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Alcohol Consumption, Finasteride and Prostate Cancer Risk: Results from the Prostate Cancer Prevention Trial

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Abstract

Background—Current research is inconclusive regarding the relationship between alcohol consumption and prostate cancer risk. We examined the associations of total alcohol, type of alcoholic beverage, and drinking pattern with risks of total, low- and high-grade prostate cancer.

Methods—Data are from the 2,129 participants in the Prostate Cancer Prevention Trial (PCPT) who had cancer detected during the 7-year trial and 8,791 who were determined by biopsy to be free of cancer at the trial end. Poisson regression was used to calculate relative risks (RRs) and 95% confidence intervals (CIs) for associations of alcohol intake with prostate cancer risk.

Results—Associations of drinking with high-grade disease did not differ by treatment arm. In combined arms, heavy alcohol consumption (≥50 g alcohol/day) and regular heavy drinking (≥4 drinks/day on ≥5 days per week) were associated with increased risks of high-grade prostate cancer (RR: 2.01, 95% CI: 1.33-3.05 and 2.17, 95% CI: 1.42 -3.30, respectively); less heavy drinking was not associated with risk. Associations of drinking with low-grade cancer differed by treatment arm. In the placebo arm, there was no association of drinking with risk of low-grade cancer. In the finasteride arm, drinking ≥50 g of alcohol/day was associated an increased risk of low-grade disease (RR: 1.89, 95% CI: 1.39-2.56); this finding was due to the 43% reduction in risk of low-grade cancer attributable to finasteride treatment in men drinking <50g alcohol per day and the lack of an effect of finasteride in men drinking ≥50 g of alcohol/day per day ($P_{interaction}$=0.03).

Conclusion—Heavy, daily drinking increases the risk of high-grade prostate cancer. Heavy drinking made finasteride ineffective for reducing prostate cancer risk.

Keywords

Alcohol consumption; finasteride; low-grade prostate cancer; high-grade prostate cancer

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Informed consent was obtained from all participants.

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Introduction

Whether or not alcohol affects prostate cancer risk is uncertain. Most studies have found no significant associations,[1-7] although two meta-analyses reported an approximate 20% increase in risk among heavy drinkers.[2, 4] Among the studies that have found significant associations, there is little consistency in the effect size or direction, pattern of dose-response, or associations specific to type of alcoholic beverage, clinical stage or pathological grade.[8-16] Studies that can better clarify the association of alcohol consumption with prostate cancer risk are important, because beyond obesity,[17] smoking,[18-21] and perhaps diet [18,22,23] prostate cancer has no well-established, modifiable risk factors.

Here we give results on the association of alcohol consumption and risk of prostate cancer from the Prostate Cancer Prevention Trial (PCPT). We examine the relationships of total alcohol consumption, alcohol from different types of beverages, and usual drinking pattern with risks of total, low- and high-grade prostate cancer. We also examine whether the effects of finasteride (the PCPT study drug) were modified by alcohol consumption, because both affect the metabolism of testosterone.[24, 25] Results of this study address whether alcohol consumption is associated with risks of biopsy-detected presence or absence of local stage prostate cancer and whether alcohol consumption should be considered when making clinical recommendations for the use of finasteride for prostate cancer prevention.

Materials and Methods

Study Design and Study Population

All data for this study were collected as part of the PCPT, a randomized, placebo-controlled trial testing whether finasteride, a 5α-reductase inhibitor, could reduce the 7-year period prevalence of prostate cancer. Informed consent was obtained from each participant prior to the study. Details of the study design and participant characteristics have been described previously. [26] Briefly, a total of 18,880 men age 55 years and older with a normal digital rectal exam (DRE) and prostate-specific antigen (PSA) level of 3.0 ng/ml or below, were randomized to receive finasteride (5 mg/day) or placebo. During the PCPT, men underwent DRE and PSA determinations annually, and a prostate biopsy was recommended for participants with an abnormal DRE or a PSA of 4.0 ng/ml or greater. At the final study visit at year 7, all men not previously diagnosed with prostate cancer were offered an end-of-study biopsy. All biopsies were collected under transrectal ultrasonographic guidance, and involved a minimum of six specimens (cores). All biopsies were reviewed to confirm the diagnosis of adenocarcinoma by both the pathologist at the local study site and a central pathology laboratory. Tumors were graded centrally and categorized as low- (Gleason sum 2-6) or high-grade (Gleason sum 7-10) prostate cancer.

Of 18,880 participants, we excluded 7,539 (39.9%) men who did not have an end-of-study biopsy, which included 1,393 who died, 6,141 who were medically unable or refused, and 5 who had prostatectomy for reasons other than cancer, leaving 2,400 cases and 8,941 non-cases. We then excluded 173 cases diagnosed after the trial end date (06/23/2003), 90 cases diagnosed 180 days or more after their planned end-of-study visit and 99 non-cases whose end-of-study biopsy was completed 180 days or more before their end-of-study visit. From the 10,979 men remaining for study, we further excluded 59 men who had incomplete or missing questionnaire data on any of the following factors: alcohol consumption (n=4), current smoking status (n=5), physical activity (n=48), education (n=1), and both education and physical activity (n=1), leaving 10,920 men for these analyses.

Data Collection

Details regarding age, race, education, diabetes status, family history of prostate cancer in first-degree relatives, physical activity, history of smoking, and usual alcohol consumption were collected at baseline using self-administered questionnaires. Participants reported the frequency of consuming each type of beverage (beer, wine, and liquor) over the past year in 7 categories ("never", "1 day/month", "2-3 days/month", "1-2 days/week", "3-4 days/week", "5-6 days/week" or "every day"). They reported the usual number of drinks on each drinking day, and the usual size of each drink (small, medium, or large, treated as 0.5, 1.0 and 1.5 in analyses). We calculated the number of standard servings per week for each type of alcoholic beverage by multiplying days of drinking per week by number of drinks per drinking day and serving size. Standard servings were converted into grams of ethanol (beer = 12.96g, wine = 12.35g, and liquor = 13.93g), and these were summed to obtain total alcohol intake in grams per week. Daily average grams of alcohol was categorized as 0, 0.1 - <3, 3 - <15, 15 - <30, 30 - <50, and 50 or more.

Statistical Analysis

Multivariable models were used to estimate associations of alcohol intake with risks of total, low- and high-grade prostate cancer while controlling for covariates. We used Poisson regression with a robust error variance, a modified Poisson regression approach proposed by Zou 27 to calculate relative risks (RRs) and 95% confidence intervals (CIs). Regressions were completed using the SAS GENMOD procedure with the Log link function, and the robust error variances were estimated by using a repeated statement and the subject identifier as the class variable.27 Results are given adjusted for age (<60, 60-69, ≥70), race (White, African-American, other) and body mass index (BMI: <25 kg/m^2, 25-29.9 kg/m^2, ≥30 kg/m^2). Further control for education, diabetes, smoking, family history of prostate cancer, physical activity, and baseline PSA level (<1 ng/mL, 1-1.9 ng/mL, ≥2 ng/mL) did not affect results. In the analyses of a specific type of alcoholic beverage other types of alcoholic beverages were included as covariates. Tests for linear trend across categories were based on an ordinal variable corresponding to rank from lowest to highest category, as described by Breslow and Day.28

Drinking pattern was defined as the number of days per week on which men drank alcoholic beverages (<1, 1-4, and ≥5) stratified by numbers of drinks per drinking day (1-3, ≥4). This distinguishes men drinking heavily on a few days from those drinking modestly on many days.

Primary analyses were completed in each treatment arm separately. When there were no differences between arms, post-hoc analyses are given for both study arms combined. We also examined whether the effect of finasteride was modified by level of alcohol consumption. All statistical tests were two-sided and considered statistically significant when $p < 0.05$. Statistical analyses were conducted using SAS software V9.1 (SAS Institute, Inc., Cary, NC).

Results

Among the total 10,920 men in this analysis, 2,129 (19.5%) men were diagnosed with prostate cancer (1,425 (66.9%) Gleason score 2-6; 564 (26.5%) Gleason score 7 or higher; and 140 (6.5%) Gleason score unknown). Among the 2,129 cases, 1,515 (71.2%) were stage T1, 505 (23.7%) were stage T2, 37 (1.7%) were stage T3 and 72 (3.4%) were unknown stage. Younger age, white race, advanced education, no diabetes, BMI <30, smoking, and physical inactivity were all associated with higher alcohol consumption (Table 1). Other strong predictors of prostate cancer risk in this cohort, including PSA at baseline, finasteride

treatment and family history of prostate cancer, were not associated with alcohol consumption.

Only heavy drinking (≥50 g of alcohol per day) was associated with cancer risk, with no dose-response at lower levels of alcohol intake (Table 2). In the placebo arm, heavy alcohol intake was not associated with risk of total or low-grade cancer, but was associated with a non-significant 67% increase in the risk of high-grade cancer. In the finasteride arm, heavy drinking was associated with a 89% increased risk of total cancer, a 101% increased risk for low-grade cancer and a 115% increased risk of high-grade cancer (all $P<0.01$). In a post-hoc analysis, the relative risk for high-grade cancer associated with heavy drinking in the combined study arms was 2.01 (95% CI: 1.33-3.05; $P=0.009$).

Table 3 shows associations of specific types of alcoholic beverages with prostate cancer risk. Heavy beer consumption was associated with a significant and large increased risk of high-grade cancer in both study arms; the relative risk for high-grade cancer contrasting none to heavy beer intake in the combined arms was 2.89 (95% CI: 1.76-4.76; $P<0.0001$). In the placebo arm, heavy wine consumption was associated with a 79% increased risk of low-grade cancer ($P=0.03$), while in the finasteride arm heavy beer drinking was associated with 103% increased risk of low-grade cancer ($P<0.0001$). There were no significant associations of liquor with cancer risk.

Occasional heavy drinking (≥4 drinks per day on fewer than 5 days per week) was not associated with cancer risk (data not shown). Heavy drinking on 5 or more days per week, compared to not drinking, was associated with significantly increased risk of high-grade cancer in both the placebo (RR: 2.05, 95% CI: 1.04-4.04; $P=0.04$) and finasteride (RR: 2.25, 95% CI: 1.31-3.86; $P=0.003$) arms. In the combined arms, the relative risk was 2.17 (95% CI: 1.42-3.30; $P=0.0003$).

Table 4 presents the effects of finasteride treatment in prostate cancer risk by levels of alcohol consumption. We dichotomized alcohol intake into <50 g/day vs. ≥50 g/day based on results in Table 2, and note that the effects of finasteride were similar across all levels of alcohol intake under 50 g/day (data not shown). For total cancer, finasteride lowered risk by 29% among men drinking <50 g of alcohol per day but increased risk by 17% among heavy alcohol drinkers ($P_{interaction}=0.03$). For low-grade cancer, finasteride decreased risk by 43% among men drinking <50 g of alcohol per day and increased risk by 12% among heavy drinkers ($P_{interaction}=0.03$). For high-grade cancer, finasteride increased risk by 19% among men drinking < 50 g of alcohol per day and by 78% among heavy drinkers ($P_{interaction}=0.36$).

Discussion

In this large cohort of men with biopsy-determined presence or absence of prostate cancer, heavy alcohol consumption (≥50 g per day) was associated with a 101% increased risk of high-grade prostate cancer. Heavy beer drinking was independently associated with a 189% increased risk of high-grade cancer; due to lower consumption the independent associations with heavy wine and liquor consumption could not be rigorously evaluated. The pattern of occasional heavy drinking (≥4 drinks per day on <5 days per week) was not associated with risk of cancer, but heavy drinking on ≥5 days per week was associated with a 117% increased risk of high-grade cancer. Finally, there was a significant interaction between heavy alcohol consumption and finasteride treatment for low-grade cancer. Finasteride reduced the risk of low-grade cancer by 43% in men drinking <50 g of alcohol per day, but finasteride had no effect in heavy drinkers.

Overall, our results are consistent with findings from two meta-analyses and one review concluding that light to moderate alcohol consumption is not associated with prostate cancer risk.[1, 2, 4] Our findings on heavy drinking, and in particular, its association with risk for high-grade cancer only, are not consistent with relevant published studies. For comparison, we examined the 6 studies with alcohol intake categories that are at least as high as our heavy drinking category (≥4 drinks per day) [3, 5, 29-32] plus an additional 4 studies with a highest alcohol intake category at least as high as ≥2 drinks per day.[8, 14, 16, 33] Of these 10 studies, two reported relative risks <0.80 [5, 8] and one reported a relative risk >1.20 [31] associated with heavy drinking; statistically significant relative risks were limited to 0.23 (95% CI=0.06 to 0.95) associated with ≥22 drinks per week (based on 2 cases),[8] and 1.4 (95%CI=1.0 to 1.8) and 1.9 (95% CI=1.3 to 2.7) associated 22-56 drinks and ≥57 drinks per week (based on 211 and 96 cases),[31] respectively. Further, there were no differences in findings by measures of tumor aggressiveness in studies that conducted stratified analyses.[3, 14, 16, 31, 32] Several of these studies were small, used case-control designs or did not comprehensively assess usual alcohol intake, but the inconsistency of this study with other large and well-conducted studies is difficult to explain. It is possible that other studies were affected by a PSA detection bias, which would mask an association if heavy drinkers were less likely to get PSA screening.[34] It is also possible that the characteristics of cancer cases in the PCPT, which were almost all screen-detected and local stage, could have affected our findings, for example if heavy alcohol consumption reduced prostate size or modified the appearance of small, intermediate-grade cancers. Mean prostate volume was smaller in heavy drinkers compared to others (25.7 cc vs. 28.0 cc, p=0.04), but this magnitude of difference is not likely to substantially affect disease detection. Clearly, replication of these findings and an investigation into potential biases affecting studies of alcohol and prostate cancer are needed.

Among the different types of alcoholic beverages, only heavy beer consumption was consistently associated with prostate cancer risk. Results of previous studies examining type of alcoholic beverages and prostate cancer risk have been inconsistent. [3, 5-7, 9-16, 35-37] Most reported no differences in prostate cancer risk between different types of alcoholic beverages; [3, 5-7, 11-13] some studies found higher risks associated with beer consumption [9, 36] and others for liquor consumption.[10, 37] Whether beer is uniquely associated with risk of prostate cancer is uncertain. Few studies, including ours, had enough heavy liquor or wine consumers to detect a unique effect and it is possible that unique effects of beer are attributable to its high consumption relative to other alcoholic beverages. Effects of wine may also be masked due to differences between red and white wines; [3, 12, 35] however we lacked data to address this question.

Only two studies have examined associations of patterns of heavy drinking with risk of prostate cancer. One found an increased risk (RR: 1.64, 95% CI: 1.13- 2.38) among men drinking large amounts of alcohol (≥105 g/week) in 1 or 2 days per week, but no risk when drinking on average a similar daily amount (≥50 g/day) every day of the week.[13] A second study found a non-significant trend for increasing risk among men drinking ≥140 g/week when spread over few days of the week (RR for 7, 4-6 and 1-3 days: 1.00, 1.20 and 1.56, respectively), but no increase in risk associated with drinking on average a similar daily amount (≥60 g/day) every day of the week.[3] We found no evidence that drinking 4 or more drinks per day on fewer than 5 days per week was associated cancer risk. It is difficult to hypothesize a mechanism whereby occasional but not regular heavy drinking would increase cancer risk, and findings in previous studies, which are based on very small numbers, could be due to chance. Indeed, binge drinking is rare in middle-aged and older men [38] and is rarer still in the men participating in most research studies; much larger studies with detailed alcohol assessment will be needed to address this association in the future. Based on current

evidence, there appears to be no association on occasional heavy drinking with prostate cancer risk.

There are several mechanisms whereby alcohol consumption could influence prostate carcinogenesis. Alcohol itself may be carcinogenic,39 it affects metabolism of carcinogens and suppresses DNA repair,40, 41 it may increase DNA damage due to oxidative stress,42, 43 and at high levels it impairs immune response and increases the risk of micronutrient deficiencies.44 Unlike the digestive tract and liver, which have characteristics making them uniquely susceptible one or more of these effects of alcohol, we know of no such characteristics of the prostate. Planned future analyses of circulating steroid hormones, genetic characteristics, markers of oxidative stress and prostate tissue pathology in the PCPT may better elucidate the mechanisms underlying the effects of alcohol reported here.

The observation that finasteride did not reduce the risk of low-grade cancer among heavy drinkers is notable. In the sample of PCPT participants used in these analyses, finasteride treatment decreased the risk of total and low-grade prostate cancer by 28% (95% CI: 33% to 22%) and 42% (95% CI: 47% to 36%), respectively, and it increased the risk of high-grade cancer by 22% (95% CI: 4% to 43%). Our results suggest that finasteride will not lower prostate cancer risk among men who are heavy drinkers. This finding is not due to poor adherence, as compliance based on pill counts was 66% in both heavy and not heavy drinkers. Several mechanisms are plausible: alcohol induces expression of 5α-reductase (the action of finasteride is through competitive inhibition of 5α-reductase) 45 and it affects enzyme expression and oxidative stress in liver 46 (where finasteride is primarily metabolized). Future studies in the PCPT will examine whether heavy drinking affected finasteride metabolism or finasteride-induced changes in steroid hormone metabolism.

Our study has several strengths. First, all men had biopsy-proved absence or presence of prostate cancer, and this minimizes the potential misclassification bias. Second, alcohol intake was assessed using a detailed questionnaire and not by food frequency questionnaire, allowing us to examine effects of specific types of alcoholic beverages as well as heavy or binge drinking patterns. Third, all men were screened for prostate cancer by both PSA level and DRE during the study period, which eliminates any potential bias from PSA screening. This study also has several limitations. The number of men who were heavy drinkers was modest and when results were stratified by study arm and cancer grade the statistical power was limited. Data on alcohol consumption were available only for the year preceding study entry. Finally, because cases of prostate cancer were almost all screen detected we could not examine associations with regional or distant stage disease.

In summary, we found that heavy drinking was associated with an increased risk of high-grade, screen-detected prostate cancer. This finding is somewhat unique in the literature and requires replication; however physicians may choose to consider this finding when counseling men on reducing prostate cancer risk. We also found that heavy drinkers did not benefit from finasteride treatment. It would be prudent for physicians who are recommending finasteride for prostate cancer prevention to assess their patients' alcohol consumption and recommend drinking no more than 2 or 3 drinks per day.

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Table 1

Associations of demographic, health, and lifestyle characteristics with alcohol consumption, the Prostate Cancer Prevention Trial (PCPT)

Characteristics	Total cohort (n=10920) n (%)	Total alcohol intake (g/day)				*P*-value†
		0 (n=8655) (%)‡	0.1-14.9 (n=1357) (%)‡	15-49.9 (n=648) (%)‡	≥50 (n=260) (%)‡	
Age						
<60	3528 (32.3)	21.8	57.5	18.0	2.7	0.007
60-69	5993 (54.9)	24.3	54.6	18.7	2.4	
≥70	1399 (12.8)	25.3	55.3	17.9	1.5	
Race						0.02
White	10167 (93.1)	23.6	55.4	18.6	2.4	
African-American	370 (3.4)	26.2	59.2	14.1	0.5	
Other	383 (3.5)	23.8	58.7	15.1	2.4	
Education level						
High school	2445 (22.4)	31.7	51.7	13.9	2.7	<.0001
College degree	4434 (40.6)	22.2	55.8	19.7	2.3	
Advanced degree	4041 (37.0)	20.4	57.7	19.6	2.3	
Family history of prostate cancer						
No	9080 (83.2)	23.8	55.5	18.3	2.4	0.84
Yes	1840 (16.8)	23.0	56.2	18.6	2.2	
Diabetes						
No	10204 (93.4)	23.2	55.8	18.6	2.4	0.0001
Yes	716 (6.6)	30.3	52.7	14.8	2.2	
Treatment						
Placebo	5587 (51.2)	23.4	55.8	18.6	2.2	0.37
Finasteride	5333 (48.8)	23.9	55.4	18.1	2.6	
Body mass index (kg/m^2)						
<25	2768 (25.4)	24.1	55.4	18.2	2.3	0.01
25-29	5546 (50.8)	22.5	55.7	19.4	2.4	
≥30	2506 (22.9)	25.6	55.7	16.1	2.6	
Missing	100 (0.9)	27.0	52.0	21.0	0	

Characteristics	Total cohort (n=10920) n (%)	Total alcohol intake (g/day)				*P*-value†
		0 (n=8655) (%)‡	0.1-14.9 (n=1357) (%)‡	15-49.9 (n=648) (%)‡	≥50 (n=260) (%)‡	
Current smoking						
No	10184 (93.3)	23.8	56.0	18.0	2.2	<.0001
Yes	736 (6.7)	21.5	50.5	23.5	4.5	
PSA* level (ng/mL)						
<1	4541 (41.6)	24.2	55.4	18.0	2.4	0.87
1-1.9	4239 (38.8)	23.1	55.7	18.9	2.3	
≥2.0	2140 (19.6)	23.6	55.9	18.1	2.4	
Physical activity						
Sedentary	1897 (17.4)	26.5	54.7	16.3	2.5	0.01
Light	4526 (41.5)	22.2	56.8	18.6	2.4	
Moderate	3411 (31.2)	23.4	55.0	19.3	2.3	
Very active	1086 (9.9)	25.4	53.9	18.4	2.3	

† *P*-value of χ^2 test

‡ Row percentage

* PSA: Prostate Specific Antigen

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Table 2

Associations of alcohol consumption with risks of total, low- and high-grade prostate cancer, stratified by study arm, the Prostate Cancer Prevention Trial (PCPT)

	Total cancers		Low-grade cancers‡		High-grade cancers	
Total alcohol consumption (g/day)	**Cases / Cohort**	**RR† (95% CI)**	**Cases / Cohort**	**RR† (95% CI)**	**Cases / Cohort**	**RR† (95% CI)**
Placebo arm*						
No alcohol consumption	296/1306	1.00	217/1227	1.00	57/1284	1.00
>0-<3	327/1488	0.97 (0.85-1.11)	245/1406	0.99 (0.84-1.16)	67/1473	1.03 (0.73-1.45)
3-<15	359/1631	0.98 (0.85-1.12)	252/1524	0.94 (0.79-1.10)	81/1605	1.17 (0.84-1.62)
15-<30	168/708	1.05 (0.89-1.23)	126/666	1.06 (0.87-1.30)	29/695	0.96 (0.62-1.48)
30-<50	82/333	1.09 (0.88-1.35)	59/310	1.08 (0.83-1.40)	17/327	1.20 (0.71-2.04)
≥50	28/121	1.05 (0.75-1.46)	17/110	0.88 (0.56-1.38)	8/118	1.67 (0.81-3.41)
P for trend		0.39		0.82		0.31
Finasteride arm*						
No alcohol consumption	192/1277	1.00	106/1191	1.00	73/1264	1.00
>0-<3	229/1444	1.08 (0.91-1.29)	136/1351	1.15 (0.90-1.46)	77/1428	0.97 (0.71-1.32)
3-<15	260/1509	1.17 (0.98-1.38)	151/1400	1.23 (0.97-1.55)	93/1493	1.10 (0.82-1.49)
15-<30	105/649	1.10 (0.88-1.36)	67/611	1.24 (0.93-1.66)	30/641	0.84 (0.56-1.28)
30-<50	46/315	1.00 (0.74-1.35)	28/297	1.08 (0.72-1.60)	16/313	0.93 (0.55-1.60)
≥50	37/139	1.89 (1.39-2.56)	21/123	2.01 (1.30-3.09)	16/139	2.15 (1.33-3.71)
P for trend		0.02		0.02		0.26
P-interaction (alcohol intake as 6-level ordinal variable)		0.22		0.09		0.93

† Relative risk: adjusted for age, race, and body mass index.

‡ Men diagnosed with high-grade cancer were excluded from the cohort in the low-grade cancer analyses.

* 85 cases in the placebo arm and 55 cases in the finasteride arm with missing Gleason score were not included in the analyses by grade.

Table 3

Associations of specific types of alcohol consumption with risks of total, low- and high-grade prostate cancer, stratified by study arm, the Prostate Cancer Prevention Trial (PCPT)

	Total cancers		Low-grade cancers‡		High-grade cancers	
Alcohol consumption (g/day)	**Cases / Cohort**	**RR† (95% CI)**	**Cases / Cohort**	**RR† (95% CI)**	**Cases / Cohort**	**RR† (95% CI)**
Placebo arm*						
Alcohol from beer						
No beer consumption	454/2044	1.00	325/1915	1.00	96/2011	1.00
>0-<15	722/3165	1.02 (0.89-1.16)	532/2975	1.08 (0.92-1.26)	142/3117	0.83 (0.61-1.14)
15-<50	64/286	1.02 (0.80-1.29)	48/270	1.08 (0.82-1.44)	13/283	0.87 (0.48-1.58)
≥50	12/55	1.10 (0.67-1.82)	5/48	0.72 (0.30-1.60)	6/54	2.65 (1.19-5.92)
P for trend		0.99		0.94		0.85
Alcohol from wine						
No wine consumption	452/2067	1.00	328/1943	1.00	91/2034	1.00
>0-<15	742/3271	1.03 (0.91-1.17)	543/3072	1.04 (0.90-1.21)	151/3223	1.04 (0.76-1.43)
15-<30	44/172	1.16 (0.88-1.53)	30/158	1.12 (0.79-1.59)	10/168	1.34 (0.70-2.56)
≥30§	12/35	1.58 (1.00-2.51)	10/33	1.79 (1.06-3.02)	2/35	1.36 (0.35-5.34)
P for trend		0.23		0.20		0.66
Alcohol from liquor						
No liquor consumption	548/2467	1.00	412/2331	1.00	102/2433	1.00
>0-<15	624/2766	0.98 (0.86-1.10)	443/2585	0.91 (0.78-1.05)	138/2723	1.24 (0.91-1.69)
15-<50	76/305	1.05 (0.85-1.31)	53/282	0.97 (0.74-1.27)	16/298	1.32 (0.77-2.29)
≥50	7/20	1.60 (0.89-2.87)	5/18	1.59 (0.75-3.34)	1/19	1.39 (0.20-9.62)
P for trend		0.76		0.66		0.38
Finasteride arm*						
Alcohol from beer						
No beer consumption	306/1949	1.00	176/1819	1.00	114/1933	1.00
>0-<15	500/3018	1.04 (0.88-1.22)	299/2817	1.00 (0.80-1.25)	164/2981	0.94 (0.70-1.27)
15-<50	42/287	0.92 (0.67-1.26)	23/268	0.83 (0.54-1.28)	17/285	1.00 (0.58-1.70)
≥50	18/55	2.20 (1.49-3.26)	9/46	2.03 (1.11-3.71)	9/55	3.04 (1.61-5.76)
P for trend		0.18		0.71		0.24

Alcohol consumption (g/day)	Total cancers		Low-grade cancers‡		High-grade cancers	
	Cases / Cohort	RR† (95% CI)	Cases / Cohort	RR† (95% CI)	Cases / Cohort	RR† (95% CI)
Alcohol from wine						
No wine consumption	317/2001	1.00	171/1855	1.00	123/1978	1.00
>0-<15	509/3087	1.04 (0.89-1.23)	312/2890	1.19 (0.95-1.49)	167/3057	0.88 (0.66-1.18)
15-<30	30/157	1.26 (0.88-1.79)	18/145	1.39 (0.86-2.25)	11/156	1.24 (0.66-2.33)
≥30§	7/43	1.03 (0.51-2.08)	5/41	1.29 (0.54-3.03)	2/43	0.79 (0.20-3.19)
P for trend		0.54		0.13		0.46
Alcohol from liquor						
No liquor consumption	395/2455	1.00	226/2286	1.00	138/2424	1.00
>0-<15	416/2528	0.99 (0.85-1.15)	245/2357	0.97 (0.79-1.20)	149/2506	1.14 (0.87-1.51)
15-<50	50/296	1.00 (0.76-1.34)	34/280	1.14 (0.79-1.64)	14/294	0.91 (0.52-1.60)
≥50	4/20	1.18 (0.50-2.81)	2/18	1.08 (0.30-3.84)	2/20	1.72 (0.44-6.76)
P for trend		0.77		0.86		0.96

†Relative risk: adjusted for age, race, body mass index, and other types of beverage intake for each specific type of alcohol intake.

‡Men diagnosed with high-grade cancer were excluded from the cohort in the low-grade cancer analyses.

§This category is reduced to ≥30 g/day of alcohol due to small numbers of heavy wine drinkers.

*85 cases in the placebo arm and 55 cases in the finasteride arm with missing Gleason score were not included in the analyses by grade.

Table 4

Associations of finasteride treatment with risk of prostate cancer, stratified by alcohol consumption, the Prostate Cancer Prevention Trial (PCPT)

	Total cancers		Low-grade cancers‡		High-grade cancers	
	Cases / Cohort	RR† (95% CI)	Cases / Cohort	RR† (95% CI)	Cases / Cohort	RR† (95% CI)
< 50 g/day						
Placebo	1232/5466	1.00	899/5133	1.00	251/5384	1.00
Finasteride	832/5194	0.71 (0.66-0.77)	488/4850	0.57 (0.52-0.64)	289/5139	1.19 (1.01-1.41)
≥ 50 g/day						
Placebo	28/121	1.00	17/110	1.00	8/118	1.00
Finasteride	37/139	1.17 (0.77-1.79)	21/123	1.12 (0.62-2.00)	16/139	1.78 (0.79-4.01)
P for interaction		0.03		0.03		0.36

†Relative risk: adjusted for age, race, and body mass index.

‡Men diagnosed with high-grade cancer were excluded from the cohort in the low-grade cancer analyses.

*85 cases in the placebo arm and 55 cases in the finasteride arm with missing Gleason score were not included in the analyses by grade.