Response to Walsh

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We thank Dr Walsh for the insightful comments. Before addressing our concerns we would like to clarify that the numbers that Walsh refer to are not risks but relate to instantaneous hazard rates at the end of the study period. The magnitude of these rates can to a large extent be explained as an artifact of the fact that men starting treatment of 5α-reductase inhibitors (5-ARIs) have more contact with urologists and are hence often diagnosed earlier than they otherwise would have been. A risk measure that is more relevant is seen in Figure 1 (1), where the cumulative incidence shows approximately one-half the 8-year risk of prostate cancer in the exposed group and no decrease in Gleason Score of at least 8 disease.

Nonetheless, these values are still remarkably low and, as pointed out by Dr Walsh, need to be interpreted with caution. We certainly agree with this and hope this caution was conveyed in our discussion about potential study biases and by the fact that our conclusion did not focus on a potential decreased risk of 5-ARI use but rather on the reassuring results of not observing any increased risk. To further draw attention to this, Thompson et al. wrote in the accompanying editorial “...with the fall in prostate specific antigen (PSA) with treatment, there may have been fewer biopsies among this group of subjects. While some of these factors may bias the study against finasteride, others have the opposite effect. In a cohort design, it is impossible to correct for these biases, and the results should be interpreted with caution” (2).

The Swedish guidelines state that PSA among 5-ARI patients should be corrected when deciding about prostate biopsy referrals for these men. Although a recent publication found that the Swedish prostate biopsy guidelines are not followed satisfactorily (3), we argue that ascertainment bias is unlikely to explain all of the reduction in prostate cancer risk among 5-ARI users. In fact, we estimated the relative risk of 5-ARI users vs nonusers by means of data from the prospective and population-based Stockholm3 prostate cancer diagnostic trial (4), which used prespecified rules for biopsy decisions. Among 160 biopsied 5-ARI users, we observed a relative risk of 0.61 (95% confidence interval [CI] = 0.42 to 0.84) for all prostate cancer and 0.73 (95% CI = 0.45 to 1.11) for a Gleason score of at least 7 cancer compared with biopsied nonusers (n = 6535 men).

Our article reports results from the largest population-based study of its kind, and because it represents a clinical cohort it includes all levels of PSA and reflects the target population for 5-ARI prescriptions. Despite its inherent limitations, we believe it adds to the evidence that 5-ARIs can be used without increased risk for high-grade prostate cancer. However, we do not believe that there is adequate evidence for using the drug as prevention for prostate cancer. For this we have to rely on clinical trials. Dr Walsh preferred using the phrase “risk of prostate cancer diagnosis,” and in reflection of the discussion above, we agree that this is a more accurate phrasing.

Note

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References