Original Article

Abrogation of Survival Disparity Between Black and White Individuals After the USPSTF's 2012 Prostate-Specific Antigen–Based Prostate Cancer Screening Recommendation

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BACKGROUND: In May 2012, the US Preventive Services Task Force (USPSTF) recommended against prostate-specific antigen (PSA)–based screening for prostate cancer (PCa), assigning it a grade D. This decision then was modified in 2018 to a grade C for men aged 55 to 69 years. The authors hypothesized that changes in screening practices would reduce survival outcomes for both Black and White men but maintain racial discrepancies in outcomes. **METHODS:** Using the Surveillance, Epidemiology, and End Results database, the authors examined PCa-specific survival based on race and year of diagnosis. The period between January 2010 and December 2012 was categorized as the pre-USPSTF era, whereas the period between January 2014 and December 2016 was classified as the post-USPSTF era. The year 2013 was considered the transition year and was excluded from the analysis. **RESULTS:** A total of 49,388 men were identified in the pre-USPSTF era who were diagnosed with PCa, approximately 83.7% of whom were White and 16.3% of whom were Black. In the post-USPSTF era, a total of 41,829 men were diagnosed with PCa, approximately 82.7% of whom were White and 17.3% of whom were Black. When compared with the pre-USPSTF era, men diagnosed in the post-USPSTF era were found to have more adverse clinical features. In the pre-USPSTF era, White men were less likely to die of PCa than Black men. This survival disparity between White and Black men was no longer observed in the post-USPSTF era. **CONCLUSIONS:** In men diagnosed with PCa between 2014 and 2016, a survival disparity between White and Black men was not observed due to a decrease in survival among White men while the survival of Black men remained steady. ***Cancer* 2020;126:5114-5123**. © *2020 American Cancer Society*.

KEYWORDS: prostate cancer, prostate-specific antigen, racial disparity, screening, Surveillance, Epidemiology, and End Results (SEER).

INTRODUCTION

There is a wide disparity in prostate cancer (PCa) outcomes between White and Black men. In 2019, it was reported that, compared with White men, Black men have a 1.75-fold higher incidence and 2.20-fold higher mortality.[1] Proposed explanations for such differences include both biology and socioeconomics. For example, divergent androgen signaling involving *SRD5A2*, TA repeat alleles, androgen synthesis, CYP17, androgen deactivation, CYP3A4, AR, and CAG repeats all have been proposed as contributing factors because higher levels of free testosterone have been reported in Black compared with White men.[2] Similarly, based on a limited sample size, various growth factors and apoptosis-related proteins such as IGF-1, EGFR, EphB2, BCL-2, and MDM2; inflammation; and various cytokines also have been implicated in the racial disparities noted in PCa.[3-7] In contrast, some have pointed to socioeconomic factors such as unequal access and differences in attitudes toward screening.[8-10] Indeed, it recently was reported that when various socioeconomic factors were adjusted, disparities in PCa outcomes between White and Black men no longer exist.[11,12] Accordingly, it is likely that the impact of any significant changes in PCa screening policies may vary based on race.

Since its introduction as a screening test for PCa in 1987, the effectiveness of prostate-specific antigen (PSA) has drawn considerable controversy, largely due to the possibility of overdiagnosis and overtreatment of PCa.[13] Studies from the European Randomised study of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial found overdiagnosis rates ranging from 17% to 50% of PCa cases detected using the PSA screening test.[14] Furthermore, Lu-Yao et al reported that the majority of deaths among men with PCa are due to non-PCa causes.[15] Treatments of PCa also carry the risk of death, cardiovascular events, urinary incontinence,

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erectile dysfunction, and bowel dysfunction.[14] For example, although radical prostatectomy is considered a definitive procedure for the treatment of PCa, approximately 7% of patients who undergo the procedure experienced major medical or surgical complications, with 0.29% dying within 30 days of surgery based on data from trials and cohort studies.[16]

Regardless, the adoption of PSA screening has coincided with considerable improvements in mortality rates and features of PCa at the time of presentation, with PCa mortality rates in the United States declining by nearly 30% in the 1990s. Etzioni et al found that the stage shift induced by PSA screening was responsible for 45% to 70% of this decline.[17] The ERSPC study reported that PSA screening was responsible for a reduction in PCa mortality of 27%.[18] Likewise, van Leeuwen et al found that PSA screening led to reductions in PCa metastases of 53% after 8.5 years of observation.[19]

In May 2012, the US Preventive Services Task Force (USPSTF) recommended against PSA-based screening for PCa, assigning it a grade D.[14] This guideline was based in part on the PLCO trial, which was conducted in the United States and reported no evidence of a mortality benefit with PSA testing.[20] However, after accounting for differential screening intensity between the control and intervention groups, Tsodikov et al found that the PLCO trial actually demonstrated a 27% to 32% lower risk of PCa mortality with PSA screening.[21]

Thus, in May 2018, the USPSTF upgraded its recommendation for PSA-based screening for men aged 55 to 69 years to a grade C.[22] Nevertheless, the USPSTF's guidelines discouraging PCa screening have had lasting effects on screening rates and features of PCa at the time of presentation. Studies have demonstrated that between 2010 and 2013, screening rates for men aged 50 to 59 years, aged 60 to 74 years, and aged ≥75 years decreased from 33.2% to 24.8%, 51.2% to 43.6%, and 43.9% to 37.1%, respectively.[23] Similarly, Ahlering et al reported a 22.6% reduction in surgical volume, increases in the median PSA from 5.1 ng/mL to 5.8 ng/mL, and increases in mean age at diagnosis from 60.8 years to 62.0 years.[24] They found that the percentage of low-grade Gleason score (GS) 3+3 cancers decreased from 30.2% to 17.1%, whereas that of the high-grade GS ≥8 cancers increased from 8.4% to 13.5%.

Although several studies have demonstrated increases in more aggressive features of PCa at the time of presentation,[25,26] to our knowledge, there have been no studies examining the effect of the USPSTF's 2012 PCa screening recommendation on racial disparities, specifically survival differences between White and Black men. We hypothesized that survival outcomes for both Black and White men would decrease due to changes in screening practices, but that the racial discrepancies in outcomes would persist. Therefore, we investigated how the USPSTF's recommendations may have affected survival differences between Black and White men diagnosed with PCa.

MATERIALS AND METHODS

Data Sources

The study cohort consisted of patients from the Surveillance, Epidemiology, and End Results (SEER) program, which collects cancer incidence data from population-based cancer registries across the United States using the SEER*Stat database. SEER registries record data concerning patient demographics, primary tumor site, tumor morphology, stage of disease at the time of diagnosis, first course of treatment, and follow-up. Information regarding incident cancer cases was available from the SEER 9 registry (1975-2016), which covers approximately 9.4% of the US population. The following geographic areas were covered: San Francisco-Oakland standard metropolitan statistical area, Connecticut, Detroit (Metropolitan), Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, and Atlanta.

Study Variables

Information regarding the following study variables was extracted for each population subset: age, PSA level, clinical GS, pathologic GS, and summary stage. Summary stage incorporates the most precise clinical and pathologic documentation of the extent of PCa.

Statistical Analysis

The primary study outcome was PCa-specific survival based on race and the diagnostic time period. Secondary study outcomes examined changes in the distribution of age, PSA, clinical GS, pathologic GS, and summary stage over time. PCa-specific survival for each diagnostic time period was measured using the Kaplan-Meier method. Disparities between the races within each time period were analyzed using the log-rank test and Cox proportional hazards model. Given that the maximum follow-up for patients diagnosed in 2016 was 36 months, the temporal endpoints for both survival curves were capped at 36 months. Differences in the distribution of patients over time by PSA, clinical GS, pathologic GS, and summary stage were analyzed using the Pearson chi-square test.

TABLE 1. Patient Characteristics in the Pre-USPSTF Era Versus the Post-USPSTF Era

	Pre-USPSTF Era (2010-2012) No. (%)	Post-USPSTF Era (2014-2016) No. (%)	*P*
Sample size	49,388	41,829	
White	41,378	34,607	
Black	8010	7222	
PCa-specific mortality	1895 (3.8)	1173 (2.8)	
Median age, y	65	66	<.001[a]
PSA, ng/mL			<.001[b]
Median	6.3	7.3	
≤10	31,636 (74.4)	24,675 (66.9)	
10 < PSA ≤20	5867 (13.8)	6195 (16.8)	
>20	5020 (11.8)	6005 (16.3)	
Total	42,523	36,875	
Clinical Gleason score			<.001[b]
≤3+3	19,505 (42.5)	12,819 (33.2)	
3+4	12,943 (28.2)	11,245 (29.1)	
4+3	5695 (12.4)	5687 (14.7)	
≥8	7788 (17.0)	8882 (23.0)	
Total	45,931	38,633	
Pathologic Gleason score			<.001[b]
≤3+3	4384 (26.4)	1812 (14.1)	
3+4	7778 (46.8)	6218 (48.4)	
4+3	2765 (16.6)	2771 (21.6)	
≥8	1709 (10.3)	2042 (15.9)	
Total	16,636	12,843	
Stage			<.001[b]
Localized	39,625 (81.5)	31,065 (75.9)	
Regional	6492 (13.4)	6576 (16.1)	
Distant	2497 (5.1)	3278 (8.0)	
Total	48,614	40,919	

Abbreviations: PCa, prostate cancer; PSA, prostate-specific antigen; USPSTF, US Preventive Services Task Force.
[a]Derived using the Wilcoxon rank sum test.
[b]Derived using the Pearson chi-square correlation.

The period between January 2010 and December 2012 was designated as the pre-USPSTF era, whereas the period between January 2014 and December 2016 was designated as the post-USPSTF era. A 1-year buffer in 2013 between the 2 eras accounted for the time it would take for the recommendations to take effect. All analyses were conducted using Stata/SE 15.0 statistical software. A *P* value ≤.05 was considered to be statistically significant for all analyses.

RESULTS

Significant Decrease in Survival Correlates With Grade and Stage Migration in the Post-USPSTF Era

The study population was composed of 91,217 patients who were diagnosed with PCa from January 2010 to December 2012 and January 2014 to December 2016 based on the SEER cause-specific death classification for PCa. Because PCa screening was discouraged in 2012, the total number of new PCa cases diagnosed decreased from the pre-USPSTF era to the post-USPSTF era (49,388 cases to 41,829 cases) (Table 1). PSA at the time of diagnosis tended to be higher after the recommendation against PSA-based PCa screening, because the median level in the pre-USPSTF and post-USPSTF eras were 6.3 ng/mL and 7.3 ng/ml, respectively ($P < .001$). The lower incidence of PCa in the post-USPSTF era was accompanied by a decrease and an increase in the percentage of low-risk and more aggressive PCa, respectively. Specifically, between the 2 eras, the number of men with clinical GS 6 (3+3) disease decreased from 19,505 (42.5%) to 12,819 (33.2%), whereas the number of men with tumors of GS ≥8 increased from 7788 (17%) to 8882 (23%) ($P < .001$). Likewise, among men who chose to undergo radical prostatectomy over the same time periods, the number of men with a pathologic GS of 6 decreased from 4384 (26.4%) to 1812 (14.1%), whereas the number of men with a GS of 8 increased from 1709 (10.3%) to 2042 (15.9%) ($P < .001$). Finally, the number of men with localized disease at the time of diagnosis decreased from 39,625 (81.5%) to 31,065 (75.9%), whereas that of men with distant disease increased from 2497 (5.1%) to 3278 (8%) ($P < .001$) between the 2 eras. When cause-specific survival was analyzed between the 2 eras, a significantly shorter survival was detected in the post-USPSTF era ($P < .0001$, log-rank test) (Fig. 1).

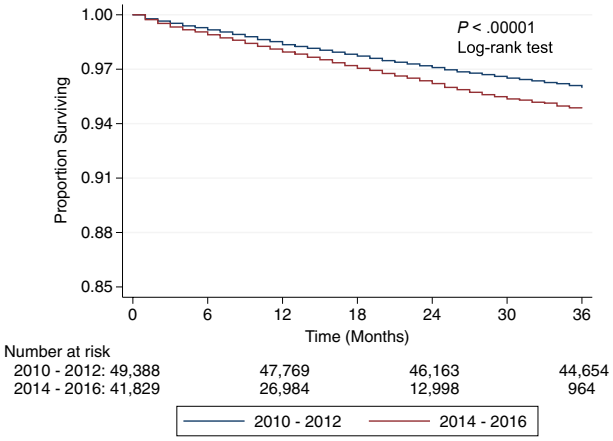

FIGURE 1. Prostate cancer–specific survival in the pre-US Preventive Services Task Force (USPSTF) (2010-2012) and post-USPSTF (2014-2016) eras. After the USPSTF's recommendation against prostate-specific antigen–based prostate cancer screening in 2012, prostate cancer–specific survival decreased significantly.

When factors associated with cause-specific survival were analyzed using the Cox proportional hazards model, era of diagnosis, age, PSA level, clinical GS, and stage of disease at the time of presentation were found to be significant. However, race was not found to be associated with death from PCa ($P = .0624$) (Table 2).

PCa Disparities in Survival Between Black and White Men Are No Longer Present in the Post-USPSTF Era

In the pre-USPSTF era, there were 41,378 White men and 8010 Black men diagnosed with PCa. The numbers during the post-USPSTF era were 34,607 and 7222, respectively, for White and Black men (Table 3). As expected, the median PSA for both White and Black men increased from the pre-USPSTF era to the post-USPSTF era (6.2 ng/mL to 7.2 ng/mL for White men and 6.9 ng/mL to 8.0 ng/mL for Black men). Distribution of the PSA level at the time of presentation for White and Black men demonstrated a significant change from the pre-USPSTF era to the post-USPSTF era ($P < .0001$ for both eras). When compared between the 2 groups, PSA distribution remained statistically significantly different in both eras ($P < .0001$ for both eras). However, the magnitude of the change in PSA for White and Black men from the pre-USPSTF era to the post-USPSTF era was not statistically significantly different ($P = .1007$, multinomial logistic regression with generalized logit function). The percentage of White men with a PSA level ≤10 ng/mL at the time of diagnosis decreased from 75.6% in the pre-USPSTF era to 68.1% in the post-USPSTF era. For Black men, the change in the percentage of men with a PSA level ≤10 ng/mL during the same time periods was 68.4% to 61.1%. Conversely, the percentages of White and Black men with a PSA level >20 ng/mL increased in the post-USPSTF era from 11% to 15.2% and 15.9% to 21.5%, respectively.

With respect to the clinical distribution of GS, both White and Black men demonstrated a significant difference between the pre-USPSTF and post-USPSTF eras ($P < .0001$ for both eras). For example, the percentage of White men with low-risk (GS 6) disease decreased from 43.4% to 34%. With regard to Black men, the percentage of patients with GS 6 PCa during the same periods decreased from 37.4% to 28.8%. In contrast, the percentages of White and Black men with high-risk disease (GS ≥8) increased from 16.9% to 22.9% and from 17.3% to 23.4%, respectively, when the 2 eras were analyzed. However, when the change in the distribution of clinical GS between the pre-USPSTF and post-USPSTF eras was compared between the 2 races, the difference was not statistically significant ($P = .2844$, multinomial logistic regression with generalized logit function).

With regard to pathologic GS distribution, a significant difference between the 2 eras was observed for both races ($P < .0001$ for both eras). Between the pre-USPSTF and post-USPSTF eras, the percentage of White men with a pathologic GS of 6 decreased from 26.5% to 14.2%, whereas among Black men the percentage decreased from 25.3% to 13.5%. The percentage of White men with a pathologic GS ≥8 increased from 10.6% in the pre-USPSTF era to 16.3% in the post-USPSTF era. For Black men, the change in the number of individuals with pathologically high-risk PCa also increased between the 2 eras (from 8.3% to 13.6%). Again, the change in the distribution of the pathologic GS from the pre-USPSTF era to the post-USPSTF era between the 2 races was not found to be statistically significant ($P = .9631$, multinomial logistic regression with generalized logit function).

With regard to clinical stage at the time of presentation, both White and Black men demonstrated a significant change from the pre-USPSTF era to the post-USPSTF era ($P < .0001$ for both eras). In the pre-USPSTF era, the percentages of White and Black men presenting with regional and distant disease were 18.7% and 17.6%, respectively ($P = .024$). In comparison, in the post-USPSTF era, the percentages for White and Black men were 24.6% and 21.6%, respectively ($P < .0001$). When the change in the distribution of clinical stage between the pre-USPSTF and post-USPSTF eras was compared between the Black and White men, the difference

TABLE 2. Cox Proportional Hazards Analysis of Factors Associated With Prostate Cancer Cause-Specific Survival

	Sample Size (%)	HR (95% CI)	*P*
Era			
2010-2012 (pre-USPSTF)	49,388	1 (referent)	
2014-2016 (post-USPSTF)	41,829	1.312 (1.25-1.414)	<.0001
Age, y			
<55	9455 (10.37)	1 (referent)	
55-70	55,831 (61.21)	1.177 (0.99-1.40)	.061
>70	25,931 (28.43)	5.419 (4.58-6.41)	<.0001
Race			
White	75,985 (83.30)	1 (referent)	
Black	15,232 (16.70)	1.093 (1.00-1.20)	.0624
PSA, ng/mL			
≤10	56,311 (70.92)	1 (referent)	
10 < PSA ≤20	12,062 (15.19)	3.090 (2.60-3.67)	<.0001
>20	11,025 (13.89)	34.548 (30.80-38.75)	<.0001
Clinical Gleason score			
≤3+3	32,324 (38.22)	1 (referent)	
3+4	24,188 (28.60)	2.190 (1.72-2.80)	<.0001
4+3	11,382 (13.46)	6.629 (5.26-8.35)	<.0001
≥8	16,671 (19.71)	41.804 (34.42-50.78)	<.0001
Stage			
Localized	70,690 (78.95)	1 (referent)	
Regional	13,068 (14.60)	2.248 (1.92-2.63)	<.0001
Distant	5775 (6.45)	72.677 (66.08-79.93)	<.0001

Abbreviations: HR, hazard ratio; PSA, prostate-specific antigen; USPSTF, US Preventive Services Task Force.

TABLE 3. Characteristics of White and Black Men Diagnosed With PCa in the Pre-USPSTF and Post-USPSTF Eras

	White		Black		
	Pre-USPSTF (2010-2012) No. (%)	Post-USPSTF (2014-2016) No. (%)	Pre-USPSTF (2010-2012) No. (%)	Post-USPSTF (2014-2016) No. (%)	*P*[a]
Sample size	41,378	34,607	8010	7222	
PCa-specific mortality	1524 (3.68%)	985 (2.85%)	353 (4.4%)	188 (2.6%)	
Median age, y	66	66	63	63	
PSA, ng/mL					.1423
Median	6.2	7.2	6.9	8.0	
≤10	26,760 (75.7)	20,767 (68.1)	4876 (68.4)	3908 (61.2)	
10 < PSA ≤20	4747 (13.4)	5079 (16.7)	1120 (15.7)	1116 (17.4)	
>20	3884 (11.0)	4633 (15.2)	1136 (15.9)	1372 (21.4)	
Total	35,391	30,479	7132	6396	
Clinical Gleason score					.2844
≤3 + 3	16,739 (43.4)	10,902 (34.1)	2766 (37.4)	1917 (28.8)	
3+4	10,582 (27.5)	9164 (28.7)	2361 (31.9)	2081 (31.3)	
4+3	4705 (12.2)	4589 (14.4)	990 (13.4)	1098 (16.5)	
≥8	6511 (16.9)	7329 (22.9)	1277 (17.3)	1554 (23.4)	
Total	38,537	31,984	7394	6650	
Pathologic Gleason score					.9631
≤3 + 3	3844 (26.5)	1557 (14.2)	540 (25.3)	255 (13.5)	
3+4	6712 (46.3)	5237 (47.8)	1066 (50.0)	981 (51.8)	
4+3	2415 (16.6)	2372 (21.7)	350 (16.4)	399 (21.1)	
≥8	1531 (10.6)	1785 (16.3)	178 (8.3)	257 (13.6)	
Total	14,502	10,951	2134	1892	
Stage					<.0001
Localized	33,134 (81.3)	25,530 (75.4)	6491 (82.4)	5535 (78.4)	
Regional	5605 (13.8)	5683 (16.8)	887 (11.3)	893 (12.6)	
Distant	1999 (4.9)	2642 (7.8)	498 (6.3)	636 (9.0)	
Total	40,738	33,855	7876	7064	

Abbreviations: PCa, prostate cancer; PSA, prostate-specific antigen; USPSTF, US Preventive Services Task Force.
[a]Multinomial logistic regression with generalized logit function.

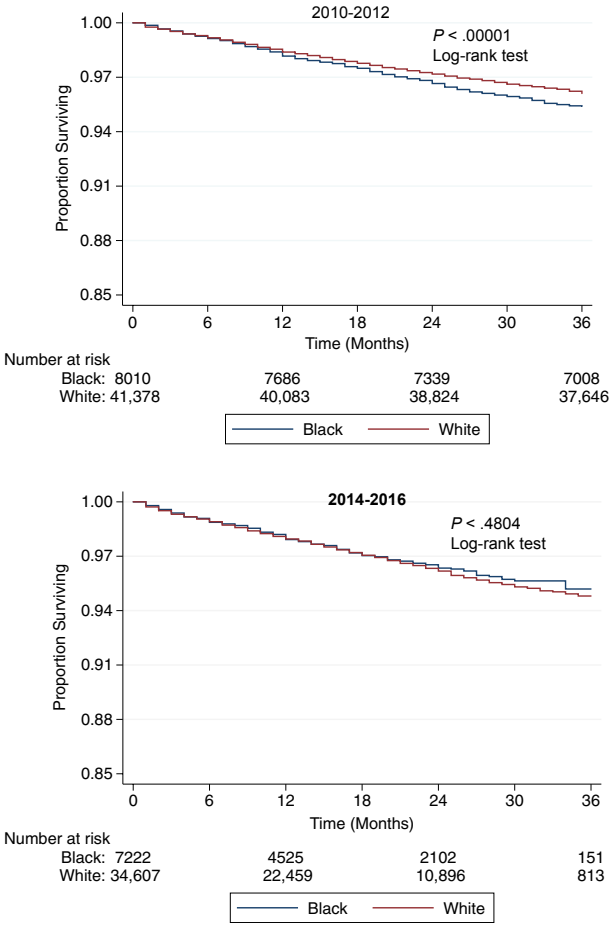

FIGURE 2. Prostate cancer–specific survival between Black and White men in the (*Top*) pre–US Preventive Services Task Force (USPSTF) and (*Bottom*) post-USPSTF eras. Compared with White men, Black men had a poorer survival in the pre-USPSTF era but not in the post-USPSTF era.

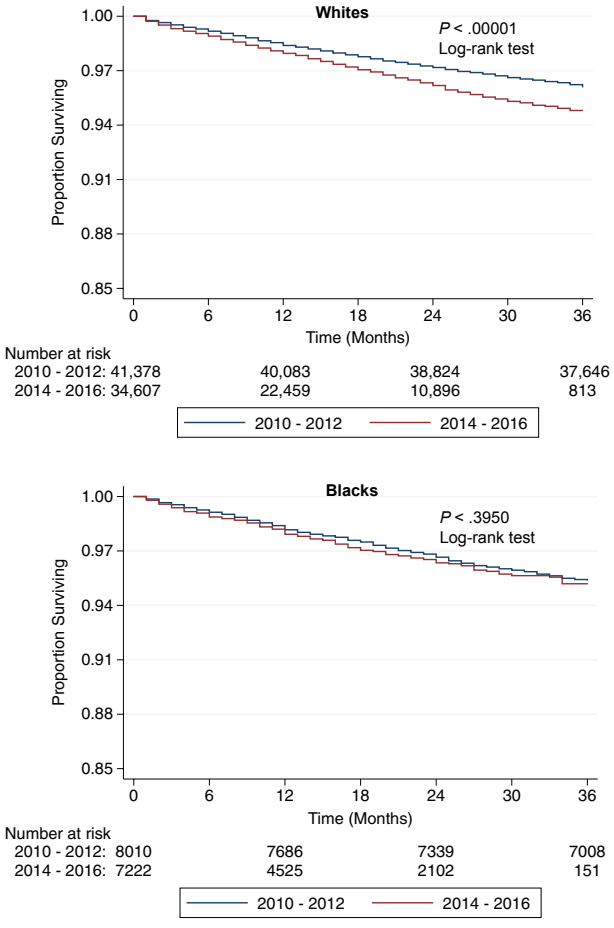

FIGURE 3. Prostate cancer–specific survival in the pre–US Preventive Services Task Force (USPSTF) and post-USPSTF eras between (*Top*) White patients and (*Bottom*) Black patients. White patients demonstrated a decrease in survival in the post-USPSTF era when compared with the pre-USPSTF era. In contrast, Black patients demonstrated no change in survival between the pre-USPSTF and post-USPSTF eras.

was found to be statistically significant ($P < .0001$, multinomial logistic regression with generalized logit function).

To determine the impact of the above changes on the survival disparities between White and Black men, we assessed cause-specific survival in the pre-USPSTF and post-USPSTF eras. During the pre-USPSTF era, Black men were found to have a significantly worse survival ($P < .0001$, log-rank test) (Fig. 2). However, the disparity in survival between White and Black men was no longer observed in the post-USPSTF era ($P = .4804$, log-rank test). Comparing the same data within each race demonstrated that White men experienced a significant decrease in survival whereas Black men did not ($P < .0001$ for White men and $P = .3960$ for Black men, log-rank test) (Fig. 3). A multivariate analysis was performed to determine which factors were associated with cause-specific survival in both eras (Tables 4 and 5). The results demonstrated that age, serum PSA level, clinical GS, and stage of disease at the time of presentation correlated with survival in both eras. However, race was found to be associated with survival only in the pre-USPSTF era ($P = .4781$ vs $.0045$).

Survival Disparities Between Black and White Men Are Not Present in Men Aged ≥75 Years in the Pre-USPSTF Era

The absence of a survival disparity between White and Black men in the post-USPSTF era was surprising and suggested that the superior survival observed in White men with PCa in the pre-USPSTF era may be due to a difference in PCa screening intensity. To assess this possibility, we examined the outcomes between White and Black men among individuals aged ≥75 years in the

TABLE 4. Cox Proportional Hazards Analysis of Factors Associated With PCa Cause-Specific Survival in the Pre-USPSTF Era: 2010 to 2012

	Sample Size No. (%)	HR (95% CI)	*P*
Age, y			
<55	5508 (11.15)	1 (referent)	
55-70	30,151 (61.05)	1.0166 (0.83-1.24)	.8715
>70	13,729 (27.80)	4.470 (3.69-5.42)	<.0001
Race			
White	41,378 (83.78)	1 (referent)	
Black	8010 (16.22)	1.185 (1.06-1.33)	.0045
PSA, ng/mL			
≤10	31,636 (74.40)	1 (referent)	
10 < PSA ≤20	5867 (13.80)	3.395 (2.75-4.19)	<.0001
>20	5020 (11.81)	37.558 (32.60-43.27)	<.0001
Clinical Gleason score			
≤3+3	19,505 (42.47)	1 (referent)	
3+4	12,943 (28.18)	2.131 (1.66-2.78)	<.0001
4+3	5695 (12.40)	2.595 (2.29-2.94)	<.0001
≥8	7788 (16.96)	41.033 (33.29-50.58)	<.0001
Stage			
Localized	39,625 (81.51)	1 (referent)	
Regional	6492 (13.35)	2.264 (1.87-2.74)	<.0001
Distant	2497 (5.14)	76.350 (68.10-85.60)	<.0001

Abbreviations: HR, hazard ratio; PCa, prostate cancer; PSA, prostate-specific antigen; USPSTF, US Preventive Services Task Force.

TABLE 5. Cox Proportional Hazards Analysis of Factors Associated With PCa Cause-Specific Survival in the Post-USPSTF Era: 2014 to 2016

	Sample Size No. (%)	HR (95% CI)	*P*
Age, y			
<55	3947 (9.44)	1 (referent)	
55-70	25,680 (61.39)	1.687 (1.18-2.41)	.0020
>70	12,202 (29.17)	8.4367 (5.96-11.95)	<.0001
Race			
White	34,607 (82.73)	1 (referent)	
Black	7222 (17.27)	0.9454353 (0.80-1.10)	.4781
PSA, ng/mL			
≤10	24,675 (66.92)	1 (referent)	
10 < PSA ≤20	6195 (16.80)	2.494 (1.85-3.36)	<.0001
>20	6005 (16.28)	29.074 (23.89-35.38)	<.0001
Clinical Gleason score			
≤3+3	12,819 (33.18)	1 (referent)	
3+4	11,245 (29.11)	2.645 (1.41-4.96)	.0015
4+3	5687 (14.72)	6.430 (3.48-11.87)	<.0001
≥8	8883 (22.99)	49.255 (28.92-83.86)	<.0001
Stage			
Localized	31,065 (75.92)	1 (referent)	
Regional	6576 (16.07)	2.182 (1.65-2.89)	<.0001
Distant	3278 (8.01)	66.759 (56.21-79.29)	<.0001

Abbreviations: HR, hazard ratio; PCa, prostate cancer; PSA, prostate-specific antigen; USPSTF, US Preventive Services Task Force.

TABLE 6. Characteristics of White and Black Men Aged ≥75 Years Who Were Diagnosed With PCa in the Pre-USPSTF Era

	White No. (%)	Black No. (%)	*P*
Sample size	7234	855	
PCa-specific mortality	849 (11.7)	114 (13.3)	
Median age, y	79	78	<.001[a]
PSA, ng/mL			.002[b]
Median	9.5	11	
4 < PSA ≤10	2886 (51.3)	319 (46.6)	
10 < PSA ≤20	1144 (20.3)	144 (21.1)	
>20	1494 (26.6)	221 (32.3)	
Total	5624	684	
Clinical Gleason score			.143[b]
≤3 + 3	1606 (26.4)	184 (26.2)	
3+4	1433 (23.6)	192 (27.4)	
4+3	982 (16.2)	104 (14.8)	
≥8	2052 (33.8)	221 (31.5)	
Total	6073	701	
Stage			.070[b]
Localized	5594 (80.9)	652 (81.3)	
Regional	420 (6.1)	34 (4.2)	
Distant	898 (13.0)	116 (14.5)	
Total	6912	802	

Abbreviations: PCa, prostate cancer; PSA, prostate-specific antigen; USPSTF, US Preventive Services Task Force.
[a]Derived using the Wilcoxon rank sum test.
[b]Derived using the Pearson chi-square correlation.

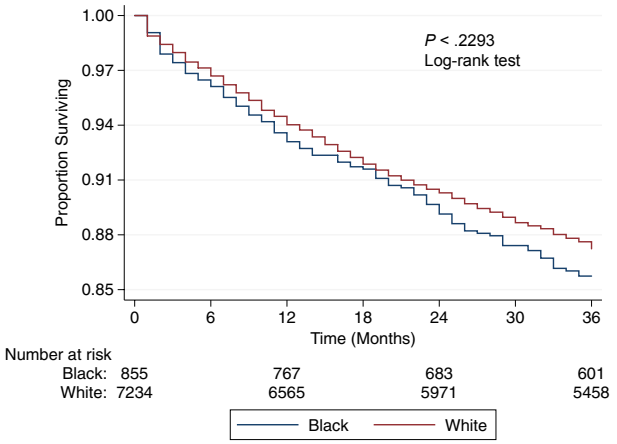

FIGURE 4. Prostate cancer–specific survival in the pre-US Preventive Services Task Force (USPSTF) era between White and Black patients aged ≥75 years. Survival was not found to be significantly different between the 2 groups.

pre-USPSTF era (2010-2012) because the recommendation against PSA-based PCa screening in this age group was made in 2008. The total number of men in this category was 7234 White men and 855 Black men (Table 6). PSA distribution between men in the 2 racial groups who were aged ≥75 years was found to be statistically significantly different ($P = .002$). Percentages of White and Black men with a PSA level ≤10 ng/mL were 53.1% and

46.6%, respectively. However, the difference in clinical GS distribution between White and Black men was not statistically significant ($P = .143$). Due to a low sample size in men aged ≥75 years who opted for radical prostatectomy (only 22 of whom were Black), pathologic GS was not analyzed. Stage of disease at the time of presentation also was found to be similar between the 2 racial groups if the age was ≥75 years in the pre-USPSTF era ($P = .070$). Finally, cause-specific survival between White and Black men aged ≥75 years was not significantly different in the pre-USPSTF era ($P = .2293$, log-rank test) (Fig. 4).

DISCUSSION

Results of the current study found multiple significant changes in the epidemiology of PCa between the pre-USPSTF and post-USPSTF eras. As expected, there was a significant shift toward the diagnosis of more aggressive PCa after the USPSTF recommendation against PSA-based PCa screening in 2012. However, this shift toward a higher risk disease coincided with a decreased cause-specific survival for White men but not Black men. Collectively, the findings of the current study pose significant questions for PCa screening and PCa disparities between White and Black men.

The observation that there was a migration toward disease of a higher grade and stage after the USPSTF's grade D recommendation for PSA-based PCa screening has been proposed by multiple investigators.[24-26] In the current study, the percentage of men with low-risk disease (GS 6) and localized disease decreased dramatically from the pre-USPSTF to the post-USPSTF era. Simultaneously, a significant decrease in cause-specific survival for men newly diagnosed with PCa was found in the years after the USPSTF's recommendation against using PSA in 2012. Such temporal changes in PCa survival after diagnosis were confirmed to be independent of age, PSA level, clinical GS, and stage of disease at the time of presentation. Because the temporal trend toward decreasing PCa mortality over the last decade appears to have stopped recently, it is reasonable to conclude that the USPSTF's 2012 recommendation has had an adverse effect on PCa outcomes.

The most important observation of the current study was that the USPSTF's recommendation against PSA-based PCa screening in 2012 may have had an unintended effect on PCa survival disparities between White and Black men. Specifically, the disparity in cause-specific survival between White and Black men that was noted in the pre-USPSTF era was not observed in the post-USPSTF era. However, the abrogation of this disparity was not due to an increase in survival for Black men with PCa but rather was the result of decreased survival for the White cohort. A detailed analysis of changes in the racial differences regarding serum PSA, clinical GS, pathologic GS, and the distribution of stage of disease at the time of presentation between the 2 eras using multinomial logistic regression with generalized logit function demonstrated that only change in stage of disease was statistically significantly different ($P < .0001$) (Table 3). Specifically, the percentage of White men with regional and distant disease at the time of diagnosis increased from 18.7% to 24.6% between the pre-USPSTF and post-USPSTF eras. In comparison, the change among Black men was from 17.6% to 21.6%. Moreover, as shown in Tables 4 and 5, the hazard ratios for regional and distant stages of disease were 2.264 and 76.350, respectively, in the pre-USPSTF era and 2.182 and 66.759, respectively, in the post-USPSTF era ($P < .0001$ for all). Taken together, the decreased survival noted among White men in the post-USPSTF era was explained, at least in part, by the increased percentage of regional and/or distant disease.

To the best of our knowledge, the precise explanation for the decreased survival in White men in the post-USPSTF era is not clear. However, because race was independent of standard clinical variables (serum PSA, clinical GS, and stage of disease) in predicting survival only in the pre-USPSTF era, it is likely that there was a nonbiologic factor that disappeared after the USPSTF's 2012 recommendation. In this regard, a provocative hypothesis is that the screening intensity for White men in the pre-USPSTF era was higher than that of Black men. As a result, more White men may have benefitted from an early definitive intervention. Indeed, this proposed difference in screening intensity between White and Black men may be a surrogate of access to care and health care insurance status. Such a concept is supported by the observation that after the USPSTF's 2008 recommendation against PCa screening in men aged ≥75 years, the odds ratio of having PCa screening decreased in White men but not in Black men.[23] Notwithstanding, the abrogation of disparities in survival outcomes in the post-USPSTF era suggests that PSA-based PCa screening may have benefitted White men more than Black men. This concept is consistent with the observation that the PCa survival disparity between White and Black men aged ≥75 years was not present in the pre-USPSTF era examined in this study (2010-2012); in this age group, PSA-based PCa screening was discouraged in 2008. Regardless of

the underlying explanation, the observation from the current study raises a serious concern in that the disparity in outcome noted between White and Black men appeared to resolve in the post-USPSTF era by downward leveling of the outcome in White men rather than an improvement in outcomes in Black men.

The abrogation of survival disparities after the recommendation against PSA-based PCa screening also shed additional light on potential reasons for racial disparities in PCa. Specifically, understanding the extent to which socioeconomic factors and biology each play a role in mortality among Black men is critical to understanding the worse PCa outcomes observed in Black men. The results of the current study have suggested that racial disparities in PCa-specific survival are significantly affected by socioeconomics because a change in PCa screening policy was associated with a significant impact on PCa outcomes between White and Black men. This concept is consistent with a recent report in which PCa outcomes were found to be similar between White and Black men when adjusted for socioeconomic factors in an equal-access setting.[11,12] Therefore, because it has been reported that the outcomes of radical prostatectomy have wide variations across high-volume tertiary centers,[27] we contend that the optimal approach to addressing PCa disparities in Black men is through community education and identifying and addressing critical socioeconomic disadvantages in Black individuals.

The distribution of the clinical GS observed in the current study suggests the possibility that the opportunity to make a difference in PCa outcomes may lie with patients with low-risk and intermediate-risk disease rather than those with high-risk disease. Indeed, due to the near-negligible metastatic rate noted in patients with GS 6 PCa, active surveillance currently is the recommended treatment in men with low-risk PCa. According to this concept, a meaningful impact on outcome is made when the disease is detected in men with high-risk disease using screening. However, the data from the current study demonstrated that the percentage of men who present with high-risk PCa of GS $\geq$8 essentially was the same between White and Black men in both the pre-USPSTF and post-USPSTF eras (16.9% vs 17.2% in the pre-USPSTF era and 22.9% vs 23.4% in the post-USPSTF era). Thus, it is likely that there are low-risk patients who may benefit from definitive therapy and that identifying these men early may be an effective strategy toward improving PCa outcomes.

The strength of the current study was its use of a population-based database. Therefore, the results represented real-world practice patterns, trends, and outcomes that cannot be ascertained from a randomized controlled trial. Nevertheless, when interpreting the current study results, the following limitations should be considered. First, the SEER database is an observational cohort and as such, potential biases such as differing preferences in treatment choice cannot be removed. Second, the main endpoint of the current study was the cause-specific survival over a 3-year period. In assessing PCa outcomes, this is a very short follow-up period. Nevertheless, the observation that the disparity existed in one period but not the other supports the validity of the current analysis. Last, because SEER does not contain PCa screening data, to the best of our knowledge, the magnitude of the impact of the USPSTF's 2012 recommendation on the PCa screening rate between White and Black men is not clear at the current time. Indeed, not having actual screening data with which to demonstrate a direct cause-and-effect relationship was a main limitation of the current study. Accordingly, the current study should be considered to be a hypothesis-generating investigation and additional studies using different population-based databases should be performed to confirm the results.

Conclusions

Racial disparities in PCa-specific survival remain a challenge. The results of the current study suggested that a carefully developed and disseminated PCa screening strategy may be the optimal approach to improving PCa outcomes in both White and Black men.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Isaac E. Kim Jr: Conception of the study, data analysis, and drafting and editing the article. **Thomas L. Jang:** Data analysis and drafting and editing the article. **Sinae Kim:** Statistics, data analysis, and drafting and editing the article. **Parth K. Modi:** Data analysis and drafting and editing the article. **Eric A. Singer:** Data analysis and drafting and editing the article. **Sammy E. Elsamra:** Drafting and editing the article. **Isaac Yi Kim:** Supervision of the entire project, conception of the study, drafting and editing the article, and funding.

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