

Alcohol Intake and Risk of Lethal Prostate Cancer in the Health Professionals Follow-Up Study

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PURPOSE It is unknown whether alcohol intake is associated with the risk of lethal (metastatic or fatal) prostate cancer. We examine (1) whether alcohol intake among men at risk of prostate cancer is associated with diagnosis of lethal prostate cancer and (2) whether intake among men with nonmetastatic prostate cancer is associated with metastasis or death.

METHODS This prospective cohort study uses the Health Professionals Follow-Up Study (1986 to 2012). Our analysis of alcohol intake among men at risk of prostate cancer included 47,568 cancer-free men. Our analysis of alcohol intake among men with prostate cancer was restricted to 5,182 men diagnosed with nonmetastatic prostate cancer during follow-up. We examine the association of total alcohol, red and white wine, beer, and liquor with lethal prostate cancer and death. Multivariate Cox proportional hazards regression estimated hazard ratios (HRs) and 95% CIs.

RESULTS Alcohol drinkers had a lower risk of lethal prostate cancer (any v none: HR, 0.84 [95% CI, 0.71 to 0.99]) without a dose-response relationship. Total alcohol intake among patients with prostate cancer was not associated with progression to lethal prostate cancer (any v none: HR, 0.99 [95% CI, 0.57 to 1.72]), whereas moderate red wine intake was associated with a lower risk (any v none: HR, 0.50 [95% CI, 0.29 to 0.86]; *P*trend = .05). Compared with none, 15 to 30 g/d of total alcohol after prostate cancer diagnosis was associated with a lower risk of death (HR, 0.71 [95% CI, 0.50 to 1.00]), as was red wine (any v none: HR, 0.74 [95% CI, 0.57 to 0.97]; *P* trend = .007).

CONCLUSION Cancer-free men who consumed alcohol had a slightly lower risk of lethal prostate cancer compared with abstainers. Among men with prostate cancer, red wine was associated with a lower risk of progression to lethal disease. These observed associations merit additional study but provide assurance that moderate alcohol consumption is safe for patients with prostate cancer.

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INTRODUCTION

More than three million men in the United States are living with diagnosed prostate cancer.^{1,2} Epidemiologic studies consistently demonstrate a lower risk of death among moderate alcohol drinkers compared with abstainers, likely because of cardiovascular benefits.^{3,4} However, alcohol intake is associated with an increased risk of several cancers.⁵ It remains unknown whether moderate alcohol intake (total and by type) is associated with prostate cancer, and no study has examined intake after diagnosis.

Studies of alcohol and prostate cancer report mixed results.⁶⁻¹⁸ Prospective studies^{6,7,17,18} have observed inverse associations between alcohol and the risk of advanced or fatal prostate cancer, but these studies have been limited by small numbers of events. We reported previously that, on the basis of follow-up through 1998, daily alcohol drinkers had a 24%

lower risk of lethal prostate cancer (distant metastases or prostate cancer death) compared with abstainers, without statistical significance.⁷

In this article, we updated these findings with 14 more years of follow-up and 611 lethal prostate cancer events. We prospectively examined alcohol intake in relation to the risk of lethal prostate cancer. First, we investigated alcohol intake and the risk of developing lethal prostate cancer among men at risk of prostate cancer. Second, among the subset of participants diagnosed with nonmetastatic prostate cancer during follow-up, we investigated postdiagnostic alcohol intake and the risk of progression to lethal prostate cancer and death.

METHODS

Study Population

The Health Professionals Follow-Up Study is a prospective cohort study of 51,529 male health

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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professionals 40 to 75 years of age in the United States. Biennial questionnaires beginning in 1986 ask men to report on their medical history, lifestyle, diet (including alcohol every 4 years), and medications. Average follow-up rates exceed 90%.

The analysis of alcohol intake among men at risk of prostate cancer excluded participants who did not complete the baseline food frequency questionnaire (FFQ), those with cancer before baseline (with the exception of non-melanoma skin cancer), and those who reported clinician-diagnosed alcohol dependency at baseline ($n = 325$), leaving 47,568 participants for analysis.

The analysis of alcohol intake among men with non-metastatic prostate cancer was further restricted to participants diagnosed between 1986 and 2012 ($n = 5,182$).

Exposure

Participants completed validated semiquantitative FFQs every 4 years, described in detail elsewhere.¹⁹ Alcoholic beverages included red and white wine separately (4 ounces, increasing to 5 ounces in 2006), beer (one glass, can, or bottle), and liquor (one drink or shot). We multiplied the amount of alcohol in grams per specified portion size by servings/day, determined the midpoint of the frequency category, and summed across all beverages to estimate total alcohol intake (grams/day [g/d]). The amount of alcohol for the specified portion size was based on United States Department of Agriculture nutrient composition tables. In a subset of questionnaires, the men were also asked to report the number of days per week that they consumed alcohol. In a validation study, the de-attenuated correlation coefficients between diet records and FFQs were 0.83 for red wine, 0.78 for white wine, 0.88 for beer, and 0.85 for liquor.^{19,20} The correlation between alcohol measured by the FFQ and high-density lipoprotein cholesterol, a biomarker sensitive, but not specific, to alcohol intake, was 0.40.²¹

Outcomes

Our primary end point for all analyses, chosen a priori on the basis of clinical significance, was lethal prostate cancer (cancer that metastasized to bone or distant organs or that was identified as a cause of death). Overall mortality was an additional end point in our analysis of alcohol intake among men with nonmetastatic prostate cancer, because most patients with prostate cancer die as a result of other causes.

The men reported incident prostate cancer diagnoses on biennial questionnaires; this information was confirmed by manual medical record review. We extracted TNM stage (85% complete), biopsy Gleason grade (80% complete), and initial treatment (82% complete) from medical records. Starting in 2000, participants reported metastases, and other clinical information, on prostate cancer follow-up questionnaires. Deaths were identified through the postal system, by next of kin, and by the National Death Index.

Study physicians reviewed medical records and death certificate information to determine the cause of death, including those deaths resulting from prostate cancer. Follow-up for overall and prostate cancer mortality was virtually complete through 2012.²²

Statistical Analysis

We used multivariate Cox proportional hazards regression to estimate hazard ratios (HR) and 95% CIs. Age (months) was the time scale and we stratified by age and calendar year.

Analysis of alcohol intake among men at risk of prostate cancer. Person-time accrued from 1986 baseline until prostate cancer diagnosis, death, or end of follow-up (January 2012). For men who developed lethal prostate cancer over follow-up, their event date was their date of prostate cancer diagnosis. To focus on associations between alcohol intake among cancer-free men and lethal prostate cancer, those men diagnosed with nonmetastatic prostate cancer were censored at diagnosis.

We first categorized intake for all alcohol exposures into any or none. On the basis of the distribution of intake, and to distinguish men drinking more than the recommended limit of two servings per day (approximately 30 g/d), we further categorized total alcohol intake as zero, more than zero to fewer than 10, 10 to fewer than 15, 15 to fewer than 30, and 30 or more grams/day. We categorized the wine, beer, and liquor as zero, more than zero to fewer than one, more than one to fewer than three, more than three to fewer than seven, and seven or more servings per week. To evaluate a dose-response relationships, we created a semi-continuous variable using the median of each category of intake, and used the Wald test P value to assess the significance of the trend. We categorized drinking frequency as 0, 1 to 2, 3 to 4, 5 to 6, or 7 days per week. Cumulative average alcohol intake (across all reports from baseline until most recent questionnaire) was updated every 4 years. For missing values, we carried forward the previous value one cycle; if a second consecutive value was missing, individuals did not contribute person-time for the subsequent 4-year time periods.

We adjusted multivariate models for factors associated with lethal prostate cancer and alcohol intake, on the basis of prior literature. This included total energy intake (kilocalories/day, continuous), smoking (never, quit more than 10 years ago, quit 10 years ago or less, current and fewer than 40 pack-years, current and 40 pack-years or more), body mass index (kg/m^2 ; less than 25, 25 to less than 30, 30 or higher), vigorous physical activity (hours per week; less than 3, 3 or more), choline (milligrams/day, quintiles), vegetable fat (grams/day, quintiles), coffee (servings/day, quintiles), lycopene (servings/day, quintiles), whole milk (servings/day, quintiles), and diabetes (yes or no). We also adjusted for prostate-specific antigen (PSA) screening beginning in 1994 (report of screening on the previous

cycle [yes or no] and report of PSA screening on 50% or more of previous cycles [yes or no]). Beer, wine, and liquor were mutually adjusted for each other, as were red and white wine. To avoid misclassifying diagnostic PSA tests as screening tests, we did not include screening reports from the questionnaire on which a prostate cancer diagnosis was reported. All covariates were updated over follow-up. We also ran models adjusting for other possible confounders, but including those covariates did not meaningfully change the associations.

We conducted several sensitivity analyses. First, because PSA screening may confound the association (ie, health-conscious men may screen more frequently and drink alcohol moderately; screening reduces risk of lethal prostate cancer), we restricted our analyses to men who reported PSA screening on both 1994 and 1996 questionnaires (starting follow-up in 1996; PSA screening was first assessed in 1994). Second, we restricted our analyses to never-smokers because of potential confounding by smoking. Third, because men may significantly decrease alcohol intake for unidentifiable reasons that may be associated with prostate cancer risk (eg, health consciousness, comorbidities, and so forth), we excluded those men who reported at baseline that they had decreased their alcohol intake in the past 10 years. Fourth, we assessed alcohol intake on the basis of the most recent exposure only, to analyze the impact of current intake (rather than cumulative average). Fifth, to further explore recent alcohol intake, we continued updating cumulative alcohol exposure after prostate cancer diagnosis instead of censoring at diagnosis, with outcome defined as date of lethal prostate cancer diagnosis (metastasis or prostate cancer death, whichever came first). Sixth, to examine reverse causation (whereby men with a greater likelihood of lethal prostate cancer decrease their intake as a result of their disease), we applied alcohol exposures from 2 to 4, 4 to 6, and 6 to 8 years before the current exposure period to the current period (lagged analyses). Last, we made no alcohol (rather than zero servings/d of the specific beverage) the referent group for beer, wine, and liquor.

We also analyzed alcohol in relation to overall mortality as a secondary outcome. Here, alcohol intake was updated until death or end of follow-up. However, if a participant was diagnosed with prostate cancer, we censored him at diagnosis.

To evaluate interaction between the amount and frequency of alcohol intake, we stratified total alcohol analyses on drinking frequency (2 or fewer v more than 2 days per week) among drinkers, testing for interaction with a likelihood ratio test.

Analysis of alcohol intake among men with nonmetastatic prostate cancer. Cox models were stratified on years since diagnosis, age, and calendar year. Person-time was accrued from first postdiagnostic alcohol report until outcome. Exposures were identical to our analysis of alcohol

intake among men at risk of prostate cancer, but we used only reports after diagnosis.

Using the same approach as discussed earlier, our multivariate models were adjusted for energy intake, smoking, body mass index, vigorous physical activity, diabetes, coffee intake, and other alcohol subtypes (where applicable) measured at the time of diagnosis. We also adjusted for clinical variables: primary treatment (radical prostatectomy, radiation, hormones, other, missing), TNM stage at diagnosis (T1, T2, T3+, missing), Gleason grade (less than 7, 7, higher than 7, missing), PSA at diagnosis (less than 4 ng/dL, 4 to less than 10 ng/dL, 10 to less than 20 ng/dL, 20 ng/dL or greater, missing), and PSA screening (screening on cycle before diagnosis [yes or no]; intensity of prediagnosis screening [50% or more of previous cycles (yes or no)]). Models for overall mortality also adjusted for parental history of myocardial infarction before age 60 years (yes or no), comorbidities updated over follow-up (yes or no [yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease]), high blood pressure (yes or no), and high cholesterol (yes or no).

We conducted several sensitivity analyses. To evaluate residual confounding from missing TNM stage ($n = 451$), we excluded men missing that stage. To further examine confounding by PSA screening, we separately restricted our analyses to men who reported one or more and two or more PSA screens before diagnosis. To further address potential confounding by smoking, we restricted our analyses to never-smokers. To examine the possibility of reverse causation, we defined alcohol exposure on the basis of the first postdiagnostic report only (no updating). We also applied alcohol exposure from 2 to 4 years before the current period (lagged analysis). Last, we examined whether change in alcohol intake from the last prediagnostic questionnaire to the first postdiagnostic questionnaire was associated with our outcomes. All statistical analyses were performed using SAS (Version 9.3, SAS Institute, Cary, NC) and two-sided P values $< .05$ were considered statistically significant.

RESULTS

Analysis of Alcohol Intake Among Men at Risk of Prostate Cancer

We observed 869 lethal prostate cancer events among 47,568 participants observed for a median of 25.3 years (interquartile range, 24.8-25.8 years). At the 1986 baseline, men who drank more alcohol were more likely to be white, smokers, active, and nondiabetic, and to consume more calories, less vegetable fat, and more coffee (Table 1). Individual alcohol beverages were associated with similar variables.

Among cancer-free men, alcohol intake was associated with a lower risk of lethal prostate cancer (any v none: HR, 0.84 [95% CI, 0.71 to 0.99]), with no dose-response relationship

(*P* trend = .37). There were no statistically significant associations with lethal prostate cancer (Table 2).

In sensitivity analyses, associations were virtually unchanged when restricting to nonsmokers (*n* = 44,179), updating alcohol exposure after initial diagnosis (*n* = 47,568), censoring at date of lethal prostate cancer (rather than at diagnosis), or updating intake every 4 years (rather than cumulative average; *n* = 47,568). After restricting our analyses to men screened in 1994 and 1996 (*n* = 13,426), the association became stronger (HR, 0.74 [95% CI, 0.47 to 1.15]). After excluding men who reported decreased intake at baseline (*n* = 29,057), the association was attenuated (HR, 1.04 [95% CI, 0.79 to 1.38]; Appendix Table A1, online only). Lagged analyses did not meaningfully change the results (Appendix Table A2, online only).

Changing the referent group for individual alcohol beverages to nondrinkers (rather than zero servings/d of the specific beverage) did not meaningfully change the results. There was no association between drinking frequency and risk of lethal prostate cancer, and no interaction between drinking frequency and total alcohol intake (results not shown). Total alcohol, wine (total, red, and white) and beer were associated with lower overall mortality (Appendix Table A3, online only).

Analysis of Alcohol Intake Among Men With Nonmetastatic Prostate Cancer

At diagnosis, men who drank more alcohol were more likely to be white, smokers, and nondiabetic. They consumed

less vegetable fat and more coffee, engaged in more vigorous activity, and were more likely to be diagnosed with T1 disease and a Gleason score of less than 7 (Table 3). Specific alcoholic beverages were associated with similar variables overall.

Among the 5,182 men diagnosed with nonmetastatic prostate cancer, alcohol intake after diagnosis was not associated with progression to lethal prostate cancer (any *v* none: HR, 0.99 [95% CI, 0.57 to 1.72]). However, red wine intake after diagnosis was inversely associated (HR, 0.50 [95% CI, 0.29 to 0.86]; *P* trend across five categories of intake = .05). Total alcohol intake was borderline inversely associated with lower overall mortality (any *v* none: HR, 0.82 [95% CI, 0.64 to 1.04]; *P* trend = .20), with the lowest risk in the 15 to 30 g/d category (HR, 0.71 [95% CI, 0.50 to 1.00]). Red wine intake after prostate cancer diagnosis was also associated with lower overall mortality (any *v* none: HR, 0.74 [95% CI, 0.57 to 0.97]; *P* trend = .007). Other alcohol beverages were not associated with either outcome (Table 4).

Overall, associations did not change meaningfully in sensitivity analyses, although we observed wide CIs because of diminished statistical power for many analyses. Associations between red wine and lethal prostate cancer and overall mortality were attenuated when only the first post-diagnostic report of alcohol was used (Appendix Tables A4 and A5, online only). Point estimates were largely unchanged when lagging exposures 2 to 4 years, although the CIs were wide (Appendix Table A6, online only). Change in

TABLE 1. Age-Standardized Baseline Characteristics of Cancer-Free Men in the Health Professionals Follow-Up Study, by Alcohol Intake (Analysis of Alcohol Intake Among Men at Risk for Prostate Cancer, 1986 to 2012; N = 47,568)

Characteristic	Alcohol Intake at Baseline (g/d)				
	None	> 0 to < 10	10 to < 15	15 to < 30	≥ 30
<i>n</i>	11,128	18,504	6,056	6,263	6,518
Age, years	54	54	55	55	55
White, %	89	91	92	92	93
BMI, kg/m ²	25.7	25.5	25.4	25.3	25.6
Vigorous physical activity, MET-h/wk	8.9	10.7	11.3	11.6	9.4
Family history of prostate cancer, %	12	12	12	12	12
Current smoker, %	7	8	10	10	22
Diabetes, %	5	3	2	2	2
PSA screening reported on 1994 questionnaire, %	31	37	36	36	33
Energy, kcal/d	1,921	1,933	1,956	2,073	2,214
Vegetable fat, g/d	31.4	30.5	30.2	29.9	26.4
Coffee, servings/d	1.4	1.8	2.1	2.3	2.6
Whole milk, servings/d	0.2	0.2	0.2	0.1	0.2
Choline, mg/d	398	400	404	400	399
Lycopene, μg/d	723	759	736	749	677

NOTE. Data are presented as means unless indicated otherwise.

Abbreviations: BMI, body mass index; PSA, prostate-specific antigen.

TABLE 2. Alcohol Intake and Risk of Lethal Prostate Cancer (Analysis of Alcohol Intake Among Men at Risk for Prostate Cancer; N = 47,568)

Alcohol Intake	Median (IQR)	No. of Patients	Person-Years	Age Adjusted			Fully Adjusted*		
				HR	95% CI	HR	95% CI	HR	95% CI
Total alcohol, g/d									
None	0 (0-0)	193	181,975		1.00 (ref)		1.00 (ref)		1.00 (ref)
> 0 to < 10	3.7 (1.8-6.4)	337	462,271	0.79	0.66 to 0.94	0.81	0.67 to 0.97		
> 10 to < 15	12.3 (11.2-13.6)	103	129,522	0.80	0.63 to 1.02	0.82	0.64 to 1.05		
15 to < 30	19.9 (17.1-24.1)	130	160,997	0.85	0.68 to 1.07	0.88	0.70 to 1.11		
≥ 30	39.2 (35.0-48.3)	106	102,050	0.96	0.75 to 1.22	0.97	0.75 to 1.26		
<i>P</i> trend					.40		.37		
None		193	181,975		1.00 (ref)		1.00 (ref)		
Any		676	854,840	0.83	0.70 to 0.97	0.84	0.71 to 0.99		
Total wine, servings/wk									
None	0 (0-0)	328	314,319		1.00 (ref)		1.00 (ref)		
> 0 to < 1	0.5 (0.3-0.6)	181	246,022	0.85	0.71 to 1.03	0.87	0.72 to 1.05		
1 to < 3	1.4 (0.7-2.1)	201	269,407	0.97	0.81 to 1.16	0.98	0.82 to 1.18		
3 to < 7	4.2 (3.5-5.6)	118	148,521	1.03	0.83 to 1.27	1.05	0.84 to 1.31		
≥ 7	9.8 (7.7-14)	41	58,547	0.93	0.67 to 1.29	0.96	0.69 to 1.35		
<i>P</i> trend					.92		.72		
None		328	314,319		1.00 (ref)		1.00 (ref)		
Any		541	722,497	0.94	0.81 to 1.08	0.98	0.83 to 1.15		
Beer, servings/wk									
None	0 (0-0)	368	358,077		1.00 (ref)		1.00 (ref)		
> 0 to < 1	0.49 (0.3-0.5)	218	280,806	0.90	0.75 to 1.06	0.89	0.75 to 1.07		
1 to < 3	1.4 (0.7-2.1)	116	184,033	0.89	0.72 to 1.10	0.88	0.70 to 1.09		
3 to < 7	3.5 (2.8-4.9)	113	146,329	1.11	0.89 to 1.38	1.07	0.85 to 1.34		
≥ 7	11.2 (7-17.5)	54	67,569	1.16	0.87 to 1.55	1.08	0.80 to 1.46		
<i>P</i> trend					.12		.25		
None		368	358,077		1.00 (ref)		1.00 (ref)		
Any		501	678,737	0.96	0.84 to 1.10	0.99	0.84 to 1.16		
Liquor, servings/wk									
None	0 (0-0)	355	415,688		1.00 (ref)		1.00 (ref)		
> 0 to < 1	0.5 (0.3-0.5)	165	250,040	0.90	0.75 to 1.09	0.87	0.72 to 1.06		
1 to < 3	1.4 (0.7-2.1)	95	132,682	0.90	0.71 to 1.13	0.86	0.68 to 1.09		

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TABLE 2. Alcohol Intake and Risk of Lethal Prostate Cancer (Analysis of Alcohol Intake Among Men at Risk for Prostate Cancer; N = 47,568) (continued)

Alcohol Intake	Median (IQR)	No. of Patients	Person-Years	Age Adjusted			Fully Adjusted*		
				HR	95% CI	HR	95% CI	HR	95% CI
3 to < 7	3.5 (2.8-5.6)	139	139,756	0.99	0.81 to 1.21	0.95	0.77 to 1.17		
≥ 7	12.6 (7.7-17.5)	115	98,647	0.92	0.75 to 1.14	0.89	0.71 to 1.12		
<i>P</i> trend					.71		.74		
None		355	415,688		1.00 (ref)		1.00 (ref)		
Any		514	621,125	0.93	0.81 to 1.06	0.96	0.81 to 1.12		
Red wine, servings/wk									
None	0 (0-0)	446	451,112		1.00 (ref)		1.00 (ref)		
> 0 to < 1	0.49 (0.3-0.5)	233	338,240	0.89	0.75 to 1.05	0.89	0.75 to 1.05		
1 to < 3	1.4 (0.7-2.1)	121	153,914	1.15	0.93 to 1.41	1.16	0.93 to 1.44		
3 to < 7	3.5 (2.8-4.2)	54	74,365	1.07	0.81 to 1.43	1.08	0.81 to 1.46		
≥ 7	9.1 (7-13.3)	15	19,183	1.01	0.60 to 1.71	1.03	0.61 to 1.76		
<i>P</i> trend					.22		.19		
None		446	451,112		1.00 (ref)		1.00 (ref)		
Any		423	585,702	0.98	0.85 to 1.12	1.06	0.89 to 1.26		
White wine, servings/wk									
None	0 (0-0)	360	349,571		1.00 (ref)		1.00 (ref)		
> 0 to < 1	0.5 (0.5-0.6)	271	389,280	0.85	0.72 to 1.00	0.86	0.73 to 1.01		
1 to < 3	0.7 (0.7-1.4)	137	174,887	1.04	0.85 to 1.27	1.04	0.85 to 1.29		
3 to < 7	2.8 (2.1-3.5)	91	97,477	1.10	0.87 to 1.39	1.11	0.87 to 1.41		
≥ 7	7 (5.6-12.6)	10	25,599	0.44	0.23 to 0.83	0.45	0.24 to 0.85		
<i>P</i> trend					.85		.28		
None		360	349,571		1.00 (ref)		1.00 (ref)		
Any		509	687,243	0.92	0.80 to 1.05	0.93	0.77 to 1.11		

Abbreviations: HR, hazard ratio; IQR, interquartile range.

*Fully adjusted models are adjusted for total energy intake (kilocalories/day, continuous); smoking status (never, past [quit > 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m^2 : < 25 , 25 to < 30 , ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); choline (milligrams/day, quintiles); vegetable fat (grams/day, quintiles); coffee (servings/day, quintiles); lycopene (servings/day, quintiles); whole milk (servings/day, quintiles); prostate-specific antigen screening beginning in 1994 (report of screening on the previous cycle [yes or no] and report of prostate-specific antigen screening on $\geq 50\%$ of previous cycles [yes or no]); and diabetes (yes or no).

TABLE 3. Age-Standardized Characteristics of Men in the Health Professionals Follow-Up Study Diagnosed With Nonmetastatic Prostate Cancer During Follow-Up, by Alcohol Intake at Diagnosis (Analysis of Alcohol Intake Among Men With Nonmetastatic Prostate Cancer; N = 5,182)

Characteristic at Diagnosis	Alcohol Intake at Diagnosis (g/d)				
	None	> 0 to < 10 g	10 to < 15 g	15 to < 30 g	≥ 30 g
n*	1,225	1,770	691	923	573
Age at diagnosis, years	70	70	70	70	70
White, %	90	91	93	95	97
BMI, kg/m ²	26.0	26.1	25.6	25.7	26.0
Vigorous physical activity, MET-h/wk	7.5	8.4	9.8	9.3	7.6
Family history of prostate cancer, %	24	21	18	20	22
Current smoker, %	3	3	3	3	7
History of diabetes, %	12	10	5	8	6
Total energy intake, kcal/d	1,880	1,926	1,954	2,105	2,252
Vegetable fat, g/d	37.8	37.2	137.5	38.5	37.9
Coffee, servings/d	1.3	1.5	1.5	1.6	1.8
Whole milk, servings/d	0.08	0.07	0.07	0.04	0.04
Choline, mg/d	375	382	375	380	356
Lycopene, μg/d	665	753	719	771	720
Year of diagnosis	1,999	1,999	2,000	2,000	2,000
No. of PSA screenings before diagnosis	2.3	2.4	2.4	2.9	2.6
TNM stage, %					
T1	48	53	56	59	59
T2	35	32	31	30	30
T3	3	3	4	3	2
T4/N1	1	1	1	1	1
Missing	13	11	8	7	8
Gleason grade, %					
< 7	43	46	46	46	49
7	30	30	33	33	29
> 7	11	10	9	12	9
Missing	16	14	12	9	13
PSA level, %					
< 4	11	12	10	12	9
4 to < 10	47	51	53	56	52
10 to < 20	15	16	17	14	17
≥ 20	8	6	8	6	8
Missing	19	15	12	12	14
Primary treatment, %					
RP	40	43	44	45	42
Radiation	30	32	34	34	34
Hormones	5	4	4	4	4
Other or active surveillance	9	10	10	8	11
Missing	16	11	8	9	9

NOTE. Data are presented as means unless indicated otherwise.

Abbreviations: BMI, body mass index; PSA, prostate-specific antigen; RP, radical prostatectomy.

*Includes all participants with an alcohol report on the first postdiagnosis questionnaire (n = 5,097). This totals to < 5,182, the number of participants included in the primary analysis of alcohol intake among men with nonmetastatic prostate cancer (Table 4), because the main analysis includes participants who provided postdiagnosis alcohol information on later questionnaires.

TABLE 4. Postdiagnosis Alcohol Intake and Progression to Lethal Prostate Cancer and Overall Mortality Among Men Diagnosed Initially With Nonmetastatic Prostate Cancer in Health Professionals Follow-Up Study (N = 5,182)

Alcohol Intake	Median (IQR)	No. of Patients	Lethal Prostate Cancer			
			Age Adjusted		Fully Adjusted*	
			HR	95% CI	HR	95% CI
Lethal prostate cancer						
Total alcohol, g/d						
None	0 (0-0)	124	1.00 (ref)		1.00 (ref)	
> 0 to < 10	3.6 (2.0-6.5)	146	0.87	0.53 to 1.42	1.17	0.63 to 2.19
> 10 to < 15	12.7 (11.4-14.0)	50	0.79	0.42 to 1.47	1.02	0.45 to 2.29
15 to < 30	18.5 (16.5-22.0)	65	0.73	0.41 to 1.31	0.63	0.31 to 1.31
≥ 30	41.0 (36.1-51.0)	39	0.71	0.35 to 1.44	1.32	0.53 to 3.25
<i>P</i> trend				.29		.87
None		124	1.00 (ref)		1.00 (ref)	
Any		300	0.80	0.52 to 1.23	0.99	0.57 to 1.72
Total wine, servings/wk						
None	0 (0-0)	200	1.00 (ref)		1.00 (ref)	
> 0 to < 1	0.5 (0.5-0.5)	57	2.08	1.13 to 3.84	3.17	1.35 to 7.44
1 to < 3	0.7 (0.7-1.4)	79	1.06	0.62 to 1.80	1.41	0.72 to 2.79
3 to < 7	4.2 (3.5-6.3)	57	0.64	0.37 to 1.11	0.53	0.26 to 1.07
≥ 7	8.4 (7.7-17.5)	31	0.86	0.43 to 1.70	0.84	0.36 to 1.99
<i>P</i> trend				.12		.03
None		200	1.00 (ref)		1.00 (ref)	
Any		224	0.99	0.68 to 1.46	1.09	0.65 to 1.85
Beer, servings/wk						
None	0 (0-0)	249	1.00 (ref)		1.00 (ref)	
> 0 to < 1	0.5 (0.5-0.5)	56	0.60	0.34 to 1.06	0.65	0.31 to 1.37
1 to < 3	0.7 (0.7-1.4)	57	1.05	0.60 to 1.85	1.27	0.61 to 2.63
3 to < 7	2.8 (2.8-5.6)	47	1.50	0.83 to 2.73	1.87	0.85 to 4.09
≥ 7	7.7 (7-17.5)	15	1.44	0.46 to 4.47	2.64	0.58 to 12.06
<i>P</i> trend				.16		.05
None		249	1.00 (ref)		1.00 (ref)	
Any		175	0.97	0.66 to 1.41	1.00	0.58 to 1.70
Liquor, servings/wk						
None	0 (0-0)	234	1.00 (ref)		1.00 (ref)	
> 0 to < 1	0.5 (0.5-0.5)	50	0.82	0.46 to 1.44	0.98	0.48 to 2.01
1 to < 3	0.7 (0.7-0.7)	33	0.92	0.44 to 1.91	1.09	0.41 to 2.86
3 to < 7	2.8 (2.8-5.6)	50	0.72	0.41 to 1.29	0.88	0.42 to 1.86
≥ 7	7 (7-17.5)	57	1.01	0.55 to 1.83	1.39	0.64 to 3.00
<i>P</i> trend				.88		.88
None		234	1.00 (ref)		1.00 (ref)	
Any		190	0.84	0.58 to 1.22	0.93	0.56 to 1.55
Red wine, servings/wk						
None	0 (0-0)	252	1.00 (ref)		1.00 (ref)	
> 0 to < 1	0.5 (0.5-0.5)	69	0.84	0.51 to 1.39	0.79	0.41 to 1.51

(continued on following page)

TABLE 4. Postdiagnosis Alcohol Intake and Progression to Lethal Prostate Cancer and Overall Mortality Among Men Diagnosed Initially With Nonmetastatic Prostate Cancer in Health Professionals Follow-Up Study (N = 5,182) (continued)

Alcohol Intake	Median (IQR)	No. of Patients	Lethal Prostate Cancer			
			Age Adjusted		Fully Adjusted*	
			HR	95% CI	HR	95% CI
1 to < 3	0.7 (0.7-0.7)	27	0.65	0.31 to 1.39	0.46	0.17 to 1.25
3 to < 7	2.8 (2.8-2.8)	56	0.66	0.39 to 1.13	0.49	0.25 to 0.97
≥ 7	7 (7-17.5)	20	0.60	0.26 to 1.39	0.51	0.18 to 1.40
<i>P</i> trend				.12		.05
None		252		1.00 (ref)		1.00 (ref)
Any		172	0.72	0.49 to 1.05	0.50	0.29 to 0.86
White wine, servings/wk						
None	0 (0-0)	243		1.00 (ref)		1.00 (ref)
> 0 to < 1	0.5 (0.5-0.5)	102	1.31	0.79 to 2.18	1.76	0.92 to 3.34
1 to < 3	0.7 (0.7-0.7)	35	0.96	0.51 to 1.84	1.00	0.44 to 2.29
3 to < 7	2.8 (2.8-2.8)	35	0.65	0.35 to 1.20	0.53	0.24 to 1.15
≥ 7	7 (7-17.5)	9	0.66	0.22 to 1.96	0.69	0.17 to 2.77
<i>P</i> trend				.14		.12
None		243		1.00 (ref)		1.00 (ref)
Any		181	0.95	0.65 to 1.39	1.25	0.73 to 2.15
Overall mortality						
Total alcohol, g/d						
None	0 (0-0)	520		1.00 (ref)		1.00 (ref)
> 0 to < 10	3.6 (2.0-6.5)	521	0.78	0.61 to 1.00	0.84	0.64 to 1.10
> 10 to < 15	12.7 (11.4-14.0)	177	0.63	0.45 to 0.88	0.77	0.54 to 1.10
15 to < 30	18.5 (16.5-22.0)	219	0.63	0.46 to 0.86	0.71	0.50 to 1.00
≥ 30	41.0 (36.1-51.0)	157	0.74	0.52 to 1.04	0.76	0.52 to 1.12
<i>P</i> trend				.03		.20
None		520		1.00 (ref)		1.00 (ref)
Any		1,074	0.71	0.58 to 0.88	0.82	0.64 to 1.04
Total wine, servings/wk						
None	0 (0-0)	864		1.00 (ref)		1.00 (ref)
> 0 to < 1	0.5 (0.5-0.5)	135	0.83	0.58 to 1.19	0.89	0.60 to 1.34 to
1 to < 3	0.7 (0.7-1.4)	302	0.89	0.69 to 1.16	1.00	0.75 to 1.34
3 to < 7	4.2 (3.5-6.3)	179	0.52	0.38 to 0.71	0.57	0.40 to 0.81
≥ 7	8.4 (7.7-17.5)	114	0.79	0.54 to 1.15	0.84	0.55 to 1.29
<i>P</i> trend				.01		.08
None		864		1.00 (ref)		1.00 (ref)
Any		730	0.75	0.61 to 0.91	0.84	0.66 to 1.08
Beer, servings/wk						
None	0 (0-0)	1,030		1.00 (ref)		1.00 (ref)
> 0 to < 1	0.5 (0.5-0.5)	190	0.70	0.52 to 0.94	0.78	0.56 to 1.09
1 to < 3	0.7 (0.7-1.4)	197	0.91	0.67 to 1.22	0.99	0.71 to 1.39
3 to < 7	2.8 (2.8-5.6)	132	0.89	0.63 to 1.25	1.04	0.70 to 1.54

(continued on following page)

TABLE 4. Postdiagnosis Alcohol Intake and Progression to Lethal Prostate Cancer and Overall Mortality Among Men Diagnosed Initially With Nonmetastatic Prostate Cancer in Health Professionals Follow-Up Study (N = 5,182) (continued)

Alcohol Intake	Median (IQR)	No. of Patients	Lethal Prostate Cancer			
			Age Adjusted		Fully Adjusted*	
			HR	95% CI	HR	95% CI
≥ 7	7.7 (7-17.5)	45	1.15	0.67 to 1.97	1.19	0.65 to 2.17
<i>P</i> trend				.92		.45
None		1,030		1.00 (ref)		1.00 (ref)
Any		564	0.84	0.69 to 1.03	0.96	0.75 to 1.22
Liquor, servings/wk						
None	0 (0-0)	921		1.00 (ref)		1.00 (ref)
> 0 to < 1	0.5 (0.5-0.5)	178	0.81	0.59 to 1.10	0.99	0.69 to 1.40
1 to < 3	0.7 (0.7-0.7)	98	0.95	0.63 to 1.44	1.08	0.67 to 1.72
3 to < 7	2.8 (2.8-5.6)	180	0.80	0.60 to 1.08	1.01	0.72 to 1.42
≥ 7	7 (7-17.5)	217	0.99	0.74 to 1.32	1.09	0.79 to 1.52
<i>P</i> trend				.79		.67
None		921		1.00 (ref)		1.00 (ref)
Any		673	0.88	0.73 to 1.06	1.08	0.85 to 1.36
Red wine, servings/wk						
None	0 (0-0)	965		1.00 (ref)		1.00 (ref)
> 0 to < 1	0.5 (0.5-0.5)	263	0.99	0.76 to 1.28	1.06	0.78 to 1.42
1 to < 3	0.7 (0.7-0.7)	123	0.66	0.46 to 0.94	0.67	0.45 to 0.99
3 to < 7	2.8 (2.8-2.8)	168	0.60	0.44 to 0.81	0.64	0.45 to 0.90
≥ 7	7 (7-17.5)	75	0.58	0.35 to 0.95	0.58	0.33 to 1.01
<i>P</i> trend				.0007		.007
None		965		1.00 (ref)		1.00 (ref)
Any		629	0.75	0.62 to 0.91	0.74	0.57 to 0.97
White wine, servings/wk						
None	0 (0-0)	989		1.00 (ref)		1.00 (ref)
> 0 to < 1	0.5 (0.5-0.5)	304	1.03	0.79 to 1.34	1.26	0.94 to 1.70
1 to < 3	0.7 (0.7-0.7)	148	0.94	0.68 to 1.30	1.12	0.78 to 1.62
3 to < 7	2.8 (2.8-2.8)	119	0.69	0.49 to 0.97	0.76	0.51 to 1.12
≥ 7	7 (7-17.5)	34	0.87	0.47 to 1.60	0.96	0.49 to 1.91
<i>P</i> trend				.10		.60
None		989		1.00 (ref)		1.00 (ref)
Any		605	0.90	0.73 to 1.10	1.24	0.94 to 1.63

Abbreviations: HR, hazard ratio; IQR, interquartile range.

*Adjusted for energy intake (kilocalories/day); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m²: < 25, 25 to < 30, ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); coffee intake (servings/day, quintiles); diabetes (yes or no); primary treatment (radical prostatectomy, radiation, hormones, other, missing); stage at diagnosis (T1, T2, T3+, missing); Gleason grade at diagnosis (< 7, 7, > 7, missing); prostate-specific antigen at diagnosis (ng/dL; < 4, 4 to <10, 10 to < 20, ≥ 20, missing); prostate-specific antigen screening (screening on the cycle before prostate cancer diagnosis was reported [yes or no] and intensity of screening [≥ 50% of previous cycles, yes or no]); diabetes (yes or no). Beer, wine, and liquor mutually adjusted for each other. Red wine and white wine were also mutually adjusted. Models for all-cause mortality also adjusted for parental history of myocardial infarction before 60 years of age (yes or no); comorbidities (yes or no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease); high blood pressure (yes or no); and high cholesterol (yes or no).

alcohol intake from before to after diagnosis was not associated with risk of either outcome (Appendix Table A7, online only). Among drinkers, the frequency of alcohol intake was not associated with either outcome, and there were no interactions between amount and frequency (results not shown).

DISCUSSION

In this prospective cohort study with 26 years of follow-up among 47,568 men in the United States, alcohol intake was associated with a lower risk of lethal prostate cancer, but there was no dose-response relationship. No specific alcohol subtype seemed to be driving this association. Among the 5,182 men diagnosed with nonmetastatic prostate cancer, red wine after diagnosis was associated with a lower risk of lethal prostate cancer and overall mortality, with a dose-response relationship for both outcomes.

Our data support the possibility that alcohol intake, particularly red wine, may inhibit prostate cancer progression. There are several plausible biologic mechanisms to explain these inverse associations. Alcohol may increase sex hormone-binding globulin levels²³ and lower testosterone,²⁴⁻²⁷ which may reduce hormonal promotion of prostate tumor growth later in disease progression. Alcohol intake may also be associated with lower insulin-like growth factor-1,^{28,29} a well-established risk factor for advanced prostate cancer. Randomized controlled trials indicate that wine improves insulin metabolism and increases antioxidant status,³⁰ pathways thought to play an important role in prostate cancer progression. Red wine may also lower inflammation, because it has been associated with decreased circulating soluble inflammatory mediators levels, including plasma fibrinogen and interleukin-1 α , decreased C-reactive protein levels, and decreased monocyte and endothelial adhesion molecules.^{31,32} In addition, studies examining the potential effects of wine polyphenols on prostate cancer cells have reported inhibition of tumor growth, migration, and invasiveness.³³⁻⁴⁷

Our data also support the possibility that moderate alcohol intake is associated with a lower risk of overall mortality among patients with prostate cancer. These findings align with epidemiologic data that consistently indicate that moderate alcohol is associated with a lower risk of

cardiovascular disease, ischemic stroke, diabetes, and overall mortality.⁴ However, we observed no benefit of beer or liquor on overall mortality among men with prostate cancer. This is in contrast to studies focused on cardiovascular disease, which have demonstrated a benefit from alcohol itself, regardless of source.⁴⁸

Our results should be interpreted conservatively. First, the lack of a dose-response relationship for total alcohol casts doubt on a causal interpretation of our findings. Second, our red wine findings could partly be a result of unmeasured confounding; health-conscious characteristics of red wine drinkers may reduce the risk of prostate cancer death. However, the results in all analyses were qualitatively unchanged when adjusting for known and potential clinical, demographic, and lifestyle risk factors and screening behavior, and the results were essentially unchanged when restricting to never-smokers. Third, reverse causation cannot be ruled out, particularly in the analysis of men with nonmetastatic prostate cancer. Here, our results were attenuated when we used the first postdiagnostic questionnaire (completed 6.3 years before death as a result of prostate cancer, on average) and when lagging our alcohol exposures, although we had limited power.

The strengths of our study include multiple, validated, and prospective exposure and covariates, detailed clinical data, complete and long follow-up, a large number of events, and clinically relevant end points. Our study also has limitations. It is possible that unmeasured confounding affected the observed associations. Alcohol intake was self-reported. However, validation studies have shown that exposure measurement error is small, and measurement error is expected to be nondifferential because of our prospective assessments. Last, our homogenous study population limits generalizability to other racial and ethnic populations but reduces confounding by sociodemographic factors.

We conclude that moderate alcohol intake is not associated with a higher risk of being diagnosed with lethal prostate cancer. Our results indicate that moderate alcohol intake among men with prostate cancer is not associated with a higher risk of progression to lethal disease or overall mortality. The potential benefit of red wine on prostate cancer progression merits additional research.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI <https://doi.org/10.1200/JCO.18.02462>.

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Alcohol Intake and Risk of Lethal Prostate Cancer in the Health Professionals Follow-Up Study

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APPENDIX

TABLE A1. Risk Sensitivity Analyses: Alcohol Intake and Risk of Lethal Prostate Cancer Among Participants in the Health Professionals Follow-Up Study
Screened in 1994, 1996 (n = 13,426) **Never-Smokers (n = 44,179)**

Alcohol Intake	Screened in 1994, 1996 (n = 13,426)			Never-Smokers (n = 44,179)		
	Patients	HR	95% CI	Patients	HR	95% CI
Total alcohol, g/d						
None	27	1.00 (ref)		179	1.00 (ref)	
> 0 to < 10	68	0.54	0.35 to 0.84	307	0.76	0.64 to 0.92
> 10 to < 15	8	0.44	0.23 to 0.84	95	0.97	0.76 to 1.22
15 to < 30	26	0.59	0.34 to 1.01	122	0.82	0.64 to 1.04
≥ 30	17	0.80	0.44 to 1.44	86	0.95	0.74 to 1.23
Any	119	0.74	0.47 to 1.15	610	0.84	0.70 to 1.00
Total wine, servings/wk						
None	38	1.00 (ref)		294	1.00 (ref)	
> 0 to < 1	43	0.96	0.60 to 1.53	167	0.87	0.71 to 1.06
1 to < 3	45	1.16	0.72 to 1.89	186	1.00	0.82 to 1.21
3 to < 7	13	0.76	0.40 to 1.44	105	1.01	0.79 to 1.27
≥ 7	7	0.87	0.37 to 2.00	37	0.94	0.66 to 1.34
Any	108	1.10	0.70 to 1.71	495	1.00	0.84 to 1.19
Beer, servings/wk						
None	60	1.00 (ref)		340	1.00 (ref)	
> 0 to < 1	41	0.66	0.42 to 1.01	195	0.86	0.71 to 1.04
1 to < 3	20	0.56	0.32 to 0.99	101	0.80	0.63 to 1.02
3 to < 7	14	0.73	0.38 to 1.42	107	1.08	0.85 to 1.37
≥ 7	11	1.87	0.93 to 3.76	46	1.05	0.76 to 1.46
Any	86	0.78	0.52 to 1.17	449	0.98	0.82 to 1.16
Liquor, servings/wk						
None	58	1.00 (ref)		336	1.00 (ref)	
> 0 to < 1	33	0.86	0.55 to 1.36	147	0.81	0.66 to 0.99
1 to < 3	14	0.69	0.38 to 1.24	86	0.82	0.64 to 1.05
3 to < 7	21	0.94	0.54 to 1.65	121	0.87	0.70 to 1.09
≥ 7	20	1.00	0.56 to 1.79	99	0.88	0.70 to 1.12
Any	88	0.85	0.56 to 1.29	453	0.90	0.76 to 1.07
Red wine, servings/wk						
None	58	1.00 (ref)		403	1.00 (ref)	
> 0 to < 1	50	0.91	0.60 to 1.38	212	0.88	0.74 to 1.05
1 to < 3	29	1.06	0.64 to 1.76	114	1.16	0.93 to 1.45
3 to < 7	5	0.71	0.30 to 1.70	48	1.05	0.77 to 1.44
≥ 7	4	1.22	0.40 to 3.73	12	0.91	0.50 to 1.65
Any	88	0.99	0.63 to 1.56	386	1.04	0.87 to 1.26
White wine, servings/wk						
None	43	1.00 (ref)		323	1.00 (ref)	
> 0 to < 1	64	0.99	0.65 to 1.52	244	0.85	0.71 to 1.01

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TABLE A1. Risk Sensitivity Analyses: Alcohol Intake and Risk of Lethal Prostate Cancer Among Participants in the Health Professionals Follow-Up Study (continued)

Alcohol Intake	Screened in 1994, 1996 (n = 13,426)			Never-Smokers (n = 44,179)		
	Patients	HR	95% CI	Patients	HR	95% CI
1 to < 3	29	1.03	0.61 to 1.74	131	1.08	0.87 to 1.34
3 to < 7	10	0.97	0.46 to 2.04	82	1.08	0.84 to 1.40
≥ 7	0	0.47	0.09 to 2.38	9	0.44	0.22 to 0.86
Any	103	1.10	0.68 to 1.78	466	0.95	0.79 to 1.15
Alcohol Intake	Excluded Men Who Reported Decreased Alcohol at Baseline* (n = 29,057)			Alcohol Value From Most Recent Questionnaire Instead of Cumulative Average (n = 47,568)		
	Patients	HR	95% CI	Patients	HR	95% CI
Total alcohol, g/d						
None	67	1.00 (ref)		193	1.00 (ref)	
> 0 to < 10	162	0.94	0.72 to 1.23	337	0.81	0.67 to 0.97
> 10 to < 15	74	1.23	0.90 to 1.67	103	0.82	0.64 to 1.05
15 to < 30	107	1.03	0.75 to 1.40	130	0.88	0.70 to 1.11
≥ 30	91	1.10	0.80 to 1.52	106	0.97	0.75 to 1.26
Any	434	1.04	0.79 to 1.38	676	0.84	0.71 to 0.99
Total wine, servings/wk						
None	151	1.00 (ref)		328	1.00 (ref)	
> 0 to < 1	96	0.95	0.73 to 1.25	181	0.87	0.72 to 1.05
1 to < 3	132	1.14	0.89 to 1.46	201	0.98	0.82 to 1.18
3 to < 7	86	1.21	0.92 to 1.61	118	1.05	0.84 to 1.31
≥ 7	36	1.17	0.80 to 1.71	41	0.96	0.69 to 1.35
Any	350	1.10	0.87 to 1.37	541	0.98	0.83 to 1.15
Beer, servings/wk						
None	163	1.00 (ref)		368	1.00 (ref)	
> 0 to < 1	138	1.08	0.85 to 1.37	218	0.89	0.75 to 1.07
1 to < 3	76	0.98	0.73 to 1.32	116	0.88	0.70 to 1.09
3 to < 7	81	1.21	0.90 to 1.61	113	1.07	0.85 to 1.34
≥ 7	43	1.15	0.81 to 1.65	54	1.08	0.80 to 1.46
Any	338	1.14	0.91 to 1.42	501	0.99	0.84 to 1.16
Liquor, servings/wk						
None	147	1.00 (ref)		355	1.00 (ref)	
> 0 to < 1	80	0.86	0.64 to 1.14	165	0.87	0.72 to 1.06
1 to < 3	59	0.84	0.61 to 1.15	95	0.86	0.68 to 1.09
3 to < 7	115	1.05	0.80 to 1.36	139	0.95	0.77 to 1.17
≥ 7	100	0.89	0.67 to 1.18	115	0.89	0.71 to 1.12
Any	354	0.90	0.72 to 1.13	514	0.96	0.81 to 1.12
Red wine, servings/wk						
None	217	1.00 (ref)		446	1.00 (ref)	
> 0 to < 1	142	0.98	0.78 to 1.22	233	0.89	0.75 to 1.05
1 to < 3	85	1.31	1.00 to 1.71	121	1.16	0.93 to 1.44
3 to < 7	44	1.29	0.92 to 1.82	54	1.08	0.81 to 1.46
≥ 7	13	1.13	0.63 to 2.02	15	1.03	0.61 to 1.76

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TABLE A1. Risk Sensitivity Analyses: Alcohol Intake and Risk of Lethal Prostate Cancer Among Participants in the Health Professionals Follow-Up Study (continued)

Alcohol Intake	Excluded Men Who Reported Decreased Alcohol at Baseline* (n = 29,057)			Alcohol Value From Most Recent Questionnaire Instead of Cumulative Average (n = 47,568)		
	Patients	HR	95% CI	Patients	HR	95% CI
Any	284	1.20	0.95 to 1.51	423	1.06	0.89 to 1.26
White wine, servings/wk						
None	177		1.00 (ref)	360		1.00 (ref)
> 0 to < 1	157	0.88	0.70 to 1.10	271	0.86	0.73 to 1.01
1 to < 3	87	1.04	0.79 to 1.37	137	1.04	0.85 to 1.29
3 to < 7	71	1.24	0.92 to 1.66	91	1.11	0.87 to 1.41
≥ 7	9	0.52	0.26 to 1.02	10	0.45	0.24 to 0.85
Any	324	0.87	0.68 to 1.11	509	0.93	0.77 to 1.11
Alcohol Intake Updated After Prostate Cancer Diagnosis* (n = 47,568)						
Alcohol Intake	Patients	HR	95% CI			
Total alcohol, g/d						
None	193		1.00 (ref)			
> 0 to < 10	337	0.81	0.67 to 0.97			
> 10 to < 15	103	0.82	0.64 to 1.05			
15 to < 30	130	0.88	0.70 to 1.11			
≥ 30	106	0.97	0.75 to 1.26			
Any	676	0.84	0.71 to 0.99			
Total wine, servings/wk						
None	328		1.00 (ref)			
> 0 to < 1	181	0.87	0.72 to 1.05			
1 to < 3	201	0.98	0.82 to 1.18			
3 to < 7	118	1.05	0.84 to 1.31			
≥ 7	41	0.96	0.69 to 1.35			
Any	541	0.98	0.83 to 1.15			
Beer, servings/wk						
None	368		1.00 (ref)			
> 0 to < 1	218	0.89	0.75 to 1.07			
1 to < 3	116	0.88	0.70 to 1.09			
3 to < 7	113	1.07	0.85 to 1.34			
≥ 7	54	1.08	0.80 to 1.46			
Any	501	0.99	0.84 to 1.16			
Liquor, servings/wk						
None	355		1.00 (ref)			
> 0 to < 1	165	0.87	0.72 to 1.06			
1 to < 3	95	0.86	0.68 to 1.09			
3 to < 7	139	0.95	0.77 to 1.17			
≥ 7	115	0.89	0.71 to 1.12			

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TABLE A1. Risk Sensitivity Analyses: Alcohol Intake and Risk of Lethal Prostate Cancer Among Participants in the Health Professionals Follow-Up Study (continued)

Alcohol Intake Updated After Prostate Cancer Diagnosis* (n = 47,568)			
Alcohol Intake	Patients	HR	95% CI
Any	514	0.96	0.81 to 1.12
Red wine, servings/wk			
None	446		1.00 (ref)
> 0 to < 1	233	0.89	0.75 to 1.05
1 to < 3	121	1.16	0.93 to 1.44
3 to < 7	54	1.08	0.81 to 1.46
≥ 7	15	1.03	0.61 to 1.76
Any	423	1.06	0.89 to 1.26
White wine, servings/wk			
None	360		1.00 (ref)
> 0 to < 1	271	0.86	0.73 to 1.01
1 to < 3	137	1.04	0.85 to 1.29
3 to < 7	91	1.11	0.87 to 1.41
≥ 7	10	0.45	0.24 to 0.85
Any	509	0.93	0.77 to 1.11

Abbreviation: HR, hazard ratio.

*Adjusted for energy intake (kilocalories/day); age at diagnosis (years); smoking status (current, past, never); body mass index (kg/m²: < 25, 25 to < 30, ≥ 30); vigorous physical activity (< 3 or ≥ 3 h/wk); primary treatment (radical prostatectomy, radiation, hormones, other, missing); stage at diagnosis (T1, T2, T3+, missing); Gleason grade at diagnosis (< 7, 7, > 7, missing); prostate-specific antigen at diagnosis (ng/dL: < 4, 4 to < 10, 10 to < 20, ≥ 20, missing); prostate-specific antigen screening (screening on the cycle before prostate cancer diagnosis was reported [yes or no] and intensity of screening [≥ 50% of previous cycles, yes or no]). Beer, wine, and liquor mutually adjusted for each other. Red wine and white wine also mutually adjusted. Models for all-cause mortality also adjusted for parental history of myocardial infarction before 60 years of age (yes or no); comorbidities (yes or no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease); high blood pressure (yes or no); and high cholesterol (yes or no).

TABLE A2. Lagged Analysis of Alcohol Intake Among Men at Risk of Prostate Cancer: Alcohol Intake and Risk of Lethal Prostate Cancer Among Participants in the Health Professionals Follow-Up Study

Alcohol Intake	2- to 4-Year Lag (n = 47,199)			4- to 6-Year Lag (n = 46,563)			6- to 8-Year Lag (n = 45,723)		
	Patients	HR*	95% CI	Patients	HR*	95% CI	Patients	HR*	95% CI
Total alcohol, g/d									
None	183	1.00 (ref)		162	1.00 (ref)		135	1.00 (ref)	
> 0 to < 10	306	0.81	0.67 to 0.98	272	0.83	0.68 to 1.02	226	0.84	0.67 to 1.05
> 10 to < 15	103	0.89	0.69 to 1.15	98	1.00	0.77 to 1.30	70	0.88	0.65 to 1.18
15 to < 30	129	0.98	0.77 to 1.24	109	0.97	0.75 to 1.25	96	1.06	0.80 to 1.39
≥ 30	95	0.93	0.71 to 1.21	85	0.97	0.73 to 1.29	74	1.04	0.76 to 1.41
Total wine, servings/wk									
None	318	1.00 (ref)		285	1.00 (ref)		237	1.00 (ref)	
> 0 to < 1	160	0.88	0.72 to 1.07	138	0.91	0.73 to 1.12	110	0.89	0.70 to 1.13
1 to < 3	174	0.90	0.74 to 1.09	147	0.85	0.69 to 1.05	121	0.84	0.67 to 1.05
3 to < 7	124	1.15	0.93 to 1.43	122	1.29	1.03 to 1.61	105	1.36	1.07 to 1.73
≥ 7	40	0.98	0.70 to 1.37	34	0.95	0.66 to 1.48	28	0.93	0.62 to 1.39
Beer, servings/wk									
None	343	1.00 (ref)		319	1.00 (ref)		275	1.00 (ref)	
> 0 to < 1	205	0.98	0.81 to 1.17	165	0.88	0.73 to 1.07	132	0.81	0.65 to 1.00
1 to < 3	102	0.90	0.71 to 1.14	82	0.82	0.63 to 1.05	61	0.70	0.52 to 0.93
3 to < 7	110	1.10	0.88 to 1.39	102	1.08	0.86 to 1.37	84	0.97	0.75 to 1.25
≥ 7	56	1.19	0.88 to 1.61	58	1.30	0.96 to 1.75	49	1.21	0.87 to 1.67
Liquor, servings/wk									
None	343	1.00 (ref)		316	1.00 (ref)		264	1.00 (ref)	
> 0 to < 1	152	0.92	0.76 to 1.12	129	0.89	0.72 to 1.10	101	0.84	0.66 to 1.06
1 to < 3	81	0.87	0.68 to 1.12	72	0.88	0.68 to 1.15	66	0.99	0.75 to 1.30
3 to < 7	131	0.98	0.80 to 1.21	119	0.97	0.78 to 1.20	94	0.91	0.71 to 1.16
≥ 7	109	0.93	0.74 to 1.18	90	0.86	0.67 to 1.10	76	0.91	0.69 to 1.19
Red wine, servings/wk									
None	435	1.00 (ref)		391	1.00 (ref)		323	1.00 (ref)	
> 0 to < 1	215	0.90	0.76 to 1.07	188	0.93	0.78 to 1.12	154	0.95	0.77 to 1.16
1 to < 3	102	1.11	0.88 to 1.39	83	1.07	0.83 to 1.37	74	1.22	0.94 to 1.60
3 to < 7	48	0.97	0.71 to 1.32	52	1.17	0.87 to 1.59	41	1.12	0.80 to 1.57
≥ 7	16	1.11	0.66 to 1.86	12	0.90	0.50 to 1.63	9	0.85	0.43 to 1.67
White wine, servings/wk									
None	347	1.00 (ref)		309	1.00 (ref)		255	1.00 (ref)	
> 0 to < 1	252	0.88	0.74 to 1.04	219	0.91	0.75 to 1.09	180	0.92	0.75 to 1.12
1 to < 3	108	0.91	0.72 to 1.15	94	0.93	0.73 to 1.18	77	0.92	0.71 to 1.21
3 to < 7	95	1.15	0.90 to 1.46	90	1.21	0.94 to 1.55	77	1.25	0.96 to 1.64
≥ 7	14	0.62	0.36 to 1.07	14	0.70	0.40 to 1.20	12	0.70	0.39 to 1.26

Abbreviation: HR, hazard ratio.

*Fully adjusted models are adjusted for total energy intake (kilocalories/day, continuous); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m^2 : < 25 , 25 to < 30 , ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); choline (milligrams/day, quintiles); vegetable fat (grams/day, quintiles); coffee (servings/day, quintiles); lycopene (servings/day, quintiles); whole milk (servings/day, quintiles); prostate-specific antigen screening beginning in 1994 (report of screening on the previous cycle [yes or no] and report of prostate-specific antigen screening on $\geq 50\%$ of previous cycles [yes or no]); and diabetes (yes or no).

TABLE A3. Alcohol Intake and Risk of Overall Mortality (N = 47,568)

Alcohol Intake	No. of Patients	Person-Years	Age Adjusted		Fully Adjusted*	
			HR	95% CI	HR	95% CI
Total alcohol, g/d						
None	1,737	183,391		1.00 (ref)		1.00 (ref)
> 0 to < 10	1,508	464,674	0.83	0.80 to 0.87	0.85	0.82 to 0.89
> 10 to < 15	1,407	130,209	0.79	0.74 to 0.84	0.82	0.78 to 0.87
15 to < 30	1,497	161,910	0.80	0.76 to 0.84	0.81	0.77 to 0.86
≥ 30	1,830	102,769	1.02	0.96 to 1.08	0.91	0.85 to 0.96
Any	6,242	859,562	0.84	0.81 to 0.88	0.85	0.81 to 0.88
Total wine, servings/wk						
None	1,881	316,642		1.00 (ref)		1.00 (ref)
> 0 to < 1	1,765	247,193	0.80	0.77 to 0.84	0.86	0.83 to 0.90
1 to < 3	1,289	270,936	0.74	0.71 to 0.77	0.81	0.78 to 0.85
3 to < 7	1,207	149,381	0.70	0.66 to 0.74	0.79	0.74 to 0.83
≥ 7	1,214	58,801	0.71	0.66 to 0.77	0.80	0.74 to 0.86
Any	5,475	726,311	0.75	0.73 to 0.78	0.85	0.82 to 0.89
Beer, servings/wk						
None	1,865	360,658		1.00 (ref)		1.00 (ref)
> 0 to < 1	1,678	282,290	0.84	0.81 to 0.87	0.87	0.84 to 0.91
1 to < 3	1,324	184,919	0.80	0.76 to 0.84	0.85	0.81 to 0.90
3 to < 7	1,065	147,144	0.85	0.81 to 0.90	0.87	0.82 to 0.92
≥ 7	1,251	67,942	1.05	0.98 to 1.13	0.89	0.83 to 0.96
Any	5,318	682,295	0.85	0.82 to 0.87	0.91	0.88 to 0.95
Liquor, servings/wk						
None	1,494	418,275		1.00 (ref)		1.00 (ref)
> 0 to < 1	1,356	251,147	0.89	0.85 to 0.92	0.92	0.88 to 0.96
1 to < 3	1,492	133,353	0.88	0.84 to 0.93	0.93	0.88 to 0.98
3 to < 7	1,645	140,766	0.92	0.87 to 0.96	0.93	0.89 to 0.98
≥ 7	2,384	99,412	1.13	1.08 to 1.19	1.04	0.99 to 1.09
Any	6,877	624,678	0.94	0.91 to 0.97	1.02	0.99 to 1.06
Red wine, servings/wk						
None	1,752	454,335		1.00 (ref)		1.00 (ref)
> 0 to < 1	1,529	339,850	0.81	0.78 to 0.84	0.87	0.84 to 0.90
1 to < 3	1,336	154,773	0.74	0.70 to 0.78	0.83	0.78 to 0.87
3 to < 7	1,132	74,705	0.73	0.68 to 0.78	0.80	0.74 to 0.86
≥ 7	1,358	19,290	0.80	0.71 to 0.91	0.82	0.73 to 0.94
Any	5,355	588,618	0.78	0.76 to 0.81	0.93	0.89 to 0.97
White wine, servings/wk						
None	1,869	352,156		1.00 (ref)		1.00 (ref)
> 0 to < 1	1,539	391,096	0.78	0.75 to 0.81	0.85	0.82 to 0.88
1 to < 3	1,306	175,856	0.72	0.68 to 0.75	0.81	0.77 to 0.85
3 to < 7	1,127	98,156	0.73	0.69 to 0.78	0.82	0.77 to 0.88
≥ 7	1,257	25,689	0.79	0.71 to 0.89	0.86	0.76 to 0.96
Any	5,229	690,797	0.76	0.74 to 0.79	0.89	0.85 to 0.93

Abbreviation: HR, hazard ratio.

*Fully adjusted models are adjusted for total energy intake (kilocalories/day, continuous); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m²: < 25, 25 to < 30, ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); choline (milligrams/day, quintiles); vegetable fat (grams/day, quintiles); coffee (servings/day, quintiles); lycopene (servings/day, quintiles); whole milk (servings/day, quintiles); prostate-specific antigen screening beginning in 1994 (report of screening on the previous cycle [yes or no] and report of prostate-specific antigen screening on ≥ 50% of previous cycles [yes or no]); and diabetes (yes or no). Models for all-cause mortality also adjusted for parental history of myocardial infarction before 60 years of age (yes or no); comorbidities (yes or no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease); high blood pressure (yes or no); and high cholesterol (yes or no).

TABLE A4. Postdiagnosis Alcohol Intake and Progression to Lethal Prostate Cancer Among Men Diagnosed With Nonmetastatic Prostate Cancer in the Health Professionals Follow-Up Study (N = 5,182)

Alcohol Intake	Exclude Missing Stage (n = 4,731)			Restricted to Men Who Reported ≥ Two Prediagnosis PSA Screenings (n = 2,963)		
	Patients	HR*	95% CI	Patients	HR*	95% CI
Total alcohol, g/d						
None	100		1.00 (ref)	38		1.00 (ref)
> 0 to < 10	133	1.18	0.58 to 2.42	42	0.49	0.10 to 2.35
> 10 to < 15	46	0.95	0.39 to 2.31	16	0.30	0.03 to 2.79
15 to < 30	61	0.65	0.29 to 1.43	19	0.39	0.07 to 2.20
≥ 30	35	1.06	0.39 to 2.87	13	0.09	0.00 to 1.67
Any	275	0.95	0.51 to 1.79	90	0.35	0.09 to 1.35
Total wine, servings/wk						
None	168		1.00 (ref)	55		1.00 (ref)
> 0 to < 1	52	3.41	1.26 to 9.24	14	9.23	1.04 to 82.26
1 to < 3	73	1.29	0.62 to 2.69	25	0.49	0.07 to 3.32
3 to < 7	55	0.53	0.24 to 1.20	21	0.29	0.03 to 2.61
≥ 7	27	0.74	0.29 to 1.88	13	0.16	0.01 to 3.69
Any	207	0.99	0.55 to 1.78	73	1.16	0.33 to 4.13
Beer, servings/wk						
None	216		1.00 (ref)	79		1.00 (ref)
> 0 to < 1	52	0.77	0.34 to 1.77	12	0.21	0.02 to 2.10
1 to < 3	52	1.29	0.60 to 2.79	19	0.38	0.04 to 3.29
3 to < 7	43	1.58	0.68 to 3.67	13	4.15	0.39 to 44.66
≥ 7	12	3.19	0.59 to 17.26	5	5.71	0.09 to 375.42
Any	159	1.04	0.57 to 1.87	49	0.44	0.12 to 1.54
Liquor, servings/wk						
None	200		1.00 (ref)	77		1.00 (ref)
> 0 to < 1	46	1.12	0.50 to 2.48	12	0.50	0.09 to 2.83
1 to < 3	30	1.38	0.49 to 3.86	8	1.41	0.15 to 13.42
3 to < 7	47	1.18	0.50 to 2.76	17	0.30	0.03 to 3.18
≥ 7	52	1.22	0.55 to 2.69	14	1.05	0.11 to 10.15
Any	175	1.05	0.60 to 1.85	51	0.64	0.18 to 2.25
Red wine, servings/wk						
None	218		1.00 (ref)	67		1.00 (ref)
> 0 to < 1	62	0.77	0.38 to 1.56	20	0.49	0.07 to 3.21
1 to < 3	25	0.43	0.14 to 1.25	10	0.29	0.02 to 4.53
3 to < 7	54	0.47	0.22 to 1.01	22	0.31	0.05 to 1.91
≥ 7	16	0.43	0.14 to 1.29	9	0.00	0.00 to 0.36
Any	157	0.48	0.27 to 0.87	61	0.56	0.15 to 2.03
White wine, servings/wk						
None	206		1.00 (ref)	76		1.00 (ref)
> 0 to < 1	93	1.48	0.72 to 3.05	29	0.47	0.08 to 2.84
1 to < 3	34	1.18	0.47 to 2.98	10	0.56	0.05 to 6.57
3 to < 7	34	0.52	0.22 to 1.23	10	0.17	0.01 to 2.00

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TABLE A4. Postdiagnosis Alcohol Intake and Progression to Lethal Prostate Cancer Among Men Diagnosed With Nonmetastatic Prostate Cancer in the Health Professionals Follow-Up Study (N = 5,182) (continued)

Alcohol Intake	Exclude Missing Stage (n = 4,731)			Restricted to Men Who Reported ≥ Two Prediagnosis PSA Screenings (n = 2,963)		
	Patients	HR*	95% CI	Patients	HR*	95% CI
≥ 7	8	0.65	0.14 to 2.93	3	5.50	0.03 to 1,009.49
Any	169	1.14	0.61 to 2.14	52	0.66	0.13 to 3.43
Alcohol Intake	Nonsmokers (n = 5,005)			Using Alcohol Report From First Postdiagnosis Questionnaire Only (n = 4,645)		
	Patients	HR*	95% CI	Patients	HR*	95% CI
Total alcohol, g/d						
None	121		1.00 (ref)	105		1.00 (ref)
> 0 to < 10	139	1.19	0.63 to 2.25	127	1.00	0.51 to 1.96
> 10 to < 15	46	1.09	0.47 to 2.53	57	1.07	0.44 to 2.65
15 to < 30	63	0.69	0.33 to 1.45	61	0.93	0.41 to 2.11
≥ 30	35	1.50	0.59 to 3.83	39	0.96	0.36 to 2.56
Any	283	1.04	0.59 to 1.83	284	0.99	0.54 to 1.84
Total wine, servings/wk						
None	193		1.00 (ref)	174		1.00 (ref)
> 0 to < 1	55	2.94	1.23 to 7.03	48	1.65	0.66 to 4.15
1 to < 3	75	1.38	0.69 to 2.77	78	0.76	0.38 to 1.51
3 to < 7	53	0.53	0.26 to 1.08	70	0.90	0.44 to 1.87
≥ 7	28	0.97	0.40 to 2.32	20	0.57	0.22 to 1.52
Any	211	1.12	0.65 to 1.92	216	0.90	0.50 to 1.60
Beer, servings/wk						
None	240		1.00 (ref)	200		1.00 (ref)
> 0 to < 1	52	0.60	0.29 to 1.26	52	0.62	0.28 to 1.34
1 to < 3	53	1.17	0.56 to 2.43	59	1.06	0.50 to 2.24
3 to < 7	46	1.66	0.75 to 3.66	60	1.16	0.53 to 2.53
≥ 7	13	2.65	0.57 to 12.19	18	1.39	0.38 to 5.06
Any	164	0.91	0.53 to 1.57	189	0.93	0.56 to 1.56
Liquor, servings/wk						
None	227		1.00 (ref)	201		1.00 (ref)
> 0 to < 1	48	0.99	0.48 to 2.05	49	1.08	0.52 to 2.23
1 to < 3	29	1.08	0.40 to 2.88	25	0.73	0.23 to 2.29
3 to < 7	47	0.99	0.45 to 2.16	57	1.14	0.53 to 2.48
≥ 7	53	1.52	0.69 to 3.32	57	1.08	0.47 to 2.47
Any	177	1.02	0.61 to 1.72	188	1.05	0.60 to 1.84
Red wine, servings/wk						
None	242		1.00 (ref)	228		1.00 (ref)
> 0 to < 1	65	0.82	0.41 to 1.61	66	0.80	0.40 to 1.61
1 to < 3	25	0.45	0.16 to 1.20	28	1.10	0.40 to 2.98
3 to < 7	53	0.49	0.24 to 0.98	58	0.81	0.37 to 1.78

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TABLE A4. Postdiagnosis Alcohol Intake and Progression to Lethal Prostate Cancer Among Men Diagnosed With Nonmetastatic Prostate Cancer in the Health Professionals Follow-Up Study (N = 5,182) (continued)

Alcohol Intake	Nonsmokers (n = 5,005)			Using Alcohol Report From First Postdiagnosis Questionnaire Only (n = 4,645)		
	Patients	HR*	95% CI	Patients	HR*	95% CI
≥ 7	19	0.56	0.20 to 1.61	10	0.60	0.17 to 2.12
Any	162	0.53	0.31 to 0.91	162	0.91	0.50 to 1.67
White wine, servings/wk						
None	232		1.00 (ref)	206		1.00 (ref)
> 0 to < 1	98	1.60	0.82 to 3.10	85	0.90	0.46 to 1.77
1 to < 3	34	1.05	0.45 to 2.43	45	0.37	0.16 to 0.87
3 to < 7	33	0.53	0.24 to 1.15	46	1.23	0.54 to 2.79
≥ 7	7	0.93	0.21 to 4.15	8	0.40	0.08 to 1.98
Any	172	1.23	0.70 to 2.15	184	0.76	0.43 to 1.36

Abbreviations: HR, hazard ratio; PSA, prostate-specific antigen.

*Adjusted for energy intake (kilocalories/day); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m^2 : < 25 , 25 to < 30 , ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); coffee intake (servings/day, quintiles); diabetes (yes or no); primary treatment (radical prostatectomy, radiation, hormones, other, missing); stage at diagnosis (T1, T2, T3+, missing); Gleason grade at diagnosis (< 7 , 7 , > 7 , missing); PSA at diagnosis (ng/dL : < 4 , 4 to < 10 , 10 to < 20 , ≥ 20 , missing); PSA screening (screening on the cycle before prostate cancer diagnosis was reported [yes or no] and intensity of screening [$\geq 50\%$ of previous cycles, yes or no]); and diabetes (yes or no). Beer, wine, and liquor mutually adjusted for each other. Red wine and white wine also mutually adjusted.

TABLE A5. Postdiagnosis Alcohol Intake and Overall Mortality Among Men Diagnosed With Nonmetastatic Prostate Cancer in the Health Professionals Follow-Up Study (N = 5,182)

Alcohol Intake	Exclude Missing Stage (n = 4,731)			Restricted to Men Who Reported ≥ Two Prediagnosis PSA Screen (n = 2,963)				
	Patients	HR*	95% CI	Patients	HR*	95% CI		
Total alcohol, g/d								
None	433		1.00 (ref)	162		1.00 (ref)		
> 0 to < 10	450	0.91	0.67 to 1.22	141	0.89	0.52 to 1.52		
> 10 to < 15	155	0.82	0.56 to 1.21	57	0.53	0.27 to 1.04		
15 to < 30	205	0.76	0.53 to 1.11	67	0.51	0.27 to 0.99		
≥ 30	142	0.82	0.54 to 1.24	54	0.43	0.18 to 1.02		
Any	952	0.85	0.65 to 1.10	319	0.66	0.42 to 1.03		
Total wine, servings/wk								
None	727		1.00 (ref)	251		1.00 (ref)		
> 0 to < 1	115	0.76	0.49 to 1.18	33	1.32	0.53 to 3.33		
1 to < 3	269	0.97	0.71 to 1.34	95	1.13	0.63 to 2.03		
3 to < 7	167	0.52	0.36 to 0.77	60	0.58	0.29 to 1.14		
≥ 7	107	0.84	0.53 to 1.31	42	0.54	0.23 to 1.28		
Any	658	0.78	0.60 to 1.02	230	1.08	0.66 to 1.78		
Beer, servings/wk								
None	889		1.00 (ref)	328		1.00 (ref)		
> 0 to < 1	168	0.78	0.54 to 1.12	43	0.51	0.25 to 1.05		
1 to < 3	164	0.91	0.63 to 1.31	61	0.49	0.24 to 0.99		
3 to < 7	124	1.05	0.69 to 1.59	37	0.54	0.22 to 1.30		
≥ 7	40	1.13	0.60 to 2.15	12	0.75	0.19 to 3.00		
Any	496	0.92	0.71 to 1.20	153	0.52	0.31 to 0.88		
Liquor, servings/wk								
None	787		1.00 (ref)	282		1.00 (ref)		
> 0 to < 1	154	1.05	0.72 to 1.54	48	0.77	0.39 to 1.50		
1 to < 3	88	1.38	0.84 to 2.26	31	1.02	0.40 to 2.61		
3 to < 7	156	1.01	0.69 to 1.46	61	0.84	0.45 to 1.56		
≥ 7	200	1.17	0.82 to 1.67	59	0.72	0.35 to 1.47		
Any	598	1.20	0.93 to 1.54	199	0.89	0.57 to 1.40		
Red wine, servings/wk								
None	818		1.00 (ref)	278		1.00 (ref)		
> 0 to < 1	231	1.08	0.79 to 1.49	74	1.28	0.66 to 2.48		
1 to < 3	112	0.60	0.39 to 0.92	46	0.60	0.28 to 1.28		
3 to < 7	157	0.63	0.44 to 0.92	54	0.58	0.29 to 1.16		
≥ 7	67	0.54	0.30 to 0.97	29	0.17	0.05 to 0.58		
Any	567	0.75	0.57 to 0.99	203	0.68	0.38 to 1.20		
White wine, servings/wk								
None	843		1.00 (ref)	291		1.00 (ref)		
> 0 to < 1	269	1.16	0.84	1.59	92	1.57	0.86	2.88
1 to < 3	132	1.15	0.77	1.70	49	1.10	0.55	2.18

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TABLE A5. Postdiagnosis Alcohol Intake and Overall Mortality Among Men Diagnosed With Nonmetastatic Prostate Cancer in the Health Professionals Follow-Up Study (N = 5,182) (continued)

Alcohol Intake	Exclude Missing Stage (n = 4,731)			Restricted to Men Who Reported ≥ Two Prediagnosis PSA Screen (n = 2,963)			
	Patients	HR*	95% CI	Patients	HR*	95% CI	
3 to < 7	110	0.70	0.46 to 1.06	37	0.86	0.39 to 1.92	
≥ 7	31	1.03	0.51 to 2.10	12	2.16	0.46 to 10.08	
Any	542	1.15	0.86 to 1.54	190	1.63	0.91 to 2.92	
Alcohol Intake	Nonsmokers (n = 5,005)			Using Alcohol Report From First Postdiagnosis Questionnaire Only (n = 4,645)			
	Patients	HR*	95% CI	Patients	HR*	95% CI	
Total alcohol, g/d							
None	500		1.00 (ref)	366		1.00 (ref)	
> 0 to < 10	491	0.97	0.73 to 1.29	501	1.08	0.78 to 1.50	
> 10 to < 15	162	0.89	0.61 to 1.30	194	0.95	0.63 to 1.42	
15 to < 30	213	0.79	0.55 to 1.12	207	0.99	0.67 to 1.45	
≥ 30	141	0.87	0.58 to 1.32	175	0.99	0.64 to 1.51	
Any	1007	0.90	0.70 to 1.16	1077	1.02	0.76 to 1.36	
Total wine, servings/wk							
None	811		1.00 (ref)	685		1.00 (ref)	
> 0 to < 1	124	0.84	0.55 to 1.29	156	0.75	0.49 to 1.13	
1 to < 3	293	1.10	0.81 to 1.49	313	1.17	0.86 to 1.60	
3 to < 7	171	0.60	0.42 to 0.87	186	0.72	0.50 to 1.03	
≥ 7	108	0.85	0.54 to 1.34	104	0.73	0.47 to 1.14	
Any	696	0.87	0.68 to 1.13	759	0.89	0.69 to 1.16	
Beer, servings/wk							
None	978		1.00 (ref)	797		1.00 (ref)	
> 0 to < 1	176	0.76	0.53 to 1.07	212	0.92	0.65 to 1.29	
1 to < 3	188	1.01	0.71 to 1.42	204	0.93	0.65 to 1.32	
3 to < 7	124	1.08	0.71 to 1.63	159	0.82	0.55 to 1.22	
≥ 7	41	1.28	0.68 to 2.42	72	1.01	0.58 to 1.74	
Any	529	0.93	0.72 to 1.20	647	0.86	0.67 to 1.11	
Liquor, servings/wk							
None	884		1.00 (ref)	710		1.00 (ref)	
> 0 to < 1	167	1.02	0.71 to 1.47	200	1.26	0.87 to 1.83	
1 to < 3	92	1.30	0.80 to 2.11	80	0.77	0.46 to 1.30	
3 to < 7	170	1.07	0.75 to 1.53	212	1.57	1.09 to 2.28	
≥ 7	194	1.05	0.74 to 1.49	242	1.31	0.92 to 1.86	
Any	623	1.12	0.88 to 1.44	734	1.29	0.98 to 1.68	
Red wine, servings/wk							
None	908		1.00 (ref)	861		1.00 (ref)	
> 0 to < 1	247	1.03	0.76 to 1.41	260	0.85	0.62 to 1.18	
1 to < 3	119	0.70	0.46 to 1.05	127	1.32	0.84 to 2.07	
3 to < 7	161	0.65	0.45 to 0.93	139	0.60	0.40 to 0.89	
≥ 7	72	0.56	0.31 to 1.01	58	0.69	0.40 to 1.18	
Any	599	0.73	0.55 to 0.95	584	0.81	0.61 to 1.08	

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TABLE A5. Postdiagnosis Alcohol Intake and Overall Mortality Among Men Diagnosed With Nonmetastatic Prostate Cancer in the Health Professionals Follow-Up Study (N = 5,182) (continued)

Alcohol Intake	Nonsmokers (n = 5,005)			Using Alcohol Report From First Postdiagnosis Questionnaire Only (n = 4,645)		
	Patients	HR*	95% CI	Patients	HR*	95% CI
White wine, servings/wk						
None	926		1.00 (ref)	772		1.00 (ref)
> 0 to < 1	292	1.27	0.93 to 1.73	317	0.97	0.71 to 1.32
1 to < 3	144	1.28	0.87 to 1.87	162	1.67	1.14 to 2.44
3 to < 7	114	0.82	0.54 to 1.24	143	0.83	0.56 to 1.22
≥ 7	31	0.96	0.45 to 2.04	50	0.80	0.40 to 1.60
Any	581	1.31	0.98 to 1.74	672	1.13	0.85 to 1.50

Abbreviations: HR, hazard ratio; PSA, prostate-specific antigen; RP, radical prostatectomy.

*Adjusted for energy intake (kilocalories/day); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m²: < 25, 25 to < 30, ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); coffee intake (servings/day, quintiles); diabetes (yes or no); primary treatment (radical prostatectomy, radiation, hormones, other, missing); stage at diagnosis (T1, T2, T3+, missing); Gleason grade at diagnosis (< 7, 7, > 7, missing); PSA at diagnosis (ng/dL: < 4, 4 to < 10, 10 to < 20, ≥ 20, missing); PSA screening (screening on the cycle before prostate cancer diagnosis was reported [yes or no] and intensity of screening [≥ 50% of previous cycles, yes or no]); and diabetes (yes or no). Beer, wine, and liquor mutually adjusted for each other. Red wine and white wine also mutually adjusted. Models for all-cause mortality also adjusted for parental history of myocardial infarction before 60 years of age (yes or no); comorbidities (yes or no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease); high blood pressure (yes or no); and high cholesterol (yes or no).

TABLE A6. Postdiagnosis Alcohol Intake and Survival Among Patients With Prostate Cancer Diagnosed With Nonmetastatic Disease in the Health Professionals Follow-Up Study, Using Alcohol Report From 2 to 4 Years Before Current Time Period (N = 4,057)

Alcohol Intake	Lethal Prostate Cancer			Overall Mortality		
	Patients	HR*	95% CI	Patients	HR*	95% CI
Total alcohol, g/d						
None	91		1.00 (ref)	431		1.00 (ref)
> 0 to < 10	105	1.28	0.58 to 2.83	450	0.89	0.65 to 1.22
10 to < 15	40	0.97	0.36 to 2.61	175	1.11	0.75 to 1.64
15 to < 30	59	0.88	0.35 to 2.19	201	0.86	0.59 to 1.25
≥ 30	37	2.15	0.65 to 7.18	155	0.88	0.58 to 1.32
Total wine, servings/wk						
None	148		1.00 (ref)	903		1.00 (ref)
> 0 to < 1	47	3.68	1.25 to 10.84	172	1.14	0.77 to 1.70
1 to < 3	65	1.96	0.87 to 4.41	170	0.89	0.65 to 1.22
3 to < 7	46	0.70	0.29 to 1.68	119	0.64	0.45 to 0.92
≥ 7	26	0.74	0.24 to 2.28	48	0.88	0.57 to 1.38
Beer, servings/wk						
None	189		1.00 (ref)	741		1.00 (ref)
> 0 to < 1	45	0.29	0.10 to 0.81	137	0.73	0.51 to 1.03
1 to < 3	46	0.96	0.41 to 2.27	254	0.87	0.60 to 1.24
3 to < 7	36	0.97	0.37 to 2.53	177	0.93	0.61 to 1.41
≥ 7	16	10.11	0.83 to 123.22	103	1.27	0.70 to 2.31
Liquor, servings/wk						
None	169		1.00 (ref)	855		1.00 (ref)
> 0 to < 1	41	1.35	0.56 to 3.29	220	1.05	0.72 to 1.53
1 to < 3	24	1.19	0.31 to 4.51	102	1.10	0.68 to 1.77
3 to < 7	45	0.69	0.30 to 1.61	166	1.16	0.81 to 1.65
≥ 7	53	3.11	1.16 to 8.39	69	1.05	0.75 to 1.48
Red wine, servings/wk						
None	193		1.00 (ref)	846		1.00 (ref)
> 0 to < 1	54	1.17	0.51 to 2.64	281	1.01	0.73 to 1.39
1 to < 3	24	0.70	0.22 to 2.20	138	0.54	0.34 to 0.83
3 to < 7	46	0.47	0.19 to 1.15	116	0.62	0.43 to 0.89
White wine, servings/wk						
None	183		1.00 (ref)	779		1.00 (ref)
> 0 to < 1	74	2.46	1.09 to 5.54	161	1.25	0.92 to 1.71
1 to < 3	41	2.45	0.98 to 6.07	90	1.05	0.71 to 1.55
3 to < 7	25	0.64	0.24 to 1.71	178	0.74	0.49 to 1.11
≥ 7	9	2.55	0.34 to 19.37	204	0.81	0.38 to 1.73

Abbreviation: HR, hazard ratio.

*Adjusted for energy intake (kilocalories/day); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m²: < 25, 25 to < 30, ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); coffee intake (servings/day, quintiles); diabetes (yes or no); primary treatment (radical prostatectomy, radiation, hormones, other, missing); stage at diagnosis (T1, T2, T3+, missing); Gleason grade at diagnosis (< 7, 7, > 7, missing); prostate-specific antigen at diagnosis (ng/dL: < 4, 4 to < 10, 10 to < 20, ≥ 20, missing); prostate-specific antigen screening (screening on the cycle before prostate cancer diagnosis was reported [yes or no] and intensity of screening [≥ 50% of previous cycles, yes or no]); and diabetes (yes or no). Beer, wine, and liquor mutually adjusted for each other. Red wine and white wine also mutually adjusted. Models for all-cause mortality also adjusted for parental history of myocardial infarction before 60 years of age (yes or no); comorbidities (yes or no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease); high blood pressure (yes or no); and high cholesterol (yes or no).

TABLE A7. Change in Alcohol Intake From Last Prediagnosis Questionnaire to First Postdiagnosis Questionnaire (N = 4,411)

Alcohol Intake	Lethal Prostate Cancer			Overall Mortality		
	Patients	HR*	95% CI	Patients	HR*	95% CI
Decreased	64	1.33	0.59 to 3.00	192	1.35	0.93 to 1.95
Same	205		1.00 (ref)	645		1.00 (ref)
Increased	68	1.12	0.53 to 2.34	215	1.15	0.81 to 1.63

Abbreviation: HR, hazard ratio.

*Adjusted for energy intake (kilocalories/day); smoking status (never, past [quit > 10 years ago], past [quit ≤ 10 years ago], current [< 40 pack-years], current [≥ 40 pack-years]); body mass index (kg/m^2 : < 25 , 25 to < 30 , ≥ 30); vigorous physical activity (< 3 h/wk, ≥ 3 h/wk); coffee intake (servings/day, quintiles); diabetes (yes or no); primary treatment (radical prostatectomy, radiation, hormones, other, missing); stage at diagnosis (T1, T2, T3+, missing); Gleason grade at diagnosis (< 7 , 7 , > 7 , missing); prostate-specific antigen at diagnosis (ng/dL : < 4 , 4 to < 10 , 10 to < 20 , ≥ 20 , missing); prostate-specific antigen screening (screening on the cycle before prostate cancer diagnosis was reported [yes or no] and intensity of screening [$\geq 50\%$ of previous cycles, yes or no]); and diabetes (yes or no). Beer, wine, and liquor mutually adjusted for each other. Red wine and white wine also mutually adjusted. Models for all-cause mortality also adjusted for parental history of myocardial infarction before 60 years of age (yes or no); comorbidities (yes or no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disease, or Parkinson's disease); high blood pressure (yes or no); and high cholesterol (yes or no).