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Statin use and risk of prostate cancer: results from the Southern Community Cohort Study

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Abstract

Background—Epidemiologic studies suggest that statin use may be inversely associated with risk of prostate cancer, but prior studies have focused predominantly on non-Hispanic white populations.

Methods—We evaluated the association between statin use and prostate cancer risk in the Southern Community Cohort Study (SCCS). Study participants were 32,091 men aged 40–79 at baseline, 67% of whom were non-Hispanic black. Between study enrollment (2002–2009) and December 31, 2010, 570 prostate cancer cases were diagnosed, including 324 low-grade cancers (Gleason score <7 or Gleason pattern 3+4) and 107 high-grade cancers (Gleason score >7 or Gleason pattern 4+3). Analyses of overall prostate cancer were conducted using Cox regression and analyses of grade-specific cancer were conducted using competing risks models.

Results—Ten percent of non-Hispanic black men and 22% of non-Hispanic white men reported use of statins at study enrollment. As compared to non-use, statin use was associated with a non-significant 14% lower risk of prostate cancer in multivariable models (Hazard Ratio [HR]:0.86; 95% Confidence Interval [CI]:0.63–1.18). This association was stronger for high-grade cancer (HR: 0.62; 95% CI: 0.30, 1.28) than low-grade cancer (HR:0.98; 95% CI:0.65–1.48). Results were similar by race/ethnicity (p-interaction:0.41) and did not vary by history of prostate-specific antigen [PSA] screening (p-interaction:0.65).

Conclusions—Results suggest no strong association between statin use and prostate cancer risk overall, and further suggest that if a modest protective effect does exist, it does not vary by race/ethnicity and may be restricted to high-grade tumors, although power to detect differences by subgroup was limited.

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Keywords

African Americans; Chemoprevention; Epidemiologic Studies; Prostate Cancer; Statins

Introduction

Various lines of research suggest that statins, or 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA) inhibitors, taken for control of hypercholesterolemia, may have chemopreventive properties, including anti-proliferative, pro-apoptotic, and anti-inflammatory effects.[1-5] Supporting epidemiologic studies suggest that these drugs may be inversely associated with risk of several cancers,[6-11] including prostate cancer,[12-16] the most commonly diagnosed cancer among men in the United States.[17]

While many studies indicate a modest inverse association between statin use and overall prostate cancer risk, the literature is inconsistent.[12-16, 18-24] This conflicting evidence may be due, in part, to the inclusion of indolent cancers identified by prostate-specific antigen (PSA) screening.[25] Risk factors for these tumors differ from those of clinically meaningful cancers,[26] and it is therefore possible that the proportion of indolent cancers affects the strength of observed association. The inclusion of screen-detected indolent prostate cancers is a particular concern for exposures related to screening, such as statin use, [27] as residual confounding by screening practices might obscure a protective association. Conversely, statins have been shown to decrease PSA levels, which may alternatively generate a non-causal inverse association between statins and prostate cancer.[28, 29] Clinically meaningful cancers are less susceptible to these biases, and accordingly, the inverse association between statin use and prostate cancer has been more consistent for advanced/lethal prostate cancers compared to overall prostate cancer.[18, 25, 30] Even so, two recent studies embedded within trials of regularly screened individuals indicated no protective association between statin use and high-grade prostate cancer.[23, 24]

Prior studies of statin use and prostate cancer have been conducted in predominantly non-Hispanic white populations, yet non-Hispanic black men experience a disproportionate burden of prostate cancer[31] and are also at increased risk of aggressive forms of the disease.[32] To our knowledge, no prior studies have evaluated whether statin use is associated with risk of prostate cancer among black men. Thus, our objective was to prospectively evaluate the association between statin use and prostate cancer risk in a predominantly non-Hispanic black cohort with control for screening practices and factors influencing access to care, such as health insurance coverage and household income.

Materials and Methods

Study Population

Study participants were drawn from the Southern Community Cohort Study (SCCS), an ongoing prospective cohort study focused on cancer disparities.[33, 34] Participants included over 85,000 men and women recruited from 2002-2009 in 12 southeastern states, including: Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North

Carolina, South Carolina, Tennessee, Virginia, and West Virginia. English-speaking persons between the ages of 40 and 79 were eligible for inclusion if they reported no history of cancer in the prior year (except non-melanoma skin cancer). Approximately 85% of participants were recruited in-person from one of 71 participating Community Health Centers (CHCs), which provide health care to low-income and under-insured individuals; the remainder were recruited from the general population by mail. CHC-recruited participants completed an in-person structured interview, while participants from the general population answered the same questions using a self-administered questionnaire.

Of the 34,284 men enrolled in the SCCS, we excluded those with a history of prostate cancer prior to baseline (n=598), as well as those missing information on statin use (n=1,619), leaving 32,091 men, 67% of whom were non-Hispanic black. All study participants provided written informed consent, and the study was approved by the Institutional Review Boards of Vanderbilt University, Meharry Medical College, and the Harvard School of Public Health.

Exposure assessment

Statin use was ascertained by a series of questions about history of high cholesterol and current use of cholesterol-lowering medications. Participants were first asked if they had ever been diagnosed with high cholesterol; respondents answering 'yes' were then queried on whether they were currently taking medication to lower their cholesterol, and if so, they were asked to list the specific cholesterol-lowering drug(s) currently used. From this information, participants were then classified as statin users or non-users at baseline. Participants taking Caduet for high blood pressure were also classified as statin users, as this drug contains a statin (n=7).

To better parse apart statin use from history of high cholesterol, statin use was alternatively defined as a three-level variable defined as follows: no history of high cholesterol, history of high cholesterol and statin use, and untreated high cholesterol (history of high cholesterol without statin use). Analyses of this three-level variable further exclude individuals using non-statin cholesterol lowering medications (n=476).

Outcome ascertainment

Prostate cancer cases were identified by linkage to state cancer registries in the 12 states of SCCS enrollment (98.1%, n=559 cases) and by linkage to the National Death Index, which identified deaths due to prostate cancer for a small number of cases not reported by these cancer registries (1.9%, n=11 cases). Cases thus included 570 incident, invasive cancers of the prostate diagnosed between study enrollment (baseline) and December 31, 2010 over an average of 5.2 years of follow-up. Of the 570 cases, 324 were low-grade (defined by Gleason score<7 or Gleason pattern 3+4), 107 were high-grade (defined by Gleason score>7 or Gleason pattern 4+3), [35] and 139 had no registry-reported Gleason score.

Statistical analysis

Cox proportional hazards models were used to estimate hazard ratios (HRs) and corresponding 95% confidence intervals (95% CIs) between statins and prostate cancer risk,

with age used as the time metric of analysis. Person-time was accrued for each participant from their date of study enrollment until the earliest of the following: date diagnosed with prostate cancer, date of death, or December 31, 2010. For the 11 cases of prostate cancer identified only through the National Death Index, date of death was used as a surrogate for date of diagnosis. Baseline statin use was modeled as a binary yes/no variable. Additional analyses were conducted with statin use alternatively defined as a 3-level variable (no high cholesterol, high cholesterol with statin use, and untreated high cholesterol).

Confounders were selected in a two-step process. We first selected a core set of confounders for inclusion in all fully-adjusted models, including: age (time metric of analysis), race/ethnicity (categorical: non-Hispanic black, non-Hispanic white, other), enrollment source (CHC versus general population), family history of prostate cancer (categorical: no first degree relatives, 1 first degree relatives, missing), history of high cholesterol (no/yes), as well as the following factors associated with access to care/receipt of screening: annual household income (categorical: <\$15,000, \$15,000- <\$25,000, \$25,000- <\$50,000, \$50,000+), health insurance coverage (no/yes), history of PSA screening (categorical: never, screened in the last 2 years, more than 2 years since last screening), history of digital rectal exam (DRE; categorical: never, screened in the last 2 years, more than 2 years since last screening), and time since last visit to a doctor (categorical: 3 months, >3- 12 months, >12 months). Family history was the only covariate coded using a missing indicator because >10% were missing this variable. Next, other factors potentially associated with both statins and prostate cancer were considered for inclusion. These factors included marital status, educational attainment, body mass index, height, history of diabetes, history of cardiovascular disease, regular use of low-dose aspirin, regular aspirin, or other non-steroidal anti-inflammatory drugs, supplemental calcium use, physical activity, alcohol consumption, smoking, and various dietary exposures (fried foods, dairy, lycopene, calcium, and total energy intake). When added to the core model, none of these variables changed the main effect estimate by > 10% and were not included in the final model.

We evaluated associations separately for high-grade and low-grade cancer using the Fine and Gray competing risks model.[36] Analyses were also stratified by history of PSA screening at baseline (never/ever) and race/ethnicity (non-Hispanic black/non-Hispanic white), with the “p-interaction” corresponding to a Wald test for a given interaction term(s). We have confirmed that Cox models meet the proportional hazards assumption. All analyses were conducted using Stata (version 12, College Station, TX).

Results

Of the 32,091 men included in this study, 570 were diagnosed with prostate cancer over 167,518 person-years of follow-up, with an average age of diagnosis of 62 years. Fourteen percent of study participants (n=4,503) reported current use of statin medications at baseline, with 10% of non-Hispanic black men and 22% of non-Hispanic white men reporting use of statins. As compared to non-users, statin users tended to be older and were more likely to be obese, insured, have a higher household income, and to have recently seen a doctor (Table 1). Statin users were also more likely to received PSA screening in the past two years (66% versus 37% of non-users). Similarly, statin users were more likely than non-users to report

receipt of a DRE in the two years prior to baseline (58% versus 37%, respectively). Associations between covariates and statin use were generally stronger among non-Hispanic black men than among non-Hispanic white men, especially for factors such as household income, screening, and BMI (Supplemental Table 1). For example, severely obese non-Hispanic black men were 4.81 times as likely to report use of statins at baseline as underweight/normal weight black men, while severely obese non-Hispanic white men were 2.50 times as likely as their underweight/normal weight counterparts to report use of statins at baseline.

In models adjusted for only age and race/ethnicity, statin use was not associated with risk of prostate cancer (HR:0.98; 95% CI:0.79-1.22) (Table 2), and this association remained null with further adjustment for history of PSA screening (HR:0.94; 95% CI:0.75-1.18; results not shown in tables). Adjusting for additional potential confounders, the HR fell to 0.86 (95% CI:0.63-1.18), although the effect estimate did not reach statistical significance. The association between baseline statin use and prostate cancer was stronger for high-grade cancer (HR:0.62; 95% CI:0.30-1.28) than low-grade cancer (HR:0.98; 95% CI:0.65-1.48).

Compared to men who were not diagnosed with prostate cancer during follow-up, prostate cancer cases were more likely to have ever received PSA screening before baseline: 69% of cases vs. 48% of non-cases. To better understand the influence of screening on the association between statin use and prostate cancer, results were stratified by history of PSA screening, with no difference in association observed (p-interaction:0.65; data not shown in tables). Specifically, among men with no history of PSA screening prior to baseline, a HR of 0.76 was observed for the association between statin use and prostate cancer risk (95% CI: 0.41-1.41), while a HR of 0.88 was observed among men with a history of PSA screening (95% CI:0.64-1.22).

The association between statin use and prostate cancer did not significantly differ by race/ethnicity (p-interaction:0.41), with a HR of 0.81 observed among non-Hispanic black men (95% CI:0.56-1.17) and a HR of 1.00 observed among non-Hispanic white men (95% CI: 0.64-1.57) (Table 3). For high-grade tumors, a HR of 0.65 (95% CI:0.29-1.44) was observed among non-Hispanic black men and a HR of 0.56 (95% CI:0.17-1.83) was observed among non-Hispanic white men (p-interaction: 0.81). With regard to low-grade cancers, a HR of 0.82 was observed among black men (95% CI:0.49-1.35) as compared to a HR of 1.35 (HR: 0.76-2.42) among non-Hispanic white men (p-interaction:0.13).

We conducted additional analyses using a 3-level variable to better parse apart the effect of statin use from history of high cholesterol (Tables 2 and 3). As compared to persons without a history of high cholesterol, use of statins was associated with 16% lower risk of prostate cancer (HR:0.84; 95% CI:0.65-1.07), while high cholesterol in the absence of statin use was not associated with prostate cancer risk (HR:1.01; 95% CI:0.78-1.32). A similar pattern was observed for low-grade cancers. However, for high-grade prostate cancer, the pattern differed: as compared to persons with no history of high cholesterol, persons reporting history of high cholesterol and statin use experienced a 24% reduced risk of high-grade prostate cancer (HR:0.76; 95% CI:0.41-1.40), while high cholesterol in the absence of statin

use associated with a 25% increased risk of high-grade prostate cancer (HR:1.25; 95% CI: 0.70-2.23).

The association between statin use and overall prostate cancer did not materially change after accounting for clustering of participants based on enrollment site (data not shown), or when the first year of follow-up was excluded (data not shown). Lastly, analyses excluding the 11 cases identified by the National Death Index did not materially change the observed association between statin use and prostate cancer (data not shown).

Discussion

In this large prospective cohort study of men living in the southeastern United States, statin use was associated with a non-significant 14% lower risk of prostate cancer overall, and results were suggestive of a stronger inverse association for high-grade cancer. The association between statin use and prostate cancer was comparable between non-Hispanic white men and non-Hispanic black men, especially with regard to high-grade prostate cancer.

Although our findings were not statistically significant, the main effect estimate (HR:0.86) aligns with a recent meta-analysis of 15 cohort studies and 12 case-control studies, which reported a summary risk ratio (RR) of 0.93 (95% CI:0.87-0.99) for the association between statin use and prostate cancer.[18] An earlier meta-analysis of 19 studies, including 6 randomized controlled trials (RCTs), 6 cohort studies, and 7 case-control studies, observed an overall pooled RR of 0.95 (95% CI:0.73-1.23), with no indication of association among the RCTs (RR: 1.06;95% CI:0.93-1.20).[30] It should be noted that there was significant heterogeneity in both of these meta-analyses, and it is possible that the heterogeneity stemmed from differences in the degree to which results were influenced by cancer screening practices. To address this concern in our analyses, we carefully adjusted for past screening practices, and also stratified by history of PSA screening, with no strong differences observed by history of PSA screening. Others have exploited the built-in homogeneity of screening practices within trials to evaluate the association between statin use and prostate cancer independently of screening differences, and these studies have yielded mixed results.[15] [23, 24] While two of these trials, the Prostate Cancer Prevention Trial (PCPT) and the REDUCE study, did not observe an inverse association between statin use and overall prostate cancer risk,[23, 24] a significant inverse association (HR:0.75; 95% CI:0.63-0.89) was observed between statin use and prostate cancer in a Finnish screening cohort.[15] However, it should be noted that study authors also observed a protective association between *non-statin* cholesterol-lowering medications (HR:0.62; 95%:0.28-1.38), indicating that perhaps it is the control of cholesterol, rather than another preventive property of the statins, which is acting to reduce prostate cancer risk. In our study, we were unable to evaluate the association between non-statin cholesterol-lowering medications and prostate cancer, given the small number of persons taking these drugs. Even so, comparison across these studies is hindered by differences in eligibility criteria regarding baseline health and PSA levels, screening intervals, and mode of prostate cancer detection.

To further address concern about detection bias, we examined associations separately for high-grade and low-grade cancers, as we hypothesized that high-grade cancers may be less prone to bias by screening practices. As expected, we detected a protective association for high-grade cancers and a null association for low-grade cancers, although neither reached statistical significance. Our results regarding high-grade cancers support a growing body of literature suggesting that the association between statin use and prostate cancer may be strongest for advanced or lethal prostate cancers. When the aforementioned meta-analyses of statin use and prostate cancer were restricted to the studies which evaluated advanced prostate cancer (defined mostly as stage T3/T4 cancer), the summary RRs similarly strengthened (RR:0.80; 95% CI:0.70-0.90;[18] RR:0.77; 95% CI:0.64-0.93).[30] Since the time of the most recent meta-analysis in 2012, additional studies have provided further support for an inverse association between use of statins and advanced prostate cancer, as well as cancer mortality after diagnosis.[37-41] In notable contrast, however, a modest *positive* association was observed between statin use and high-grade prostate cancer, as defined by Gleason score 7-10 (HR:1.27; 95% CI:0.85-1.90) in the PCPT,[24] a trial in which all men had low PSA at baseline, had been previously biopsied and were found to be without prostate cancer, and received annual PSA screening and DRE. In a secondary analysis of men in the REDUCE trial, in which all men had a negative biopsy at baseline and elevated PSA and received PSA-independent biopsies, no evidence of association between statin use and high-grade prostate cancer was observed (OR:1.11; 95% CI: 0.85-1.45).[23] While these results suggest that a protective association does not exist even for high-grade prostate cancer independent of screening and regardless of baseline PSA, it should be noted that the generalizability of the PCPT and REDUCE trials is unclear.

In order to better understand the relationship between statin use and prostate cancer risk, we disaggregated non-statin users into two groups: those without history of high cholesterol and those with high cholesterol in the absence of statin use. In this secondary analysis, we observed no association between ‘untreated’ high cholesterol and overall prostate cancer risk. However, when examining the association between our 3-level variable and high-grade prostate cancer, we observed statin use, relative to no history of high cholesterol, to be modestly inversely associated with high-grade prostate cancer and a modest positive association between untreated high cholesterol and high-grade prostate cancer. As such an association was not observed for overall prostate cancer, these results suggest that the stronger association between binary statin use and high-grade (versus overall) prostate cancer may be, in part, driven by the positive association between untreated high cholesterol and high-grade prostate cancer. This is further supported by prior work showing that high cholesterol is associated with increased risk of high-grade prostate cancer, but not overall prostate cancer.[42-44]

To our knowledge, no prior studies of statin use and prostate cancer have evaluated whether the association varies by race/ethnicity. Here, we observed no significant effect modification by race/ethnicity, although our results did suggest a 19% reduced risk among non-Hispanic black men and no association among non-Hispanic whites. As black men generally experience a higher burden of aggressive disease,[32] it is possible that the race-stratified findings reflect differences in association by aggressiveness of disease. To address this

concern, we examined the association between statin use and high-grade prostate cancer by race/ethnicity, and noted that the association between statin use and high-grade prostate cancer among non-Hispanic whites (HR:0.56) is similar to that of non-Hispanic black men (HR:0.65). With regard to low-grade prostate cancer, there was some suggestion of different associations among non-Hispanic blacks (HR:0.82) and non-Hispanic whites (HR:1.35), although this difference was not significant. The low-grade cancer group is likely enriched with screen-detected indolent cancers, and any difference between racial/ethnic groups for this outcome likely reflects residual screening differences between racial/ethnic groups. Our results therefore do not support an interaction between statins and race/ethnicity, especially with regard to the more clinically meaningful high-grade cancers. Even so, results regarding interaction with race/ethnicity should be interpreted conservatively, given the limited number of non-Hispanic white men in our study. Further, although the relative association is comparable across racial/ethnic groups, it is important to consider that the population-level implications differ, as non-Hispanic black men were half as likely to be taking a statin as non-Hispanic white men.

An important limitation of our study is that we did not have information on participants' history of statin use prior to study enrollment, nor did we have information on total duration of statin use. With an average of 5.2 years between the date of baseline exposure assessment and censoring date, our statin variable is capturing exposure relatively soon before diagnosis. While statin use is assumed to be persistent throughout follow-up, it is possible that our statin variable may not represent exposure in the most etiologically relevant time period. However, such non-differential measurement error would be expected to attenuate results toward the null. Regarding exposure assessment, it should also be noted that we were underpowered to evaluate differences in association by the type of statin used (lipophilic versus hydrophilic). While it may have been informative to evaluate associations between non-statin cholesterol-lowering medications and prostate cancer, we were underpowered to do so in this study, given the small number of men using non-statin cholesterol-lowering medications. Further, as prostate cancer has high survival, we were not powered to define our outcome by lethal prostate cancer.[25] However, we were able to evaluate the association between statin use and prostate cancer by tumor grade,[24], [45, 46] but even so, high-grade cases still contain localized cancers. Lastly, while we made an effort to control for past screening practices and address concerns about detection bias, it is still possible that our results are subject to bias induced by screening practices.

This study also has several strengths. For the first time, we were able to evaluate the statin-prostate cancer association among non-Hispanic black men, and we were able to explore whether this association varies across racial/ethnic groups. Although the number of cases among white men in our study was relatively small, we detected no strong signal of a differential association by race/ethnicity. Furthermore, we were able to address this question in a predominantly low-income population in which the racial/ethnic groups were more similar with respect to socioeconomic status and screening than might otherwise be observed, reducing some concern about residual confounding by socioeconomic status when comparing results across strata. Also, given the large number of persons with untreated high cholesterol (12% of the cohort), we were able to disaggregate users into a group which was untreated and a group which did not have a history of high cholesterol. We were also able to

account for screening history and other factors which might reflect access to care (health insurance status, socioeconomic status, and time since last doctor visit).

Conclusion

In conclusion, our study suggests no strong association between statin use and prostate cancer risk, and further suggests that if a modest protective effect does exist, it may be restricted to high-grade tumors. This association does not appear to vary by race/ethnicity, especially with regard to the more clinically-relevant high-grade tumors. Given the high prevalence of statin use and burden of prostate cancer in the population, even a modest protective association, if one exists, could have public health importance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Distribution of selected characteristics of the study population, by baseline statin use
(n=32,091)^a

	Statin Non-users (n=27,558) n (%)	Statin Users (n=4,503) n (%)	Age-Adjusted Prevalence Ratio for Statin Use (95% CI)
Age at Baseline (yrs) ^b			
40-<45	7,072 (25.6)	397 (8.82)	1.00 (Ref)
45-<50	7,014 (25.4)	637 (14.2)	1.57 (1.39, 1.77)
50-<55	5,698 (20.7)	845 (18.8)	2.43 (2.17, 2.72)
55-<60	3,747 (13.6)	911 (20.2)	3.68 (3.29, 4.12)
60-<65	2,212 (8.02)	826 (18.3)	5.12 (4.57, 5.72)
65+	1,845 (6.69)	887 (19.7)	6.11 (5.47, 6.82)
Race/Ethnicity			
Non-Hispanic black	19,264 (70.3)	2,215 (49.7)	1.00 (Ref)
Non-Hispanic white	7,231 (26.4)	2,017 (45.3)	1.70 (1.61, 1.80)
Other	923 (3.37)	221 (4.96)	1.70 (1.50, 1.91)
Enrollment Source			
Community Health Center	23,612 (85.6)	3,057 (67.9)	1.00 (Ref)
General Population	3,976 (14.4)	1,446 (32.1)	1.65 (1.56, 1.75)
Household Income			
<\$15,000	15,238 (55.9)	1,795 (40.6)	1.00 (Ref)
\$15,000- <25,000	5,535 (20.3)	837 (18.9)	1.23 (1.15, 1.33)
\$25,000- <50,000	3,694 (13.6)	819 (18.5)	1.52 (1.41, 1.63)
\$50,000 +	2,794 (10.3)	976 (22.1)	1.87 (1.74, 2.00)
Insurance Coverage			
No	12,983 (47.2)	961 (21.4)	1.00 (Ref)
Yes	14,508 (52.8)	3,522 (78.6)	2.04 (1.90, 2.19)
Time Since Last Doctor Visit			
3 months	16,102 (60.2)	3,661 (85.0)	1.00 (Ref)
>3 - 12 months	6,754 (25.3)	577 (13.4)	0.49 (0.45, 0.53)
>1 year	3,891 (14.6)	67 (1.56)	0.12 (0.09, 0.15)
Prostate-Specific Antigen Screening			
Never	14,455 (55.9)	1,141 (27.5)	1.00 (Ref)
Ever, 2 Years Since Last Screen	9,614 (37.2)	2,751 (66.3)	2.07 (1.93, 2.22)
Ever, >2 Years Since Last Screen	1,798 (6.95)	260 (6.26)	1.33 (1.17, 1.51)
Digital Rectal Exam Screening			
Never	11,981 (44.1)	1,096 (24.8)	1.00 (Ref)
Ever, 2 Years Since Last Screen	10,159 (37.4)	2,581 (58.3)	1.66 (1.55, 1.77)
Ever, >2 Years Since Last Screen	5,014 (18.5)	750 (16.9)	1.24 (1.14, 1.35)
Family History Prostate Cancer (No. of 1 st degree relatives)			
0	22,993 (83.3)	3,571 (79.3)	1.00 (Ref)
1+	1,362 (4.94)	320 (7.11)	1.21 (1.09, 1.34)
Missing	3,233 (11.7)	612 (13.6)	1.05 (0.98, 1.14)

	Statin Non-users (n=27,558) n (%)	Statin Users (n=4,503) n (%)	Age-Adjusted Prevalence Ratio for Statin Use (95% CI)
Body Mass Index (kg/m ²)			
Underweight/Normal Weight (<25)	10,235 (37.4)	692 (15.5)	1.00 (Ref)
Overweight (25- <30)	9,685 (35.4)	1,669 (37.5)	2.13 (1.97, 2.32)
Obese (30- <35)	4,721 (17.3)	1,206 (27.1)	2.91 (2.67, 3.18)
Severely Obese (35+)	2,722 (9.95)	888 (19.9)	3.74 (3.41, 4.09)

^aNumber of persons missing each variable is as follows: race/ethnicity (n=220); household income (n=403); insurance coverage (n=117); time since last doctor visit (n=1039); prostate specific antigen screening (n=2072); digital rectal exam (n=510); body mass index (n=273)

^bUnadjusted prevalence ratio

Table 2
Association between baseline statin use and prostate cancer risk

	Cohort N=32,091	Cases N=570	Age and Race Adjusted		Fully Adjusted ^a	
	N (%)	N (%)	HR	95% CI	HR	95% CI
ALL CASES						
Statin Use (2-level)						
No Use	27,588 (86.0)	455 (79.8)	1.00	Ref	1.00	Ref
Use	4,503 (14.0)	115 (20.2)	0.98	0.79, 1.22	0.86	0.63, 1.18
Statin Use (3-level) ^b						
No High Cholesterol	23,391 (74.0)	376 (67.3)	1.00	Ref	1.00	Ref
High Cholesterol, Statin Use	4,306 (13.6)	108 (19.3)	0.97	0.77, 1.21	0.84	0.65, 1.07
Untreated High Cholesterol	3,918 (12.4)	75 (13.4)	1.07	0.83, 1.37	1.01	0.78, 1.32
HIGH-GRADE TUMORS						
Statin Use (2-level)						
No Use	27,475 (86.0)	87 (81.3)	1.00	Ref	1.00	Ref
Use	4,477 (14.0)	20 (18.7)	0.89	0.54, 1.48	0.62	0.30, 1.28
Statin Use (3-level) ^b						
No High Cholesterol	23,295 (74.0)	71 (67.6)	1.00	Ref	1.00	Ref
High Cholesterol, Statin Use	4,282 (13.6)	19 (18.1)	0.91	0.53, 1.53	0.76	0.41, 1.40
Untreated High Cholesterol	3,903 (12.4)	15 (14.3)	1.15	0.66, 2.01	1.25	0.70, 2.23
LOW-GRADE TUMORS						
Statin Use (2-level)						
No Use	27,475 (86.0)	255 (78.7)	1.00	Ref	1.00	Ref
Use	4,477 (14.0)	69 (21.3)	1.13	0.86, 1.48	0.98	0.65, 1.48
Statin Use (3-level) ^b						
No High Cholesterol	23,295 (74.0)	209 (65.5)	1.00	Ref	1.00	Ref
High Cholesterol, Statin Use	4,282 (13.6)	65 (20.4)	1.12	0.84, 1.49	0.90	0.66, 1.25
Untreated High Cholesterol	3,903 (12.4)	45 (14.1)	1.16	0.83, 1.61	1.00	0.70, 1.43

ABBREVIATIONS: 95% CI (95% Confidence Interval); HR (hazard ratio)

^a Adjusted for age, race/ethnicity, enrollment source, household income, insurance coverage, time since last doctor visit, history of prostate specific-antigen screening, history of digital rectal exam, history of high cholesterol, and family history of prostate cancer.

^b Excludes those taking other cholesterol-lowering medications, leaving 31,615 persons, among whom 559 cases occurred

Table 3
Association between baseline statin use and prostate cancer risk, by race/ethnicity

	Non-Hispanic Black				Non-Hispanic White			
	Cohort N (%)	Cases N (%)	Fully Adjusted ^a		Cohort N (%)	Cases N (%)	Fully Adjusted ^a	
			HR	95% CI			HR	95% CI
ALL CASES								
Statin Use (2-level)								
No Use	19,264 (89.7)	357 (84.8)	1.00	Ref	7,231 (78.2)	86 (65.7)	1.00	Ref
Use	2,215 (10.3)	64 (15.2)	0.81	0.56, 1.17	2,017 (21.8)	45 (34.4)	1.00	0.64, 1.57
Statin Use (3-level) ^b								
No High Cholesterol	16,746 (78.5)	298 (71.1)	1.00	Ref	5,761 (64.4)	70 (56.5)	1.00	Ref
High Cholesterol, Statin Use	2,181 (10.2)	64 (15.3)	0.81	0.60, 1.09	1,870 (20.9)	40 (32.3)	0.89	0.57, 1.38
Untreated High Cholesterol	2,418 (11.3)	57 (13.6)	1.05	0.78, 1.42	1,311 (14.7)	14 (11.3)	0.76	0.41, 1.41
HIGH-GRADE TUMORS								
Statin Use (2-level)								
No Use	19,182 (89.7)	72 (84.7)	1.00	Ref	7,203 (78.2)	14 (70.0)	1.00	Ref
Use	2,200 (10.3)	13 (15.3)	0.65	0.29, 1.44	2,006 (21.8)	6 (30.0)	0.56	0.17, 1.83
LOW-GRADE TUMORS								
Statin Use (2-level)								
No Use	19,182 (89.7)	203 (84.9)	1.00	Ref	7,203 (78.2)	44 (61.1)	1.00	Ref
Use	2,200 (10.3)	36 (15.1)	0.82	0.49, 1.35	2,006 (21.8)	28 (38.9)	1.35	0.76, 2.42

ABBREVIATIONS: 95% CI (95% Confidence Interval); HR (hazard ratio)

^a Adjusted for age, race/ethnicity, enrollment source, household income, insurance coverage, time since last doctor visit, history of prostate specific-antigen screening, history of digital rectal exam, history of high cholesterol, and family history of prostate cancer.

^b Excludes those taking other cholesterol-lowering medications, leaving 30,287 non-Hispanic black and non-Hispanic white men, among whom 543 cases occurred