

PROSTATE CANCER

PSA screening—more data, more debate

New evidence published in the *Journal of the National Cancer Institute* adds to the prostate cancer screening discussion, demonstrating that there is no survival benefit associated with annual PSA tests for asymptomatic men. Long-term results of the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial confirm the findings of the initial report, which was published in 2009 after 7–10 years of follow-up. This might be construed as another blow for advocates of PSA screening, after the US Preventive Service Task Force (USPSTF) advised against screening in their draft recommendation issued a few months ago.

The PLCO study was one of two large high-quality randomized trials considered by the USPSTF when making their recommendation. The other—the European Randomized Study of Screening for Prostate Cancer (ERSPC)—demonstrated a 20% decrease in risk of death from prostate cancer for men aged 55–69 years who underwent regular screening, when it was reported in 2009. Overall, however, the USPSTF concluded that the mortality benefits of

PSA screening are outweighed by the harms, the impact of which cannot be denied. For their review, the USPSTF analyzed US data on the harms associated with PSA detection itself (such as complications related to biopsy) and with the most commonly used interventions—prostatectomy and radiation therapy (such as incontinence and erectile dysfunction).

The PLCO cohort consists of 76,685 men aged 55–74 years who were enrolled at 10 screening centers across the USA between November 1993 and July 2001. 38,340 men were randomly assigned to undergo PSA screening once a year for 6 years plus annual digital rectal examination for 4 years; 38,345 patients received usual care. Screening finished in October 2006. The 2009 PLCO report demonstrated no significant difference in prostate-cancer-specific mortality between patients who underwent screening and those who did not, but was criticized for its short follow-up given the long natural history of prostate cancer. It was hoped, by some, that prolonged follow-up would reveal a greater survival benefit for PSA screening.

Now, Gerald Andriole and colleagues report a lack of such benefit at 13 years. Although 12% more prostate tumors were detected in the screened group than in those who received usual care (4,250 versus 3,815; RR 1.12; 95% CI 1.07–1.17), the number of deaths did not differ significantly between groups (158 versus 145; RR 1.09; 95% CI 0.87–1.36). Furthermore, the investigators found that age, pretrial PSA testing and baseline comorbidity status did not influence the effect of screening on prostate cancer mortality.

These data certainly add weight to the USPSTF's draft recommendation, although it is still unclear why the ERSPC and PLCO report such contradictory results. Andriole and his team plan to update their findings at 15 years, but it's unlikely that the controversy surrounding PSA screening will die down in the meantime.

The effect of PSA screening on overdiagnosis and overtreatment of patients whose prostate cancer might not have resulted in death is certainly troubling. However, many experts continue to point out that it is the best available tool for the detection of aggressive disease, and strict adherence to the USPSTF recommendation would result in the deaths of many men with curable prostate cancer.

Research efforts should be focused on refining the screening procedure in order to target only the men who are most likely to benefit (young, at high risk of prostate cancer, with a family history of disease), as well as improving the current treatment options by reducing the adverse effects of therapies, improving active surveillance and developing new less-invasive techniques.

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Original article Andriole, G. L. *et al.* Prostate cancer screening in the randomized Prostate, Lung, Colorectal and Ovarian cancer screening trial: mortality results after 13 years of follow-up. *J. Natl Cancer Inst.* 104, 125–132 (2012)



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