

DON'T TEST - DON'T TREAT

The New Paradigm for the Treatment of Prostate Cancer?

by Justin M. Albani, MD

The recommendation to abandon all PSA screening is based on faulty methodology and an oversimplification, as well as a complete ignorance of the most important published studies of PSA screening.



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Prostate cancer is the second most common malignancy affecting men in the United States and the second leading cause of cancer deaths in men (after lung cancer).¹ There will be over 240,000 new cases and 33,720 deaths in 2011 alone. One in six men will develop prostate cancer in their lifetime and one in thirty-six will subsequently die of this disease.¹ Aware of these facts, physicians for over two decades have been utilizing the serum prostate specific antigen (PSA) test to help identify men at increased risk for developing this disease and initiate early diagnosis and treatment to decrease prostate cancer-specific mortality. In the first decade of PSA use, epidemiologic studies noted an initial increase in the detection rate of prostate cancers and a well described stage migration such that many more cancers are now detected long before patients become overtly symptomatic. Epidemiologic data from the National Cancer Institute's SEER (Surveillance, Epidemiology and End Results) database has reported a 40% decrease in the age-adjusted prostate cancer specific mortality in what is now known as the modern PSA era.²

However, valid concerns about the test's lack of specificity for detecting prostate cancer has led to criticism and continual debate about the effectiveness of screening protocols for the general male population.

This has been addressed with careful consideration and review by the American Urological Association (AUA) which regularly puts forth new recommendations as does the American Cancer Society (ACS). Both organizations, representing the physicians most involved and with the greatest expertise in diagnosis and treatment of prostate cancer, acknowledge that patients should have the opportunity to make an informed decision with their health care provider about whether to be screened for prostate cancer.^{3, 4} Many additional isoforms (% free PSA, pro-PSA), other assays (PCA-3, EPCA-2, urine sarcosine), and instruments such as PSA velocity, density, and age-specific PSA have all been used in an attempt to give the screening tool more predictive power.

Continued review of this data led to the decision by the USPSTF (United States Preventive Services Task Force) in 2008 to recommend no further prostate cancer screening in men over 75 years of age, and the most recent recommendation by the same task force **against PSA-based screening for prostate cancer in all men.** The committee gave the PSA test a grade D recommendation. This rating denotes that "there is a moderate or high certainty that the service has no net benefit or that the harm outweighs the benefits."^{5, 6} Of

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interest, the USPSTF body making this sweeping, radical and highly controversial statement to end all prostate cancer screening is a government panel comprised of 16 primary care clinicians and does not include a single urologist, medical oncologist, radiation oncologist, or even a physician-consultant who actually treats patients with this disease in any capacity on a regular basis.

The USPSTF panel should be applauded for its extensive review and analysis of the five randomized trials of screening and three trials and 23 cohort studies of treatments, but it glosses over and effectively ignores the evidence that supports the benefits of prostate cancer screening and its effect on the reduction of prostate cancer mortality. The task force illustrates the complexity of screening by reviewing the two largest trials of PSA screening that had conflicting results and seems to use this as an example to decry the futility of its usefulness.^{7,8} Unfortunately, the USPSTF does not elucidate on the specifics of the studies nor, incredibly, the two additional investigations that were later reported as extensions of these reports. They both note a benefit to prostate cancer screening.^{9,10} The European Randomized Study of Screening for Prostate Cancer (ERSPC) trial randomized 182,000 men in Europe to PSA screening every two to seven years or usual care and reported a 20% reduction in prostate cancer mortality and a 41% decrease in metastatic disease in the screening arm in men followed for nine years.⁸ The greatest criticism of this study noted the high number of men needed to be treated (48) to save one life.⁸ Interestingly, an additional trial (Göteborg) that was a subset of this patient population comprised of 20,000 men aged 50-64 screened every two years with a lower PSA cutoff (2.5-3.4) recently reported a 44% lower prostate cancer death rate in screened men at a follow up of 14 years.¹⁰ Not only did this study demonstrate that prostate cancer screening lowered the cancer death rate, perhaps more importantly, it reported a much lower number needed to treat (NNT) to save one life at only 12 patients.¹⁰ (This is comparable to breast cancer with a NNT of 10).

Additionally, the USPSTF panel reviewed the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, (PCLO) conducted in the United States that was reported in the same journal at the same time as the ESPRC trial and noted this study showed no reduction in prostate cancer deaths among those who had regular PSA tests.⁷ However, it failed to mention that this study was widely criticized for the fact that up to 52% of the ‘nonscreened’

control men in that study were actually getting PSAs and digital rectal exams by their primary care physicians; this severely contaminated the study. Interestingly, again, a reanalysis of the same study found that if PSA screening was performed in men with low or no comorbidity, there was a 44% decrease in prostate cancer mortality; the NNT was calculated to be a commendable five treated to save one life.⁹ Unfortunately, this important update to the previously well publicized negative study garnered little to no media attention, and was completely overlooked in the USPSTF evaluation. This study buttresses the belief that the true benefit of prostate screening is, as most oncologists and urologists recognize, realized in screening younger and healthier men. An additional smaller study again noted the benefits of screening as it compared the screening rate of 6% of men of Northern Ireland to the ESPRC screening arm (94%), and found a 53% lower incidence of metastases and a 37% decrease in prostate cancer mortality rates in the highly PSA screened population.¹¹

The USPSTF should not be criticized for its exhaustive review of the very complex data regarding prostate screening, but should be faulted for its assumption that all screening leads immediately and always to treatment, and thus potentially overtreatment. Pediatrician Virginia Moyer, MD, the chair of the USPSTF task force notes correctly that PSA ‘cannot distinguish cancer that will never make a difference in a man’s lifetime from cancers that will make a difference.’¹² While she is absolutely correct about the limitations of PSA, she fails to recognize that it is not the PSA at all that can make this distinction, but rather it is the *prostate biopsy* that establishes a patient’s true prognosis. The risk of overtreatment is real, but the USPSTF panel makes a gross generalization assuming that physicians do not take into consideration a patient’s age, comorbidities, volume of disease, or Gleason score when coming to a decision to recommend treatment or no treatment.

Risk stratification has been developed and in practice for years, and this allows physicians to appropriately counsel men on what treatment, or *non-treatment* may be most appropriate for him. The concept and practice of active surveillance for prostate cancer has grown systematically in the recent years as a very acceptable practice, and urologists have embraced this as they recognized that some prostate cancer is indeed indolent and likely may never present a problem in a patient’s lifetime. However, the USPSTF panel makes

no allowance for this possibility and simply submits a blanket generalization that screening causes more harm than good. As physicians, we all can offer more than just anecdotal evidence of the young, healthy and completely asymptomatic patient with an elevated PSA that subsequently led to a prostate biopsy noting Gleason 9 and 10 disease in multiple cores. This patient will die of disease and will suffer immensely if left untreated. What happens to these patients if we physicians accept the USPSTF plan to assign the PSA test a grade D and completely discard the exam? You know the answer? They die painfully, prematurely, and preventably!

Admittedly, PSA is imperfect, but it is the only tool physicians presently have to allow the detection of cancer that can be debilitating and life-threatening. Weekly, I personally hear complaints from frustrated patients who are diagnosed with clinically significant high grade (Gleason 8-10) prostate cancer, who are told by friends or family members that they are just fine because they *'only have prostate cancer.'* Because the media has often propagated the myth that all prostate cancer is indolent and insignificant, and that they have been told that they *'always will die of something else first,'* these patients feel their suffering, endurance, perseverance, and even death is deeply cheapened by this misinformation.

The morbidity of treatments for prostate cancer is real, but this should not be confused with the morbidity of screening which unavoidably creates some anxiety and may involve a prostate biopsy, which, while uncomfortable, is rarely life threatening (0.5% urosepsis).¹³ The question must be to treat, or not to treat – not, should we screen?

Much is made and discussed about the cost of health care in the United States, and certainly by ignoring prostate cancer, the second most common cancer in men, a great deal of money would likely be saved by not treating this disease. However, a strong argument can be made that prostate cancer screening may actually help to decrease the cost of health care by identifying cancer before it metastasizes and precluding the need to treat patients with incurable and debilitating advanced disease with expensive and often ineffective treatment regimens. Dr. Donald Berwick, appointed administrator of the Centers for Medicare and Medicaid in July 2010, has proclaimed his mission of the 'Triple Aim' of providing better care for patients, better health for populations, and reducing per-capita costs, but he has promised that costs *'should not be reduced by eliminating any helpful care.'*^{14, 15} The

USPSTF recommendation that PSA screening be labeled grade D and not be performed gives insurance companies and state and federal governments a free pass to lower their costs by denying needed care and effectively taking away the ability of the physician and patient to make a personal choice regarding that patient's health care. A similar pattern of restricting breast screening mammograms was made by the same USPSTF panel without any input from gynecologists, breast surgeons, or medical or radiation oncologists- the very doctors who treat this disease every day.¹⁶

Conclusion

The USPSTF panel recommendation to abandon all PSA screening is based on faulty methodology and an oversimplification as well as, in some instances, a complete ignorance of the most important published studies of PSA screening. Given the lack of prostate cancer experts on the panel, perhaps these errors were inevitable. If implemented the USPSTF recommendations will cause many preventable deaths of men from prostate cancer. Much better recommendations about the use of life-saving PSA testing come from the American Cancer Society and American Urological Association. The screening and treatment algorithms for prostate cancer can and should be improved, but absolutely not abandoned. The true power of the AUA and ACS's recommendations regarding prostate cancer screening is that they specifically involve a discussion between the patient and the physician regarding a medical decision rather than a governmental entity, under pressure to reduce healthcare costs, arbitrarily dictating a deadly wrong course of action.^{3, 4}

Call for Action

Health care professionals and patients alike need to take action now to preserve control of their health care and to protect the patient's right to prostate cancer screening. Patients and their doctors are best equipped to decide when a PSA test is indicated – not a government panel with little or no experience with treating this disease.

We would encourage all patients and physicians to respond to the USPSTF in opposition and request they rescind their recommendation to stop PSA screening on all men. An opportunity to comment on this statement is at the following web address: www.uspreventiveservicestaskforce.org/uspstf_form3/ Additionally, we encourage you to contact your US

Senators and Representatives to reject this recommendation by contacting Congress at 202-224-3121 as well as visit the PSA Test Action Center at www.tinyurl.com/AACU-PSA.

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Disclosure

None reported.



Saving Dollars at the Cost of Saving Lives

by John C. Hagan, III, MD

My paternal Uncle Ray and maternal Uncle Tom were tough World War II combat veterans. Both died painfully from metastatic prostate cancer. They were old school and didn't go to physicians unless my aunts put them in a car and drove them to the office. Early and regular PSA screening may have lead to an earlier diagnosis and a later, less painful death.

The current generation of Hagan males over 40 have regular prostate exams and PSA screenings. In his mid 50s, one of my cousins was found to have accelerating PSA readings. He was worked up, found to have a high Gleason prostate cancer and, after careful counseling of his options by his urologist and a radiation oncologist, opted for a radical nerve sparing prostatectomy. Six years later he's doing well with no sign of reoccurrence. The PSA test, costing as little as \$70, saved his life. Sounds like a bargain to me but not to the USPSTF.

Because of family history, I am at high risk for prostate cancer. There is no happier day each year than when my PSA comes back less than 1.0 and prostate exam shows only stable asymptomatic hypertrophy. In my 60s, I'm awash in an epidemic of prostate cancer among friends and relatives. I can name 10 male friends that have had their prostate cancers diagnosed by PSA screening. The last funeral I went to was a death at 62 from metastatic prostate cancer in a neighbor.

I am stunned and angered at the USPSTF panel recommendation that PSA screening no longer be done on any male. There are no prostate cancer experts on this government-sponsored (and -influenced) panel. The Chair is a pediatrician. This group of pseudo-experts last recommendation would dramatically cut back breast cancer screening mammograms. There are no breast cancer experts on this panel. Small comfort they are gender blind when it comes to really bad screening conclusions. The USPSTF committee is undoubtedly under pressure from government and insurance industry to reduce health care costs by cutting back on screenings. These deeply flawed recommendations if adopted will create huge male life wastage.

So what is it with this dysfunctional panel? Don't know? Or don't care? In either case USPSTF with its healthcare rationing agenda has created a horrific PSA recommendation.

Disclosures

None reported.

