## EDITORIAL

## Aligning Prostate Cancer Screening Recommendations for Patients and Providers

ther than skin cancer, prostate cancer is the most common cancer in American men. The United States estimates for 2021 are 248,530 new cases of prostate cancer with 34,130 deaths. Prostate cancer is the second leading cause of cancer death in American men, behind only lung cancer, with 1 man in 41 dying of this disease. Approximately 60% of newly diagnosed prostate cancer is in US men over 65 years of age with this group growing from 54 million today to 83.7 million by 2050. The debate surrounding PSA prostate cancer screening of this common cancer will likely intensify with the growth of this at-risk population. Screening for prostate cancer is commonly defined as the detection of cancer using a PSA test with our without a rectal exam in patients without symptoms.

The prostate cancer death rate declined from 39/100,000 in 1992 to 18/100,000 in 2019. While treatments have improved, PSA based screening, introduced in the early 1990's, has also contributed to this decline. Today 9% of all new prostate cancer cases present with advanced incurable disease, compared with 32% before the PSA era. The European Randomized Study of Screening for Prostate Cancer (ERSPC) published their 13-year follow up with a 21% reduction in prostate cancer deaths in the screened group versus the controls.¹ A recent review of over 400,000 men from Kaiser Permanente demonstrated that yearly PSA screening is beneficial, reducing prostate cancer deaths by 64% for men aged 55-75 years and all-cause mortality by 24%.² In addition to advanced age and family history being risk factors, African American men are at an increased risk of prostate cancer. Younger African American men undergoing frequent prostate cancer screening have a lower risk of metastasis and fatal disease.³ Other large screening studies have been less convincing with some dismissed due to poor methodology or data contamination. With evidence that some level of prostate cancer screening is appropriate, PSA screening remains controversial.

While some scientific support exists for screening, many professional groups are opposed or send mixed messages on the role of PSA testing. Even within the groups that support PSA based screening, some differences in guideline recommendations exist.

There are similarities in the PSA based screening recommendations from professional groups who support the effort such as, for example, the American Cancer Society, the American Urological Association, the National Comprehensive Cancer Network (NCCN) among others. Restricting screening to healthy men with relatively long-life expectancies, focusing on higher risk populations (age, race, family history) and shared decision-making are common themes. Subtle differences include age cutoffs, PSA levels and testing intervals. Many patient advocacy groups such as the Prostate Conditions Education Council (PCEC), ZERO – The End of Prostate Cancer, The Prostate Health Education Network (PHEN) and others present the risks and benefits of prostate cancer screening in many different venues. All these groups advocate for prostate cancer early detection through screening.

The Unites States Preventive Services Task Force (USPSTF) has issued six recommendations since 2002 including a controversial 'do not screen" recommendation in 2012. Studies have suggested this 2012 recommendation may have been responsible for an increase in the metastatic prostate cancer rates for several years that followed.<sup>4</sup> In their 2018 update, however, the USPSTF now recognizes that some men under the age of 70 might benefit from screening and encourage patient-provider shared decisions.

The American College of Physicians does not recommend PSA based screening unless the patient expresses a clear preference for it. Potential harms of a prostate biopsy in terms of over diagnosis and over treatment are noted but this group considers there "may be" value to a PSA after an abnormal DRE in terms of decreasing mortality.

There is one influential public forum that addresses the screening issue in both widely available print and web formats and engages with professional societies that deserves a closer look. "Choosing Wisely" campaign was started in 2012 as an initiative of the American Board of Internal Medicine Foundation in collaboration with the *Consumer Reports* magazine. The goal was to encourage physicians to have conversations with patients on potentially wasteful or unneeded treatments and procedures.<sup>5</sup>

"Choosing Wisely" is to be commended for summarizing the various high level professional society recommendations on prostate cancer screening on the "Clinician Lists" portion of their web site. There are several sections on the site relating to prostate cancer in general and PSA screening specifically. In particular the "For Patient's" section of the web site carries mostly negative screening messaging. These include highlighted statements such as "This test is often not needed", "There are risks to getting prostate cancer tests and treatments" and "Screenings can lead to high costs". This portion of the site does ultimately conclude that "....you should discuss the PSA test with your doctor", or shared decision-making. Another section by ASCO leads off by saying "Don't routinely perform PSA testing for prostate cancer screening in men with no symptoms of the disease" with no reference to shared decision-making. However, on their own *cancer.net* website there is the following statement: "ASCO recommends that people with no symptoms of prostate cancer and who are expected to live less than 10 years do not receive PSA screening. For those expected to live longer than 10 years, ASCO recommends that they talk with their doctor to find out if the test is appropriate for them". In a 2019 issue of *Consumer Reports* "Don't routinely screen for prostate cancer using a PSA test or digital rectal exam" was listed as part of the campaign.

"Choosing Wisely" also references a 2018 JAMA review that concludes: ".....services for which harms are likely to outweigh benefits include treatment for early-stage prostate cancer, which provides no mortality benefit but increases absolute risk of erectile dysfunction by 10% to 30%". Such an emphatic statement does not give fair balance to studies that have demonstrated benefit to screening in the setting of younger healthy patients with high-risk disease.

One of the sections that addresses PSA screening on the "Choosing Wisely" site was updated in 2018 in cooperation with the American Urological Association. It appears more balanced, and it includes active surveillance as an option for screen detected cancer. The American Academy of Family Practice (AAFP) that represents many primary care providers on the front lines of PSA screening decisions, has contributed a section as well. The AAFP states " .....for men who express a desire for prostate cancer screening, it should only be performed following a discussion of the potential benefits and harms. Routine screening for prostate cancer should not be done".

The reluctance to endorse prostate cancer screening does have merit. The PSA blood test, while arguable the best tumor marker of any cancer for follow up after treatment, has limitations as a screening tool. Falsely elevated PSA is a consequence of benign prostatic enlargement, infection and recent prostate instrumentation. A unique feature of prostate cancer is the fact that "more men die with prostate cancer rather than of prostate cancer". This reinforces the need to be cautious in screening approaches to avoid over diagnosis and treatment of insignificant prostate cancers, often referred to as "autopsy cancer", that will never harm a man in his lifetime.

The use of MRI, a variety of newer urine and blood tests and risk calculators<sup>1</sup> are refining our screening approach. These tests have shown the potential to reduce the over diagnosis of insignificant prostate cancer. Precision medicine and the role of genetic testing to assess prostate cancer risk is rapidly evolving to identify men who should consider screening. Improvements in prostate biopsy complications such as the increased use of transperineal biopsy are welcomed. The concept of active surveillance for low-risk disease should be considered in any screening discussion. Lastly, it should also be noted that our screening efforts may not always be successful. The nature of some aggressive prostate cancers may allow it to spread early, escaping routine screening efforts.

Another aspect of the prostate cancer screening debate relates to malpractice, often placing providers at risk depending on which professional society guidelines are followed. According to a 2021 Medscape report on malpractice, 31% of lawsuits were due to "failure to diagnose" with "disease progression and delayed treatment" accounting for another 42% of lawsuits. These are areas of concern for any prostate cancer screening decision.

How will we ever align PSA based prostate cancer screening opinions? Consistency in recommendations from groups that support screening would be a good first step as their guidelines are based on the same peer reviewed publications. This consistency should also apply to groups that have different statements on different web sites as noted previously. Groups that do not support screening should objectively review the latest literature as well and include findings that support or challenge their position. In general, consistency in messaging can be found for screening guidelines for other common male cancers such as colon and lung for a variety of reasons. This would be welcomed for prostate cancer. The trend that more groups on both sides of the argument are suggesting shared decision-making is an important step in aligning recommendations.

The goal should not be broad based PSA screening of all adult males but targeted screening for men at highest risk of aggressive life-threatening disease. These men could benefit from early treatment. Embracing this might help bring all parties into closer alignment.

Many professional medical societies continue to disagree on the role of prostate cancer PSA screening. While there a few areas of common ground, the controversy continues. What is more commonly highlighted in the messaging directed to patients is to avoid PSA screening. In this brief editorial it is impossible to review in detail all of the data that frames both sides of the discussion. How to align all of these stake holders and develop a consistent objective message will continue to be a challenge for both patients and providers. Consensus on screening for prostate cancer while getting closer may still be a long way off.

Leonard G. Gomella, MD Editor-in-Chief Philadelphia, PA, USA

## References

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