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Alcohol Consumption and the Risk of Hypertension in Women and Men

Howard D. Sesso, Nancy R. Cook, Julie E. Buring, JoAnn E. Manson, J. Michael Gaziano

Abstract—Heavy alcohol intake increases the risk of hypertension, but the relationship between light-to-moderate alcohol consumption and incident hypertension remains controversial. We prospectively followed 28 848 women from the Women's Health Study and 13 455 men from the Physicians' Health Study free of baseline hypertension, cardiovascular disease, and cancer. Self-reported lifestyle and clinical risk factors were collected. In women, total alcohol intake was summed from liquor, red wine, white wine, and beer; men reported total alcohol intake from a single combined question. During 10.9 and 21.8 years of follow-up, 8680 women and 6012 men developed hypertension (defined as new physician diagnosis, antihypertensive treatment, reported systolic blood pressure ≥ 140 mm Hg, or diastolic blood pressure ≥ 90 mm Hg). In women, we found a J-shaped association between alcohol intake and hypertension in age- and lifestyle-adjusted models. Adding potential intermediates (body mass index, diabetes, and high cholesterol) attenuated the benefits of alcohol in the light-to-moderate range and strengthened the adverse effects of heavy alcohol intake. Beverage-specific relative risks paralleled those for total alcohol intake. In men, alcohol intake was positively and significantly associated with the risk of hypertension and persisted after multivariate adjustment. Models stratified by baseline systolic blood pressure (< 120 versus ≥ 120 mm Hg) or diastolic blood pressure (< 75 versus ≥ 75 mm Hg) did not alter the relative risks in women and men. In conclusion, light-to-moderate alcohol consumption decreased hypertension risk in women and increased risk in men. The threshold above which alcohol became deleterious for hypertension risk emerged at ≥ 4 drinks per day in women versus a moderate level of ≥ 1 drink per day in men. (*Hypertension*. 2008;51:1080-1087.)

Key Words: alcohol ■ hypertension ■ blood pressure ■ prospective study ■ men ■ women

Considerable evidence supports an association between excessive alcohol intake and an increased risk of hypertension.¹⁻³ This association persists regardless of beverage type,⁴ implicating ethanol in this etiologic process, although few studies have compared beverage types.^{5,6} A meta-analysis of randomized clinical trials among subjects initially consuming 3 to 6 drinks per day found that reductions in alcohol intake significantly decreased both systolic and diastolic blood pressure (BP; SBP and DBP, respectively).⁷ Clinically meaningful BP reductions occur within weeks after reductions in alcohol intake among hypertensive subjects,⁸ but few data exist among normotensive individuals.

Clinical guidelines on the primary prevention of hypertension recommend limiting alcohol intake ≤ 2 drinks per day in men and ≤ 1 drink per day in women.^{9,10} However, uncertainty remains regarding any benefits or risks attributable to light-to-moderate alcohol intake on the risk of hypertension. Conflicting studies have noted beneficial,⁶ unassociated,^{2,3,5,11} and deleterious^{12,13} effects on the risk of hyperten-

sion or elevations in BP. Additional data on the relative merits of overall or beverage-specific alcohol intake with hypertension risk may clarify any role of alcohol in hypertension prevention. Therefore, we examined the association between alcohol intake and the risk of developing hypertension in 2 large prospective cohorts of women and men.

Methods

Study Populations

The Women's Health Study (WHS) is a recently completed trial of aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer.^{14,15} In 1992, a total of 39 876 female US health professionals aged ≥ 45 years who were postmenopausal or not intending to become pregnant and free from previous myocardial infarction (MI), stroke, transient ischemic attack, and cancer (except nonmelanoma skin cancer) were enrolled. The Physicians' Health Study (PHS) is a completed trial of aspirin and β -carotene in the primary prevention of cardiovascular disease and cancer.¹⁶ In 1982, 22 071 US male physicians, aged 40 to 84 years of age and free from similar diseases as the WHS, were enrolled.

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Data Collection

On the baseline questionnaire in WHS, women responded to a question on their average consumption of 4 different beverages over the past year, including beer (1 glass, bottle, or can), red wine (4-oz glass), white wine (4-oz glass), and liquor (1 drink or shot). Nine possible responses (never or <1 per month, 1 to 3 per month, 1 per week, 2 to 4 per week, 5 to 6 per week, 1 per day, 2 to 3 per day, 4 to 5 per day, and ≥ 6 per day) were converted into the beverage-specific number of alcoholic drinks consumed weekly (0.0, 0.5, 1.0, 3.0, 5.5, 7.0, 18.0, 32.0, or 46.0 drinks per week, respectively) and then summed for total alcohol consumption and categorized as above. At baseline in PHS, subjects reported current alcohol intake by responding to a question on how often they consumed alcoholic beverages, without regard to the amount of alcohol consumption for each episode. As done previously in the PHS,¹⁷ we interpreted these responses as the number of drinks consumed in the specified time period, converting 7 response categories (rarely or never, 1 to 3 per month, 1 per week, 2 to 4 per week, 5 to 6 per week, daily, and ≥ 2 per day) to the number of alcoholic drinks consumed weekly (0.0, 0.5, 1.0, 3.0, 5.5, 7.0, and 18.0 drinks per week, respectively). Self-reported alcohol intake has been found to be reliable and valid in health professionals^{18,19} and other populations.²⁰

Men also provided self-reports of baseline risk factors including age, smoking, parental history of MI before age 60 years, vigorous exercise, BP and hypertension, history of high cholesterol (treatment, diagnosis, or total cholesterol ≥ 240 mg/dL), and diabetes mellitus. Body mass index (BMI; in kilograms per meter squared) was calculated from height and weight. Women provided baseline information on the above variables plus postmenopausal status and postmenopausal hormone use.

Among 39 876 randomly assigned WHS participants, we excluded women with no data on alcohol consumption or those with prerandomization revascularization or angina. Women with baseline hypertension, defined as self-reported past or current antihypertensive treatment, SBP ≥ 140 mm Hg, or DBP ≥ 90 mm Hg at study entry, were also excluded, resulting in a study population of 28 848 women. A similar set of exclusions in PHS reduced the study population from 22 071 to 13 455 men.

Outcome Ascertainment

Incident cases of hypertension in WHS must meet ≥ 1 of 4 criteria: (1) self-report of a new physician diagnosis on follow-up questionnaires at years 1, 3, or annually thereafter; (2) self-report of newly initiated antihypertensive treatment at years 1, 3, or 4; (3) self-reported SBP ≥ 140 mm Hg; or (4) self-reported DBP ≥ 90 mm Hg. Women reporting physician-diagnosed hypertension also provided the month and year of diagnosis. A missing date for a physician diagnosis or hypertension defined by another criterion was assigned a date of incident hypertension by selecting a random date between the current and previous annual questionnaire. Those developing major concomitant diseases that may impact BP, including MI, stroke, or revascularization, during follow-up and before the potential development of hypertension were censored at the date of antecedent disease and not considered to have developed hypertension. Based on this definition, there were 8680 women who developed hypertension during a median follow-up of 9.8 years (maximum follow-up: 10.9 years).

Follow-up in PHS was accomplished using similar methods, with minor differences. Incident cases of hypertension in PHS met ≥ 1 of 3 criteria: (1) self-report of newly initiated antihypertensive treatment at years 2, 7, or annually thereafter; (2) self-reported SBP ≥ 140 mm Hg; or (3) self-reported DBP ≥ 90 mm Hg. If the date of incident hypertension was missing, it was randomly assigned between the current and previous annual questionnaire. Concomitant diseases during follow-up that may impact BP were censored as done for WHS. As a result, 6012 men developed hypertension during a median follow-up of 17.0 years (maximum follow-up: 21.8 years).

Hypertension Validation

We assessed the accuracy of self-reported incident hypertension in WHS and PHS by randomly choosing 50 initially normotensive

subjects who recently reported a new hypertension diagnosis (WHS women) or antihypertensive treatment (PHS men). We also randomly selected 50 women in WHS and 50 men in PHS who never reported a hypertension diagnosis, antihypertensive medication use, SBP ≥ 140 , or DBP ≥ 90 mm Hg. In standardized telephone interviews, we found that 96% of women and 90% of men verified the details of their self-reported hypertension. In addition, $\geq 90\%$ of WHS and 92% of PHS participants reporting no hypertension throughout decades of follow-up verified their normotensive status. Because hypertension status can be accurately determined from self-reports, we believe that any misclassification would only slightly bias our risk estimates for hypertension.

Data Analyses

Separate analyses were done for women and men. Participants were examined by categories of total alcohol intake using ANCOVA to compare mean values or χ^2 tests to compare proportions of baseline risk factors. Cox proportional hazards models estimated the relative risk (RR) and 95% CI of developing hypertension. We examined age-adjusted models, then adjusted for BMI, smoking status, exercise, and parental history of MI. Additional covariates in models for men included aspirin and β -carotene treatment and for women included aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use. Linear trend tests included the median level for each alcohol category as an ordinal variable. We assessed potential deviations from linearity across alcohol intake categories by adding a squared trend variable to a model already with the ordinal trend variable and conducting likelihood ratio tests.

In secondary analyses, we examined whether adjustment for variables potentially on the causal pathway (diabetes and history of high cholesterol) altered the findings. Models also considered whether any association between alcohol intake and hypertension was independent of baseline BP. Finally, time-varying models updated alcohol data from the 4-year and 7-year follow-up questionnaires in women and men, respectively, in multivariate models.

Gender-specific stratified models assessed how alcohol and hypertension differed by baseline SBP (<120 and 120 to 139 mm Hg) and DBP (<75 and 75 to 89 mm Hg). Because the ordinal DBP categories in WHS included 75 to 84 and 85 to 89 mm Hg, not perfectly replicating the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure categorization, we chose consistent BP strata for women and men. Finally, we tested the interaction among alcohol intake (ordinal variable), BP (dichotomized), and the risk of hypertension.

Results

Overall, a greater proportion (43%) of women reported rarely or never consuming alcohol compared with men (15.2%). A greater proportion of men consumed light-to-moderate amounts of alcohol, ranging from 1 drink per month to 1 drink per day, compared with women. In women, for whom beverage-specific information was collected, the majority of alcohol intake was from white (39.0%) and red (16.3%) wine, followed by liquor (26.3%) and beer (18.4%) intake. Individual beverage types were modestly correlated with one another, with Spearman correlation coefficients ranging from 0.25 to 0.42.

In Table 1, we examined differences in baseline characteristics according to levels of alcohol consumption among 28 848 women and 13 455 men. In men, there was a possible J-shaped relation between alcohol intake and age. BMI demonstrated a modest inverse association with increasing alcohol intake among women and men. Subjects in the highest levels of alcohol intake had SBP and DBP levels that were ≈ 2 and 1 mm Hg higher, respectively. Among other

Table 1. Baseline Characteristics According to Categories of Total Alcohol Consumption in 28 848 Women and 13 455 Men

Baseline Characteristics	Baseline Level of Total Alcohol Consumption, No. of Drinks								
	Rarely or Never	1 to 3 per Month	1 per Week	2 to 4 per Week	5 to 6 per Week	1 per Day	2 to 3 per Day	4 to 5 per Day	≥6 per Day
Women, n (%)	12 408 (43.0)	4444 (15.4)	3784 (13.1)	3772 (13.1)	1485 (5.2)	1897 (6.6)	956 (3.3)	102 (0.4)	
Age, mean (SD), y	53.9 (6.7)	53.3 (6.4)	53.0 (6.1)	53.6 (6.4)	53.7 (6.4)	54.4 (6.9)	55.0 (6.9)	54.1 (6.3)	
BMI, mean (SD), kg/m ²	25.8 (4.9)	25.2 (4.4)	25.2 (4.3)	24.5 (3.8)	24.2 (3.7)	23.8 (3.4)	23.8 (3.5)	24.1 (3.5)	
SBP, mean (SD), mm Hg	118.8 (9.6)	118.2 (9.5)	118.2 (9.5)	118.1 (9.2)	118.1 (9.2)	118.3 (9.4)	119.9 (9.5)	120.6 (9.1)	
DBP, mean (SD), mm Hg	74.2 (7.6)	73.8 (7.6)	74.0 (7.6)	73.8 (7.6)	73.9 (7.6)	74.1 (7.6)	75.0 (7.5)	75.4 (7.6)	
High cholesterol, %*	26.7	25.2	22.4	22.8	20.1	23.9	24.7	24.5	
Diabetes, %	2.1	1.1	0.6	0.5	0.7	0.6	0.4	0.0	
Parental history of MI <60 y, %	12.4	12.2	13.0	12.7	12.2	12.2	12.5	8.0	
Smoking status, %									
Never	60.1	50.9	49.8	43.2	37.8	32.6	27.0	11.8	
Former	26.6	36.4	39.8	44.2	48.3	52.5	48.9	52.9	
Current <15 cigarettes/d	4.7	4.6	4.4	5.4	6.0	6.3	6.9	10.8	
Current ≥15 cigarettes/d	8.6	8.1	6.1	7.2	7.9	8.6	17.2	24.5	
Exercise, %									
None	41.0	35.6	30.3	30.0	29.8	31.3	36.9	55.9	
<2 times per week	30.0	30.7	32.9	31.9	25.9	28.2	26.7	15.7	
≥2 times per week	29.0	33.7	36.8	38.1	44.3	40.6	36.4	28.4	
Postmenopausal, %	52.1	48.9	46.8	50.0	49.3	54.6	57.6	50.0	
Hormone replacement, %									
Never	51.5	52.7	51.6	50.0	48.7	47.9	48.8	58.4	
Past	9.2	7.4	7.1	6.6	8.4	6.7	8.7	5.9	
Current	39.3	39.9	41.4	43.5	42.9	45.4	42.5	35.6	
Men, n (%)	2039 (15.2)	1536 (11.4)	1980 (14.7)	3186 (23.7)	1713 (12.7)	2675 (19.9)	326 (2.4)		
Age, mean (SD), y	52.8 (9.3)	50.4 (8.8)	50.5 (8.5)	50.9 (8.3)	51.6 (8.7)	53.8 (9.3)	54.2 (9.2)		
BMI, mean (SD), kg/m ²	24.6 (2.7)	24.7 (2.8)	24.7 (2.8)	24.5 (2.5)	24.4 (2.4)	24.2 (2.4)	24.4 (2.6)		
SBP, mean (SD), mm Hg	121.0 (9.0)	121.3 (8.6)	121.5 (8.3)	121.4 (8.4)	122.0 (8.6)	122.4 (8.3)	122.8 (7.9)		
DBP, mean (SD), mm Hg	76.1 (6.6)	76.4 (6.4)	76.5 (6.1)	76.3 (6.4)	76.7 (6.3)	76.9 (6.2)	76.9 (6.5)		
High cholesterol, %*	10.0	9.6	11.2	11.0	11.6	13.0	13.5		
Diabetes, %	2.5	2.3	1.8	0.9	0.9	2.0	0.9		
Parental history of MI <60 y, %	8.2	8.3	9.6	10.7	10.3	9.3	6.9		
Smoking status, %									
Never	69.5	57.6	57.0	51.7	44.9	38.6	28.0		
Former	22.6	30.8	34.0	38.9	44.8	47.3	52.6		
Current <20 cigarettes/d	2.2	3.0	2.6	3.2	3.7	3.8	3.1		
Current ≥20 cigarettes/d	5.8	8.6	6.4	6.2	6.5	10.2	16.3		
Exercise, %									
None	15.1	15.4	12.6	8.7	9.2	11.8	16.4		
<2 times per week	30.7	35.9	33.1	32.0	30.9	30.0	29.0		
≥2 times per week	54.2	48.7	54.3	59.3	60.0	58.3	54.6		

*High cholesterol is defined as having either any history of cholesterol-lowering treatment, a physician diagnosis, or self-reported total cholesterol ≥240 mg/dL.

baseline characteristics, those consuming more alcohol tended to be current or former smokers.

There were 8680 women and 6012 men who developed hypertension during a median (maximum) follow-up of 9.8 (10.9) and 17.0 (21.8) years, respectively. We examined total alcohol consumption and the risk of developing hypertension

in Table 2. Light-to-moderate alcohol consumption from 1 drink per month to 1 drink per day was associated with significant 8% to 21% reductions in the risk of hypertension. Additional adjustment for BMI, diabetes, and history of high cholesterol attenuated these risk reductions, largely because of BMI, with a nadir remaining at 5 to 6 drinks per week (RR:

Table 2. Association Between Baseline Total Alcohol Intake and Risk of Developing Hypertension in Women and Men

Model	Total Alcohol Intake, No. of Drinks					
	Rarely or Never	1 to 3 per Month	1 per Week	2 to 4 per Week	5 to 6 per Week	1 per Day
Women	3984*	1316	1092	1032	386	533
Age-adjusted RR (95% CI)	1.00 (ref)	0.92 (0.86 to 0.98)	0.90 (0.85 to 0.97)	0.83 (0.78 to 0.89)	0.77 (0.70 to 0.86)	0.84 (0.77 to 0.92)
Multivariate RR (95% CI)†	1.00 (ref)	0.92 (0.86 to 0.99)	0.92 (0.86 to 0.99)	0.85 (0.79 to 0.91)	0.79 (0.71 to 0.89)	0.83 (0.76 to 0.92)
Multivariate RR (95% CI)‡	1.00 (ref)	0.98 (0.91 to 1.05)	0.98 (0.91 to 1.06)	0.95 (0.88 to 1.03)	0.90 (0.80 to 1.00)	0.96 (0.87 to 1.06)
Men	852*	679	866	1,362	786	1,311
Age-adjusted RR (95% CI)	1.00 (ref)	1.12 (1.01 to 1.23)	1.10 (1.00 to 1.20)	1.04 (0.95 to 1.13)	1.14 (1.03 to 1.25)	1.24 (1.13 to 1.35)
Multivariate RR (95% CI)†	1.00 (ref)	1.10 (0.99 to 1.22)	1.08 (0.98 to 1.19)	1.02 (0.93 to 1.11)	1.10 (1.00 to 1.22)	1.19 (1.09 to 1.31)
Multivariate RR (95% CI)‡	1.00 (ref)	1.11 (1.00 to 1.23)	1.07 (0.97 to 1.18)	1.03 (0.94 to 1.12)	1.15 (1.04 to 1.27)	1.26 (1.15 to 1.37)

(Continued)

ref indicates reference.

*Cases of incident hypertension.

†Adjusted for age (in years), exercise (none, <2 times per week, ≥2 times per week), and parental history of MI <60 years (no or yes). Additional covariates for men included aspirin and β-carotene treatment and smoking status (never, former, current <20 cigarettes per day, or current ≥20 cigarettes per day); for women they included aspirin, α-carotene, and vitamin E treatment, postmenopausal status (never, former, or current), smoking status (never, former, current <15 cigarettes per day, or current ≥15 cigarettes per day), and hormone replacement therapy (never, former, or current).

‡Adjusted for the covariates above plus BMI (in kilograms per meter squared), history of high cholesterol (no or yes), and history of diabetes mellitus (no or yes).

0.90; 95% CI: 0.80 to 1.00) and a significant increased risk when consuming ≥4 drinks per day. This apparent J-shaped association between alcohol and hypertension in women significantly deviated from linearity (ordinal trend versus 7 indicator variables for alcohol [6 degrees of freedom]; $P < 0.001$); adding a squared trend variable was also significant ($P < 0.001$). In men, we found a strong positive association between higher alcohol consumption and an increased risk of developing hypertension (P for trend < 0.001 for all of the models), with no evidence of benefit in the light-to-moderate drinking. The RRs of hypertension did not remain significantly elevated in men until total alcohol consumption exceeded 5 drinks per week.

Secondary analyses tested the strength of the associations observed in Table 2. Models that additionally adjusted for baseline BP altered the RRs of hypertension in women, but a J-shaped association remained with a significant 15% reduction in hypertension risk for women consuming 5 to 6 drinks per week and a significant 54% increase in hypertension risk for women consuming ≥4 drinks per day. Adding baseline BP to the multivariate model in men reduced RRs, but a significant positive linear trend ($P = 0.001$) remained. Next, adjustment for various dietary factors in women only minimally altered the multivariate RRs of hypertension. Finally, excluding subjects with baseline diabetes, hypercholesterolemia, or a BMI ≥30 kg/m² resulted in nearly identical RRs. Because alcohol consumption may change over time, we updated alcohol intake at 4- and 7-year of follow-up in women and men, respectively, for the risk of hypertension. In women, significant 15% and 65% increased risks of hypertension occurred at 2 to 3 and ≥4 drinks per day, respectively, as compared with women reporting little or no alcohol intake. In men, the significant positive linear trend of RRs remained when updating alcohol at 7-year follow-up.

In the Figure, beer, red wine, and white wine each had a significant reduction in the risk of hypertension between 2 and 7 drinks per week. However, drinking ≥2 drinks per week of beer, liquor, and white wine resulted in significant or borderline significant elevations in hypertension risk, suggesting a J-shaped association paralleling that for total alcohol consumption. Adjustment for total alcohol intake modestly attenuated the RRs and maintained the finding that heavy intake of individual alcohol beverages was associated with incident hypertension.

Finally, in Table 3 we considered whether the association between alcohol and hypertension differed in subjects with low or high baseline SBP or DBP levels. Overall, there were no significant interactions (all P s for interaction > 0.05) between alcohol intake and either SBP (<120 and 120 to 139 mm Hg) or DBP (<75 and 75 to 89 mm Hg) with the risk of hypertension in women and men. We also examined effect modification by baseline BMI (normal, overweight, and obese subjects, as defined by the World Health Organization²¹), noting a borderline significant interaction in women ($P = 0.02$) but not men. Overweight and obese women had lower risks of developing hypertension for light-to-moderate alcohol consumption, whereas normal-weight women had a significant increased risk (RR: 2.45) of hypertension when consuming ≥4 drinks per day.

Discussion

We found that the association between light-to-moderate alcohol intake and the risk of developing hypertension differed in women and men and confirmed that heavy alcohol intake increases hypertension risk.²² In women, we found a possible J-shaped association in which light-to-moderate alcohol consumption modestly lowered hypertension risk, whereas heavier consumption of ≥4 drinks per day significantly increased hypertension risk. This association largely

Table 2. Continued

Total Alcohol Intake, No. of Drinks			P for Trend
2 to 3 per Day	4 to 5 per Day	≥6 per Day	
293	44		
0.92 (0.82 to 1.03)	1.53 (1.13 to 2.05)		0.041
0.92 (0.81 to 1.05)	1.51 (1.11 to 2.04)		0.11
1.10 (0.97 to 1.25)	1.84 (1.36 to 2.48)		0.026
156			
	1.27 (1.07 to 1.50)		<0.0001
	1.23 (1.03 to 1.46)		0.0003
	1.29 (1.08 to 1.53)		<0.0001

persisted when we considered specific types of alcoholic beverages. In men, using a slightly different assessment of alcohol intake, there were no benefits of light-to-moderate alcohol consumption. We instead found a consistent and strong positive linear trend in which a significant increased risk of hypertension began at just 5 drinks per week. None of our reported associations were affected in analyses stratified by baseline BP levels.

There is consistent evidence that alcohol consumption of ≥2 drinks per day increases BP and the long-term risk of

developing hypertension in men and women.²³ In 1 meta-analysis of subjects consuming ≥1 drink per day, typically as liquor, there were corresponding 2.7 and 1.4 mm Hg increases in SBP and DBP.²⁴ For alcohol consumption >2 drinks per day, BP levels rose by 5 mm Hg.²⁵ Conversely, a pooled analysis by Xin et al⁷ found that 67% reductions in alcohol consumption among those consuming 3 to 6 drinks per day reduced SBP and DBP by 3.3 and 2.0 mm Hg, respectively.

Of greater debate is whether light-to-moderate alcohol consumption up to 2 drinks per day beneficially or deleteriously affects hypertension risk. In men, light-to-moderate alcohol consumption was simply part of a strong, positive, linear association between increasing alcohol consumption and risk of hypertension, as corroborated in Japanese^{12,13,26} cohorts. In the Atherosclerosis Risk in Communities cohort, white men consuming 1 to 209 g/wk (<14 drinks per week) had a nonsignificant 12% reduction in hypertension risk.² In contrast, in women we found a J-shaped association between increasing alcohol intake and hypertension, with the nadir in risk within the range of light-to-moderate intake at 5 to 6 drinks per week. Comparatively, in the Nurse's Health Study and Nurse's Health Study II, the corresponding nadirs in risk were 1 drink per day⁵ and 0.25 to 0.50 drinks per day.⁶ In white and black women drinking 1 to 209 g/wk (<14 drinks per week), there was a small but nonsignificant reduction in incident hypertension compared with nondrinkers.² In Japa-

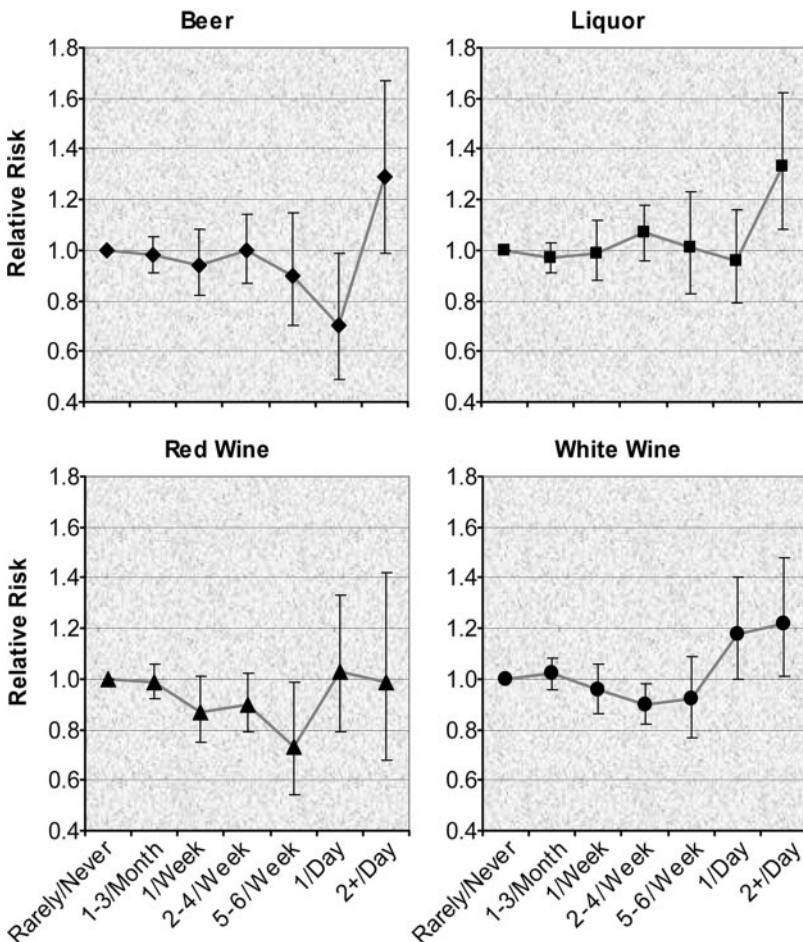


Figure. A comparison of the associations among beer, liquor, red, and white wine intake and the multivariate risk of developing hypertension in women, adjusting for age (in years), smoking status (never, former, current <15 cigarettes per day, or current ≥15 cigarettes per day), exercise (none, <2 times per week, or ≥2 times per week), and parental history of MI <60 years (no or yes), aspirin, β-carotene and vitamin E treatment, postmenopausal status (never, former, or current), hormone replacement therapy (never, former, or current), body mass index (in kilograms per meter squared), history of high cholesterol (no or yes), and history of diabetes mellitus (no or yes).

Table 3. Multivariate RRs (95% CIs) of Developing Hypertension According to Baseline Total Alcohol Intake, Stratified by Baseline SBP and DBP in Women and Men

Blood Pressure Category	Total Alcohol Intake, No. of Drinks					
	Rarely or Never	1 to 3 per Month	1 per Week	2 to 4 per Week	5 to 6 per Week	1 per Day
Women, RR (95% CI)*						
SBP (<i>P</i> interaction=0.39)						
<120 mm Hg	1.00 (ref)	0.99 (0.88 to 1.11)	0.87 (0.76 to 0.99)	0.96 (0.85 to 1.09)	0.88 (0.73 to 1.07)	0.98 (0.83 to 1.16)
120 to 139 mm Hg	1.00 (ref)	0.98 (0.90 to 1.06)	1.05 (0.96 to 1.14)	0.93 (0.85 to 1.02)	0.87 (0.76 to 1.00)	0.93 (0.82 to 1.05)
DBP (<i>P</i> interaction=0.40)						
<75 mm Hg	1.00 (ref)	0.93 (0.82 to 1.04)	0.91 (0.80 to 1.03)	0.87 (0.76 to 0.99)	0.80 (0.66 to 0.98)	0.87 (0.73 to 1.04)
75 to 89 mm Hg	1.00 (ref)	1.00 (0.92 to 1.08)	0.98 (0.90 to 1.07)	0.95 (0.87 to 1.04)	0.90 (0.79 to 1.04)	0.94 (0.83 to 1.06)
Men, RR (95% CI)†						
SBP (<i>P</i> interaction=0.25)						
<120 mm Hg	1.00 (ref)	0.96 (0.76 to 1.21)	1.11 (0.89 to 1.38)	1.05 (0.86 to 1.27)	1.05 (0.84 to 1.33)	1.03 (0.84 to 1.27)
120 to 139 mm Hg	1.00 (ref)	1.13 (1.01 to 1.27)	1.02 (0.92 to 1.13)	0.99 (0.90 to 1.09)	1.12 (1.01 to 1.25)	1.24 (1.13 to 1.37)
DBP (<i>P</i> interaction=0.13)						
<75 mm Hg	1.00 (ref)	1.03 (0.83 to 1.27)	1.19 (0.98 to 1.44)	1.05 (0.89 to 1.25)	1.13 (0.92 to 1.38)	1.27 (1.07 to 1.52)
75 to 89 mm Hg	1.00 (ref)	1.11 (0.99 to 1.25)	1.01 (0.90 to 1.12)	1.01 (0.91 to 1.12)	1.13 (1.01 to 1.26)	1.21 (1.09 to 1.34)

(Continued)

Data were adjusted for age (in years), exercise (none, <2 times per week, or ≥2 times per week), parental history of MI <60 years (no or yes), BMI (in kilograms per meter squared), history of high cholesterol (no or yes), and history of diabetes mellitus (no or yes). Additional covariates for men included aspirin and β-carotene treatment, and smoking status (never, former, current <20 cigarettes per day, or current ≥20 cigarettes per day); for women the covariates included aspirin, β-carotene, and vitamin E treatment, postmenopausal status (never, former, or current), smoking status (never, former, current <15 cigarettes per day, or current ≥15 cigarettes per day), and hormone replacement therapy (never, former, or current).

*No. of hypertension cases/No. of women in each blood pressure category includes 2865/16 681 for SBP <120 mm Hg, 5815/12 167 for SBP 120 to 139 mm Hg, 2826/15 313 for DBP <75 mm Hg, and 5854/13 535 for DBP 75 to 89 mm Hg.

†No. of hypertension cases/No. of men in each blood pressure category includes 1075/3770 for SBP <120 mm Hg, 4937/9685 for SBP 120 to 139 mm Hg, 1481/4569 for DBP <75 mm Hg, and 4531/8886 for DBP 75 to 89 mm Hg.

nese women, alcohol has been positively associated with hypertension risk.¹²

Therefore, does light-to-moderate alcohol consumption reduce hypertension risk? The mechanisms underlying any inverse association between light-to-moderate alcohol consumption and hypertension may differ from those for coronary heart disease, because only women appeared to benefit with a reduction in hypertension risk. In men, light-to-moderate alcohol intake was associated with both greater BP levels; in women, alcohol intake of 1 drink per month to 1 drink per day was associated with lower BP levels than nondrinkers. Although light-to-moderate alcohol intake may reduce hypertension risk via favorable changes in high-density lipoprotein cholesterol and other hemostatic factors,²⁷ this mechanism would not appear to differ and explain our discrepant results in women and men. Alternatively, differences in the pattern of drinking, beverage choices, and lifestyle and dietary correlates of light-to-moderate alcohol consumption may account for our observed gender differences.

Clinical guidelines for the primary prevention of hypertension consistently limit alcohol consumption to <2 drinks per day in men and <1 drink per day in women.^{9,10} These long-standing recommendations, respecting the protective effect of light-to-moderate alcohol intake on coronary heart disease,²⁸ persist, although light-to-moderate alcohol con-

sumption within the recommended range may increase BP levels and hypertension risk.¹⁰

Another important consideration is the type and pattern of alcohol consumption. Among women, we found no appreciable differences for wine, beer, or liquor and risk of hypertension. A crossover study in 24 normotensive men found that red wine and beer raised BP to a similar extent, whereas dealcoholized red wine did not impact BP.²⁹ The timing of alcohol consumption relative to meals may also matter,³⁰ although such data were not collected in our cohorts. Those drinking even lightly to moderately outside of meals are more likely to have hypertension.¹¹ Subjects in the present study were not explicitly asked about how many drinks they may have at 1 time, although binge drinking may be an important factor when considering the association among alcohol intake, BP, and risk of hypertension.³¹ Binge drinking also increases ambulatory SBP and DBP by 5 mm Hg during the time of intoxication.²⁵

Heavy alcohol intake increases BP and the risk of hypertension through several potential mechanisms, such as directly influencing the heart or the vascular smooth muscle or stimulating the sympathetic nervous system or the renin-angiotensin-aldosterone system. Alcohol may increase plasma cortisol levels through magnesium loss into the urine, by an increase in endothelin release, or by a decrease in NO production in the arterial endothelium.^{32,33}

Table 3. Continued

Baseline Level of Total Alcohol Consumption, No. of Drinks			
2 to 3 per Day	4 to 5 per Day	≥6 per Day	P for Trend
1.17 (0.94 to 1.47)	1.74 (0.98 to 3.07)		0.09
0.92 (0.79 to 1.08)	1.55 (1.09 to 2.22)		0.59
1.13 (0.90 to 1.41)	2.16 (1.29 to 3.60)		0.22
0.95 (0.82 to 1.11)	1.45 (1.00 to 2.11)		0.83
	1.24 (0.80 to 1.92)		0.47
	1.21 (1.00 to 1.46)		<0.0001
	1.71 (1.23 to 2.38)		0.0004
	1.12 (0.91 to 1.37)		0.002

Among potential limitations, self-reported alcohol intake has been reliably reported in health professionals similar to WHS and PHS.^{18,19} Any alcohol misclassification is likely random, biasing our RRs toward the null, although differential underreporting may occur among moderate drinkers.³⁴ We lacked beverage-specific intake in men, yet the effects of alcohol are driven by its ethanol content.³⁵ Summing 4 individual alcoholic beverages may explain why proportionately more women drank heavily than men. We also lacked details on drinking patterns and could not differentiate a subject consuming 1 drink each day from 7 drinks 1 day per week.

Among men in PHS, we asked about frequency and not about the amount of alcohol consumed, which may underestimate the amount of alcohol intake, particularly in higher intake categories. Any resulting misclassification would lower the nadir of any alcohol-associated risk of hypertension than the true nadir. However, because we only observed a positive association between alcohol and hypertension in men, with no nadir in risk, this potential misclassification should be minimal. Yet, data from PHS on alcohol and coronary heart disease¹⁷ had a nadir in risk consistent with the broader literature.

Next, we used self-reported incident hypertension. However, self-reported BP in physicians is highly correlated with measured SBP ($r=0.72$) and DBP ($r=0.60$).³⁶ We also conducted a confirmation study of 100 WHS and 100 PHS subjects, including 50 hypertensive subjects and 50 subjects remaining normotensive as identified from recent follow-up questionnaires for each cohort. The presence of self-reported hypertension was highly confirmed in WHS (96%) and PHS (92%), along with the absence of hypertension in participants not reporting hypertension in WHS (90%) and PHS (92%),³⁷ consistent with similar cohorts.³⁸ Finally, subjects in WHS

and PHS represent initially healthy health professionals with relatively low levels of alcohol consumption, so these results may not be generalizable to those with heavier alcohol consumption.

Perspectives

We confirmed that heavier alcohol consumption exceeding 2 drinks per day increased the risk of developing hypertension in both women and men. Detailed categorization of alcohol intake within the light-to-moderate range allowed us to precisely characterize where any reduction in hypertension risk may exist in women versus men. Surprisingly, we found discrepant results for light-to-moderate alcohol intake, as women had a potential reduced risk of hypertension and men had an increased risk of hypertension. We must better understand how light-to-moderate alcohol intake impacts BP and hypertension risk in women and men to determine whether light-to-moderate alcohol intake should be more strongly encouraged in hypertension prevention guidelines, while emphasizing the importance of individual recommendations that balance the complexity of the metabolic, physiological, and psychological effects of alcohol.³⁹

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Disclosures

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