Can PSA testing become appropriate public health policy?

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Over 30 years ago, Catalona et al proposed using prostate-specific antigen (PSA) as a screening test for prostate cancer.1 Their recommendation was based on the ability of PSA to find more prostate cancer when compared with transrectal ultrasound or a digital rectal examination. The impact on prostate cancer mortality was not evaluated. Many urologists in North America rapidly embraced PSA testing and transrectal prostate biopsy and the incidence of prostate cancer nearly tripled within the next 5 years. Subsequent trials confirmed that more than half of the cancers identified by PSA testing are low grade and are unlikely to progress during a patient’s lifetime.2 Despite these findings, widespread opportunistic PSA testing persists in many Western countries and often leads to interventions that do not lower prostate cancer mortality but do compromise quality of life. For this reason, most European countries have declined to support PSA-based screening programmes.

In the manuscript entitled The prevalence of MRI lesions in men responding to a GP-led invitation for a prostate health check: a prospective cohort study by Moore et al, the authors propose a new screening strategy.3 They suggest combining PSA with an MRI and restricting biopsies to men with demonstrable lesions and those with a PSA density >0.12 ng/mL. Their pilot study has raised an important finding that several men with normal PSA values appear to harbour clinically significant disease. The authors join several other researchers seeking to improve the performance of PSA testing. Most efforts combine the use of MRI, more extensive measurement of serum markers including prostate kallikreins and a measure of prostate volume, usually PSA density.

The European Association of Urology recently proposed a ‘risk-adapted early detection strategy for prostate cancer’ for men aged 50–70 years that relies on a PSA threshold of 3 ng/mL to trigger a cascade of risk evaluations including family history, PSA density, PSA velocity and a risk calculator that leads to an MRI for men likely to harbour intermediate or high-grade disease.4 The Swedish National Board of Health and Welfare has implemented an organised prostate cancer testing programme designed for men aged 50–74 years in two regions within Sweden.5 The programme is a risk stratified diagnostic algorithm based on PSA (>3 ng/mL), PSA density (>0.15 ng/mL/cm³) and/or a suspicious MRI lesion and age. Bratt et al recently published a detailed summary of the problems associated with traditional PSA screening and the current trials underway designed to improve PSA-based testing algorithms.6

Moore et al wisely state that they need to evaluate their proposed screening strategy in a larger UK population. Over 20% of the invitees were referred for prostate biopsy. This is an extraordinarily high number compared with the number of men likely to die from prostate cancer and raises concerns whether their algorithm will resolve the problems of overdiagnosis and overtreatment. The trial protocol by Moore et al also raises several questions. When should MRI/PSA testing commence? How often does an MRI scan need to be performed? At what age does testing cease? The incidence of prostate cancer rises with age, but many older men do not succumb to their disease. How should older men be monitored? Researchers conducting the ProScreen trial in Finland and the Probase trial in Germany have struggled with the same issues.7,8

Any new prostate cancer screening protocol needs to be accompanied by treatment algorithms that ultimately prove the efficacy of the screening programme. Simply finding ‘clinically significant disease’ is insufficient. We assume that surgery and radiation will alter the outcomes of newly diagnosed localised disease, but we lack sufficient data from randomised trials that detail the true impact of these interventions in men with intermediate and high-grade prostate cancer. Ultimately, any screening programme must meet public health criteria.
that balance the economic cost and the impact on quality of life against the potential gain in increased life expectancy. The natural history of most screen-detected prostate cancers extends well over a decade. This is a long time to validate a screening protocol, but necessary to prove its value.

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