Re: Lest We Abandon Digital Rectal Examination as a Screening Test for Prostate Cancer

The editorial by Basler and Thompson (1) on the report by Schröder et al. (2) necessitates comment by me. We are happy that Basler and Thompson agree with the final conclusion of the report that “more sensitive methods will have to be found to replace DRE (digital rectal examination) in men with low PSA (prostate-specific antigen) values.” Fur-
thermore, we acknowledge that the editorial points out a number of limitations of our material. Most of these points are correct, such as the possible bias by selecting case subjects for radical prostatectomy, the change of the protocol on one occasion during the study period, that palpable lesions were not directly subjected to biopsy examination, but were entered into sextant biopsy schemes, and the fact that only 90% of eligible men were subjected to biopsy examination; most of these are acknowledged in our report.

Several issues raised in the editorial, however, require at least short comments; other issues require more comment.

Screening before randomization (contamination): Contamination not only before, but also after, subjects were randomly assigned to the screening and control arms is subject to extensive study. The data will be presented elsewhere shortly. In the present context, only the contamination rate before subjects were randomly assigned is of relevance. This rate can be evaluated from the intake form and varies between 9% and 11%. Characteristics of the refusers are the subject of a separate study (3). Bias in the direction of selectively excluding men who might have a positive DRE is highly unlikely.

Low biopsy rate with low PSA: Basler and Thompson suggest that the number of cancers in the low PSA ranges may be substantially underestimated because the DRE-driven biopsy rate is lower in the lower ranges of PSA. In considering this issue, it is important to realize that the examiners did not know the PSA values before performing the DRE. Furthermore, other authors (4, 5) have encountered the same phenomenon. The fact that the positive predictive value (PPV) of DRE increases with rising PSA in a blind fashion shows that the value of DRE as a test is, in fact, PSA dependent.

Minimal prostate cancer, metastatic disease, and prostatic intraepithelial neoplasia (PIN): Basler and Thompson state that the definition of minimal prostate cancer is somewhat arbitrary. The definitions used are documented by Hoedemaeker et al. (6). All definitions of minimal, moderate, and advanced disease are arbitrary because they have not been clinically tested. Unfortunately, on pages 1820 and 1821 of our report, in spite of rigorous editing, contradictory information regarding the percentage of advanced tumors found for PSA levels of less than 4 ng/mL was retained. On page 1821, left column, line 3, the sentence should read as follows: "... whereas six tumors (16%) showed characteristics of advanced cancer." This statement is consistent with information several lines later in the same column, where we said that the proportions of men with PSA values of less than 4.0 ng/mL who had minimal, moderate, and advanced disease were 42%, 42%, and 16%, respectively. Our report indeed does not mention the proportion of cases with metastatic disease, which was 0.6%, 14 times lower than in the control arm. PIN has been subject to a separate report (7).

Basler and Thompson state that the assumption that DRE-detected tumors with PSA levels of less than 4 ng/mL might still be curable after 4 years is "an unsubstantiated leap of faith." We fully agree with this statement. Our report does not make this assumption. On the contrary, we anticipated a discussion of this issue. We state that the study group has decided to subject all men with a PSA level of greater than 3 ng/mL to a biopsy examination on the basis of the experience with the first 10,523 men screened. The question is whether cases of prostate cancer detected in men with a PSA level of less than 3 ng/mL might still be amenable to curative measures in the second round of screening. In this context, it is of interest that preliminary data indicate an identical detection rate with the regimen described in this paper, and the new regimen in which men with a PSA level of less than 3 ng/mL get an all-clear message, while men with a PSA level of 3 ng/mL or higher are subjected to a biopsy examination (Schroder FH: oral communication). This suggests that a large proportion of cases of prostate cancer are missed by DRE in men with PSA levels of 3–3.9 ng/mL.

Our report does not state that DRE should be abandoned, as suggested by the title of the editorial. The conclusion drawn is that a positive DRE and low PSA levels have a less than desirable PPV. DRE should be replaced by a better regimen that detects a larger proportion of cancers with fewer biopsy examinations.

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References


Note

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