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Total, free, and complexed prostate-specific antigen levels among US men, 2007–2010

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Abstract

Background: Screening for prostate cancer using prostate-specific antigen (PSA) is common. Prostate cancer has been associated with higher total PSA (tPSA), lower free PSA (fPSA), lower percent free PSA (%fPSA), and higher complexed PSA (cPSA).

Methods: Total, free and complexed PSAs were performed on 3251 men ≥40 years in the 2007–2010 National Health and Nutrition Examination Survey. Distributions of the PSA tests were examined by age, race and ethnicity, and body mass index (BMI) groups. Percentages of men at PSA thresholds were examined.

Results: Total PSA geometric mean was 0.96 μg/l among men aged ≥40 years and increased from 0.74 μg/l for men 40–49 years, to 1.82 μg/l for men 80 years and older. Non-Hispanic Whites had lower age-adjusted mean tPSA (1.03 μg/l) and cPSA (0.56 μg/l) than non-Hispanic Blacks (tPSA 1.25 μg/l and cPSA 0.72 μg/l). Obese men had lower age-adjusted mean total, free and complexed PSAs (0.94, 0.27, and 0.51 μg/l, respectively) than men with normal BMI (tPSA 1.21, fPSA 0.32, and cPSA 0.68 μg/l, respectively).

Conclusion: Total, free and complexed PSAs increased with age; tPSA and cPSAs were highest in non-Hispanic Blacks; and total, free, and complexed PSAs were lowest in obese men.

Keywords

Prostate-specific antigen; National health survey; Prostate cancer

1. Introduction

Prostate cancer is a common non-dermatologic cancer in US men [1]. Most prostate cancers represent indolent disease, but aggressive forms of prostate cancer exist. There is approximately a 2.7% lifetime risk for dying of prostate cancer which results in approximately 30,000 deaths/year in the US. The common screening tests for prostate cancer are digital rectal examination and the biomarker serum total PSA. Prostate cancer

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screening is common but has been controversial for many years [2–4]. Hayes and Barry recently reviewed randomized trials and modeling studies of screening for prostate cancer with the PSA test and found that two major trials have examined the role of PSA in screening for prostate cancer [5]. The European Randomized Study of Screening for Prostate Cancer (ERSPC) found a reduction in prostate cancer mortality using PSA testing [6,7]. The Prostate, Lung, Colorectal and Ovarian (PLCO) screening trial did not show a prostate cancer-specific mortality benefit with PSA screening [8,9]. In 2012, the United States Preventive Services Task Force recommended against PSA-based screening for men of any age [10]. The American Urological Association recently recommended shared decision-making for PSA-based screening for men ages 55 to 69 years [11]. The American Urological Association did not recommend PSA screening in men under age 40 years, in men 40–55 years at average risk, in men 70 years and older or in men with less than 10–15 years life expectancy. However, PSA tests are useful for the monitoring of treatment of prostate cancer [10].

In blood, total PSA is composed of free PSA and complexed PSA, primarily bound to α-1-antichymotrypsin and α-2-macroglobulin [12,13]. Most blood PSA immunoassays measure free or α-1-antichymotrypsin complexed PSA. Free and complexed PSAs have been proposed as supplemental tests to total PSA to increase the sensitivity and specificity of detecting prostate cancer, especially at lower concentrations of total PSA [14–19]. Prostate cancer has been associated with higher total and complexed PSAs and lower free PSA. Percent free PSA (fPSA / tPSA × 100%), percent complexed PSA (%cPSA = cPSA / tPSA × 100%) and free/complexed PSA ratio (f/cPSA) have also been examined in prostate cancer screening. The distributions of total, free and percent free PSAs have been examined in the 2001–2004 National Health and Nutrition Examination Survey (NHANES) [20].

The objective of this study was to examine the distributions of total, free and complexed PSA levels, percent free and complexed PSAs, and the free/complexed PSA in men who were examined in the 2007-2010 NHANES. The relationship of age, race and ethnicity, and body mass index to PSA tests were examined. Also, the percentage of men at PSA test threshold values was assessed.

2. Materials and methods

2.1. Study population and sample design

The National Health and Nutrition Examination Survey is a nationally representative, multistage probability sample designed to measure the health and nutritional status of the US civilian, non-institutionalized population. The multistage sample is based on a selection of counties or contiguous counties, blocks, households, and persons within households. NHANES has been conducted periodically since 1960 and continuously since 1999. NHANES participants receive an in-person home interview followed by physical measurements including laboratory testing at a mobile examination center. In this study, male participants ≥40 years who underwent PSA testing were selected from the 2007 to 2008 and from 2009 to 2010 NHANES survey cycles. Hispanic, non-Hispanic Black, low income persons and adults 80 years and older were over-sampled in NHANES 2007–2010 [21]. The procedures for selecting the sample and conducting the interviews and

examinations for NHANES 2007–2010 have been described [22]. Written informed consent was obtained from each participant and the National Center for Health Statistics Research Ethics Review Board approved the NHANES 2007–2010 protocols.

For NHANES 2007–2010, 5567 men aged 40 years or older were sampled, of whom 3989 (71.7%) were interviewed and 3868 (69.5%) were interviewed and underwent physical examination. After these men received general information about the PSA test from the examining NHANES physician, they were offered the opportunity to be tested. Of these 3868 men, 51 (1.3%) did not give permission for the PSA test. In addition, men were excluded from PSA testing if they reported, refused to answer, or did not know if they had procedures or conditions that could alter PSA results. These exclusion criteria were current infection or inflammation of the prostate, digital rectal exam in the past week, prostate biopsy or surgery in the past 4 weeks, cystoscopy in the past 4 weeks, or history of prostate cancer. An additional 467 (12.1%) had one or more of the exclusion criteria. Also, 99 (2.6%) of eligible men had a missing value for total PSA. Hence, 3251 of 3868 or 84.0% of interviewed and examined men ages 40 years and older participated in the NHANES PSA testing.

2.2. Specimen collection and laboratory methods

PSA testing consisted of the measurement of total, free and complexed PSAs. Also, the percent free PSA, the percent complexed PSA and the free to complexed PSA ratio were calculated. All PSA tests were conducted on venous serum samples that were collected in the NHANES mobile examination center and were frozen at −20 °C within 1 hour of phlebotomy. Within one week, the specimens were shipped on dry ice to the University of Washington Medical Center, Department of Laboratory Medicine, where the specimens were stored at −70 °C.

For 2007–2010, total and free PSA immunoassays were performed using the Beckman Coulter (Brea, CA) Access Hybritech instrument using a two-site immunoenzymatic “sandwich” assay [23–26]. Hybritech calibrators were used for the total and free PSA immunoassays. The complexed PSA immunoassay was measured using the Siemens (Malvern, PA) ADVIA Centaur instrument in 2007–2008 [27] and the ADVIA Centaur XP instrument in 2009–2010 using a two-site chemiluminometric assay [28].

The total PSA had an inter-run imprecision coefficient of variation (CV) ≤ 5.8% for quality control pool means of 0.15–16.28 μg/l. The free PSA had a CV ≤ 5.0% for means of 0.52–1.75 μg/l and the complex PSA had a CV ≤ 5.1% for means of 0.95–12.24 μg/l. A crossover study revealed that the ADVIA XP (2009–2010) resulted, on average, 5% higher cPSA than the cPSA on the ADVIA (2007–2008). A Deming regression was used to adjust the 2007–2008 cPSA to equivalent 2009–2010 cPSA values [29]. The Deming regression used was Y (2009–2010 estimated cPSA) = 1.047 × X (2007–2008 measured cPSA).

2.3. Independent variables

Independent variables included in the analysis were age, race and ethnicity, and body mass index groups. Age groups were categorized as 40 to 49, 50 to 59, 60 to 69, 70 to 79, and 80 years and older. Race and ethnicity was self-reported and categorized as Hispanic, non-

Hispanic White, non-Hispanic Black, and “other”. The “other” race and ethnicity category was included in the total sample analyses, but was not shown separately due to insufficient sample size. BMI was calculated from measured weight in kilograms divided by measured height in meters squared and then rounded to the nearest hundredths. BMI was categorized into 4 groups: < 18.50,18.50 to 24.99, 25.00 to 29.99 and 30.00 or more kg/m^2 which correspond to underweight, normal (healthy), overweight and obese, respectively [30]. There were only a small number of respondents who were underweight, and therefore data for the underweight group was not shown separately but it was included in the total sample analyses.

2.4. Statistical analysis

The distributions of PSA tests for 2007–2010 NHANES were estimated for age groups (Table 1), race and ethnicity (Table 2), race and ethnicity for different age groups (Table 3) and body mass index group (Table 4). In addition, the weighted mean (standard error of the mean) and selected percentiles (5th, 10th, 25th, 50th, 75th, 90th and 95th) for total, free and complexed PSAs are seen in Supplemental Table 1, Supplemental Table 2 and Supplemental Table 3, respectively. All PSA tests were log-normal in distribution except percent complexed PSA, which was normally distributed. Geometric means (GMs) were calculated for all PSA tests (except cPSA for which an arithmetic mean was calculated) along with standard error (SE) of the means, and selected percentiles. The mean and SE of PSA tests were age-adjusted for race and ethnicity and BMI groups by the direct method to the year 2000 US Census population estimates [31]. Examination sample weights, which account for the differential probabilities of selection, nonresponse, and non-coverage are incorporated into the estimation process. The standard errors of the mean were estimated by Taylor series linearization [32]. Orthogonal linear contrasts were used to test for linear trends, analysis of variance was used to compare means for 3 or more groups, and orthogonal contrasts were used for pairwise comparisons.

Proportions at different threshold values for total, percent free, and percent complexed PSAs were estimated for race and ethnicity (Fig. 1). Statistical hypotheses were tested at the alpha level of 0.05 of significance with Bonferroni correction for multiple comparisons. For the three possible race and ethnicity comparisons, the Bonferroni corrected significant p-value was 0.05/3 or 0.017. All data analyses were performed using the statistical packages SAS (SAS Institute, Inc., Cary, NC) version 9.3 and SAS-callable SUDAAN (RTI International, Research Triangle Park, NC) version 11.0.

3. Results

The geometric means, SEs of the mean, and selected percentiles for total PSA, free PSA, complexed PSA, percent free and complexed PSAs, and free/complexed PSA ratio are shown for age groups in Table 1. The total, free and complexed PSAs increased with age (linear trend, $p < 0.001$), but the percent free and complexed PSA and the free/complexed PSA did not change significantly with age. Total PSA GM increased from 0.74 μg/l, for men 40–49 years, to 1.82 μg/l for men 80 years and older. Free PSA GM increased from 0.22

μg/l, for men 40–49 years, to 0.51 μg/l for men ≥80 years, and complexed PSA GM increased from 0.40 μg/l, for men 40–49 years, to 0.99 μg/l for men ≥80 years.

There were significant differences ($p < 0.05$ with Bonferroni correction) in age-adjusted means for PSA tests for race and ethnic groups (Table 2). Non-Hispanic Black men had higher total PSA (1.25 μg/l), complexed PSA (0.72 μg/l), and percent complexed PSA (57.7%) than non-Hispanic White men (tPSA 1.03 μg/l, cPSA 0.56 μg/l and %cPSA 55.4%). Non-Hispanic Black men had lower percent free PSA (25.8%) and free/complexed PSA ratio (0.46) than non-Hispanic White men (%fPSA 28.8% and f/cPSA 0.53). Hispanic men had higher cPSA (0.64 μg/l) and %cPSA (59.2%) than non-Hispanic White men. Hispanic men had lower %fPSA (26.2%) and f/cPSA (0.45) than non-Hispanic White men. There was no significant difference in age-adjusted means for PSA tests between non-Hispanic Black and Hispanic men.

All men, Hispanic, non-Hispanic White and Black men had increasing age group linear trends ($p < 0.001$) for total, free and complexed PSAs (Table 3). Non-Hispanic Black men had the greatest age increase in total PSA (0.74 μg/l for 40–49 years to 2.44 μg/l for ≥70 years) compared to non-Hispanic White men (0.73 μg/l for 40–49 years to 1.64 μg/l for ≥70 years) and Hispanic men (0.79 μg/l for 40–49 years to 1.74 μg/l for ≥70 years). Similarly, non-Hispanic Black men had the steepest increase in age linear trends for free and complexed PSAs when compared to non-Hispanic White and Hispanic men.

There were significant differences ($p < 0.05$ with Bonferroni correction) in age-adjusted means for PSA tests for body mass index groups (Table 4). Normal (healthy) BMI men had higher tPSA (1.21 μg/l), fPSA (0.32 μg/l), and cPSA (0.68 μg/l) than obese men (tPSA 0.94 μg/l, fPSA 0.27 μg/l and cPSA 0.51 μg/l). Also, overweight men had higher tPSA (1.09 μg/l), fPSA (0.31 μg/l) and cPSA (0.59 μg/l) than obese men. There was no significant difference in age-adjusted means for PSA tests between normal (healthy) BMI men and overweight men.

The distribution of selected threshold values for PSA tests by race and ethnicity is seen in Fig. 1. Overall, 6.1% of men over 40 years had a total PSA greater than 4.0 μg/l, a common screening threshold for tPSA, with 1.0% of men with a tPSA ≥ 10 μg/l. Approximately 13.9% of men had a total PSA greater than 2.5 μg/l, the lower suggested screening threshold for prostate cancer. The total PSA from 4.0 to less than 10.0 μg/l was higher for non-Hispanic Blacks (5.6%) than non-Hispanic Whites (5.2%) and Hispanics (3.7%), but was not significant. For total PSA ≥ 10.0 μg/l, non-Hispanic Black men had the highest proportion (2.2%) compared to non-Hispanic White men (0.8%) and was significant ($p = 0.036$).

The distribution of percent free PSA threshold values was different for race and ethnicity. For all men, approximately 38% had %fPSA ≤ 25%, a suggested upper threshold for screening for prostate cancer, and 8.5% of men had ≤ 15% percent free PSA. A higher proportion of non-Hispanic Black men (12.3%) compared to non-Hispanic White men (8.1%) had %fPSA ≤ 15% ($p = 0.029$). Hispanic men had a higher proportion (36.8%) compared to non-Hispanic White men (28.1%) for %fPSA greater than 15% to 25% ($p < 0.001$).

The percent complexed PSA threshold values were determined by quartiles of %cPSA values. Of all men, 5.6% had a %cPSA greater than 75%. Hispanics (8.2%) had the highest %PSA greater than 75% compared to non-Hispanic White men (5.2%, $p < 0.001$). Also, Hispanic men had a higher %cPSA (69.2%) than non-Hispanic White men (62.1%, $p < 0.001$) for %cPSA greater than 50% and ≤75%.

4. Discussion

The distribution of PSA tests for NHANES 2001–2004 was previously described for total, free and percent free PSAs by age and race and ethnicity [20]. In this report, more recent data from NHANES 2007–2010 was examined and included complexed PSA in addition to total and free PSAs by body mass index, age and race and ethnicity. Prostate cancer has been associated with higher complexed PSA levels [15–19]. We also examined the percent complexed PSA that may be higher in people with prostate cancer. In addition, we calculated the free/complexed PSA ratio. With a decreased free PSA and an increased complexed PSA, the f/cPSA should be lower in prostate cancer.

The age group distribution of PSA tests is seen in Table 1. The total, free and complexed PSAs increased with age. The geometric mean (SE) of total PSA was 0.96 (0.02) μg/l for all men in NHANES 2007–2010 which was similar to the tPSA GM of 0.94 (0.02) μg/l for all men in NHANES 2001–2004. Also, the age group trend for tPSA was similar for men in 2007–2010 (0.74 μg/l for ages 40–49 years to 1.66 μg/l for ages 70–79 years) compared with men in 2001–2004 (0.73 μg/l for ages 40–49 years to 1.56 μg/l for ages 70–79 years). For NHANES 2007–2010, total PSA increased with age for non-Hispanic Whites and Blacks and Hispanic men (Table 3). In NHANES 2001–2004, the total PSA increased with age for all non-Hispanic Whites and Blacks and Mexican Americans [20]. The GM (SE) of free PSA was 0.30 (0.005) μg/l for all men in NHANES 2007–2010 and compared with 0.27 (0.001) μg/l for all men in 2001–2004. Furthermore, the increasing age trend of fPSA was similar for the two NHANES periods. Free PSA also increased for all race and ethnic groups for 2001–2004. For 2007–2010, the complexed PSA geometric mean (SE) was 0.53 μg/l for all men and there was an increasing age trend (0.40 μg/l for 40–49 years to 0.99 μg/l for men ages 80 years and over). No age trends were seen for percent free PSA for NHANES 2007–2010 and 2001–2004. In addition, no age trend was seen for percent complexed and free/complexed PSA ratio for 2007–2010.

The age-adjusted means for PSA tests were examined by race and ethnic groups for NHANES 2007–2010 (Table 2). Non-Hispanic Black men had higher total PSA, complexed PSA and percent complexed PSA compared with non-Hispanic White men. But non-Hispanic Black men had lower percent free PSA and free/complexed PSA compared with non-Hispanic White men. This suggested a possible increased prevalence of prostate cancer in non-Hispanic Black men compared to White men and this has been seen in the National Cancer Institute's SEER study [1]. Hispanic men had higher complexed and percent complexed PSAs and lower percent free and free/complexed PSAs than non-Hispanic White men. There was no difference in age-adjusted means of PSA tests between non-Hispanic Black and Hispanic men.

For NHANES 2007–2010, non-Hispanic Black men had the greatest linear increase in total, free and complexed PSAs with increasing age compared with non-Hispanic White and Hispanic men (Table 3). This suggested a potentially greater prevalence of prostate cancer in non-Hispanic Black men compared to non-Hispanic White and Hispanic men with increasing age. In NHANES 2001–2004, non-Hispanic Black men also had steeper linear trend increases in total and free PSAs with increasing age compared with non-Hispanic White and Mexican American men [20]. Interestingly, in NHANES 2001–2004, there was a nonlinear relationship between percent free PSA and age for non-Hispanic Black men. The percent free PSA decreased for increasing age up to 60 years and then %fPSA increased above 60 years with increasing age.

Body mass index had a significant effect on the distribution of PSA tests (Table 4). Normal (healthy) and overweight men had higher tPSA, fPSA, and cPSA than obese men. There was no significant difference in age-adjusted means for PSA tests between normal (healthy) BMI men and overweight men. Obesity has also been shown to be inversely related to PSA in NHANES 2001–2004. Werny et al. found that total PSA decreased with increasing BMI, weight, waist circumference, and triceps skinfold while controlling for age and race and ethnicity [33]. Fowke and Matthews examined the relationship of total PSA to body composition measured by dual X-ray absorptiometry in NHANES 2001–2004 [34]. They found that lower total PSA was associated with the highest levels of total, lean and fat masses. This suggested a PSA plasma hemodilution with higher BMI. Hence, there is a dilution of a fixed amount of PSA in a larger body mass with a greater plasma volume. Other studies have shown an inverse relationship between BMI and total PSA [35–38].

Studies have not shown consistently that obesity is associated with increased prevalence of prostate cancer [33]. However, obesity may be related to more advance stages of prostate cancer and mortality rate from prostate cancer [39–41]. Allott et al. showed evidence that obesity was linked with aggressive prostatic cancer [39]. Freedland reviewed possible biological mechanisms of obesity leading to advanced stages of prostate cancer and increased mortality [42]. Obese men have decreased serum free testosterone, increased serum estradiol and insulin, and consume diets high in fats and calories, all factors that are associated with more aggressive prostate cancer.

The distribution of men for selected thresholds for total, percent free and percent complexed PSAs for NHANES 2007–2010 is seen in Fig. 1. Generally, the distributions of thresholds for total and percent free PSAs were very similar to NHANES 2001–2004 [20]. For all men, the total PSA > 4.0 μg/l was 6.1% in NHANES 2007–2010 and 6.2% in NHANES 2001–2004. The tPSA > 2.5 μg/l was 13.9% in NHANES 2007–2010 and 13.1% during NHANES 2001–2004. For NHANES 2007–2010, there were no statistically significant differences ($p >$ 0.035, significant at $p > 0.05$ with Bonferroni correction) in the distributions at various total PSA thresholds between non-Hispanic Black and White men and Hispanic men (Fig. 1).

The distribution of percent free PSA thresholds for NHANES 2007–2010 was similar to NHANES 2001–2004. For all men, the %fPSA ≤ 25% was 38% in NHANES 2007–2010 compared to 37% in NHANES 2001–2004. For %fPSA threshold ≤ 15%, the proportion was 8.5% of men in NHANES 2007–2010 and 9.2% of men in NHANES 2001–2004. In

NHANES 2007–2010, non-Hispanic Black men had a higher proportion of men with a %fPSA ≤ 15% compared with non-Hispanic White men. Also, Hispanic men (45.4%) and non-Hispanic Black men (44.2%) had a significantly ($p < 0.05$ with Bonferroni correction) higher proportion of %fPSA ≤ 25% compared with non-Hispanic White men (36.2%). Catalona et al. showed that a %fPSA cutoff of ≤25% for patients with total PSA of 4–10 μg/l could reduce unnecessary prostate biopsies with minimal loss in sensitivity in detecting prostate cancer [43]. Roddam et al. did a systemic review of studies using %fPSA and complexed PSA with total PSA of 2–10 μg/l and concluded that these tests could reduce unnecessary prostate biopsies while maintaining a high detection of prostate cancer [44].

The distribution of percent complexed PSA has not been reported previously and threshold values for %cPSA have not been established. A higher complexed PSA and perhaps percent complexed PSA could indicate a possible increased prevalence for prostate cancer. Of all men, 5.6% had %cPSA exceeding 75%. Hispanic men (8.2%) had a significantly ($p < 0.05$ with Bonferroni correction) higher proportion of %cPSA ≥ 75% compared with non-Hispanic White men (5.2%).

A major limitation of NHANES data is that the surveys are cross-sectional and the diagnosis and outcome of prostate cancer using PSA tests cannot be obtained immediately. NHANES cannot directly implicate the association of PSA tests and prostate cancer. Potential long-term follow-up of NHANES data is possible using NHANES data linked to Medicare enrollment and claims records collected from the Centers for Medicare and Medicaid Services [45] and mortality data from the National Death Index [46]. Another limitation is only 84.0% of interviewed and examined men ≥40 years participated in PSA testing in NHANES 2007–2010, and this can lead to possible self-selection bias. Also, PSA tests can be affected by benign prostatic hypertrophy and other non-prostatic diseases such as renal failure that are not evenly distributed across different population subgroups.

5. Conclusions

The screening for prostate cancer using the total prostate-specific antigen is common but remains controversial [2–4]. PSA tests are used to monitor patients with prostate cancer along with other diagnostic modalities. In this study, total, free and complexed PSAs increased with age. Non-Hispanic Black men had the highest total and complexed PSAs. Also, obese men had the lowest total, free and complexed PSAs.

Laboratory tests are needed to identify more aggressive forms of prostate cancer. Recently, molecular diagnosis of prostate cancer has been introduced to screen, monitor and treat prostate cancer [47–49]. New prostate biomarkers include molecular markers in serum, urine and tissue, and molecular gene-based tests. The use of free and complexed PSAs may help in the diagnosis and monitoring of prostate cancer, but longitudinal studies will be needed to ascertain the utility of these tests.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

List of abbreviations

%cPSA	percent complexed prostate-specific antigen
%fPSA	percent free prostate-specific antigen
cPSA	complexed prostate-specific antigen
fPSA	free prostate-specific antigen
f/cPSA	free/complexed prostate-specific antigen ratio
GM	geometric mean
NHANES	National Health and Nutrition Examination Survey
tPSA	total prostate-specific antigen

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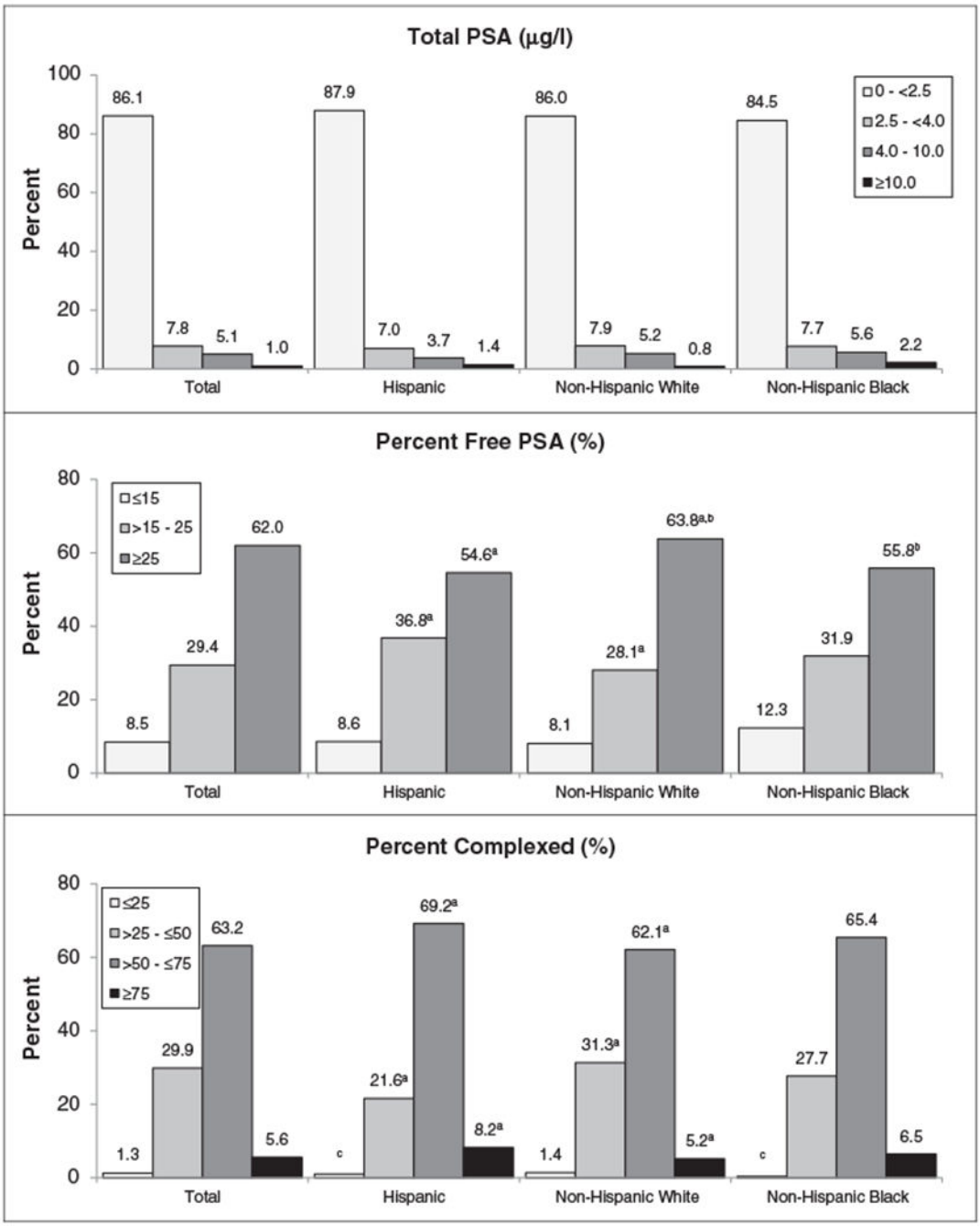

Fig. 1.

Distribution of thresholds for total PSA, percent free PSA and percent complexed PSA by race and ethnicity. [a]Non-Hispanic White is different from Hispanic ($p < 0.05$ with Bonferroni correction). [b]Non-Hispanic White is different from non-Hispanic Black ($p < 0.05$ with Bonferroni correction). [c]Relative standard error > 40%.

Table 1

Weighted mean, standard error of the mean, and selected percentiles for PSA tests among US men aged 40 and over by age group.

	Age group	*n*	Mean (SE)[a]	Percentiles						
				5%	10%	25%	50%	75%	90%	95%
Total PSA (μg/l)	All ages	3251	0.96 (0.02)	0.28	0.37	0.54	0.88	1.59	3.03	4.57
	40–49 years	854	0.74 (0.01)	0.28	0.35	0.49	0.70	1.04	1.64	2.21
	50–59 years	833	0.87 (0.04)	0.29	0.38	0.52	0.84	1.47	2.31	3.00
	60–69 years	787	1.19 (0.04)	0.28	0.38	0.65	1.10	2.18	4.02	5.60
	70–79 years	511	1.66 (0.06)	0.27	0.42	0.86	1.71	3.53	5.50	8.46
	≥80 years	266	1.82 (0.16)	0.24	0.35	0.82	1.94	3.92	8.39	11.85
	p value[b]		<0.001							
Free PSA (μg/l)	All ages	3251	0.27 (<0.01)	0.08	0.11	0.16	0.26	0.41	0.69	0.94
	40–49 years	854	0.22 (<0.01)	0.08	0.10	0.15	0.21	0.30	0.44	0.56
	50–59 years	833	0.24 (0.01)	0.08	0.11	0.16	0.24	0.37	0.51	0.64
	60–69 years	787	0.31 (0.01)	0.09	0.12	0.18	0.32	0.56	0.77	1.02
	70–79 years	511	0.46 (0.02)	0.10	0.14	0.25	0.48	0.88	1.49	1.97
	≥80 years	266	0.51 (0.04)	0.08	0.11	0.26	0.53	1.02	1.96	2.74
	p value[b]		<0.001							
Complexed PSA (μg/l)	All ages	3250	0.53 (0.01)	0.11	0.16	0.27	0.49	0.96	1.97	2.94
	40–49 years	853	0.40 (0.01)	0.11	0.16	0.25	0.39	0.61	1.08	1.43
	50–59 years	833	0.47 (0.03)	0.11	0.17	0.25	0.45	0.87	1.50	2.09
	60–69 years	787	0.66 (0.03)	0.12	0.17	0.33	0.66	1.29	2.65	3.58
	70–79 years	511	0.90 (0.04)	0.10	0.15	0.45	0.95	2.10	3.48	5.05
	≥80 years	266	0.99 (0.09)	0.10	0.17	0.41	1.03	2.28	5.12	7.85
	p value[b]		<0.001							
Percent free PSA (%)	All ages	3251	28.1 (0.3)	12.5	15.7	21.1	28.8	37.5	46.8	52.7
	40–49 years	854	29.6 (0.5)	13.0	16.5	22.7	30.1	39.0	47.6	53.0
	50–59 years	833	28.0 (0.6)	12.4	16.0	20.7	28.7	37.9	46.4	50.9
	60–69 years	787	26.1 (0.6)	10.9	13.9	20.0	26.7	34.9	43.3	50.8
	70–79 years	511	27.9 (0.7)	13.9	16.2	21.0	27.2	36.0	48.7	56.3

	Age group	*n*	Mean (SE)[a]	Percentiles						
				5%	10%	25%	50%	75%	90%	95%
	≥80 years	266	28.0 (0.9)	11.6	15.6	21.6	28.9	37.2	44.6	54.7
	p value[b]		NS							
Percent complexed PSA (%)	All ages	3250	56.0 (0.5)	33.9	39.6	47.4	56.9	64.8	71.6	75.5
	40–49 years	853	55.7 (0.5)	33.4	39.3	47.1	56.2	64.2	71.4	75.1
	50–59 years	833	55.6 (0.9)	33.8	39.3	46.7	56.1	64.6	71.1	75.1
	60–69 years	787	57.4 (0.7)	35.8	40.5	49.4	58.0	66.0	72.2	76.3
	70–79 years	511	56.3 (0.9)	32.2	38.1	48.7	57.6	64.8	70.9	74.4
	≥80 years	266	55.9 (0.7)	33.7	39.6	47.8	56.5	63.3	71.4	76.8
	p value[b]		NS							
Free/complexed PSA ratio	All ages	3250	0.52 (0.01)	0.18	0.23	0.34	0.51	0.79	1.11	1.43
	40–49 years	853	0.55 (0.01)	0.19	0.25	0.36	0.55	0.82	1.15	1.49
	50–59 years	833	0.52 (0.02)	0.17	0.23	0.34	0.51	0.82	1.11	1.44
	60–69 years	787	0.47 (0.01)	0.17	0.21	0.32	0.47	0.70	1.02	1.26
	70–79 years	511	0.51 (0.02)	0.21	0.25	0.33	0.47	0.76	1.12	1.69
	≥80 years	266	0.52 (0.02)	0.16	0.23	0.36	0.53	0.77	1.10	1.40
	p value[b]		NS							

[a]The geometric weighted mean and SE of the mean are shown for all PSA tests except percent complexed PSA, for which the arithmetic weighted mean is shown.

[b]*p* value for linear trend.

Table 2

Age-adjusted weighted mean[a], standard error of the mean, and selected percentiles for PSA tests by race and ethnicity status.

	Race and ethnicity	*n*	Mean (SE)[b]	Percentiles						
				5%	10%	25%	50%	75%	90%	95%
Total PSA (μg/l)	Total[c]	3251	1.06 (0.02)							
	Hispanic	864	1.11 (0.06)	0.30	0.39	0.57	0.86	1.39	2.76	4.00
	Non-Hispanic White	1700	1.03 (0.02)[d]	0.28	0.37	0.54	0.88	1.61	3.07	4.41
	Non-Hispanic Black	560	1.25 (0.07)	0.25	0.33	0.53	0.96	1.70	3.22	5.44
Free PSA (μg/l)	Total	3251	0.30 (0.005)							
	Hispanic	864	0.29 (0.01)	0.08	0.11	0.15	0.24	0.37	0.60	0.82
	Non-Hispanic White	1700	0.29 (0.01)	0.09	0.11	0.16	0.26	0.42	0.71	0.95
	Non-Hispanic Black	560	0.31 (0.01)	0.07	0.10	0.16	0.25	0.43	0.68	0.95
Complexed PSA (μg/l)	Total	3250	0.58 (0.01)							
	Hispanic	864	0.64 (0.03)[e]	0.14	0.19	0.31	0.50	0.90	1.83	2.82
	Non-Hispanic White	1699	0.56 (0.01)[d]	0.11	0.16	0.27	0.49	0.97	1.97	2.75
	Non-Hispanic Black	560	0.72 (0.04)	0.11	0.16	0.27	0.50	1.07	2.10	3.51
Percent free PSA (%)	Total	3251	28.2 (0.3)							
	Hispanic	864	26.2 (0.5)[e]	11.7	15.4	19.8	26.2	35.2	43.8	49.3
	Non-Hispanic White	1700	28.8 (0.3)[d]	12.8	16.1	21.6	29.1	37.7	47.2	53.5
	Non-Hispanic Black	560	25.8 (0.6)	11.5	13.8	19.3	26.8	35.5	44.9	50.2
Percent complexed PSA (%)	Total	3250	56.0 (0.5)							
	Hispanic	864	59.2 (0.8)[e]	38.4	42.3	51.6	59.9	67.7	73.8	78.4
	Non-Hispanic White	1699	55.4 (0.5)[d]	33.6	39.2	46.8	56.3	64.3	71.2	75.2
	Non-Hispanic Black	560	57.7 (0.7)	34.3	40.7	49.1	58.0	65.2	72.5	76.5
Free-to-complexed ratio	Total	3251	0.52 (0.01)							
	Hispanic	864	0.45 (0.01)[e]	0.16	0.22	0.30	0.44	0.67	1.02	1.23
	Non-Hispanic White	1699	0.53 (0.01)[d]	0.18	0.24	0.35	0.52	0.80	1.15	1.47
	Non-Hispanic Black	560	0.46 (0.01)	0.16	0.21	0.31	0.47	0.72	1.05	1.33

[a] Weighted means are age-adjusted by the direct method to year 2000 population estimates using age groups 40–49, 50–59, 60–69, 70–79, and 80 and over.

[b] The weighted geometric mean and the SE of the mean are shown for all PSA tests except percent complexed PSA, for which the weighted arithmetic mean is shown.

[c] The total includes "other" race and ethnic group (not shown).

[d] Significant difference between non-Hispanic White and non-Hispanic Black ($p < 0.05$ with Bonferroni correction).

[e] Significant difference between Hispanic and non-Hispanic White ($p < 0.05$ with Bonferroni correction).

Table 3

Weighted mean and standard error of the mean for selected PSA tests for race and ethnicity groups by age groups.

Race and ethnicity	Age group	Total PSA		Free PSA		Complexed PSA	
		n	Mean[a] (SE)	*n*	Mean[a] (SE)	*n*	Mean[a] (SE)
All men	≥40 years	3251	0.96 (0.02)	3251	0.27 (0.00)	3250	0.53 (0.01)
	40–49 years	854	0.74 (0.01)	854	0.22 (0.00)	853	0.40 (0.01)
	50–59 years	833	0.87 (0.04)	833	0.24 (0.01)	833	0.47 (0.03)
	60–69 years	787	1.19 (0.04)	787	0.31 (0.01)	787	0.66 (0.03)
	≥70 years	777	1.71 (0.06)	777	0.48 (0.02)	777	0.93 (0.04)
	p value[b]		<0.001		<0.001		<0.001
Hispanic	≥40 years	864	0.96 (0.02)	864	0.25 (0.01)	864	0.55 (0.01)
	40–49 years	275	0.79 (0.03)	275	0.21 (0.01)	275	0.46 (0.02)
	50–59 years	264	0.92 (0.04)	264	0.23 (0.01)	264	0.54 (0.03)
	60–69 years	222	1.36 (0.09)	222	0.36 (0.02)	222	0.77 (0.06)
	≥70 years	103	1.74 (0.27)	103	0.44 (0.06)	103	0.99 (0.16)
	p value[b]		<0.001		<0.001		<0.001
Non-Hispanic White	≥40 years	1700	0.96 (0.02)	1700	0.27 (0.01)	1699	0.52 (0.01)
	40–49 years	396	0.73 (0.02)	396	0.22 (0.01)	395	0.39 (0.01)
	50–59 years	372	0.86 (0.04)	372	0.24 (0.01)	372	0.46 (0.03)
	60–69 years	363	1.16 (0.05)	363	0.30 (0.01)	363	0.64 (0.03)
	≥70 years	569	1.64 (0.07)	569	0.47 (0.02)	569	0.88 (0.04)
	p value[b]		<0.001		<0.001		<0.001
Non-Hispanic Black	≥40 years	560	1.02 (0.04)	560	0.26 (0.01)	560	0.57 (0.03)
	40–49 years	147	0.74 (0.04)	147	0.20 (0.01)	147	0.40 (0.03)
	50–59 years	162	1.00 (0.07)	162	0.26 (0.02)	162	0.56 (0.05)
	60–69 years	175	1.35 (0.10)	175	0.35 (0.02)	175	0.77 (0.06)
	≥70 years	76	2.44 (0.26)	76	0.55 (0.06)	76	1.48 (0.18)
	p value[b]		<0.001		<0.001		<0.001

[a]The weighted geometric mean and SE of the mean are shown.

[b] p value for linear trend.

Table 4

Age-adjusted weighted mean[a], standard error of the mean, and selected percentiles for PSA tests by body mass index group.

	Body mass index group[b]	*n*	Mean (SE)[c]	Percentiles						
				5%	10%	25%	50%	75%	90%	95%
Total PSA (μg/l)	Total[d]	3203	1.06 (0.19)							
	Normal	702	1.21 (0.06)[e]	0.29	0.38	0.59	0.98	1.78	3.65	5.36
	Overweight	1315	1.09 (0.03)[f]	0.31	0.39	0.55	0.90	1.63	3.01	4.64
	Obese	1152	0.94 (0.03)	0.24	0.34	0.49	0.80	1.48	2.77	3.85
	p value		NS							
Free PSA (μg/l)	Total	3203	0.30 (0.005)							
	Normal	702	0.32 (0.01)[e]	0.08	0.11	0.16	0.28	0.47	0.72	1.10
	Overweight	1315	0.31 (0.01)[f]	0.09	0.12	0.18	0.26	0.42	0.69	0.94
	Obese	1152	0.27 (0.01)	0.08	0.10	0.15	0.23	0.38	0.67	0.90
	p value		NS							
Complexed PSA (μg/l)	Total	3202	0.58 (0.01)							
	Normal	702	0.68 (0.03)[e]	0.11	0.17	0.30	0.52	1.08	2.28	3.55
	Overweight	1314	0.59 (0.02)[f]	0.13	0.17	0.28	0.49	1.00	1.96	2.83
	Obese	1152	0.51 (0.02)	0.10	0.15	0.25	0.45	0.81	1.82	2.52
	p value		0.048							
Percent free PSA (%)	Total	3203	28.2 (0.3)							
	Normal	702	26.9 (0.7)	11.0	14.9	20.6	27.8	35.6	43.7	49.8
	Overweight	1315	28.5 (0.4)	13.0	15.6	21.1	29.1	37.5	47.3	52.5
	Obese	1152	28.9 (0.4)	13.2	16.2	21.5	29.1	38.2	47.4	53.1
	p value		NS							
Percent complexed PSA (%)	Total	3202	56.0 (0.5)							
	Normal	702	56.9 (0.7)	36.2	40.7	48.7	57.2	65.4	71.8	77.3
	Overweight	1314	55.9 (0.6)	33.9	39.6	46.8	56.9	64.8	72.1	75.3
	Obese	1152	55.7 (0.6)	33.1	39.1	47.4	56.7	64.6	71.0	74.8
	p value		NS							

	Body mass index group[b]	n	Mean (SE)[c]	Percentiles						
				5%	10%	25%	50%	75%	90%	95%
Free-to-complexed ratio	Total	3202	0.52 (0.01)							
	Normal	702	0.49 (0.02)	0.15	0.23	0.33	0.50	0.74	1.04	1.22
	Overweight	1314	0.52 (0.01)	0.19	0.24	0.34	0.51	0.81	1.13	1.47
	Obese	1152	0.54 (0.01)	0.19	0.24	0.34	0.52	0.79	1.15	1.48
	p value		NS							

[a] Weighted means are age-adjusted by the direct method to year 2000 population estimates using age groups 40–49, 50–59, 60–69, 70–79, and 80 and over.

[b] A body mass index (kg/m^2) from 18.5 to 24.9 is considered normal, from 25.0 to 29.9 is overweight and 30.0 or more is obese.

[c] The weighted geometric mean and the SE of the mean (SE) are shown for all PSA tests except percent complexed PSA, for which the weighted arithmetic mean is shown.

[d] Total includes underweight body mass index (<18.5 kg/m^2). Underweight is not shown separately because of insufficient sample size.

[e] Significant difference between normal and obese ($p < 0.05$ with Bonferroni correction).

[f] Significant difference between overweight and obese ($p < 0.05$ with Bonferroni correction).

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