Screening for Prostate Cancer: Prostate-Specific Antigen Testing Is Not Effective

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Drs. Hitzeman and Molina present a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at http://www.cochrane.org/reviews/en/ab004720.html.

Clinical Scenario
A 51-year-old man with no significant family history of cancer presents for a general health examination. He asks if his testing should include a prostate-specific antigen (PSA) test.

Clinical Question
Does the PSA test have a role in prostate cancer screening? Does it lead to better outcomes?

Evidence-Based Answer
Several large randomized controlled trials show that PSA screening does not significantly reduce prostate cancer mortality, even in a U.S. study that included black men and men with a family history of prostate cancer. However, PSA screening does lead to overdiagnosis, overtreatment, and treatment-associated morbidity. (Strength of Recommendation = A, based on consistent, good-quality patient-oriented evidence)

Practice Pointers
Prostate cancer is the second leading cause of cancer death in U.S. men, with 32,050 deaths estimated in 2010 (11 percent of deaths in men with cancer). They identified five randomized controlled trials involving a total of 341,351 participants in the United States, Canada, and Europe. The meta-analysis—whether viewed as a whole or by individual study—showed that PSA screening conferred no benefit in prostate cancer mortality with the exception of one subgroup in the European Randomized Study of Screening for Prostate Cancer. This subgroup of screened men 55 to 69 years of age had a relative risk reduction of 20 percent in prostate cancer mortality after a mean follow-up of nine years. Although this sounds encouraging, the small absolute benefit translates to 1,410 men needing to be screened and 48 men needing to be diagnosed to prevent one prostate cancer death over a decade. Additionally, it...
Cochrane Abstract

Background: Any form of screening aims to reduce disease-specific and overall mortality and improve a person’s future quality of life. Screening for prostate cancer has generated considerable debate within the medical and broader community, as demonstrated by the varying recommendations made by medical organizations and governed by national policies. Much of this debate is caused by the limited availability of high-quality research and the influence of false-positive or false-negative results generated by use of the screening techniques, such as the digital rectal examination and prostate-specific antigen (PSA) blood test. Our 2006 Cochrane review identified insufficient evidence to support or refute the use of routine mass, selective, or opportunistic screening for prostate cancer. This article is an update of that review.

Objectives: To determine whether screening for prostate cancer reduces prostate cancer–specific mortality, all-cause mortality, and its impact on quality of life, including adverse events.

Search Strategy: An updated search of electronic databases (PROS- TATE register, CENTRAL the Cochrane Central Register of Controlled Trials, Medline, EMBASE, CANCERLIT, and the NHS EED) was performed, in addition to hand searching of specific journals and bibliographies in an effort to identify published and unpublished trials.

Selection Criteria: All randomized controlled trials (RCTs) of screening versus no screening for prostate cancer were eligible for inclusion in this review.

Data Collection and Analysis: The authors assessed eligibility and trial quality, and extracted and double-entered data.

Main Results: Five RCTs with a total of 341,351 participants were included in this review. All involved PSA testing, although the interval and threshold for further evaluation varied across trials. The age of participants ranged from 50 to 74 years, and duration of follow-up from seven to 15 years. The methodological quality of three of the studies was assessed as posing a high risk of bias. Analysis of the five studies showed no statistically significant reduction in prostate cancer–specific or all-cause mortality among the whole population of men randomized to screening versus controls. A preplanned analysis of a core age group of men 55 to 69 years of age from the largest trial (European Randomized Study of Screening for Prostate Cancer [ERSPC]) reported a significant 20 percent relative reduction in prostate cancer–specific mortality; (95% confidence interval [CI], 0.65 to 0.98; absolute relative risk = 0.71 per 1,000 men).

Meta-analysis of the five included studies indicated no statistically significant difference in prostate cancer–specific mortality between men randomized to screening and control (relative risk [RR] = 0.95; 95% CI, 0.85 to 1.07). Subgroup analyses indicated that prostate cancer-specific mortality was not affected by the age at which participants were screened. Meta-analysis of two studies investigating all-cause mortality did not determine any significant differences between men randomized to screening or control (RR = 1.00; 95% CI, 0.98 to 1.02). A diagnosis of prostate cancer was significantly greater in men randomized to screening compared with those randomized to control (RR = 1.35; 95% CI, 1.06 to 1.72). None of the studies provided detailed assessment of the effect of screening on quality of life or costs associated with screening. Harms of screening included high rates of false-positive results for the PSA test (up to 75.9 percent), overdiagnosis (up to 50 percent in the ERSPC study) and adverse events associated with transrectal ultrasonography-guided biopsies, such as infection, bleeding, and pain.

Authors’ Conclusions: Prostate cancer screening did not significantly decrease prostate cancer–specific mortality in a combined meta-analysis of five RCTs. Only one study (ERSPC) reported a benefit in a subgroup of men 55 to 69 years of age. Within this subgroup of men, it was determined that 1,410 men needed to be invited to screening, and 48 additional men subsequently diagnosed with prostate cancer needed to receive early intervention, to prevent one additional prostate cancer death at 10 years. Men should be informed of this and the demonstrated adverse effects when deciding whether to undertake screening for prostate cancer. Any benefits from prostate cancer screening may take up to 10 years to accrue; therefore, men who have a life expectancy less than 10 to 15 years should be informed that screening for prostate cancer is unlikely to be beneficial.

These summaries have been derived from Cochrane reviews published in the Cochrane Database of Systematic Reviews in the Cochrane Library. Their content has, as far as possible, been checked with the authors of the original reviews, but the summaries should not be regarded as an official product of the Cochrane Collaboration; minor editing changes have been made to the text (http://www.cochrane.org).
Force provides no recommendation for or against PSA screening apart from discouraging its use in men 75 years and older, although it is currently updating its 2008 recommendations. The United Kingdom disallows PSA testing for prostate cancer screening.

In light of the controversy regarding PSA screening, most guidelines encourage a shared decision-making approach between the patient and physician. A booklet about prostate cancer screening for patients is provided through the Centers for Disease Control and Prevention at http://www.cdc.gov/cancer/prostate/pdf/prosguide.pdf. How to fit this discussion into a 15- to 30-minute office visit remains a challenge when most patients are already sold on the benefits of cancer screening. In a busy practice, it is sometimes easier to fulfill a request for a PSA test. However, in doing so, physicians may be doing harm by exposing their patients to unacceptably high risks of false-positive results, overdiagnosis, and adverse effects of unnecessary treatment for indolent cancers.

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REFERENCES


