

# Guidelines for Physicians REGARDING PROSTATE CANCER SCREENING

By Peter Grimm, DO



*Prostate cancer (PC) is the second leading cause of cancer-related mortality in men, with approximately 28,000 deaths per year. Screening for PC with the prostate-specific antigen (PSA) test carries some controversy, and patient questions arise about how to interpret the test results, as well as what can be done to mitigate the risk.*

The incidence of prostate cancer increased after the introduction of screening and has remained higher ever since. This increase appears to be due to screening practices that pick up more early-stage cancers. Screening has also coincided with decreasing PC mortality. Prostate cancer deaths rates decreased 4 percent per year from 1991 to 2002, from 40 per 100,000 in 1990 to approximately 30 per 100,000 in 2002. Clearly, screening results in finding cancers in an early, more curable stage.

## The Controversy Over Screening

Screening can also lead to over-diagnosis, over-treatment and side effects. Some question whether it really does decrease mortality.

Three recent trials have looked at screening and mortality reduction. The European Randomized Study of Prostate Cancer (ERSPC) suggested that screening saved lives but an American screening trial (Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial) showed no reduction in prostate cancer death. More recently, a Swedish screening trial based on the PSA test showed dramatically reduced mortality.

The American trial was criticized because 52 percent of the control group had prior PSA screening and these patients were allowed into the trial, which meant a larger number of patients with cancer would have been eliminated prior to entering the trial. Also the efficacy of PSA screening in detecting prostate cancer was lower in the U.S. than in ERSPC trial.

The European trial showed a 20 percent reduction in PC death, but 1,400 men needed to be screened and 48 treated to prevent one death, and 24 treated to prevent one case of metastatic PC. It would be valuable to identify these high-risk patients, however it is often not possible to determine if one person's cancer is more aggressive (requiring treatment) than another person's less aggressive (not requiring treatment). This is true even if both patients' grade of cancer is the same.

In the Swedish trial of 10,000 men in the city of Göteborg, death rates associated with prostate cancer in men recruited for PSA screening in 1994 were 0.50%, compared with 0.90% in a similar group not invited for testing.<sup>1</sup>

***Bottom Line** Although the screening question is still not completely resolved, it appears that screening can reduce mortality.*

## Risk Factors

It is important to know what increases the risk of PC and what does not. Genetics, race and age are definite risk factors, but other potential risk factors are questionable.

These factors do not increase risk for PC: social class, occupation, marital status, sexual activity, religion, vasectomy, lifestyle, smoking, physical activity/obesity, infectious agents,

continues

<sup>1</sup> Hugosson J, et al "Mortality results from the Göteborg randomized population-based prostate-cancer screening trial" *Lancet Oncol* 2010; DOI: 10.1016/S1470-2045(10)70146-7.

diabetes or environmental risk factors. A high-fat diet probably does not increase the risk, but recently studies have indicated that milk products may increase the risk.

**We know that genetics, race and age are contributing factors.**

Regarding genetics, the younger the father with PC, the higher the risk. The risk increases four times if the father’s onset was at age 70, five times if the father’s onset was at age 60 and seven times if the father’s onset was at age 50. In addition, if more than two first-degree relatives (e.g., father, brother) had PC, the risk increases five to eight times. However, most PC patients—80 percent—have no family history of PC.

**Bottom Line** *If your patient has a family history of PC, start screening earlier than 50 years old.*

Figure 1 Age and Normal PSAs

AGE	ASIAN	AFRICAN AMERICAN	CAUCASIAN	MEAN
40 – 49	0 – 2.0	0 – 2.0	0 – 2.5	0.7
50 – 59	0 – 3.0	0 – 4.0	0 – 3.5	0.9
60 – 69	0 – 4.0	0 – 4.5	0 – 4.5	1.2
70 – 79	0 – 5.0	0 – 5.5	0 – 6.5	1.5

Regarding race, African Americans have a higher incidence of PC. The CDC’s 2006 publication “Prostate Cancer Screening: A Decision Guide for African Americans” states that African Americans have a one in five lifetime risk, versus one in six for Caucasian men. See Figure 1 for a chart of normal PSA levels for men of different races.

**Bottom Line** *If your patient is African American, he may wish to start screening earlier than 50 years old.*

Regarding age, the older the man, the more likely he has PC. The incidence increases significantly after age 60. A strict age cutoff of 75 years, as recommended by the U.S. Preventative Task Force, can reduce over-screening but also will prevent finding potentially lethal PC in healthy older men who have a long life expectancy.

**Bottom Line** *High-risk patients should consider annual screening beginning at 40 and most others after 50. Overall health issues should be considered in screening men older than 75 years old.*

**Who Should Be Screened, and When?**

The American Cancer Society recommends that all patients be informed about screening issues. PC screening should be considered in the general health discussion at age 40, and if the patient is willing, he should establish a baseline PSA. Prostate cancer is rare prior to this time. Most men, with the exception of those with risk factors such as race or family history as discussed, can begin after age 50. PC is typically a slow growing cancer in most men; therefore most of the organizations recommend screening only in healthy men with a life expectancy greater than five to 10 years.

**What Tests?**

Total PSA is the single best test to detect early disease. A digital rectal exam (DRE) is also recommended, particularly if the PSA is in the normal range. Free PSA is used for specific circumstances to distinguish possible benign versus malignant disease. Monitoring PSA should be done at a single laboratory, as there can be some variability between labs.

**If Tests Are Abnormal, What Next?**

Prostatitis, BPH, urethral or prostate trauma can cause an elevation of PSA. Finasteride or Duasteride can reduce the PSA levels as much as 50 percent. A repeat PSA should be done to confirm abnormal results. Biopsy is the only sure way to know if there is cancer in the prostate.

The side effects of modern treatment have been significantly reduced. Advances in surgery, external radiation and brachytherapy approaches have reduced the side effects significantly. A thorough discussion with a surgeon, radiation oncologist and a brachytherapy specialist is appropriate.

**PSA Value and Risk of Prostate Cancer**

There is no PSA value in which the chance of finding PC is zero. As the PSA rises, the risk increases proportionately. Therefore, there is no threshold value to recommend a biopsy. See Figure 2 for the level of risk based on the PSA result.

Figure 2 **PSA Value and Chance of Finding PCA in a Man Age 50 or Older**

<b>PSA VALUE</b>	<b>PERCENT</b>
< 0.5	6.6%
0.6 – 2.0	10%
2.0 – 2.9	7.4 – 17%
3.0 – 3.9	12 – 26 %
< 4 – 10	20 – 30%
10 – 20	50 – 75%
> 20	90%

**Bottom Line** If the PSA level is 1-2 ng/ml, probably screen every two years. If higher, screening at least once per year is recommended. Despite the absence of an established cut point, it seems reasonable to consider an evaluation and discussion of PC with a PSA of 2.5-4.0 ng/ml. Race, family history, results of previous biopsies, and DRE result should weigh into the decision to pursue possible biopsy.

Also, a rapid rise in PSA numbers over a short period (1 year) increases risk of PC. Therefore, if PSA numbers from same lab shows an increase of greater than 0.75 ng/ml per year, it is reasonable to increase surveillance or refer the patient for evaluation.

### When to Refer a Patient

Patients should read a summary discussion about screening and risks (see Figure 3). If the patient is healthy and wishes screening, evaluate the PSA results and follow the outline.

### A Positive DRE is an Indication for a Referral Regardless of PSA.

A PSA level of 2.5 ng/ml is a reasonable cut point for men under 55; for men older than 65, that cut point would be 4.0 ng/ml. In between those ages, if the patient has a family history, is African American, has a PSA velocity of more than 0.75 ng/ml, or has a positive DRE, it is reasonable to have him evaluated. ■

Figure 3 **Key Information for Patients About Screening**

- ◆ Screening with the PSA blood test detects cancer at an earlier stage than if no screening is performed.
- ◆ Prostate cancer screening might be associated with a reduction in the risk of dying from prostate cancer; however, evidence is conflicting.
- ◆ For men whose prostate cancer is detected by screening, it is not currently possible to predict which men are likely to benefit from treatment.
- ◆ Treatment for prostate cancer can lead to urinary, bowel, sexual, and other health problems that can be significant or minimal, permanent or temporary.
- ◆ The PSA and DRE can produce false-positive or false-negative results.
- ◆ Abnormal results from screening with PSA and DRE require prostate biopsies, which can be painful and lead to complications like infection or bleeding.
- ◆ Not all men whose prostate cancer is detected through screening require immediate treatment. Some require periodic blood tests and prostate biopsies to determine the need for future treatment

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