Prostate-Specific Antigen in a Community Screening Program

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Background. This study was designed to determine who participates in community-based prostate-specific antigen (PSA) screening programs and what serum PSA levels can be expected.

Methods. A descriptive analysis of men who participated in an annual community health screening program was used to compare men who chose PSA screening with those who did not. The relationship of demographic variables to PSA level was evaluated by multivariate regression analysis. Data were available on 5548 men, 6% of whom were black.

Results. The population of PSA screening participants included proportionately more middle-aged white men with higher median income, as compared with men who did not participate. Those who did not participate in the screening were more likely to be either very old or very young. PSA levels increased with age, and the percentage of men with elevated PSA levels increased with age. One tenth (9.6%) of all participants had PSAs between 4 ng/mL and 10 ng/mL, and 1.9% had levels greater than 10 ng/mL. Within 1 year of the screening, 1.7% of the screened participants had a diagnosis of prostate cancer. The mean PSA in this group was 15.9 ng/mL.

Conclusions. These data confirm the need for age-specific PSA reference ranges. It is likely that the same reference range can be used for all racial and ethnic populations.

Key words. Prostate; prostate-specific antigen; prostate cancer screening; community health screening; community health services. (*J Fam Pract 1995; 41:163-168*)

In the United States, prostate cancer has surpassed lung cancer as the most commonly diagnosed cancer among men and is the second leading cause of cancer death in men. The association between age and prostate cancer is well known: the incidence rate in men over 65 years of age is almost 40 times greater than in men under 65 years.[1] As the at-risk population continues to increase, the number of prostate cancer cases also is expected to rise.

Prostate-specific antigen (PSA) has been proposed as a screening tool for prostate cancer, although its value as such has not been completely determined. Its main proven utility has been to monitor the progress of prostate cancer and the response to therapy.[2] However, the American Cancer Society currently recommends a PSA determination along with digital rectal examination annually for screening all asymptomatic men aged 50 years and older.[3] Other cancer-interest groups such as the US Preventive Services Task Force and the International Union Against Cancer do not recommend mass screening for prostate cancer because such screening has not been shown to have an impact on prostate cancer mortality.[4]

Project Health-O-Rama (PHR) is an annual community-based health-screening program in southeast Michigan that offered PSA testing as part of its screening program for the first time in 1992. Data from the 1992 program were used to determine the predictors of participation in PSA screening and predictors of PSA level in men who had a PSA test. The PHR data set permitted the following: (1) examination of the demographics of participants vs nonparticipants in PSA screening; (2) evaluation of variables associated with elevated PSA levels in a

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volunteer population; and (3) matching of the PHR data set against the Surveillance, Epidemiology, and End Results (SEER)[1] database for metropolitan Detroit to determine subsequent prostate cancer diagnosis. Specifically, the authors assessed whether age, race/ethnicity, and socioeconomic status influenced the likelihood of having a PSA test, and evaluated the association of age, race/ethnicity, and subsequent diagnosis of prostate cancer with PSA level.

Methods

The goal of PHR, an annual community-based health-screening program in southeastern Michigan, is to encourage individuals in the community to assume responsibility for their health and well-being by adopting and maintaining good health and lifestyle habits. In 1992, a total of 37,334 persons 18 years of age and older participated in screenings at 99 different neighborhood sites, such as shopping malls, hospitals, and churches. A multitude of screening tests and services, such as blood pressure measurement, Papanicolaou smear, prostate/testicular examination, blood chemistries, and tests for visual and hearing acuity, glaucoma, and stool occult blood, were available. Although not all tests were available at each site, blood testing was available at all sites, and because of the large number of participants, all laboratory tests, including PSA, were offered at a reduced cost.

A total of 14,022 men participated in PHR. All were offered a PSA test at a cost of $25. Solicitation regarding the PSA test consisted of distributing a 1-page handout about PSA screening to all men. The handout explained the test, its limitations, and the need for further evaluation if the PSA level was found to be elevated.

Of the 14,022 male PHR participants, 6001 purchased a PSA test (PSA participants). PSA participants were characterized by the demographic information obtained from registration forms and laboratory result forms.

To determine the characteristics of the 8021 men who did not have a PSA test (PSA nonparticipants), a sample of approximately 10% of this population was identified by selecting all men whose registration number ended with a 5; registration numbers had been assigned sequentially to each PHR attendee on his arrival.

All laboratory analyses were performed at Continental Bio-Clinical Laboratory Service, Inc, in Grand Rapids, Michigan. PSA determinations were performed with an IMx/PSA assay (Abbott Laboratories, North Chicago, Ill). The reference ranges were those recommended by the manufacturer: values of 4 ng/mL or less were considered normal, values of 4.1 to 9.9 ng/mL were suspect, and values of 10 ng/mL or greater were considered abnormal. In the data analysis, log PSA was used in order to stabilize the variance.

Because individual socioeconomic status data were unavailable, 1990 US census track data on median household income level were used as a surrogate measurement of SES.

The National Cancer Institute's SEER database for metropolitan Detroit was used to match cancer cases against the PHR database. The last match was performed in July 1994. At that time, the data set for 1992 and approximately the first half of 1993 was complete. The SEER database includes the tri-county area of Wayne, Oakland, and Macomb counties surrounding Detroit. Some of the PHR participants resided outside the SEER area, and thus were not included in any analyses in which "subsequent prostate cancer diagnosis" was a variable.

Statistical analyses were performed using SAS.[5] Simple descriptive statistics and correlation coefficients for relationships between PSA and other variables were computed. Associations between categorical variables were tested using chi-square, and between continuous variables using Student's t test. Multiple linear regression was employed to evaluate the effects of potential important covariates on log PSA.

Results

Of the 14,022 men who participated in the community health program, 6001 (42.8%) men purchased a PSA test. A match was obtained between the laboratory and registration files on 5548 of these men. Most of the difference was attributable to missing records. Some matched records had incomplete demographic data: information about race/ethnicity was missing from 95 records, age from 60, and both from one.

PSA participants ranged in age from 20 to 93 years. As shown in Table 1, 5050 (91.0%) of the participants classified themselves as white, 327 (5.9%) as black, and 76 (1.4%) as other (Mexican-American, Asian-Oriental, and Middle Eastern). Ninety-five (1.7%) did not respond to the race/ethnicity question. Compared with nonparticipants, PSA participants had a higher median income and were predominantly white. The age distribution of the two groups also differed significantly. PSA nonparticipants were more likely to be at either end of the age spectrum, whereas PSA participants were more likely to be 50 to 69 years old.

There was no statistically significant difference in mean log PSA between blacks, whites, and other or unknown racial/ethnic groups after adjusting for age ($P>.05$, Table 2). The range of PSA in black men was

Table 1. Characteristics of PSA Participants and Nonparticipants

Characteristic	% of Screening Participants (n=5548)	% of Screening Nonparticipants (n=909*)	*P* Value†
Race			
Black	5.9	12.4	
White	91.0	81.7	
Other	1.4	4.2	<.001
Unknown	1.7	1.7	
Age, y			
<50	20.8	33.1	
50–59	23.6	10.6	
60–69	35.1	27.4	<.001
70–79	17.6	23.8	
≥80	1.9	3.9	
Unknown	1.1	1.3	
Median annual income, $			
<15,000	3.1	5.9	
15,000–25,000	4.5	6.3	
25,000–30,000	6.1	8.1	<.001
>30,000	48.5	46.3	
Unknown	37.8	33.3	

**Characteristics of PSA nonparticipants were obtained based on an approximate 10% sample of the total number of Project Health-O-Rama (PHR) participants (n=8021). This sample was identified by selecting all men whose PHR registration number ended in 5.*
†Chi-square test.
PSA denotes prostate-specific antigen.

0.1 ng/mL to 136 ng/mL (mean, 1.15 ng/mL). In white men, the range was 0.1 ng/mL to 254 ng/mL (mean, 1.13 ng/mL); in the other or unknown group, the range was 0.1 ng/mL to 24.4 ng/mL (mean, 1.08 ng/mL). The lowest detectable PSA level was 0.1 ng/mL.

The multivariate analysis included black and white PSA participants who were of known age and resided in the tri-county area (n=3865). With PSA as the dependent variable, the independent variables evaluated in the regression model were race/ethnicity (included in every model), age, subsequent prostate cancer diagnosis, and the interaction terms for these variables. No interaction terms made a significant contribution to the models, although a quadratic term for age (age^2) was significant (P=.002). A subsequent diagnosis of prostate cancer was

Table 2. Serum PSA Level of PSA Participants, by Race Adjusted for Age

PSA Level	Race		
	Black (n=319)	White (n=4992)	Other/Unknown (n=169)
Mean (SEM)	1.15 (±1.1)	1.13 (±1.0)	1.08 (±1.1)
Range	0.1–136.0	0.1–254.0	0.1–24.4

NOTE: Differences in mean PSA values between black and white participants are not statistically significant. Total number of participants does not add to 5548 because of missing data.
PSA denotes prostate-specific antigen; SEM, standard error of the mean.

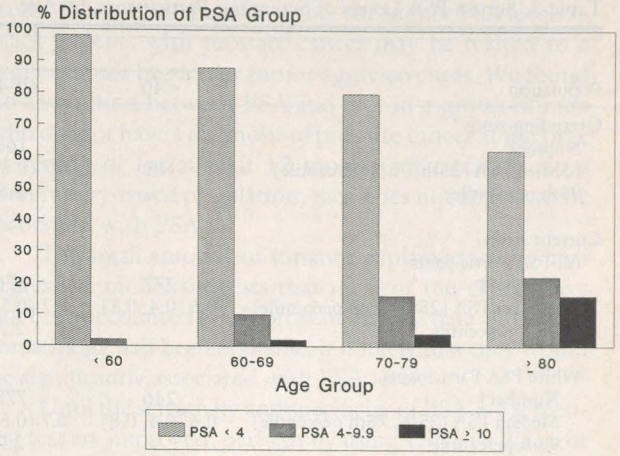

Figure. Distribution of prostate-screening antigen (PSA) by age among participants in the screening program.

associated with higher PSA levels (P<.001). After controlling for age and subsequent prostate cancer, race/ethnicity was not associated with PSA level (P>.05).

Age and subsequent prostate cancer diagnosis accounted for 22.6% of the variance in the final model. Age represents the majority of the variance that was accounted for (R^2=.162). Prostate cancer diagnosis essentially accounts for the remainder (R^2=.063).

The Figure illustrates the association between age and PSA range. As the age increases, the percentage of participants with elevated PSA also increases. Table 3 also demonstrates this association in a format similar to that published by Oesterling et al,[6] whose results are included for comparison. The median PSA values with 25th and 75th percentiles were determined for similar age ranges. The 95th percentile PSA levels obtained from the regression model at the midpoint of the 10-year age ranges between 40 and 79 years (eg, the 95% value for 65-year-old men in the 60- to 69-year-old group) are likewise included for comparison.

PSA participants and nonparticipants were matched against the 1992 and early 1993 SEER data set for cancer diagnosis. Of the 5548 PSA participants, 4015 lived in the SEER tri-county area, and 70 (1.7%) were found to have prostate cancer diagnosed. Of the 909 PSA nonparticipants, 691 lived in the SEER area, and 12 (1.7%) had a prostate cancer diagnosis. The mean PSA level among the subsequent prostate cancer cases was 15.9 ng/mL (range 0.4 to 115 ng/mL); the median PSA value was 8.5 ng/mL.

Discussion

Men with a higher median income were more likely to purchase the PSA test, which cost $25, the most expen-

Table 3. Serum PSA Levels of Screening Participants, by Age

Population	Age Group, y					
	<40	40–49	50–59	60–69	70–79	≥80
Oesterling study*						
Number		165	144	94	68	
Median PSA (25th, 75th percentile)	NA	0.7 (0.5, 1.1)	1.0 (0.6, 1.4)	1.4 (0.9, 3.0)	2.0 (0.9, 3.0)	NA
95th percentile		2.5	3.5	4.5	6.5	
Current study						
All PSA Participants						
Number†	277	876	1308	1919	961	100
Median PSA (25th, 75th percentile)	0.6 (0.4, 0.8)	0.7 (0.5, 1.0)	0.9 (0.5, 1.4)	1.3 (0.7, 2.4)	1.7 (0.9, 3.4)	2.6 (1.0, 6.6)
95th percentile		2.7	3.8	5.3	7.5	—
White PSA Participants						
Number†	246	773	1205	1756	884	92
Median PSA (25th, 75th percentile)	0.6 (0.4, 0.8)	0.7 (0.5, 1.0)	0.9 (0.5, 1.4)	1.3 (0.7, 2.4)	1.6 (0.9, 3.4)	2.6 (1.0, 6.3)
95th percentile		2.7	3.8	5.3	7.3	—
Black PSA Participants						
Number†	20	69	59	104	57	8
Median PSA 25th, 75th percentile)	0.5 (0.4, 0.8)	0.6 (0.5, 1.0)	0.9 (0.6, 1.6)	1.2 (0.6, 2.4)	2.2 (1.3, 5.6)	3.2 (1.0, 13.1)
95th percentile		3.2	4.8	7.1	10.5	—

**Oesterling JE, Jacobsen SJ, Chute CG, et al. Serum prostate-specific antigen in a community-based population of healthy men. JAMA 1993;270:860–4.*
†Numbers of participants across age groups do not add to the total for each category because of exclusion criteria for analysis and missing data.
PSA denotes prostate-specific antigen; NA, not available.

sive blood test offered by Health-O-Rama. Black men were less likely to purchase the PSA test, perhaps because black men have different attitudes and perceptions regarding cancer screening than white men.[7] Black men also represented a larger proportion of the low-income groups as compared with whites among PSA participants and nonparticipants alike ($P<.001$), indicating that there may have been financial reasons for not purchasing PSA.

The skewed distribution of the PSA nonparticipants to both extremes of age may also be related to the cost of the test, since both groups may be less likely to afford the PSA fee. The larger proportion of young men in the PSA nonparticipant category may also be explained by the possibility that most men participating in PHR are aware that prostate cancer is generally a cancer of older men. The older age group may represent a group of elderly men who feel they are too old for testing to result in any benefit.

If society decides that screening for prostate cancer should be performed, black men will likely be a target population because of their higher prostate cancer incidence and mortality rates as compared with white men.[8–10] These results suggest that testing at reduced cost in a convenient and accessible neighborhood location is insufficient in adequately targeting this population and that more aggressive measures are required. Perhaps an intense educational campaign might include not only black men, but also their families, who could, in turn, encourage them to be tested. If mass PSA screening is determined to be beneficial, it may be necessary to offer the test at an even lower fee or free of charge.

Although PHR participants who chose to have the PSA test differed in age, race/ethnicity, and socioeconomic status profiles from those who did not participate, they appear to be similar to PSA screening populations reported by others.[11,12] In these reports, men who were ≥50 years and did not have prostate cancer were recruited through news reports or direct-mail advertising to undergo screening.[11,12] Our participants were not queried directly about whether they had a history of prostate cancer.

Another indication of the similarity between our PSA participants and those of other studies is the proportion of abnormal PSA levels, which agrees well with the study by Catalona et al[11] of PSA in a group of 1653 men older than 50 years. This study found PSA levels of 4.0 to 9.9 ng/mL in 6.5% men, compared with 7.6% of men in our study with the same values, and a level of 10 ng/mL or greater in 1.8%, compared with 1.9% in our study population.

In contrast to other reports,[11,13] we found a statistically significant association between age and PSA among PSA-screening volunteers. Age accounted for most of the variation of PSA levels in the multivariate regression analysis. Since PSA is known to be associated with volume of the prostate gland and benign prostatic hyperplasia,[14,15] both of which increase with age, our findings were not surprising.

The association between age and PSA has been reported in other populations. Recently, in a single study of a community-based population of 471 white men,[6] PSA was shown to be significantly correlated with both age and prostatic volume, while age was also significantly correlated with prostatic volume. The authors concluded that age-specific reference ranges for PSA, prostatic volume, and PSA density are needed.

Our study population is a community-based volunteer population, but with a much larger population that includes approximately 6% black men. Our median values and 25th and 75th percentile ranges for all the PSA participants are very similar to those reported by Oesterling et al,[6] indicating that the median PSA values for these age groups are stable. Based on our multivariate regression results, we do not believe it is necessary to determine separate age-specific references ranges for black men.

The age-specific reference ranges reported by Oesterling et al[6] used the 95th percentile determined in a regression model as the upper reference value. We determined the 95th percentile in our PSA participants between the ages of 40 and 79 years for comparison (Table 3). The results are similar to those of Oesterling et al[6] in the younger age groups but less so in the older groups. This is especially true for older black men. As noted previously, our population was not as thoroughly screened for prostate cancer as in the study of Oesterling and colleagues.[6] Although we attempted to remove prostate cancer cases from our data set for comparison with the subjects investigated by Oesterling et al, our population is probably more skewed in the higher PSA ranges, especially among older men, in whom prostate cancer is more prevalent. Also, the number of black men in each age group is small compared with white men, increasing the variance and, therefore, the 95th percentile.

We also attempted to determine the 95th percentile based on a quadratic model, as this model was the most accurate description of the relationship between age and PSA in our multivariate analysis. When the analysis is restricted to 40 to 79 years of age, however, the association between age and PSA is linear.

We agree that there is a need for an age-adjustment factor or population-based age-specific reference ranges when interpreting PSA values. At this time, the first such age-specific ranges have been published using a community-based population of men with no evidence of prostate cancer.[6] Our results would indicate that these reference ranges are reasonable and may even be conservative in the older age ranges.

One of our primary interests was to determine if PSA level was associated with race. The only study to address the question reported an association between race and PSA level in a group of prostate cancer patients.[16] In that study, the authors speculated that the higher PSA levels in black patients with prostate cancer may be related to a higher tumor burden or tumor aggressiveness. We found no association between PSA and race in a group of men who did not have a diagnosis of prostate cancer at the time of testing or for at least 12 months after testing. In a community-based population, race does not appear to be associated with PSA.

The small amount of variance explained in the final regression model suggests that most of the effects have not been accounted for. If prostate clinical data and symptomatology had been available, it is likely that they would be significantly associated with PSA level.

Until the sensitivity and specificity of PSA as a screening test are improved, perhaps by using PSA in a different strategy, such as longitudinal PSA,[17] it is necessary to characterize PSA to the best of our ability with the available means. The interpretation of a single, "cross-sectional" elevated level could easily lead to unnecessary testing, which would be prevented with improved interpretation. The use of population-based age-specific reference ranges would result in greater accuracy in PSA interpretation, improving the sensitivity of PSA in the younger age groups with a cutoff lower than 4 ng/mL and the specificity in older men with a cutoff greater than 4 ng/mL. The decision regarding whether PSA screening should be performed at all may best be a mutual decision by physicians and their patients within the context of a comprehensive evaluation of the individual patient's history and risk factors.

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