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Article

Prostate cancer disparities among American Indians and Alaskan Natives in the United States

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Abstract

Background: Americans Indians and Alaska Natives face disparities in cancer care with lower rates of screening, limited treatment access, and worse survival. Prostate cancer treatment access and patterns of care remain unknown.

Methods: We used Surveillance, Epidemiology, and End Results data to compare incidence, primary treatment, and cancer-specific mortality across American Indian and Alaska Native, Asian and Pacific Islander, Black, and White patients. Baseline characteristics included prostate-specific antigen (PSA), Gleason score (GS), tumor stage, 9-level Cancer of the Prostate Risk Assessment risk score, county characteristics, and health-care provider density. Primary outcomes were first definitive treatment and prostate cancer-specific mortality (PCSM).

Results: American Indian and Alaska Native patients were more frequently diagnosed with higher PSA, GS greater than or equal or 8, stage greater than or equal to cT3, high-risk disease overall (Cancer of the Prostate Risk Assessment risk score $\geq$ 6), and metastases at diagnosis than any other group. Adjusting for age, PSA, GS, and clinical stage, American Indian or Alaska Native patients with localized prostate cancer were more likely to undergo external beam radiation than radical prostatectomy and had the highest rates of no documented treatment. Five-year PCSM was higher among American Indian and Alaska Natives than any other racial group. However, after multivariable adjustment accounting for clinical and pathologic factors, county-level demographics, and provider density, American Indian and Alaska Native patient PCSM hazards were no different than those of White patients.

Conclusions: American Indian or Alaska Native patients have more advanced prostate cancer, lower rates of definitive treatment, higher mortality, and reside in areas of less specialty care. Disparities in access appear to account for excess risks of PCSM. Focused health policy interventions are needed to address these disparities.

Native American (recorded in US census data as American Indian and Alaskan Native) individuals face considerable disparities with respect to all cancers, including lower rates of screening (1,2), delayed diagnosis (3,4), decreased treatment access (5), and poorer health outcomes and mortality rates (6). Prostate cancer is the most common cancer among American Indian and Alaska Native men in the United States (7) and the third-leading cause of cancer death (8). Whereas mortality rates from prostate cancer have declined for White men between 1999 and 2009, they remained relatively constant among American Indian and Alaska Native men (9,10). With concurrent changes in prostate-specific antigen (PSA) screening recommendations, the incidence rates of all prostate cancer gradually increased from 2014 to 2017 in American Indian and Alaska Native men, but distant disease incidence also increased after 2008 for yet unclear reasons (11). In fact, American Indian and Alaska Native individuals have experienced the smallest decrease in overall prostate cancer mortality rates among all major racial and ethnic groups in the United States and are often excluded from population studies on cancer disparities (8,12).

Although such disparities among American Indian and Alaska Native patients are frequently described, little is known about the natural history and definitive treatment patterns for prostate cancer within this population. This picture is further clouded by historical underreporting of cancer outcomes within this population and frequent racial misclassification (13). In this study, we sought to characterize the disparity in prostate cancer outcomes using nationwide data from the Surveillance, Epidemiology, and End Results (SEER) cancer registry. In addition, we account for provider and hospital density by county. We examine the risk and stage distribution of prostate cancer at the time of diagnosis across American Indian and Alaska Native, Asian and Pacific Islander, Black, and White patients and compare rates of definitive treatment modalities and prostate cancer–specific mortality (PCSM).

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Methods

Our study included all men diagnosed with prostate cancer in 4 racial groups (American Indian and Alaska Native, Asian and Pacific Islander, Black, and White) residing in the 18 SEER program geographic areas between 2000 and 2016. SEER collects cancer incidence and survival information from 18 population-based cancer registries. To address historical racial misclassification of American Indian and Alaska Natives, these registries were linked with the Contract Health Service Delivery Areas database. Contract Health Service Delivery Areas are defined geographical regions within which health services are provided by the Indian Health Services to registered American Indian and Alaska Native individuals residing in that area. To be eligible for these services, the individual must document American Indian and Alaska Native descent, own tax-exempt or -restricted land, and/or be enrolled within a native tribe or group under federal supervision (14). The most recent data encompass 28% of the total US population and 43% of the full national American Indian and Alaska Native population. We excluded men classified as "Other" or missing key demographic or clinical data, including birthdate, clinical stage, Gleason score (GS), or PSA. SEER*Stat software was used to identify men diagnosed with prostate cancer between 2000 and 2016.

We compared registry-based demographic data, diagnostic GS, clinical T-stage at diagnosis, PSA, primary treatment modality, PCSM, county characteristics, and Cancer of the Prostate Risk Assessment (CAPRA)-9 scores (15) among each ethnic group. Demographic data were also merged with Area Health Resource File 2015 (https://data.hrsa.gov/topics/health-workforce/ahrf) by state and county code to include population density and healthcare workforce per county, including per capita numbers of physicians, radiation oncologists, urologists, operating room capacity, and hospital bed capacity.

Statistical analysis

Covariates were analyzed using linear analysis of variance for continuous variables and χ^2 for categorical variables. Primary outcomes of interest were PCSM and treatment modality. Treatment rates were assessed using multinomial logistic regression modeling, with race as an independent variable and adjusted rates calculated using the least square means of each variable (age, T-stage, metastases at diagnosis, GS, and PSA). American Indian and Alaska Native was the reference category for this analysis. A principal components analysis was used to assess the effect of collinearity in the multiple variables included (Supplementary Methods, available online).

We performed a Kaplan-Meier survival analysis and Cox proportional hazards regression adjusting for age group, marital status, metastases at diagnosis, PSA range, GS, clinical stage, and county characteristics including low education level (>68% of residents with less than high school education), poverty (>68% of residents living below federal poverty level), unemployment (percent of population), and provider density (total physicians, urologists, radiation oncologists, hospital beds, and operating rooms). Analyses were performed with SAS software (v. 9.4, Cary, NC, USA), and a 2-tailed P less than .05 was considered statistically significant.

Results

We identified 486 817 patients, including 1528 American Indian and Alaska Native men, 23 026 Asian and Pacific Islander men, 71 037 Black men, and 391 226 White men (Table 1). Our median follow-up time was 6.0 years (interquartile range = 2.9-9.0 years). American Indian and Alaska Native men were diagnosed at a similar median age as White men and slightly later than Black men (65.0 years vs 66.0 years vs 63.0 years, respectively; $P < .001$). American Indian and Alaska Native men were much more likely than White men to reside in rural areas (22.0% vs 12.0%, $P < .001$), be unmarried (21.8% vs 13.6%, $P < .001$), reside in counties with a lower level of education (38.3% vs 32.6%, $P < .001$), live in areas of greater poverty (42.7% vs 30.6%, $P < .001$), and live in areas of high unemployment rates (46.3% vs 30.3%). American Indian and Alaska Native men also resided in areas with lower density per capita of physicians, urologists, and radiation oncologists specifically, with fewer hospital beds per county (Table 1).

Our results demonstrate later stage at presentation among American Indian and Alaska Native men compared with all other races, with a higher proportion of high-risk disease at diagnosis (Figure 1). A total of 15.1% of American Indian and Alaska Native men presented with T3-T4 disease compared with 12.3% of White and 10.1% of Black men ($P < .001$). American Indian and Alaska Native men also had the most GS 7 or higher disease (65.2%), closely followed by Black men (64.6%). By multivariable risk assessment using the CAPRA-9 score, a shift in risk stratification was also noted—16.5% of American Indian and Alaska Native men presented with high-risk disease compared with 10.5% of White men and 13.6% of Black men ($P < .001$) (Table 1). Finally, American Indian and Alaska Native men were also more likely to present with metastatic disease than either White or Black patients (6.1% vs 3.6% vs 3.8%, respectively, $P < .001$).

A greater percentage of American Indian and Alaska Native men with localized intermediate or high-risk prostate cancer had no documented definitive treatment (8.9%) compared with Asian and Pacific Islander (6.3%), Black (5.7%), and White (6.8%) men (Table 2). With respect to type of treatment, American Indian/Alaska Native men were less likely to undergo surgery than Asian and Pacific Islander and White men, but not Black men, after adjustment for age, PSA, T-stage, and GS (Table 2). Conversely, American Indian and Alaska Native men, but not Black or White men, were more likely to undergo treatment than Asian and Pacific Islander men (Table 2).

In our study, the overall PCSM rate was highest among American Indian and Alaska Native men (3.1%, compared with 1.6% among Asian and Pacific Islander men, 2.5% among Black men, and 2.0% among White men; $P < .001$; Supplementary Figure 1, available online). On univariate analysis, American Indian and Alaska Native race was associated with increased risk of PCSM relative to White men (hazard ratio [HR] = 1.6, 95% confidence interval [CI] = 1.3 to 2.0), which was also observed with Black men (HR = 1.2, 95% CI = 1.1 to 1.2). Age, rurality, single status, PSA, GS, and clinical stage were all associated with PCSM. Although absolute effects were low, county-level characteristics of lower education status, higher poverty rates, and higher unemployment rates were correlated with higher PCSM, whereas increased urologist, radiation oncologist, and hospital bed availability were associated with lower PCSM (Table 3). With adjustment, American Indian and Alaska Native race was no longer associated with PCSM, whereas Asian and Pacific Islander race was associated with improved survival (HR = 0.7, 95% CI = 0.7 to 0.8) and Black race worse survival (HR = 1.2, 95% CI = 1.1 to 1.2).

Discussion

Our study demonstrates that American Indian and Alaska Native patients are more likely to be diagnosed with higher stage and

Table 1. Baseline patient cohort characteristics

Individual characteristics	All patients, No. (%)	Race				
		American Indian and Alaska Native, No. (%)	Asian and Pacific Islander No. (%)	Black No. (%)	White No. (%)	P
All patients	486 817 (100.0)	1528 (0.3)	23 026 (4.7)	71 037 (14.6)	391 226 (80.4)	
Age categories, y						
<50	15 690 (3.2)	51 (3.3)	407 (1.8)	4343 (6.1)	10 889 (2.8)	<.001
50-59	112 195 (23.0)	372 (24.3)	3916 (17.0)	21 693 (30.5)	86 214 (22.0)	
60-69	207 252 (42.6)	685 (44.8)	9624 (41.8)	30 089 (42.4)	166 854 (42.6)	
70-74	78 835 (16.2)	223 (14.6)	4436 (19.3)	8917 (12.6)	65 259 (16.7)	
≥75	72 845 (15.0)	197 (12.9)	4643 (20.2)	5995 (8.4)	62 010 (15.9)	
Mean age (SD)	65.3 (8.8)	64.8 (8.7)	67.2 (8.6)	62.6 (8.6)	65.7 (8.8)	<.001
Median age (IQR)	65.0 (59.0-71.0)	65.0 (59.0-70.0)	67.0 (61.0-73.0)	63.0 (57.0-68.0)	66.0 (60.0-72.0)	<.001
Rural vs urban						
Urban	433 479 (89.0)	1192 (78.0)	22 374 (97.2)	65 708 (92.5)	344 205 (88.0)	<.001
Rural	53 338 (11.0)	336 (22.0)	652 (2.8)	5329 (7.5)	47 021 (12.0)	
Marital status						
Married	346 257 (71.1)	964 (63.1)	18 146 (78.8)	40 543 (57.1)	286 604 (73.3)	<.001
Single	55 547 (11.4)	231 (15.1)	1759 (7.6)	11 376 (16.0)	42 181 (10.8)	
Unmarried or unknown	85 013 (17.5)	333 (21.8)	3121 (13.6)	19 118 (26.9)	62 441 (16.0)	
Clinical stage						
T1ab	18 176 (4.0)	76 (5.3)	841 (3.9)	1728 (2.6)	15 531 (4.2)	<.001
T1c	135 227 (29.7)	382 (26.8)	6438 (30.1)	25 761 (39.1)	102 646 (28.0)	
T2	237 137 (52.1)	698 (48.9)	10 576 (49.5)	30 320 (46.0)	195 543 (53.4)	
T3	51 166 (11.2)	198 (13.9)	2675 (12.5)	6082 (9.2)	42 211 (11.5)	
T4	7282 (1.6)	32 (2.2)	443 (2.1)	1047 (1.6)	5760 (1.6)	
Missing	6136 (1.3)	40 (2.8)	408 (1.9)	960 (1.5)	4728 (1.3)	
Metastases at diagnosis						
No	437 483 (89.9)	1333 (87.2)	20 458 (88.8)	63 207 (89.0)	352 485 (90.1)	<.001
Yes	17 641 (3.6)	93 (6.1)	923 (4.0)	2691 (3.8)	13 934 (3.6)	
Missing	31 693 (6.5)	102 (6.7)	1645 (7.1)	5139 (7.2)	24 807 (6.3)	
PSA						
<10 ng/mL	325 812 (66.9)	899 (58.8)	14 266 (62.0)	44 646 (62.8)	266 001 (68.0)	<.001
10-20 ng/mL	66 284 (13.6)	260 (17.0)	4208 (18.3)	11 189 (15.8)	50 627 (12.9)	
>20 ng/mL	39 812 (8.2)	189 (12.4)	2550 (11.1)	8229 (11.6)	28 844 (7.4)	
Missing	54 909 (11.3)	180 (11.8)	2002 (8.7)	6973 (9.8)	45 754 (11.7)	
Mean PSA (SD), ng/mL	10.8 (15.6)	14.2 (20.3)	12.7 (17.1)	13.0 (18.7)	10.3 (14.8)	<.001
Median PSA (IQR), ng/mL	6.3 (4.7-9.8)	7.3 (5.2-12.3)	7.4 (5.3-11.8)	6.8 (4.9-11.5)	6.2 (4.6-9.5)	<.001
Gleason score						
6	173 304 (35.6)	483 (31.6)	6885 (29.9)	23 664 (33.3)	142 272 (36.4)	<.001
7	219 525 (45.1)	672 (44.0)	10 104 (43.9)	33 947 (47.8)	174 802 (44.7)	
8	45 143 (9.3)	146 (9.6)	3001 (13.0)	6973 (9.8)	35 023 (9.0)	
9	35 462 (7.3)	161 (10.5)	2296 (10.0)	4489 (6.3)	28 516 (7.3)	
10	3904 (0.8)	17 (1.1)	245 (1.1)	464 (0.7)	3178 (0.8)	
Missing	9479 (1.9)	49 (3.2)	495 (2.1)	1500 (2.1)	7435 (1.9)	
Mean (SD)	6.9 (1.0)	7.0 (1.1)	7.0 (1.1)	6.9 (1.0)	6.9 (1.0)	<.001
Median (IQR)	7.0 (6.0-7.0)	7.0 (6.0-7.0)	7.0 (6.0-7.0)	7.0 (6.0-7.0)	7.0 (6.0-7.0)	<.001
CAPRA-9						
0 to 2	229 375 (47.1)	586 (38.4)	8476 (36.8)	30 988 (43.6)	189 325 (48.4)	<.001
3 to 5	192 162 (39.5)	635 (41.6)	10 292 (44.7)	28 815 (40.6)	152 420 (39.0)	
6 to 9	54 542 (11.2)	252 (16.5)	3730 (16.2)	9635 (13.6)	40 925 (10.5)	
Missing	10 738 (2.2)	55 (3.6)	528 (2.3)	1599 (2.3)	8556 (2.2)	
Mean (SD)	3.0 (1.9)	3.4 (2.0)	3.5 (2.0)	3.2 (2.0)	2.9 (1.9)	<.001
Median (IQR)	3.0 (1.0-4.0)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	3.0 (2.0-4.0)	3.0 (1.0-4.0)	<.001
County characteristics						
Less than high school education						
<34%	162 582 (33.4)	490 (32.1)	7447 (32.3)	15 657 (22.0)	138 988 (35.5)	<.001
34%-66%	165 993 (34.1)	453 (29.6)	8127 (35.3)	32 599 (45.9)	124 814 (31.9)	
67%-100%	158 242 (32.5)	585 (38.3)	7452 (32.4)	22 781 (32.1)	127 424 (32.6)	
Below federal poverty level						
<34%	162 289 (33.3)	375 (24.5)	10 213 (44.4)	13 612 (19.2)	138 089 (35.3)	<.001
34%-66%	161 807 (33.2)	500 (32.7)	6337 (27.5)	21 419 (30.2)	133 551 (34.1)	
67%-100%	162 721 (33.4)	653 (42.7)	6476 (28.1)	36 006 (50.7)	119 586 (30.6)	
Unemployment level						
<34%	161 821 (33.2)	363 (23.8)	11 210 (48.7)	12 603 (17.7)	137 645 (35.2)	<.001
34%-66%	163 941 (33.7)	458 (30.0)	4967 (21.6)	23 344 (32.9)	135 172 (34.6)	
67%-100%	161 055 (33.1)	707 (46.3)	6849 (29.7)	35 090 (49.4)	118 409 (30.3)	
Urban (population)						
1 million or more	297 906 (61.2)	680 (44.5)	15 979 (69.4)	47 969 (67.5)	233 278 (59.6)	<.001
250 000 to 1 million	98 598 (20.3)	320 (20.9)	5863 (25.5)	12 376 (17.4)	80 039 (20.5)	
Fewer than 250 000	36 975 (7.6)	192 (12.6)	532 (2.3)	5363 (7.5)	30 888 (7.9)	
Rural (population)						
20 000 or more	19 555 (4.0)	224 (14.7)	605 (2.6)	1807 (2.5)	16 919 (4.3)	
<20 000	33 783 (6.9)	112 (7.3)	47 (0.2)	3522 (5.0)	30 102 (7.7)	
Health-care workforce, total (by county)						
Active physicians, median (IQR)	2026.0 (407.0-5243.0)	1039.0 (190.0-4028.0)	4636.0 (3373.0-10 198.0)	2886.0 (592.0-5243.0)	1813.0 (363.0-4895.0)	<.001
	10.0 (2.0-25.0)	5.0 (1.0-19.0)	20.0 (11.0-43.0)	12.0 (3.0-25.0)	9.0 (2.0-25.0)	<.001

(continued)

Table 1. (continued)

Individual characteristics	All patients, No. (%)	Race				
		American Indian and Alaska Native, No. (%)	Asian and Pacific Islander No. (%)	Black No. (%)	White No. (%)	P
Radiation oncologists, median (IQR)						
Urologists, median (IQR)	26.0 (5.0-47.0)	13.0 (2.0-41.0)	46.0 (30.0-113.0)	31.0 (7.0-47.0)	23.0 (4.0-47.0)	<.001
Hospital beds, median (IQR)	1672.0 (462.0-4019.0)	1033.0 (214.0-3095.0)	3048.0 (2010.0-5685.0)	2271.0 (908.0-4313.0)	1548.0 (384.0-3897.0)	<.001
Operating rooms, mean (SD)	8.9 (17.7)	5.6 (13.7)	17.1 (22.2)	8.8 (17.0)	8.4 (17.4)	<.001
Treatment (CAPRA 3-9)						
Radical prostatectomy	112 343 (23.1)	359 (23.5)	6165 (26.8)	14 963 (21.1)	90 856 (23.2)	<.001
External beam radiation	117 568 (24.2)	446 (29.2)	6950 (30.2)	21 217 (29.9)	88 955 (22.7)	
Brachytherapy	337 (0.1)	3 (0.2)	10 (0.0)	62 (0.1)	262 (0.1)	
No treatment	256 569 (52.7)	720 (47.1)	9901 (43.0)	34 795 (49.0)	211 153 (54.0)	
Outcome						
Prostate cancer–specific death	18 199 (3.7)	84 (5.5)	791 (3.4)	2911 (4.1)	14 413 (3.7)	<.001
Follow-up, mean (SD), y	6.0 (3.6)	5.7 (3.6)	5.9 (3.6)	5.7 (3.6)	6.1 (3.6)	<.001
Follow-up, median (IQR), y	6.0 (2.9-9.0)	5.3 (2.5-8.7)	5.8 (2.7-8.8)	5.6 (2.6-8.6)	6.1 (3.0-9.1)	<.001

PSA = prostate specific antigen; CAPRA-9 = Cancer of the Prostate Risk Assessment score, 9-level version; IQR = interquartile range.

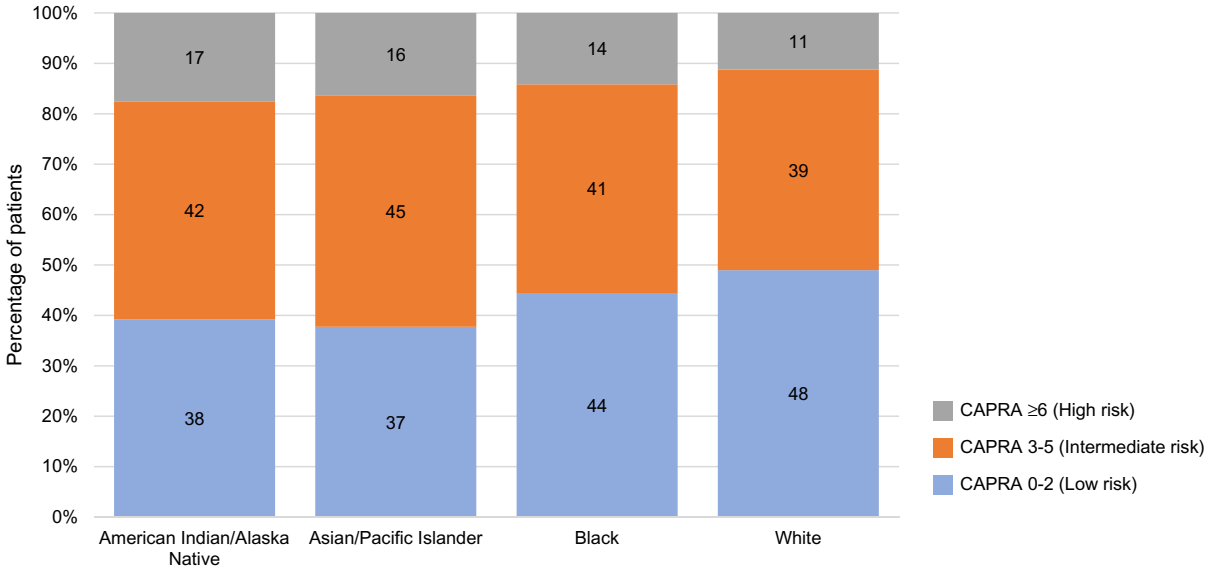

Figure 1. Distribution of 9-level Cancer of the Prostate Risk Assessment (CAPRA-9) score at diagnosis by race.

Gleason grade prostate cancer, present with metastases, and die from their disease than any other racial group, including Black men. American Indian/Alaska Native patients are less likely to undergo definitive treatment and, when they do, undergo radiation therapy more often than surgery. Our findings are consistent with prior studies indicating that American Indian and Alaska Native men may have a lower incidence of prostate cancer than White men (9) yet have the highest risk of prostate cancer mortality of any racial group (14,16), statistics that, together, reflect inadequate access to screening.

American Indian and Alaska Native men were diagnosed at a similar median age as White men but later than Black men (65 years vs 66 years vs 63 years, respectively; $P < .001$). Our finding that Black men are diagnosed at an earlier median age than other groups is consistent with other groups (17) and may demonstrate the effects of earlier screening implementation—a hypothesis that is also supported by a higher proportion of T1c disease in Black men. Despite earlier screening, however, Black men harbor a higher proportion of GS7 or higher prostate cancer than White men and a higher risk of death in multivariable modeling.

American Indian and Alaska Native patients face prominent system-level barriers to accessing care for chronic illnesses and all cancers, including lack of care coordination, insurance reimbursement structures, guideline-based treatment, provider density, and geography, as well as historical social barriers (14,18,19). Indian Health Service (IHS) hospitals and clinics located on American Indian and Alaska Native reservations provide care to approximately 2.2 of the 3.7 million individuals in the United States who identify as American Indian and Alaska Native (18). Because the IHS does not directly provide tertiary care (eg, urologist or radiation oncologist), referrals must be approved through the Purchased/Referred Care program, constituting another potential barrier to care. Furthermore, funding for the IHS is far below health expenditures per capita for the remaining US

Table 2. Treatment percentage by race estimated by squares means from the multinomial logistic model, in univariate analysis and adjusted for age, T-stage, metastasis at diagnosis, PSA, AJCC stage, and Gleason score

Procedure type	Race	Total No.	No. treated	Univariate model results (% of procedures)		Multivariable model results (% of procedures)	
				LSMean (95% CI)	$P_{adjusted}$[a]	LSMean (95% CI)	$P_{adjusted}$[a]
RP vs none	American Indian and Alaska Native (Ref.)	883	359	40.8 (37.4 to 43.9)	Ref.	20.9 (17.4 to 24.4)	Ref.
	Asian and Pacific Islander	13 931	6148	44.1 (43.3 to 45.0)	<.001	34.7 (33.0 to 36.5)	<.001
	Black	38 166	14 920	39.1 (38.6 to 39.6)	<.001	21.7 (20.5 to 23.0)	0.19
	White	191 971	90 551	47.2 (46.9 to 47.4)	<.001	30.5 (29.0 to 32.1)	<.001
EBRT vs RP	American Indian and Alaska Native (Ref.)	883	442	50.0 (46.8 to 53.3)	Ref.	65.1 (59.4 to 70.8)	Ref.
	Asian and Pacific Islander	13 931	6891	49.5 (48.6 to 50.3)	.05	57.4 (55.6 to 59.2)	.02
	Black	38 166	21 008	55.0 (54.5 to 55.5)	<.001	68.1 (65.8 to 70.3)	.08
	White	191 971	88 105	45.9 (45.7 to 46.1)	.76	59.8 (57.7 to 61.8)	.32
BT vs RP	American Indian and Alaska Native (Ref.)	883	3	0.34 (0.00 to 0.73)	Ref.	0.93 (0.00 to 7.43)	Ref.
	Asian and Pacific Islander	13 931	9	0.06 (0.02 to 0.11)	0.30	0.18 (0.00 to 1.44)	0.62
	Black	38 166	61	0.16 (0.12 to 0.20)	>.99	0.40 (0.00 to 3.15)	>.99
	White	191 971	252	0.13 (0.12 to 0.15)	>.99	0.39 (0.00 to 3.08)	>.99
None vs RP	American Indian and Alaska Native (Ref.)	883	79	8.95 (7.06 to 10.83)	Ref.	11.10 (8.44 to 13.77)	Ref.
	Asian and Pacific Islander	13 931	883	6.34 (5.93 to 6.74)	<.001	5.97 (5.44 to 6.50)	<.001
	Black	38 166	2177	5.70 (5.47 to 5.94)	<.001	8.44 (7.88 to 9.00)	0.58
	White	191 971	13 063	6.80 (6.69 to 6.92)	<.001	7.41 (7.00 to 7.82)	<.001

[a] *P* values were adjusted by Bonferroni method. AJCC = American Joint Committee on Cancer; BT = brachytherapy; CI = confidence interval; EBRT = external beam radiation therapy; LSMean = least square mean; None = no treatment; PSA = prostate-specific antigen; Ref. = reference group; RP = radical prostatectomy.

population (13). As our analysis demonstrates, American Indian and Alaska Native individuals are more likely to reside in areas of lower specialist density and fewer hospital beds and operating rooms, and these factors are directly associated with prostate cancer mortality.

The patterns of definitive treatment selection among American Indian and Alaska Native men compared with others are notable, with a greater use of radiation modalities even after multivariable adjustment. Although American Indian and Alaska Native men appeared to have lower rates of definitive treatment, this outcome was no longer statistically significant after adjustment for baseline clinical and pathologic features. Differences in patient-, provider-, and systems-based practices may explain differences in treatment uptake across racial groups. A study of Medicare-SEER data found that guideline-concordant prostate cancer treatment occurred in only 39% in American Indian and Alaska Native men compared with 60% of White men. Despite uniformity of insurance, lack of guideline-concordant treatment is also associated with worse cancer-specific survival (19).

Our initial finding that PCSM is increased among American Indian and Alaska Native men is in agreement with another study, which showed that prostate cancer mortality declined from 1999 to 2009 for White men but not for American Indian and Alaska Native men (20) and that the prostate cancer mortality to incidence ratio from 1999 to 2009 was higher among American Indian and Alaska Native men than White men (21). A more contemporary study of over 500 American Indian and Alaska Native men in California seen in the Kaiser Permanente system also found that, despite stable health insurance, American Indian and Alaska Native men with prostate cancer had nearly twice the PCSM risk compared with White men (HR = 1.87, 95% CI = 1.14 to 3.06) as well as higher all-cause and cancer-specific mortality rates, which were not attenuated after further adjusting for comorbidity (14).

However, the finding that American Indian and Alaska Native race was associated with PCSM on univariate analysis but not multivariable analysis suggests that measurable differences in clinical, pathologic, and demographic factors may be driving the poorer outcomes initially observed. Interestingly, after accounting for these factors, American Indian and Alaska Native race was no longer associated with PCSM, whereas Asian and Pacific Islander race was associated with improved survival and Black race with worse survival. There are several possible explanations for this finding. Our model contained several variables associated with rurality, and it is well known than American Indian and Alaska Native patients are highly concentrated in rural regions. In contrast, Asian and Black patients have less rural and urban differentiation, and this model may not have fully adjusted to other variables associated with their access to care (20,22,23). These observations speak to the complex social constructs reflected in categorized "race" and the uniquely constrained environments in which patients seek care and treatment.

Other studies have suggested that social environmental factors contribute to the cancer disparities seen in American Indian and Alaska Native men in delays in diagnosis with resultant stage migration, reduced access to specialty care, and associated lack of definitive treatment. A recent SEER database study examined prostate cancer characteristics at diagnosis from 2004 to 2016 using PSA, stage, and grade and found that after propensity score matching and competing-risks-regression-models, race alone was not an independent predictor of cancer-specific mortality (24). Our model supports this finding and includes county-level demographic and health-care characteristics to account for differences in social environment and access.

Unique strengths of our study include its large sample size, focus on definitive treatment patterns, and inclusion of county characteristics, including accessibility of health-care resources and specialty care into the multivariable model. These factors highlight the importance of the environment and health-care system in determining prostate cancer outcomes. In addition, SEER currently has the highest representation of American Indian and Alaska Native patients of any cancer registry in the United States, and we were able to leverage these data to study a traditionally underrepresented population in existing prostate cancer literature.

Our study is not without several important limitations inherent to national cancer registry analysis. We were not able to

Table 3. Univariate and multivariable Cox regression model for prostate cancer–specific mortality outcomes[a]

Variable	Univariate Cox model			Multivariable Cox model		
	HR (95% CI)	P	P_{global}	HR (95% CI)	P	P_{global}
Race						
American Indian and Alaska Native	Ref.		<.001	Ref.		<.001
Asian and Pacific Islander	0.60 (0.48 to 0.76)	<.001		0.63 (0.50 to 0.79)	<.001	
Black	0.74 (0.60 to 0.92)	.01		0.97 (0.78 to 1.20)	.75	
White	0.62 (0.50 to 0.77)	<.001		0.84 (0.68 to 1.04)	.11	
Age group, y						
<50	Ref.		<.001	Ref.		<.001
50-59	1.04 (0.94 to 1.16)	.44		1.12 (1.00 to 1.24)	.04	
60-69	1.29 (1.17 to 1.43)	<.001		1.29 (1.16 to 1.43)	<.001	
70-79	2.23 (2.01 to 2.47)	<.001		1.81 (1.63 to 2.01)	<.001	
≥80	8.42 (7.58 to 9.36)	<.001		3.50 (3.14 to 3.90)	<.001	
Living area						
Urban	Ref.		<.001	Ref.		.79
Rural	1.22 (1.17 to 1.27)	<.001		1.01 (0.96 to 1.07)	.79	
Marital status						
Married	Ref.		<.001	Ref.		<.001
Single	2.01 (1.93 to 2.09)	<.001		1.34 (1.29 to 1.39)	<.001	
Unmarried or unknown	1.38 (1.33 to 1.44)	<.001		1.18 (1.14 to 1.23)	<.001	
PSA						
<10 ng/mL	Ref.		<.001	Ref.		<.001
10-20	2.52 (2.41 to 2.64)	<.001		1.56 (1.49 to 1.64)	<.001	
>20	11.56 (11.17 to 11.98)	<.001		2.58 (2.47 to 2.69)	<.001	
Missing	2.99 (2.86 to 3.13)	<.001		1.86 (1.77 to 1.95)	<.001	
Gleason score						
6	Ref.		<.001	Ref.		<.001
7	1.67 (1.59 to 1.76)	<.001		1.78 (1.69 to 1.87)	<.001	
8	6.14 (5.82 to 6.47)	<.001		3.86 (3.64 to 4.10)	<.001	
9	15.61 (14.88 to 16.37)	<.001		7.13 (6.74 to 7.53)	<.001	
10	42.37 (39.54 to 45.40)	<.001		11.13 (10.31 to 12.01)	<.001	
Missing	24.40 (23.04 to 25.85)	<.001		5.44 (5.07 to 5.84)	<.001	
Clinical stage						
T1/T2a	Ref.		<.001	Ref.		<.001
T2b/T2c	0.81 (0.78 to 0.84)	<.001		0.93 (0.90 to 0.97)	<.001	
T3/T4	2.65 (2.55 to 2.76)	<.001		1.57 (1.50 to 1.65)	<.001	
Missing	11.04 (10.48 to 11.63)	<.001		2.17 (2.03 to 2.32)	<.001	
Met at diagnosis						
No	Ref.		<.001	Ref.		<.001
Yes	23.02 (22.31 to 23.75)	<.001		6.23 (5.98 to 6.48)	<.001	
Less than high school education level						
0%-33%	Ref.		<.001	Ref.		<.001
34%-67%	1.17 (1.12 to 1.21)	<.001		1.08 (1.03 to 1.13)	<.001	
≥68%	1.35 (1.30 to 1.40)	<.001		1.21 (1.15 to 1.27)	<.001	
Below federal poverty level						
0%-33%	Ref.		<.001	Ref.		<.001
34%-67%	1.21 (1.16 to 1.25)	<.001		1.09 (1.05 to 1.14)	<.001	
≥68%	1.36 (1.31 to 1.41)	<.001		1.11 (1.04 to 1.18)	<.001	
Unemployment level						
0%-33%	Ref.		<.001	Ref.		0.45
34%-67%	1.06 (1.03 to 1.10)	<.001		1.00 (0.95 to 1.04)	.81	
≥68%	1.27 (1.23 to 1.32)	<.001		1.03 (0.97 to 1.08)	.33	
First definitive treatment						
Radical prostatectomy	Ref.		<.001	Ref.		<.001
External beam radiation	3.08 (2.95 to 3.22)	<.001		2.63 (2.50 to 2.77)	<.001	
Brachytherapy	5.90 (4.35 to 8.00)	<.001		5.42 (3.99 to 7.37)	<.001	
No treatment	1.08 (1.04 to 1.13)	<.001		2.49 (2.36 to 2.64)	<.001	
Total physicians in county, No.						
0-999	Ref.		<.001	Ref.		.90
1000-3999	0.88 (0.85 to 0.91)	<.001		0.98 (0.89 to 1.08)	.73	
≥4000	0.95 (0.92 to 0.98)	.002		0.96 (0.83 to 1.12)	.64	
Radiation oncologists in county, No.						
0-5	Ref.		<.001	Ref.		.59
6-20	0.90 (0.87 to 0.94)	<.001		0.97 (0.91 to 1.03)	. 30	
≥20	0.96 (0.93 to 0.99)	.01		0.97 (0.87 to 1.07)	.50	
Urologists in county, No.						
0-9	Ref.		<.001	Ref.		.32
10-39	0.86 (0.83 to 0.90)	<.001		0.95 (0.86 to 1.05)	.28	
≥40	0.93 (0.90 to 0.96)	<.001		0.90 (0.78 to 1.03)	.13	

(continued)

Table 3. (continued)

Variable	Univariate Cox model			Multivariable Cox model		
	HR (95% CI)	P	P_{global}	HR (95% CI)	P	P_{global}
Operating rooms in county, No.						
0	Ref.		<.001	Ref.		.38
1-12	1.04 (1.00 to 1.08)	.08		1.03 (0.98 to 1.08)	.25	
≥12	1.08 (1.04 to 1.12)	<.001		1.04 (0.98 to 1.10)	.22	
Hospital beds in county						
0-999	Ref.		<.001	Ref.		.26
1000-2499	0.93 (0.90 to 0.97)	<.001		1.04 (0.98 to 1.10)	.20	
≥2500	0.97 (0.94 to 1.00)	.07		1.08 (0.98 to 1.19)	.11	

[a] CI = confidence interval; PSA = prostate-specific antigen; Ref. = reference group.

adjust comorbidities and other lifestyle factors such as smoking and alcohol use, which may vary across racial groups. In addition, the accuracy of definitive treatment rates was dependent on timely reporting, and regional variation in reporting may exist. Lastly, the use, timing, and duration of androgen-deprivation therapy is unreliable in SEER and was not included as a clinical variable, nor was use of active surveillance or watchful waiting. Despite these limitations, the data clearly demonstrate that American Indian and Alaska Native men present with higher-risk prostate cancer, are less likely to undergo definitive treatment, and are more likely to die of their disease that any other racial group in the United States. Although both genetic and social environmental factors may drive this disparity in combination, community-level health policy interventions to improve access to screening, diagnosis, and timely treatment could plausibly ameliorate the PCSM disparity faced by American Indian and Alaska Native men.

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Data availability

Datasets analyzed during the current study are available in the SEER*Stat publicly available dataset (https://seer.cancer.gov/data-software/documentation/seerstat/). All SAS code for statistical analysis and raw data can be shared per request.

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