

The New England Journal of Medicine

©Copyright, 1995, by the Massachusetts Medical Society

Volume 332

MAY 11, 1995

Number 19

ALCOHOL CONSUMPTION AND MORTALITY AMONG WOMEN

CHARLES S. FUCHS, M.D., MEIR J. STAMPFER, M.D., GRAHAM A. COLDITZ, M.B., B.S.,
EDWARD L. GIOVANNUCCI, M.D., JOANN E. MANSON, M.D., ICHIRO KAWACHI, M.B., CH.B.,
DAVID J. HUNTER, M.B., B.S., SUSAN E. HANKINSON, R.N., SC.D., CHARLES H. HENNEKENS, M.D.,
BERNARD ROSNER, PH.D., FRANK E. SPEIZER, M.D., AND WALTER C. WILLETT, M.D.

Abstract Background. Studies in men suggest that light-to-moderate alcohol intake is associated with a reduction in overall mortality, due primarily to a reduced risk of coronary heart disease. Among women with similar levels of alcohol consumption, an increased risk of breast cancer has been noted that complicates the balance of risks and benefits.

Methods. We conducted a prospective study among 85,709 women, 34 to 59 years of age and without a history of myocardial infarction, angina, stroke, or cancer, who completed a dietary questionnaire in 1980. During the 12-year follow-up period, 2658 deaths were documented.

Results. The relative risks of death in drinkers as compared with nondrinkers were 0.83 (95 percent confidence interval, 0.74 to 0.93) for women who consumed 1.5 to 4.9 g of alcohol per day (one to three drinks per week),

0.88 (95 percent confidence interval, 0.80 to 0.98) for those who consumed 5.0 to 29.9 g per day, and 1.19 (95 percent confidence interval, 1.02 to 1.38) for those who consumed 30 g or more per day, after adjustment for other predictors of mortality. Light-to-moderate drinking (1.5 to 29.9 g per day) was associated with a decreased risk of death from cardiovascular disease; heavier drinking was associated with an increased risk of death from other causes, particularly breast cancer and cirrhosis. The benefit associated with light-to-moderate drinking was most apparent among women with risk factors for coronary heart disease and those 50 years of age or older.

Conclusions. Among women, light-to-moderate alcohol consumption is associated with a reduced mortality rate, but this apparent survival benefit appears largely confined to women at greater risk for coronary heart disease. (N Engl J Med 1995;332:1245-50.)

IN prospective cohort studies, conducted predominantly among men, light-to-moderate drinkers of alcoholic beverages have been found to have lower total mortality rates than either nondrinkers or heavier drinkers.¹⁻¹⁴ This reduced mortality is due largely to a reduced risk of fatal coronary heart disease. Studies among women have been fewer, and the results have been conflicting.^{3,8,9,11,15,16}

Whether the apparent overall benefit of light-to-moderate alcohol intake among men can be extrapolated to women is unclear. As compared with men, women have a lower risk of coronary heart disease,¹⁷ attain higher blood alcohol concentrations for a given amount of alcohol consumed,¹⁸ and are more susceptible to al-

coholic liver disease.^{19,20} Moreover, women who consume moderate quantities of alcohol have an increased risk of breast cancer.²¹⁻²³

We therefore examined prospectively the relation between alcohol intake and mortality in a large cohort of women. Furthermore, we specifically examined this relation among women at low risk for coronary heart disease, for whom increased rates of breast cancer and other adverse events may outweigh the reduction in coronary heart disease.

METHODS

Study Cohort

The Nurses' Health Study was established in 1976 when 121,700 female registered nurses 30 to 55 years of age, residing in the United States, completed a mailed questionnaire on known or suspected risk factors for cancer²² and coronary heart disease.²⁴ Every two years since then, the participants have been sent follow-up questionnaires to update information on potential risk factors and to identify newly diagnosed cases of cancer, coronary heart disease, and other diseases.

Semiquantitative Food-Frequency Questionnaire

In 1980, 1984, and 1986, the participants were asked to report their average frequency of consumption of specified foods and beverages during the previous 12 months. In 1980, we also asked whether

From the Channing Laboratory (C.S.F., M.J.S., G.A.C., E.L.G., J.E.M., I.K., D.J.H., S.E.H., C.H.H., B.R., F.E.S., W.C.W.) and the Division of Preventive Medicine (J.E.M., C.H.H., B.R.), Brigham and Women's Hospital and Harvard Medical School; the Division of Medical Oncology, Dana-Farber Cancer Institute (C.S.F.); and the Departments of Epidemiology (M.J.S., G.A.C., D.J.H., S.E.H., C.H.H., W.C.W.), Nutrition (M.J.S., W.C.W.), Health and Social Behavior (I.K.), and Biostatistics (B.R.), Harvard School of Public Health — all in Boston. Address reprint requests to Dr. Fuchs at the Dana-Farber Cancer Institute, 44 Binney St., Boston, MA 02115.

Supported by grants (HL 34594 and CA 40356) from the National Institutes of Health and by Faculty Research Awards from the American Cancer Society (FRA-398 to Dr. Colditz and FRA-455 to Dr. Hunter).

consumption of each item had greatly increased or greatly decreased during the previous 10 years. The reproducibility and validity of these questionnaires have been documented previously.²⁵⁻²⁹

Questions about the consumption of beer, wine, and spirits were included as separate items. Total alcohol intake was the sum of the values for all three beverages; a 12-oz (360-ml) can or bottle of beer was assumed to contain 13.2 g of alcohol, a 4-oz (120-ml) glass of wine 10.8 g, and a standard drink of spirits 15.1 g.³⁰ The Spearman rank-correlation coefficient for alcohol intake as measured by the questionnaire and as calculated from the dietary records of participants was 0.90.²² Similarly, the correlation between the alcohol consumption reported in response to the 1984 questionnaire and that found in the 1980 diet records was 0.84.²⁹ In addition, alcohol intake as measured by each of the methods was correlated with plasma concentrations of high-density lipoprotein ($r = 0.40$, $P < 0.001$).²²⁻²⁹

Population for Analysis

The dietary questionnaire was returned by 98,462 nurses in 1980. We excluded from our study women with 10 or more food items left blank (4 percent) or with implausibly high or low scores for total food intake (2.7 percent). We also excluded women with a history of cancer (except nonmelanoma skin cancer), angina, myocardial infarction, or stroke. Because the group of women who now abstain from alcohol may include former heavy drinkers and women who stopped drinking because of illness, we excluded from our primary analysis 2957 women who reported no alcohol intake in 1980 but had greatly decreased their alcohol intake in the previous 10 years. This left 85,709 women in the analysis.

Identification of Deaths

Our primary end point was death from any cause. We made systematic searches of the vital records of the states and the National Death Index to discover deaths among women who did not respond during each questionnaire cycle. This search was supplemented by reports from family members or from postal authorities. We estimate that we were able to ascertain more than 98 percent of the deaths in the cohort by these methods.³¹

A physician, blinded to data on alcohol consumption and other risk factors, reviewed death certificates and medical records to classify the cause of death according to the *International Classification of Diseases, Eighth Revision* (ICD-8).³² The following subgroups were analyzed: participants whose deaths were due to any cardiovascular disease (ICD-8 codes 390 to 459 and 795); coronary heart disease (codes 410 to 414); stroke (codes 430 to 437); any noncardiovascular cause (all codes except 390 to 459 and 795); any cancer (codes 140 to 207); breast cancer (code 174); cirrhosis of the liver (code 571); and any injury with an external cause (codes 800 to 999 and all "E" codes), which included accidents and suicides.

Statistical Analysis

In our primary analysis, we used incidence rates with person-years of follow-up as the denominators. For each woman, person-years of follow-up were counted from the date of return of the 1980 questionnaire to May 31, 1992 or, for those who died, until the date of death. Because our focus was on mortality, and because people tend to reduce alcohol consumption markedly or to discontinue consumption after a major illness is diagnosed, levels of alcohol intake reported after 1980 were not taken into consideration in the primary analysis. For all other covariates, person-years of follow-up were assigned according to the risk-factor status reported on the most recently completed questionnaire. Follow-up terminated at the date of death. If no questionnaire was returned for a follow-up cycle, the most recently recorded data were used for the subsequent follow-up period.

We calculated relative risk as the incidence of death among women with a given alcohol intake divided by the corresponding rate among women who did not consume alcohol. Relative risks were adjusted for age, in five-year categories, and for the history and amount of cigarette smoking (participants were grouped into those who never smoked, those who had formerly smoked, and those who smoked less than 15, 15 to 24, and more than 24 cigarettes per day)³³; 95 percent confidence intervals were calculated.³⁴ We used a proportional-hazards model to adjust for multiple risk factors simultaneously.³⁵ Any

curvilinear association between alcohol intake and mortality was assessed by including both linear and quadratic terms (average alcohol intake and that value squared) in our model.³⁶ Stratified analyses were conducted to determine whether the effect of alcohol consumption was modified by age or coronary-risk-factor status. In both these analyses, the value for the relevant variable, age or coronary-risk-factor status, was updated biennially. Tests for interaction were performed by entering into the proportional-hazards model cross-product terms for alcohol consumption (as indicator variables for each level of intake) and either age or coronary-risk-factor status.³⁶

To address the potential misclassification of alcohol intake due to the passage of time, secondary analyses were performed on the basis of updated measurements of alcohol consumption, although these data were not used in the primary analysis.

Employing a model with separate continuous variables for alcohol intake according to type of beverage — beer, wine, or spirits — we used the Wald test to examine differences between logistic-regression coefficients.³⁶

RESULTS

Among the 85,709 women eligible for analysis, 29.8 percent reported no alcohol consumption in 1980, and the majority reported consuming only low-to-moderate amounts (Table 1). Approximately 1 percent of the cohort drank more than 50 g per day. Most base-line characteristics were distributed similarly among drinkers and nondrinkers, although diabetes mellitus and obesity were more common among nondrinkers and regular aspirin use, oral-contraceptive use, and smoking were more common among drinkers.

During the 12 years of follow-up (1,010,209 person-years), 2658 of the women died. A total of 503 women died of cardiovascular disorders; 1495 of any cancer, including 350 of breast cancer; 203 of injury from external causes, including accidents and suicides; 52 of cirrhosis of the liver; and 405 from other causes.

As compared with nondrinkers and heavy drinkers, light-to-moderate drinkers (1.5 to 29.9 g of alcohol per day) had a significantly lower overall risk of death (Table 2). Even after we controlled for several known or suspected predictors of mortality, the data for mortality according to alcohol consumption fitted a U-shaped curve with a nadir at approximately 1.5 to 4.9 g per day (one to three drinks per week). The lower risk associated with light drinking was principally due to a lower risk of fatal cardiovascular disease. The higher death rate among women who consumed 30 g or more per day was largely due to a higher number of deaths from noncardiovascular diseases, including breast cancer and cirrhosis. Furthermore, controlling for risk factors for breast cancer (age at menarche less than 13 years, one or more pregnancies, age at first pregnancy less than 22 years, history of benign breast disease, or family history of breast cancer) did not materially affect the association of alcohol consumption with mortality from all causes.

To assess the nonlinear relation between alcohol intake and mortality from all causes, we performed analyses in which alcohol consumption, measured continuously, was entered into the multivariate model as both linear and quadratic terms (average alcohol intake and that value squared). A negative regression coefficient for the linear term ($\beta = -1.3 \times 10^{-2}$, $P = 0.02$) and a positive coefficient for the quadratic term

Table 1. Base-Line Characteristics of the Cohort, According to Alcohol Intake.

CHARACTERISTIC*	AVERAGE ALCOHOL INTAKE (g/DAY)					
	0 (N = 25,535)	0.1–1.4 (N = 11,304)	1.5–4.9 (N = 18,460)	5.0–14.9 (N = 17,783)	15.0–29.9 (N = 8106)	≥30.0 (N = 4521)
Median age (yr)	47	46	46	46	47	49
Current smoking (%)	22	27	27	31	38	54
Body-mass index†	25	25	24	24	23	23
Regular aspirin use (%)‡	25	26	26	28	30	31
Regular vigorous exercise (%)§	40	44	46	50	50	44
High plasma cholesterol (%)¶	6.0	5.3	5.3	4.9	4.8	5.2
Diabetes mellitus (%)	3.6	2.3	1.6	1.1	1.0	1.3
Myocardial infarction in parent ≤60 yr of age (%)	14	15	15	15	15	15
Hypertension (%)	17	16	15	14	16	20
Breast cancer in mother or sibling (%)	5.8	5.9	6.1	6.3	7.0	5.9
Past or present oral-contraceptive use (%)	46	48	50	52	55	54
Parity ≥1 (%)	93	93	93	92	91	89
Age at first pregnancy <22 yr (%)	23	23	22	22	21	23
Menopausal status (% premenopausal)	70	70	71	71	72	71
Age at menarche <13 yr (%)	52	50	50	48	47	48
Postmenopausal hormone use (%)	22	22	22	22	23	23
Dietary intake						
Fiber (g/day)	17	17	17	17	16	13
Saturated fat (g/day)	29	29	29	28	27	24
Cholesterol (mg/day)	339	341	340	336	333	304

*All values are directly standardized according to the age distribution of the cohort. Nutrient values represent the mean energy-adjusted intake for each alcohol-intake group.

†The weight in kilograms divided by the square of the height in meters.

‡Two or more days per week.

§Vigorous physical activity (long enough to work up a sweat) at least one or more days per week.

¶Self-report of physician-diagnosed hypercholesterolemia.

||Self-report of physician-diagnosed hypertension.

($\beta = 4.9 \times 10^{-4}$, $P = 0.001$) were derived, results consistent with the observed U-shaped relation.

We excluded from our primary analysis former heavy drinkers who reported current abstinence, but we examined the data on these women separately. As compared with long-term nondrinkers, these former drinkers had a relative risk of death, after adjustment for age and smoking status, of 1.49 (95 percent confidence interval, 1.27 to 1.74) as well as a significantly higher risk of death from any cardiovascular cause (relative risk, 2.48; 95 percent confidence interval, 1.88 to 3.25) and from any noncardiovascular cause (relative risk, 1.24; 95 percent confidence interval, 1.02 to 1.50).

Age strongly affected the relation between alcohol intake and mortality from all causes. For women 34 to 39 years of age, the relative risk of death in all categories of drinkers was slightly but not significantly increased (Table 3). Among women in this age group who consumed 5.0 g or more of alcohol per day, external causes of injury accounted for 50 percent of the deaths. In contrast, among women 50 or older, light-to-moderate drinkers (1.5 to 29.9 g per day) had a significant reduction in mortality from all causes, which appeared to be the result of a substantially lower risk of fatal cardiovascular disease. Among light-to-moderate drinkers, the relative risk of death from a cardiovascular cause was 0.59 (95 percent confidence interval, 0.47 to 0.73) for women 50 years of age or older. To test whether age

significantly affected the association between alcohol intake and total mortality, we added to the multivariate model the cross-product interaction terms of age (measured continuously) and each of the levels of alcohol consumption specified in Table 3. For light-to-moderate drinkers, the decrease in the relative risk of death with increasing age was at the margin of statistical significance (P for trend = 0.05).

The apparent benefit associated with light-to-moderate alcohol consumption was greatest among women with one or more risk factors for coronary heart disease (Table 4). Among women reporting at least one coronary risk factor (73.2 percent of the study population in 1980), light-to-moderate drinkers had a significantly lower total mortality ($P < 0.001$). In contrast, among women with no coronary risk factors (26.8 percent of the population in 1980), light-to-moderate drinking was not associated with any appreciable reduction in total mortality ($P = 0.70$); consumption of 30 g or more of alcohol per day by these women markedly increased mortality. This higher total mortality among heavier drinkers without coronary risk factors was largely due to

a higher risk of death from noncardiovascular disease (relative risk, 2.22; 95 percent confidence interval, 1.31 to 3.72), most notably breast cancer (relative risk, 3.43; 95 percent confidence interval, 1.36 to 8.66). The result of a test for interaction between the consumption of 1.5 to 29.9 g of alcohol per day and the presence or absence of cardiac risk factors was not significant in a multivariate model ($P = 0.09$), although the relative risks associated with the consumption of 30 g or more per day did differ significantly among women with and without cardiac risk factors ($P = 0.04$).

To determine whether the interaction between alcohol consumption and coronary-risk-factor status was independent of age, we then limited our analysis to women 50 years of age or older. Among these older women, the reduction in mortality associated with light-to-moderate drinking was again confined to women with one or more coronary risk factors. As was the case when younger women were included, the interaction between the risk of death associated with the consumption of 1.5 to 29.9 g of alcohol per day and coronary-risk-factor status was not significant ($P = 0.08$).

Although we excluded women with serious illnesses at base line, the group of long-term nondrinkers could include women who refrained from drinking because of early symptoms of disease. If so, the higher mortality among nondrinkers might be due in part to undiagnosed, preexisting disease. Such an effect would ac-

Table 2. Number of Deaths and Relative Risks of Death According to Cause and Alcohol Intake.

VARIABLE*	AVERAGE ALCOHOL INTAKE (g/DAY)					
	0	0.1-1.4	1.5-4.9	5.0-14.9	15.0-29.9	≥30.0
Death from all causes						
No.	837	321	460	509	272	259
Adjusted RR (95% CI)	1.0	0.86 (0.75-0.98)	0.76 (0.68-0.86)	0.80 (0.71-0.89)	0.81 (0.71-0.93)	1.19 (1.03-1.38)
Multivariate RR (95% CI)†	1.0	0.91 (0.80-1.03)	0.83 (0.74-0.93)	0.88 (0.79-0.99)	0.89 (0.77-1.02)	1.19 (1.02-1.38)
Death from cardiovascular disease						
No.	202	64	67	87	44	39
Multivariate RR (95% CI)	1.0	0.79 (0.59-1.05)	0.57 (0.43-0.76)	0.73 (0.56-0.95)	0.66 (0.47-0.93)	0.74 (0.51-1.08)
Death from noncardiovascular causes						
No.	635	257	393	422	228	220
Multivariate RR (95% CI)	1.0	0.94 (0.81-1.09)	0.91 (0.80-1.03)	0.93 (0.83-1.05)	0.95 (0.81-1.11)	1.33 (1.12-1.57)
Death from coronary heart disease						
No.	145	47	41	50	28	9
Multivariate RR (95% CI)	1.0	0.82 (0.59-1.15)	0.51 (0.36-0.73)	0.64 (0.46-0.89)	0.65 (0.43-0.99)	0.59 (0.35-0.99)
Death from cancer						
No.	429	182	290	293	162	139
Multivariate RR (95% CI)	1.0	0.98 (0.82-1.16)	0.97 (0.83-1.13)	0.93 (0.80-1.09)	0.99 (0.82-1.20)	1.28 (1.04-1.58)
Death from breast cancer						
No.	107	30	61	69	48	35
Multivariate RR (95% CI)	1.0	0.67 (0.45-1.01)	0.85 (0.61-1.16)	0.96 (0.71-1.32)	1.37 (0.96-1.96)	1.67 (1.10-2.53)
Death from injury with an external cause						
No.	62	20	30	50	24	17
Multivariate RR (95% CI)	1.0	0.75 (0.45-1.24)	0.70 (0.45-1.09)	1.15 (0.78-1.69)	1.17 (0.66-1.75)	1.08 (1.61-1.94)
Death from hepatic cirrhosis						
No.	12	1	5	10	9	15
Multivariate RR (95% CI)	1.0	0.21 (0.27-1.59)	0.69 (0.24-1.98)	1.27 (0.54-3.01)	1.86 (0.76-4.59)	2.55 (1.06-6.11)

*RR denotes relative risk, and CI confidence interval. Relative risks are expressed for each alcohol-intake group as compared with the group of women who drank no alcohol. Adjusted RR has been adjusted for age (in five-year categories) and smoking status. Multivariate RRs have been adjusted for age (in five-year categories), smoking status, body-mass index (in quintiles), regular aspirin use (≥ 2 days per week), regular vigorous exercise (≥ 1 day per week), high plasma cholesterol level (yes or no), diabetes (yes or no), hypertension (yes or no), myocardial infarction in a parent at ≤ 60 years of age (yes or no), past or present oral-contraceptive use (yes or no), menopausal status, past or present postmenopausal hormone use (yes or no), and energy-adjusted intake of dietary fiber and saturated fat (in quintiles).

†Multivariate test for trend: linear term, $\chi^2 = -2.23$, $P = 0.02$; quadratic term, $\chi^2 = 3.22$, $P = 0.001$.

count for higher rates of death in the earlier years of follow-up but would be expected to diminish in later years of observation. To address this issue, we repeated our analyses after excluding deaths in the first four years of follow-up (Table 5). With the analysis restricted to the final eight years of follow-up, a significant U-shaped relation remained between the average alcohol intake reported in 1980 and total mortality ($P = 0.002$ for the quadratic term [average alcohol intake]²).

Because people may alter their drinking habits over time, longitudinal studies that assess alcohol intake only at base line may result in misclassification. There-

fore, we repeated our analyses using updated measurements of alcohol consumption obtained in 1984 and 1986, and still observed a significant U-shaped relation between alcohol consumption and mortality ($P < 0.001$ for the quadratic term [average alcohol intake]²) (Table 5). In performing analyses in which the data on alcohol intake were updated, we considered the possibility that a disproportionate number of the women who had recently stopped drinking did so because of ill health, which might have resulted in a misleading elevation of mortality among abstainers. Therefore, we performed further analyses in which women were excluded from follow-up if they reported nonfatal myocardial infarction, angina, stroke, or cancer during subsequent assessments of alcohol intake. With 2043 deaths left in the analysis, we continued to observe a significant U-shaped relation between alcohol intake and total mortality ($P = 0.001$ for the quadratic term [average alcohol intake]²).

We examined separately the association between mortality and alcohol intake according to type of beverage — beer, wine, or spirits. In a regression model controlled for other predictors of mortality, the associations between alcohol intake (measured as a continuous variable) from beer, wine, or spirits and the risk of death did not differ significantly, although there was a nonsig-

Table 3. Number of Deaths and Relative Risk of Death According to Age and Alcohol Intake.

AGE AND VARIABLE*	AVERAGE ALCOHOL INTAKE (g/DAY)			
	0	0.1-1.4	1.5-29.9†	≥30.0
34-39 yr				
No. of deaths	8	7	25	2
Multivariate RR (95% CI)	1.0	1.89 (0.68-5.19)	2.08 (0.92-4.71)	2.46 (0.50-12.4)
40-49 yr				
No. of deaths	113	53	183	29
Multivariate RR (95% CI)	1.0	1.02 (0.73-1.41)	0.95 (0.74-1.20)	1.47 (0.95-2.27)
50-59 yr				
No. of deaths	364	132	560	126
Multivariate RR (95% CI)	1.0	0.88 (0.72-1.06)	0.88 (0.77-0.99)	1.26 (1.01-1.57)
≥60 yr				
No. of deaths	352	129	473	102
Multivariate RR (95% CI)	1.0	0.88 (0.72-1.08)	0.79 (0.68-0.91)	1.02 (0.80-1.30)

*RR denotes relative risk, and CI confidence interval. Relative risks are expressed for each alcohol-intake group as compared with the group of women who drank no alcohol. Multivariate RRs have been adjusted for age (in five-year categories), smoking status, body-mass index (in quintiles), regular aspirin use (≥ 2 days per week), regular vigorous exercise (≥ 1 day per week), high plasma cholesterol level (yes or no), diabetes (yes or no), hypertension (yes or no), myocardial infarction in a parent at ≤ 60 years of age (yes or no), past or present oral-contraceptive use (yes or no), menopausal status, past or present postmenopausal hormone use (yes or no), and energy-adjusted intake of dietary fiber and saturated fat (in quintiles).

† $P = 0.05$ for the interaction between age and the consumption of 1.5 to 29.9 g of alcohol per day.

Table 4. Number of Deaths from All Causes and Relative Risk of Death According to Cardiac Risk Status and Alcohol Intake.

POPULATION AND VARIABLE*	AVERAGE ALCOHOL INTAKE (g/DAY)			
	0	0.1-1.4	1.5-29.9†	≥30.0‡
All women				
No cardiac risk factor				
No. of deaths	144	38	153	17
Multivariate RR (95% CI)	1.0	0.75 (0.52-1.06)	0.95 (0.75-1.19)	2.22 (1.31-3.72)
≥1 cardiac risk factor				
No. of deaths	693	283	1088	242
Multivariate RR (95% CI)	1.0	0.93 (0.81-1.07)	0.84 (0.76-0.93)	1.12 (0.95-1.31)
Women 50 or older				
No cardiac risk factors				
No. of deaths	107	31	115	11
Multivariate RR (95% CI)	1.0	0.84 (0.56-1.25)	0.96 (0.74-1.25)	1.89 (1.00-3.58)
≥1 cardiac risk factor				
No. of deaths	609	230	918	217
Multivariate RR (95% CI)	1.0	0.88 (0.75-1.02)	0.81 (0.74-0.91)	1.08 (0.91-1.28)

*RR denotes relative risk, and CI confidence interval. Relative risks are expressed for each alcohol-intake group as compared with the group of women who drank no alcohol. Multivariate RRs have been adjusted for age (in five-year categories), smoking status, body-mass index (in quintiles), regular aspirin use (≥2 days per week), regular vigorous exercise (≥1 day per week), high plasma cholesterol level (yes or no), diabetes (yes or no), hypertension (yes or no), myocardial infarction in a parent at ≤60 years of age (yes or no), past or present oral-contraceptive use (yes or no), menopausal status, past or present postmenopausal hormone use (yes or no), and energy-adjusted intake of dietary fiber and saturated fat (in quintiles). Cardiac risk factors are defined as a history of hypertension or diabetes, smoking, a high cholesterol level, a myocardial infarction in a parent at ≤60 years of age, and a body-mass index >29.0.

†P=0.09 for the interaction between cardiac-risk-factor status and the consumption of 1.5 to 29.9 g of alcohol per day, in all women. For women 50 or older, P=0.08.

‡P=0.04 for the interaction between cardiac-risk-factor status and the consumption of 30 g or more of alcohol per day, in all women.

nificant trend toward more protection with wine (data not shown).

DISCUSSION

Our results, from a large prospective study of women, provide strong evidence for a U-shaped relation between alcohol intake and mortality in women. As compared with abstinence, light-to-moderate alcohol consumption was associated with a significantly reduced risk of death due largely to a lower risk of fatal cardiovascular disease. In contrast, heavier drinking was associated with increased mortality, due largely to an increased risk of death from noncardiovascular diseases, including breast cancer. In a manner consistent with these competing effects, the apparent benefit of

light-to-moderate alcohol consumption was mainly confined to women at greater risk for coronary heart disease, specifically older women and women with one or more coronary risk factors.

Bias is unlikely to explain the observed relations. The dietary questionnaires reliably measured alcohol intake.²⁹ Moreover, our results remained unchanged even after we accounted for variations in alcohol consumption over time. The prospective design precluded recall bias. Differential follow-up is unlikely to have made a material contribution to these findings, since we estimate that we accurately identified more than 98 percent of the deaths in this cohort.³¹

We observed a reduction in mortality for light-to-moderate drinkers only among women 50 years of age or older, although our cohort did not include women over 70. For women

34 to 39 years of age, we observed elevated risks of death for all levels of alcohol consumption, but the number of deaths in this subgroup was small. Two previous studies have reported an increased mortality among younger drinkers, largely as a result of alcohol-related accidents.^{11,37} Although a recent analysis of British physicians reported lower mortality for moderate drinkers at all ages, the study population consisted of men over the age of 50 who were predominantly former or current smokers.⁵

The women in the Nurses' Health Study have patterns of alcohol consumption that are quite similar to those found in a general survey of U.S. women.³⁸ Thus, our results may be applicable to the wider population of women. Since only a small percentage of our cohort

Table 5. Results of Secondary Analyses.

ANALYSIS AND VARIABLE*	AVERAGE ALCOHOL INTAKE (g/DAY)					
	0	0.1-1.4	1.5-4.9	5.0-14.9	15.0-29.9	≥30.0
Excluding first 4 yr of follow-up†						
No. of deaths	667	263	382	405	218	207
Multivariate RR (95% CI)‡	1.0	0.93 (0.81-1.08)	0.86 (0.76-0.98)	0.88 (0.77-1.00)	0.89 (0.76-1.04)	1.19 (1.01-1.42)
Using updated alcohol-intake reports§						
No. of deaths	1055	306	488	424	152	233
Multivariate RR (95% CI)¶	1.0	0.83 (0.73-0.94)	0.73 (0.65-0.82)	0.75 (0.67-0.85)	0.78 (0.66-0.93)	1.02 (0.87-1.19)
Using updated alcohol-intake reports and excluding new cases of nonfatal disease						
No. of deaths	767	242	370	339	130	195
Multivariate RR (95% CI)**	1.0	0.87 (0.75-1.01)	0.74 (0.66-0.85)	0.81 (0.71-0.92)	0.89 (0.73-1.07)	1.12 (0.94-1.33)

*RR denotes relative risk, and CI confidence interval. Relative risks are expressed for each alcohol-intake group as compared with the group of women who drank no alcohol. Multivariate RRs have been adjusted for age (in five-year categories), smoking status, body-mass index (in quintiles), regular aspirin use (≥2 days per week), regular vigorous exercise (≥1 day per week), high plasma cholesterol level (yes or no), diabetes (yes or no), hypertension (yes or no), myocardial infarction in a parent at ≤60 years of age (yes or no), past or present oral-contraceptive use (yes or no), menopausal status, postmenopausal hormone use (yes or no), and energy-adjusted intake of dietary fiber and saturated fat (in quintiles).

†Based on 1980 reports of alcohol intake but excluding deaths from 1980 through 1984.

‡Multivariate test for trend: linear term, $\chi^2 = -2.22$, $P = 0.02$; quadratic term, $\chi^2 = 3.04$, $P = 0.002$.

§Based on reports of alcohol intake from 1980, 1984, and 1986, and including deaths from 1980 through 1992.

¶Multivariate test for trend: linear term, $\chi^2 = -4.25$, $P < 0.001$; quadratic term, $\chi^2 = 4.16$, $P < 0.001$.

||Based on reports of alcohol intake from 1980, 1984, and 1986, including deaths from 1980 through 1992, but excluding women who reported nonfatal disease in 1984 or 1986 (see the text for details).

**Multivariate test for trend: linear term, $\chi^2 = -2.46$, $P = 0.01$; quadratic term, $\chi^2 = 3.22$, $P = 0.001$.

consumed more than 50 g of alcohol per day, our ability to examine the health consequences of excessive drinking is limited.

The relations between alcohol consumption and the risk of death from breast cancer or cardiovascular disease reflect the previously described association of alcohol with the incidence of these illnesses.^{21-23,39-42} In addition, several other diseases have been positively linked to alcohol consumption, including colorectal cancer, cancers of the upper aerodigestive tract (the oral cavity and esophagus), hemorrhagic stroke, cirrhosis of the liver, accidents, and suicide.^{2,11,43,44} Our mortality analysis does not address nonfatal disease and may therefore be less useful in addressing causal relations. However, data on mortality provide one measure of the overall balance of risks and benefits of alcohol consumption.

In conclusion, these findings indicate that for women as a group light-to-moderate alcohol consumption confers a significant overall survival advantage. Among younger women and those without risk factors for coronary heart disease, however, light-to-moderate alcohol consumption is not associated with a reduction in total mortality and heavier drinking is associated with a substantial increase in mortality. For older women and women with coronary risk factors, light-to-moderate alcohol consumption is associated with a reduction in total mortality, although with heavier intake mortality is increased.

REFERENCES

- Blackwelder WC, Yano K, Rhoads GG, Kagan A, Gordon T, Palesch Y. Alcohol and mortality: the Honolulu Heart Study. *Am J Med* 1980;68:164-9.
- Boffetta P, Garfinkel L. Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. *Epidemiology* 1990;1:342-8.
- Cullen KJ, Knuiman MW, Ward NJ. Alcohol and mortality in Busselton, Western Australia. *Am J Epidemiol* 1993;137:242-8.
- De Labry LO, Glynn RJ, Levenson MR, Hermos JA, LoCastro JS, Vokonas PS. Alcohol consumption and mortality in an American male population: recovering the U-shaped curve — findings from the normative aging study. *J Stud Alcohol* 1992;53:25-32.
- 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.
- Dyer AR, Stamler J, Paul O, et al. Alcohol consumption, cardiovascular risk factors, and mortality in two Chicago epidemiologic studies. *Circulation* 1977;56:1067-74.
- Gordon T, Doyle JT. Drinking and mortality: the Albany Study. *Am J Epidemiol* 1987;125:263-70.
- Gronbaek M, Deis A, Sorensen TI, et al. Influence of sex, age, body mass index, and smoking on alcohol intake and mortality. *BMJ* 1994;308:302-6.
- Friedman LA, Kimball AW. Coronary heart disease mortality and alcohol consumption in Framingham. *Am J Epidemiol* 1986;124:481-9.
- 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.
- Klatsky AL, Armstrong MA, Friedman GD. Alcohol and mortality. *Ann Intern Med* 1992;117:646-54.
- Kono S, Ikeda M, Tokudome S, Nishizumi M, Kuratsune M. Alcohol and mortality: a cohort study of male Japanese physicians. *Int J Epidemiol* 1986;15:527-32.
- Kozaravaevic D, McGee D, Vojvodic N, et al. Frequency of alcohol consumption and morbidity and mortality: the Yugoslavia Cardiovascular Disease Study. *Lancet* 1980;1:613-6.
- Marmot MG, Rose G, Shipley M, Thomas B. Alcohol and mortality: a U-shaped curve. *Lancet* 1981;1:580-3.
- Garfinkel L, Boffetta P, Stellman S. Alcohol and breast cancer: a cohort study. *Prev Med* 1988;17:686-93.
- Camacho TC, Kaplan GA, Cohen RD. Alcohol consumption and mortality in Alameda County. *J Chronic Dis* 1987;40:229-36.
- National Center for Health Statistics. Vital statistics of the United States: mortality series. Washington, D.C.: Government Printing Office, 1968-1988.
- Frezza M, di Padova C, Pozzato G, Terpin M, Baraona E, Lieber CS. High blood alcohol levels in women: the role of decreased gastric alcohol dehydrogenase activity and first-pass metabolism. *N Engl J Med* 1990;322:95-9.
- Norton R, Batey R, Dwyer T, MacMahon S. Alcohol consumption and the risk of alcohol cirrhosis in women. *BMJ* 1987;295:80-2.
- Saunders JB, Davis M, Williams R. Do women develop alcoholic liver disease more readily than men? *BMJ* 1981;282:1140-3.
- Longnecker MP. Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. *Cancer Causes Control* 1994;5:73-82.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Hennekens CH, Speizer FE. Moderate alcohol consumption and the risk of breast cancer. *N Engl J Med* 1987;316:1174-80.
- Schatzkin A, Jones DY, Hoover RN, et al. Alcohol consumption and breast cancer in the Epidemiologic Follow-up Study of the first National Health and Nutrition Examination Survey. *N Engl J Med* 1987;316:1169-73.
- Stampfer MJ, Willett WC, Colditz GA, Rosner B, Speizer FE, Hennekens CH. A prospective study of postmenopausal estrogen therapy and coronary heart disease. *N Engl J Med* 1985;313:1044-9.
- Colditz GA, Willett WC, Stampfer MJ, et al. The influence of age, relative weight, smoking, and alcohol intake on the reproducibility of a dietary questionnaire. *Int J Epidemiol* 1987;16:392-8.
- Colditz G, Martin P, Stampfer MJ, et al. Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort study of women. *Am J Epidemiol* 1986;123:894-900.
- Willett WC, Sampson L, Browne ML, et al. The use of a self-administered questionnaire to assess diet four years in the past. *Am J Epidemiol* 1988;127:188-99.
- Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;122:51-65.
- Giovannucci E, Colditz G, Stampfer M, et al. The assessment of alcohol consumption by a simple self-administered questionnaire. *Am J Epidemiol* 1991;133:810-7.
- Nutrition Information Service. Human provisional table on nutrient content of beverages. Washington, D.C.: Department of Agriculture, 1982.
- Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. *Am J Epidemiol* 1984;119:837-9.
- Department of Health, Education, and Welfare. International classification of diseases, 8th rev., adapted for use in the United States: ICDA. Vol. 1. Tabular list. Washington, D.C.: Government Printing Office, 1967. (DHEW publication no. (PHS) 1693.)
- Rothman KJ. Modern epidemiology. Boston: Little, Brown, 1986.
- Miettinen O. Estimability and estimation in case-referent studies. *Am J Epidemiol* 1976;103:226-35.
- Cox D. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187-220.
- Hosmer DW Jr, Lemeshow S. Applied logistic regression. New York: John Wiley, 1989.
- Andreasson S, Allebeck P, Romelsjo A. Alcohol and mortality among young men: longitudinal study of Swedish conscripts. *BMJ* 1988;296:1021-5.
- Wilsnack R, Wilsnack S, Klassen A. Women's drinking and drinking problems: patterns from a 1981 national survey. *Am J Public Health* 1984;74:1231-8.
- Stampfer MJ, Colditz 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.
- Gaziano JM, Buring JR, Breslow JL, et al. Moderate alcohol intake, increased levels of high-density lipoprotein and its subfractions, and decreased risk of myocardial infarction. *N Engl J Med* 1993;329:1829-34.
- Rimm EB, Giovannucci EL, Willett WC, et al. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 1991;338:464-8.
- Klatsky AL, Armstrong MA, Friedman GD. Risk of cardiovascular mortality in alcohol drinkers, ex-drinkers and nondrinkers. *Am J Cardiol* 1990;66:1237-42.
- Alcohol and cancer. *Lancet* 1990;335:634-5.
- McGinnis JM, Foege WH. Actual causes of death in the United States. *JAMA* 1993;270:2207-12.

CORRECTION

Alcohol Consumption and Mortality among Women

Alcohol Consumption and Mortality among Women . On page 1248, in Table 2, the 95 percent confidence interval for death from injury with an external cause at an average alcohol intake of >30.0 g per day should have read, "0.61–1.94," not "1.61–1.94," as printed. We regret the error.