary depending on the distribution of cause-specific mortality or differing drinking patterns in each study population, as well as methodologic differences between studies.

Alcohol and cause-specific mortality. In this study, the risk reduction in CVD mortality was primarily driven by a significant 32% to 47% reduction in MI that persisted in the highest drinking category. These findings are consistent with a recent meta-analysis suggesting an L-shaped effect of moderate alcohol on risk of nonfatal MI (36). In that study the reduction in risk began at 1/2 drink per day and reached maximal benefit at 1 drink per day. There was a nonsignificant suggestion of lower stroke risk in the present analysis among the light drinkers—between 1 to 4 drinks per week. Prior reports in both men and women have suggested that light alcohol consumption may decrease the risk of stroke,

Table 5. RR (95% CI) of Cancer Mortality According to Level of Alcohol Consumption

	Number of Drinks						
	Rarely/Never	1–3/Month	1/Week	2–4/Week	5–6/Week	1/Day	≥2/Day
Total Cancer							
Age adjusted (n = 944)*	1.00 (Ref)	0.91 (0.71–1.17)	0.77 (0.60–0.98)	0.83 (0.67–1.03)	0.83 (0.64–1.08)	1.00 (0.83–1.20)	1.53 (1.15–2.05)
RF† adjusted (n = 864)*	1.00 (Ref)	0.92 (0.72–1.19)	0.71 (0.55–0.93)	0.83 (0.66–1.04)	0.81 (0.62–1.06)	0.92 (0.76–1.12)	1.18 (0.87–1.62)
Lung Cancer							
Age adjusted (n = 207)*	1.00 (Ref)	0.55 (0.28–1.08)	0.68 (0.38–1.21)	1.02 (0.64–1.62)	1.03 (0.60–1.77)	1.22 (0.82–1.81)	2.53 (1.47–4.35)
RF† adjusted (n = 181)	1.00 (Ref)	0.50 (0.25–1.01)	0.63 (0.34–1.16)	0.97 (0.60–1.57)	0.85 (0.48–1.52)	0.89 (0.58–1.36)	1.30 (0.72–2.34)
Colon Cancer							
Age adjusted (n = 112)	1.00 (Ref)	1.17 (0.57–2.42)	0.82 (0.38–1.76)	1.12 (0.60–2.11)	0.79 (0.35–1.82)	1.37 (0.79–2.38)	1.26 (0.47–3.37)
RF† adjusted (n = 101)	1.00 (Ref)	1.28 (0.61–2.69)	0.88 (0.40–1.93)	1.08 (0.55–2.11)	0.84 (0.36–1.97)	1.21 (0.66–2.20)	1.01 (0.34–3.02)
Prostate Cancer							
Age adjusted (n = 78)*	1.00 (Ref)	0.56 (0.21–1.50)	0.10 (0.01–0.71)	0.93 (0.46–1.89)	0.70 (0.28–1.77)	1.19 (0.67–2.13)	0.80 (0.24–2.71)
RF† adjusted (n = 74)*	1.00 (Ref)	0.56 (0.21–1.50)	0.09 (0.01–0.71)	0.86 (0.42–1.78)	0.69 (0.27–1.76)	1.01 (0.55–1.85)	0.69 (0.20–2.37)
Pancreatic Cancer							
Age adjusted (n = 85)	1.00 (Ref)	0.95 (0.46–1.97)	0.50 (0.21–1.19)	0.44 (0.20–0.97)	0.70 (0.31–1.58)	0.73 (0.40–1.32)	1.62 (0.69–3.81)
RF† adjusted (n = 78)	1.00 (Ref)	0.89 (0.40–1.97)	0.50 (0.20–1.25)	0.52 (0.23–1.15)	0.72 (0.30–1.72)	0.79 (0.42–1.49)	1.77 (0.73–4.29)
Hematologic Cancers‡							
Age adjusted (n = 137)	1.00 (Ref)	0.98 (0.54–1.81)	1.15 (0.66–2.00)	0.90 (0.53–1.53)	0.76 (0.39–1.49)	0.62 (0.37–1.05)	0.79 (0.31–2.04)
RF† adjusted (n = 124)	1.00 (Ref)	1.09 (0.59–2.04)	1.08 (0.60–1.96)	0.87 (0.49–1.53)	0.70 (0.33–1.45)	0.67 (0.38–1.15)	0.70 (0.24–2.02)
Other Cancers							
Age adjusted (n = 325)	1.00 (Ref)	1.08 (0.73–1.62)	0.88 (0.59–1.33)	0.72 (0.49–1.06)	0.84 (0.54–1.31)	0.97 (0.71–1.33)	1.56 (0.96–2.56)
RF† adjusted (n = 296)	1.00 (Ref)	1.10 (0.72–1.68)	0.78 (0.50–1.22)	0.75 (0.50–1.12)	0.88 (0.56–1.39)	0.98 (0.70–1.37)	1.28 (0.74–2.21)

*p for nonlinear association < 0.05. †Adjusted for age and other coronary risk factors, including smoking, diabetes, exercise and body mass index. ‡Hematologic includes both lymphoma and leukemia.
RF = risk factor.

Table 6. RR (95% CI) of Other Mortality According to Level of Alcohol Consumption

	Number of Drinks						
	Rarely/Never	1–3/Month	1/Week	2–4/Week	5–6/Week	1/Day	≥2/Day
Other Death*							
Age adjusted (n = 822)†	1.00 (Ref)	0.76 (0.58–0.98)	0.64 (0.50–0.83)	0.59 (0.46–0.74)	0.71 (0.55–0.93)	0.87 (0.72–1.05)	1.11 (0.80–1.53)
RF‡ adjusted (n = 720)†	1.00 (Ref)	0.69 (0.51–0.92)	0.71 (0.54–0.93)	0.68 (0.53–0.87)	0.70 (0.52–0.95)	0.88 (0.71–1.08)	1.07 (0.75–1.51)
Violent Death							
Age adjusted (n = 189)	1.00 (Ref)	0.94 (0.53–1.67)	1.15 (0.69–1.91)	0.94 (0.58–1.52)	0.95 (0.54–1.68)	1.12 (0.72–1.75)	1.10 (0.49–2.50)
RF‡ adjusted (n = 177)	1.00 (Ref)	0.88 (0.48–1.60)	1.08 (0.63–1.84)	0.93 (0.56–1.54)	0.95 (0.53–1.72)	1.11 (0.70–1.77)	1.06 (0.46–2.43)
Pulmonary Death							
Age adjusted (n = 174)	1.00 (Ref)	0.85 (0.49–1.47)	0.53 (0.28–0.98)	0.49 (0.28–0.86)	0.46 (0.22–0.94)	1.03 (0.70–1.51)	1.00 (0.49–2.05)
RF‡ adjusted (n = 144)	1.00 (Ref)	0.96 (0.52–1.78)	0.68 (0.35–1.32)	0.65 (0.35–1.20)	0.47 (0.21–1.07)	1.03 (0.66–1.61)	0.88 (0.40–1.93)
Suicide Death							
Age adjusted (n = 122)	1.00 (Ref)	0.99 (0.52–1.90)	0.60 (0.29–1.23)	0.58 (0.31–1.11)	1.41 (0.78–2.54)	0.92 (0.53–1.59)	1.57 (0.67–3.66)
RF‡ adjusted (n = 109)	1.00 (Ref)	0.80 (0.38–1.68)	0.68 (0.32–1.42)	0.63 (0.32–1.24)	1.39 (0.73–2.65)	0.97 (0.54–1.75)	1.58 (0.66–3.79)

*Includes death from liver disease. †p for nonlinear trend < 0.05. ‡Adjusted for age and other coronary risk factors, including smoking, diabetes, exercise and body mass index.
RF = risk factor.

but that at higher levels of consumption there may be an increased risk of stroke (23, 37–39). This apparent reduction at light drinking levels, if confirmed in other studies, may be explained by different effects of alcohol on ischemic and hemorrhagic strokes.

Among light-to-moderate drinkers, there was no clear association with total cancer mortality. None of the more common individual cancers among men—lung, colon, prostate, lymphoma or leukemia—was clearly associated with alcohol intake after controlling for potential confounders. These results support prior findings of little or no increased overall cancer risk among male, light-to-moderate drinkers (6). The apparent increase in age-adjusted lung cancer risk among those consuming ≥2 drinks per day appeared to be due entirely to confounding by cigarette smoking. There was a suggestion of decreased risk for prostate and lung cancer among lighter drinkers and increased risk of pancreatic cancer among those who drank ≥2 drinks per day, but this study was underpowered to draw any definitive conclusions. Only in the remainder of cause-specific cancer deaths—"other cancers"—was there a borderline nonsignificant increased risk of death among those drinking ≥2 drinks per day. This group includes less common malignancies including cancers of the stomach, oropharynx and esophagus which have previously been associated with alcohol use.

The explanation for the U-shaped relationship between drinking and all "other causes" (non-cancer, non-CVD) of death is not entirely clear. This category includes a wide variety of specific causes of death with potentially disparate associations with alcohol, and the small numbers of end points for many causes yielded imprecise estimates. Many of the deaths due to unknown or miscellaneous causes (n = 266) may have been due to ischemic heart disease. This misclassification could explain a portion of the risk reduction. Also, unmeasured variables may confound the relationship between alcohol and risk of "other causes" of death, biasing our risk estimates. It is also possible that comorbid CHD could lead to increased mortality due to other causes; thus reductions in CHD associated with alcohol intake could result in lower mortality from other causes. There was no clear association for traumatic (violent/accidental and suicide) deaths among light-to-moderate drinkers. While there is a clear association between heavy drinking and acute alcohol intoxication and traumatic death (40), light drinkers are not reported to be at increased risk of fatal injury (41–44). The increased risk of traumatic death associated with alcohol is reported to be predominantly among young men (45) with high peak blood alcohol levels (43). Given the age of our population and a cohort consisting almost entirely of light-to-moderate drinkers, we anticipated no increased risk of traumatic death and alcohol. Among other causes of death we found a suggestive inverse association between alcohol and pulmonary death at light-to-moderate levels of intake, but since this was not an a priori hypothesis it requires further exploration. Liver deaths, which were a

part of the other causes category, showed increased association with alcohol consumption at ≥1 drink per day though these estimates are based on only a few cases. The small numbers of deaths in this category possibly reflect the small number of heavy drinkers in this group of male physicians and the relative infrequency of deaths due to liver disease in the U.S. population. The limited number of renal or genitourinary deaths also hindered our ability to detect an association.

Possible limitations. Several potential limitations of this study are worth discussion. First, this study relied on self-reported data. If there were a systematic underestimation of alcohol consumption, this may artificially shift the reported associations towards lower drinking categories and lead to underestimation of the nadir of the alcohol-mortality relationship. However, studies, including those of health professionals, have found self-reporting to be reliable for general classification of drinking habits (46–48). Second, our study used a single measure of alcohol consumption at one point in time. Since intake may change over time, this could also lead to some misclassification; however, drinking patterns among middle-aged and older individuals tend to be stable over time (49). Third, our study requested information on average intake; thus, we were unable to explore relationships by drinking pattern. The risks and benefits may be quite different for the individual who has 1 drink per day with dinner and the person who has seven drinks on Friday night, despite the two individuals sharing the same average daily intake. Fourth, the questionnaire used did not allow us to identify heavy drinkers. The highest drinking category was ≥2 drinks per day. While we feel that the number of heavy drinkers was likely to be low given the overall distribution of drinking in this cohort, it would have been preferable to exclude heavy drinkers from this drinking category. It remains possible that some of the apparent excess risk observed in this highest category may have been confined to heavier drinkers. Fifth, we did not distinguish between the types of beverage consumed and, thus, could not compare risks and benefits of wine, beer or liquor consumption. Sixth, Shaper et al. (50) have suggested that the reduction in CVD risk among drinkers could be in part explained by an excess risk among those in the nondrinking categories who stopped drinking because of underlying disease. While we were unable to exclude recent exdrinkers, we excluded anyone who reported a history of MI, stroke, cancer or liver disease. Further, there was no material difference in rates of various coronary risk factors between rare/never drinkers or light drinkers (1 to 3 drinks per month). Most recent studies have excluded recent exdrinkers and have reported similar results (22, 51, 52). Finally, residual confounding by unmeasured variables is likely small, since adjustment for the known major confounders had little affect on the RRs.

We cannot add to the debate regarding the risks and benefits among women, particularly given their lower rates of CHD (53), increased risk of breast cancer (54, 55) and potentially increased susceptibility to alcoholic liver disease (56, 57). Recently, Fuchs et al. (58) found a similar U-shaped relation between light-to-moderate alcohol consumption and mortality among women in the Nurses' Health Study, which was largely due to a decrease in CVD at light-to-moderate levels (1.5 to 29.9 g per day [1 to 2½ drinks per day]) with an increase in breast cancer at higher levels (≥30 g per day [≥2½ drinks per day]). Overall, we analyzed, after exclusions, a group of relatively healthy men with a higher level of education, a higher socioeconomic status and easier access to health care than the general population. If, in fact, this population of men was healthier than the general population, then our findings argue against other studies that suggest the benefit of moderate alcohol consumption is only present among those sicker populations (50, 59). It may be possible to generalize these findings to other populations by summing disease specific curves weighted by the cause-specific death distribution for any given population.

Conclusions. In summary, this study reveals the complex effects of alcohol consumption on various chronic diseases as reflected in the overall U-shaped relationship between light-to-moderate alcohol consumption and total mortality in men. Reductions in risk of death among light drinkers are largely due to lower risk of CVD and no clear increases in cancer; however, the CVD benefits may begin to be offset by increasing risk of some of the less common cancers at a level of ≥2 drinks per day. In addition to these effects revealed in our study, alcohol has many other proposed metabolic, physiologic and psychologic effects on the individual as well as many societal repercussions related to heavier drinking. Alcohol-related deaths are still a major cause of preventable death in this country. Given the complex nature of the relationship of alcohol with various diseases, alcohol consumption can neither be viewed as a primary preventive strategy nor should it necessarily be viewed as an unhealthy behavior. A discussion of alcohol intake should be a part of routine preventive counseling, but any individual or public health recommendations must consider the totality of evidence, which includes deleterious metabolic, physiologic and psychologic consequences.

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