

## Prostate Cancer Screening: Benefits Remain Uncertain

Lin K, Lipsitz R, Miller T, Janakiraman S. Benefits and harms of prostate-specific antigen screening for prostate cancer: an evidence update for the U.S. Preventive Services Task Force. *Ann Intern Med* 2008;149:192–9.

### Study Overview

**Objective.** To review new evidence on the effect of prostate-specific antigen (PSA) screening on health outcomes.

**Design.** Systematic review and planned meta-analysis.

**Methods.** Search of PubMed for articles addressing health outcomes associated with PSA screening indexed between 1 January 2002 and 12 July 2007 (randomized controlled trials [RCTs], systematic reviews, and meta-analyses); the harms of screening for prostate cancer, excluding harms from treatment of prostate cancer, indexed between 1 January 2002 and 12 July 2007 (randomized or nonrandomized comparative studies); and the natural history of PSA-detected, nonpalpable, localized prostate cancer indexed between 1 January 2002 and 23 August 2007 (RCTs and cohort studies). Additional articles were identified through searches of the Cochrane Library and reference lists from major review articles and consultation with experts. Two reviewers independently assessed the articles to determine if inclusion criteria were met. Qualitative and quantitative data syntheses were planned.

**Main outcome measures.** Morbidity and mortality resulting from prostate cancer screening and anxiety and pain associated with PSA screening.

**Main results.** Reviewers assessed 390 articles addressing health outcomes associated with PSA screening, 421 articles on the harms of prostate cancer screening, and 91 articles on the natural history of PSA-detected, nonpalpable localized prostate cancer. Only 9 research studies (described in 10 articles) met criteria for inclusion, and thus plans for a quantitative synthesis of data were abandoned. In 2 poorly conducted RCTs assessing health outcomes with PSA screening, no difference in morbidity and mortality was found independently or in a meta-analysis between the screened and control groups, as assessed in intent-to-screen analysis. In 1 cross-sectional and 2 prospective cohort studies (fair to good quality), no overall increase in anxiety or decrease in health-related quality of life was evident; however, increased worry about prostate cancer was reported after false-positive test results in 2 of the 3 studies. One study found a decrease

in sexual function among men with false-positive results, and another found moderate to severe pain in men who had prostate biopsies that were later found to be benign. In 3 fair-quality cohort studies assessing the natural history of PSA-detected prostate cancer, good prognosis was found up to 10 years after diagnosis in elderly men selected for surveillance because of preexisting favorable risk for prostate cancer progression.

**Conclusion.** Limited new evidence is available to assess the harms and benefits of PSA screening for prostate cancer. No clear health benefit from screening is yet evident, and some harm can result from PSA testing.

### Commentary

Prostate cancer screening is one of the most controversial issues in cancer screening. Professional societies, including the American College of Physicians, generally call for physicians to have informed consent discussions with their patients regarding the potential benefits and harms of screening [1]. Other societies differ somewhat in their emphasis. The American Urological Association and the American Cancer Society recommend that physicians offer screening to patients starting at age 50 years after discussion about the associated benefits and harms [2,3]. The American Association of Family Physicians endorses the 2002 U.S. Preventive Services Task Force (USPSTF) findings, which stated that insufficient evidence was available to recommend for or against prostate cancer screening [4,5]. These somewhat diverging recommendations have created confusion for physicians and patients.

The current study by Lin et al sought to uncover any new evidence that could inform this discussion to aid in the updating of the USPSTF recommendations. The authors discovered few new studies. Studies that addressed health outcomes related to screening were of poor quality and provided no clear evidence in support of screening, and studies that assessed the natural history of PSA-discovered prostate cancer in elderly men found limited evidence that prostate cancer was the ultimate source of major morbidity and mortality over a mean of 10 years of follow-up. Some studies documented anxiety regarding prostate cancer risk in the aftermath of false-positive tests.

In response to these findings, the USPSTF recommendations

mostly remain the same: there is insufficient evidence to make a recommendation for or against PSA screening in men younger than age 75 years [6]. However, the USPSTF did conclude that the harms of PSA screening outweigh the benefits in men over age 75 years and therefore recommended against screening in this age-group [6].

The weakness of this study is the weakness of the research available to inform it. The studies were limited and of insufficient quality to truly assess the effectiveness of prostate cancer screening. As a result, this study is solely a qualitative review given the lack of available data. Another limitation was the decision to exclude some observational studies, which could have informed USPSTF decision making, especially given the lack of good RCTs.

Results of future large-scale clinical trials will likely be available to aid in this difficult decision for patients and their physicians. The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial is a multicenter RCT being conducted in 10 screening centers in the United States. The trial includes a large prostate cancer screening component, with over 38,000 men aged 55 to 74 years randomized to receive PSA and digital rectal examination (DRE) screening with a similar number of controls [7]. The European Randomized Screening for Prostate Cancer (ERSPC) Trial is an RCT being conducted in 8 countries in Europe. This study has enrolled over 163,000 men aged 55 to 69 years, with participants randomized to receive PSA screening with subsets also receiving DRE screening and transrectal ultrasonography [8]. Preliminary results from the ERSPC have been published as an observational case-control study and found a 49% reduction in metastatic prostate cancer in a subset of patients who received screening as compared with those who were not screened [9]. However, mortality from prostate cancer is the true endpoint, and results are still pending. These studies will provide complementary evidence that either supports or opposes prostate cancer screening. In the meantime, the USPSTF has provided helpful insight to guide screening in some populations.

### **Applications for Clinical Practice**

No clear evidence has emerged to support prostate cancer screening as a means of reducing morbidity and mortality

from prostate cancer, and some modest harms can result from screening. The USPSTF recommends against prostate cancer screening in men over the age of 75 years and has determined that there is insufficient evidence to make a recommendation for men in younger age-groups. Results from large-scale RCTs are pending and will provide more definitive evidence.

—Review by Jason P. Block, MD, MPH

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