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Probability of an Abnormal Screening PSA Result Based on Age, Race, and PSA Threshold

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Abstract

Objective—To determine the distribution of screening PSA values in older men and how different PSA thresholds affect the proportion of white, black, and Latino men who would have an abnormal screening result across advancing age groups.

Methods—We used linked national VA and Medicare data to determine the value of the first screening PSA test (ng/mL) of 327,284 men age 65+ who underwent PSA screening in the VA healthcare system in 2003. We calculated the proportion of men with an abnormal PSA result based on age, race, and common PSA thresholds.

Results—Among men age 65+, 8.4% had a PSA >4.0ng/mL. The percentage of men with a PSA >4.0ng/mL increased with age and was highest in black men (13.8%) versus white (8.0%) or Latino men (10.0%) (P<0.001). Combining age and race, the probability of having a PSA >4.0ng/mL ranged from 5.1% of Latino men age 65–69 to 27.4% of black men age 85+. Raising the PSA threshold from >4.0ng/mL to >10.0ng/mL, reclassified the greatest percentage of black men age 85+ (18.3% absolute change) and the lowest percentage of Latino men age 65–69 (4.8% absolute change) as being under the biopsy threshold (P<0.001).

Conclusions—Age, race, and PSA threshold together affect the pre-test probability of an abnormal screening PSA result. Based on screening PSA distributions, stopping screening among men whose PSA < 3ng/ml means over 80% of white and Latino men age 70+ would stop further

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screening, and increasing the biopsy threshold to >10ng/ml has the greatest effect on reducing the number of older black men who will face biopsy decisions after screening.

Keywords

Geriatrics; Prostate-Specific Antigen; Prostate Neoplasm; Early Detection of Cancer

INTRODUCTION

Screening for prostate cancer continues to be common practice among older men.[1, 2] For example, 44% of men age 75 years and older reported a recent PSA test in the 2010 National Health Interview Study (NHIS), which remains similar to rates reported in 2005 and 2008.[3,4] White men reported the highest screening rates, although approximately a third of black and Latino men age 80 years and older also reported a PSA test in the past year. More than half of older men recalled a clinician recommending screening, despite no evidence for screening benefit in this population and strong evidence for harm.[4, 5]

To potentially improve the benefit-to-harm ratio of PSA screening, the American Urological Association recently published guidelines recommending that among men over age 70 who wished to be screened the PSA threshold for biopsy should be increased to >10ng/ml. [6] This is based on evidence that older men with a PSA level above 10ng/ml are more likely to have aggressive prostate cancer that would benefit from treatment compared with those with a PSA below 10ng/ml. [7] These guidelines also recommended discontinuation of PSA screening in men over age 70 with a PSA < 3.0ng/ml.

However, the distribution of screening PSA values has not been determined in a national population according to the combination of factors that predict an abnormal screening result: age, race, and threshold value of PSA used to define abnormal.[8–14] While prior studies have calculated PSA values according to age and race, none included enough older men to determine the distribution of abnormal PSA results according to race at advanced ages and none have determined how Latino race/ethnicity affects the distribution of screening PSA values. This is despite Latinos being one of the fastest growing demographic groups in the United States.[15]

Therefore, among men age 65 years and older, we linked national VA and Medicare data to determine the probability of having an abnormal screening PSA result based on age, race (white, black, Latino), and common PSA thresholds for biopsy (>2.5 ng/ml, >4.0ng/ml, >6.5ng/ml, and >10.0ng/ml). The distribution of screening PSA values and probabilities of having an abnormal screening result from this study can inform patients and clinicians about the likelihood that they will face biopsy decisions after PSA screening.

METHODS

Data Sources and Subjects

We conducted a cross-sectional study of 327,284 men age 65 years and older who underwent PSA screening in the VA healthcare system in 2003. We used the VA National Patient Care Database (VA NCPD) and linked Medicare data to identify the 701,399 men age ≥65 who identified as black, white, or Latino with at least 1 outpatient visit in both 2002 and 2003 and had an index PSA test in 2003 at one of 104 VA facilities (Figure 1).[16] An index PSA test was defined as the first outpatient PSA in the 2003 Decision Support System (DSS) National Data Extracts Laboratory Results dataset (which captured PSA results for 104 of the 127 VA facilities).[2, 17] We did not include other race groups in this study because each constituted less than 1.0% of the population. We also did not include 1,464 men with

unknown race. We excluded 92,069 (13.0%) men enrolled in Medicare managed care from 01/01/02–12/31/03 because they lacked Medicare claims, which was used to determine whether patients had a medical history that made them ineligible for PSA screening. For example, we used VA and Medicare inpatient and outpatient claims and VA Central Cancer Registry between 01/01/99 and the date of the index PSA test in 2003 to exclude 201,842 (28.4%) men with a history of prostate cancer, prostatectomy, androgen deprivation therapy, or elevated PSA (in VA or Medicare) because such history defines men for whom PSA testing is not routine screening (Figure 1). We also used claims to exclude 72,377 (10.2%) men who experienced symptoms (e.g. urinary obstruction, hematuria, prostatitis, benign prostatic hypertrophy, other disorders of the prostate, unexplained weight loss, and back pain) within 3 months before the index PSA was performed because this PSA was considered a diagnostic test rather than a screening test. Lastly, using VA pharmacy data, we excluded 7,827 (1.1%) men on medications that affect PSA values (e.g., testosterone and finasteride). This left a final screening cohort of 327,284 men.

Predictor Variables

Age on the date of the index screening PSA was categorized into five groups: 65–69 years, 70–74 years, 75–79 years, 80–84 years, and ≥85 years. Race/Ethnicity was determined primarily from Medicare data. Medicare derives race/ethnicity data from Social Security applications, which use a two-question format that separates Hispanic/Latino ethnicity from race. Applicants were asked to self-identify as ethnically Hispanic/Latino and/or racially as White, Black, Asian, North American Native, or Other. This standard for classification of race/ethnicity is based on directives from the Office of Management and Budget.[18] Medicare then combines and categorizes race/ethnicity variables, making Hispanic/Latino ethnicity a mutually exclusive designation. For instance, if a patient identifies as ethnically Hispanic/Latino, he is categorized as Latino regardless of his racial identification. VA race data was used to fill in missing cases. Prior studies have shown that the combination of Medicare and VA datasets improved race data completeness to nearly 100% among older patients (≥65 years).[19] Other factors known to influence the use and outcomes of PSA screening were obtained from VA and Medicare data and linkage to the 2000 US census (Table 1).[2, 20, 21]

Outcome Variable

The main outcome variable was the index screening PSA value (ng/mL) from the VA DSS National Data Extracts Laboratory Results Data Set, which extracts PSA results obtained in the course of clinical practice from each VA facility. PSA values were examined across the continuum and according to four published thresholds for defining abnormal (>2.5, >4.0, >6.5, and >10.0 ng/mL).[6, 8–10]

Analyses

Baseline characteristics were compared between white, black and Latino men using chi-square tests. Median PSA values were compared according to age and race/ethnicity using chi-square tests. Percentages of men with different PSA values (0–2.5, >2.5–4.0, >4.0–6.5, >6.5–10.0, and >10.0 ng/mL) were calculated for each agerace/ ethnicity group to provide men with the probability for having a screening PSA value within a certain range based on their age and race combined, rather than based on age or race alone. In addition, because there are different PSA biopsy thresholds[6, 8–10], we calculated the percentage of men with PSA values that exceeded four commonly used thresholds (>2.5, >4.0, >6.5, and >10.0 ng/mL) according to age and race to provide men with the probability of having an abnormal screening PSA result based on the combination of age, race, and selected PSA threshold. We also calculated the percentage of men in each age-race/ethnicity group who would be reclassified based on different PSA thresholds and compared percentages using chi-square

tests. All analyses were performed using SAS version 9.2 statistical software. The Committee on Human Research at the University of California, San Francisco and the Committee for Research and Development at the San Francisco Veterans Affairs Medical Center approved this study.

RESULTS

Participant Characteristics

Baseline characteristics of the 327,284 men who had a screening PSA in 2003 at one of 104 VA facilities are presented in Table 1. Mean age was 73.2 (range, 65.0 to 106.5). 296,477 (90%) were white; 25,058 (8.5%) were black; and 5,748 (1.9%) were Latino. Baseline characteristics differed between race/ethnic groups for all variables in Table 1 (P<0.001). For example, black men were younger and less likely to be married than other race/ethnic groups, while Latino men were older and more likely to live in low income zip code tabulation areas.

Screening PSA Results

The median screening PSA value for our cohort was 1.3 ng/mL (interquartile range, 0.7, 2.3). Scores were skewed to the left with PSA values ranging from 0.00002 ng/mL to 2,929.7 ng/mL. Of the total cohort, 21.7% had a PSA >2.5 ng/ml; 8.4% had a PSA >4.0 ng/ml; 2.4% had a PSA of >6.5ng/ml; and 0.9% had a PSA >10.0 ng/ml.

PSA values increased with advancing age ranging from a median PSA value of 1.1 ng/mL for men age 65–69 to 1.6 ng/mL for men age 85+ (P<0.001). Using the most common PSA threshold >4.0 ng/mL, the percentage of men who had an abnormal screening PSA result ranged from 5.9% in men age 65–69 to 13.7% in men age 85+ (P<0.001) (Table 2). Using a PSA threshold >10.0ng/mL, the percentage of men with an abnormal result ranged from 0.5% in men age 65–69 to 3.6% in men age 85+.

PSA values also varied across race/ethnic groups. The median PSA value was 1.3 ng/mL for white men, 1.3 ng/mL for Latino men and 1.5 ng/mL for black men (P<0.001). Using the PSA threshold >4.0ng/mL, the percentage of men who had an abnormal screening PSA result was 8.0% in white men, 10.0% in Latino men, and 13.8% in black men (P<0.001) (Table 2). Using the PSA threshold > 10ng/ml, the percentage of men in our cohort with an abnormal result was 0.8% in white men, 1.0% in Latino men, and 2.6% in black men.

Combining age and race, the most frequently observed screening PSA result was < 2.5ng/ml for all age-race/ethnicity groups (See electronic supplementary material). In fact, among men over age 70, the PSA result was <3.0ng/ml for 82.4% of white men, 80.9% of Latino men, and 74.0% of black men. The probability of having a PSA >4.0 ng/mL ranged from 5.1% (47/918) in Latino men age 65–69 to 27.4% (144/525) in black men age 85+. If the PSA threshold was increased to >10.0ng/mL, abnormal results ranged from 0.3% (3/918) in Latino men age 65–69 to 9.1% (48/525) in black men age 85+ (Figure 2).

Older black men were the most likely to be reclassified when the PSA threshold was changed. For example, only 5.2% (5,134/99,762) of white men aged 65–69 and 4.8% (44/918) of Latino men age 65–69 were reclassified below the biopsy threshold by raising the PSA threshold from >4.0 ng/mL to >10.0ng/mL compared to 18.3% (96/525) of black men aged 85+ (P<0.001). However, if the PSA threshold was lowered from >4.0 ng/mL to >2.5 ng/mL, 11% (10,974/99,762) of white men aged 65–69 and 12.1% (111/918) of Latino men age 65–69 were reclassified above the biopsy threshold compared to 17.5% (92/525) of black men aged 85+ (P<0.001).

DISCUSSION

This is the largest national study to present the distribution of screening PSA values in clinical practice for the three most common race/ethnicity groups: white, black and Latino, including the probabilities of having an abnormal screening PSA result as a function of age and different PSA thresholds. In this study, over 27% of black men age 85+ had screening PSA values >4.0 ng/mL. Latino and white men had PSA distributions that were similar to each other and consistently had a lower probability of an abnormal result than black men across all age groups and PSA thresholds. However, even among Latino and white men, more than one in six men age 85+ had a screening PSA >4ng/ml. Using a PSA threshold >10.0ng/mL, 9% of black men age 85+ would have an abnormal PSA result as compared to 45% if the PSA threshold is >2.5ng/mL. Applying new American Urological Association guidelines to increase the PSA threshold for biopsy to >10ng/ml will have the greatest effect on reducing the number of older black men who will face biopsy decisions after screening.

While prior studies of the association between age, race and PSA values have consistently shown older black men have higher PSA values than white or Latino men, these studies involved smaller cohorts, which were predominantly comprised of younger men age 40–60 years old and had upper age limits of 79 years. For example, De Antoni et al studied PSA values in men age 40–79 who participated in a prostate cancer awareness week program. He found a mean PSA value of 2.5 ng/mL for black men age 70–79 compared with a mean value of 2.3 ng/mL for white men in this age group.[12] Another study of men over age 40 found 37.2% of black men age ≥70 had a PSA >4 ng/mL.[13] This is a higher percentage than what we found (16.3%) likely because we used stricter exclusion criteria to define our screening cohort. For example, we excluded men who had urinary symptoms suggestive of prostate cancer , which are associated with higher PSA values. Our cohort also included a much larger number of older men, including over 100,000 men age 75+ who underwent PSA screening as part of clinical practice, which allows greater precision of our percentages.

Using this large cohort of older men, we found that black men were more likely to have an abnormal screening PSA result across all age groups and PSA thresholds compared to white or Latino men. This is true even among men age 80+ in whom racial distributions of PSA have not been previously published. In addition, few PSA screening studies have included Latino men of any age. The few studies of predominantly younger men that included Latinos found that white and Latino men have similar PSA values.[12–14] Our study, which included nearly six thousand Latino men age 65+, found Latino and white men generally had similar PSA values, with Latino men age 70+ having a slightly higher probability of a screening PSA result >4.0 ng/mL compared to white men in this same age group. This was the reverse in men age 65–69. However, these differences were small compared to black men who were 1.5 times more likely to have a screening PSA >4.0 ng/mL than white or Latino men combined.

While this cross-sectional study did not determine which men ultimately were diagnosed with prostate cancer after PSA screening, our findings of higher PSA values among older black men are consistent with U.S. population statistics which show the incidence of prostate cancer increases with advancing age and is highest in older black men compared to other racial groups.[22] Current U.S. prostate cancer statistics show black men are 1.6 times more likely to be diagnosed with prostate cancer than white and Latino men, although black men are generally less likely to undergo PSA screening.[2, 4]

In addition, because black men have higher screening PSA values at every age, they are most affected by the PSA threshold chosen to define an abnormal result. While Welch et al discussed implications of various PSA thresholds according to advancing age [10], our study is

the first to show how various PSA thresholds affect the proportion of men with an abnormal PSA result according to race/ethnicity and advancing age. Across all age groups black men had the greatest likelihood of being reclassified as having an abnormal or normal screening PSA based on the PSA threshold chosen. Choosing a higher PSA threshold is based on the Prostate Cancer Intervention versus Observation Trial (PIVOT) study, which found that men over age 70 with a PSA >10.0ng/mL are more likely to benefit from treatment of prostate cancer than men with a PSA below 10ng/ml.[7] Knowing upfront which PSA threshold will be used informs men about the likelihood they will be faced with making a biopsy decision if they undergo screening.

Alternatively, the American Urological Association also recently recommended discontinuing PSA screening among men over age 70 with a PSA below 3ng/ml[6], which is most likely to affect white and Latino men. For example, using a PSA threshold of <3ng/ml to discontinue screening translates into more than 80% of white and Latino men age 70+ in our cohort stopping further screening. Discontinuing screening among men with a PSA <3ng/ml is based on a study by Schaeffer et al., which found men age 75–80, who had a PSA result of <3.0ng/mL, were unlikely to be diagnosed with high-risk prostate cancer or die from prostate cancer in their remaining years of life.[23] Our study has several limitations. First, because we did not determine who was ultimately diagnosed with high-risk prostate cancer or who died, we do not provide evidence about which threshold should be used to define an abnormal screening result. The main goal of our study was to present more individualized pre-test probabilities of having an abnormal screening PSA result according to age and race and varying PSA thresholds. Second, laboratory data do not indicate the reasons for ordering PSA tests. As a result, some of the tests may have been performed for non-screening reasons. However, we conducted chart reviews that showed most PSA tests in our cohort were screening tests [2], and our median PSA values are lower than many published studies suggesting our exclusions effectively defined a primarily lower-risk screening cohort. Third, race/ethnicity was self-reported, and definitions can vary. However, prior studies have shown that because race/ethnicity is a social construct, self-identity is its most accurate and valid measure.[19] Lastly, our cohort consists of men who received care in the VA healthcare system, so the generalizability of PSA values in this study to non-veterans is uncertain. Regardless, the VA is the largest health care system for men in the nation and has the largest number of PSA results across the U.S. compared to any other data source.[24]

In conclusion, this study provides granular data of the probability of having an abnormal screening PSA result according to advancing age, race and PSA threshold among elderly U.S. veterans. These findings can provide useful information to patients and clinicians who are considering PSA screening. Knowing the probability of an abnormal PSA result informs men about the probability they will need to think about follow-up testing and biopsies, and expands the PSA screening decision to consider downstream decisions, such as “what would I do if the result comes back abnormal.” For example, if a patient knows he has more than a 1 in 4 chance of having to face a downstream decision about a prostate biopsy, based on his age, race and PSA threshold, this frames screening as being more than just getting a “simple” blood test. This framing is important to ensuring informed PSA screening decisions by older men and their clinicians.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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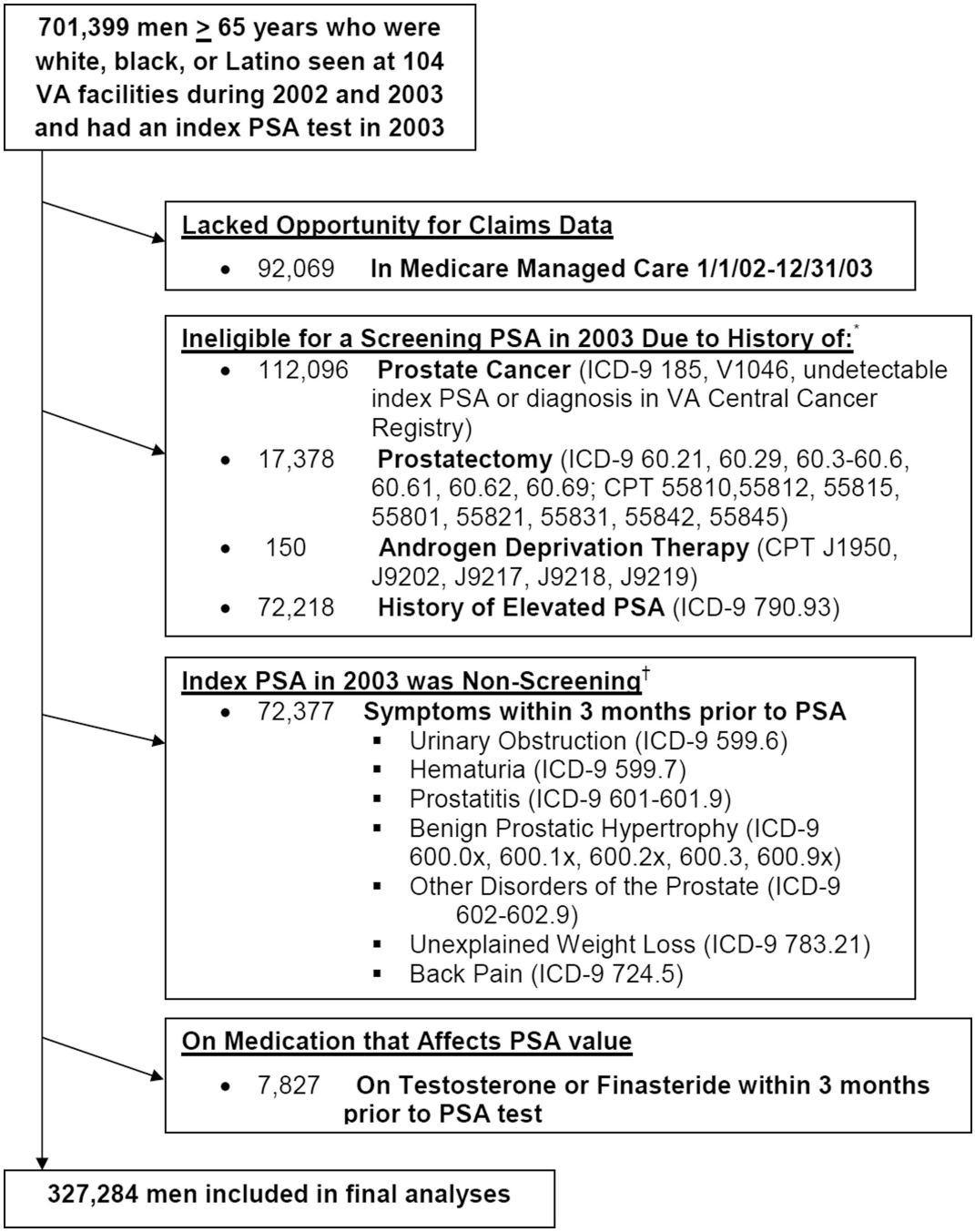

Figure 1.
Exclusions used to define the final cohort of elderly men who received a screening PSA test in 2003 at a VA facility.

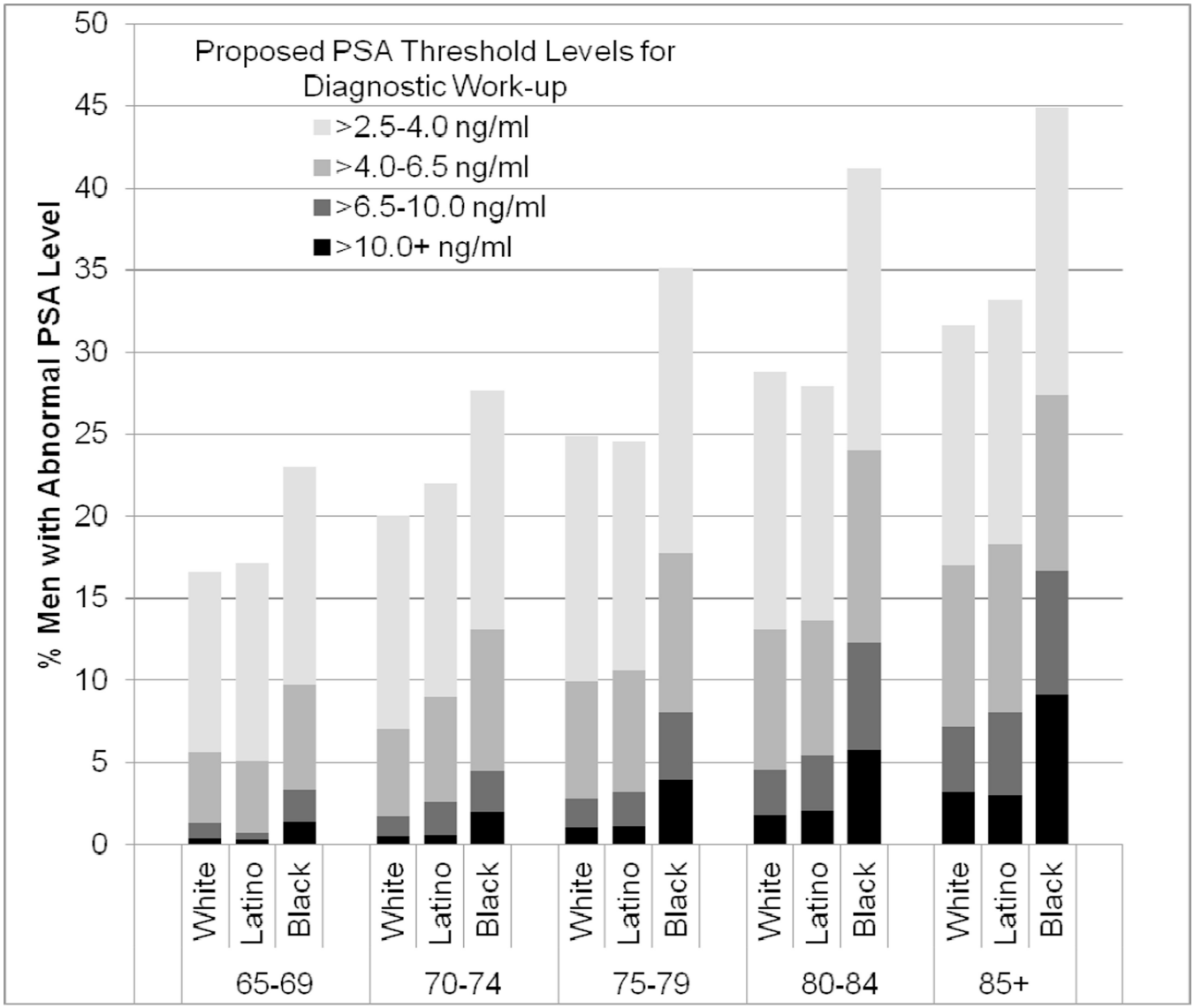

Figure 2.
Percent of men with an Abnormal PSA Result Based on Age, Race, and PSA Threshold (N=327,284).

Table 1

Baseline Characteristics of Study Participants (N=327,284)

Characteristic	Total N (%)*	White	Black	Latino
	N= 327,284	296,477 (90.6)	25,058 (7.7)	5,749 (1.8)
Age				
65–69	110,412(33.7)	33.7	38.8	16.0
70–74	105,083(32.1)	32.0	33.5	33.6
75– 79	71,466(21.8)	22.0	17.9	31.1
80–84	32,599(10.0)	10.1	7.7	15.2
85+	7,724(2.4)	2.4	2.1	4.1
Charlson Score†				
0 (best health)	205,278(62.7)	62.1	68.7	69.1
1–3 (average health)	106,588(32.6)	33.2	26.8	27.1
≥ 4 (worst health)	15,418 (4.7)	4.7	4.5	3.8
Married‡				
Yes	234,016 (71.9)	73.6	52.5	70.5
No	91,396 (28.1)	26.4	47.5	29.5
Lived in ZCTA in which ≥ 25% of adults had a college education§				
Yes	88,326 (27.8)	28.5	22.2	16.2
No	229,070 (72.2)	71.5	77.8	83.8
ZCTA Median Income in Tertiles				
< $32,407	104,855 (33.0)	30.8	50.7	75.3
$32,407–$41,143	107,691 (33.9)	34.9	26.1	14.0
≥ $41,144	104,912 (33.1)	34.3	23.2	10.7

*The percent values are presented as column percents

†Charlson-Deyo comorbidity scores were calculated from VA and Medicare inpatient and outpatient claims during the 12 months before the index PSA date. Men were categorized as being in best health if they had a Charlson score=0, average health if they had a Charlson score = 1–3, and worst health if they had a Charlson score ≥4. These cutoffs have been used in prior studies.[2, 21]

‡Marital Status is obtained from the Veterans Affairs National Patient Care Database which includes inpatient and outpatient claims. Data were missing from 0.6% of men.

§ZCTA=Zip Code Tabulation Area. Through linkage to the 2000 US Census, we determined the percentage of adults with a college degree who lived with a veteran's ZCTA and the median income for adults ages 65 years and older who lived within than ZCTA. Education and Income data were missing for 3.0% of men in the cohort.

Table 2

Number and percentage of men with an index screening PSA value above various PSA thresholds, according to age and race (N=327,284)

Age	N	>2.5 ng/mL	>4.0 ng/mL	>6.5 ng/mL	>10.0 ng/mL
65–69	110,412	18,889 (17.1)	6,508 (5.9)	1,550 (1.4)	519 (0.5)
70–74	105,083	21, 713 (20.7)	7,871 (7.5)	1,978 (1.9)	644 (0.6)
75–79	71,466	18,187 (25.5)	7,385 (10.3)	2,206 (3.1)	823 (1.2)
80–84	32,599	9,598 (29.4)	4, 452 (13.7)	1,635 (5.0)	660 (2.0)
85+	7,724	2,512 (32.5)	1,367 (17.7)	606 (7.9)	276 (3.6)
Race					
White	296,477	62,408 (21.1)	23,558 (8.0)	6,412 (2.2)	2,224 (0.8)
Black	25,058	7,145 (28.5)	3,450 (13.8)	1,381 (5.5)	638 (2.6)
Latino	5,749	1,346 (23.4)	575 (10.0)	182 (3.2)	60 (1.0)

[*] History was defined by searching VA and Medicare inpatient and outpatient claims and the VA Central Cancer Registry between 1/1/99 and the date of the index PSA test in 2003.

[†] VA and Medicare claims were used to exclude men with prostate symptoms during the 3 months before their index PSA, because this PSA was considered a diagnostic test rather than a screening test.