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Alcohol Use, Comorbidity, and Mortality

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OBJECTIVES: To examine the combined influence of alcohol use and comorbidity on 20-year mortality in older adults (average age 66 at the time of the baseline survey).

DESIGN: Longitudinal analysis of a national probability sample–based cohort study.

SETTING: Data sources were the National Health and Nutrition Examination Survey I (NHANES I), 1971–1974, and the NHANES Epidemiologic Followup Survey, 1992.

PARTICIPANTS: Four thousand six hundred ninety-one adults aged 60 and older who provided data on alcohol use.

MEASUREMENTS: The prevalence of at-risk drinking in older adults in the United States and the 20-year all-cause mortality risk associated with it. At-risk drinking status was determined from amount of alcohol consumed and comorbidities, using a previously validated method.

RESULTS: The prevalence of at-risk drinking in the United States between 1971 and 1974 in older adults was 10% (18% of men, 5% of women). The majority of at-risk drinkers were identified as such because of their use of alcohol in amounts deemed risky in the presence of relevant comorbidities (69%) (e.g., drinking 2–3 drinks per day and having gout or anxiety or taking a medication for pain). In men, at-risk drinking was associated with higher mortality rates than not-at-risk drinking (hazard ratio = 1.20, 95% confidence interval = 1.01–1.41); abstinence was not associated with greater mortality. In women, neither abstinence nor at-risk drinking was associated with greater mortality rates.

CONCLUSION: In this first, large population-based study of older adults examining the mortality risks of alcohol use and comorbidity, at-risk drinking was associated with greater mortality rates in men. These findings suggest that a lower threshold of alcohol use should be recommended for older adults with specific comorbidities to reduce mortality risks. **J Am Geriatr Soc 54:757–762, 2006.**

Key words: aged; alcohol; epidemiology; mortality

The relationship between alcohol use and all-cause mortality in adults is generally U- or J-shaped, with abstainers and heavy drinkers having higher mortality than light and moderate drinkers,[1–5] but in older adults, this relationship has been less clear, with some studies supporting[1,6,7] and others challenging the association.[3,7–9] One possible explanation for the inconsistencies observed in older populations in these studies is that older persons are more likely than younger persons to have multiple comorbidities. Alcohol may interact differently with different chronic conditions (e.g., depression, gastrointestinal reflux disease) and with medications (e.g., sedatives and arthritis medications) to adversely affect health outcomes. Previous research has largely examined the effect of alcohol use on health outcomes, while treating indicators of comorbidity as covariates,[9] rather than considering their interactions with alcohol use.[8,10] The effect of alcohol on mortality and other health outcomes may vary significantly, depending on the presence of specific chronic conditions (which alcohol may worsen) or the use of specific medications (whose efficacy alcohol may diminish or that may negatively interact with it). Thus, explicitly addressing the interaction of alcohol use with specific chronic conditions and medications may improve the prediction of health risks and better illuminate the adverse health effects of alcohol use in older adults with comorbidity.

This idea has been previously addressed by developing and testing measures to identify older adults who are at risk for harm from their alcohol use, because of excessive alcohol consumption or of alcohol consumption in the presence of select comorbidities.[11–14] These measures have been validated using an expert panel process,[15] with existing alcoholism screening measures,[12] and against a criterion standard for at-risk drinking.[11] One of these measures is the Comorbidity–Alcohol Risk Evaluation Tool (CARET).[11] The CARET uses comorbidity-specific drinking thresholds to place individuals in one of two risk groups:

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at risk or not at risk. The at-risk and not-at-risk drinking definitions are based on data demonstrating that certain amounts of alcohol consumption may be safe for those without comorbidities but not for those with selected comorbidities.[14–17] Actual mortality associations with CARET-defined at-risk drinking have not been examined before.

To determine the prevalence of at-risk drinking as defined by the CARET and to determine mortality associations with CARET-defined at-risk drinking, data from a nationally representative sample of persons aged 60 and older from the National Health and Nutrition Examination Survey 1971–1975 (NHANES I),[18] and the NHANES Epidemiologic Followup Survey 1992 (NHEFS) were examined.[19] The following questions were asked. How much do different factors (e.g., excessive alcohol use, select chronic medical conditions, and regular use of select medications) contribute to drinkers being at risk? Over a 20-year follow-up, do CARET-defined at-risk drinkers have greater mortality rates than CARET-defined not-at-risk drinkers?

METHODS

Study Population

NHANES I included a multistage, stratified, probability sampling design to select a representative sample of the U.S. civilian noninstitutionalized population aged 1 to 74.[18] To investigate the development of health conditions, including death, in NHANES I survey participants, three longitudinal NHEFS follow-up surveys (1982–1984, 1987, 1992) were conducted in persons who were aged 25 and older at NHANES I. In each survey, the subjects or their proxies were interviewed, and death certificates were obtained for decedents.

At baseline, 4,700 people were aged 60 to 74. Of this sample, 3,033 (65%) reported drinking fewer than 12 drinks in the previous year, 1,658 (35%) reported drinking at least 12 drinks in the previous year, and nine (< 1%) had no data on drinking. The descriptive analyses were confined to the group of 4,691 persons for whom data on drinking were available. Data on mortality were missing for 227 persons (4.8%) of the original sample. The longitudinal mortality analyses included only those persons for whom data on mortality status at the time of NHEFS 1992 and complete data on covariates associated with drinking and death (n = 3,726) were also available. Consistent with other large cohort studies, participants who were not included in the longitudinal analyses (because they were missing data on mortality or covariate data, n = 965) had higher mortality and were more often male, not white, not married, of lower income and education, not working, and less active than participants who were included in the analyses ($P < .02$ for all). The median length of follow-up for survivors in the study sample was 20 years (range 17–22 years).

Alcohol Variables

The questions on alcohol consumption asked at baseline were as follows. "During the past year, have you had at least one drink of beer, wine, or liquor?" (Response options were yes or no.) "How often do you drink beer, wine, or liquor?" (Response options were every day, just about every day, about two or three times a week, about one to four times a month, or more than three but less than 12 times a year.) "When you drink, how much do you usually drink over 24 hours?" (Responses obtained ranged from 1 to 25 drinks.) Abstainers were defined as persons who reported no drinking in the previous year or those who reported drinking on fewer than 12 occasions in the past year. This definition of abstainers has been used in the National Health Interview Surveys.[20] Drinkers were defined as those who reported drinking on at least 12 occasions in the previous year.

Drinking Risk Groups

Using the CARET's items and decision rules as a model, at-risk drinking was defined in the study sample using respondents' answers to NHANES I items on quantity and frequency of drinking and selected comorbidities (e.g., medical and psychiatric conditions and medications regularly used). Medical and psychiatric conditions included having been told by a doctor that they had gout, hepatitis, or ulcer disease, or having been told by a doctor in the previous year that they had a nervous breakdown (or were taking a medication for nerves). Medications included were those used for insomnia, seizures, allergies, indigestion, or pain. Table 1 includes definitions of at-risk and not-at-risk drinking using variables available in NHANES I and modeled on those used in the CARET. Respondents who met one or more criteria for at-risk drinking were considered at-risk drinkers.

Table 1. At-Risk and Not-at-Risk Drinking Variables Based on Comorbidity-Alcohol Risk Evaluation Tool Definitions

Item	Amount of Drinking Considered at Risk	Amount of Drinking Considered Not at Risk
Alcohol use alone	3 drinks/day, ≥4 times a week or ≥4 drinks/day at any frequency	3 drinks/day < 4 times a week or 1–2 drinks/day at any frequency
Alcohol use and comorbidity		
Medical/psychiatric conditions		
Gout, anxiety disorder (history of nervous breakdown or takes medication for nerves)	2–3 drinks/day ≥2 times a week or ≥4 drinks/day at any frequency	2–3 drinks/day < 2 times a week or 1 drink/day at any frequency
Hepatitis, ulcer disease	Any amount of drinking	Not applicable
Medications for insomnia, seizures, allergies, indigestion, pain	2–3 drinks/day ≥2 times a week or ≥4 drinks/day at any frequency	2–3 drinks/day < 2 times a week or 1 drink/day at any frequency

Demographic and Health-Related Variables

The following demographic variables were examined: age, sex, marital status (married vs other), work status (working vs other), income (split at the median; <\$7,000 vs ≥\$7,000), race (white vs other), and education (<12th grade vs ≥12th grade). The health-related variables included body mass index (weight in kilograms divided by square of height in meters) and current smoking status (yes vs no), and usual physical activity (very or moderately active vs quite inactive). Smoking status was available at baseline for only part of the sample. For those without baseline smoking data, smoking status was based on recall information from survivors or proxy interviewees at the 1982–1984 NHEFS follow-up interview, thus increasing baseline smoking status availability (n = 4,096).[21,22] The following conditions were also examined as potential confounders, because they are strong predictors of mortality and may be associated with alcohol use: previous heart attack, previous stroke, hypertension, and diabetes mellitus.[23]

Statistical Analyses

Sampling weights from NHANES I were used to estimate distributions of drinking and demographic and health-related characteristics for the U.S. population.[24] The SAS 8.01 procedure PROC SURVEYMEANS (SAS Institute, Inc., Cary, NC) was used to incorporate the effect of the complex survey design, including stratification and clustering, for the population estimates. Stata 7.0 commands, SVYREGRESS, and SVY LOGIT (Stata Corp., College Station, TX) were also used to compare demographic and health-related characteristics of persons in the drinking-risk groups and abstainers.

To ascertain why older at-risk drinkers were identified as such, the prevalence of individual risks identifying at-risk drinkers as listed in Table 1 were examined. The number of risks identifying at-risk drinkers was then summed. Both of these analyses were conducted for the entire sample of at-risk drinkers and in men and women separately.

Cox proportional hazards analyses[25] were used to estimate the hazard ratios and 95% confidence intervals for death of abstainers and at-risk drinkers and compare them with those of not-at-risk drinkers. The referent group for all models was not-at-risk drinkers. The first model included 14 covariates (age; sex; race; marital status; education; income; employment; body mass index; smoking status; activity level; and prior history of heart attack, stroke, hypertension, and diabetes mellitus). The second model included these same covariates (with the exception of sex) and was stratified by sex, because others have found that women and men have differing mortality risks from alcohol use.[9,26] All variables in these models met the proportional hazards assumptions based on visual inspection of cumulative hazard logarithm plots.

An interaction between drinking-risk group and comorbidity (having one or more of the comorbidities listed in Table 1) was tested for. This interaction term was not statistically significant in the combined sex analyses ($P = .94$) or the sex-stratified analyses ($P = .92$ for men, $P = .83$ for women), so the analyses were not stratified by comorbidity status.

Because smoking was the largest source of missing data in these analyses (n = 595), these analyses were also conducted using a multiple imputation method for this missing data using SAS PROC MI based on MCMC algorithm (SAS Institute, Inc.). Because the results of these analyses did not differ substantially from those excluding those with missing smoking data, they are not reported here.

RESULTS

Demographic and Health-Related Characteristics of the Risk Groups

At the time of the baseline survey, the average age of U.S. adults aged 60 to 74 was 66, and they were 56% female (n = 2,476 in the sample), 91% white (n = 3,903), 68% married (n = 3,029), and 77% nonsmoking (n = 3,235); 81% had less than a high school education (n = 3,940). Abstainers were 61% (n = 3,033) of the population. Drinkers constituted 39% of the U.S. adult population (n = 1,658 in the sample), and at-risk drinkers constituted 10% of this population (n = 425), including 18% of drinking men (n = 336) and 5% of drinking women (n = 89).

Men, married people, and smokers were more likely than women, unmarried people, and nonsmokers to be at-risk drinkers and less likely to be abstainers (Table 2). Those who were less educated, had lower incomes, and had hypertension and diabetes mellitus were more likely to be abstainers than those with higher education, with higher income, without hypertension, and without diabetes mellitus.

Prevalence of Individual Risks Identifying At-Risk Drinkers

Thirty-one percent of at-risk drinkers (33% of men, 27% of women) were identified as such solely because of the amount of alcohol they reported consuming, and 69% of at-risk drinkers were classified as such, because their reported amount of alcohol use was deemed risky when combined with comorbidities (67% of men, 73% of women) (Table 3). The most common medical and psychiatric conditions responsible for identifying at-risk-drinking men were gout (22%) and ulcer disease (16%). Ulcer disease (20%) and anxiety disorder (defined as having a nervous breakdown or taking medications for nerves) (17%) were the most common conditions identifying at-risk-drinking women. Pain medication was the most common medication used to identify at-risk drinkers in men and women (13% of men, 22% of women).

Mortality Associations

After approximately 20 years of follow-up, 2,673 persons (1,379 men, 1,294 women) had died: 65% (76% of men, n = 445; 60% of women, n = 239) of abstainers, 62% (68% of men, n = 720; 56% of women, n = 1,018) of not-at-risk drinkers, and 70% of at-risk drinkers (77% of men, n = 214; 49% of women, n = 37).

In proportional hazard analyses, after adjusting for the potential confounders, at-risk drinkers and abstainers had marginally higher hazard rates for death than not-at-risk drinkers (12% and 8% greater hazard rates, respectively) (Table 4). An interaction between drinking-risk group and comorbidity (having one or more of the comorbidities listed in Table 1) was tested for. This interaction term was not

Table 2. Demographic and Health-Related Characteristics of the U.S. Population, Aged 60 and Older at the Time of the National Health and Nutrition Examination Survey I (1971–1975)

Characteristic	At-Risk Drinkers (n = 425)	Abstainers (n = 3,033)	Not-at-Risk Drinkers (n = 1,233)	*P*-value
Age, mean		66	66	<.001
Sex, %				<.001
Female	26	66	47	
Male	74	34	53	
Race, %				.04
White	92	90	93	
Other	8	10	7	
Marital status, %				<.001
Married	80	63	72	
Other than married	20	36	28	
Education, %*				<.001
<High school	74	84	77	
≥High school	25	15	22	
Annual income, \$, %†				<.001
<7,000	42	60	43	
≥7,000	51	36	52	
Employment, %				.03
Working	46	41	47	
Other	54	59	53	
Body mass index, kg/m^2, mean	26	26	26	.045
Usual activity level, %				.47
Very/moderately active	87	87	89	
Quite inactive	13	13	11	
Smoker, %‡				<.001
Smoker	35	16	27	
Nonsmoker	54	75	64	
Hypertension, %	26	37	27	.01
Heart attack, %	9	11	9	.16
Stroke, %	4	4	3	.56
Diabetes mellitus, %	4	10	5	<.001

* 1% in each of the drinking groups had missing data on education.
† 7% of the at-risk drinking group, 4% of the abstainer group, and 5% of the not-at-risk drinking group had missing data on annual income.
‡ 11% of the at-risk drinking group, 9% of the abstainer group, and 9% of the not-at-risk drinking group had missing data on smoking.

statistically significant ($P = .94$). An interaction with sex was also tested for, and it was found that sex marginally modified the association between at-risk drinking and mortality ($P = .07$) but did not modify the association between abstinence and mortality ($P = .94$). In sex-stratified analyses, in men, at-risk drinkers had a 20% greater hazard rate for death, whereas abstainers had no greater hazard rate for death. In women, neither at-risk drinkers nor abstainers had greater hazard rates for death.

DISCUSSION

In this large, population-based sample of older persons, it was found that at-risk drinking (defined using comorbidity-specific drinking thresholds) was common in drinkers (27%) during the NHANES I study period. Men and smokers were more likely than women and nonsmokers, respectively, to be at-risk drinkers. Most older drinkers were considered at-risk drinkers because of their alcohol use in the presence of relevant comorbidities (69%). Although older drinkers currently consume less alcohol than older drinkers did during the time of NHANES I,[27] it is still likely that at-risk drinking is common, given that more recent data show that 40% to 50% of older men and 30% to 40% of older women drink alcohol.[27] In addition, 82% of persons aged 65 and older have one or more chronic condition.[28]

In mortality analyses, it was found that at-risk-drinking men had a 20% higher mortality rate than did not-at-risk-drinking men. In contrast, men and women abstainers had a marginally significant 8% higher mortality rate than not-at-risk drinkers, whereas at-risk-drinking women had no greater mortality than not-at-risk-drinking women. Some studies have observed similar associations between heavy drinking and mortality,[5,8] whereas others have not observed this association.[7,9] The risk groups in the current study differ from the alcohol-risk groups examined in prior studies; in this study, older adults consuming what is typically considered light to moderate amounts of alcohol use (e.g., two drinks twice a week) were considered at-risk drinkers if they also had selected comorbidities that could increase risk for harm from alcohol (e.g., have gout, take a medication for insomnia regularly).

Table 3. Reasons for Identifying At-Risk Drinkers (N = 425)

Reason	Men n (%)	Women n (%)	Total n (%)
Alcohol use alone	117 (33)	23 (27)	140 (31)
Alcohol use with comorbidity	219 (67)	66 (73)	285 (69)
Medical/psychiatric conditions			
Gout	61 (22)	4 (5)	65 (18)
Anxiety disorder*	25 (7)	13 (17)	38 (9)
Hepatitis	2 (1)	1 (<1)	3 (1)
Ulcer	45 (16)	18 (20)	63 (17)
Medications			
Insomnia	11 (4)	8 (12)	19 (6)
Seizures	2 (<1)	1 (<1)	3 (<1)
Allergies	6 (2)	3 (3)	9 (2)
Indigestion	22 (8)	9 (9)	31 (8)
Pain	49 (13)	19 (22)	68 (15)

* History of nervous breakdown or takes a medication for nerves.

Others have also found the association between mortality and alcohol use in women to be nonsignificant,[26] and this null finding has been thought to be related to small numbers of heavy-drinking women in these samples.[9,26] In the sample in the current study, there were only 89 at-risk-drinking women (compared with 336 at-risk-drinking men) and only 37 deaths in this group (49%, vs 77% of men). Perhaps it was not possible to observe an association between at-risk drinking and mortality in women only because of the small sample size and the lower mortality rate in women.

None of these previous studies have examined mortality risks in groups of persons identified as at-risk drinkers because of their use of specific amounts of alcohol in combination with comorbidities. Because most older persons who drink have comorbidities, and different comorbidities have differing health effects when combined with alcohol use, it is important to use comorbidity-specific thresholds of alcohol use to define at-risk drinking. Unlike a previous study[9] that found no association between alcohol use and mortality after stratifying by disease status, the current study found, in the same population, that at-risk drinking defined using comorbidity-specific thresholds was associated with greater mortality in men (but not in women). The difference between the findings in the previous study[9] and the current study (at least with respect to at-risk drinking in men) underlines the need to use different alcohol-use thresholds for different comorbid conditions, as in the CARET.

An interaction between at-risk drinking and the presence or absence of any relevant comorbidity (using the list in Table 1) was tested for, and no evidence was found of an interaction. This suggests that the mortality rate in drinkers who are at risk because of the amount of alcohol they consume alone is similar to the rate in drinkers who are at risk because of the amount of their alcohol use combined with selected comorbidities. Because the amounts of alcohol used to classify at-risk drinking among those drinkers having comorbidity were lower than in those at-risk drinkers without comorbidity, this finding provides additional support for using lower thresholds to identify at-risk drinking in older adults with selected comorbidities.

Only a marginally significant association was found between abstention and mortality risk and not-at-risk drinking. This finding adds to the evidence suggesting that even the low amounts of alcohol consumption in the not-at-risk drinkers may not have big mortality benefits in older adults.[1–9] It is also possible that the inability to find a strong mortality benefit for not-at-risk drinking (compared with abstention) reflects the need for even lower alcohol consumption thresholds to identify at-risk drinking than used by CARET. Future work will investigate whether and how the CARET may have to be refined by examining longitudinal associations with a variety of health outcomes (including hospitalization and declines in physical and cognitive functioning) in older adults with and without relevant comorbidities.

There are some limitations to this study. First, it was not possible to assess all potential risks associated with alcohol use in this population, because data were not collected on other factors important in evaluating these risks (e.g., use of medications that may cause gastrointestinal bleeding, evidence of depression). Second, at-risk drinking could be assessed only at baseline, because the dataset did not include the same set of comorbidities at each of the survey periods. This prevented the mortality effects of changes in at-risk drinking from being studied over time. Third, the sample was more than 90% white, which reflected the racial composition of the United States in 1971 through 1975; comparisons with other racial groups are therefore limited. Fourth, no

Table 4. Risk of Death for At-Risk Drinkers and Abstainers Aged 60 and Older

Subjects	At-Risk Drinker (322 Deaths)	Abstainer (2,426 deaths)
	Adjusted Hazard Ratio (95% Confidence Interval)	
All (N = 3,726; 2,673 deaths)	1.12 (0.97–1.30)	1.08 (0.98–1.19)
Men (n = 1,711; 1,379 deaths)*	1.20 (1.01–1.41)	No sex interaction
Women (n = 2,015; 1,294 deaths)*	0.87 (0.61–1.24)	

Note: Not-at-risk drinkers were the referent group for all hazard ratios. Model adjusted for age, race (white vs other), income (<\$7,000 vs ≥\$7,000), education (<12th grade vs ≥12th grade), marital status (married vs other), employment status (working, retired, or other), current smoking status (yes vs no), usual physical activity (very or moderately active vs quite inactive), hypertension, heart attack, stroke, and diabetes mellitus.
* *P*-values for test of sex interaction: with at-risk drinking, $P = .07$; with abstinence, $P = .94$.

data on episodic heavy drinking were available. Such drinking has been shown to influence mortality risks associated with average alcohol consumption.[26]

This is the first study to examine the combined effects of alcohol use and comorbidities that may contribute to mortality risk. The findings help to explain the relationship between alcohol, comorbidity, and mortality by identifying groups of older drinkers, specifically men, whose use of alcohol with their comorbidity increases their risk for death. The findings also suggest that a lower threshold of alcohol use should be recommended for older adults with specific comorbidities to reduce mortality risks. The CARET was used as the model to define at-risk drinking and was developed to identify those at risk for a variety of harms, not only limited to mortality. It is possible that other outcomes such as disability, depression, or falls may have stronger associations with at-risk drinking. Future studies examining these outcomes and others that the use of alcohol in the presence of comorbidities may influence will help to better understand the benefits and risks of alcohol use in older adults with comorbidity.

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