

Authors' Response

The Quebec Study Shows a 69% Decrease in Prostate Cancer Death

To the Editor:

It is true and well-recognized that only 23.1% of the 30,956 men invited for screening were screened. This was due to a lack of awareness in the population of the potential benefits of screening and, consequently, a lack of interest in men towards screening. On the other side, a unique strength of our study is the high quality of the control unscreened group, with minimal (6.4%) contamination by screening. Contamination of the control group by screening is a major problem, with no available solution in any other study on prostate cancer screening.

The 46,732 men were randomized between screening and no screening. Despite what was said by Alexander and Prescott, the first analysis was performed on an intent-to-treat basis from the time of enrollment, since deaths were analyzed independent of follow-up, the groups being definitively assigned from the day of first visit, with no censoring at a later date for any reason.

It is true that the mean follow-up time was longer in the unscreened men. This, however, was taken into account by expressing the data per 100,000 man-years. Contrary to what was mentioned by Alexander and Prescott, the potential bias should rather be in favor of the unscreened group, since their follow-up, on average, started 3 years earlier, and thus at a younger age where prostate cancer death is known to be lower. There was no "problem with the identification of the time when the follow-up clock starts ticking." As stated in the text, for the first analysis, it started on November 15, 1988 for the control unscreened group, and at first visit for the screened men.

It should be added that we have sufficient data to evaluate with precision the prostate cancer death rate in a screening-free population as a function of the number of years of follow-up. Those death rates were used to estimate the expected number of deaths that should have occurred in the screened group, adjusting for the number of years of follow-up available due to progressive entry into the study. According to this approach, screening reduced the cause-specific mortality by 2.9-fold. This is only 4% lower than the estimate of 3.03-fold reported in our paper and certainly very far from the estimate suggested by Alexander and Prescott that gradual enrollment caused a 43% reduction in deaths. Clearly, the "crude examination of the Scottish survival data for PC" performed by Alexander and Prescott does not apply. The Scottish survival data are for diagnosed prostate cancer cases;

this was not the situation in our study, since prior diagnosis of prostate cancer was an exclusion criterion in both groups.

Alexander and Prescott indicated that an intent-to-screen analysis is required, because "those who accept screening differ from those who do not." We appreciate that these authors also say that we performed such an analysis with "more scientific rigor." In fact, we used the best statistical methods available to analyze any possible bias, especially due to low compliance or low response to the invitation to be screened.

Thus, in agreement with the suggestion of Alexander and Prescott, the second analysis was made on an intent-to-treat basis at randomization. This analysis gave a 6% advantage in favor of screening, despite a dilution of the effect of screening by 76.9% of men who were not screened. However, it is not correct, as suggested by Alexander and Prescott, to eliminate years of follow-up postrandomization in such an intent-to-treat analysis (as seen later, Boer and Schroder suggest the opposite). Despite this, based upon approximate numbers, Alexander and Prescott estimated a 5% advantage in favor of the randomized invited group, a figure close to the 6% benefit that we reported. Since the correction for exposure is appropriate, why then mention numbers which do not apply and prepare a table with results that are similar to our data and thus lead to the same conclusion? The method of Cuzick et al. was applied, thus meeting the last suggestion of Alexander and Prescott.

We thus feel that all the statistical requirements have been met and that the Quebec study shows a 69% decrease in prostate cancer death resulting from screening and, most importantly, early treatment. If one wants only to compare the men originally invited to be screened and screened with those not invited and not screened, the advantage is 67% in favor of screening, a value not too different from the 69% obtained by pooling the data.

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