Published in final edited form as:

Stroke. 2015 November ; 46(11): 3124–3130. doi:10.1161/STROKEAHA.115.010601.

Midlife Alcohol Consumption and the Risk of Stroke in the Atherosclerosis Risk in Communities Study

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Abstract

Background and Purpose—Alcohol consumption is common in the US and may confer beneficial cardiovascular effects at light-to-moderate doses. The alcohol-stroke relationship remains debated. We estimated the relationship between mid-life, self-reported alcohol consumption and ischemic stroke (IS) and intracerebral hemorrhage (ICH) in a biracial cohort.

Methods—We examined 12,433 never and current drinkers in the Atherosclerosis Risk in Communities Study, aged 45-64 at baseline. Participants self-reported usual drinks/week of beer, wine, and liquor at baseline. We used multivariate Cox proportional hazards regression to assess the association of current alcohol consumption relative to lifetime abstention with incident IS and ICH and modification by sex-race group. We modeled alcohol intake with quadratic splines to further assess dose-response relationships.

Results—One-third of participants self-reported abstention, 39% and 24%, respectively, consumed ≤3 and 4-17 drinks/week, and only 5% reported heavier drinking. There were 773 IS and 81 ICH over follow-up (median ~22.6 years). For IS, light and moderate alcohol consumption were not associated with incidence (HR=0.98, 95% CI 0.79-1.21; 1.06, 0.84-1.34) while heavier drinking was associated with a 31% increased rate relative to abstention (HR=1.31, 0.92-1.86). For ICH, moderate-to-heavy (HR=1.99, 1.07-3.70), but not light, consumption increased incidence.

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Disclosures

The authors report no disclosures.

Conclusion—Self-reported light-to-moderate alcohol consumption at mid-life was not associated with reduced stroke risk compared with abstention over 20 years of follow-up in the ARIC study. Heavier consumption increased the risk for both outcomes as did moderate intake for ICH.

Keywords

ischemic stroke; alcohol; intracerebral hemorrhage

INTRODUCTION

Stroke is a leading cause of mortality and disability worldwide, a major contributor to U.S. healthcare costs, and is projected to increase in burden as the population ages.[1-3] As such, continued examination of modifiable risk factors and behaviors that may prevent disease occurrence is needed. One such factor may be alcohol, a prevalent exposure both in the U.S. and worldwide. Seventy percent of U.S. adults report current drinking and more than one-quarter report excessive drinking.[4, 5]

The relationship between alcohol intake and stroke has been widely studied, yet uncertainties remain; results from observational studies are inconsistent and randomized trials are infeasible. Light-to-moderate alcohol consumption (usually defined as 1-2 drinks per day in the U.S.) may reduce the risk of stroke, but some studies, particularly older ones, have not found beneficial effects.[6-8] Current meta-analyses suggest that moderate intake is protective for ischemic stroke (IS), but not intracerebral hemorrhagic (ICH), with possible differential dose-responses by sex.[6-8] Limitations of our understanding stem from 1) the assessment of alcohol intake late in life, a period that may not reflect the most critical exposure window for disease risk and that may be influenced by other medical conditions developing in later life; 2) alcohol measurement error and misspecification due to variations in drinking patterns; and 3) limited generalizability.[6-15] Furthermore, some studies lack adjustment for lifestyle and socioeconomic factors that may account for protective effects in light drinkers, or combine former and never drinkers in a single referent group. In contrast to the evidence on light-to-moderate intake, consistent and convincing evidence supports the harmful effects of heavy consumption on stroke risk. The precise dose-response relationship, however, is unclear.

Despite the large body of work on alcohol and stroke, few studies have included substantial numbers of minority individuals. Blacks have higher stroke incidence and different drinking patterns from whites and therefore warrant investigation.[3] In addition, few studies have accounted for the competing risk of mortality, which may be substantial in prospective studies. Subdistribution hazard estimation is particularly useful to public health scientists interested in assessing risks and benefits of alcohol in a population experiencing competing risks.[16] In our study, we estimated the dose-response relationship between usual, mid-life alcohol consumption and incident stroke among black and white adults in the Atherosclerosis Risk in Communities (ARIC) study, a population-based cohort drawn from 4 US communities.

METHODS

Study Population

The ARIC study is a population-based cohort recruited using probability sampling of adults aged 45-64 years from 4 US communities: Forsyth County, NC; Jackson, MS; suburbs of Minneapolis, MN; and Washington County, MD. The ARIC study design and rationale are described in detail elsewhere.[17] A total of 15,792 participants were enrolled at Visit 1 (1987-1989) and underwent an in-home interview and physical examination, with four additional study visits over the subsequent 25 years. For analysis, we excluded race-ethnicities other than white or black (N= 48), blacks from Minnesota or Washington County (N=55), participants missing alcohol intake (N=106), and those with prevalent stroke (N=284). After these exclusions, the analytic cohort totaled 15,305. We further limited our population to current or never drinkers (N=12,433) because of the heterogeneity in exposure among former drinkers in our population with regard to duration and quantity of consumption and time since cessation.[12]

Alcohol Assessment

Alcohol consumption was measured at baseline using an interviewer-administered questionnaire developed in accordance with the validated Willett 66-item food frequency questionnaire (FFQ).[18] Participants were asked to report whether they currently consumed alcoholic beverages and if so, their usual intake of drinks per week; those reporting values under 0.5 were recorded as '0'. Separate intake frequency questions were asked for standard drinks of wine (4-oz), beer (12-oz), and hard liquor (1.5-oz). Total drinks per week was calculated as the sum of standard drinks of each type.

Stroke Definition

Suspected stroke hospitalizations were ascertained by self-report, at study visits, during annual follow-up, and surveillance of local hospital discharge lists. Validation of suspected events and stroke diagnosis were conducted independently by a computer-derived algorithm and a physician reviewer using data abstracted from the medical record; differences were adjudicated by a second physician reviewer. Strokes were classified using criteria adopted from the National Survey of Stroke[19] and required, at a minimum, evidence of sudden or rapid onset of neurological symptoms lasting >24 hours or leading to death in the absence of evidence for a nonstroke cause. Out-of-hospital fatal strokes (N=19) were not validated and were not included. Additional details of stroke subtype classification have been published.[20]

Covariates

Confounders were identified based on substantive knowledge and directed acyclic graph analysis was used to obtain a minimally sufficient set of adjustment variables: age, sex, race, study center, baseline comorbid conditions, diet score, low-density lipoprotein cholesterol, education, smoking status, and marital status.[21] Causal intermediates included blood pressure, high-density lipoprotein cholesterol, and atrial fibrillation.

Dietary factors were assessed using an interviewer-administered 66-item FFQ measuring usual intake of foods over the past year. We calculated a diet score as described elsewhere[22]

based on quintile values for 6 dietary components: percent energy from trans and omega-3 fatty acids, fiber, folate, glycemic load, and polyunsaturated:saturated fatty acid ratio. Physical activity was measured using the Baecke physical activity questionnaire.[23] Baseline medical history included diabetes (self-reported physician diagnosis, fasting glucose ≥126 mg/dL, non-fasting ≥200 mg/dL, or self-reported pharmacologic treatment) and coronary artery disease (electrocardiogram-adjudicated or self-reported myocardial infarction or any of self-reported heart/arterial surgery, coronary bypass, or angioplasty).

Statistical methods

Descriptive statistics for participant characteristics were calculated according to alcohol intake category. Cox proportional hazards regression was used to estimate hazard ratios and 95% confidence intervals for the association between alcohol and incident IS, ICH, and total stroke. Participants contributed person-time until the earliest of: incident stroke, death, loss to follow-up, or end of follow-up on December 31, 2011. The proportional hazards assumption was tested using interaction terms between exposure and time.

Alcohol consumption was categorized as drinks per week by examining the dose-response relationship as well as using *a priori* values selected to align with prior research and recommended guidelines. Results were robust to different category boundaries and are presented herein as ≤3, 4-17, and 18 or more drinks per week, which reflect our data-informed categorization and cut-points of previous studies.[14] In a second alcohol assessment at year 6, 67% of participants were categorized the same as at baseline. We assessed possible non-linear relationships using quadratic splines and polynomial terms. Knots were selected based on AIC values compared across models with 2, 3, and 4 knots located at percentile values.[24] Secondary models for IS were stratified by sex-race group.

In secondary analysis, we estimated sub-distribution hazard ratios (HR_{SD}) to assess the risk of stroke given the relatively high proportion of death (26%) over follow-up. Cause-specific hazards models, which censor deaths, yield estimates reflecting the relative *rate* of stroke. HR_{SD}, on the other hand, reflect the relative *risk* over a period of time.[16] These were obtained using the SAS macro PSHREG based on the proportional sub-distribution hazards model proposed by Fine and Grey.[25] All analyses were conducted using Statistical Analysis Software Version 9.2 (SAS Inc., Cary, N.C.).

RESULTS

Over one-third of the ARIC participants were light alcohol drinkers, consuming ≤3 drinks/week (Table 1). Roughly one-third reported lifetime abstention from alcohol, one-quarter were moderate drinkers of 4-17 drinks/week, and only 5% consumed >18 drinks/week. Women comprised the largest proportion of abstainers and white men accounted for nearly three-quarters of heavier drinkers. Light-to-moderate drinkers were of higher socioeconomic status – in the form of greater educational attainment, more managerial occupations, and higher family income - than heavier drinkers and lifetime abstainers. Current smoking was reported by 46% of heavier drinkers but only 23% of light drinkers. The prevalence proportion of diabetes was low overall (8.6%) and roughly twice as high in abstainers

compared with current drinkers. Finally, blood pressure and HDL-C increased across alcohol consumption level.

Over a median follow-up of 22.6 and 22.7 years, respectively, there were 773 IS and 81 ICH. Ischemic stroke incidence rates per 100,000 person-years increased across alcohol intake categories: 251 for ≤3/week, 313 for 4-17/week, 435 for ≥18/week, and 368 for abstainers (Table 2). Estimates were attenuated after adjustment for covariates; most of this attenuation occurred with model 1 covariates. In fully-adjusted Cox models, light and moderate drinking were not associated with IS compared with lifetime abstention (HR=0.98, 95% CI 0.79-1.21; 1.06, 0.84-1.34, respectively; Table 2). Heavier drinking was associated with a 31% increase relative to abstainers (HR=1.31, 0.92-1.86). Confidence intervals for these associations were wide and overlapped the null.

Associations of light-to-moderate drinking versus abstention were in opposite directions in whites compared with blacks and confidence intervals overlapped considerably and therefore we cannot conclude that hazard ratios differ by sex-race group (Supplemental Figure I; p=0.5). Hazard ratios ranged from 0.78 (0.56-1.10) in white women to 1.20 (0.75-1.92) in black men.

ICH incidence rates ranged from 20 per 100,000 person-years among light drinkers to 41 among moderate-to-heavier drinkers. We found no clear association of light drinking compared with abstention (HR=1.04, 0.56-1.94) after adjustment for age, race, sex, smoking status and education (Table 2). Moderate-to-heavier drinking, however, was associated with higher ICH rates compared with abstention (HR=1.99, 1.07-3.70); this estimate was unchanged when heavier drinkers were removed. The precision of these estimates was low because of small numbers of events, which also precluded adjustment for additional lifestyle factors. Effect estimates for total stroke were similar to those for IS alone: HR_{light}=0.98, 0.80-1.20; $HR_{moderate}$=1.13, 0.91-1.42; and HR_{heavy}=1.36, 0.97-1.91.

Results from models with quadratic splines representing alcohol intake did not support a J-shaped relationship (Figure 1); higher-order spline terms were not significant, although these analyses were under-powered to estimate dose-response relationships. The log-hazard ratio of IS was roughly linear across intake (β=0.06 for a 1 drink-per-week increase; HR=1.06, 0.99-1.13; p=0.1) and also non-significant. Additional quadratic (p=0.3) and cubic terms (p=0.9) were not statistically significant compared with the linear model.

More than one-quarter of the participants died over follow-up, ranging from 24% in light to 42% in heavier drinkers. The estimated HR_{SD} account for this underlying mortality and reflect the relative cumulative incidence in our population. As expected, effect estimates were attenuated slightly for heavy drinkers; light and moderate alcohol consumption were not associated with reduced IS risk compared with abstention and moderate intake may increase ICH risk (Table 3). Lastly, we explored the impact of former versus never drinking on stroke. Estimates were non-significant with wide confidence intervals; interpretation of these estimates is difficult because of heterogeneity in consumption levels among former drinkers.

CONCLUSIONS

We did not find a protective effect of light-to-moderate mid-life alcohol consumption on IS or ICH in this analysis of a bi-racial population-based cohort of US adults. Heavier intake tended to increase rates of IS and ICH compared with abstention, though confidence intervals were wide. The dose-response relationship we estimated for IS was imprecise, and did not support a clear J-shaped or linear relationship.

Alcohol consumed moderately in mid-life may lower IS risk through beneficial alterations in vascular risk factors including HDL-cholesterol, blood pressure, platelet aggregation, inflammatory markers and insulin sensitivity compared with no drinking.[7, 26-28] In contrast, high doses of alcohol have well-established deleterious effects including elevated blood pressure, inflammation, and development of atrial fibrillation. Low-dose alcohol may also increase the risk for hemorrhage through hemostatic changes that promote bleeding. Dose-specific effects may differ by sex; women attain higher blood alcohol levels than men because of different body composition and alcohol metabolism.[29]

A J-shaped relationship between alcohol and ischemic stroke is frequently reported in meta-analyses.[7, 8, 13-15] Consumption of 1-2 drinks/day was associated with 28% lower risk and >4 drinks per day with 69% increased risk.[7] Meta-analyzed results may be limited by inclusion of studies with non-validated stroke events, no adjustment for lifestyle factors, and inclusion of causal intermediates (e.g. blood pressure and HDL-C) in regression models. Our results, based on well-validated events with adjustment for important confounders, suggest no clear association between alcohol and stroke until heavier intake levels. Inconsistencies in estimates across studies could be due to differential distributions of etiologic subtypes in these cohorts coupled with a different mechanistic role of alcohol in their etiology (i.e. larger protective effect for thrombotic vs. cardioembolic strokes). Differences may also result from heterogeneity according to drinking pattern or sex-race or from measurement and selection biases.

Stronger protective effects of low-dose alcohol are reported for women compared with men (HR=0.66, 95% CI 0.61-0.71 vs. 0.80, 0.67-0.96).[7, 8] Women consuming <2 drinks/day in the Nurses' Health Study (a primarily white cohort) had a 12-18% lower risk of IS compared with non-drinkers.[14] This aligns with results for white, but not black, women in the ARIC study. Our results for men were similar to those reported by the Health Professionals Follow-up Study that found no association for <1 drink/day and slightly elevated risk of ≥1 drinks/day.[12] We noted non-significantly higher HRs for blacks compared with whites that could be explained by different drinking patterns between whites and blacks.[30] Evidence suggests that moderate quantities of alcohol may be beneficial when consumed at moderate, but not high, frequency.[12]

Meta-analyzed data indicate that ICH risk increases log-linearly with increasing alcohol consumption for men, with possible J-shaped curves for women.[6, 7, 14] Consumption of ≤2 drinks/day is associated with 12-24% lower hemorrhage risk compared with abstention.[6, 7, 14] We did not find evidence of a protective effect of light drinking in our

population. ICH rates were increased even at moderate drinking levels compared with abstention. Our results, however, were limited by small numbers of events.

Our results should be interpreted in light of several limitations. Participants may under-report alcohol consumption leading to misclassification. While we were unable to quantify errors, construct and rank-order validity was supported by positive correlations of alcohol with both HDL-C and blood pressure. Residual confounding is possible. We had low power to estimate precise effects, particularly among heavier drinkers and for ICH. Finally, race-specific results may not generalize to the U.S. population outside of the ARIC communities.

Strengths of our study include a prospective study design with >20 years of follow-up, a bi-racial population, and robust stroke ascertainment. Alcohol consumption was assessed using a validated instrument with beverage-specific questions (thus reducing under-reporting) that differentiated never from former drinkers. We had rich covariate data that permitted adjustment for lifestyle factors, smoking, and SES.

Public health recommendations for alcohol consumption must consider both its benefits and risks. While light-to-moderate intake may reduce the risk of some cardiovascular outcomes, other harmful effects exist even at low doses (e.g., dependency, cancer). As such, the American Heart Association does not recommend initiation of drinking for disease prevention.[31] Our results support this recommendation. We found no significant risk reduction for IS or ICH with light-to-moderate mid-life alcohol consumption and increased risks at heavier intake levels. Understanding the alcohol-stroke relationship would be advanced by assessing dose-dependent exposure measurement errors, updating meta-analyses to include only high-quality studies and to explore modification by drinking pattern, etiologic subtype, and sex-race.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors thank the staff and participants of the ARIC study for their important contributions.

Funding Sources

The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HSN268201100011C, and HHSN268201100012C).

References

1. Andrews, R.; Elixhauser, A. Healthcare Cost and Utilization Project Statistical Briefs. Agency for Health Care Policy and Research; Rockville, MD: Dec. 2007 The National Hospital Bill: Growth trends and 2005 update on the most expensive conditions by payer: Statistical Brief #42.
2. Seshadri S, Wolf PA. Lifetime risk of stroke and dementia: current concepts, and estimates from the Framingham Study. Lancet Neurol. 2007; 6:1106–1114. [PubMed: 18031707]

3. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2013 update: a report from the American Heart Association. Circulation. 2013; 127:e6–e245. [PubMed: 23239837]
4. Healthy People 2020 leading health indicators: substance abuse. US Department of Health and Human Services, Office of Disease Prevention and Health Promotion; website. https://www.healthypeople.gov/2020/leading-health-indicators/2020-lhi-topics/Substance-Abuse/data [Accessed June 26, 2015]
5. Fryar CD, Hirsch R, Porter KS, Kottiri B, Brody DJ, Louis T. Smoking and Alcohol Behaviors Reported by Adults: United States, 1999-2002. Advance Data from Vital and Health Statistics. 2006; 378:1–25.
6. Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, Mohapatra S, et al. Alcohol consumption and the risk of morbidity and mortality for different stroke types--a systematic review and meta-analysis. BMC Public Health. 2010; 10:258. [PubMed: 20482788]
7. Reynolds K, Lewis B, Nolen JD, Kinney GL, Sathya B, He J. Alcohol consumption and risk of stroke: a meta-analysis. JAMA. 2003; 289:579–588. [PubMed: 12578491]
8. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ. 2011; 342:d671. [PubMed: 21343207]
9. Berger K, Ajani UA, Kase CS, Gaziano JM, Buring JE, Glynn RJ, et al. Light-to-moderate alcohol consumption and risk of stroke among U.S. male physicians. N Engl J Med. 1999; 341:1557–1564. [PubMed: 10564684]
10. Djousse L, Himali JJ, Beiser A, Kelly-Hayes M, Wolf PA. Apolipoprotein e, alcohol consumption, and risk of ischemic stroke: the Framingham Heart Study revisited. J Stroke Cerebrovasc Dis. 2009; 18:384–388. [PubMed: 19717024]
11. Elkind MS, Sciacca R, Boden-Albala B, Rundek T, Paik MC, Sacco RL. Moderate alcohol consumption reduces risk of ischemic stroke: the Northern Manhattan Study. Stroke. 2006; 37:13–19. [PubMed: 16306464]
12. Mukamal KJ, Ascherio A, Mittleman MA, Conigrave KM, Camargo CA Jr. Kawachi I, et al. Alcohol and risk for ischemic stroke in men: the role of drinking patterns and usual beverage. Ann Intern Med. 2005; 142:11–19. [PubMed: 15630105]
13. Mukamal KJ, Chung H, Jenny NS, Kuller LH, Longstreth WT Jr. Mittleman MA, et al. Alcohol use and risk of ischemic stroke among older adults: the cardiovascular health study. Stroke. 2005; 36:1830–1834. [PubMed: 16081863]
14. Jimenez M, Chiuve SE, Glynn RJ, Stampfer MJ, Camargo CA Jr. Willett WC, et al. Alcohol consumption and risk of stroke in women. Stroke. 2012; 43:939–945. [PubMed: 22403048]
15. Sacco RL, Elkind M, Boden-Albala B, Lin IF, Kargman DE, Hauser WA, et al. The protective effect of moderate alcohol consumption on ischemic stroke. JAMA. 1999; 281:53–60. [PubMed: 9892451]
16. Lau B, Cole SR, Gange SJ. Competing risk regression models for epidemiologic data. Am J Epidemiol. 2009; 170:244–256. [PubMed: 19494242]
17. The ARIC investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol. 1989; 129:687–702. [PubMed: 2646917]
18. Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol. 1985; 122:51–65. [PubMed: 4014201]
19. The National Survey of Stroke. National Institute of Neurological and Communicative Disorders and Stroke. Stroke. 1981; 12:I1–91. [PubMed: 7222163]
20. Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, et al. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. Stroke. 1999; 30:736–743. [PubMed: 10187871]
21. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology. 1999; 10:37–48. [PubMed: 9888278]

22. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. N Engl J Med. 2000; 343:16–22. [PubMed: 10882764]

23. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. American Journal of Clinical Nutrition. 1982; 36:936–942. [PubMed: 7137077]

24. Harrell, FE. General Aspects of Fitting Regression Models. In: Bickel, P.; Diggle, P.; Fienberg, SE., et al., editors. Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis. 1st Ed. Springer; New York: 2001. p. 13-44.

25. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association. 1999; 94:496–509.

26. Stampfer MJ, Colditz GA, Willett WC, Speizer FE, Hennekens CH. A prospective study of moderate alcohol consumption and the risk of coronary disease and stroke in women. N Engl J Med. 1988; 319:267–273. [PubMed: 3393181]

27. Zakhari S. Alcohol and the cardiovascular system: molecular mechanisms for beneficial and harmful action. Alcohol Health Res World. 1997; 21:21–29. [PubMed: 15706760]

28. Agarwal DP. Cardioprotective effects of light-moderate consumption of alcohol: a review of putative mechanisms. Alcohol Alcohol. 2002; 37:409–415. [PubMed: 12217928]

29. Ferreira MP, Weems MK. Alcohol consumption by aging adults in the United States: health benefits and detriments. J Am Diet Assoc. 2008; 108:1668–1676. [PubMed: 18926132]

30. Dawson DA, Grant BF, Stinson FS, Chou PS. Toward the attainment of low-risk drinking goals: a 10-year progress report. Alcohol Clin Exp Res. 2004; 28:1371–1378. [PubMed: 15365308]

31. Alcohol and Heart Health. American Heart Association; web site. http://www.heart.org/HEARTORG/GettingHealthy/NutritionCenter/HealthyEating/Alcohol-and-Heart-Health_UCM_305173_Article.jsp [Accessed September 1, 2015]

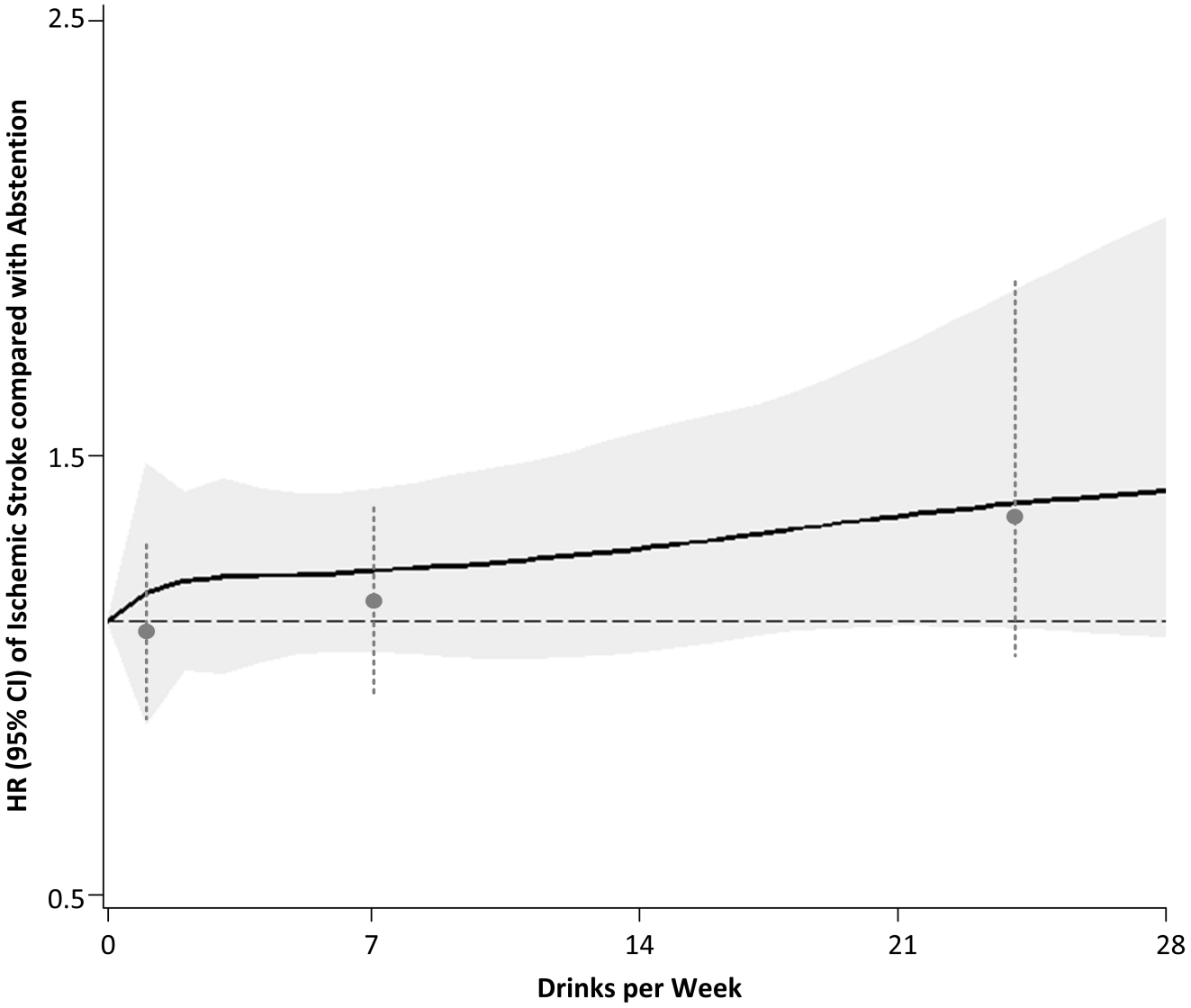

Figure 1.

Dose-response relationship between midlife alcohol consumption and IS estimated with quadratic splines. Shading indicates 95% confidence bands. Knots were placed at 0.5, 3, and 17 drinks/week. Point estimates and 95% confidence intervals from categorical analysis are overlaid on the curve at the median of each category.

TABLE 1

Characteristics of ARIC participants according to self-reported usual alcohol consumption at baseline.*

	Alcohol consumption, drinks per week			
	Lifetime abstainer	**Light (≤3)**	**Moderate (4-17)**	**Heavier (18+)**
Number of participants	3851	4876	3042	664
Person-years	76974.8	99125.5	60479.2	11947.2
Alcohol consumption, median (25^{th}-75^{th} percentile)				
Grams ethanol per week		0 (0-24)	95 (68-151)	317 (277-415)
Glasses per week		0 (0-2)	7 (5-11)	24 (20-30)
Age, years	54.6 (5.7)	53.7 (5.8)	53.8 (5.7)	53.9 (5.8)
Sex-race group				
White men	14	34	50	71
White women	40	55	34	11
Black men	8	4	11	17
Black women	38	7	5	2
Educational attainment				
<High school	30	13	14	19
High school or vocational	41	45	38	43
College degree or higher	29	43	49	38
Occupation				
Managerial	18	29	34	25
Non-managerial	69	59	53	57
Retired	13	13	14	19
Income				
<$12,000	22	7	7	10
$12,000-$49,999	65	60	52	60
$50,000+	13	34	41	30
Physical activity index score	2.2 (0.7)	2.5 (0.8)	2.6 (0.8)	2.4 (0.8)
Diet score	12.3 (3.8)	11.8 (3.9)	12.0 (3.8)	12.0 (3.7)
Cigarette smoking				
Current	13	23	30	46
Former	16	33	43	43
Never	71	44	27	12
Blood pressure, mmHg				
Systolic	124.0 (19.9)	117.9 (17.3)	120.9 (18.4)	127.1 (18.8)
Diastolic	74.5 (11.5)	72.2 (10.6)	74.3 (11.2)	77.0 (11.5)
LDL-c, mg/dL	139.4 (40.7)	136.3 (38.1)	135.3 (39.7)	132.4 (39.8)
HDL-c, mg/dL	37.8 (10.7)	37.0 (10.9)	39.4 (11.7)	40.5 (12.1)
Body mass index, kg/m^2	29.0 (6.1)	27.1 (4.9)	26.6 (4.5)	26.7 (4.5)
Coronary artery disease	2	3	3	4
Diabetes	13	7	7	7

*Population includes never and current drinkers, excluding prevalent strokes, non-white or black, blacks from Washington County or Minnesota, and missing alcohol information for a total N=12,433. Proportions reflect person-time distributions of covariates; all p<0.001. Values are presented as %, or mean (SD), unless otherwise specified.

TABLE 2

Hazard ratios and 95% confidence intervals (CI) for the association of alcohol consumption and IS and ICH

	Alcohol Consumption, drinks per week			
	Lifetime abstainer	**≤3**	**4-17**	**18+**
Ischemic stroke				
Events	283	249	189	52
Person-years	76,975	99,126	60,479	11,947
Incidence rate per 100,000 PY (95% CI)	367.7 (326.7-412.4)	251.2 (221.4-286.9)	312.5 (270.3-359.5)	435.2 (328.7-566.0)
Hazard ratio (95% CI)				
Unadjusted	1	0.68 (0.57-0.81)	0.85 (0.71-1.02)	1.22 (0.91-1.64)
Model 1*	1	0.90 (0.74-1.10)	0.97 (0.78-1.20)	1.17 (0.84-1.63)
Model 2**	1	0.98 (0.79-1.21)	1.06 (0.84-1.34)	1.31 (0.92-1.86)
	Lifetime abstainer	**≤3**	**4+**	
Intracerebral hemorrhage				
Events	31	20	30	
Person-years	78,599	100,456	73,711	
Incidence rate per 100,000 PY (95% CI)	39.4 (27.3-55.2)	19.9 (11.2-28.6)	40.7 (28.0-57.3)	
Hazard ratio (95% CI)				
Unadjusted	1	0.50 (0.29-0.89)	1.04 (0.63-1.71)	
Model 1*	1	1.04 (0.56-1.94)	1.99 (1.07-3.70)	

* **Model 1** is adjusted for age (linear), center-race interaction (5-level), sex, educational attainment (<high school, high school, college or higher), and cigarette smoking (current, former, never).

** **Model 2** is additionally adjusted for marital status, LDL-C (quadratic), diet score (linear), physical activity (linear), and prevalence of coronary artery disease and diabetes at baseline.

TABLE 3

Cause-specific and subdistribution hazard ratios and 95% confidence intervals (CI) for the association of alcohol consumption and IS and ICH

	Alcohol Consumption, drinks per week			
	Lifetime abstainer	**≤3**	**4-17**	**18+**
Ischemic stroke *				
Hazard ratio (95% CI)				
Cause-specific	1	0.98 (0.79-1.21)	1.06 (0.84-1.34)	1.31 (0.92-1.86)
Subdistribution	1	0.97 (0.79-1.21)	1.06 (0.84-1.35)	1.19 (0.83-1.72)
	Lifetime abstainer	**≤3**	**4+**	
Intracerebral hemorrhage *				
Hazard ratio (95% CI)				
Cause-specific	1	1.04 (0.56-1.94)	1.99 (1.07-3.70)	
Subdistribution	1	1.07 (0.55-2.05)	1.95 (1.00-3.81)	

* IS and ICH models are adjusted for covariates listed in Model 2 and Model 1, respectively of Table 2