

# Initial Prostate Specific Antigen 1.5 ng/ml or Greater in Men 50 Years Old or Younger Predicts Higher Prostate Cancer Risk

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## Abbreviations and Acronyms

AUA = American Urological Association

NCCN = National Comprehensive Cancer Network

PCa = prostate cancer

PSA = prostate specific antigen

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**Purpose:** Studies show that initial prostate specific antigen higher than the median in young men predicts a subsequent higher risk of prostate cancer. To our knowledge this relationship has not been studied in patients stratified by race.

**Materials and Methods:** A cohort of 3,530 black and 6,118 white men 50 years or younger with prostate specific antigen 4 ng/ml or less at the first prostate specific antigen screening was retrieved from the prostate center database at our institution. Patients were divided into groups based on initial prostate specific antigen 0.1 to 0.6, 0.7 to 1.4, 1.5 to 2.4 and 2.5 to 4.0 ng/ml. Univariate and age adjusted multivariate logistic regression was done to estimate the cancer RR in these prostate specific antigen groups. We calculated the prostate cancer rate at subsequent followups.

**Results:** Median prostate specific antigen in black and white men was 0.7 ng/ml at age 50 years or less. The prostate cancer rate was not significantly different in the groups with prostate specific antigen less than 0.6 and 0.7 to 1.4 ng/ml in black or white men. Black and white men with initial prostate specific antigen in the 1.5 to 2.4 ng/ml range had a 9.3 and 6.7-fold increase in the age adjusted prostate cancer RR, respectively. At up to 9 years of followup initial prostate specific antigen 1.5 ng/ml or greater was associated with gradually increased detection at followup in black and white men.

**Conclusions:** An initial prostate specific antigen cutoff of 1.5 ng/ml may be better than median prostate specific antigen 0.7 ng/ml to determine the risk of prostate cancer in black and white men 50 years old or younger.

**Key Words:** prostate, prostatic neoplasms, prostate-specific antigen, mass screening, continental population groups

SCREENING with PSA has been widely used to detect PCa for 2 decades but it continues to be controversial. The results of 2 large randomized, controlled trials were recently released<sup>1,2</sup> but due to conflicting results the usefulness of PSA screening for decreasing PCa mortality remains hotly debated.

The NCCN recommends that men 40 to 49 years old with baseline PSA greater than 0.6 ng/ml (the median in 40 to 49-year-old men) undergo an-

nual screening thereafter. However, no definitive evidence in the literature supports this recommendation.<sup>3</sup> A number of studies show that men with initial PSA higher than the age specific median are at significantly higher risk for PCa.<sup>4-6</sup> Fang et al reported 3.6-fold higher PCa RR in men 40 to 50 years old when PSA was greater than the age specific median of 0.60 ng/ml.<sup>4</sup> Also, the cumulative projection of cancer-free survival in

men with greater vs lesser PSA with time was significantly different. An even higher relative risk of PCa (22-fold) was found in another study of men with initial PSA greater than the age specific median.<sup>5</sup> Loeb et al reported that men 40 to 50 years old with PSA less than the age specific median had a low PCa incidence in the short term.<sup>6</sup> These previous studies indicate that initial PSA greater than the age specific median should be the criterion to start regular annual PSA screening.

To our knowledge no prior group has investigated the relationship between initial PSA and the subsequent PCa rate by race. Little is known about the PCa incidence at different followups in young men with initial PSA in specific ranges. Thus, we examined the relationship between initial PSA and the subsequent PCa rate in black and white men 50 years old or younger. We also investigated the PCa incidence at different followups in men with initial PSA in different ranges.

## MATERIALS AND METHODS

A total of 138,103 PSA values collected between 1990 and 2008 were retrieved from the prostate center database at our institution. PSA tests done after a PCa diagnosis were excluded from analysis, leaving 108,536 in a total of 43,066 men. Of this group we included in the study 3,530 black and 6,118 white men in whom PSA was first measured at age 50 years or less and initial PSA was 4 ng/ml or less. Clinical variables studied were race (black and white), age (less than 30, 30 to 39 and 40 to 50 years), initial PSA (0 to 0.6, 0.7 to 1.4, 1.5 to 2.4 and 2.5 to 4.0 ng/ml), time to diagnosis (0.0 years or immediate, 0.1 to

2.0, 2.1 to 4.0 and greater than 4.0), and PCa presence or absence (yes or no). The PCa incidence was also assessed for the different initial PSA levels at different followups. Serum PSA was measured using the Tandem®-R immunoradiometric assay (Tandem-E assay before 2000) and the Access® assay. The criteria for performing a prostatic biopsy were a positive digital rectal examination or a PSA considered high based on clinician practice.

The chi-square and Mann-Whitney U tests were used as appropriate to compare the PCa incidence in the black vs white groups. Univariate and multivariate logistic regression was done to estimate and compare the PCa RR in various PSA and age adjusted PSA groups. Men with initial PSA less than 0.6 ng/ml served as controls during analysis. Statistical analysis was done using SPSS® 16.0.

## RESULTS

### PCa by Age, Initial PSA and Followup Stratified by Race

At ages less than 30, 30 to 39 and 40 to 50 years 0, 0 and 28 black men (0.9%), and 0, 1 (0.1%) and 39 white men (0.7%) had PCa, respectively. In black and white men with initial PSA less than 1.5 ng/ml the overall PCa rate was less than 0.4%. Of those with initial PSA between 1.5 and 2.5 ng/ml the PCa rate was greater in black than in white men but the difference was not significant (4.0% vs 2.2%,  $p = 0.174$ ). At PSA 2.5 to 4.0 ng/ml black men had a lower PCa incidence than white men but again the difference was not significant (7.8% vs 9.0%,  $p = 0.739$ , table 1).

Of the 28 black men with PCa the diagnosis was made in 9 at time 0.0 (immediately), in 5 at 0.1 to 2.0

**Table 1.** Study population characteristics

	Black		White		p Value
	PCa	No PCa	PCa	No PCa	
No. pts (%)	28 (0.8)	3,502 (99.2)	40 (0.7)	6,078 (99.3)	0.430 (chi-square test)
PSA (ng/ml):					
No. 0–0.6 (%)	7 (0.4)	1,891 (99.6)	10 (0.4)	3,355 (99.7)	0.660 (chi-square test)
No. 0.7–1.4 (%)	3 (0.2)	1,261 (99.8)	7 (0.3)	2,152 (99.7)	0.754 (Fisher's exact test)
No. 1.5–2.4 (%)	11 (4.0)	267 (96.0)	10 (2.2)	440 (97.8)	0.174 (chi-square test)
No. 2.5–4.0 (%)	7 (7.8)	83 (92.2)	13 (9.0)	131 (91.0)	0.739 (chi-square test)
Median (IQR)	0.7 (0.5–1.1)		0.7 (0.5–1.0)		0.211 (Mann-Whitney U test)
Mean ± SD	0.86 ± 0.59		0.84 ± 0.57		
Age:					
No. less than 30 (%)	0	43 (100)	0	135 (100)	
No. 30–39 (%)	0	445 (100)	1 (0.1)	673 (99.9)	
No. 40–50 (%)	28 (0.9)	3,014 (99.1)	39 (0.7)	5,270 (99.3)	
Median (IQR)	45.7 (42.3–48.2)		44.6 (41.4–47.5)		<0.001 (Mann-Whitney U test)
Mean ± SD	44.0 ± 4.6		44.5 ± 5.1		
Yrs to PCa diagnosis:					
No. 0.0 (Immediate diagnosis)	9 (0.5)	1,989 (99.5)	16 (0.4)	3,855 (99.6)	0.836 (chi-square test)
No. 0.1–2.0 (%)	5 (0.9)	582 (99.1)	8 (0.9)	910 (99.1)	0.968 (chi-square test)
No. 2.1–4.0 (%)	3 (0.7)	414 (99.3)	5 (0.9)	544 (99.1)	1.000 (Fisher's exact test)
No. greater than 4.0 (%)	11 (2.1)	517 (97.9)	11 (1.4)	769 (98.6)	0.353 (chi-square test)
Median (IQR)	0.0 (0.0–1.5)		0.0 (0.0–2.2)		<0.001 (Mann-Whitney U test)
Mean ± SD (range)	1.4 ± 2.2 (0–9.1)		1.2 ± 2.1 (0–9.2)		

**Table 2.** PCa RR in men with different initial PSA by race

	Black RR (96% CI)	p Value	White RR (96% CI)	p Value
PSA (ng/ml):				
0.0–0.6	Referent		Referent	
0.7–1.4	0.6 (0.2–2.5)	0.520	1.1 (0.4–2.9)	0.860
1.5–2.4	11.1 (4.3–29.0)	<0.001	7.6 (3.2–18.4)	<0.001
2.5–4.0	22.8 (7.8–66.5)	<0.001	33.3 (14.3–77.3)	<0.001
Age adjusted				
PSA (ng/ml):				
0.0–0.6	Referent		Referent	
0.7–1.4	0.6 (0.2–2.4)	0.51	1.0 (0.4–2.7)	0.960
1.5–2.4	9.3 (3.5–24.3)	<0.001	6.7 (2.7–16.2)	<0.001
2.5–4.0	16.6 (5.6–49.0)	<0.001	27.1 (11.7–64.7)	<0.001
Age	1.2 (1.0–1.4)	<0.001	1.1 (1.0–1.2)	<0.001

years, in 3 at 2.1 to 4.0 years and in 11 at more than 4.0 years of followup. Of the 40 white men with PCa the diagnosis was made in 16 at time 0.0 (immediately), in 8 at years 0.1 to 2.0, in 5 at years 2.1 to 4.0 and in 11 at more than 4.0 years of followup (table 1). In black and white men 50 years old or younger median PSA was 0.7 ng/ml. From initial PSA measurement to diagnosis the followup 75th percentile was 1.5 (range 0.0 to 9.1) and 2.2 years (range 0.0 to 9.2) in black and white men, respectively (table 1).

#### PCa RR by Initial PSA and Race

On univariate analysis the PCa RR was not significantly different between the groups with initial PSA 0 to 0.6 and 0.7 to 1.5 ng/ml in black and white men ( $p = 0.520$  and  $0.860$ , respectively). On multivariate analysis including initial PSA and age the age adjusted PCa RR was still not significantly different between the groups with initial PSA 0 to 0.6 and 0.7 to 1.5 ng/ml in black and white men ( $p = 0.510$  and  $0.960$ , respectively). However, when initial PSA increased to 1.5 to 2.5 ng/ml, the PCa RR was 11.1-fold higher in black men and 7.6-fold higher in white men than in men with initial PSA 0.6 ng/ml or less

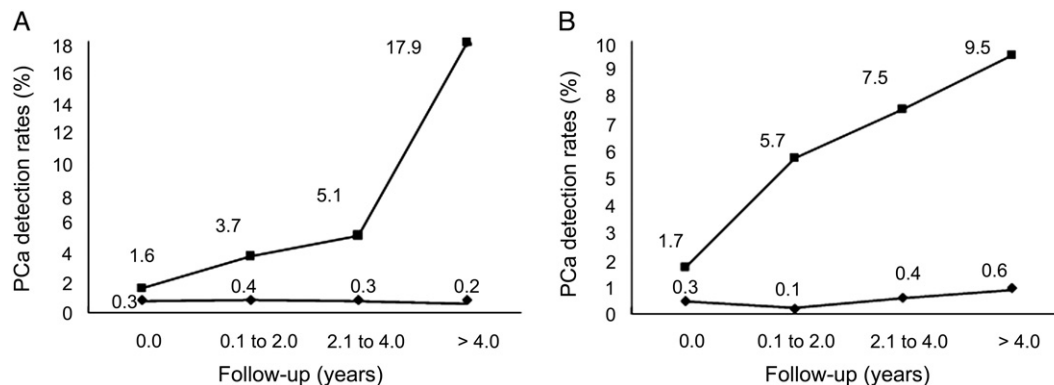
(each  $p < 0.001$ ). The age adjusted PCa RR was also significantly increased 9.3-fold in black men and 6.7-fold in white men (each  $p < 0.001$ ). In the group with initial PSA 2.5 to 4.0 ng/ml the age adjusted RR was 27.1 in black men and 16.6 in white men (each  $p < 0.001$ ). Table 2 lists results.

#### PCa by Followup PSA Less Than 1.5 vs 1.5 ng/ml or Greater

The PCa rate increased gradually and significantly at longer followup in black and white men with baseline PSA 1.5 ng/ml or greater ( $p < 0.001$  and  $0.017$ , respectively). Black and white men with initial PSA 1.5 ng/ml or less had a low PCa incidence at all followups. The PCa rate at followup did not change significantly in black and white men with baseline PSA 1.5 ng/ml or less ( $p = 0.647$  and  $0.323$ , respectively, see figure).

#### DISCUSSION

Although the PCa prevalence in men 50 years old or younger is low,<sup>7</sup> 1/5 in this age group have had a PSA test in the last year.<sup>8</sup> Of those in the prostate center database at our institution who had a PSA test 3,612 black (8.4%) and 6,209 white (14.4%) men underwent it at or before age 50 years, an age at which we found a 1.5% and 1.0% PCa incidence, respectively (data not shown). Of them 3,530 black (97.7%) and 6,118 white (98.5%) men had baseline PSA 4 ng/ml or less. The PCa rate in these men was 0.8% and 0.7%, respectively. The clinical significance of detecting PCa in these cases is unclear. Lane et al reported that the PCa prevalence in men 50 years old or younger with threshold PSA 1.5 ng/ml was similar to that in older men with threshold PSA 3.0 ng/ml.<sup>7</sup> Others reported that younger men have a higher long-term cancer control rate than older men after radical prostatectomy.<sup>9,10</sup>



With time PCa incidence increased significantly in black (A) and white (B) men with initial PSA 1.5 ng/ml or greater (squares) ( $p < 0.001$  and  $0.017$ ) but did not change significantly when initial PSA was less than 1.5 ng/ml (circles) ( $p = 0.647$  and  $0.323$ , respectively).

In our series median PSA in black and white men 50 years old or younger was 0.7 ng/ml, similar to values in previous studies.<sup>4,5</sup> Initial PSA 0.7 to 1.5 ng/ml did not increase the risk of PCa compared to initial PSA 0 to 0.6 ng/ml. However, initial PSA 1.5 to 2.5 ng/ml increased the age adjusted PCa RR 9.3-fold in black men and 6.7-fold in white men. Even more striking was the finding in the group with initial PSA 2.5 to 4.0 ng/ml that age adjusted PCa RR was 16.6 in black men and 27.1 in white men. These findings are in agreement with those in previous studies showing that increased initial PSA in young men is associated with an increased PCa risk.<sup>4-6,11</sup> Our results differ from previously published studies indicating that age specific PSA medians should be used as a cutoff for risk stratification to detect PCa.<sup>4-6</sup> Our findings reveal that initial PSA 1.5 ng/ml or greater and not a median of greater than 0.7 ng/ml may be a better cutoff to determine which men 50 years old or younger are at higher risk for PCa in the future and who may benefit from more frequent PSA testing.

Two major differences between our study and previously published series may provide a rationale for some findings. 1) To our knowledge our cohort is the largest in the literature, and the first in which black and white men were evaluated independently. 2) The initial PSA range in our series only included PSA 4.0 ng/ml or less but other studies included PSA 4.0 ng/ml or greater.

In our cohort of men 50 years old or younger with initial PSA 4.0 ng/ml or less the incidence of PCa in black and white men with initial PSA less than 1.5 ng/ml was always less than 0.6% even at up to 9 years of followup. In contrast, the PCa rate in men with initial PSA 1.5 ng/ml or greater was significantly higher than that in men with PSA less than 1.5 ng/ml and it increased with time. At greater than 4-year followup (maximum 9) the PCa incidence in the group with initial PSA greater than 1.5 ng/ml was almost 18.0% in black men and 9.5% in white men (see figure). These findings indicate that PSA 1.5 ng/ml is a better cutoff to stratify PCa risk in men 50 years old or younger.

Results of the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer show that the rate of detected cancer at 8 years of followup with 2 subsequent screening visits was 0.47% in men with PSA 1.0 ng/ml or less, representing 42% of screened men in the 55 to 65-year age range.<sup>12</sup> The investigators suggested that PSA screening every 8 years in men with PSA 1.0 ng/ml or less would lead to a considerable decrease in the number of screening visits, and associated costs and stress, and the strategy would carry minimal risk for missing aggressive cancer at a curable stage.<sup>12</sup> Loeb et al reported that men 40 to 50 years old with PSA

less than the age specific median were at low risk for PCa detection in the short term.<sup>6</sup>

Initial PSA less than 1.5 ng/ml was associated with a low PCa incidence at different followups in our series, in agreement with previous results. Higher initial PSA also predicted a higher PCa incidence with time in our study. This further confirms that initial PSA 1.5 ng/ml or greater rather than a median of greater than 0.7 ng/ml may be a better cutoff to determine which men 50 years old or younger are at higher risk for PCa in the future. However, prospective studies with long-term followup are warranted.

The biological basis for the relationship between initial PSA and PCa risk remains unclear but theories exist on the cause. 1) Since PCa is generally a gradual process, men with higher initial PSA may be more likely to harbor PCa at an early stage or as a premalignant lesion that can progress and become clinically apparent with time. 2) High grade PIN is 6-fold more common in the biopsies of men with high PSA. Since high grade PIN is considered precancerous, some groups suggest that it may induce higher PSA.<sup>4,13</sup> 3) Prostatic inflammation can lead to increased PSA and in young men may result in a higher risk of subsequent PCa.<sup>14</sup> 4) Insulin-like growth factor-1, and the androgen related genes CYP17, CYP3A4 and SRD5A2 are associated with PCa risk.<sup>15,16</sup>

Our series has several limitations. It is retrospective. We did not evaluate PCa family history. We used data from a large tertiary medical center. This is partly counteracted by our cohort size, which may mitigate the limitation. We did not evaluate digital rectal examination results. However, European Randomized Study of Screening for Prostate Cancer results indicate that the overall characteristics of detected PCa cases differ little based on how they are detected, that is by increased PSA, digital rectal examination or transrectal ultrasound.<sup>17</sup> Also, our findings may not be applicable to all racial groups since we only included black and white men in our analysis.

## CONCLUSIONS

In men 50 years old or younger low initial PSA is associated with a subsequent low PCa rate. Initial PSA less than 1.5 ng/ml was associated with a low PCa rate even at up to 9 years of followup. In contrast, men with initial PSA 1.5 ng/ml or greater were at significantly higher risk for PCa and this incidence increased with time. Based on our findings baseline PSA 1.5 ng/ml is a better risk stratification cutoff than age adjusted median PSA 0.7 ng/ml in black and white men 50 years old or younger. This

recommendation is based on 28 and 40 events in black and white men, respectively, in a large study

cohort with up to 9 years of followup. Further studies are warranted.

## REFERENCES

1. Andriole GL, Grubb RL 3rd, Buys SS et al: Mortality results from a randomized prostate-cancer screening trial. *N Engl J Med* 2009; **360**: 1310.
2. Schroder FH, Hugosson J, Roobol MJ et al: Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med* 2009; **360**: 1320.
3. National Comprehensive Cancer Network Clinical Practice Guideline in Oncology. Prostate Cancer Early Detection, version V.2.2007. National Comprehensive Cancer Network. Available at [http://www.nccn.org/professionals/physician\\_gls/PDF/prostate\\_detection.pdf](http://www.nccn.org/professionals/physician_gls/PDF/prostate_detection.pdf). Accessed November 25, 2008.
4. Fang J, Metter EJ, Landis P et al: Low levels of prostate-specific antigen predict long-term risk of prostate cancer: results from the Baltimore Longitudinal Study of Aging. *Urology* 2001; **58**: 411.
5. Antenor JA, Han M, Roehl KA et al: Relationship between initial prostate specific antigen level and subsequent prostate cancer detection in a longitudinal screening study. *J Urol* 2004; **172**: 90.
6. Loeb S, Nadler RB, Roehl KA et al: Risk of prostate cancer for young men with a prostate specific antigen less than their age specific median. *J Urol* 2007; **177**: 1745.
7. Lane JA, Howson J, Donovan JL et al: Detection of prostate cancer in unselected young men: prospective cohort nested within a randomised controlled trial. *BMJ* 2007; **335**: 1139.
8. Scales CD Jr, Antonelli J, Curtis LH et al: Prostate-specific antigen screening among young men in the United States. *Cancer* 2008; **113**: 1315.
9. Smith CV, Bauer JJ, Connelly RR et al: Prostate cancer in men age 50 years or younger: a review of the Department of Defense Center for Prostate Disease Research multicenter prostate cancer database. *J Urol* 2000; **164**: 1964.
10. Khan MA, Han M, Partin AW et al: Long-term cancer control of radical prostatectomy in men younger than 50 years of age: update 2003. *Urology* 2003; **62**: 86.
11. Whittemore AS, Cirillo PM, Feldman D et al: Prostate specific antigen levels in young adulthood predict prostate cancer risk: results from a cohort of black and white Americans. *J Urol* 2005; **174**: 872.
12. Roobol MJ, Roobol DW and Schroder FH: Is additional testing necessary in men with prostate-specific antigen levels of 1.0 ng/mL or less in a population-based screening setting? (ERSPC, section Rotterdam). *Urology* 2005; **65**: 343.
13. Fowler JE Jr, Bigler SA, Lynch C et al: Prospective study of correlations between biopsy-detected high grade prostatic intraepithelial neoplasia, serum prostate specific antigen concentration, and race. *Cancer* 2001; **91**: 1291.
14. De Marzo AM, Marchi VL, Epstein JI et al: Proliferative inflammatory atrophy of the prostate: implications for prostatic carcinogenesis. *Am J Pathol* 1999; **155**: 1985.
15. Winter DL, Hanlon AL, Raysor SL et al: Plasma levels of IGF-1, IGF-2, and IGFBP-3 in white and African-American men at increased risk of prostate cancer. *Urology* 2001; **58**: 614.
16. Williams H and Powell IJ: Epidemiology, pathology, and genetics of prostate cancer among African Americans compared with other ethnicities. *Methods Mol Biol* 2009; **472**: 439.
17. Schroder FH, Roobol-Bouts M, Vis AN et al: Prostate-specific antigen-based early detection of prostate cancer—validation of screening without rectal examination. *Urology* 2001; **57**: 83.

## EDITORIAL COMMENT

These authors conclude that a PSA cutoff of 1.5 ng/ml or greater can be used for risk stratification in men 50 years or younger, a group that may benefit from more frequent PSA testing. 1) This study suffers from verification bias. The biopsy rate in PSA subgroups was not known and is likely to differ. 2) Of the men 4% were diagnosed with prostate cancer (96% were not) at a mean of 1.4 years with a total followup of up to 9 years. In a clinical setting these values are 2.3% and 17 years, respectively.<sup>1</sup> We now know that PSA based

screening can decrease disease specific mortality but this coincides with considerable over diagnosis even when starting at age 55 years and applying a 4-year screening interval.<sup>3</sup> The question is now when and on what basis we label men as at increased risk, keeping in mind the possible consequences of such an approach.<sup>2</sup>

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## REFERENCES

1. Lilja H, Ulmert D, Björk T et al: Long-term prediction of prostate cancer up to 25 years before diagnosis of prostate cancer using prostate kallikreins measured at age 44 to 50 years. *J Clin Oncol* 2007; **25**: 431.
2. Schröder FH, Hugosson J, Roobol MJ et al: Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med* 2009; **360**: 1320.

## REPLY BY AUTHORS

The risk/benefit of PSA screening is an issue and there is a need to develop a method to identify high

risk men for periodic PSA screening.<sup>1</sup> Currently the AUA and NCCN guidelines recommend that men

should have a baseline PSA test at age 40 years, and that high risk men should start annual screening thereafter.<sup>2,3</sup> The AUA guidelines consider that men in their forties with a PSA higher than the median (0.6 to 0.7 ng/ml) are at high risk. The NCCN guidelines recommend that men with PSA 1.0 ng/ml or greater should undergo PSA screening more frequently. There is still no definitive evidence support-

ing these recommendations. Based on our large cohort of men and PSA testing during the last 2 decades, we found that a PSA of 1.5 ng/ml or greater is a better cutoff for identifying high risk men younger than 50 years. This PSA cutoff is higher than that recommended by the AUA and NCCN, and would potentially avoid unnecessary PSA tests and improve cost-effectiveness.

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## REFERENCES

1. Uhlman MA, Moul JW, Robertson CN et al: Prostate-specific antigen screening and prostate cancer mortality: implications of a randomized European study. *Aging Health* 2009; **5**: 281.
2. Carroll P, Albertsen PC, Greene K et al: Prostate-Specific Antigen Best Practice Statement: 2009 Update. Available at [www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/psa09.pdf](http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/psa09.pdf). Accessed July 8, 2009.
3. National Comprehensive Cancer Network: NCCN clinical practice guideline in oncology. NCCN stresses importance of PSA testing in high-risk men. Available at [www.nccn.org/about/news/newsinfo.asp?NewsID=218](http://www.nccn.org/about/news/newsinfo.asp?NewsID=218). Accessed August 10, 2009.