



March 2010

Revised and Discordant PSA Screening Guidelines

Prostate cancer is by far the most commonly diagnosed cancer among American men and remains the second leading cause of cancer death in men. Widespread screening using the PSA blood test started in 1991 after the publication of a high-profile study demonstrating that elevations in PSA in asymptomatic men were associated with a higher risk of having prostate cancer. Since its introduction, PSA testing has dramatically changed the landscape of prostate cancer, creating a significant rise in cancer incidence and shifting the stage of disease at the time of diagnosis to a much earlier and potentially more curable stage. Today only 5% of men have metastatic disease at the time of diagnosis compared to 50% before the advent of PSA testing. Although prostate cancer mortality has declined approximately 30% during this time, some experts argue that this decline is more attributable to improvements in treatment than screening. Two recent prospective randomized trials that were expected to resolve this issue provided conflicting results (N Engl J Med. 2009;360:1310–1319 & 1320-1328). The European Randomized Study of Screening for Prostate Cancer (ERSPC) demonstrated a 20% reduction in prostate cancer-specific mortality in men randomized to screening compared with controls, while the prostate arm of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial in the United States did not demonstrate any benefit.

Although the evidence remains conflicted regarding whether prostate cancer screening is associated with a reduction in mortality, it is clear that any benefit is accompanied by a significant rate of overdiagnosis and overtreatment. Overdiagnosis increases with age, rising from about 27% in men age 55 to about 56% at age 75. The ERSPC study demonstrated that 1410 men would need to be screened and 48 cases of prostate cancer would need to be treated to prevent one death over 10 years. Despite the fact that active surveillance is an option, more than 90% of men in the United States choose to undergo aggressive treatment, even if

they have low grade cancer. This degree of potential overdiagnosis and overtreatment is greater than that for any other cancer for which routine screening occurs. Potential adverse effects of overtreatment include bleeding, infection, erectile dysfunction and urinary and fecal incontinence. Moreover, the harms of screening accrue immediately, whereas potential benefits are realized only many years later.

The cloud of controversy surrounding overdiagnosis and overtreatment exists at least partially because there is no evidence-based, standardized threshold for a clinically actionable PSA level. Amid this continuing controversy regarding the merits of early detection of prostate cancer, the Prostate Cancer Advisory Committee of the American Cancer Society (ACS) revised its guideline on the early detection of prostate cancer (CA Cancer J Clin 2010;60:70-98). The revision states that prostate cancer screening should not occur without an informed discussion about risks and benefits. If the patient decides to undergo screening, PSA is the recommended screening test with or without digital rectal exam (DRE). The age at which screening should be initiated depends on the patient's estimated risk of developing prostate cancer:

- Age 50 years for men at average risk
- Age 45 years for men at higher risk including African American men and men who have a father or brother diagnosed with prostate cancer before age 65 years
- Age 40 years for men at appreciably higher risk such as those with multiple family members diagnosed with prostate cancer before age 65 years

Asymptomatic men who have less than a 10-year life expectancy based on age and health status should not be offered prostate cancer screening. At age 75 years, only about half of men have a life expectancy of 10 years or more. Men in this age group with significant comorbidities, as well as younger men with life-limiting comorbid conditions, are not likely to benefit from screening.

ACS recommends the following PSA thresholds to guide test frequency and referral for further evaluation:

- Screening should be conducted yearly for men whose PSA level is 2.5 ng/mL or greater
- Screening can be extended to every 2 years for men whose PSA is less than 2.5 ng/mL
- A PSA level of 4.0 ng/mL remains a reasonable level to recommend referral for further evaluation or biopsy in men at average risk for prostate cancer
- PSA levels between 2.5 ng/mL and 4.0 ng/mL may be used to recommend biopsy in individuals at increased risk of high-grade cancer.

The American Urological Association (AUA) also recently published their Prostate Specific Antigen Best Practice Policy in November 2009 (J Urol 2009;182:2232-2241). This policy differs significantly from the ACS guideline. AUA stated that prostate cancer testing is an individual decision that patients of any age should make in conjunction with their physician or urologist. It recommended that prostate cancer screening with both PSA and DRE should be offered to men beginning at age 40 years and repeated annually. AUA no longer recommends a single PSA threshold value to prompt prostate biopsy. The decision to proceed to biopsy should be based primarily on PSA and DRE results but should also consider free and total PSA, patient age, PSA velocity, PSA density, family history, ethnicity, prior biopsy history and comorbidities. The AUA guidelines have been criticized because they are not supported by any convincing evidence.

At the other extreme, the US Preventive Services Task Force (USPSTF) concluded in 2008 that for men younger than age 75 years, the benefit of screening for prostate cancer was uncertain and the balance of benefits and harms could not be determined (<http://www.ahrq.gov>). They recommended against screening men age 75 years or older. If screening was eventually shown to reduce deaths, the USPSTF concluded that PSA screening as infrequently as every 4 years would yield as much of a benefit as annual screening.

These 3 sets of discordant guidelines have done little to quell the controversy regarding prostate cancer screening. Physicians are still left with a bewildering array of disparate guidelines. Despite all of these ambiguities, PSA testing will remain the mainstay of prostate cancer screening for the foreseeable future.

Stool Parasite Diagnostics

Testing for stool pathogens has been extensively examined in the literature for more than a decade, due to low yield and high cost of stool cultures and ova & parasite (O&P) examinations. *Giardia* is by far the most common parasitic stool pathogen in the U.S. with an estimated 2 million infections annually, followed by *Cryptosporidium* with 300,000 infections. A previous review of Saint Luke's Regional Laboratory O&P results revealed that <1% of positive tests yielded a pathogen other than *Giardia*.

Microscopic examination for stool parasites was the diagnostic test of choice for many years, however, the traditional O&P is actually less sensitive than antigen detection for *Giardia* and does not detect *Cryptosporidium*. Stool antigen detection for *Giardia* and *Cryptosporidium* are the tests of choice to detect most fecal parasites in the United States. Saint Luke's Regional Laboratories has performed *Giardia* antigen testing instead of microscopic exams for all routine O&P requests since December 1999, due to the prevalence of this parasite compared to other pathogens and the superiority of antigen testing for detection.

Microscopic O&P examinations are suggested for immunocompromised patients, patients with a travel history outside the U.S., and patients with persistent symptoms despite negative stool culture, *Giardia* antigen, & *Cryptosporidium* antigen testing. Physicians should indicate on the requisition when one of these circumstances is met for microscopic O&P. *Cryptosporidium* antigen testing requires a separate request, and is indicated for immunocompromised patients, and patients exposed to day care situations or farm animals. Testing is performed daily and samples are retained for one week.