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Alcohol Consumption and Functional Outcome after Stroke in Men

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Abstract

Background and Purpose—Light-to-moderate alcohol consumption has been associated with reduced risk of total and ischemic stroke. However, data on the relationship between alcohol consumption and functional outcomes from stroke is sparse.

Method—Prospective cohort study among 21,862 men enrolled in the Physicians' Health Study who provided information on alcohol consumption at baseline, had no prior history of stroke or transient ischemic attack (TIA). Alcohol consumption was divided into five categories: <1 drink/week, 1 drink/week, 2–4 drinks/week, 5–6 drinks/week and ≥ 1 drink/day. Possible functional outcomes included TIA, modified Rankin Scale (MRS)=0–1, MRS=2–3, and MRS=4–6. We used multinomial logistic regression to evaluate the relationship between levels of alcohol consumption and functional outcomes from stroke.

Results—During a mean of 21.6 years of follow-up, 767 TIAs and 1393 strokes (1157 ischemic, 222 hemorrhagic and 14 unknown type) occurred. Men who consumed 1 drink/week had lowest

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Conflicts on Interest Disclosures

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associated odds for any outcome. Compared with men who did not experience a TIA or stroke and who consumed <1 drink/week, men who consumed 1 drink/week had odds ratio (95% confidence interval) for total stroke of 0.85 (0.60–1.21) for MRS=0–1, 0.84 (0.64–1.10) for MRS=2–3, and 0.60 (0.37–0.97) for MRS=4–6. The OR for TIA was 0.95 (0.73–1.22). The pattern of association did not substantially differ for ischemic and hemorrhagic stroke. Higher alcohol consumption showed no association with functional outcome after stroke.

Conclusions—Our data do not show strong associations between alcohol consumption and functional outcome after stroke. Modest beneficial associations exist with low alcohol consumption.

Keywords

Stroke; epidemiology; alcohol; men

Stroke is one of the leading causes of disability and death worldwide and is expected to become a more prevalent cause of disability in the future due to the aging population.^{1,2} Several behavior dependent risk factors for stroke are established. While single risk factors, such as smoking, were the target of earlier prevention campaigns, efforts to reduce stroke morbidity and mortality now often aim to influence individuals towards a more “healthy lifestyle.” This approach is based on studies that found that the risk of total and ischemic stroke was significantly decreased with an increasing healthy lifestyle index score.^{3,4} Such an index is composed of behavior dependent lifestyle factors, such as smoking, physical activity and includes alcohol consumption. Studies evaluating the single relationship between alcohol consumption and risk of stroke showed J-shaped associations between risk of total stroke and alcohol consumption.^{3,4} A meta-analysis found that consuming less than one drink per day was associated with a significantly reduced risk of stroke compared to non-drinkers.⁵ Consumption of more than five drinks per day was associated with a significantly increased risk of stroke compared to non-drinkers. A previous analysis in the Physicians’ Health Study (PHS) showed that men who consumed two to four alcoholic drinks per week had the lowest risk of total and ischemic stroke compared to men who consumed less than one alcoholic drink per week after an average of 12.2 years of follow-up.⁶ Data on the association of alcohol consumption on functional outcome from stroke, however, are sparse. A few studies have examined factors that affect stroke morbidity, but none of focused specifically on the association between alcohol consumption and short-term outcomes from stroke.^{7,8} Due to the large projected morbidity burden of stroke, finding factors that may reduce stroke morbidity is becoming increasingly important. In this study, we aimed to evaluate the relationship between alcohol consumption and risk of functional outcomes upon hospital discharge after stroke.

Methods

The PHS was a randomized primary prevention trial of the effect of low-dose aspirin on cardiovascular disease and the effect of beta-carotene on the risk of cancer. The design, methods, and results have been previously described.^{9,10} In brief, 22,071 US male physicians between the ages of 40 and 84 in 1982 who were free of a history of stroke, transient ischemic attack (TIA), myocardial infarction, and other major diseases were randomly assigned to receive aspirin, beta carotene, both active agents or both placebos. After the end of the aspirin component in 1988 and the beta carotene component in 1995, the men continued to be followed either on an observational basis or as part of Physicians Health Study II.^{11, 12} This analysis included data available as of March 2008. Morbidity and mortality follow-up is >99%. Informed consent was obtained from all participants and the institutional review board at Brigham and Women’s Hospital approved the PHS.

Assessment of Exposure

Information on demographic and lifestyle characteristics and medical history was collected in yearly questionnaires. At baseline the participating physicians answered the question “How often do you usually consume alcoholic beverages (beer, wine, or liquor)?” The possible response categories were rarely or never, one to three per month, one per week, two to four per week, five or six per week, one per day, or two or more alcoholic drinks per day.¹³ To be consistent with a previous study of alcohol consumption and risk of stroke in the PHS cohort, we combined the alcohol consumption categories of rarely or never and one to three drinks per month to create one larger reference category. Additionally, we a priori combined the categories of one drink per day and two or more drinks per day to create one category (≥ 1 /day) according to previous categorization in the PHS.⁶

Assessment of Outcome

Every six months for the first year and annually thereafter, participants were sent a follow-up questionnaire asking about any newly diagnosed medical conditions, including stroke and TIA. For all reported trial outcomes events, permission was asked to review medical records. An endpoints committee of physicians confirmed all trial outcomes. A nonfatal stroke was defined as a focal neurological deficit with sudden or rapid onset attributable to a cerebrovascular event that lasted more than 24 hours. A TIA was defined as a focal-neurological deficit with sudden or rapid onset attributable to a cerebrovascular event that lasted less than 24 hours. If family members or postal authorities reported that the participant had died, the death was verified by reviewing all available medical records, death certificates, and eyewitness accounts. Stroke cases were further classified as ischemic, hemorrhagic or unknown type with high interobserver agreement.¹⁴ Medical record information was also used to determine the functional outcome from the stroke according to the modified Rankin scale (MRS). The MRS is a six-point scale (0=no symptoms at all; 1=no significant disability despite symptoms; 2=slight disability; 3=moderate disability; 4=moderately severe disability; 5=severe disability; 6=death).¹⁵ To avoid problems with model convergence due to sparse data, we a priori categorized the MRS score into three levels (0–1, 2–3, 4–6).¹⁷ The possible functional outcomes were no stroke, TIA, and the three categories of the MRS. In the event that a participant experienced multiple strokes and/or TIAs, the only first event was used in our analysis.

Statistical Analysis

We excluded participants who were missing information on alcohol consumption ($n=194$), had missing MRS scores ($n=2$), or reported a stroke or TIA prior to receiving the baseline questionnaire ($n=9$), leaving a total of 21,862 men for this analysis.

We used Cox proportional hazards models to calculate the relative risk of TIA and total, ischemic, and hemorrhagic stroke for each level of alcohol consumption using the category of less than one drink per week as the reference. We tested the assumption of proportional hazards by including an interaction term between the log transformation of time on study and alcohol consumption category and found no significant violation.

We used multinomial logistic regression to evaluate the relationship between levels of alcohol consumption and functional outcomes from stroke. Multinomial logistic regression is an extension of binary logistic regression that allows the dependent variable to have more than two categories. Each category is then simultaneously compared to a reference category. We calculated odds ratios of each functional outcome according to level of alcohol consumption from the multinomial logistic regression model, using men in the less than one drink per week category who did not experience a stroke or TIA as the reference group. For the analyses examining the relationship between alcohol consumption and functional outcome after hemorrhagic stroke, TIA was not included as a potential outcome.

We distinguished two multivariable models for both our risk of stroke and functional outcomes from stroke analyses. The first model controlled for age, randomized treatment assignments, systolic blood pressure, smoking, body mass index, exercise, history of diabetes, current treatment for hypertension, and history of migraine, variables that we believed could be confounders based on plausible biological mechanisms. In a second model, we included variables that are potential intermediates on the causal pathway between alcohol consumption and functional outcome from stroke. These variables were diastolic blood pressure, history of hypertension, history of high cholesterol, and cholesterol medication use.

Finally, we examined whether age, cigarette use, obesity, history of hypertension, or randomized assignment to aspirin modified the relationship between alcohol consumption and risk of total stroke or functional outcomes from total stroke by including an interaction term between alcohol consumption and each variable in separate models.

For all models, we included an indicator variable for variables that had >100 missing (exercise, migraine history, history of hypertension, hypertension medication use, history of high cholesterol and cholesterol medication use). We created a separate category for those missing information on systolic and diastolic blood pressure. Less than 100 men were missing information on history of diabetes, smoking and body mass index and were assigned to no history of diabetes, past smoking and the mean body mass index respectively in our analysis. All statistical analyses were performed using SAS 9.1 (Cary, NC). All p-values are two-tailed and we considered $p < 0.05$ as statistically significant.

Results

Table 1 summarizes the baseline characteristics of the 21,862 participants according to categories of alcohol consumption. Men who drank one or more alcoholic drinks per day were slightly older and were more likely to have a history of hypertension than the men in the other categories of alcohol consumption. The percentage of men who were never smokers decreased with increasing alcohol intake. The percentage of men with a history of migraine or diabetes was highest in among the men who drank less than one alcoholic drink per week.

Risk of Stroke

During a mean of 21.6 years of follow-up (473,053 person years) a total of 767 TIAs and 1393 strokes (1157 ischemic strokes, 222 hemorrhagic strokes and 14 strokes of unknown type) occurred. Table 2 shows the relative risk of total, ischemic, and hemorrhagic stroke and TIA by level of alcohol consumption. Compared to the less than one drink per week category, the lowest risk of total, ischemic and hemorrhagic stroke was observed for the one drink per week category. Only the decrease in total stroke risk among men who consumed one drink per week compared to less than one drink per week reached statistical significance (relative risk = 0.80, 95% CI: 0.66, 0.97; $p = 0.03$). No level of alcohol consumption resulted in a statistically significant increased risk of TIA or ischemic or hemorrhagic stroke. Adjusting for potential intermediates had very little impact on our results (results not shown). Stratified analyses to test as to whether age, cigarette use, obesity, history of hypertension, and randomized assignment to aspirin modified the relationship between alcohol consumption and risk of total stroke did not show any significant interaction between these variables and alcohol consumption (all $p > 0.05$).

Functional Outcomes from Stroke

The association of alcohol consumption with functional outcomes from stroke after adjusting for possible confounders is summarized in Table 3. Men who consumed one drink per week had lowest associated risk for any of the outcomes. With regard to total stroke, compared with

men who did not experience a TIA or stroke and who consumed less than one drink per week, men who consumed one drink per week had a relative risk (95% CI) 0.85 (0.60–1.21) for MRS=0–1, 0.84 (0.64–1.10) for MRS=2–3, and 0.60 (0.37–0.97) for MRS=4–6. Higher alcohol consumption showed no association with functional outcome after stroke. Using less than one drink per week as the reference group, no level of increased alcohol consumption resulted in a statistically significant increase or decrease in the risk of TIA compared to the reference group (relative risk (95% confidence interval) of 0.95 (0.73, 1.22) for 1 drink/week, 1.07 (0.86, 1.33) for two-four drinks per week, 0.98 (0.75, 1.27) for five-six drinks per week and 1.16 (0.95, 1.41) for one or more drinks per day). Adjusting for possible intermediates had very little impact on our results (results not shown).

The pattern of association with the MRS was similar for ischemic stroke (Table 3). No clear pattern was observed between alcohol consumption and functional outcomes from hemorrhagic stroke (Table 3).

We found no significant effect modification between age, cigarette use, obesity, history of hypertension, or randomized assignment to aspirin on the relationship between alcohol consumption and functional outcomes from total stroke (all $P > 0.10$).

Discussion

Data from this large, prospective cohort study in men do not support a strong association between alcohol consumption and functional outcome after stroke. Our data suggest lowest risks of incident TIA and total, ischemic or hemorrhagic stroke among men who consume one alcohol drink per week. However, this decrease in risk only reached statistical significance for total stroke. When examining the relationship between alcohol consumption and short-term functional outcomes after stroke, most of the categories of alcohol consumption did not show a statistically significant association with functional outcomes after stroke. Only men who consumed one drink per week had a significantly decreased risk of having an MRS score of 4–6 (i.e., the most severely affected group) as compared with men who had no stroke or TIA and who consumed less than one drink per day.

Our results with regard to the association between alcohol consumption and stroke incidence are somewhat different from those found in an earlier study of the relationship between alcohol consumption and risk of stroke using PHS data.⁶ Berger et al found that men who consumed two to four alcohol drinks per week had a statistically significant decreased risk of total and ischemic stroke. The differences in the results between our study and Berger's study and other studies that have also shown statistically significant decreased risk of stroke among light to moderate drinkers^{18,19} may be explained by the longer follow-up time and, thus, the aging of the cohort. Moderate to light alcohol consumption may reduce the risk of stroke in shorter follow-up periods but has reduced influence in long periods.

Only a few studies have looked at the effect of pre-stroke alcohol consumption on stroke outcomes. The North East Melbourne Stroke Incidence Study (NEMESIS) did not find pre-stroke alcohol consumption to be a factor that independently predicted handicap two years after stroke in multivariate analysis.⁸ The Copenhagen Stroke Study examined a population of patients with severe stroke to determine factors that predicted good outcome after rehabilitation. Daily alcohol consumption compared to non-daily alcohol consumption was an independent predictor of good outcome only in univariate but not in multivariate analysis.⁷ Our study shows similar results to NEMESIS and the Copenhagen Stroke Study and extends their findings because the large number of participants and outcome events allow us to use finer categories of alcohol consumption and functional stroke outcome. Additionally, our results are not limited to only the most severe cases of stroke.

We used the MRS scores as a measurement of functional outcome from stroke. Although the MRS claims to be a measure of handicap, its strong emphasis on mobility makes it more a measure of disability or a “global health index.”^{20,21} Despite its limitations,^{22,23} the MRS score is widely accepted for use in clinical trials and is an appropriate outcome measure for this study. The MRS is simple to administer, can be assessed retrospectively from medical records, and has strong test-retest reliability, inter-rater reliability, and validity.²³ Additionally, the MRS can be used to compare patients with many different types of neurological limitations and allows pre-stroke disability to be taken into consideration when determining post-stroke Rankin score.¹⁵ Another advantage to MRS is that it does not seem to have a “ceiling effect” as can sometimes be observed when using the Barthel Index.²⁴

Other strengths to our study include the large number of participants and outcome events, prospective design, confirmed outcome definition with high interobserver agreement¹⁴ and the homogenous structure of the cohort, which limits confounding by access to medical care.

One limitation to our study is the possible bias arising from the use of self-reported alcohol consumption. However, misclassification of alcohol consumption at baseline is most likely nondifferential because of the prospective design. Only using alcohol consumption at baseline may not accurately reflect alcohol consumption over the course of the study. However, we found a high correlation between alcohol consumption at baseline and at 84 months [$r=0.75$]. In addition, when we evaluated the association between alcohol consumption and risk of stroke and functional outcomes from stroke using alcohol consumption at 84 months and cases of stroke after 84 months, we found very similar results (data not shown). We combined the two highest alcohol intake categories because only few physicians drank >1 drink per day, which may have mask potential harmful effects. However, dividing the highest category of alcohol consumption (≥ 1 drink/day) into two categories (1 drink/day and ≥ 2 drinks/day) did not reveal any further increased or decreased risk of our functional outcomes (data not shown).

Using nondrinkers as the reference category when examining the relationship between alcohol consumption and risk of stroke or functional outcomes from stroke has been questioned because of the potential for ex-drinkers who quit for health reasons to be included in the non-drinkers category. Including ex-drinkers in the non-drinker category may result in an attenuation of the relationship between alcohol consumption and risk of stroke or functional outcomes from stroke. However, the inclusion of many ex-drinkers in the non-drinker category is unlikely in this cohort because the men were free of many disabling conditions and of major diseases at baseline that could lead one to abstain from alcohol.

Having limited information about the men’s functional status pre-stroke is unlikely to be a large source of bias. In general the men were most likely healthy and able-bodied since they had to be free of many major diseases to be included in the study base. Additionally, the MRS scale takes pre-stroke disability into account when measuring functional outcomes from stroke.

Another limitation is that since very few men in our study were underweight, we are unable to make any inferences about possible interactions between body weight and alcohol consumption on our functional outcomes.

Our study participants were all male physicians who presumably live a healthier lifestyle compared to the general population. Thus, our results may not be generalizable to other populations and we cannot exclude potential harmful effects of very high alcohol consumption on the evaluated outcomes. Since gender differences in alcohol metabolism may exist²⁵ and women have different risk factors for stroke and poorer outcomes from stroke than men,²⁶ future research will need to examine the association of alcohol consumption on the risk of stroke and functional outcomes from stroke among women.

In conclusion, our data do not show strong association between alcohol consumption, which is a component of the lifestyle of many individuals, with functional outcome after stroke. A modest beneficial association was observed for those men who had low alcohol consumption. Future studies are warranted to evaluate potential factors influencing functional outcome after stroke.

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Table 1

Baseline characteristics according to level of alcohol consumption in the Physicians' Health Study (N=21,862).

Characteristic	Alcohol Consumption (no. of drinks)			
	<1/wk (N=5694)	1/wk (N=3059)	2-4/wk (N=4897)	5-6/wk (N=2771)
Mean age (yr)	53.7	52.2	52.5	53.2
Cigarette use (%)				56.1
Never smoked	62.7	55.8	49.5	43.6
Smoked in the past	27.9	34.8	40.7	45.5
Currently smokes <20 cig/day	2.9	3.2	3.7	4.9
Currently smokes ≥20 cig/day	6.2	5.9	5.8	5.7
Exercise frequency (%)				10.7
Daily	6.2	4.8	4.4	5.0
5-6 times/week	10.1	8.6	11.6	13.2
2-4 times/week	32.5	37.8	40.8	38.8
1 time/week	17.4	19.8	18.5	18.4
1-3/month	15.4	14.6	14.1	13.4
Rarely/Never	17.4	13.7	9.8	10.4
History of migraine (%)	2.7	2.5	2.1	2.0
History of diabetes (%)	4.9	3.0	1.7	1.7
Mean blood pressure (mm Hg)				2.7
Systolic	125.6	125.3	125.3	126.0
Diastolic	78.5	78.5	78.4	78.9
History of hypertension (%) [*]	23.0	20.6	21.1	22.7
Hypertension medication use (%)				28.5
Never	83.4	84.1	84.5	82.2
Ever	2.6	1.5	1.9	2.0
Current	10.1	9.5	9.3	11.1
History of high cholesterol (%) [†]	9.8	10.2	9.8	10.9
Cholesterol medication use (%)				11.7
Never	86.0	82.8	83.3	82.3
Ever	0.9	1.0	1.0	0.9
				1.2

Characteristic	Alcohol Consumption (no. of drinks)			
	<1/wk (N=5694)	1/wk (N=3059)	2-4/wk (N=4897)	5-6/wk (N=2771)
Current	0.3	0.2	0.1	0.3
Mean body mass index (kg/m ²)	25.0	25.0	24.7	24.6
Random assignment to aspirin group (%)	49.2	51.2	49.9	50.8
				≥1/day (N=5441)
				0.2
				24.6
				49.9

Numbers may not add up to 100% because of missing data.

* History of hypertension was defined as self-reported systolic blood pressure of 140 mm Hg or higher, diastolic blood pressure 90 mm Hg or higher, or past or current treatment for hypertension (regardless of blood pressure).

[†] History of high cholesterol was defined as blood cholesterol 240 mg/100mL or higher or past or current cholesterol medication

Table 2

Multivariable-adjusted relative risk of TIA, total stroke, ischemic or hemorrhagic stroke according to alcohol consumption (N=21,862).*

Alcohol Consumption	TIA			Total Stroke			Ischemic Stroke			Hemorrhagic Stroke		
	No. of cases	Relative risk (95% CI) [†]	No. of cases	Relative risk (95% CI) [†]	No. of cases	Relative risk (95% CI) [†]	No. of cases	Relative risk (95% CI) [†]	No. of cases	Relative risk (95% CI) [†]	No. of cases	Relative risk (95% CI) [†]
<1 drink/wk	191	1.00	381	1.00	308	1.00	66	1.00	66	1.00		
1 drink /wk	90	0.95 (0.74, 1.23)	146	0.80 (0.66, 0.97)	123	0.84 (0.68, 1.04)	23	0.70 (0.44, 1.13)	23	0.70 (0.44, 1.13)		
2-4 drinks/wk	161	1.05 (0.85, 1.30)	276	0.98 (0.83, 1.14)	226	1.00 (0.84, 1.19)	48	0.92 (0.63, 1.33)	48	0.92 (0.63, 1.33)		
5-6 drinks/wk	87	0.97 (0.75, 1.25)	182	1.08 (0.90, 1.29)	155	1.15 (0.94, 1.39)	25	0.82 (0.52, 1.30)	25	0.82 (0.52, 1.30)		
≥1 drink/day	238	1.18 (0.97, 1.43)	408	1.03 (0.89, 1.18)	345	1.08 (0.92, 1.26)	60	0.88 (0.62, 1.25)	60	0.88 (0.62, 1.25)		

* CI denotes confidence interval. Men who consumed less than one drink per week served as the reference category.

[†] Values have also been adjusted for age, systolic blood pressure, treatment for hypertension, smoking, history of diabetes, body mass index, exercise, and history of migraine.

Table 3

Multivariable-adjusted* odds ratios of functional outcomes after stroke and stroke subtypes according to alcohol consumption in the Physicians' Health Study (N=21,862).

	No TIA or stroke			MRS 0-1			MRS 2-3			MRS 4-6				
	N	%	N	%	RR (95% CI)	N	%	RR (95% CI)	N	%	RR (95% CI)	N	%	RR (95% CI)
Total Stroke														
					(n = 426)			(n = 709)			(n = 258)			
<1 drink/wk	5122	26.0	110	25.8	1.00	193	27.2	1.00	78	30.2	1.00			
1 drink /wk	2823	14.3	45	10.6	0.85 (0.60, 1.21)	79	11.1	0.84 (0.64, 1.10)	22	8.5	0.60 (0.37, 0.97)			
2-4 drinks/wk	4460	22.6	90	21.1	1.13 (0.85, 1.50)	130	18.3	0.91 (0.72, 1.15)	56	21.7	1.02 (0.72, 1.45)			
5-6 drinks/wk	2502	12.7	56	13.1	1.17 (0.84, 1.63)	99	14.0	1.16 (0.90, 1.49)	27	10.5	0.80 (0.51, 1.25)			
≥1 drink/day	4795	24.3	125	29.3	1.09 (0.84, 1.42)	208	29.3	1.03 (0.84, 1.26)	75	29.1	0.86 (0.62, 1.19)			
Ischemic Stroke														
					(n = 393)			(n = 633)			(n = 131)			
<1 drink/wk	5122	26.0	100	25.4	1.00	171	27.0	1.00	37	28.2	1.00			
1 drink /wk	2823	14.3	42	10.7	0.88 (0.61, 1.27)	67	10.6	0.81 (0.61, 1.08)	14	10.7	0.82 (0.44, 1.53)			
2-4 drinks/wk	4460	22.6	82	20.9	1.14 (0.84, 1.54)	110	17.4	0.88 (0.69, 1.12)	34	26.0	1.36 (0.85, 2.20)			
5-6 drinks/wk	2502	12.7	50	12.7	1.16 (0.82, 1.63)	92	14.5	1.23 (0.94, 1.59)	13	9.9	0.84 (0.44, 1.59)			
≥1 drink/day	4795	24.3	119	30.3	1.13 (0.86, 1.49)	193	30.5	1.07 (0.86, 1.32)	33	25.2	0.79 (0.49, 1.28)			
Hemorrhagic Stroke														
					(n = 30)			(n = 75)			(n = 117)			
<1 drink/wk	5122	26.0	8	26.7	1.00	22	29.3	1.00	36	30.8	1.00			
1 drink /wk	2823	14.3	3	10.0	0.72 (0.19, 2.72)	12	16.0	1.06 (0.52, 2.15)	8	6.8	0.45 (0.21, 0.98)			

	No TIA or stroke		MRS 0-1		MRS 2-3		MRS 4-6	
	N	%	N	%	N	%	N	%
			(n = 426)		(n = 709)		(n = 258)	
			RR (95% CI)		RR (95% CI)		RR (95% CI)	
2-4 drinks/wk	4460	22.6	8	26.7	19	25.3	21	17.9
			(0.47, 3.43)		(0.58, 2.00)		(0.45, 1.34)	
5-6 drinks/wk	2502	12.7	5	16.7	7	9.3	13	11.1
			(0.45, 4.29)		(0.29, 1.60)		(0.42, 1.51)	
≥1 drink/day	4795	24.3	6	20.0	15	20.0	39	33.3
			(0.27, 2.32)		(0.35, 1.32)		(0.62, 1.54)	

Comparison group consists of men without stroke or transient ischemic attack (TIA) who consumed <1 drink/wk alcohol. MRS refers to modified Rankin Scale; CI refers to confidence interval.

* Adjusted for age, systolic blood pressure, treatment for hypertension, smoking, history of diabetes, body mass index, exercise, history of migraine, and TIA.