Editorials

Prostate Cancer Screening: The Pendulum Has Swung, and the Burden of Proof Is with Proponents

VINAY PRASAD, MD, MPH, *National Cancer Institute, National Institutes of Health, Bethesda, Maryland*

▶ **See related article on page 683.**

Because prostate cancer screening guidelines have wide implications and generate strong opinions, the debate has spilled outside the pages of the peer-reviewed biomedical literature and into the popular press. In July 2015, Dr. Deepak Kapoor, a urologist, published an op-ed piece in the *New York Times* entitled, "Bring Back Prostate Screening."[1] In it, he counsels that advances in magnetic resonance imaging technology, a better understanding of prostate-specific antigen (PSA) kinetics, and novel genetic tests will differentiate low- from high-risk prostate cancer. He argues that screening, by itself, does not commit men to further treatment, and he advises men in their 40s to get a baseline PSA test. In short, Kapoor believes that PSA screening should be modified and tweaked as we go, and that its use should not be even temporarily halted. Based on other articles, editorials, and blogs written by urologists and others, Kapoor appears to be in good company.

In this issue of *American Family Physician*, Mulhem and colleagues make a case as to why Dr. Kapoor and others are mistaken.[2] The use of PSA screening is a troubled public health strategy, and primary care physicians are justified in omitting this test from their routine health maintenance visits. When it comes to large-scale public health efforts, it is not sufficient to merely hope that advances in science and new screening algorithms will improve outcomes; rather, improved outcomes must be shown explicitly in well-designed, prospective clinical trials. Retrospective, post hoc, or other modeling studies are insufficient given the importance of the issue and the well-known limitations of these types of evidence.

The goal of any intervention performed on a healthy person is to improve overall mortality or quality of life.[3] Consider the facts for PSA screening. Prostate cancer screening does not improve overall mortality according to individual randomized controlled trials and pooled analysis. In a 2013 update to the Cochrane review on prostate cancer screening, five randomized controlled trials including 341,342 total participants compared PSA screening with observation. Screening did not reduce prostate cancer mortality when pooling the five trials or overall mortality in the four trials that examined these outcomes.[4] Only one trial showed that screening decreased prostate cancer–specific mortality (21% reduction) in a prespecified subgroup of men between 55 and 69 years of age, although this came at the price of substantial overdiagnosis (50%).[4] Also, improvements occurred in just two of the seven countries included in the trial.[5] This study contradicts results from a large, meticulously conducted American trial, which found no reduction in prostate cancer mortality.[6] As in all cases in which outcomes are different by study site and contradict other data, closer examination of the participant-level data is critical, particularly to assess for potential elements of bias. Yet, alarmingly, data from the positive European randomized trial are not being shared.[7]

If a patient undergoes PSA screening, and the cascade of downstream testing detects prostate cancer, the only randomized controlled trial conducted in the PSA era (PIVOT) showed no benefit of radical prostatectomy compared with active surveillance.[8] Yet, physicians are rarely using active surveillance in the care of these patients.[9] Using three criteria to identify patients in whom active surveillance is appropriate, rates of active surveillance are poor, ranging from 6.5% to 12.1%.[9]

It is unclear whether current PSA screening protocols yield any improvement in any patient-centered outcome, although it's unlikely, and PSA screening definitely leads to excess downstream interventions (unnecessary biopsies and prostatectomies, excess radiation, overuse of androgen deprivation therapy), anxiety, treatment adverse effects, costs, and missed opportunities to address general health and well-being. Mulhem and colleagues describe these issues in detail.[2]

When it comes to PSA screening, the pendulum has swung. Not only has our understanding of the benefits and harms shifted, as reflected by a continual change in guidelines away from testing, but the burden to justify screening has also swung. For decades, critics of PSA testing have shown the many unintended repercussions of the test, cautioning that our initial widespread adoption was not justified. Moving forward, it must be the proponents of screening who shoulder the burden of proof. Their task will be to show in a future randomized study whether any PSA screening algorithm can improve survival or quality of life compared with what is now the standard of care—no routine screening. Before primary care physicians consider reintroducing the PSA test, they must have proof that it improves outcomes. ▶

A busy primary care physician seeing a 40-, 50-, or 60-year-old man for a brief visit has one of the most challenging tasks in medicine. The physician must prioritize interventions and advice that reduce mortality, while simultaneously addressing the patient's concerns and questions, which are often related to different topics. In this context, a clinician may discuss with patients the uncertain benefits and known risks of PSA screening, as well as the U.S. Preventive Services Task Force recommendation against PSA screening.[10] Screening campaigns must be based on proven benefits, and routine PSA screening currently does not meet this standard.[11]

Address correspondence to Vinay Prasad, MD, MPH, at vinayak.k.prasad@gmail.com. Reprints are not available from the author.

Author disclosure: No relevant financial affiliations.

REFERENCES

1. Kapoor DA. Bring back prostate screening. *The New York Times*. July 5, 2015. http://www.nytimes.com/2015/07/06/opinion/bring-back-prostate-screening.html. Accessed July 5, 2015.
2. Mulhem E, Fulbright N, Duncan N. Prostate cancer screening. *Am Fam Physician*. 2015;92(8):683-688.
3. Prasad V. But how many people died? Health outcomes in perspective. *Cleve Clin J Med*. 2015;82(3):146-150.
4. Ilic D, Neuberger MM, Djulbegovic M, Dahm P. Screening for prostate cancer. *Cochrane Database Syst Rev*. 2013;(1):CD004720.
5. Salzberg S. PSA screening does more harm than good. *Forbes*. May 19, 2014. http://www.forbes.com/sites/stevensalzberg/2014/05/19/psa-screening-does-more-harm-than-good/. Accessed July 26, 2015.
6. Andriole GL, Crawford ED, Grubb RL III, et al.; PLCO Project Team. Mortality results from a randomized prostate-cancer screening trial [published correction appears in *N Engl J Med*. 2009;360(17):1797]. *N Engl J Med*. 2009;360(13):1310-1319.
7. Ablin RJ. The problem with prostate screening. *The New York Times*. November 25, 2014. http://www.nytimes.com/2014/11/26/opinion/the-problem-with-prostate-screening.html. Accessed July 15, 2015.
8. Wilt TJ, Brawer MK, Jones KM, et al.; Prostate Cancer Intervention versus Observation Trial (PIVOT) Study Group. Radical prostatectomy versus observation for localized prostate cancer [published correction appears in *N Engl J Med*. 2012;367(6):582]. *N Engl J Med*. 2012;367(3):203-213.
9. Maurice MJ, Abouassaly R, Kim SP, Zhu H. Contemporary nationwide patterns of active surveillance use for prostate cancer. *JAMA Intern Med*. 2015;175(9):1569-1571.
10. U.S. Preventive Services Task Force. Prostate cancer: screening. May 2012. http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/prostate-cancer-screening. Accessed August 20, 2015.
11. Prasad V. It is time to stop screening for prostate cancer. *JAMA Intern Med*. 2014;174(11):1841-1842. ■