Original Article

Ultraviolet Index and Racial Differences in Prostate Cancer Incidence and Mortality

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BACKGROUND: Studies suggest that low levels of vitamin D may be associated with prostate cancer, and darker skin reduces the body's ability to generate vitamin D from sunshine. The impact of sunshine on racial disparities in prostate cancer incidence and mortality is unknown. **METHODS:** Using the Surveillance, Epidemiology, and End Results program database, the authors calculated age-adjusted prostate cancer incidence rates among black and white men aged ≥45 years by race and county between 2000 and 2009 (N = 906,381 men). Similarly, county-level prostate cancer mortality rates were calculated from the National Vital Statistics System (N = 288,874). These data were linked with the average monthly solar ultraviolet (UV) radiation index by county and data regarding health, wellness, and demographics. Multivariable regression analysis was used to assess whether increases in the UV index (in deciles) moderated the association between black race and the incidence and mortality of prostate cancer. **RESULTS:** Compared with counties in the lowest UV index decile, prostate cancer incidence rates for white and black men were lower in counties with a higher UV index (all $Ps \leq .0.051$). Incidence rates were higher for black men versus white men, but the difference by race was less for counties in the fourth to fifth UV index deciles versus those in the first decile ($Ps \leq 0.02$). Mortality rates also were found to decrease with increasing UV index for white men ($Ps \leq 0.003$), but increase for black men, and an unexplained increase in racial differences in mortality rates was observed with an increasing UV index. **CONCLUSIONS:** Racial disparities in the incidence of prostate cancer were larger in some areas with less sunshine. Additional research should confirm the findings of the current study and assess whether optimizing vitamin D levels among black men can reduce disparities. ***Cancer*** **2013;119:3195-203.** © *2013 American Cancer Society.*

KEYWORDS: prostate cancer; disparities; vitamins; survival.

INTRODUCTION

Prostate cancer is the cancer with the highest incidence in the United States, with >241,000 new diagnoses occurring in 2012,[1] and is the second most fatal among men.[2] Prostate cancer also demonstrates striking racial and ethnic disparities. In 2009, black men had an annual death rate from prostate cancer that was 2.5 times that of whites,[2] translating into an estimated 61,028 lives lost between 2000 and 2009.[2,3]

A growing literature has considered whether vitamin D may reduce cancer mortality[4-9] by promoting cell differentiation and apoptosis,[10,11] and inhibiting metastasis[12] and angiogenesis.[13] For the majority of individuals, approximately 90% of vitamin D is estimated to derive from sunshine,[14] with the liver converting solar ultraviolet (UV) radiation into 25-hydroxyvitamin D_3 ($25(OH)D_3$), the form of vitamin D typically measured in blood serum. $25(OH)D_3$ has a reported half-life of 15 days,[15] and therefore cannot be stored from summer (when solar radiation is highest) to winter. Indeed, studies suggest higher cancer mortality rates for patients diagnosed in winter[16,17] and at northern latitudes.[18,19] Some studies focused on prostate cancer have suggested a J-shaped or U-shaped association between vitamin D and the incidence of prostate cancer,[18-21] particularly in younger men,[20] although others have found no significant relationship.[22-24] There are conflicting results from randomized clinical trials examining vitamin D (calcitriol) supplementation, with one trial suggesting a positive association with survival[25] and another trial that was discontinued early because of an inverse association.[26]

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Black individuals synthesize less vitamin D per unit of sun exposure than white individuals, because a darker complexion acts as a natural sunscreen.[27] The Institute of Medicine estimates that 54% of non-Hispanic blacks have very low levels of vitamin D (25(OH)D<16 ng/mL), versus 27% of Mexican Americans and 11% of non-Hispanic whites.[28] To the best of our knowledge, the possible link between sun exposure and racial differences in prostate cancer incidence and mortality has not been thoroughly investigated.

In the current study, we assessed whether the racial disparity noted in prostate cancer incidence and mortality was greater in US regions with more UV radiation from sunshine, in which whites benefited disproportionately from solar absorption of vitamin D.

MATERIALS AND METHODS

Data and Patients

We obtained data on UV irradiance from the National Aeronautics and Space Administration (NASA) in increments of 1° latitude and 1.25° longitude throughout the United States from 1978 through 2005.[29,30] To understand prostate cancer incidence, we used data from the Surveillance, Epidemiology, and End Results program, which provides population-based cancer registry data from areas covering 28% of the US population.[31,32] We identified 773,964 white men and 132,417 black men aged ≥45 years with a first primary diagnosis of prostate cancer made between 2000 and 2009. Individuals were white or black and not diagnosed by autopsy or death certificate.

For data regarding prostate cancer mortality, we used the National Vital Statistics System, which releases cause of death nationwide by county.[33] We identified 239,689 white men and 49,185 black men aged ≥45 years who died of prostate cancer between 2000 and 2009.[32]

We obtained county-level data concerning health, wellness, and sociodemographic factors from the US Census Bureau[34] and the Behavioral Risk Factors Surveillance System.[35]

UV Index

Because the UV index is seasonal, we first investigated the month in which racial disparities in the ability to convert sunshine into vitamin D were the largest. Using NASA data, we characterized the average noontime UV index in each calendar month for the coordinates of the centroid of each man's county.[36,37] The UV index measures UV radiation reaching the earth's surface; in the continental United States, it ranges from 0 to 5 in January to 4 to 12 in July.[36] The index is a function of latitude, time, solar irradiation, elevation, ozone, and cloud cover.[36,37] Established formulae allow for the conversion of the index into the number of minutes outdoors required to sunburn and to synthesize various amounts of vitamin D, based on an individual's skin tone.[36,38]

We next estimated the number of minutes of sun exposure in each calendar month for individuals of the lightest and darkest skin types to synthesize 600 international units (IU) of vitamin D, the recommended dietary allowance (RDA) for adults aged ≤70 years.[28,38] We assumed a relationship between average maximum daily temperature and body parts exposed to sunlight (≥75°F: face, neck, hands, and arms exposed; 60°F-74°F: face, neck, hands, and lower arms exposed; 30°F-59°F: face, neck, and hands exposed; 15°F-29°F: face and neck exposed; and ≤14°F: face exposed).[39,40] The month with the largest racial differences noted in sun exposure to obtain the RDA of vitamin D was considered the most relevant for further analysis with prostate cancer incidence and mortality. For example, in January, Phoenix, Arizona, had an average noontime UV index of 3.2,[29] with an average maximum temperature of 68°F.[39] Individuals of the lightest and darkest skin tones were estimated to synthesize 600 IU of vitamin D in 27 minutes and 137 minutes, respectively,[29,36-38] for a racial difference of 110 minutes.

Prostate Cancer Incidence and Mortality

For each county, we calculated the prostate cancer incidence by race and stage of disease (any, local/regional, and metastatic). The numerator was the number of men aged ≥45 years diagnosed with prostate cancer and the denominator was the number of men aged ≥45 years residing in each county, in person-years. Similarly, from the National Vital Statistics System, we calculated prostate cancer mortality for men aged ≥45 years by race. In counties with <10 deaths, the Vital Statistics system suppressed data, and therefore we used the average mortality rate in geographically adjacent counties, weighted by the at-risk population of each race. If data were suppressed for all adjacent counties, we assumed zero mortality. Rates were age-adjusted using the 2000 US standard population.

Control Variables

For each county, we documented the median income by race; the number of physicians (general practice and urologists) and short-term general hospital beds, each nonfederal per 100,000 population; whether the county included a federally designated Health Professional Shortage Area in primary care; less urban or rural geography; and census division.

TABLE 1. Summary Statistics for Prostate Cancer Incidence and Mortality Cohorts, Males Aged ≥45 Years: 2000 to 2009

Variable	Incidence Cohort			Mortality Cohort		
	White (N=773,964)	Black (N=132,417)	P^a	White (N=239,689)	Black (N=49,185)	P^a
No. of counties	336	336		2203	2203	
Age-adjusted incidence/100,000 men	398.3	646.6	<.001	—	—	
Age-adjusted mortality/100,000 men	—	—		68.2	164.3	<.001
Median county-level income	$63,922	$39,555	<.001	$57,724	$36,571	<.001
Health and wellness						
Males aged ≥40 y who reported undergoing a PSA test within the prior 2 y	53.5%	55.0%	.29	55.4%	56.4%	.12
Population aged ≥18 y who smoked	23.0%	25.3%	.037	25.5%	24.8%	.22
BMI, kg/m^2	26.3	27.9	<.001	26.4	28.1	<.001
Daily servings of fruits and vegetables	2.2	2.0	<.001	2.2	1.9	<.001
Access to physicians, county-level						
General practice physicians/100,000 persons	28.0	24.6	.037	28.9	26.3	.004
Urologists/100,000 persons	3.3	3.8	.14	3.4	4.0	.003
Short-term hospital beds/100,000 persons	232.3	275.6	.015	271.2	336.4	<.001
Counties federally designated as a Health Professional Shortage Area	64.1%	67.3%	.74	60.5%	71.2%	.004
Geography, county-level						
Counties designated as less urban or rural	4.9%	3.6%	.30	8.7%	7.3%	.12
Census division						
New England	5.8%	3.9%	.044	5.8%	2.2%	.003
Middle Atlantic	12.6%	15.1%		14.6%	16.1%	
South Atlantic	3.2%	12.7%		19.1%	32.5%	
East North Central	5.4%	12.7%		16.1%	14.8%	
East South Central	6.2%	3.8%		5.9%	9.3%	
West North Central	3.7%	0.7%		6.3%	2.9%	
West South Central	5.1%	15.9%		10.6%	12.4%	
Mountain	5.5%	0.9%		6.6%	1.8%	
Pacific	52.6%	34.3%		14.9%	7.9%	

Abbreviations: BMI, body mass index; PSA, prostate-specific antigen.
[a] Determined using the chi-square or Student *t* test as appropriate; results were weighted by the at-risk population of each race and county.

From the Behavioral Risk Factors Surveillance System, we characterized by county and race the percentage of men aged ≥40 years who obtained a prostate-specific antigen (PSA) test within the prior 2 years (2001-2009), the percentage of individuals aged ≥18 years who smoked (1984-2009), average body mass index (1984-2009), and average daily servings of fruits and vegetables (annually from 1990-1993 and biannually for 1996-2002 and 2003-2009). If a variable had <20 observations for either race, across all years, we aggregated at the metropolitan statistical area (MSA; if there were ≥20 observations for each race across all years) or state levels. The majority of MSA-level and state-level aggregation occurred for counties in the sixth to seventh and ninth deciles of the January UV index. Results for alternate cutoffs were similar.

The current study was considered exempt by the Institutional Review Board of Harvard Medical School and did not meet criteria for human subjects review for the Institutional Review Board of New York University School of Medicine.

Statistical Analyses

We described each cohort and tested for racial differences using the Student *t* test or Pearson chi-square test, as appropriate (Shapiro-Wilk tests suggested the data were normally distributed). We used multivariate regressions to analyze the association between the UV index and prostate cancer incidence and mortality. The dependent variable was the log of countywide prostate cancer incidence or mortality for men aged ≥45 years between 2000 and 2009. Logs allowed us to consider results in relative terms; for example, a coefficient of −0.10 would suggest a 10% decline in incidence or mortality. Each county had 2 observations, 1 per race. To avoid potential bias that might be introduced by small denominators, we only included those counties with ≥20 at-risk men of each race. To reflect each county's relative importance in national data, observations were weighted by the at-risk population of each county and race. Herein, we report 2-sided significance tests at the 5% level.

We considered 3 key independent variables: the UV index, black versus white race, and the interaction

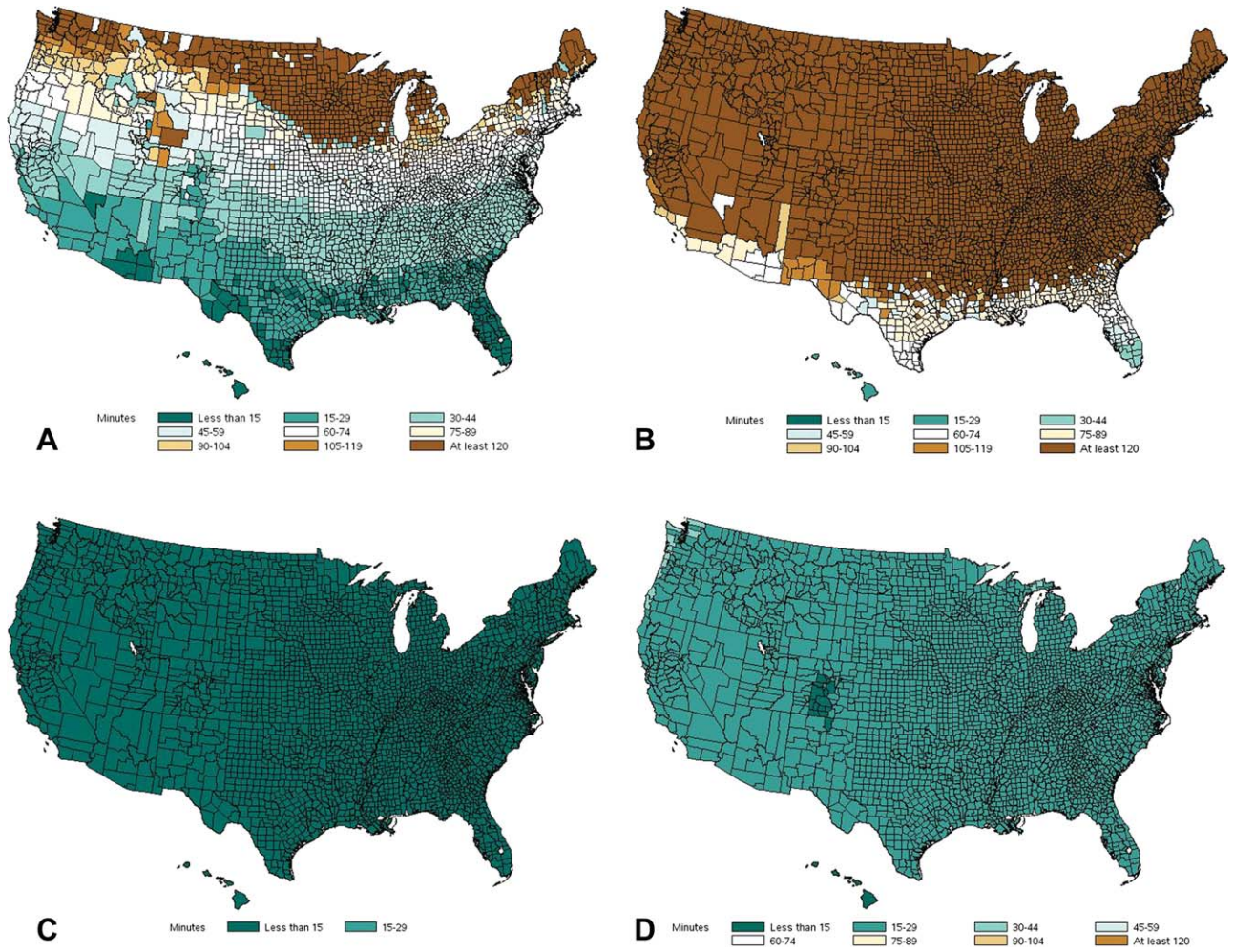

Figure 1. Estimated number of minutes required to synthesize 600 international units of vitamin D from sunlight is shown. Results are shown for noontime, assuming no sunscreen is used and a relationship between the average maximum daily temperature and sun exposure ($\geq$ 75°F: face, neck, hands, and arms exposed; 60°F-74°F: face, neck, hands, and lower arms exposed; 30°F-59°F: face, neck, and hands exposed; 15°F-29°F: face and neck exposed; and $\leq$14°F: face exposed). Results are shown for (A) white, fairest skin in January; (B) black, darkest skin in January; (C) white, fairest skin in July; and (D) black, darkest skin in July.

between black race and the UV index. Control variables were as described above. Analyses were repeated for each cancer stage; ages $\geq$55 years, $\geq$65 years, and 45 years-74 years; and the UV index specified in deciles, quintiles, quartiles, and continuous terms.

RESULTS

Table 1 shows summary statistics for the cohorts for both prostate cancer incidence and mortality. Age-adjusted incidence rates were higher for black men compared with white men (646.6 vs 398.3 per 100,000 men), as were mortality rates (164.3 vs 68.2 per 100,000 men). Black men more often resided in poorer counties with a higher average body mass index and fewer generalist physicians.

Figure 1 shows the estimated minutes required for individuals of the lightest and darkest skin tones to synthesize 600 IU of vitamin D from sunlight in the months of January and July. In January, the month with the lowest average UV index, fair-skinned white men (eg, red hair and blue eyes) required <45 minutes of sunlight exposure in areas as far north as Virginia and northern California (Fig. 1). Dark-skinned black men required $\geq$120 minutes of sunlight exposure in areas as far south as Georgia, Texas, and southern California (Fig. 1) and $\geq$120 minutes more than fair-skinned whites in areas as far south as Georgia, the Oklahoma/Texas border, and central California (data not shown). By contrast, in July, the month with the highest average UV index, both groups required <30 minutes in the vast majority of the United

TABLE 2. Adjusted Prostate Cancer Incidence and Mortality Per 100,000 Men Versus January UV Index Decile[a]

Dependent Variable (per 100,000 Men)[b]	Incidence	*P*	Mortality	*P*
January UV Index Decile				
1	Reference		Reference	
2	−9.5	.001	0.4	.75
3	−10.4	.005	−5.5	.08
4	−10.3	.001	−5.9	.001
5	−13.2	<.001	−5.3	.003
6	−16.0	<.001	−7.8	<.001
7	−22.3	<.001	−11.7	<.001
8	−22.4	<.001	−9.1	<.001
9	−18.9	<.001	−8.9	<.001
10	−23.4	<.001	−15.9	<.001
Black vs white race	60.3	<.001	48.3	<.001
Interaction of Black Race with January UV Index Decile				
1	Reference		Reference	
2	−2.2	.55	14.8	.23
3	0.4	.91	23.7	.020
4	−9.3	.016	26.8	.013
5	−9.3	.020	15.5	.14
6	6.4	.13	44.3	<.001
7	6.8	.38	47.1	<.001
8	0.6	.84	43.5	<.001
9	2.1	.61	33.7	<.001
10	−10.8	.06	39.6	<.001
Access to Health Care				
Males aged ≥40 y who reported undergoing a PSA test within the prior 2 y, %	0.3	.003	−0.2	.003
Population aged ≥18 y who smoked, %	−0.4	.001	−0.1	.19
BMI, kg/m^2	−2.5	.022	0.4	.68
Daily servings of fruits and vegetables	14.4	.038	−11.3	.042
Access to Physicians				
General practice physicians/100,000 persons	−0.2	.026	0.1	.007
Urologists/100,000 persons	0.0	.98	−0.2	.35
Federally designated Health Professional Shortage Area in primary care	−0.4	.74	2.4	.006
Short-term hospital beds/100,000 persons	0.0	.86	0.0	.44
Median income (natural log $ × 100)	0.1	.041	0.0	.15
Less urban or rural county	−1.7	.48	4.6	.001
Constant	546.2	<.001	411.9	<.001
R-squared	0.75		0.46	
F statistic	242.14		154.83	
No. of observations	672		4406	
No. of counties	336		2203	

Abbreviations: BMI, body mass index; PSA, prostate-specific antigen; UV, ultraviolet.
[a] For all stages of disease and age ≥45 years. Coefficients for census division are not shown. Models were repeated for white (versus black) race and the interaction of white race with January UV index decile. Standard errors were clustered by county.
[b] Unit: natural log × 100.

States (Fig. 1). Due to larger racial differences in vitamin D synthesis occurring in the winter, we focused on the January UV index for the remainder of our analysis.

Incidence

Table 2 and Figure 2 show adjusted prostate cancer incidence versus decile of the January UV index, categorized

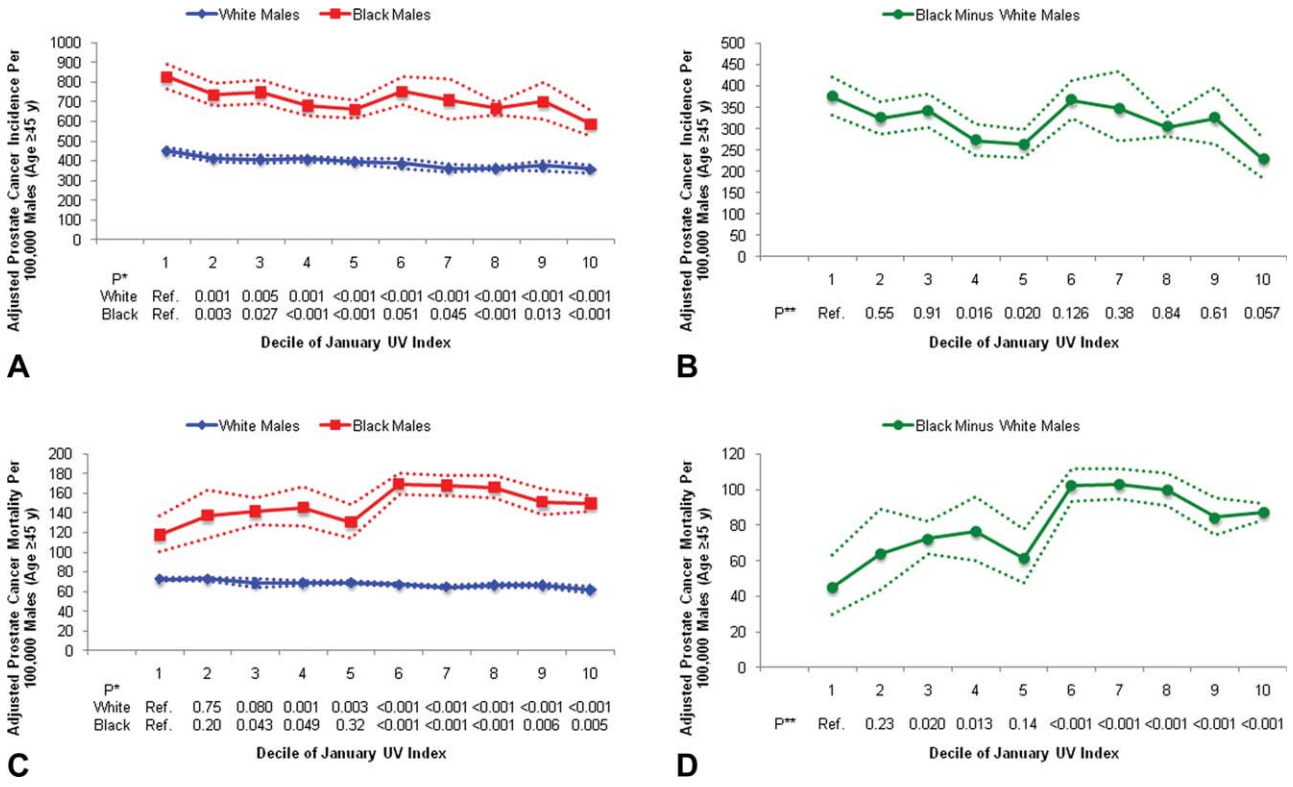

Figure 2. Adjusted prostate cancer incidence and mortality per 100,000 males versus January ultraviolet (UV) index decile are shown. This figure shows how prostate cancer incidence and mortality rates varied with the January UV index, adjusted for all variables shown in Table 1. Numeric coefficients for white males and the racial disparity (black minus white males) are shown in Table 2. Dotted lines denote 95% confidence intervals. (A) The adjusted incidence of prostate cancer is shown. (B) Racial differences in the adjusted incidence are shown. (C) Adjusted mortality of prostate cancer is shown. (D) Racial differences in the adjusted mortality are shown. Ref. indicates reference. *P values relative to decile 1. **P values for interaction term of UV index with black race, relative to decile 1.

from lowest (1st decile) (Washington State and Michigan) to highest (10th decile) (Louisiana, southern California, New Mexico, and Hawaii), calculated from the regression model. For white men, increases in the UV index were associated with lower prostate cancer incidence rates. Compared with the 1st decile, rates were 9.5% to 10.4% lower for counties in the 2nd to 4th deciles (primarily Connecticut, New Jersey, Iowa, Kentucky, and Utah), 13.2% to 16.0% lower for counties in the 5th to 6th deciles (primarily northern California and Georgia), and 18.9% to 23.4% lower for counties in the 7th to 10th deciles (central/southern California, Georgia, Louisiana, New Mexico, and Hawaii) (all $P \leq .005$) (Table 2) (Fig. 2A).

For black men, increases in the UV index were also associated with lower incidence rates (Fig. 2A). Compared with the 1st decile, rates were 11.7%, 10.0%, 19.6%, and 22.6% lower, respectively, for counties in the 2nd to 5th deciles of the UV index; 9.6% to 16.8% lower for counties in the 6th to 9th deciles; and 34.2% lower for counties in the 10th decile (all $P \leq .051$).

The racial disparity in prostate cancer incidence was significantly smaller for black men compared with white men living in counties in the 4th to 5th deciles of the UV index versus the 1st decile, with incidence rates being an additional 9.3% lower for black men than for white men in each decile (P for interaction of .016 and .020, respectively) (Table 2) (Fig. 2B). The racial disparity was not significantly different in the 6th to 10th deciles versus the 1st decile (P for interaction of .057-.84) (Table 2) (Fig. 2B). A Wald test of whether the coefficients on UV index deciles were jointly equal to 0 was rejected ($P < .001$), as was a Wald test regarding the interaction terms between black race and UV index deciles ($P = .002$).

When we repeated analyses examining prostate cancer incidence by stage of disease, the results for localized/regional tumors were similar (data not shown). The incidence of metastatic cancers did not vary significantly at higher UV index deciles, although the numbers of metastatic cancers in many counties were small (data not shown).

Mortality

For white men, increases in the UV index were associated with lower prostate cancer mortality rates. Compared with the 1st decile, mortality rates were 5.3% to 5.9% lower for counties in the 4th to 5th deciles ($P \leq .003$), and 7.8% to 15.9% lower for counties in the 6th to 10th deciles (all $P < .001$) (Table 2) (Fig. 2C). For black men, increases in the UV index were associated with higher prostate cancer mortality rates. Compared with the 1st decile, prostate cancer mortality rates were 18.2% to 36.5% higher for counties in the 3rd to 4th and 6th to 10th deciles ($P \leq .02$) (Fig. 2C). We rejected a Wald test for whether the coefficients on UV index deciles were jointly equal to 0 for black men ($P < .001$). The racial disparity in mortality rates was 23.7% to 48.3% greater in the 3rd to 4th and 6th to 10th deciles, compared with counties in the lowest decile (P for interaction of $\leq .02$) (Fig. 2D). Results for other age groups were similar but less often significant (data not shown).

For counties in which the National Vital Statistics System suppressed mortality rates, we repeated analyses after assigning a zero mortality rate. Results were similar but less significant (data not shown).

Sensitivity Analyses

For both incidence and mortality, our primary results were robust to changes in the age group (data not shown). Specifications of the UV index in quintiles, quartiles, and continuous terms yielded similar results (data not shown). The association was seasonal, with more negative coefficients on the UV index observed during the winter months (data not shown).

DISCUSSION

In the current study, we examined the association of prostate cancer incidence and mortality and corresponding racial disparities with the January UV index. We observed a decrease in prostate cancer incidence with increasing levels of the UV index. We also observed a reduction in the racial disparity in prostate cancer incidence in areas with moderately high UV indices compared with those with lower UV indices. Adjusted incidence rates in counties with more sunshine were lower for white men and black men compared with counties with less sunshine.

For black men, adjusted prostate cancer incidence rates declined with increasing levels of the UV index in 7 of the 10 deciles. Exceptions may be influenced by lack of county-level data in rural areas; 46% of health and wellness variables were aggregated at the MSA or state levels in the 6th to 7th and 9th deciles of the January UV index (predominately rural Georgia, Louisiana, and New Mexico) versus 18% in surrounding deciles. We also found a decline in black versus white disparities in prostate cancer incidence, with a reduction in the disparity noted in the 4th to 5th deciles versus the 1st decile, and nonsignificant declines in the 6th to 10th deciles of the UV index.

The results of the current study expand those of the previous literature in 3 ways. First, we addressed the potential association between vitamin D, as proxied by the UV index, and racial disparities in prostate cancer incidence and mortality. The previous literature has primarily considered white men only.[19-23] Our findings are consistent with other studies that suggest an inverse association between vitamin D (or UV index) and prostate cancer incidence[20,21] or mortality[19] for white men and suggest a similar relationship also may be present for black men with regard to prostate cancer incidence. At higher levels of the UV index, the percentage decrease in prostate cancer incidence rates was generally larger for black men compared with white men, although the confidence intervals were large.

Second, we considered the pattern in UV index versus cancer incidence and mortality throughout the United States. Previous work has considered the relative risk of cancer incidence and mortality primarily at extreme northern and southern latitudes.[30] For white men, we found that coefficients on prostate cancer incidence became progressively more negative as the UV index increased. For black men, the relationship demonstrated a general downward trend but was not uniform. These results suggest that even moderate doses of sunlight may help to reduce the incidence of prostate cancer, although they should be confirmed by future research.

Third, we evaluated the number of minutes that men must spend outdoors to obtain the RDA for vitamin D from sunshine. To our knowledge, this result has not been reported previously. In winter, it may be particularly difficult for black men to obtain enough vitamin D from sunlight, because they required $\geq$120 minutes outdoors in all but the southernmost regions of the United States, which may not be realistic in January. These issues suggest the need for future research to evaluate the potential benefits of preferential vitamin D supplementation in black men, as related to prostate cancer.

It is unclear why a positive association was found between the UV index and prostate cancer mortality in black men. Results were potentially influenced by suppressed data; 8% of counties reported $<$10 prostate cancer deaths. Alternatively, it is possible that UV radiation (and vitamin D) helps to prevent certain types of cancers, but

cancers that are not prevented have worse prognostic features. However, other recent data suggest that vitamin D may prevent aggressive prostate cancer.[41] In addition, we could not adjust for tumor characteristics, medical treatments, and individual-level socioeconomic data. Previous research has demonstrated inconsistent associations between cancer mortality and UV radiation in black individuals.[30]

Limitation of the Current Study

The results of the current study are limited by the fact that we evaluated the UV index rather than vitamin D, and serum levels of vitamin D differ by individual. For example, vitamin D is positively associated with healthy behaviors such as diet and exercise, and inversely associated with obesity.[42] In addition, the relationship between vitamin D and the UV index may differ by race. Nevertheless, for men who do not move between geographic regions, the UV index may be a proxy for lifetime vitamin D exposure, whereas plasma measures 1 point in time. Second, there may be other unobserved confounders associated with vitamin D and prostate cancer, including testosterone,[43] and the confounders we did measure, such as obesity, were measured at the county level. Third, the black population was small in some cancer areas. Finally, incidence and mortality are multifactorial, and our observational design allowed us to identify associations, not causality.

In conclusion, prostate cancer incidence for black and white men, the racial differences in incidence, and prostate cancer mortality for white men appear to be inversely associated with UV radiation from sunshine. Additional research is needed to confirm the findings of the current study and to assess whether optimizing vitamin D levels among men with dark skin tones can reduce prostate cancer disparities.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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