

PROSTATE CANCER

Does PSA screening do more harm than good?



Interim analyses of the long-awaited results of two trials of prostate cancer screening have failed to put the controversy to bed. Completion of planned follow-up will hopefully provide clinicians with the guidance they need to manage their patients most effectively.

Initiated in the early 1990s, the US-based Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial and the European Randomized Study of Screening for Prostate Cancer (ERSPC) aim to determine the effect of screening on rates of prostate-cancer-related death. Lack of comprehensive, controlled assessment of the risks and benefits of screening has led to wide variation in the advice dispensed by professional organizations, and confusion among clinicians. Unfortunately, the analyses of ERSPC and PLCO trial data, published in the March issue of *The New England Journal of Medicine* after approximately 9 and 11 years of follow-up, respectively, have generated conflicting conclusions.

The 10-institution-strong PLCO team detected no significant reduction in prostate cancer mortality in their screened cohort. Men aged between 55 and 74 years who were randomized to the

PLCO trial's screening group ($n = 38,343$) were offered annual PSA testing (for 6 years) plus digital rectal examination (DRE; for 4 years). The control group ($n = 38,350$) were assigned to usual care. Importantly, 'usual care' for 40–50% of the men in the control arm included PSA testing and/or DRE.

By contrast, the ERSPC investigators determined that screening—as measurement of PSA level only, about every 4 years—reduced the rate of prostate-cancer-related death by 20%. The superior power of this trial, in which 182,000 men between the ages of 50 and 74 years were randomized, is one factor that could underlie the apparent difference in primary outcome between the European and US-based studies.

The authors of the two papers do converge in support of one key point: screening is associated with a markedly increased likelihood of overdiagnosis and, by inference, overtreatment. Biopsy—indicated when PSA level exceeded 3 ng/ml in the European centers—revealed a 76% false-positive rate. Is the screening of 1,410 men and treatment of another 48 to prevent one death due to prostate cancer (as calculated by the ERSPC investigators) an acceptable cost/benefit ratio?

The life expectancy of individuals is an important factor in answering this question. At this stage, neither the PLCO nor ERSPC teams have collected sufficient data to draw conclusions on the basis of age. Nevertheless, the lead author of the US study, Gerald Andriole, thinks that “screening is probably not necessary for elderly men and men with significant health issues.”

This opinion is supported by a recent publication of data collected during the Baltimore Longitudinal Study of Aging. Appearing last month in *The Journal of Urology*, this cohort study of almost 850 men showed that none aged 75–80 years with a PSA level <3 ng/ml died of prostate cancer. “We need to identify where we

should best focus our health-care dollars by concentrating on patients who can actually benefit from PSA testing,” said lead investigator Edward Schaeffer. “These findings give a very strong suggestion of when we can start to counsel patients on when to stop testing.”

“Is the screening of 1,410 men ... to prevent one death ... an acceptable cost/benefit ratio?”

Counseling and consultation with individual patients seems to be the best strategy for clinicians to employ while awaiting resolution of the screening debate. In a roundtable discussion (www.nejm.org/perspective-roundtable/screening-for-prostate-cancer), Philip Kantoff, Director of the Lank Center for Genitourinary Oncology at Dana Farber Cancer Institute, stated that clinicians “need to individualize, because clearly there are many patients who are diagnosed with prostate cancer that do not need to be treated, can be observed safely, and will not die of their cancer.” Mary McNaughton-Collins, a general medicine internist at Mass General Hospital, stressed the importance of patients being “fully informed, to consider their preferences and values about their decision, this PSA test. And we physicians can help them to know that there are tradeoffs, that there are potential benefits and that there are potential harms.”

Suzanne J. Farley

Original articles Andriole, G. L. *et al.* Mortality results from a randomized prostate-cancer screening trial. *N. Engl. J. Med.* **360**, 1310–1319 (2009). Schröder, F. H. *et al.* Screening and prostate-cancer mortality in a randomized European study. *N. Engl. J. Med.* **360**, 1320–1328 (2009). Schaeffer, E. M. *et al.* Prostate specific antigen testing among the elderly—when to stop? *J. Urol.* **181**, 1606–1614 (2009).