

The New England Journal of Medicine

© Copyright, 1997, by the Massachusetts Medical Society

VOLUME 337

DECEMBER 11, 1997

NUMBER 24



ALCOHOL CONSUMPTION AND MORTALITY AMONG MIDDLE-AGED AND ELDERLY U.S. ADULTS

MICHAEL J. THUN, M.D., RICHARD PETO, F.R.S., ALAN D. LOPEZ, PH.D., JANE H. MONACO, M.S., S. JANE HENLEY, B.A.,
CLARK W. HEATH, JR., M.D., AND RICHARD DOLL, F.R.S.

ABSTRACT

Background Alcohol consumption has both adverse and beneficial effects on survival. We examined the balance of these in a large prospective study of mortality among U.S. adults.

Methods Of 490,000 men and women (mean age, 56 years; range, 30 to 104) who reported their alcohol and tobacco use in 1982, 46,000 died during nine years of follow-up. We compared cause-specific death rates and rates of death from all causes across categories of base-line alcohol consumption, adjusting for other risk factors, and related drinking and smoking habits to the cumulative probability of dying between the ages of 35 and 69 years.

Results Causes of death associated with drinking were cirrhosis and alcoholism; cancers of the mouth, esophagus, pharynx, larynx, and liver combined; breast cancer in women; and injuries and other external causes in men. The mortality from breast cancer was 30 percent higher among women reporting at least one drink daily than among nondrinkers (relative risk, 1.3; 95 percent confidence interval, 1.1 to 1.6). The rates of death from all cardiovascular diseases were 30 to 40 percent lower among men (relative risk, 0.7; 95 percent confidence interval, 0.7 to 0.8) and women (relative risk, 0.6; 95 percent confidence interval, 0.6 to 0.7) reporting at least one drink daily than among nondrinkers, with little relation to the level of consumption. The overall death rates were lowest among men and women reporting about one drink daily. Mortality from all causes increased with heavier drinking, particularly among adults under age 60 with lower risk of cardiovascular disease. Alcohol consumption was associated with a small reduction in the overall risk of death in middle age (ages 35 to 69), whereas smoking approximately doubled this risk.

Conclusions In this middle-aged and elderly population, moderate alcohol consumption slightly reduced overall mortality. The benefit depended in part on age and background cardiovascular risk and was far smaller than the large increase in risk produced by tobacco. (N Engl J Med 1997;337:1705-14.)

©1997, Massachusetts Medical Society.

MEN and women who drink alcoholic beverages regularly have, in comparison with abstainers, higher death rates from injuries,^{1,2} violence,² suicide,² poisoning,³ cirrhosis,⁴ certain cancers,⁵ and possibly hemorrhagic stroke,^{6,7} but lower death rates from coronary heart disease and thrombotic stroke.⁸⁻²⁷ The net balance of risks and benefits is likely to differ in different age groups and populations. Examining this balance in a particular population requires large epidemiologic studies that have information on all causes of death and include sufficient numbers of people and deaths to estimate risks reliably within subgroups defined according to age, sex, and tobacco use.

We calculated death rates according to self-reported alcohol consumption in half a million U.S. adults 30 years old or older who provided information on alcohol consumption, smoking, and other behavior in 1982 and who were followed prospectively through 1991. We had three aims: to quantify the relation between drinking at base line and specific causes of death thought to be increased or decreased by the consumption of alcohol, while controlling for smoking^{5,13}; to determine how age, sex, and background risk of cardiovascular disease modify the relation of drinking to total mortality; and to compare alcohol and cigarette smoking as risk factors for death in middle age.

From Epidemiology and Surveillance Research, American Cancer Society, Atlanta (M.J.T., J.H.M., S.J.H., C.W.H.); the Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, Oxford, England (R.P., R.D.); and the Programme on Substance Abuse, World Health Organization, Geneva (A.D.L.). Address reprint requests to Dr. Thun at Epidemiology and Surveillance Research, American Cancer Society, 1599 Clifton Rd., NE, Atlanta, GA 30329-4251.

METHODS

Study Population

The Cancer Prevention Study II is a nationwide prospective mortality study of nearly 1.2 million U.S. adults, 30 years old or older, that was begun in 1982. At the request of an American Cancer Society volunteer, each enrollee completed a confidential, four-page mailed questionnaire on his or her alcohol and tobacco use, diet, and other factors potentially affecting mortality. The present analyses include approximately 490,000 people (251,420 women and 238,206 men) who at enrollment reported either not drinking or currently drinking alcohol and who provided complete information on smoking (Table 1).^{28,29} The mean age was 56 years (range, 30 to 104). Because the study subjects were recruited by American Cancer Society volunteers, they were also more likely than the general U.S. population to be college-educated, married, middle-class, and white (Table 2).²⁸

Deaths were ascertained from the month of enrollment until December 1991 through personal inquiries by the volunteers in September 1984, 1986, and 1988, and then through linkage with the National Death Index.³⁰ By September 1988, 2 percent of the subjects had been lost to follow-up and another 0.2 percent could not be followed further because data were insufficient for linkage. By 1991, 12 percent were known to have died. Death certificates were obtained for 98 percent, and from these the underlying cause of death was coded according to the *International Classification of Diseases, Ninth Revision* (ICD-9).³¹

Alcohol Consumption

Current alcohol consumption in 1982 was assessed by the question "How many cups, glasses, or drinks of these beverages do you usually drink a day, and for how many years?" Beer, wine, and spirits were assessed separately. People who reported changing their drinking habits in the past 10 years were asked about previous consumption. We defined as nondrinkers people who explicitly recorded zero for current consumption of any alcoholic beverage and zero or blank for previous drinking. We defined as "less than daily" drinkers those who reported drinking any alcoholic beverage less than daily but at least three times per week. People who reported drinking at least 1 drink a day were classified on the basis of the sum of their reported current consumption of

all three types of alcoholic beverages, from "1 daily" to "≥6 daily." People who indicated alcohol consumption but did not quantify it were excluded from the analyses, as were people for whom all questions about alcohol were left blank (Table 1). Consumption levels were grouped into three categories in analyses of specific causes of death and into five categories for broader combinations of causes. Each drink was assumed to contain, on average, 12 g of alcohol.

Stability of Alcohol Consumption

Of the 490,000 subjects, 98,000 also completed a more detailed dietary questionnaire in 1992 that included similar questions on alcohol. In this subgroup, 95 percent of the nondrinkers in 1982 continued to abstain or drink less often than twice weekly, and 78 percent of the current drinkers in 1982 remained within the same or an adjacent (usually lower) consumption category. Furthermore, among 47,000 people who were excluded from our analyses because of missing 1982 data but who responded in 1992, 82 percent reported drinking less often than weekly (suggesting that a blank 1982 answer usually, but not always, indicated no regular alcohol consumption).

Alcohol and Specific Causes of Death

We expected death rates from certain conditions to increase with alcohol consumption¹³: cirrhosis of the liver (ICD-9 code 571; grouped with 67 deaths from alcoholic psychosis and dependence, codes 291 and 303); alcohol-related cancers (those of the oral cavity, pharynx, esophagus, liver, and larynx, but excluding the salivary glands and nasopharynx; codes 141, 143, 144, 145, 146, 148, 149, 150, 155, and 161); accidents and other external causes (codes E800 to E999); and possibly breast cancer in women (code 174), cancer of the colon or rectum (codes 153 and 154),⁵ pneumonia (codes 480 to 487),¹³ and hemorrhagic stroke (codes 430 to 432). Decreased mortality was expected from coronary heart disease (codes 410 to 414), total stroke (codes 430 to 438), and possibly "other circulatory conditions" combined (codes 390 to 405, 415 to 429, and 449 to 459). No association was expected with all "other cancers" or "other causes of death."

The subjects who reported preexisting illness in 1982 were excluded from some analyses but not from others. No exclusions for

TABLE 1. NUMBERS OF SUBJECTS AND DEATHS IN THE ANALYSIS OF ALCOHOL CONSUMPTION IN THE CANCER PREVENTION STUDY II, 1982-1991.

VARIABLE	WOMEN		MEN	
	PERSONS	DEATHS	PERSONS	DEATHS
	number (percent)			
Total cohort	676,526 (100)	59,439 (100)	508,576 (100)	76,715 (100)
Exclusions				
Smoking unquantified*	44,790 (7)	6,039 (10)	20,955 (4)	5,209 (7)
Alcohol use unquantified†	107,170 (16)	9,056 (15)	90,645 (18)	14,643 (19)
Missing all data on beer, wine, and spirits	265,056 (39)	26,106 (44)	147,249 (29)	25,803 (34)
Former drinkers, now nondrinkers‡	8,090 (1)	790 (1)	11,521 (2)	2,183 (3)
Analytic cohort§	251,420 (37)	17,448 (29)	238,206 (47)	28,877 (38)

*Persons whose smoking status or amount or duration of smoking was unclassifiable were excluded.

†Persons whose amount or duration of drinking was unclassifiable were excluded.

‡These persons, who were currently nondrinkers but reported previous drinking, were excluded only from the reference group, except where specified.

§Another 32,203 persons with cancer or cirrhosis at the beginning of the study, and 7412 deaths among these persons, were excluded from the cause-specific analyses, but not from the analysis of deaths from all causes.

TABLE 2. DEMOGRAPHIC CHARACTERISTICS OF PERSONS IN THE CANCER PREVENTION STUDY II WHO IN 1982 REPORTED CURRENT ALCOHOL DRINKING, NO CURRENT DRINKING, OR NO INFORMATION ON ALCOHOL CONSUMPTION.

CHARACTERISTIC	WOMEN			MEN		
	CURRENT DRINKERS	LIFELONG NONDRINKERS	NO ALCOHOL INFORMATION*	CURRENT DRINKERS	LIFELONG NONDRINKERS	NO ALCOHOL INFORMATION*
Subjects — no. (%)	146,015 (28)	105,405 (20)	265,056 (51)	179,951 (47)	58,255 (15)	147,249 (38)
Age — yr						
Mean	54	56	58	56	58	59
Range	30–104	30–103	30–111	30–101	30–101	30–103
White race — %	96	94	92	96	95	94
Married — %	81	76	75	94	95	95
Education — %†						
≤Grade 12	32	46	53	27	37	45
>Grade 12	69	55	47	73	63	55
Occupation — %						
White collar	54	51	45	59	50	44
Blue collar	6	9	11	21	29	32
Housewife	28	29	31	—	—	—
Unknown	12	11	14	20	21	24
Employed — %	51	47	41	77	71	66
Religion — %						
Protestant	60	66	63	59	66	64
Catholic	31	19	22	29	13	18
Jewish	4	4	4	4	6	5
Other	6	11	11	8	15	14
Smoking status — %‡						
Never smoked	39	70	67	19	47	31
Former smoker	32	16	17	45	33	40
Current smoker	29	15	17	36	20	29
Vegetable intake — % in lowest quintile	13	19	24	18	20	26
Fat intake — % in highest quintile	23	24	19	22	24	20
Incomplete nutrition data — %	7	7	14	5	4	11
Mean body-mass index§	23.7	25.1	25.1	25.8	25.9	26.0
Any current aspirin use — %	69	63	58	61	58	54

*Questions on the consumption of beer, wine, and spirits at base line were left blank.

†Percentages may not total 100 because of rounding.

‡Percentages for men include pipe and cigar smoking.

§The body-mass index was calculated as the weight in kilograms divided by the square of the height in meters.

preexisting disease have been made in Tables 1 and 2 and Figures 1 and 2. In Tables 3, 4, and 5, people with cirrhosis or cancer (except nonmelanoma skin cancer) at base line have been excluded. The relation between drinking and mortality from coronary heart disease differed in subjects with and without prevalent vascular conditions (prior heart attack, hypertension, medications for these conditions, stroke, or diabetes mellitus), and the two are presented separately in Tables 3, 4, and 5.

Statistical Analysis

We estimated the relative risks and 95 percent confidence intervals by Cox proportional-hazards analyses,³² comparing mortality at each level of base-line drinking with that in abstainers, with adjustment for certain other risk factors. All models were stratified according to exact age at enrollment and race and were adjusted for education, body-mass index, smoking, a crude index of fat consumption,³³ and the use or nonuse of estrogen-replacement therapy in women. Analyses of mortality from cardiovascular causes were also adjusted for marital status, any current aspirin use (vs. none), current employment (yes or no), blue-collar employment (yes or no), and physical activity. Analyses of mortality from breast cancer controlled for family history of breast cancer

in mother or sister, total number of sisters, age at menarche, age at first birth, age at menopause, oral-contraceptive use or nonuse, and presence or absence of breast cysts. Analyses of deaths due to other cancers controlled for vegetable consumption.³³

Multivariate-adjusted death rates were then derived by multiplying the adjusted relative risk at each level of drinking by the age-standardized death rate in nondrinkers. Variances of the log relative risks were calculated,³⁴ and the square roots of these, multiplied by the corresponding death rates, gave the standard errors of those rates.

The probabilities of death between the ages of 35 and 69 years among drinkers and smokers were estimated as follows. First, we calculated the relative risk of death from all causes at these ages for six combinations of drinking (yes or no) and cigarette smoking (currently, formerly, or never) in our cohort. We then multiplied these rates by the proportion of the U.S. population in this category in 1990³⁵ and by a constant (representing the death rate among nondrinkers) so that the weighted average of the six rates equaled the U.S. death rate per 100,000 people 35 through 69 years old in 1990 for a uniform age distribution.³⁶ The corresponding probability of death at ages 35 to 69 then equaled $1 - \exp[-35(\text{death rate per } 100,000)]$.

TABLE 3. NUMBER OF DEATHS AND MULTIVARIATE-ADJUSTED DEATH RATES ACCORDING TO CAUSE OF DEATH AND ALCOHOL CONSUMPTION AMONG MEN.*

CAUSE OF DEATH†	ALCOHOL CONSUMPTION‡					P VALUE FOR TREND
	NONE (N=55,313)	LESS THAN DAILY (N=61,426)	1 DRINK/DAY (N=31,159)	2-3 DRINKS/DAY (N=46,775)	≥4 DRINKS/DAY (N=32,198)	
Conditions potentially worsened by alcohol						
Cirrhosis, alcoholism, or both						
Death rate	5.4±1.1	6.5±1.1	6.5±1.5	13.9±1.7	40.6±3.5	<0.001
Relative risk (95% CI)	1.0	1.2 (0.7-2.0)	1.2 (0.7-2.2)	2.6 (1.6-4.0)	7.5 (4.9-11.4)	
No. of deaths	28	38	19	67	151	
Injuries and external causes						
Death rate	50.8±3.5	48.4±3.1	48.7±4.4	51.3±3.7	66.7±5.1	0.02
Relative risk (95% CI)	1.0	1.0 (0.8-1.1)	1.0 (0.8-1.2)	1.0 (0.8-1.2)	1.3 (1.1-1.6)	
No. of deaths	255	236	123	195	181	
Alcohol-related cancers (mouth, esophagus, pharynx, larynx, and liver)						
Death rate	13.0±1.6	18.3±1.8	18.6±2.4	19.7±2.0	37.0±3.2	<0.001
Relative risk (95% CI)	1.0	1.4 (1.0-1.9)	1.4 (1.0-2.0)	1.5 (1.1-2.1)	2.8 (2.1-3.8)	
No. of deaths	69	106	58	101	144	
Colorectal cancer						
Death rate	39.6±3.0	42.9±2.9	40.6±3.9	44.4±3.3	48.7±4.3	0.10
Relative risk (95% CI)	1.0	1.0 (0.9-1.3)	1.0 (0.8-1.3)	1.1 (0.9-1.4)	1.2 (1.0-1.5)	
No. of deaths	211	216	111	182	131	
Cardiovascular conditions						
Coronary heart disease (no preexisting disease)§						
Death rate	210.0±9.8	181.9±8.1	162.1±10.4	152.3±8.2	176.2±10.8	<0.001
Relative risk (95% CI)	1.0	0.9 (0.8-1.0)	0.8 (0.7-0.9)	0.7 (0.6-0.8)	0.8 (0.7-1.0)	
No. of deaths	570	504	245	346	274	
Coronary heart disease (preexisting disease)¶						
Death rate	787.5±20.3	575.7±16.3	548.9±21.3	520.6±16.5	464.6±18.7	<0.001
Relative risk (95% CI)	1.0	0.7 (0.7-0.8)	0.7 (0.6-0.8)	0.7 (0.6-0.7)	0.6 (0.5-0.6)	
No. of deaths	1917	1259	669	1006	644	
Stroke						
Death rate	85.7±4.5	59.8±3.7	59.8±4.8	64.8±4.1	62.5±4.9	0.001
Relative risk (95% CI)	1.0	0.7 (0.6-0.8)	0.7 (0.6-0.8)	0.8 (0.6-0.9)	0.7 (0.6-0.9)	
No. of deaths	461	268	158	252	168	
Other circulatory disease						
Death rate	179.9±6.5	155.1±5.6	139.4±7.2	138.4±5.8	162.3±7.6	0.002
Relative risk (95% CI)	1.0	0.9 (0.8-1.0)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.9 (0.8-1.0)	
No. of deaths	958	761	381	579	477	
All cardiovascular disease						
Death rate	731.8±13.1	585.4±11.1	512.3±13.5	512.3±11.0	512.3±13.2	<0.001
Relative risk (95% CI)	1.0	0.8 (0.7-0.8)	0.7 (0.7-0.8)	0.7 (0.7-0.7)	0.7 (0.7-0.8)	
No. of deaths	3906	2792	1453	2183	1563	
Residual conditions						
All other cancers						
Death rate	280.0±7.9	261.6±6.9	265.2±9.3	284.2±7.6	312.5±9.5	0.002
Relative risk (95% CI)	1.0	0.9 (0.9-1.0)	0.9 (0.9-1.0)	1.0 (0.9-1.1)	1.1 (1.0-1.2)	
No. of deaths	1485	1463	818	1420	1126	
All other causes						
Death rate	260.7±7.8	195.5±6.5	198.4±8.5	211.4±7.2	234.9±9.2	0.004
Relative risk (95% CI)	1.0	0.8 (0.7-0.8)	0.8 (0.7-0.8)	0.8 (0.7-0.9)	0.9 (0.8-1.0)	
No. of deaths	1394	924	546	866	683	

*The total numbers of men (226,871) and deaths in men (25,244) shown in this table exclude 11,335 men with cancer or cirrhosis at base line and 3633 deaths in those men.

†The death rate (±SE) per 100,000 is shown. CI denotes confidence interval.

‡“Less than daily” alcohol consumption was defined as drinking three or more times per week but less than once per day. One drink was considered to be 12 g of alcohol.

§Values are based on 141,880 men who reported no heart disease, hypertension, use of medications for these, stroke, or diabetes at base line.

¶Values are based on 84,991 men who reported at least one of the above conditions at base line.

TABLE 4. NUMBER OF DEATHS AND MULTIVARIATE-ADJUSTED DEATH RATES ACCORDING TO CAUSE OF DEATH AND ALCOHOL CONSUMPTION AMONG WOMEN.*

CAUSE OF DEATH†	ALCOHOL CONSUMPTION‡					P VALUE FOR TREND
	NONE (N=96,784)	LESS THAN DAILY (N=66,415)	1 DRINK/DAY (N=25,304)	2-3 DRINKS/DAY (N=30,174)	≥4 DRINKS/DAY (N=11,875)	
Conditions potentially worsened by alcohol						
Cirrhosis, alcoholism, or both						
Death rate	5.0±0.9	4.3±0.9	7.7±1.9	10.4±1.9	23.9±4.5	
Relative risk (95% CI)	1.0	0.9 (0.5-1.4)	1.5 (0.8-2.8)	2.1 (1.3-3.4)	4.8 (2.9-7.9)	
No. of deaths	44	23	16	30	30	<0.001
Injuries and external causes						
Death rate	22.7±1.9	25.5±2.2	17.7±2.8	18.9±2.7	17.1±4.0	
Relative risk (95% CI)	1.0	1.1 (0.9-1.4)	0.8 (0.6-1.1)	0.8 (0.6-1.2)	0.8 (0.5-1.2)	
No. of deaths	208	138	40	51	18	0.07
Alcohol-related cancers (mouth, esophagus, pharynx, larynx, and liver)						
Death rate	4.8±0.9	5.3±1.0	3.9±1.2	7.1±1.4	14.3±3.2	
Relative risk (95% CI)	1.0	1.1 (0.7-1.8)	0.8 (0.4-1.6)	1.5 (0.9-2.5)	3.0 (1.7-5.3)	
No. of deaths	43	30	10	26	21	0.002
Colorectal cancer						
Death rate	33.7±2.5	27.3±2.4	19.4±3.1	30.9±3.6	24.8±5.1	
Relative risk (95% CI)	1.0	0.8 (0.7-1.0)	0.6 (0.4-0.8)	0.9 (0.7-1.2)	0.7 (0.5-1.1)	
No. of deaths	305	131	40	76	24	0.06
Breast cancer§						
Death rate	30.3±2.1	33.3±2.4	37.6±4.1	45.8±4.2	29.1±5.3	
Relative risk (95% CI)	1.0	1.1 (0.9-1.3)	1.2 (1.0-1.6)	1.5 (1.2-1.9)	1.0 (0.7-1.4)	
No. of deaths	269	188	83	121	30	0.02
Cardiovascular conditions						
Coronary heart disease (no preexisting disease)¶						
Death rate	78.5±5.4	62.7±5.2	59.7±7.4	67.0±7.0	68.0±11.5	
Relative risk (95% CI)	1.0	0.8 (0.7-1.0)	0.8 (0.6-1.0)	0.9 (0.7-1.1)	0.9 (0.6-1.2)	
No. of deaths	342	145	65	95	36	0.14
Coronary heart disease (preexisting disease)¶¶						
Death rate	276.2±10.1	200.5±10.8	156.3±13.2	170.7±13.0	159.6±19.1	
Relative risk (95% CI)	1.0	0.7 (0.6-0.8)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	
No. of deaths	1397	348	141	176	73	<0.001
Stroke						
Death rate	62.3±3.3	40.5±3.1	46.9±4.8	53.1±4.8	56.3±7.7	
Relative risk (95% CI)	1.0	0.7 (0.5-0.8)	0.8 (0.6-0.9)	0.9 (0.7-1.1)	0.9 (0.7-1.2)	
No. of deaths	627	168	96	126	55	0.08
Other circulatory disease						
Death rate	96.5±4.2	66.9±4.0	63.2±5.5	60.5±4.9	81.1±8.9	
Relative risk (95% CI)	1.0	0.7 (0.6-0.8)	0.7 (0.5-0.8)	0.6 (0.5-0.8)	0.8 (0.7-1.1)	
No. of deaths	970	282	133	156	86	<0.001
All cardiovascular disease						
Death rate	334.5±7.8	229.8±7.5	212.8±10.2	227.5±9.8	251.2±16.1	
Relative risk (95% CI)	1.0	0.7 (0.6-0.7)	0.6 (0.6-0.7)	0.7 (0.6-0.8)	0.8 (0.7-0.9)	
No. of deaths	3336	943	435	553	250	<0.001
Residual conditions						
All other cancer						
Death rate	156.0±5.1	135.4±4.9	153.7±7.8	155.8±6.8	173.5±11.2	
Relative risk (95% CI)	1.0	0.9 (0.8-1.0)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.1 (1.0-1.3)	
No. of deaths	1372	775	389	541	248	0.17
All other causes						
Death rate	158.6±5.3	120.2±5.3	134.8±8.0	119.9±6.8	154.2±12.0	
Relative risk (95% CI)	1.0	0.8 (0.7-0.8)	0.9 (0.7-1.0)	0.8 (0.7-0.9)	1.0 (0.8-1.1)	
No. of deaths	1534	528	284	316	170	0.004

*The total numbers of women (230,552) and deaths in women (13,669) shown in this table exclude 20,868 women with cancer or cirrhosis at base line and 3779 deaths in these women.

†The death rate (±SE) per 100,000 is shown. CI denotes confidence interval.

‡“Less than daily” alcohol consumption was defined as drinking three or more times per week but less than once per day. One drink was considered to be 12 g of alcohol.

§When the categories of one or more drinks daily were combined for stability, the rate of death from breast cancer was 39.7, the relative risk was 1.3 (95 percent confidence interval, 1.1 to 1.6), and the P value for trend was 0.006.

¶Values are based on 159,633 women who reported no heart disease, hypertension, use of medications for these, stroke, or diabetes at base line.

¶¶Values are based on 70,919 women who reported at least one of the above conditions at base line.

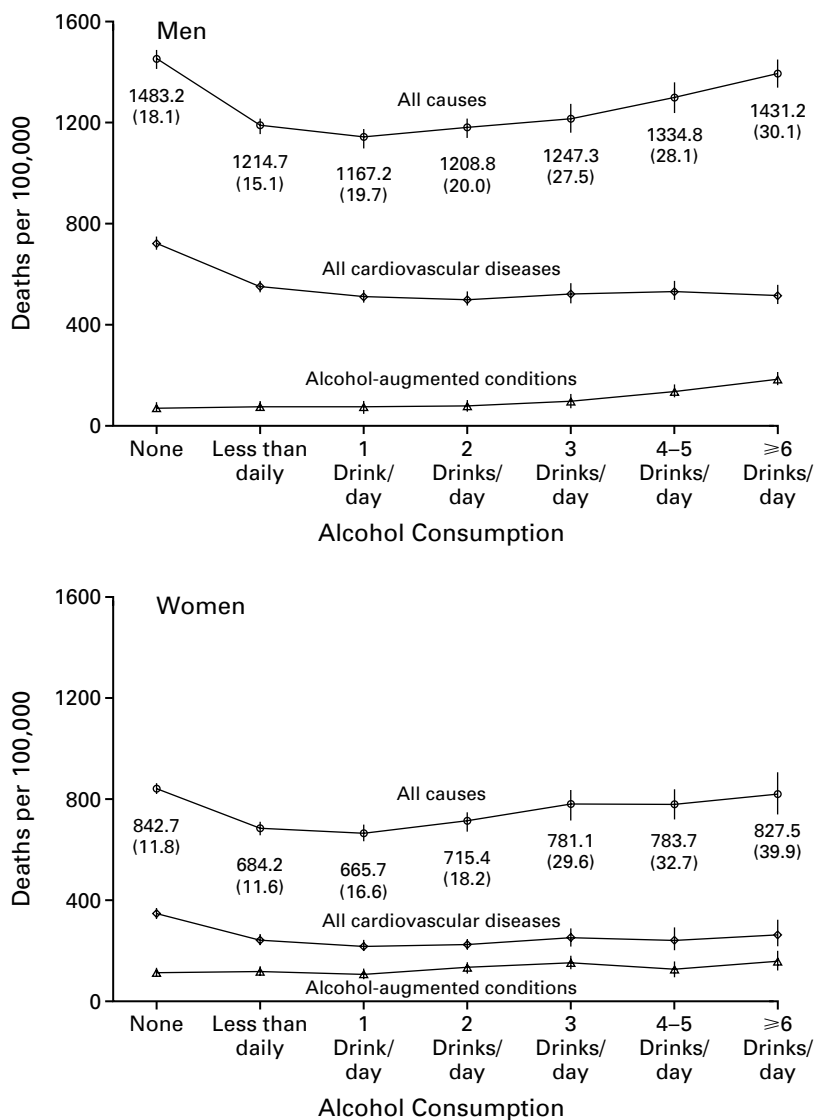


Figure 1. Rates of Death from All Causes, All Cardiovascular Diseases, and Alcohol-Augmented Conditions from 1982 to 1991, According to Base-Line Alcohol Consumption.

Alcohol-augmented conditions are cirrhosis and alcoholism, alcohol-related cancers, breast cancer in women, and injuries and other external causes. "Less than daily" alcohol consumption was defined as drinking three or more times per week but less than one drink per day. The numbers in parentheses are the standard errors of the rates of death from all causes.

RESULTS

Demographic Characteristics

As compared with nondrinkers, drinkers were more likely to smoke, to have graduated from high school, and to be Catholic (Table 2). Among the drinkers, the percentage who smoked cigarettes at the time of enrollment increased with the frequency of alcohol consumption, from 22 percent of men and women reporting less than one drink daily to 37 percent of those who consumed four or more drinks daily. The drinkers also reported eating more vege-

tables than did abstainers, but this may have been an artifact of more complete reporting of both beverage and food consumption by some subjects. People excluded from the alcohol analyses because of blank answers in 1982 resembled abstainers demographically but were somewhat older and less likely to have completed high school or to be employed (Table 2).

Specific Causes of Death

Alcohol consumption was associated with increased rates of death from cirrhosis and alcoholism and from cancers of the mouth, esophagus, pharynx,

TABLE 5. NUMBER OF DEATHS AND MULTIVARIATE-ADJUSTED DEATH RATES FROM ALL CAUSES AMONG MEN AND WOMEN ACCORDING TO BASE-LINE ALCOHOL CONSUMPTION, AGE, AND BACKGROUND RISK OF CARDIOVASCULAR DISEASE.

VARIABLE*	ALCOHOL CONSUMPTION†					
	NONE (N = 148,536)	LESS THAN DAILY (N = 127,082)	1 DRINK/DAY (N = 55,911)	2 DRINKS/DAY (N = 51,120)	3 DRINKS/DAY (N = 25,377)	≥4 DRINKS/DAY (N = 43,850)
Ages 30–59 yr						
Low cardiovascular risk‡						
No. of persons	69,499	69,588	28,693	25,219	12,443	20,850
Death rate	329.4±9.1	300.0±7.3	305.3±11.1	319.8±11.3	339.2±15.8	385.4±12.6
Relative risk (95% CI)	1.0	0.9 (0.8–1.0)	0.9 (0.8–1.0)	1.0 (0.9–1.1)	1.0 (0.9–1.1)	1.2 (1.1–1.3)
No. of deaths	1,641	1,725	766	805	467	989
High cardiovascular risk§						
No. of persons	27,179	22,430	9,111	9,328	5,222	10,197
Death rate	734.0±20.4	608.5±16.3	608.5±24.8	605.6±23.4	643.7±31.3	706.1±22.6
Relative risk (95% CI)	1.0	0.8 (0.8–0.9)	0.8 (0.8–0.9)	0.8 (0.8–0.9)	0.9 (0.8–1.0)	1.0 (0.9–1.0)
No. of deaths	1,700	1,399	604	674	428	1,036
Ages 60–79 yr						
Low cardiovascular risk‡						
No. of persons	24,877	19,318	9,979	8,829	3,932	6,409
Death rate	2052.9±45.1	1732.6±39.9	1666.9±52.1	1734.7±54.3	1835.3±80.9	2022.1±64.5
Relative risk (95% CI)	1.0	0.8 (0.8–0.9)	0.8 (0.8–0.9)	0.8 (0.8–0.9)	0.9 (0.8–1.0)	1.0 (0.9–1.1)
No. of deaths	2,840	1,914	1,031	1,028	520	1,017
High cardiovascular risk§						
No. of persons	26,981	15,746	8,128	7,744	3,780	6,394
Death rate	3783.9±59.4	3076.3±55.8	3019.6±73.4	3008.2±73.7	2985.5±102.5	2996.9±76.9
Relative risk (95% CI)	1.0	0.8 (0.8–0.9)	0.8 (0.8–0.8)	0.8 (0.8–0.8)	0.8 (0.7–0.9)	0.8 (0.7–0.8)
No. of deaths	6,084	3,064	1,708	1,676	856	1,579

*The death rate (±SE) per 100,000 is shown. CI denotes confidence interval.

†“Less than daily” alcohol consumption was defined as drinking three or more times per week but less than once per day. One drink was considered to be 12 g of alcohol.

‡Subjects with low cardiovascular risk reported no heart disease, hypertension, use of medications for these, stroke, or diabetes at base line.

§Subjects with high cardiovascular risk reported at least one of the above conditions at base line.

larynx, and liver combined (Tables 3 and 4). The death rates from these conditions were three to seven times as high among both men and women who reported at least four drinks daily as among nondrinkers. For men but not for women, mortality from external causes (mostly unintentional injuries and suicide) was 30 percent higher among those drinking at this level than among nondrinkers (relative risk, 1.3; 95 percent confidence interval, 1.1 to 1.6) (Table 3). The rate of death from breast cancer was 30 percent higher among women reporting at least one drink daily than among nondrinkers (relative risk, 1.3; 95 percent confidence interval, 1.1 to 1.6) (Table 4).

In contrast, the rates of death from all cardiovascular diseases combined were 30 to 40 percent lower among men (relative risk, 0.7; 95 percent confidence interval, 0.7 to 0.8) and women (relative risk, 0.6; 95 percent confidence interval, 0.6 to 0.7) reporting at least one drink daily than among nondrinkers. The largest reduction, in both absolute and relative terms, occurred in mortality from coronary heart disease among drinkers who, at enrollment, had reported heart disease, stroke, or some other indication of pre-existing risk of cardiovascular disease (Tables 3 and 4). This subgroup contained one third of all the people in the study but contributed nearly three quarters of all deaths from cardiovascular causes.

We found no consistent relation between alcohol consumption and rates of death from colorectal cancer (Tables 3 and 4), colon or rectal cancer separately, hemorrhagic stroke, pneumonia, or all respiratory diseases (data not shown). The death rates among subjects excluded from the analyses because of missing data on alcohol consumption, whose mortality patterns were consistent with most but not all of them being nondrinkers, are not shown.

Combined Causes of Death

Figure 1 illustrates how death rates from all alcohol-augmented conditions (cirrhosis and alcoholism, alcohol-related cancers, breast cancer in women, and external causes) compare, at various levels of drinking, with those from all cardiovascular diseases. Overall, cardiovascular causes accounted for 45 percent and 37 percent of all deaths among men and women, respectively, whereas the alcohol-augmented conditions accounted for 7 percent of all deaths among men and 15 percent among women. The percentage of deaths due to cardiovascular diseases decreased as alcohol consumption increased.

The rates of death from all causes were lowest among both men and women who reported one drink daily; the rates were about 20 percent below those of nondrinkers (Fig. 1). Above one drink per

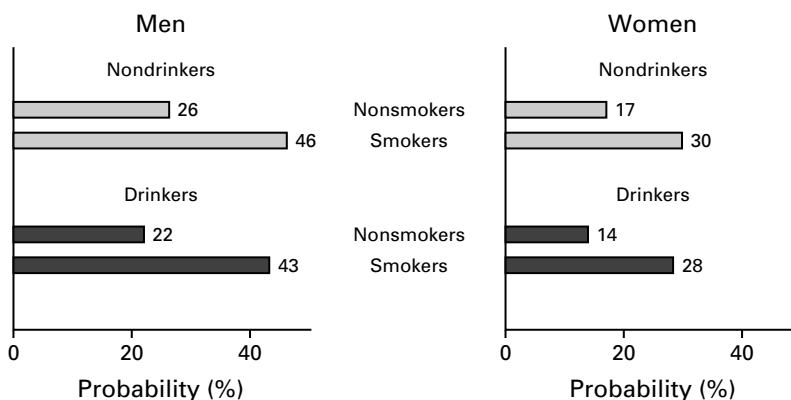


Figure 2. Estimated Probability of Death from Any Cause in the General U.S. Population from 35 to 69 Years of Age for Four Combinations of Alcohol Consumption and Smoking.

The probabilities projected for the general U.S. population are based on relative risks calculated in this study, combined with prevalence and mortality data for the U.S. population in 1990. They reflect the smoking of approximately one pack of cigarettes per day by smokers and consumption of approximately one to two drinks per day by those who reported drinking alcohol in 1982.

day, the overall death rate among drinkers increased, although the shape of the dose–response relation with alcohol consumption varied substantially in different subgroups of the population.

Table 5 illustrates how age and background risk of cardiovascular disease influence the relation between drinking and mortality from all causes. For men and women 30 to 59 years old who were at low risk for cardiovascular disease, the rates of death from all causes among those reporting four or more daily drinks exceeded the rates among nondrinkers (J-shaped pattern). In the two subgroups at intermediate risk for cardiovascular disease (30 to 59 years old with cardiovascular risk factors and 60 to 79 years old without cardiovascular risk factors), the rates of death from all causes among persons reporting four or more drinks daily nearly equaled those of nondrinkers (U-shaped pattern). In the subgroup at highest risk for cardiovascular disease (60 to 79 years old with preexisting risk factors), the rates of death from all causes among drinkers remained significantly below those among nondrinkers, even for subjects reporting four or more drinks daily (L-shaped pattern).

In Figure 1, which includes people of all ages, with or without cardiovascular risk factors, the U-shaped relation between alcohol consumption and mortality from all causes represents the average dose–response relation in the study population. Although most of the 20 percent reduction in rates of death from all causes among daily drinkers was attributable to lower mortality from cardiovascular causes, other nonneoplastic conditions, which are classified with “other causes” of death in Tables 3 and 4, also contributed. Similarly, although most of the increase in the overall death rates associated with heavier drink-

ing arose from the conditions we designated as alcohol-augmented, some resulted from “all other cancers” and “all other causes” (Tables 3 and 4).

Comparison between Alcohol and Tobacco

Continued smoking approximately doubled the risk of death between the ages of 35 and 69, whereas moderate alcohol consumption was associated with a small reduction in risk (Fig. 2). Thus, for death in middle age, the benefits of moderate alcohol consumption are much smaller than the hazards of tobacco use.

DISCUSSION

This prospective study of 490,000 people and 46,000 deaths has three main findings about alcohol consumption and mortality from all causes. First, those who consumed up to one or two drinks of alcohol daily had lower overall mortality rates than nondrinkers. Similar findings have been reported previously.^{10,13,22} An important caveat is that the subjects in all these studies were largely middle-aged and elderly middle-class people. These studies excluded or underrepresented certain high-risk groups, such as adolescents, young adults, binge drinkers or very heavy drinkers, members of groups with lower socioeconomic status, and population groups in which deaths from accidents, violence, and other external causes outnumber deaths from cardiovascular causes.

Second, the balance of adverse and beneficial effects of drinking on mortality from all causes depends not only on the amount of alcohol consumed but also on age and background cardiovascular risk. In most subgroups, the rates of death from all causes were lowest among people who reported one drink

of alcohol daily. With heavier consumption, the rate of death from all causes followed a J-, U-, or L-shaped pattern in subgroups at low, intermediate, or high risk of cardiovascular disease, respectively (Table 5). The J-shaped configuration that we observed among low-risk men and women 30 to 59 years old is similar to the pattern reported among men 40 to 59 years old in a previous American Cancer Society study.¹⁰ Differences in age and background risk of cardiovascular disease can help explain apparent inconsistencies among previous epidemiologic studies with respect to mortality from all causes at higher levels of drinking. Because overall death rates are a weighted average of the rates for specific causes of death, the relative importance of alcohol-augmented (mostly injury-related) deaths as compared with deaths from cardiovascular disease influences the relation between alcohol consumption and total mortality. At one extreme are men 18 to 29 years old, an age group not included in our study. A study of Swedish military recruits found a linear increase in rates of death from all causes (mostly from accidents, violence, and suicide) with greater alcohol consumption.² Among U.S. men 15 to 29 years old, deaths from injuries and other external causes predominate, accounting for 75 percent of all deaths, as compared with 4 percent from cardiovascular conditions.³⁵ The reverse is true among men 60 or more, for whom external causes account for 3 percent of deaths and circulatory conditions for over 45 percent.

Our third point is that drinking alcohol does not compensate for the large increase in risk produced by smoking. Whereas moderate alcohol consumption slightly reduces the risk of death between the ages of 35 and 69 years, cigarette smoking approximately doubles this risk. The analyses in Figure 2 adjust for the higher prevalence and intensity of smoking among drinkers, but not for the slightly heavier drinking by smokers than by nonsmokers. Furthermore, such calculations consider only mortality and disregard consequences to people other than the drinker. Nevertheless, despite the catastrophic harm that alcohol can cause,³ Figure 2 illustrates the more usual slight protective effects of moderate alcohol consumption on mortality among middle-aged and elderly adults.

The strengths of this study include its large size, the ability to control for tobacco smoking, the exclusion of former drinkers from the reference group (which minimized bias due to cessation because of illness caused by alcohol), and the availability of the responses to a repeated questionnaire that helped to assess the stability of drinking behavior in this population. Its limitations include the difficulty of quantifying alcohol consumption by self-report, the low prevalence of heavy drinking, the lack of information on sporadic binge drinking (and hence on its

hazards), and the exclusion of those who left the alcohol questions blank in 1982. (Few of these people, however, were heavy drinkers whose exclusion might have biased our results, given their demographic characteristics and mortality and the infrequency of regular drinking among those who completed the second questionnaire in 1992.)

An unexpected finding was the lower mortality among drinkers than among nondrinkers from the aggregate of the causes we had originally postulated would be unrelated to drinking. A similar reduction was found in a study of British doctors.¹³ This reduction, which was more evident among men than among women, needs further investigation.

Several consensus groups^{37,38} have concluded that moderate alcohol consumption reduces the overall risk of cardiovascular disease, but it is not known how long moderate alcohol consumption must continue for this benefit to occur. Alcohol consumption beginning in middle age might suffice, while averting much of the risk of accidents and cancer associated with drinking. However, many factors influence alcohol consumption besides knowledge of the potential health hazards or benefits for the drinker, and the implications of the present findings for social policy are beyond the scope of this paper.

The authors alone are responsible for the views expressed in this article.

We are indebted to Ms. Audrey Earles for preparing many drafts of the manuscript, and to Drs. Peter Anderson and Neil Collishaw for their review and comments.

REFERENCES

1. Update: alcohol-related traffic crashes and fatalities among youth and young adults — United States, 1982–1994. *MMWR Morb Mortal Wkly Rep* 1995;44:869-74.
2. Andreasson S, Allebeck P, Romelsjö A. Alcohol and mortality among young men: longitudinal study of Swedish conscripts. *BMJ* 1988;296:1021-5.
3. Anderson P. Alcohol and risk of physical harm. In: Holder HD, Edwards G, eds. *Alcohol: evidence and issues*. Oxford, England: Oxford University Press, 1995:82-113.
4. Norton R, Batey R, Dwyer T, MacMahon S. Alcohol consumption and the risk of alcohol related cirrhosis in women. *BMJ* 1987;295:80-2.
5. IARC monographs on the evaluation of carcinogenic risks to humans. Vol. 44. *Alcohol drinking*. Lyon, France: International Agency for Research on Cancer, 1988.
6. Donahue RP, Abbott RD, Reed DM, Yano K. Alcohol and hemorrhagic stroke: the Honolulu Heart Program. *JAMA* 1986;255:2311-4.
7. Klatsky AL, Armstrong MA, Friedman GD. Alcohol use and subsequent cerebrovascular disease hospitalizations. *Stroke* 1989;20:741-6.
8. Stampfer MJ, Colditz GA, Willett WG, 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.
9. 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.
10. Boffetta P, Garfinkel L. Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. *Epidemiology* 1990;1:342-8.
11. Camacho TC, Kaplan GA, Cohen RD. Alcohol consumption and mortality in Alameda County. *J Chronic Dis* 1987;40:229-36.
12. 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.

13. 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.
14. 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.
15. Friedman LA, Kimball AW. Coronary heart disease mortality and alcohol consumption in Framingham. *Am J Epidemiol* 1986;124:481-9.
16. Fuchs CS, Stampfer MJ, Colditz GA, et al. Alcohol consumption and mortality among women. *N Engl J Med* 1995;332:1245-50. [Erratum, *N Engl J Med* 1997;336:523.]
17. Gaziano JM, Buring JE, 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.
18. Gordon T, Doyle JT. Drinking and mortality: the Albany Study. *Am J Epidemiol* 1987;125:263-70.
19. Klatsky AL, Armstrong MA, Friedman GD. Risk of cardiovascular mortality in alcohol drinkers, ex-drinkers and nondrinkers. *Am J Cardiol* 1990;66:1237-42.
20. *Idem*. Alcohol and mortality. *Ann Intern Med* 1992;117:646-54.
21. 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.
22. Marmot MG, Rose G, Shipley MJ, Thomas BJ. Alcohol and mortality: a U-shaped curve. *Lancet* 1981;1:580-3.
23. Miller GJ, Beckles GLA, Maude GH, Carson DC. Alcohol consumption: protection against coronary heart disease and risks to health. *Int J Epidemiol* 1990;19:923-30.
24. 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.
25. Salonen JT, Puska P, Nissinen A. Intake of spirits and beer and risk of myocardial infarction and death — a longitudinal study in Eastern Finland. *J Chronic Dis* 1983;36:533-43.
26. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men: explaining the U-shaped curve. *Lancet* 1988;2:1267-73.
27. Klatsky AL, Armstrong MA, Friedman GD. Red wine, white wine, liquor, beer, and risk for coronary artery disease hospitalization. *Am J Cardiol* 1997;80:416-20.
28. Garfinkel L. Selection, follow-up, and analysis in the American Cancer Society prospective studies. In: Selection, follow-up, and analysis in prospective studies: a workshop. National Cancer Institute monograph 67. Washington, D.C.: Government Printing Office, 1985:49-52. (NIH publication no. 85-2713.)
29. Thun MJ, Namboodiri MM, Heath CW Jr. Aspirin use and reduced risk of fatal colon cancer. *N Engl J Med* 1991;325:1593-6.
30. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. *Am J Epidemiol* 1993;137:235-41.
31. International classification of diseases: manual of the international statistical classification of diseases, injuries, and causes of death: based on recommendations of the Ninth Revision Conference, 1975, and adopted by the Twenty-ninth World Health Assembly. Geneva: World Health Organization, 1977-1978.
32. Cox DR. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187-220.
33. Thun MJ, Calle EE, Namboodiri MM, et al. Risk factors for fatal colon cancer in a large prospective study. *J Natl Cancer Inst* 1992;84:1491-500.
34. Easton DF, Peto J, Babiker AG. Floating absolute risk: an alternative to relative risk in survival and case-control analysis avoiding an arbitrary reference group. *Stat Med* 1991;10:1025-35.
35. National Center for Health Statistics, Schoenborn CA, Marano M. Current estimates from the National Health Interview Survey: United States, 1987. Vital and health statistics. Series 10. No. 166. Washington, D.C.: Government Printing Office, 1988. (DHHS publication no. (PHS) 88-1594.)
36. Table 1-27: deaths from 282 selected causes, by 5-year age groups, race, and sex: United States, 1990. In: National Center for Health Statistics. Vital statistics of the United States, 1990. Vol. 2. Mortality. Part A. Washington, D.C.: Government Printing Office, 1994:312-71. (DHHS publication no. (PHS) 95-1101.)
37. Krauss RM, Deckelbaum RJ, Ernst N, et al. Dietary guidelines for healthy American adults: a statement for health professionals from the Nutrition Committee, American Heart Association. *Circulation* 1996;94:1795-800.
38. Dietary Guidelines Advisory Committee, Agricultural Research Service. Report of the Dietary Guidelines Advisory Committee on the dietary guidelines for Americans, 1995, to the Secretary of Health and Human Services and the Secretary of Agriculture. Washington, D.C.: National Technical Information Service, 1995. (NTIS publication no. PB 96 104 344.)