Alcohol consumption and cognitive function in late life

A longitudinal community study

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Abstract—*Objective:* To examine the association between alcohol use and cognitive decline in a longitudinal study of a representative elderly community sample free of dementia at baseline. *Methods:* Cognitive functions and self-reported drinking habits were assessed at 2-year intervals over an average of 7 years of follow-up. Cognitive measures, grouped into composites, were examined in association with alcohol consumption. Trajectory analyses identified latent homogeneous groups with respect to alcohol use frequency over time, and their association with average decline over the same period in each cognitive domain. Models controlled for age, sex, education, depression, smoking, general mental status (Mini-Mental State Examination [MMSE]), performance on the given test at baseline, and subsequent new-onset dementia during follow-up. *Results:* The authors found three homogeneous trajectories that they characterized as no drinking, minimal drinking, and moderate drinking. Few heavy drinkers were identified in this elderly cohort. Compared to no drinking, both minimal and moderate drinking were associated with lesser decline on the MMSE and Trailmaking tests. Minimal drinking was also associated with lesser decline on tests of learning and naming. These associations were more pronounced when comparing current drinkers to former drinkers (quitters) than to lifelong abstainers. *Conclusion:* In a representative elderly cohort over an average of 7 years, a pattern of mild-to-moderate drinking, compared to not drinking, was associated with lesser average decline in cognitive domains over the same period.

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Current clinical wisdom regarding alcohol and the brain is based largely on the deleterious effects of excessive alcohol consumption such as Wernicke-Korsakoff syndrome, alcohol dementia,[1-4] and hemorrhagic stroke[5]. Acute alcohol consumption adversely affects cognitive task performance in laboratory settings,[6-9] and heavy alcohol consumption impairs cognitive processing in older individuals.[10-12] In contrast, a growing literature suggests that a chronic pattern of light-to-moderate drinking, variously defined, may have a protective effect against dementia[13-28] and on cognitive function,[19-22] particularly among women.[23-26] These findings parallel contemporary reports of the beneficial effects of moderate alcohol use on cardiovascular health.[27,28]

Many previous studies examined either cognitive performance or alcohol use at a single measurement point.[10,14,29,30] Others examined only a general mental status test.[21,31] Some accounted for changes in drinking patterns over time by repeating the analyses excluding those with such changes.[17,18,25] In the present study, we used the method of trajectory analysis to examine the associations between changes in cognitive functioning over time and the patterns or trajectories of self-reported drinking over the same period, in a large community-based elderly sample of older adults.

Methods. The data reported here were collected as part of the Monongahela Valley Independent Elders Survey (MoVIES project), a prospective epidemiologic study of dementia in a largely rural, blue-collar community in Southwestern Pennsylvania. Details of the background, cohort, and methods of the study have been reported earlier.[32-34] Briefly, a total of 1,681 individuals aged 65 years or older were recruited during 1987–1989, fluent in English with at least sixth-grade education, and living in the community (i.e., not in long-term-care institutions). Of these, 1,422 study participants were recruited by random sampling from the voter registration lists for the selected area, and 259 subjects were volunteers from the same area. A covariate "recruitment status," representing original random vs volunteer selection, is always included in our analytic models.

At approximately 2-year intervals, surviving consenting subjects were reassessed in a series of data collection "waves" until 2002. Data on alcohol consumption were first collected at wave 2 (1989-1991), which therefore serves as the baseline for the current analyses. At wave 2, the MoVIES cohort consisted of 1,341 adults with mean (SD) age 74.9 (5.5) years. After excluding 64 participants with prevalent dementia (see below) with onset before baseline, data from the remaining 1,277 participants were available for the present analysis; further exclusions occurred where data were missing or not relevant for specific analyses, as will be described later.

Screening assessment. Informed consent was obtained according to procedures approved annually by the University of Pittsburgh Institutional Review Board. The standardized interview

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collected data on a range of variables including but not limited to the following.

Cognitive functioning was assessed at each wave using a test battery incorporating the neuropsychological test panel of the Consortium to Establish a Registry for Alzheimer disease (CERAD),[35] to briefly measure cognitive performance in multiple domains known to be affected in dementia. Tests included the Mini-Mental State Examination (MMSE),[36] Trailmaking Tests A and B,[37] Word List Learning and Delayed Recall,[35] Story Immediate Retell and Delayed Recall,[38] Initial Letter and Category Fluency,[39] 15-item CERAD version of the Boston Naming Test,[35,40] CERAD Constructional Praxis,[41] and Clock Drawing.[42] Composite cognitive scores were constructed as described later.

Alcohol use was assessed at baseline by the following self-reported variables: lifetime history of alcohol use (yes/no), alcohol use in the past year (yes/no), frequency of alcohol use during the past year, and number of drinks consumed per occasion. At follow-up, only drinking frequency was assessed. Based on frequency, participants were classified into six initial levels: no alcohol in the preceding year (lifelong abstainers and exdrinkers or quitters), alcohol consumed less than once a month, once a month or more but less than once a week, once a week, more than once a week but not daily, and daily.

Covariates. In addition to age, sex, educational level, and recruitment status, we also examined smoking and depressive symptoms. For these analyses, participants were classified as ever-smokers vs never-smokers based on their responses to the question: "Have you ever smoked cigarettes regularly (more than one a day for a year)?" Depression was examined using the modified Center for Epidemiologic Studies-Depression Scale (mCES-D) with a threshold of five or more symptoms used to indicate substantial depression symptoms, as previously reported.[43-44] For post-hoc subgroup analyses, as a general measure of medical morbidity, we included the number of regularly taken prescription medications, based on direct inspection of pill bottles.[45-46] We also included self-report of the following selected conditions, in response to the question: "Has a doctor or nurse ever told you that you have [heart disease, diabetes, stroke, other neurologic diseases, peptic ulcer disease (stomach, intestines), bowel disease, liver disease, or nervous/emotional condition]?"[46]

Detailed clinical assessment. Performance on the cognitive tests at each wave was used to select subgroups of individuals classified as "cognitively impaired" and "cognitively declined" for a standardized clinical diagnostic assessment based on the CERAD and Pittsburgh Alzheimer disease Research Center assessment protocols; a comparison group of cognitively intact participants was also randomly selected for this assessment.[34,47] Clinical assessments led to the diagnosis of dementia according to Diagnostic and Statistical Manual of Mental Disorders , 3rd edition, revised (DSM-III-R),[48] and of dementia stage/severity based on the Clinical Dementia Rating (CDR) scale,[49] as detailed previously.[34] For all those classified as having dementia, a symptom onset date was estimated based on all available data. For the present analyses, we excluded those with prevalent dementia, defined as CDR rating ≥ 1 and onset prior to baseline (wave 2). Subsequent development of incident dementia (with onset after baseline) was included as a covariate in the trajectory models described below.

Statistical methods. Descriptive statistics (χ^2 test, t test, or nonparametric equivalents) were used to characterize the sample and subgroups on self-reported frequency of alcohol consumption, age, sex, education, recruitment status, smoking, depression, MMSE score at baseline (wave 2) and proportion with subsequent incident dementia. The correlation between drinking frequency and quantity (number of drinks consumed per occasion) was examined using Spearman's rank-order correlation. Two subgroups of current nondrinkers (lifetime abstainers and exdrinkers) were compared with each other in post-hoc analyses.

Composite cognitive scores. The following composite cognitive scores were created by first Z-transforming scores on each individual test, based on their distribution at baseline, and then combining and averaging the Z-transformed tests according to cognitive domain, based on conceptual grounds and previous factor analysis:[50]

1. Learning (composite of the learning trials from the Word List Learning test and Story Immediate Retell);
2. Memory (composite of Word List Delayed Recall and Story Delayed Recall);
3. Visuospatial (composite of Clock Drawing and CERAD Constructional Praxis);
4. Fluency (composite of Verbal Fluency for Categories and for Initial letters);
5. Trailmaking (composite of Trail Making A and B);
6. Naming (CERAD/Boston Naming Test alone).

A specific "executive" composite was not designated. Clock Drawing can be considered a test of either or both executive and visuospatial functions, depending on scoring and interpretation. Verbal fluency can be an executive task or a language task. Trailmaking B assesses some executive functions, whereas Trailmaking A primarily measures psychomotor speed. Our composites were based primarily on the previously reported factor structure of our test battery,[50] in which Clock Drawing and Constructional Praxis loaded together on one factor, which we called Visuospatial, whereas Verbal Fluency for initial letters (P and S) as well as Verbal Fluency for categories (fruits and animals) loaded together on another factor we called Fluency, and both Trailmaking Tests loaded together on another factor. The MMSE was included as an indicator of general mental status.[36]

On these composites/tests, we examined both baseline scores and average decline per year over each participant's duration of follow-up. Those with high baseline scores might be expected to show greater decline over time because they have more room to decline than those whose scores are already low at baseline (floor effect). Alternatively, those with middle-to-low baseline scores may already have declined from previous (unmeasured) higher levels and may be on the path to further decline (e.g., as a result of underlying disease). They may therefore decline more than those with higher scores who may be stable and high-functioning. The longitudinal analyses of decline (see below) were therefore adjusted for baseline scores.

Trajectory analysis is a type of latent class analysis which identifies homogeneous groups within a heterogeneous population assumed to contain multiple latent trajectories. This procedure combines two separate statistical models simultaneously using a maximum likelihood estimation approach, the first being a multinomial regression model examining the associations of the covariates with the probability of membership in each of the homogeneous groups. The second model builds trajectories (slopes) for the different latent groups. This method (SAS procedure PROC TRAJ)[51] was used to examine trajectories of drinking frequency over time and characteristics associated with the trajectories. Here, drinking frequencies reported at each wave 2 through 6 were modeled by a censored normal distribution.

The first model included the following covariates: age at baseline, sex, education (high school graduate or more vs less than high school), recruitment status, depressive symptoms (mCES-D ≥ 5 vs ≤ 4), smoking, development of incident dementia during followup, baseline MMSE score, baseline scores and average annual decline on the given cognitive test or composite. The Bayesian Information Criteria[52] were used to identify the optimal number of homogenous groups. For each model, participants with missing longitudinal data (i.e., dropout during follow-up) were included, whereas those with missing data on baseline covariates were excluded, because the model estimates each subject's probabilities of falling into each latent trajectory by using information on baseline covariates. In post-hoc analyses, the trajectory models were fit separately for men and women, and also separately using only quitters and only lifelong abstainers as the reference group.

We assumed that elderly participants who did not meet criteria for dementia at baseline, but went on to do so later in the course of the study, already had incipient dementia at baseline. Underlying degenerative or vascular disease might have affected the rate and pattern of cognitive decline in those individuals, in addition to any effects of alcohol consumption. We therefore adjusted the models for incident dementia so as to determine the independent effect of alcohol on decline. In post-hoc analyses, we refit the trajectory models excluding the incident dementia cases.

Results. Among 1,277 nondemented (CDR <1.0) subjects at baseline, 18 subjects were excluded because of missing baseline values on at least one of the covariates. The remaining 1,259 subjects had, at baseline, a mean (SD) age of 74.6 (5.34) (range 66.8 to 97.1) years. They were 60.8% women, 97.5% white, and 61.2% with high

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Table 1 *Frequency of drinking and number of drinks per occasion as reported at baseline*

	No. of drinks per occasion							
Frequency of drinking	0	1	2	3	4	5	>5	Total
Not drinking currently/past year	487	0	0	0	0	0	0	487
Less than once a month	0	287	46	14	3	1	0	351
Once a month or more, less than weekly	0	32	20	6	0	1	1	60
Weekly (including weekends only)	0	20	11	5	2	1	1	40
More than weekly, less than daily	0	24	20	4	1	3	4	56
Daily	0	37	35	11	10	7	4	104
Total	487	400	132	40	16	13	10	1098

Data restricted to 1,098 subjects included in trajectory analyses.

school graduate or higher education. Current drinking (consumption of some alcohol over the preceding year) was reported by 54.2% of the cohort; by sex and age, this broke down to 70.6% vs 56.2% of men aged ≤74 vs ≥75 years, and 52.5% vs 39.9% of women aged ≤74 vs ≥75 years.

Mean (SD) duration of follow-up was 7.3 (2.7) years, with a range of 1.7 to 11.8 years. Exclusion of those with missing follow-up data on variables relevant to the trajectory analyses further reduced the sample size to 1,098. Within this group, crosstabulation of drinking frequency with drinking amount (table 1) revealed that only 10 participants reported consuming more than five drinks per occasion, and that frequency and quantity were strongly correlated (Spearman rank-order correlation coefficient = 0.91, $p < 0.001$).

The trajectory analysis (PROC TRAJ) identified three homogeneous groups as the best model of drinking frequencies over time. The figure shows both actual (using exact probabilities of each subject's belonging to each trajectory) and estimated (using the model-assigned group identification for each subject) trajectories, after including all covariates except the domain-specific cognitive test/composite scores. The Bayesian Information Criteria varied slightly depending on the specific cognitive measure included in the model, but in each case a three-trajectory model provided the best fit, with trajectories virtually identical to those depicted in the figure. Based on the actual drinking frequencies reflected in these trajectories, we designated them as no drinking, minimal drinking (once a month or less), and moderate drinking (more than once a month, averaging between daily and weekly). Relevant baseline characteristics of the three drinking frequency subgroups defined by the trajectories are shown in table 2.

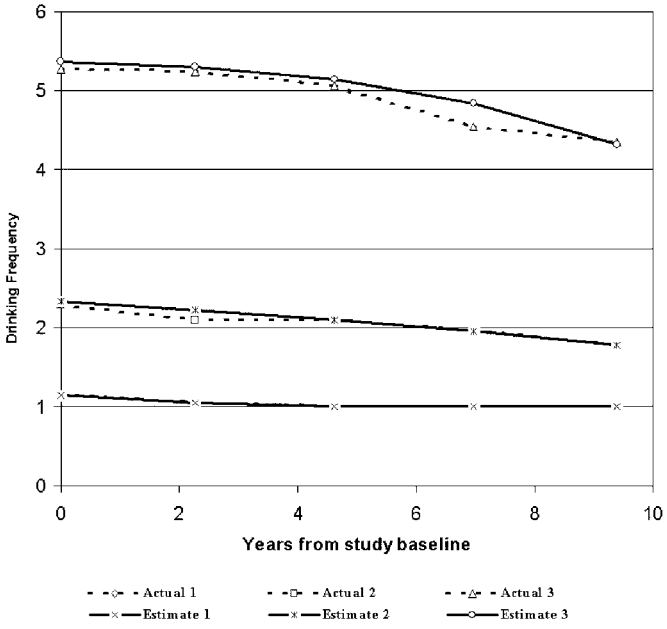

Figure. Trajectories of alcohol intake frequency.

Table 3 shows the associations of the test/composite baseline score and subsequent annual decline on the test/composite with the minimal and moderate drinking trajectories, using the no-drinking trajectory as the reference group. All models adjusted for the covariates shown in table 2; decline models also adjusted for baseline score on the given test/composite. Table 3 can be interpreted as follows: for example, a one SD increase in MMSE baseline score is associated with a 26% increase in odds of being in the minimal-drinking group (i.e., odds ratio [OR] 1.26) compared with the no-drinking group. Further, a one SD greater annualized decline in MMSE is associated with a 70% reduction in odds of being in the minimal-drinking group (OR = 0.3), compared with the no drinking group. Similarly, compared to no drinking, the minimal-drinking trajectory was associated with higher baseline scores on all tests/composites except fluency, whereas the moderate-drinking trajectory was associated with higher baseline scores on all tests/composites except Trailmaking. Both minimal- and moderate-drinking trajectories were associated with smaller decline on the MMSE and Trailmaking; minimal drinking was also associated with smaller decline on learning and naming.

For clinical reference, table 4 shows the actual mean (SD) raw baseline scores and average annual decline on the individual tests (as opposed to the composites) in the three trajectory-based groups.

Regarding the other covariates, only smoking history was consistently associated with drinking trajectory; ever-smokers were significantly more likely to be in the minimal- and moderate-drinking trajectory groups than in the no-drinking group. Those with more than a high school education comprised 57.1%, 65.5%, and 63.1% of those in groups 1, 2, and 3; this difference was significant ($p < 0.001$ by χ^2 test) in univariate analyses but not in the models after adjustment for other covariates. Female sex

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Table 2 *Baseline characteristics of all participants across categories based on drinking frequency trajectories* over time (n = 1,098)*

	No drinking trajectory (group 1)	Minimal drinking trajectory (group 2)	Moderate drinking trajectory (group 3)	Total
n	447	502	149	1,098
Mean (SD) age, y	75.1 (5.4)	73.9 (4.9)	73.9 (5.1)	74.4 (5.2)
Women, %	74.3	65.7	22.2	63.3
High school education or more, %	57.1	65.5	63.1	61.8
Ever smoked, %	34.9	50.2	65.1	46.0
Depression symptoms on mCESD ≥5, %	11.6	7.8	7.4	9.3
Mean (SD) MMSE	27.1 (2.3)	27.5 (1.9)	27.3 (2.0)	27.3 (2.1)
Volunteers, %	21.5	19.5	14.1	19.6
Developed incident dementia during follow-up, %	20.4	11.6	10.7	15.0

* See figure.

was related to different trajectories on different tests, in no consistent pattern. In post-hoc analyses, we fit the trajectory models separately in men and women (data not shown). Similar associations of higher baseline scores and lesser decline over time with minimal and moderate drinking on several tests/composites were seen in women. No associations were found between drinking trajectory and cognition among men examined separately, with the sole exception of significantly less decline on the MMSE associated with moderate drinking. Loss of power is the most likely explanation; the decrease in sample size (from 1,098 overall to 695 women and 403 men) most likely reduced the significance of some of the associations seen in the cohort as a whole.

In post-hoc analyses excluding incident dementia cases, there were minor changes in the odds ratios but the significance of all associations remained the same with one exception: the association of lesser decline on the MMSE was no longer significantly associated with group 3 (moderate drinking). We attribute this minor change in results to decrease in power from the 10% reduction in sample size.

The trajectory models in the cohort as a whole were also fit including alcohol quantity (number of drinks per occasion) as a covariate; the association between drinking frequency and quantity was so strong that associations with cognitive variables were obscured. We therefore report the models based solely on frequency, rather than quantity, of alcohol consumption.

Table 3 *Associations of baseline cognitive test scores and average annual decline with minimal and moderate drinking compared to no drinking**

	Minimal drinking (group 2) compared to no drinking (group 1)		Moderate drinking (group 3) compared to no drinking (group 1)	
Test or composite	Odds ratio	95% CI	Odds ratio	95% CI
Baseline scores				
Mini-Mental State Examination	1.26†	1.01–1.58	1.66†	1.18–2.32
Learning (composite)	1.42†	1.11–1.81	1.63†	1.13–2.34
Memory (composite)	1.30†	1.02–1.65	1.62†	1.13–2.31
Fluency (composite)	1.17	0.95–1.44	1.37†	1.02–1.85
Visuospatial	1.44†	1.12–1.85	1.66†	1.15–2.40
Trailmaking	1.27†	1.01–1.60	1.30	0.94–1.82
Naming	1.50†	1.22–1.84	1.53†	1.11–2.10
Average annual decline				
Mini-Mental State Examination	0.30†	0.14–0.65	0.08†	0.02–0.28
Learning (composite)	0.17†	0.05–0.57	0.25	0.04–1.4
Memory (composite)	0.38	0.10–1.39	1.06	0.18–6.33
Fluency (composite)	0.73	0.21–2.57	0.25	0.05–1.40
Visuospatial	0.46	0.17–1.24	0.49	0.13–1.89
Trailmaking	0.20†	0.05–0.85	0.05†	0.01–0.45
Naming	0.36†	0.15–0.84	0.48	0.14–1.64

* Results of trajectory analysis; see figure.
† Significant at $\alpha = 0.05$.

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Table 4 *Actual baseline test scores and average annual decline in the three trajectory groups*

		Overall sample		No drinking (reference group)		Minimal drinking		Moderate drinking	
Composite (if applicable)	Tests	Baseline score (SD)	Annual decline (SD)	Baseline score (SD)	Annual decline (SD)	Baseline score (SD)	Annual decline (SD)	Baseline score (SD)	Annual decline (SD)
NA	Mini-Mental State Examination	27.3 (2.1)	0.26 (0.7)	27.0 (2.3)	0.39 (0.9)	27.5 (1.9)	0.16 (0.6)	27.2 (2.0)	0.12 (0.5)
Learning	Word List Learning	19.7 (3.8)	0.21 (0.8)	19.3 (4.0)	0.36 (0.9)	20.1 (3.5)	0.09 (0.7)	19.4 (3.8)	0.16 (0.7)
	Story Retell	6.6 (2.8)	0.08 (0.5)	6.3 (2.9)	0.12 (0.6)	6.9 (2.8)	0.05 (0.5)	6.4 (2.6)	0.06 (0.5)
Memory	Word List Recall	6.6 (1.9)	0.14 (0.4)	6.4 (2.0)	0.18 (0.4)	6.76 (1.8)	0.09 (0.4)	6.76 (1.9)	0.15 (0.3)
	Story Recall	5.88 (3.0)	0.09 (0.5)	5.5 (3.1)	0.11 (0.6)	6.25 (0.1)	0.07 (0.5)	5.67 (2.9)	0.11 (0.5)
Fluency	Categories	27.04 (6.1)	0.66 (1.3)	26.27 (6.2)	0.76 (1.3)	27.66 (5.9)	0.59 (1.2)	27.19 (6.3)	0.60 (1.3)
	Initial Letters	22.67 (7.5)	0.35 (1.2)	21.80 (7.5)	0.41 (1.3)	23.29 (7.3)	0.37 (1.1)	23.06 (7.8)	0.12 (1.2)
Visuospatial	Clock Drawing	7.2 (0.9)	0.07 (0.3)	7.04 (1.1)	0.08 (0.3)	7.28 (0.8)	0.07 (0.2)	7.42 (0.8)	0.07 (0.2)
	Constructional Praxis (CERAD)	9.53 (1.4)	0.05 (0.3)	9.32 (1.5)	0.07 (0.4)	9.67 (1.3)	0.03 (0.3)	9.70 (1.3)	0.07 (0.3)
Trailmaking Test	Trails A	0.57 (0.2)	0.19 (0.2)	0.56 (0.2)	0.24 (0.2)	0.58 (0.2)	0.17 (0.2)	0.56 (0.2)	0.17 (0.2)
	Trails B	0.22 (0.1)	0.13 (0.2)	0.21 (0.1)	0.17 (0.2)	0.23 (0.1)	0.11 (0.2)	0.22 (0.1)	0.11 (0.2)
NA	Boston Naming Test (CERAD)	14.2 (0.1)	0.07 (0.3)	13.9 (1.4)	0.10 (0.3)	14.4 (1.0)	0.05 (0.2)	14.38 (0.9)	0.06 (0.2)

Two subgroup of current nondrinkers were compared: quitters and lifelong abstainers. Abstainers were more likely to be women (86.6% vs 62.8%, χ^2 test, 1 *df*, $p < 0.001$) and less likely to have ever smoked (14.5% vs 48.5%, χ^2 test, 1 *df*, $p < 0.001$) than quitters. These two subgroups were not different in age, education, depression, baseline MMSE, incident dementia, overall medical burden as measured by number of prescription medications, or self-report of the specified medical conditions. Abstainers had higher mean (± SD) baseline scores than quitters on Trails A (0.55 ± 0.21 vs 0.51 ± 0.19, $p = 0.01$ by *t* test) and lower mean (± SD) annual decline also on Trails A (0.22 ± 0.26 vs 0.24 ± 0.23, $p = 0.01$).

The trajectory models for decline were fit once again, first excluding quitters and then excluding the lifelong abstainers. Overall, the contrast between nondrinkers and drinkers was less marked when the reference group was limited to lifelong abstainers, and more pronounced when limited to quitters (i.e., much of the difference between drinkers and nondrinkers was explained by quitters).

Specifically, in the trajectory models limiting the reference group to abstainers (i.e., excluding the quitters), many of the above associations lost their statistical significance. In the minimal drinking group, the lower odds of decline on MMSE (OR = 0.05, 95% CI: 0.01–0.26) and Trailmaking (OR = 0.08, 95% CI:0.01–0.56) remained significant, and lower odds of decline on the visuospatial composite (OR = 0.18, 95% CI: 0.04–0.73) became significant. In the moderate drinking group, MMSE (OR = 0.27, 95% CI: 0.09–0.84) and Trailmaking (OR = 0.02, 95% CI: 0.001–0.22) remained significant and the lower odds of decline on Learning (OR = 0.15, 95% CI: 0.03–0.79) became significant.

In contrast, when the reference group was restricted to quitters (i.e., excluding abstainers), there were significant associations between drinking and several tests/composites. The minimal drinking trajectory had lower odds of decline on MMSE (OR = 0.26, 95% CI: 0.10–0.63), learning (OR = 0.16, 95% CI: 0.04–0.63), memory (OR = 0.24, 95% CI: 0.06–0.99), and naming (OR = 0.34, 95% CI: 0.13–0.89). The moderate drinking trajectory had lower odds of decline on MMSE (OR = 0.07, 95% CI: 0.02–0.26) and Trailmaking (OR = 0.04, 95% CI: 0.004–0.47).

Discussion. Historically, the concept of moderate alcohol drinking has evolved from a nonintoxicating and noninjurious level of drinking, to a statistically defined normative level, to the level associated with the lowest morbidity and mortality in a population.[53] Operational definitions of moderate drinking vary greatly across studies. Here, we described as "moderate" the highest trajectory of drinking frequency observed in our cohort over time (averaging between daily and weekly), and as "minimal" the intermediate group who reported drinking once a month or less often. Exclusion of former drinkers made little difference to the results. The proportions reporting current drinking were within the range reported from this age group in national samples.[54] Heavy drinking was underrepresented or underreported in this cohort, as in previous surveys,[52] for reasons we could not assess but may have included selective mortality.

Overall, our cohort showed a consistent pattern of better baseline scores and lesser decline over time in individuals who consumed alcohol minimally or moderately, compared to those who reported no drinking at baseline. These associations were seen in specific areas of cognition. When compared to no drinking, minimal drinking was associated with higher base-

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line scores on all tests/composites except fluency, and lesser decline on general mental status, learning, confrontation naming, and the Trailmaking Test. Moderate drinking was associated with better baseline scores on all tests except Trailmaking, and lesser decline on general mental status and Trailmaking. Thus, the seemingly beneficial effects of alcohol intake against cognitive decline appear concentrated in the areas of learning, executive functions (specifically, psychomotor speed and set maintenance as measured by the Trailmaking Test), and general mental status. Except in the comparison of minimal drinkers to quitters, no effect was found on decline in memory (delayed recall) in which deficits are typically seen with heavy alcohol use, as discussed later.

Post-hoc analyses revealed that much of the difference in cognitive decline between current drinkers and nondrinkers was explained by lesser declines among current drinkers when compared to quitters, rather than when compared to lifelong abstainers. The discrepancy between quitters and lifelong abstainers was not unexpected because it is usually assumed that former drinkers quit drinking because of health problems, which might independently lead to cognitive decline. However, these two subgroups of current nondrinkers differed only in sex ratio and smoking history, and were not significantly different in age, education, depression, number of prescription drugs, or self-reported history of conditions in which alcohol use might have been medically restricted. Our data do not explain the apparent cognitive advantage of continued drinking over cessation of drinking among those already accustomed to alcohol consumption. One potential explanation is that quitters quit because of perceived cognitive difficulties, partly supported by our finding that quitters had lower baseline scores and greater subsequent decline than abstainers on Trailmaking Test A, which measures psychomotor speed. Another possibility is that quitting removed a previously beneficial exposure to alcohol in these individuals, unmasking or precipitating cognitive decline.

The clinical literature to date has largely focused on the deleterious CNS effects of excessive alcohol consumption in younger and middle-aged individuals: alcohol neurotoxicity, malnutrition (particularly thiamine), and hepatic encephalopathy.[2,53,55,56] Various cognitive and behavioral measures have been used to identify the resulting deficits, most often in memory,[57-59] executive functions,[58,60-62] and occasionally visuospatial functions[63]. The two chronic cognitive syndromes typically attributed to alcohol are the Wernicke-Korsakoff syndrome,[4] characterized by dense amnesia and some executive dysfunction (usually seen in middle-aged individuals), and alcohol dementia with milder deficits in memory (usually in older persons). Some authorities consider the latter to be merely a variant of the former,[56] whereas others have suggested alcohol dementia represents comorbid AD in heavy drinkers.[64] The current psychiatric nomenclature, represented by DSM-IV-TR,[1] does not distinguish cognitive subtypes among the dementia syndromes of degenerative, vascular, substance-induced, or other origin. The cardinal feature of alcohol-related dementia is evidence that it is due to the persisting effects of previous alcohol use.[1] Thus, alcohol-related deficits may partially reverse with cessation of drinking.[65] Neither syndrome is regarded as associated with continuing cognitive decline.

In contrast, a growing epidemiologic literature derived from community-based cohorts suggests a J-shaped or U-shaped relationship between alcohol consumption and cognitive functioning, such that light to moderate drinking in middle to late life is associated with better cognitive performance and lesser cognitive decline than either no drinking or heavy drinking.[29,66] The Women's Health Initiative Memory Study found moderate alcohol intake to be associated with better scores and lesser decline over 4.2 years on the modified MMSE.[24] In the Kame study, current drinkers had higher scores than abstainers or past drinkers on the Cognitive Abilities Screening Scale.[67] Neither of these studies reported effects in specific cognitive domains. One study of a national U.S. sample showed alcohol intake to be associated with lower prevalence of verbal memory deficit, with a greater effect in more highly educated individuals.[68] In the Nurses Health Study, moderate drinkers had better cognitive scores and lower risks of substantial cognitive impairment and decline over 1.8 years than nondrinkers.[25] In the Whitehall Study, alcohol use was associated with improved performance on tests of vocabulary and fluency but not memory.[29] Other community-based prospective studies have shown moderate alcohol consumption to be associated with reduced risk of degenerative and vascular dementia.[13,14,17-18,69-70] The most likely mechanism for the apparent protective effect is indirect, via benefits to cardiovascular and cerebrovascular functioning, but actions via various neurotransmitters have also been proposed.[2,55] Clearly, such patterns cannot be detected from studying alcohol-abusing and alcohol-dependent patients. Different mechanisms may underly the adverse effects of heavy drinking and the potential beneficial effects of light to moderate drinking, and may also partly explain why deficits are reported seen in certain functions (e.g., delayed recall), whereas benefits are seen in others (e.g., learning).

Advantages of our study include the large, representative cohort followed prospectively with repeated measurements of several cognitive functions. We examined the association of alcohol use both cross-sectionally with test performance and longitudinally with decline over a fairly long follow-up period. A relative innovation is that we examined cognition in relation to trajectories of drinking frequencies over time. To maintain our focus on the association between alcohol use and cognitive function in relatively healthy individuals, we deliberately excluded preva-

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lent cases of dementia at baseline and adjusted our models for subsequent onset of incident dementia. We examined the entire distributions of cognitive performance and decline rather than only extremes of these values. We also adjusted for potential confounders[71] including demographics, education, baseline cognitive score, depression, and smoking, and undertook relevant subgroup analyses to further clarify our main findings.

Being primarily collected as part of a dementia epidemiology study, our data on alcohol use are less comprehensive and specific than those of studies designed to study alcohol abuse and its consequences. We asked only a few questions about alcohol use and our data were limited to self-report; however, previous studies have shown strong associations between retrospective self-report, food frequency questionnaires, and biologic measures reflecting alcohol consumption.[10,25] Our trajectory models focused on frequency rather than quantity of drinking, rather than combining the two variables.[54] However, there was a strong association between the two, and only a handful of participants reported heavy use. For this reason we were also unable to examine cognitive effects of heavy alcohol consumption. We did not ascertain the types of alcoholic beverages consumed by our participants, as the literature does not suggest they have different effects.[18,25] Although our models were adjusted for education as well as cognitive scores at study baseline, we lacked data on our elderly study participants' intellectual functioning in early adulthood.[71] Our study cohort included too few African Americans and other U.S. minorities to allow ascertainment of racial/ethnic differences in the association of alcohol use with cognitive functioning.[12,30] Despite the prospective design of our study, the length of follow-up, and our efforts to adjust for potential confounders, it remains possible that those who were able to maintain minimal to moderate levels of drinking were those whose health and cognition permitted their doing so.[72]

Our data should not be interpreted as recommending initiation or continuation of alcohol consumption to preserve mental functioning in the elderly. The risk-to-benefit ratio of such recommendations must clearly be considered in the individual case. The National Institute on Alcohol Abuse and Alcoholism position paper on moderate alcohol consumption states only that there is no evidence that moderate alcohol consumption causes cognitive impairment as individuals age.[73] However, in parallel with studies showing low mortality[74-75] and the potential cardiovascular benefits of light to moderate drinking,[27-28] our data support accumulating evidence that moderate alcohol intake might reduce the risk of cognitive decline and dementia in elderly populations. In contrast to the mechanisms by which excessive alcohol might cause damage to various brain structures and functions, these studies point to the need for further research on the mechanisms by which alcohol might also help to protect aspects of cognitive functioning.

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