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Article

Evaluating Prostate-Specific Antigen Screening for Young African American Men With Cancer

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Abstract

Background: Despite higher risks associated with prostate cancer, young African American men are poorly represented in prostate-specific antigen (PSA) trials, which limits proper evidence-based guidance. We evaluated the impact of PSA screening, alongside primary care provider utilization, on prostate cancer outcomes for these patients. **Methods:** We identified African American men aged 40-55 years, diagnosed with prostate cancer between 2004 and 2017 within the Veterans Health Administration. Inverse probability of treatment-weighted propensity scores were used in multivariable models to assess PSA screening on PSA levels higher than 20, Gleason score of 8 or higher, and metastatic disease at diagnosis. Lead-time adjusted Fine-Gray regression evaluated PSA screening on prostate cancer–specific mortality (PCSM), with noncancer death as competing events. All statistical tests were 2-sided. **Results:** The cohort included 4726 patients. Mean age was 51.8 years, with 84-month median follow-up. There were 1057 (22.4%) with no PSA screening prior to diagnosis. Compared with no screening, PSA screening was associated with statistically significantly reduced odds of PSA levels higher than 20 (odds ratio [OR] = 0.56, 95% confidence interval [CI] = 0.49 to 0.63; $P < .001$), Gleason score of 8 or higher (OR = 0.78, 95% CI = 0.69 to 0.88; $P < .001$), and metastatic disease at diagnosis (OR = 0.50, 95% CI = 0.39 to 0.64; $P < .001$), and decreased PCSM (subdistribution hazard ratio = 0.52, 95% CI = 0.36 to 0.76; $P < .001$). Primary care provider visits displayed similar effects. **Conclusions:** Among young African American men diagnosed with prostate cancer, PSA screening was associated with statistically significantly lower risk of PSA levels higher than 20, Gleason score of 8 or higher, and metastatic disease at diagnosis and statistically significantly reduced risk of PCSM. However, the retrospective design limits precise estimation of screening effects. Prospective studies are needed to validate these findings.

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Prostate cancer is the leading cause of cancer among African American men, representing the second leading cause of cancer-related deaths (1). African American men are more likely to develop prostate cancer, be diagnosed younger, and die from their disease compared with non-Hispanic White (NHW) men (1). Despite these disparities, African American men remain underrepresented in cancer trials. Studies have continued to identify disproportionately low percentages of African American participants (2,3). The Prostate, Lung, Colorectal, and Ovarian (PLCO) and European Randomized Study of Screening for Prostate Cancer (ERSPC) represent 2 landmark trials evaluating prostate-specific antigen (PSA) screening, yet the majority of participants were NHW men. No race-specific reporting is available for the ERSPC trial, and only 4.4% of PLCO trial participants were African American (4,5). Neither trial had participants younger than age 55 years.

Most PSA screening guidelines are based on these 2 trials, with many endorsing shared decision making beginning at age

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40 years for high-risk patients, including African American men (6-8). Many of these recommendations categorize African American men into higher risk groups that may benefit from earlier screening. However, neither the PLCO or ERSPC trial provides sufficient evidence surrounding PSA guidance for African American men between ages 40 and 55 years, and current PSA screening research for this patient population is limited. The lack of evidence has led to discordant recommendations across medical societies. For African American men younger than 55 years, the US Preventive Task Force does not recommend screening, the American Urological Association suggests shared decision making, and the National Comprehensive Cancer Network endorses shared decision making surrounding annual PSA screening. Because of these varied recommendations, young African American men represent an at-risk group that lacks proper PSA screening guidance. Additional research is needed to characterize its potential benefit for young African American men. Evaluating the role of PSA screening is important for controlling disease, reducing unnecessary procedures and costs for patients (9,10), and allowing clinicians to better discuss the risks and benefits of PSA screening. Moreover, investigating PSA screening within the overall architecture of primary care likely provides greater contextualization of its utility. Ultimately, a greater understanding of PSA screening for young African American men may partially alleviate racial disparities in prostate cancer outcomes for these patients.

Given the increased risk of prostate cancer within African American men, increased or earlier screening may be warranted. To provide better evidence for PSA screening recommendations in young African American men, we conducted a large retrospective analysis to evaluate the impact of PSA screening on prostate cancer outcomes within the Veterans' Health Administration. We identified a cohort of African American patients diagnosed with prostate cancer between the ages of 40 and 55 years and described the effects of PSA screening and primary care utilization on patients' disease severity at diagnosis and prostate cancer–specific mortality (PCSM).

Methods

Data Source

Given the paucity of young African American men in PSA screening trials, we present a nonstandard, retrospective estimation of PSA screening effect. Although we limited potential biases to the best of our ability, evaluating effectiveness of screening programs requires randomized trials.

The Veterans' Affairs Informatics and Computing Infrastructure (VINCI) provides patient-level electronic health record information for veterans within the Veterans Affairs (VA) health-care system. These include clinical notes, demographics, imaging, and operative and pathology reports. VINCI includes tumor registry information gathered by registrars at individual VA sites issued from the American College of Surgeons (11,12).

Study Population

The study population included African American men aged 40-55 years, diagnosed from 2004 to 2017. Year cutoffs represent years with complete variables, including verified PSA values. Patients with missing metastatic staging, survival follow-up, cause of death, or primary payer other than the VA were excluded (Supplementary Figure 1, available online). The following covariables were extracted: age at diagnosis, race, year of diagnosis, marital status, staging variables, Gleason score, PSA values at diagnosis, employment status, Charlson comorbidity scores, median bachelor education percentage, median income, body mass index, smoking history, and exposure to Agent Orange. PSA testing usually occurs during primary care physician (PCP) visits, and to control for possible confounding benefits of increased primary health-care utilization, PCP visit rate was included. Healthcare Common Procedure Coding System and Current Procedural Terminology codes were used to designate PSA screening or PCP visit and were additionally validated through documented PSA values within the Veterans Health Administration (Supplementary Methods, available online).

We calculated the percent of annual PSA screening and PCP visits within the 5 years before diagnosis, our prediagnostic observation period. This period started at age 40 years. If a patient received 1 or more PSA tests in each prediagnostic year, his annual PSA screening rate would be 100%. If a patient received 1 or more PSA tests in 4 out of 5 prediagnostic years, his rate would be 80%. This process was repeated for PCP visit rate.

Statistical Analysis

Table 1 summarizes patient demographic and clinical characteristics. Group comparisons were calculated with χ^2 for multigroup categorical variables, 2-proportion z test for proportion variables, and student t test for continuous variables. Patients were stratified into subgroups by PSA screening into "No previous screening" and "1 or more previous PSA." The proportion of PSA levels higher than 20, Gleason score of 8 or higher, and metastatic disease at diagnosis is shown in Figure 1. Difference of proportions was evaluated with 2-proportion z test. Cumulative incidence functions were fit (see Figure 2). Gray test evaluated difference in survival curves. Pearson test evaluated correlation between PSA screening and PCP visits. We selected severity of disease at diagnosis and PCSM as primary endpoints. High-risk features (PSA $>$ 20, Gleason $\geq$ 8) and metastatic disease were chosen as disease severity endpoints (Supplementary Methods, available online).

Observational studies are subject to potential bias introduced by systematic differences between intervention and control groups (13). To balance baseline covariates and more accurately estimate the average treatment effect of PSA screening on our disease severity endpoints, we calculated inverse probability of treatment weighted (IPTW) propensity scores with previous PSA screening as our intervention (14). Each patient's propensity score was calculated as a probability from a logistic regression model that included covariates that may affect PSA screening decisions, listed in Table 2. Separate IPTW-weighted logistic regressions were performed on our endpoints. Sensitivity analysis using a full-match algorithm was performed. Patients with unknown Gleason score or PSA at diagnosis were excluded from their respective models.

For PCSM, we fit multivariable Fine-Gray competing risk regression with noncancer death as a competing risk and PCSM as the endpoint. Lead-time bias remains an important consideration for survival analysis of screening studies and may occur when earlier detection advances survival time without impacting the natural history of the disease thereby exaggerating screening benefits (15). Draisma et al. (16) report estimated lead times controlling for PSA screening intensity and overdiagnosis. We adjusted survival times by accounting for lead time, reported in previous studies (17) (Supplementary Table 1,

Table 1. Demographic and clinical characteristics stratified by annual prostate-specific antigen (PSA) screening

Variable	Total	No previous screening	≥1 previous PSA test	*P*
Total, No. (%)	4726	1057 (22.4)	3669 (77.6)	—
Age, No. (%)	51.8 (3.0)	51.1 (3.5)	52.0 (2.9)	<.001[a]
40-45 y	207 (4.4)	84 (7.9)	123 (3.4)	
46-50 y	1117 (23.6)	312 (29.5)	805 (21.9)	
51-55 y	3402 (72.0)	661 (62.5)	2741 (74.7)	
Year diagnosed, No. (%)				<.001[a]
2004-2008	1799 (38.1)	465 (44.0)	1334 (36.4)	
2009-2012	1737 (36.8)	370 (35.0)	1367 (37.3)	
2013-2017	1190 (25.2)	222 (21.0)	968 (26.4)	
Clinical T stage, No. (%)				<.001[a]
T1	3718 (78.7)	801 (75.8)	2917 (79.5)	
T2	912 (19.3)	217 (20.5)	695 (18.9)	
T3	65 (1.4)	24 (2.3)	41 (1.1)	
T4	31 (0.7)	15 (1.4)	16 (0.4)	
Clinical N stage, No. (%)				.001[b]
N0	4657 (98.5)	1030 (97.4)	3627 (98.9)	
≥N1	69 (1.5)	27 (2.6)	42 (1.1)	
Clinical M stage, No. (%)				<.001[b]
M0	4597 (97.3)	996 (94.2)	3601 (98.1)	
M1	129 (2.7)	61 (5.8)	68 (1.9)	
Gleason score, No. (%)				<.001[a]
≤6	1838 (38.9)	330 (31.2)	1508 (41.1)	
7	2058 (43.5)	481 (45.5)	1577 (43.0)	
8	332 (7.0)	95 (9.0)	237 (6.5)	
≥9	255 (5.4)	85 (8.1)	170 (4.6)	
Unknown	243 (5.1)	66 (6.2)	177 (4.8)	
Charlson score, No. (%)				<.001[a]
0	2412 (51.0)	609 (57.6)	1803 (49.1)	
1	489 (10.3)	87 (8.2)	402 (11.0)	
≥2	1825 (38.6)	361 (34.2)	1464 (39.9)	
Employment, No. (%)				.001[b]
Yes	1498 (31.7)	292 (27.6)	1206 (32.9)	
No	3228 (68.3)	765 (72.4)	2463 (67.1)	
Marital status, No. (%)				<.001[b]
Single	3113 (65.9)	743 (70.3)	2372 (64.6)	
Married	1613 (34.1)	314 (29.7)	1297 (35.4)	
BMI, No. (%)				.03[a]
Underweight	169 (3.6)	34 (3.2)	135 (3.7)	
Normal weight	975 (20.6)	252 (23.8)	723 (19.7)	
Overweight	1489 (31.5)	326 (30.8)	1163 (31.7)	
Obese	2093 (44.3)	445 (42.1)	1648 (44.9)	
Smoking history, No. (%)				.26[a]
Yes	2849 (60.3)	660 (62.4)	2189 (59.7)	
No	1208 (25.6)	257 (24.3)	951 (25.9)	
Unknown	669 (14.2)	140 (13.2)	529 (14.4)	
Agent Orange exposure, No. (%)				.32[a]
Yes	109 (2.3)	30 (2.8)	79 (2.2)	
No	4531 (95.9)	1005 (95.1)	3526 (96.1)	
Unknown	86 (1.8)	22 (2.1)	64 (1.7)	
Mean PSA at diagnosis (SD)	13.1 (19.7)	19.7 (26.7)	11.2 (16.7)	<.001[c]
Median income[d, e] (SD)	45.2 (18.2)	44.6 (18.3)	45.4 (18.1)	.27[c]
Median bachelor[d] (SD), %	14.6 (7.1)	14.7 (7.2)	14.6 (7.1)	.65[c]
Mean PSA screening rate (SD), %	37.2 (29.0)	0 (0)	48.0 (25.2)	<.001[c]
Mean PCP visit rate (SD), %	64.1 (35.6)	28.4 (34.6)	74.4 (28.6)	<.001[c]

[a]*P* values were calculated with a 2-sided χ^2 for multigroup categorical variables. BMI = body mass index; PCP = primary care provider; — indicates no *P* value calculated for group stratification.

[b]*P* values were calculated with a 2-sided 2-proportion *z* test for proportion variables.

[c]*P* values were calculated with a 2-sided student *t* test for continuous variables.

[d]By zip code.

[e]Per $10 000.

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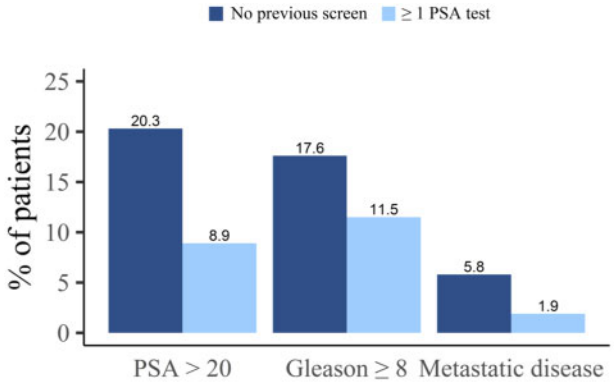

Figure 1. Prevalence of patients presenting with prostate-specific antigen (PSA) > 20, Gleason score ≥ 8, and metastatic disease at diagnosis, stratified by PSA screening status. Two-proportion z tests showed statistically significant difference in proportions for all panel comparisons ($P < .001$). All statistical tests were 2-sided.

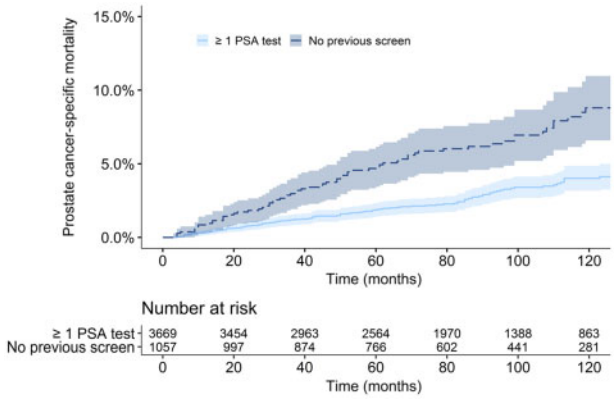

Figure 2. Cumulative incidence function (CIF) for prostate cancer–specific mortality (PCSM), stratified by prostate-specific antigen (PSA) screening status. There is a statistically significant difference between survival curves (Gray test, $P < .001$) for PSA screening cohorts. Shading indicates 95% confidence intervals. All statistical tests were 2-sided.

available online). This helped mitigate survival benefit attributed to lead time in screen-detected cancers. Similar to studies using lead-time adjusted survival analysis (18-21), we excluded staging covariates in our model. Including these with lead-time correction would likely obscure the effect of PSA screening by overcorrecting benefits from stage shift. In addition, screening programs are subject to overdiagnosis, which refers to capturing clinically irrelevant cases that increase the observed effect of screening (22). To estimate the effect of overdiagnosis, we identified patients alive at end of follow-up within the "1 or more previous PSA test" group, randomly removed 10%-50% of alive patients, and refit survival curves (Supplementary Table 2 and Supplementary Figure 2, available online). Table 2 summarizes our multivariable survival regression subdistribution hazard ratios (SHR). Secondary analysis using PSA screening rate in lieu of our binary screening variable evaluated the impact of increased PSA screening on PCSM. Supplementary Table 3 (available online) summarizes stage-stratified primary treatment for patients who received "No previous screening" and "1 or more previous PSA." All statistical tests were 2-sided, with a P value less than .05 considered statistically significant. Analyses were conducted with R, version 3.5.1 (R Core Team, Vienna, Austria) , survival (v3.2) and ggplot2 (v3.3.3). The study is covered by institutional review board #150169.

Results

Baseline Characteristics

Our cohort included 4726 patients. Mean age at diagnosis was 51.8 years with median follow-up of 84 months. Table 1 summarizes additional characteristics. Of the patients, 256 (5.4%) received annual PSA screenings and 1057 (22.4%) with no previous screening. PSA screening distribution was right skewed, with values ranging from 0% to 100% (Table 3). There were 1723 patients (36.5%) who underwent annual PCP visits and 483 (10.2%) with no previous PCP utilization. PCP visit distribution was left skewed, with values ranging from 0% to 100%. The correlation between PCP visits and PSA screening was 0.68 ($P < .001$). In general, patients with previous PSA screening were slightly older, presented with lower Gleason score and clinical staging, and had higher PCP visits than those without previous screening (Table 1).

Disease Severity at Diagnosis

At diagnosis, patients without previous PSA screening had higher proportions of PSA levels higher than 20 (20.3% vs 8.9%; $P < .001$), Gleason score of 8 or higher (17.6% vs 11.5%; $P < .001$), and metastatic disease (5.8% vs 1.9%; $P < .001$; Figure 1).

Utilizing a standardized mean difference of less than 0.1 as reference, covariates were well-balanced after IPTW-weighted balancing. On multivariable IPTW-weighted propensity score analysis, patients with 1 or more PSA screens had 44% reduced odds of PSA levels higher than 20 (odds ratio [OR] = 0.56, 95% confidence interval [CI] = 0.49 to 0.63; $P < .001$), 22% reduced odds of Gleason score of 8 or higher (OR = 0.78, 95% CI = 0.69 to 0.88; $P < .001$), and 50% reduced odds of metastatic disease at diagnosis (OR = 0.50, 95% CI = 0.39 to 0.64; $P < .001$) (Table 2). PCP utilization was also associated with statistically significantly decreased odds of PSA levels higher than 20 (OR = 0.72, 95% CI = 0.68 to 0.76; $P < .001$), Gleason score of 8 or higher (OR = 0.80, 95% CI = 0.75 to 0.85; $P < .001$), and metastatic disease at diagnosis (OR = 0.63, 95% CI = 0.57 to 0.70; $P < .001$). Across these multivariable models, higher Charlson index scores and smoking history were generally associated with higher disease severity at diagnosis (Table 2).

Prostate Cancer–Specific Mortality

Patients with previous PSA screening possessed lower cumulative incidence of PCSM at median follow-up of 84 months (2.4% vs 6.0%; $P < .001$). The cumulative incidence continues to diverge over time. At 120 months, these become 4.0% vs 8.8% ($P < .001$; Figure 2). Lead-time adjusted survival curves remain statistically significantly different at up to 40% simulated overdiagnosis (Supplementary Figure 2, available online).

In our lead-time corrected multivariable Fine-Gray competing risk regression, previous PSA screening was statistically significantly associated with 48% decreased risk of PCSM (SHR = 0.52, 95% CI = 0.36 to 0.76; $P < .001$). On secondary analysis, increased annual PSA screening was statistically significantly associated with 24% decreased odds of PCSM (SHR = 0.76, 95% CI = 0.59 to 0.98; $P = .03$). Additional factors statistically significantly

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Table 2. Full model outputs of inverse probability of treatment-weighted propensity scores analysis, performed for PSA > 20, Gleason ≥ 8, or metastatic disease at diagnosis as the endpoint[a]

Characteristic	PSA > 20 at diagnosis OR (95% CI)	Gleason ≥ 8 at diagnosis OR (95% CI)	Metastatic at diagnosis OR (95% CI)	Cancer-specific mortality SHR (95% CI)
Previous PSA screen	0.56 (0.49 to 0.63)	0.78 (0.69 to 0.88)	0.50 (0.39 to 0.64)	0.52 (0.36 to 0.76)
PCP visit rate	0.72 (0.68 to 0.76)	0.80 (0.75 to 0.85)	0.63 (0.57 to 0.70)	0.86 (0.72 to 1.03)
Age at diagnosis				
40-45 y	0.89 (0.65 to 0.76)	0.59 (0.41 to 0.82)	1.17 (0.56 to 1.97)	0.85 (0.36 to 2.02)
46-50 y	1.05 (0.91 to 1.19)	1.03 (0.89 to 1.17)	1.06 (0.65 to 1.40)	0.91 (0.63 to 1.31)
≥51 y	1.00	1.00	1.00	1.00
Year of diagnosis				
2004-2008	0.53 (0.45 to 0.62)	0.51 (0.43 to 0.60)	0.53 (0.39 to 0.72)	3.96 (1.22 to 12.86)
2009-2012	0.39 (0.33 to 0.46)	0.55 (0.47 to 0.64)	0.44 (0.32 to 0.61)	2.27 (0.70 to 7.40)
2013-2017	1.00	1.00	1.00	1.00
Charlson score				
0	1.00	1.00	1.00	1.00
1	0.57 (0.45 to 1.71)	1.22 (1.01 to 1.47)	0.42 (0.22 to 0.73)	0.95 (0.54 to 1.66)
2+	1.36 (1.20 to 1.55)	1.12 (0.98 to 1.27)	1.94 (1.53 to 2.48)	1.50 (1.09 to 2.05)
Employment				
Employed	1.00	1.00	1.00	1.00
Other/Not employed	1.08 (0.93 to 1.23)	0.83 (0.73 to 0.95)	1.14 (0.88 to 1.51)	1.10 (0.76 to 1.60)
Marital status				
Married	1.00	1.00	1.00	1.00
Other/Not married	1.07 (0.94 to 1.23)	1.07 (0.94 to 1.22)	0.91 (0.71 to 1.18)	0.84 (0.60 to 1.16)
% Bachelor education[b]				
Top 50%	0.98 (0.85 to 1.13)	1.33 (1.16 to 1.54)	0.99 (0.75 to 1.30)	1.35 (0.94 to 1.93)
Bottom 50%	1.00	1.00	1.00	1.00
Median income[b]				
Top 50%	0.68 (0.58 to 0.78)	0.73 (0.63 to 0.84)	0.55 (0.41 to 0.72)	0.81 (0.56 to 1.17)
Bottom 50%	1.00	1.00	1.00	1.00
BMI				
Underweight	0.89 (0.66 to 1.19)	1.45 (1.09 to 1.93)	2.98 (1.97 to 4.44)	2.90 (1.94 to 4.34)
Normal weight	1.00	1.00	1.00	1.00
Overweight	0.63 (0.53 to 0.73)	0.95 (0.80 to 1.14)	0.82 (0.60 to 1.12)	0.34 (0.23 to 0.52)
Obese	0.62 (0.53 to 0.72)	1.00 (0.86 to 1.18)	0.54 (0.40 to 0.74)	0.23 (0.15 to 0.36)
Agent Orange exposure				
Yes	1.27 (0.87 to 1.83)	3.88 (2.92 to 5.13)	0.49 (0.16 to 1.18)	1.28 (0.63 to 2.64)
No	1.00	1.00	1.00	1.00
Unknown	1.47 (0.92 to 2.29)	0.18 (0.05 to 0.47)	0.56 (0.13 to 1.59)	0.22 (0.02 to 1.83)
Smoking history				
Yes	1.98 (1.70 to 2.32)	1.58 (1.37 to 1.82)	1.92 (0.42 to 2.63)	1.38 (0.91 to 2.09)
No	1.00	1.00	1.00	1.00
Unknown	1.37 (1.07 to 1.74)	0.58 (0.44 to 0.77)	0.70 (0.36 to 1.26)	0.83 (0.42 to 1.34)

[a]Fine-Gray competing risk regression performed with prostate cancer mortality as the endpoint and noncancer death as competing event, survival adjusted for lead time. BMI = body mass index; CI = confidence interval; OR = odds ratio; PCP = primary care provider; PSA = prostate-specific antigen; SHR = subdistribution hazard ratio.
[b]By zip code.

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associated with increased PCSM were year of diagnosis between 2004 and 2008 (SHR = 3.96, 95% CI = 1.22 to 12.86; P = .02) and Charlson index score of 2 or higher (SHR = 1.50, 95% CI = 1.09 to 2.05; P = .01) (Table 2). PCP visit rate in the prediagnostic years was associated with a 14% risk reduction for PCSM (SHR = 0.86, 95% CI = 0.72 to 1.03; P = .09). These findings are robust to lead-time adjustments within the upper and lower bounds of their estimated 95% confidence intervals (Supplementary Table 1, available online).

Discussion

African American men possess the highest PCSM rate among racial groups (1). Current guidelines recommend shared decision making for PSA screening (23). However, like many cancer studies (2,3), these recommendations depend on PSA studies that included few African Americans (24). The generalizability of these studies may be limited. For instance, African American men develop disease at younger ages than NHW men and have higher PSA values at diagnosis (1). Many medical societies recognize that African American men likely carry greater risk for prostate cancer and suggest earlier PSA screening despite the lack of existing data (7,8,23). To our knowledge, this is the first large-scale analysis evaluating the association between prediagnostic PSA screening on prostate cancer outcomes in young African American men. Our findings suggest that PSA screening may improve prostate cancer outcomes for these patients. Compared with current guidelines, our findings are most consistent with National Comprehensive Cancer Network

Table 3. Summary of previous prostate-specific antigen (PSA) test and primary care provider (PCP) visit counts within the 5-year prediagnostic period

Prediagnostic test/visit	Counts					
	0	1	2	3	4	5
PSA test, No. (%)	1057 (22.4)	1182 (25.0)	932 (19.7)	786 (16.6)	513 (10.9)	256 (5.4)
PCP visit, No. (%)	483 (10.2)	654 (13.8)	563 (11.9)	603 (12.8)	700 (14.8)	1723 (36.5)

recommendations that endorse shared decision making focused on annual PSA screening.

For African American men between ages 40 and 55 years, we found that previous PSA screening was associated with lower disease severity at diagnosis. Propensity score analysis demonstrated that patients with 1 or more PSA tests prior to diagnosis had 44% reduced odds of PSA levels higher than 20, 22% reduced odds of Gleason score of 8 or higher, and 50% reduced odds of metastatic disease at diagnosis. Furthermore, the 5-year survival for prostate cancer in African American men approaches 100% for localized disease but decreases to 30% for more distant stages (1). Earlier diagnosis is imperative for increased curative treatment options. In our lead-time adjusted multivariable survival model, previous PSA screening was associated with a 48% reduction in PCSM, with higher PSA screening rates conveying statistically significantly reduced risk of PCSM. Our results suggest the benefit of higher PSA screening on disease severity and survival, however, additional risk stratification should be implemented to balance the risk of overdiagnosis and overtreatment. Our overdiagnosis sensitivity analysis suggests that the benefit of PSA screening on survival is mostly conserved at large proportions of simulated overdiagnosis. Nevertheless, multivariable risk prediction algorithms are growing in both accuracy and clinical significance (25), and proper utilization of these tools is needed to limit overdiagnosis and overtreatment if higher PSA screening regimens are initialized for young African American men.

Lead-time bias remains an important consideration for survival analyses. Screen-detected cancers may be more indolent, and survival time may be artificially increased through earlier presymptomatic tumor monitoring. However, increased lead time itself is not inherently negative. One goal of screening is earlier detection for increased curative treatment opportunities. Approaches to mitigate lead-time bias, while preserving benefits of early detection, have been described (17). In our secondary analysis using PSA screening rate, we find approximately 24% reduction in PCSM following lead-time bias adjustment. Combined with findings from our disease severity endpoints, these results suggest that increased PSA screening may best allow for clinical interventions in young African American men.

The factors promoting PSA screening are complex and must be considered when interpreting our results. For instance, we found a moderate correlation ($r = 0.68$, $P < .001$) between PCP visits and PSA screening. These results display the interplay between primary care and PSA screening while alluding to underlying complexities between the two. Higher primary care utilization could represent increased patient trust, lower health-care system burden, and/or improved health-care resources, which may all affect PSA screening and disease severity at diagnosis. Unmeasured variables such as these may bias our results despite balancing performed during propensity score analysis. Therefore, we recommend consideration of our results within the overall body of current PSA literature when discussing PSA screening for this patient population.

Nevertheless, primary care as a broader concept likely remains integral for prostate cancer early detection. In our models, PCP visits were associated with lower disease severity at diagnosis and lower risk of PCSM. This analysis underscores the complex and combined benefits of primary care utilization alongside PSA screening for these patients. African American men are less likely to be provided sufficient information regarding PSA screening, which may partially explain their observed lower PSA screening (26,27). In the context of shared decision making, the collaboration between primary care physicians, primary oncologists, and their patients is important to mitigate racial disparities in prostate cancer screening. The involvement of primary care during prediagnosis is critical and provides an opportunity to diminish current racial disparities in the management of prostate cancer.

The lack of diversity in clinical trials and research studies is well known (28,29). African American men remain underrepresented within trials. Given the higher rates and more aggressive disease, addressing the causes of low PSA screening for young African American men is important for reducing prostate cancer health-care disparities. We suggest one contributing factor may be the current lack of data for PSA screening in young African American men and find evidence supporting its potential implementation within this population. Many additional barriers to prostate cancer health equity remain (30). The physician–patient relationship is integral to PSA screening discussions, and our results have highlighted the importance of PCP continuity of care on reducing disease severity. Moreover, factors reflecting access to care, such as insurance status, disproportionately affect African American men and may contribute to racial differences in screening availability and treatment selection for prostate cancer (31). Ultimately, the findings of this study are one step in addressing the overall racial health-care disparities that remain within prostate cancer.

This study has limitations. First, our cohort consists of patients diagnosed with prostate cancer. The prostate cancer risk likely differs from the general African American population and likely additionally for other ethnic groups. Population-based research quantifying overdiagnosis and overtreatment is needed to better balance our results. Second, the retrospective study design is potentially limited by unmeasured confounders, and the described effects of PSA screening on our endpoints must be understood within this context. Factors driving PSA screening in young African American men are complex, and in the most extreme case, PSA screening may only be a conduit for improved health care. The propensity score analysis reduces confounders that affect both disease severity and PSA screening, such as PCP utilization. However, remaining unmeasured confounders, such as varying health-care system burden, could bias our estimated average treatment effects and require randomized trials to address the issue of confounding. Third, our survival analysis is limited by lead-time bias. We attempted to control for lead-time bias with previously established methods, though the estimated lead times were calculated from the

ERSPC trial cohort (16). The generalizability of this European population to African American men may be limited. We predict that PSA screening lead times may be longer for young African American men and expanded our corrections to the upper-bound 95% confidence interval lead times to help account for this. Residual confounding may still occur, although there is limited randomized data to provide more precise estimates of PSA screening lead times for this population. Lastly, our cohort skewed older, and our results may be less generalizable to the youngest patients. Additional prospective studies including balanced age groups are needed to validate our findings.

African American men possess the highest PCSM rate among all racial groups, and the lack of data for PSA screening among young African American men preclude proper evidence-based guidance. We found that among young African American men diagnosed with prostate cancer, previous PSA screening was associated with statistically significantly decreased risk of PSA levels higher than 20, Gleason score of 8 or higher, and metastatic disease at diagnosis as well as statistically significantly reduced risk of PCSM after lead-time adjustment. Higher PSA screening rates were associated with improved outcomes, and higher primary care utilization had similar effects on these endpoints. Overall, these data suggest that previous PSA screening in conjunction with close primary care utilization may improve prostate cancer outcomes in young African American men diagnosed with prostate cancer. Additional prospective studies are needed to validate these findings.

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Data Availability

The data that support the findings of this study are available from Veterans' Health Administration. Restrictions apply to the availability of these data, which were used under license for this study. Data are available for request at https://www.hsrd.research.va.gov/for_researchers/vinci/ with the permission of the Veterans' Health Administration.

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