Prostate cancer screening in Europe

We congratulate the investigators of the European Randomised Study of Screening for Prostate Cancer (ERSPC) for providing longer follow-up to inform our understanding of the benefits and harms of population-based prostate cancer screening. Data from ERSPC will inform updates of systematic reviews that present the totality of randomised trial evidence on this topic.

Fritz Schröder and colleagues continue to emphasise the small absolute reduction in prostate-cancer-specific mortality and downplay the absence of a statistically significant effect of screening on all-cause mortality. Disease-specific mortality relies on the assumption that cause of death can be ascertained with a very high degree of accuracy, which is unlikely. Prostate cancer deaths represent a small fraction of all deaths in the trial. Subsequently, minor inaccuracies in cause of death ascertainment can sufficiently skew estimated effect size in favour of screening and make conclusions unreliable.

All-cause mortality also encapsulates fatal adverse events that might not be attributed to prostate cancer screening or treatment, which is particularly important in settings such as prostate cancer screening, in which overdiagnosis and overtreatment are of major concern.

The reported reduction of prostate-cancer-specific mortality continues to be limited to Sweden and Netherlands, and seems to be driven by the subgroup of participants aged 65–69 years. Whether these unique findings are due to chance, variation in screening and treatment protocols, or participant characteristics is not clear, but impedes broad population application.

No references are provided to support the authors’ praise of multiparametric MRI to selectively diagnose more clinically significant prostate cancer. The lessons from initial widespread enthusiasm for prostate-specific antigen screening tell us that high quality randomised trials are needed to establish the effect on disease and overall mortality.

We declare no competing interests.

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The third update of the ERSPC trial at 13 years’ follow-up claims to confirm the widely quoted figure of a substantial 21% reduction in prostate-cancer mortality attributable to prostate-specific antigen (PSA) screening of asymptomatic men. However, specific PSA-related and unacknowledged data call this figure into serious question.

The control patients diagnosed with early-stage prostate cancer were far more likely to receive initial treatment with androgen-deprivation monotherapy for equivalent risk disease, which is a very inferior treatment compared with radiation plus androgen-deprivation therapy for high-risk early-stage prostate cancer and is not an approved treatment for low-risk or intermediate-risk early-stage prostate cancer. If this inappropriately targeted hormonal treatment caused some increased prostate-cancer deaths in control patients, then the scientific alternative is that some of this 21% difference between screened and control patients might be attributable to increased prostate-cancer mortality in the control group. The 21% figure would thus be an inflated one.

The true extent of any change in prostate-cancer mortality due to PSA screening can be easily settled. Verification only needs access to the risk group and stage of all prostate cancers diagnosed, the initial treatments received, and the mortality outcomes. Unfortunately, access to the hormonal-based treatment data has been denied, despite ERSPC being publicly funded. To place the claim of substantial life-saving benefits of PSA screening onto a solid quantifiable footing, it would be helpful for the investigators to release these pivotal data for independent analysis, as has been previously requested.

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