Screening for prostate cancer remains controversial

The effectiveness of prostate-cancer screening with prostate-specific antigen (PSA) for mortality reduction and quality-of-life improvement remains uncertain after the recent publication of two large trials—the European randomised study of screening for prostate cancer (ERSPC) and the prostate, lung, colorectal, and ovarian (PLCO) cancer screening trial.1,2,3

ERSPC studied 162 000 men randomised to receive PSA testing every 4 years or no screening.1 With a median follow-up of 9 years, prostate cancer deaths decreased by 20% in men assigned to screening, but 95% CIs were wide (2–35%); the decrease was 27% for those who were actually screened. 1410 men would need to be screened and 48 would need treatment to prevent one death, although a reduced number to treat would be needed to prevent one person having bone metastasis. PSA testing can identify and cure some men why does use of the test continue to be controversial?

Some cancers detected by PSA testing are low risk,1,2 more than a third of these cancers are unlikely to become clinically detectable.3 Moreover, the best protocol to treat men with prostate cancer detected by screening is unknown. In the Scandinavian trial,4 surgery was better than observation, but the whole cohort had disease of higher stage and grade than is usually detected by PSA testing. Surgery and radiotherapy cause side-effects on sexual, urinary, and bowel function,5 but such side-effects are reduced in frequency and severity in centres treating a high volume of patients.6 Innovations such as robotic-assisted laparoscopic radical prostatectomy could reduce these side-effects, although treatments need to be targeted more effectively to patients who will most benefit. The advantages and risks associated with active monitoring and surveillance programmes are unknown.7 The US PIVOT trial8 and UK ProtecT study9 are working to establish the most effective treatment protocol. The ProtecT study has tested more...
than 110 000 men so far, and follow-up is in progress of more than 1600 men with clinically localised prostate cancer, who have been randomly allocated to receive active monitoring, radical surgery, or radical conformal radiotherapy. We need to await these results.

PSA testing lacks sensitivity and specificity. About a third of men with a PSA concentration of 3–10 ng/mL have prostate cancer. We cannot define a lower limit at which we are certain that no cancer is present because 18% of men with a PSA concentration of 1–3 ng/mL have intermediate-grade (Gleason 7) or high-grade (Gleason 8–10) disease.23 Some men are falsely reassured by a low PSA concentration, but lowering the PSA threshold increases the probability of identifying low-risk cancers.24

The role of digital rectal examination in screening remains uncertain because the test will deter some men. In ERSPC, digital rectal examination in combination with PSA testing resulted in increased cancer detection rates, especially for cancers of Gleason grade 7 or higher.24 However, in men with low-risk prostate cancer who are undergoing active monitoring, repeat digital rectal examination is important.

The independent data-monitoring committee for the PLCO study25 of 76 000 men was reported to have terminated the trial early and recommended publication of results because of “a continuing lack of a significant difference in the death rate between the two study groups at 10 years (with complete follow-up at 7 years) and information suggesting harm from screening”. However, contamination by PSA testing in controls was substantial, increasing from 40% in year 1 to 52% in year 6. In each of the test and control groups, a third of men had undergone a PSA test before recruitment and 10% had undergone more than one; a fifth had undergone more than one digital rectal examination. Consequently, whether the study will produce interpretable findings is in doubt.

Early detection of prostate cancer by PSA testing can prevent death for a subset of men. However, the test is associated with risk of excessive diagnosis and treatment, and population-based screening for prostate cancer cannot be recommended on the basis of these new data. Full counselling for men who request a PSA test remains essential because of the continuing uncertainty. Use of biomarkers26 offers hope for targeting diagnosis26 and radical treatment for men at risk of clinically significant disease. For men with low-risk disease, we need to refine active monitoring protocols to ensure that the opportunity for cure is not lost and patients are not treated unnecessarily.

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