

Prostate Cancer Screening

The Debate Continues

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Prostate cancer screening with prostate-specific antigen (PSA) remains a hotly debated issue across North America. Undoubtedly, prostate cancer is an important public health concern, but there is significant ambivalence in the advocacy of PSA screening.

What is an ideal screening test?

An ideal screening test should detect a common disorder that is associated with significant morbidity or mortality. The test should also be able to predict who is going to develop morbidity from the disease and there should be effective treatment available. Finally, all of this should ultimately be done in a cost-effective manner.

PSA screening fits many, but certainly not all of these criteria, primarily because prostate cancer management has proven to be a moving target over the last decade.

How does PSA measure up?

Prostate cancer should represent a significant concern in the life of North American men, as it is the most common visceral cancer. However, many men diagnosed with prostate cancer will not die of their disease or even suffer any morbidity; autopsy series reveal that a vast majority of men in their eighth decade will have histologically proven cancer in their prostate that did not present clinically.

Bill's case

- Bill, 54, is being seen sporadically for symptoms of osteoarthritis.
- He is otherwise very healthy and active.
- He is interested in having a prostate-specific antigen test done to screen for prostate cancer.
- Bill has minimal lower urinary tract symptoms and gets up only once at night to void.
- He has no family history of prostate cancer and his family members tend to have a long life expectancy.
- His physical exam is unremarkable, with a symmetrical and benign-feeling prostate, which is moderately enlarged for his age.



What would you tell Bill?

- A discussion of the possible benefits (early detection of prostate cancer at a curable stage) and risks (possible need for biopsy leading to treatment of any detected cancer) would include the fact that there is only limited evidence that a PSA, in this situation, would necessarily decrease prostate cancer mortality.

Fact Box

Did you know?

- Prostate cancer makes up 29% of all male cancers and is the second or third leading cause of cancer deaths in men.
- Men have a 16% lifetime risk of being diagnosed with prostate cancer and a 3% lifetime risk of dying from the disease.

Frankel S, Smith GD, Donovan J, et al: Screening for prostate cancer. *Lancet* 2003; 361(9363):1122-8.

Many studies have demonstrated that the stage and grade of the diagnosed prostate cancer and the life expectancy of the patient are all important parameters that allow the treating physician to predict the likelihood that the disease will affect the health and life of a specific individual.¹⁻³

A major concern of PSA screening is whether or not we are detecting less aggressive tumours that do not need intervention. This could result in significant costs and morbidities associated with “curative” therapies (surgery, radiotherapy, hormones) in patients who may never have suffered from their prostate cancer.

However, most prostate cancer screening series have demonstrated that a large number of cancers (up to 90%) found through PSA screening do represent significant disease based on parameters such as grade

and volume of cancer detected.⁴ PSA screening has resulted in a stage migration of cancers detected, with many more cancers being localized to the prostate. In a contemporary, randomized trial, the treatment of men with early prostate cancer has been shown to be effective in improving cancer-specific survival.⁵

However, even in the screened population, not all men will be found to have organ-confined (and potentially curable) disease. As well, around 10% of those cancers found to be “confined” to the prostate at the time of surgery will actually recur. These results seem to suggest PSA is still not as sensitive a test as it needs to be.

A very real concern in recommending population-based screening with PSA is lead-time bias. Although the survival of a patient treated for prostate cancer may be prolonged in any one published series, this may

Table 1

Modifications to improve the sensitivity & specificity of PSA in detecting clinically significant prostate cancer

PSA modification	What is it?	How is it used?
PSA velocity	Rise of PSA over time	Risk increases when PSA rises > 0.75 ng/mL/year
Free to total PSA	The ratio of free or unbound PSA compared to total PSA	Risk increases when ratio is < 0.20
PSA density	Relationship of PSA to volume of prostate	Higher PSA values are accepted as less of a risk in men with large prostates
Age-specific ranges	Relationship of rising PSA with increasing age	Age-specific normal ranges: <ul style="list-style-type: none"> • 40-49 years: < 2.5 ng/mL • 50-59 years: < 3.5 ng/mL • 60-69 years: < 4.5 ng/mL • < 70 years: < 6.5 ng/mL

PSA: Prostate-specific antigen

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simply be a reflection of the benefit of detection earlier in its generally long natural history, without substantially affecting the course of the disease. This lead-time bias can again lead to a cure in many men who would not have otherwise suffered or died from their disease.

To date, there are no published studies demonstrating decreased prostate cancer mortality in a screened population, representing the strongest argument against a policy of widespread PSA screening.

There has, however, been a decrease in prostate cancer mortality in North America since 1994⁶ and some preliminary results of European screening initiatives have demonstrated interesting results, including decreased progression to metastatic disease in the screened population.⁷ However, given the long natural history of this disease, results will take time to be realized and may be confused by the constantly evolving management of prostate cancer.

Can we improve PSA?

There is no doubt PSA has changed our management of men with prostate cancer and remains an important tool in men presenting with lower urinary tract symptoms.

There have been several attempts at improving the sensitivity and specificity of PSA (Table 1). However, two questions remain: Can PSA screening change the natural history of prostate cancer and should it be advised for all men, symptomatic or not?

How should I use PSA?

A practical approach (Table 2) would be to offer PSA testing to men presenting with significant lower urinary tract symptoms or an abnormal rectal exam. This approach represents case detection and has to be interpreted as such.

Table 2

Practical approach to PSA testing

1. If convinced of benefits of screening, discuss risks and benefits of PSA testing with men over 45-50 years of age with a predicted lifespan of 10-15 years.
2. If not convinced of benefits of screening, consider PSA testing (after discussion of risks and benefits) for case detection in men who:
 - a) have close relatives with prostate cancer (particularly if fatal)
 - b) have voiding symptoms which may be related to prostate disease
 - c) have a prostate nodule on DRE
 - d) are worried about prostate cancer
 - e) specifically request a PSA test

DRE: Digital rectal exam
PSA: Prostate-specific antigen


Table 3

Practical patient discussion points

- Prostate cancer is generally slow-growing, but is still a significant cause of mortality and morbidity in Canadian men.
- PSA is not very specific to cancer (with a value < 10 ng/mL), but it does allow earlier detection of prostate cancer.
- PSA is a simple blood test, but may result in further invasive tests, such as transrectal ultrasound and biopsy.
- Early prostate cancer can be cured, but there are significant complications from treatment and screening has not yet been proven to decrease prostate cancer mortality.

PSA: Prostate-specific antigen

For asymptomatic men questioning the benefits of PSA screening or simply requesting the test, the pro and con discussion (Table 3) of using PSA to detect a significant prostate cancer is warranted.

If it is decided to screen for prostate cancer, a digital rectal exam and PSA should suffice, as the added benefit of a transrectal ultrasound is minimal and costly. Although the discussion of PSA screening is generally considered in men 50 to 70 years of age, those in higher risk groups, such as men with a significant family history or African-Americans, should likely be considered for earlier screening. Opening the discussion of PSA screening in low-risk, asymptomatic patients remains controversial and should be left to the individual physician's discretion on a patient-to-patient basis. 

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