Re: Is a Screening Interval of Every 4 Years for Prostate Cancer Acceptable?

In an accompanying editorial, Crawford (1) critically reviewed our paper (2) “Interval cancers in prostate cancer screening: comparing 2- and 4-year screening intervals in the European Randomized Study of Screening for Prostate Cancer, Gothenburg and Rotterdam.” We would like to respond to some of his remarks.

First, the analysis reported was not done with the intention to defend a 4-year screening interval. At the start of the European Randomized Study of Screening for Prostate Cancer (ERSPC) trial, a 4-year screening interval was chosen based on the current available knowledge on lead time. The only center, and not several centers, as is mentioned in the editorial, that chose differently was the Swedish center in Gothenburg. However, as mentioned previously in the complete overview of the ERSPC in 2003 (3), the group was awaiting data that would confirm the correctness of the screening interval of 4 years. The first data that were published with respect to this choice were reassuring (4,5). Our comparative and longer term observations are confirmatory and will be helpful in developing future screening strategies.

Second, we acknowledge that the comparison was not made in a randomized setting. However, statements in the editorial addressing age and follow-up time are not correct. To achieve a similar age distribution, only men who were 55–65 years of age at the time of first screening were included. Follow-up data in both centers were complete through December 31, 2005, with a comparable mean follow-up time of 7.16 years in Rotterdam and 7.38 years in Gothenburg.

Third, contrary to the editorial, the paper does address the issue relating the screening interval to the initial prostate-specific antigen (PSA) level. Several studies on this subject are referred to in the paper. Moreover, it is mentioned in the discussion that only five of the men with interval cancers that were detected in both centers (N = 88) had a PSA level of 1.0 ng/mL or less at their first screening. In addition to the analysis of the number and characteristics of the interval cancers, the appropriateness of the length of the screening interval was also related to the tumor characteristics of the cancers detected at repeat screenings. In both centers, the rate of non–organ-confined and/or metastatic cancers was extremely low. These data provide another strong indication that the length of either a 2-year or a 4-year interval is not too long.

Finally, the suggestion to biopsy every man at the age of 50 years is, at the least, unwise. First, a prostate biopsy is not a 100% sensitive test and, without doubt, prostate cancer will be missed. But second, and most important, the amount of overdiagnosis that would occur using such a policy would be unacceptable. In this context, we would like to refer to the positive predictive value of the end-of-study biopsies in the Prostate Cancer Prevention Trial of 24.4% (6). Thus, biopsy every man regardless of PSA level would, without doubt, lead to the detection of at least half of the prostate cancers found at autopsy (the prevalence of detection at autopsy is 40%–50%). Is this really what we want to achieve?

MONIQUE J. ROOBOL FRITZ H. SCHRÖDER

References

Crawford’s editorial looks like an advertising slogan (1). The title “Is a screening interval of every 4 years for prostate cancer acceptable?” should be changed to “Screening for prostate cancer still unacceptable.” A physician’s goal should be to maximize effectively administered therapies and minimize unnecessary therapies, particularly given that the treatment of localized prostate cancer often has major consequences on quality of life (2). Yet, the impact on mortality remains unproven despite widespread screening for more than 15 years! Of the 19 major medical organizations worldwide, only the American Cancer Society and the American and the French Urological Associations recommend screening men for prostate cancer with annual prostate-specific antigen testing (3). Two of these three organizations have a major conflict of interest. I follow the guideline of the US Preventive Services Task Force (4), which concluded that “the evidence is insufficient to recommend for or against routine screening for prostate cancer.” The main drawback of cancer screening is overdiagnosis. The risk–benefit ratio is still debated for breast cancer screening (5). For prostate cancer screening, the risk of overdiagnosis is obvious.

Again, the editorial’s conclusion looks like an advertising slogan, “Men aged 50 years could combine a routine colonoscopy and prostate biopsy!” This promotes unproven and dangerous albeit lucrative
investigations. At the present time, colorectal cancer screening is based on a noninvasive test that detects fecal occult blood.

The editorial in the Journal could have been more evidence driven.

ALAIN BRAILLON

References


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Affiliation of author: Public Health, University Hospitals, Amiens, France.

Correspondence to: Alain Braillon, MD, Public Health, University Hospitals, Amiens, France (e-mail: braillon.alain@chu-amiens.fr).

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Response

Dr Braillon expresses concern that my editorial comment is an “advertising slogan” for screening. In the editorial comment it is stated, “Screening for prostate cancer is controversial—some medical organizations support it and others are skeptical.” These controversies led to the development of a large randomized clinical trial in the United States to determine the value, if any, of early detection of prostate cancer, the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) trial. This very important randomized trial began in 1992. I don’t see how he comes to the conclusion that this is an advertisement based on the above statement!

He expressed concern over the statement, “Men aged 50 years could combine a routine colonoscopy and prostate biopsy!” Prostate-specific antigen (PSA) and digital rectal examination are not perfect screening tests, and if men really want to know if they have prostate cancer, then this may be an option. From our prostate cancer prevention trial (1), 16.7% of men with a PSA of less than 1.0 ng/mL have prostate cancer, and 22.5% of the cancers detected were high grade.

Early detection efforts have turned the tide from diagnosis of more advanced disease to more local. Accompanying this trend is the discovery of a certain number of nonthreatening cancers. Dr Braillon’s statement, “The main drawback of cancer screening is overdiagnosis,” is true to some extent. That is why we are working on less invasive management techniques as well as surveillance and then intervening only for the patients who show signs of progression.

We have instituted a large clinical trial of targeted therapy in which we treat only the cancer, not the entire prostate (2). This has...
been referred to as the male lumpectomy. Although a number of men are potentially overdiagnosed, nearly 30,000 men will die of prostate cancer in the United States this year. The latter probably wish that they would have been the victims of overdiagnosis rather than underdiagnosis.

Drs Roobol and Schröder are correct and acknowledge my concerns that their manuscript is not the result of a randomized trial between 2 and 4 years of screening. If screening is determined to be worthwhile, then most men will not need to be screened every year, especially those with PSA values of less than 1.0 ng/mL (Figs. 1 and 2). This is what we reported years ago from the PLCO trial (3). I agree with the statement that biopsy is not 100% sensitive, but it is still the definitive way to diagnose prostate cancer. We need tests that are more specific and sensitive and then molecular markers to help us determine who needs treatment.

E. DAVID CRAWFORD

References

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Affiliation of author: Division of Urologic Oncology, University of Colorado Health Sciences Center, Aurora, CO.

Correspondence to: E. David Crawford, MD, Division of Urologic Oncology, University of Colorado Health Sciences Center, Mail Stop # F710, PO Box # 6510, Aurora, CO 80045 (e-mail: david.crawford@uchsc.edu).

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