Original Article

Racial, ethnic, and socioeconomic disparities in rates of stage IV prostate cancer after USPSTF category "D" recommendation against prostate-specific antigen screening: a retrospective cohort study

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Background: In 2012 the United States Preventative Services Task Force (USPSTF) changed its prostate-specific antigen (PSA) screening recommendation to a category "D". The purpose of this study is to examine racial, ethnic, and socioeconomic differences in risk of presentation with metastatic prostate cancer (mPCa) at time of diagnosis before and after the 2012 USPSTF category "D" recommendation.

Methods: This is a population-based cohort study. We identified patients with mPCa at diagnosis within the National Cancer Database from 2004–2017. Logistic regression models were used to examine associations of mPCa with age, race, ethnicity, geographic location, education level, income, and insurance status. Linear regression models assuming underlying binomial distribution were fitted to annual percentage of mPCa at diagnosis for years 2012–2017 to evaluate the post category "D" recommendation era.

Results: From 2004 to 2017, 88,987 patients presented with mPCa. A higher percentage of mPCa was noted post-USPSTF category "D" recommendation, with a disproportionately greater increase observed among Hispanics and non-Hispanic Blacks [Δslope/year: Hispanics (0.0092), non-Hispanic Blacks (0.0073) and non-Hispanic Whites (0.0070)]. Insurance status impacts race/ethnicity differently: uninsured Hispanics were 3.66 times more likely to present with mPCa than insured Hispanics, while uninsured non-Hispanic Blacks were 2.62 times more likely to present with mPCa than insured non-Hispanic Blacks. Household income appears to be associated with differences in mPCa, particularly among non-Hispanic Blacks. Those earning <$30,000 were more likely to present with mPCa compared to higher income brackets.

Conclusions: Since the USPSTF grade "D" recommendation against PSA screening, the percentage of mPCa at diagnosis has increased, with a higher rate of increase among Hispanic and non-Hispanic Blacks compared to non-Hispanic Whites.

Keywords: African American; blood screening; Hispanics; prostate cancer (PCa); urology

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Introduction

Prostate cancer (PCa) is the second most common cause of cancer death among men in the United States (1). The National Cancer Institute estimates that one in eight men will be diagnosed with PCa during their lifetime (2). Advancements in screening techniques have enabled health care providers (HCP) to diagnose PCa prior to metastasis. The stage at which PCa is diagnosed is a critical determinant for treatment modality and mortality (3).

Randomized controlled trials confirmed that early detection through prostate-specific antigen (PSA) screenings significantly reduced PCa mortality (4). However, HCPs must balance the benefits and harms of PCa screening with PSA, as screening may lead to over-diagnosis and overtreatment with radiation or surgery that can result in deleterious effects on functional parameters (5). Recognizing these potential harms, in 2012, the United States Preventive Services Task Force (USPSTF) published a grade "D" recommendation against PSA screening for men of all ages (6).

Racial and ethnic disparities in metastatic PCa (mPCa) at diagnosis are known; however, the potential differential impact of the USPSTF screening decision on racial and ethnic minorities remains less well understood (7). Black race and Hispanic ethnicity are associated with higher odds of mPCa at presentation and Black men are more likely to be diagnosed with PCa at an earlier age (8,9). Previous studies have investigated social determinants of health including socioeconomic status, geographic location, education level, and health insurance status in relation to PCa incidence, risk, stage at presentation, and survival (10-12). However, a comprehensive contemporary analysis of the potential interactions between age, race, ethnicity, education level, income, insurance status, and the USPSTF "D" screening recommendation with the proportion of mPCa at presentation does not yet exist in the literature.

In this study, we examined risk of presentation with mPCa in the National Cancer Database (NCDB) to evaluate its relationship with race, ethnic, and socioeconomic characteristics. Furthermore, we investigated whether differences in associations between these characteristics and mPCa at presentation are observed as differential rates of change in mPCa prior to and following the USPSTF's "D" recommendation against PSA screening. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-90/rc).

Highlight box

Key findings

- Significant racial and ethnic disparities exist in metastatic prostate cancer (mPCa) diagnosis at presentation.
- Being insured is associated with decreased odds of mPCa diagnosis at presentation.
- Rates of mPCa diagnosis at presentation increased for all groups post-United States Preventative Services Task Force (USPSTF) downgrade.
- Hispanic and non-Hispanic Black patients had a disproportionately greater increase.

What is known and what is new?

- There are racial and ethnic disparities in PCa diagnosis and treatment.
- The USPSTF downgrade resulted in fewer prostate-specific antigen (PSA) screens performed.
- However, an analysis of the potential differential impact of the USPSTF screening decision on racial and ethnic minorities is not found in the literature.

What is the implication, and what should change now?

- Patients with significant racial, ethnic, insurance status, and income risk factors should receive PSA screening at a higher priority than current USPSTF guidelines.

Methods

Data source

Data for patients presenting with mPCa from 2004 to 2017 were obtained from the NCDB, thus the sample size was determined by the total number of cases during the sample period. The NCDB is the largest clinical cancer registry in the world and receives over one million cancer case reports annually. Sourced from hospital registry data, the database represents more than 70 percent of newly diagnosed cancer cases from 1,500 American College of Surgeons

Commission on Cancer accredited facilities nationwide (13). The time of the downgrade of the USPSTF recommendation to "D" was set at 2012 (6). The study was exempt from ethical review given minimal risk with the NCDB. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Outcomes and covariates under study

The primary outcome of this population-based cohort study was the percentage of mPCa during the study period, which is defined as distant metastasis of PCa (i.e., beyond regional pelvic lymph nodes) (14). Secondary outcomes included the change in percentage of mPCa within racial/ethnic populations and sociodemographic characteristics that are associated with mPCa.

Covariates included age, race, ethnicity, geographic location, county type, education level median household income, academic medical center and insurance status. Race and Hispanic ethnicity were combined into a single, four-category variable: known Hispanic, non-Hispanic (NH) White, NH Black, and other/unknown race/ethnicity. Geographic location was defined using the U.S. Census division categories of Northeast, South/Southeast, Midwest, and West (15). County type was defined as metropolitan (>250,000 residents/county), urban (2,500–250,000 residents/county), and rural (<2,500 residents/county). Education level was based on the percentage of adults within a zip code that did not graduate high school based on U.S. Census Bureau American Community Survey data (16). Likewise, median household income was defined by zip code and derived from U.S. Census Bureau. Academic medical center was defined as a hospital with an academic cancer program with more than 4 postgraduate medical education programs and more than 500 diagnosed cancer cases per year. Insurance status was defined by the patient's primary insurance carrier at the time of diagnosis, patients with unknown insurance status were grouped with uninsured patients and reported separately.

Statistical analysis

Available data on all patients with PCa diagnosis of any stage were obtained from the NCDB. Frequencies and percentages of PCa stages and covariates of interest were computed. Relationships between socioeconomic characteristics and presentation with mPCa were examined using logistic regression models. Two-way interactions between race/ethnicity and other characteristics were fitted to examine potential differential relationships between characteristics and mPCa among race/ethnicity groups. Model selection was performed using backwards elimination beginning with a model that included all main effects and their two-way interactions. Factors were eliminated one-by-one in a hierarchical framework, starting with interaction terms and continuing to main effects if all interactions involving them had been eliminated. Because the large sample size made for increased precision, only factors significant at the 0.01 alpha level (or main effects involved in a significant interaction) were retained in the final model. Linear trends in percentage of mPCa at presentation over time, overall and by race/ethnicity, were examined using generalized linear regression models assuming an underlying binomial distribution. Lines were fitted through annualized rates of mPCa with an interaction for years 2012–2017 to evaluate changes in slopes over the post PSA screening era.

Results

We identified 1,275,410 PCa cases in the NCDB from 2004–2017, of which 88,987 (7%) were metastatic at presentation. *Table 1* shows sociodemographic characteristics of the study population overall, as well as the frequency and percentage of mPCa cases at presentation by sociodemographic characteristics. We observed that 7% of NH Whites, 9% of NH Blacks, and 10% of Hispanics presented with mPCa. Percentages of mPCa at presentation varied by insurance status as 19% of uninsured patients, 16% of Medicaid patients, and 4% of privately insured patients presented with metastatic disease.

Summary results of backward variable selection (Chi-square statistics and P values) for logistic regression models to predict mPCa status at presentation are shown in Tables S1,S2. All two-way interactions between sociodemographic factors were considered for model inclusion. Interactions that remained in the final model, ranked from largest to smallest ratio of chi-square statistic to degrees-of-freedom (DF), included: age with insurance status (χ^2/DF 205.1); race/ethnicity with PSA testing era (30.4); insurance status with academic medical center (28.9); age with education (14.2); academic medical center with education (11.7); academic medical center with income (9.1); race/ethnicity with insurance status (7.8); insurance status with income (6.3); race/ethnicity with income (6.2); and insurance status with education (3.8). Tables S1,S2 give

Table 1 Characteristics of patients in NCDB 2004–2017 with prostate cancer diagnosis at presentation (n=1,275,410) overall and with metastatic disease (n=88,987)

Characteristics	Total	Metastatic PCa
Age category (years)		
<59	329,553 (26%)	15,280 (5%)
60–65	314,203 (25%)	15,107 (5%)
66–70	308,632 (24%)	16,021 (5%)
>71	323,022 (25%)	42,579 (13%)
Race		
White	1,034,324 (81%)	68,411 (7%)
Black	185,413 (15%)	16,573 (9%)
Other	37,487 (3%)	3,061 (8%)
Unknown	18,186 (1%)	942 (5%)
Ethnicity		
Hispanic	55,773 (4%)	5,470 (10%)
Non-Hispanic	1,143,786 (90%)	79,344 (7%)
Unknown	75,851 (6%)	4,173 (6%)
Race/ethnicity combined		
Hispanic (any race, including unknown)	55,773 (4%)	5,470 (10%)
Non-Hispanic White	985,707 (77%)	63,636 (6%)
Non-Hispanic Black	183,516 (14%)	16,378 (9%)
Other/unknown	50,414 (4%)	3,503 (7%)
Geographic location		
Northeast	291,028 (23%)	20,225 (7%)
South/Southeast	362,026 (28%)	22,492 (6%)
Midwest	423,272 (33%)	30,737 (7%)
West	198,355 (16%)	15,468 (8%)
Not specified	729 (0.06%)	65 (9%)
County type		
Metro	1,034,340 (81%)	73,243 (7%)
Urban	172,028 (13%)	11,721 (7%)
Rural	23,717 (2%)	1,670 (7%)
Unknown	45,325 (4%)	2,353 (5%)
Education level of population (% no high school diploma)		
≥29%	193,422 (15%)	17,045 (9%)
20–28.9%	274,098 (21%)	20,549 (7%)
14–19.9%	297,975 (23%)	20,557 (7%)
<14%	509,915 (40%)	30,836 (6%)

Table 1 *(continued)*

Table 1 *(continued)*

Characteristics	Total	Metastatic PCa
Median household income		
<$30,000	156,578 (12%)	13,936 (9%)
$30,000–$34,999	209,239 (16%)	15,950 (8%)
$35,000–$45,999	341,405 (27%)	24,514 (7%)
$46,000 or more	568,188 (45%)	34,587 (6%)
Insurance status		
Not insured	21,081 (2%)	4,045 (19%)
Private	573,758 (45%)	22,903 (4%)
Medicaid	35,429 (3%)	5,817 (16%)
Medicare or other government based	617,976 (48%)	53,960 (9%)
Not specified	27,166 (2%)	2,262 (8%)

NCDB, National Cancer Database; PCa, prostate cancer.

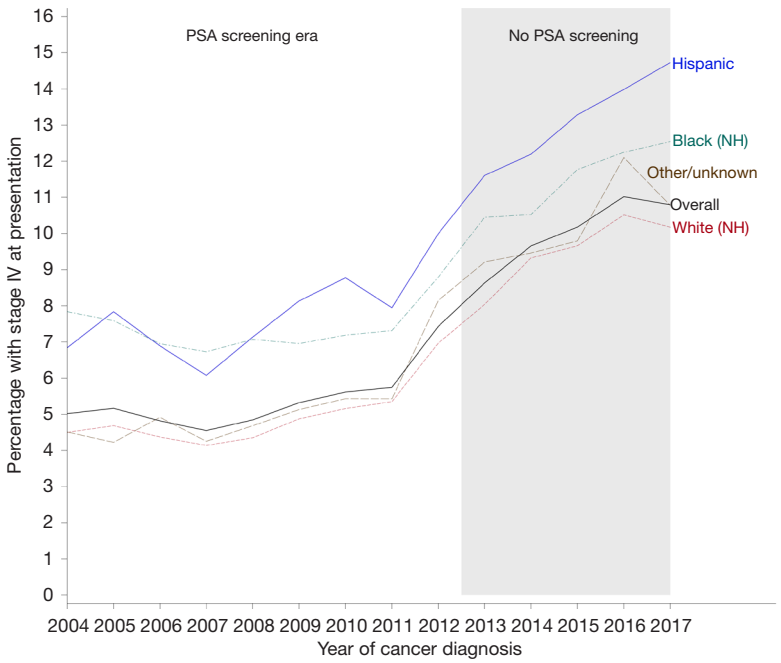

Figure 1 Percentage of metastatic prostate cancer at presentation versus year of cancer diagnosis, stratified by race/ethnicity. PSA, prostate-specific antigen; NH, non-Hispanic.

more detail including parameter estimates.

Figure 1 depicts the annual percentages of patients presenting with mPCa by year of diagnosis beginning in 2004 through 2017, overall and stratified by race/ethnicity group. Prevalence of mPCa at presentation is stable for years 2004 through 2011, which coincides with the USPSTF pre-grade "D" recommendation era. Beginning in 2012 percentages of mPCa at presentation begin to increase in a trend that continues through 2017. Hispanic and NH Black groups presented with highest percentages of mPCa for both pre- and post-USPSTF "D" recommendation eras with pre-USPSTF percentages among Hispanics

Table 2 Change per year (slope) in proportion presenting with metastatic prostate cancer, by race/ethnicity group and overall. Slopes calculated for eras with PSA testing guideline (2004–2011) and without guideline (2012–2017)

Race/ethnicity group	Testing era	Slope (Δ/year)	95% CI	P value (difference between eras)
Hispanic	PSA testing guideline 2004–2011	0.0021	0.0008, 0.0034	<0.001
	No PSA testing guideline 2012–2017	0.0092	0.0068, 0.0116	
Non-Hispanic White	PSA testing guideline 2004–2011	0.0012	0.0010, 0.0014	<0.001
	No PSA testing guideline 2012–2017	0.0070	0.0065, 0.0075	
Non-Hispanic Black	PSA testing guideline 2004–2011	–0.0005	–0.0012, 0.0002	<0.001
	No PSA testing guideline 2012–2017	0.0073	0.0061, 0.0086	
Non-Hispanic other or unknown	PSA testing guideline 2004–2011	0.0016	0.0005, 0.0027	<0.001
	No PSA testing guideline 2012–2017	0.0064	0.0021, 0.0073	
All races combined	PSA testing guideline 2004–2011	0.0011	0.0009, 0.0013	<0.001
	No PSA testing guideline 2012–2017	0.0072	0.0067, 0.0076	

PSA, prostate-specific antigen; CI, confidence interval.

ranging from 6.8% to 10% per year, 7.8% to 8.8% per year among NH Blacks, 4.5% to 7% per year among NH Whites, and 4.5% to 8.1% per year among other/unknown race/ethnicities. Post-USPSTF percentages ranged from 11.6% to 14.7% per year among Hispanics; 10.4% to 12.5% per year among NH Blacks, 8% to 10.2% per year among NH Whites, and 9.2% to 10.8% among other/unknown race/ethnicities. This increasing trend for the post-grade "D" recommendation era was consistent across all race/ethnicity groups. Analysis of differences in slopes of the lines for pre- versus post-grade "D" eras is statistically significant (P<0.001) for each race/ethnicity group (*Table 2*) with each exhibiting significantly positive slopes in the post grade "D" era (P<0.001 for each slope).

Visual depiction of interaction between race/ethnicity and income, and race/ethnicity and insurance status are shown in *Figures 2,3*, respectively. Among NH Black men, those earning <$30,000 compared to >$46,000/year had 22% greater odds of a diagnosis of mPCa at diagnosis [odds ratio (OR) 1.22, 95% confidence interval (CI), 1.14–1.30]. NH Black men earning <$30,000 versus those earning $35,000–$45,999 had 17% greater odds of mPCa at presentation (OR 1.17, 95% CI: 1.10–1.23), and NH Black men earning <$30,000 versus those earning $30,000–$34,999 had 8% greater odds (OR 1.08, 95% CI: 1.02–1.14). For other race/ethnicity groups, the relationships between median household income and mPCa at presentation were not as disparate as for NH Black males (*Figure 2*).

Relationships between insurance status and mPCa at presentation differed significantly between race/ethnicity groups (two-way interaction, P value <0.001 for all), as shown in *Figure 3*. Uninsured NH Whites had twice the odds of presenting with mPCa compared to those with Medicaid insurance (OR 2.02; 95% CI: 1.93–2.12). Notably, this magnitude of difference between the uninsured and those with Medicaid was not as large among Hispanic (OR 1.43, 95% CI: 1.29–1.59) and NH Black (OR 1.15, 95% CI: 1.07–1.23) patients.

Discussion

In this study, we used the NCDB to analyze factors that are associated with increasing presentation of mPCa and temporal effects of USPSTF's "D" recommendation for PSA screening in the United States. We observed an increasing percentage of mPCa at diagnosis in all racial/ethnic subgroups under study after the 2012 grade "D" recommendation. Increased access to health insurance was associated with decreased risk of presentation of mPCa, with a differential impact by race. When comparing the uninsured to those with Medicaid, White patients had higher odds of presenting with mPCa compared to Hispanic or NH Black patients, suggesting Medicaid may have had a greater mitigating influence on the percentage of mPCa among Whites than racial minorities. These observations may have implications for Medicaid expansion policy.

Our model suggests that being insured is associated with a decreasing odds of presenting with mPCa. Private

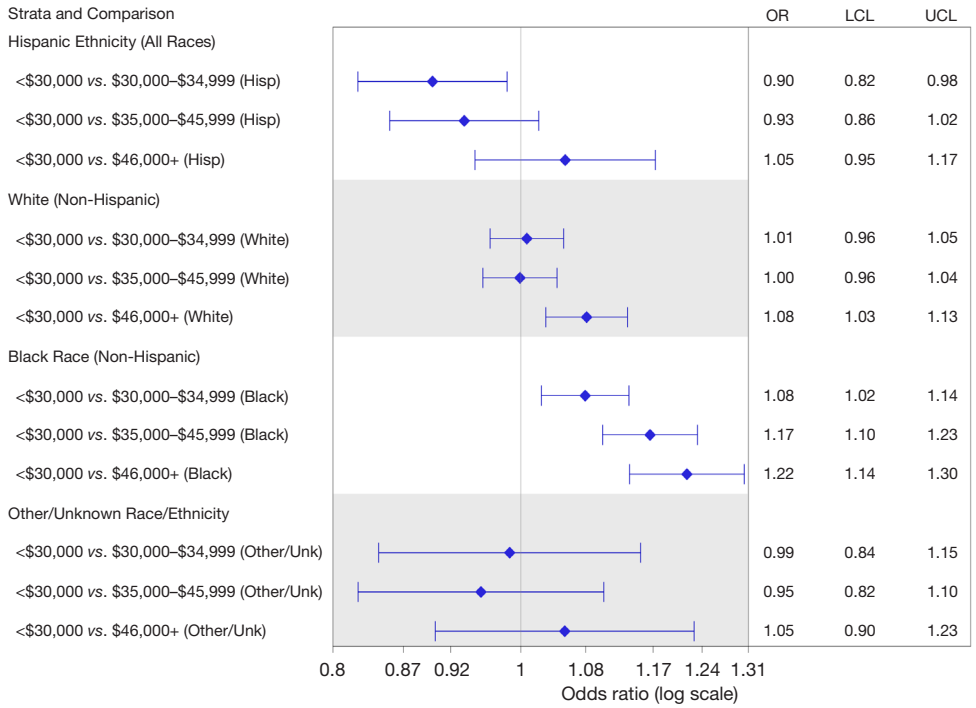

Figure 2 Odds ratios for metastatic prostate cancer at presentation, comparing median household income <$30,000 to income $35,000–$45,999 and income >$46,000, controlling for race/ethnicity. OR, odds ratio; LCL, lower control limit; UCL, upper control limit; Unk, unknown.

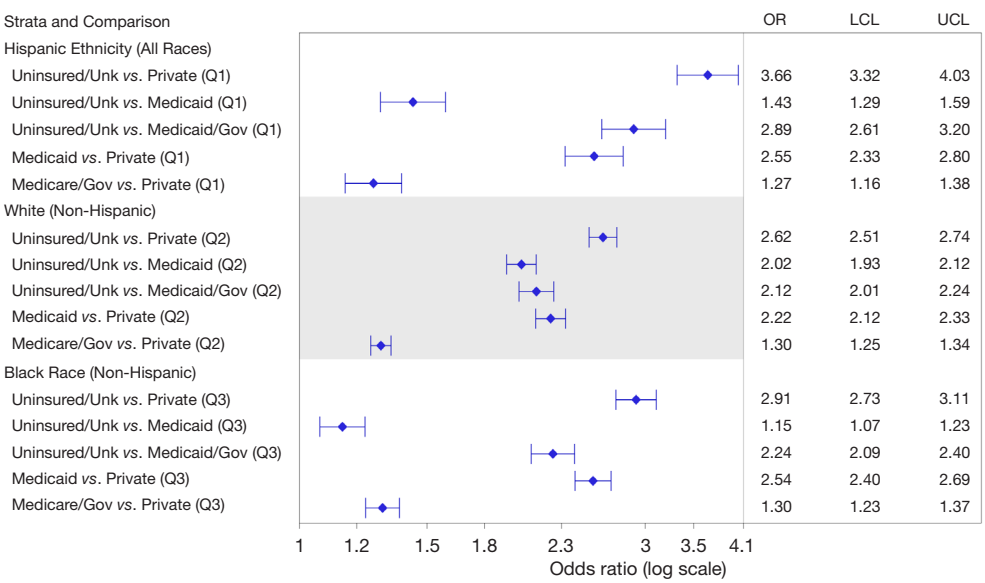

Figure 3 Odds ratios for metastatic prostate cancer at presentation for insurance status, stratified by race/ethnicity. OR, odds ratio; LCL, lower control limit; UCL, upper control limit; Unk, unknown; Gov, governmental insurance.

insurance was the largest protective factor for NH Black, Hispanic, and NH White populations (*Figure 3*). Following private insurance, Medicaid and Medicare statuses were associated with decreased odds of mPCa presentation. Uninsured status versus private insurance contributed to greatest risk of presentation with mPCa for NH Black, Hispanic, and NH White men. Our study demonstrated uninsured Hispanics may be most vulnerable with more than a three-fold increased risk of mPCa at diagnosis compared to those with private insurance. Uninsured individuals are disproportionately likely to be Black or Hispanic (17). Previous work illustrated uninsured adults are less likely to receive preventive care and screening services (18). Increased access to health insurance for Black and Hispanic individuals is associated with decreased risk of presentation of mPCa.

A decrease in the utilization of PSA screening is attributed to the grade "D" recommendations against PSA screening for men of all ages published in 2012 by the USPSTF (19,20). Contributing factors to end PSA screening included risks of treatment, costs of screening, PCa specific mortality benefit, and over-diagnosis of PCa (21). Percentage of mPCa increased 2.75% in 2012 following the USPSTF recommendation and is expected to increase through 2025 (22). On initial observation, the rise in mPCa depicted in *Figure 2* begins from 2011–2012, around the same time as the 2012 USPSTF recommendation. However, a study by Sammon *et al.* (23) demonstrated a 5% decrease in PSA testing from 2010–2013 which may contribute to the rise in mPCa prior to the 2012 recommendation. Furthermore, Abdollah *et al.* (24) found a rapid decrease in PSA testing from 34.9% to 31.9% from 2011 to 2013 which was corroborated by Jemal *et al.* (25) who found a similar 7% decrease in PSA screening during a similar time period, suggesting a rapid acceptance of the 2012 USPSTF recommendation.

Our analysis illustrated that from 2004 through 2017, NH Black and Hispanic patients were the most likely to present with mPCa (*Figure 1*). Notably, NH Black and Hispanic populations sustained the largest increases in yearly change of mPCa at presentation in comparison of the pre- and post-grade "D" eras (*Table 2*). Overall increases in the percentage of presentation with mPCa may be explained by decreased PSA testing following the grade "D" recommendation against screening. However, significantly increased percentages of presentation of mPCa for NH Blacks and Hispanics highlight disparities within racial and ethnic minority communities. Racial and ethnic differences in presentation of mPCa may reflect systemic barriers to early diagnosis with possible contributing factors being social and economic disparities.

Lower economic status, as measured by quartile of median household income in residential ZIP code, was identified as a risk factor for presentation with mPCa. According to our analysis, residing in an area with a higher median household income is a protective factor against mPCa for NH Black and NH White populations. In 2019, an analysis by the National Cancer Institute found that low income is linked to advanced stage of PCa for all races (26). Interpretation of income as a variable in isolation is less helpful than considering how income may affect access to health insurance. In the United States, most adults under 65 receive health insurance through an employer-based plan. From 1999 to 2014, fewer individuals in the workforce were offered insurance through their employer. Decreases in coverage rates have disproportionately affected families with low incomes (27). Health insurance and income, combined may perpetuate racial and ethnic differences in mPCa at presentation.

Additional elements related to social determinants of health include education, neighborhood factors, and proximity to a metropolitan area. In our model, we found few differences in mPCa at presentation in metropolitan versus rural counties. Small but significant increased risk was noted for metropolitan versus rural NH Black (OR 1.18, 95% CI: 1.01–1.38) and NH White populations (OR 1.08, 95% CI: 1.03–1.15). Education analysis by zip codes where ≥29% of individuals had less than high school degree versus <14%, demonstrated significantly increased risk for all NH Whites, NH Blacks, and Hispanics. These results demonstrate that further research with detailed neighborhood factors such as school rankings, population density, public transportation, assessment of food dessert status, and access to public parks, is needed to understand the association of mPCa risk.

The study conclusions are limited by the shortcomings of the NCDB database. First, race and ethnicity were limited to Black, White, Hispanic, and "Other", which does not properly represent the full complexity of patient identity. Second, the method by which the NCDB collects data introduces bias into its sample population. The NCDB is a hospital-based registry, meaning that only patients who receive cancer diagnosis or treatment at a hospital accredited by the American College of Surgeons Commission on Cancer are included (28). Mallin *et al.* found that between 2012 and 2014, only 58% of PCa

diagnoses were captured by the NCDB (29). Due to this sampling technique, the NCDB database has previously been found to underrepresent low-grade PCa as well as racial and ethnic minorities (30). Other study limitations include its retrospective design, which limits extrapolation to current patient demographics, and limits the ability to establish causal relationships between the variables. The study is also limited by the inability to control for changes in patient comorbidities during the study period.

Other study limitations include its retrospective design, which limits extrapolation to current patient demographics, and limits the ability to establish causal relationships between the variables. Our study is also limited by the inability to control for changes in patient comorbidities during the study period. However, our findings concerning the relationship between "D" recommendation and increased mPCa rates for NH White and Black men are consistent with previous work that used the more inclusive Surveillance, Epidemiology, and End Results (SEER) database (31). Another limitation is that measures of education and income were based on aggregated data from ZIP code of residence, rather than being ascertained from individual patients. Although ZIP code aggregation is known to incorporate bias, this statistical method is frequently used in urology literature when an alternative is not available (32-34).

It is important to note that in 2018 the USPSTF revised its 2012 guidance to make PSA screening for men ages 55 to 69 years a category "C" recommendation, with PSA screening for men over 70 remained a category "D" recommendation (35). This screening recommendation revision is outside the bounds of our study period, but represents an important topic of future analysis.

Conclusions

Significant racial, ethnic, and socioeconomic disparities exist for patients who are diagnosed with mPCa at presentation. Since the USPSTF grade "D" recommendation against PSA screening, the percentage of mPCa at diagnosis has increased disproportionately in NH Black and Hispanic populations.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-24-90/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was exempt from ethical review given minimal risk with the NCDB.

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