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## World News

# Prostate cancer: To screen, or not to screen? That is the question


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At present there is no major developed country that recommends population screening with PSA for prostate cancer. The UK position, last reviewed in 2020, is that *"screening for prostate cancer is currently not recommended in the UK. This is because the PSA test is not accurate enough to detect prostate cancer that needs treatment"*. The US Preventative Services Task Force recommended in 2018 that *"men who are 55 to 69 years old should make individual decisions about being screened for prostate cancer with a prostate specific antigen test"*. Ultimately, the current majority view is that prostate cancer screening using the PSA blood test, while potentially reducing prostate cancer deaths, does lead to overdiagnosis and overtreatment with associated morbidity and mortality.

https://view-health-screening-recommendations.service.gov.uk/prostate-cancer/
https://www.cdc.gov/cancer/prostate/basic_info/get-screened.htm

Why then is prostate cancer screening back on the agenda? The issue provided one of the centrepiece sessions at the recent meeting of the European Association of Urology, coinciding with the publication of two high impact papers that provide further data in this area.

The first of these publications was a 15-year median follow-up of the CAP trial (Clustered Randomised Trial of PSA testing for Prostate Cancer), a UK based randomised trial of screening [3], in which the ProtecT (Prostate testing for cancer and Treatment) was embedded as its intervention arm. At the time of entry into the trial, primary care practices were randomised to offer a single invitation for PSA screening to men aged 50–69 years, with a PSA level of 3 ng/mL being the threshold for further investigation. At that time this involved transrectal ultrasound biopsy of the prostate. The control practices received no invitation for screening.

Prostate-Specific Antigen Screening and 15-Year Prostate Cancer Mortality. A Secondary Analysis of the CAP Randomized Clinical Trial. Richard M. Martin, Emma L. Turner, Grace J. Young et al *JAMA* 2024; https://doi.org/10.1001/jama.2024.4011

12 013 and 12 958 men in the intervention and control groups respectively had a prostate cancer diagnosis and at 15 years, 1199 and 1451 men had died of prostate cancer (RR 0.92 95% CI 0.85–0.99). Overall, there was a small decrease (0.09% absolute reduction) in prostate cancer-specific mortality at 15 years in the screened population but no effect upon overall survival, with resulting overdiagnosis and overtreatment as demonstrated in the ProtecT trial. This means that screening resulted in one fewer prostate cancer death per 1000 men invited for screening and the results were consistent with the European Randomised Study of Prostate Cancer Screening trial, which demonstrated that at 16 years, albeit with a different PSA testing regime of interval testing, 570 men needed to be invited for screening in order to prevent one prostate cancer death.

Hugosson J, Roobol MJ, Månsson M et al; ERSPC investigators. A 16-yr follow-up of the European Randomized Study of Screening for Prostate Cancer. *Eur Urol* 2019; 76: 43–51.

The second paper reported the baseline results of ProScreen, a Finnish trial of PSA screening, with over 61 000 men aged 50 to 63 years being randomised. Those with a PSA greater than 3 ng/mL initially underwent a 4-kallikrein panel blood test and those with a panel score of 7.5% or more underwent an MRI scan of the prostate, with targeted biopsies where appropriate. The initial

results showed that screening resulted in one additional high grade prostate cancer diagnosis per 196 men screened and one additional low-grade cancer per 909 men screened. The study's primary endpoint is disease-specific mortality and the results are awaited.

Prostate Cancer Screening With PSA, Kallikrein Panel, and MRI. The ProScreen Randomized Trial. Anssi Auvinen, Teuvo L. J. Tammela, Tuomas Mirtti et al. *JAMA* 2024; https://doi.org/10.1001/jama.2024.3841

## Why the renewed interest in screening? The PRAISE-U project and MRI scanning

The recent increased interest in prostate cancer screening has arisen partly because of increased political interest and partly as a consequence of clinical change and evolution. In December 2022, the European Commission announced a new policy designed to ensure that 90% of the European population who qualify for breast, cervical and colorectal cancer screenings are offered such screening by 2025. However, in a supplementary statement they also supported further evaluation to determine the feasibility and effectiveness of organised prostate cancer screening on the basis of PSA testing in combination with MRI scanning as follow-up.

Following on from that, the European Union in conjunction with the European Association of Urology has funded the **PR**ostate cancer **A**wareness and **I**nitiative for **S**creening in the **E**uropean **U**nion (PRAISE-U) programme. The stated aims were to ensure early detection and diagnosis of prostate cancer through customised and risk-based screening programs and to align screening protocols and guidelines across member states to enable the collection and distribution of relevant data. The overall budget was over €12 million and the project duration was 1st April 2023 to 31st March 2026.

> *"The risk of the introduction of population screening will be a repeated cycle of overdetection and overtreatment in Europe, at a time when the evidence suggests that systematic screening is likely to cause more harm than good"*

The PRAISE-U project has been broken down into six work packages. Work package 1 will provide overview, coordination and quality assurance of the project. Package 2 will develop a needs assessment report, performance indicators and a knowledge hub regarding prostate cancer screening. One of the outputs of work package 2, which is a systematic review regarding a detailed picture of screening policies and guidelines that are currently in place in Europe has already been published. Package 3 will design protocols and other research tools for the different pilots to evaluate risk-based screening. Package 4 will involve the set-up and coordination of pilot studies in the host countries, while work package 5 will assess functionality, feasibility and sustainability of the screening pilots. Finally, work package 6 will focus on communication and dissemination of the project aims and results.

At present five pilot sites have been identified. In Poland the focus of the project will be on important issues when setting up a screening program where little infrastructure currently exists. An Irish project will focus on streamlining opportunistic testing, while a Spanish project (in Galicia) will focus on the feasibility of risk-based screening. A second Spanish project (in Manresa) will focus upon compliance, particularly in relation to primary care and a project in Lithuania will use a risk-stratified population screening approach to align algorithms with the one proposed by the PRAISE-U project. The risk of such a programme, however, will be the introduction of population screening in the pilot sites, with a repeated cycle of overdetection and overtreatment in Europe, at a time when the evidence suggests that systematic screening is likely to cause more harm than good. Researchers will have to be vigilant in that respect.

https://health.ec.europa.eu/non-communicable-diseases/cancer/europes-beating-cancer-plan-eu4health-financed-projects/projects/praise-u_en
Beyer K, Leenen R, Venderbos LDF et al. Health Policy for Prostate Cancer Early Detection in the European Union and the Impact of Opportunistic Screening: PRAISE-U Consortium. *J Pers Med* 2024; 14: 84. https://doi.org/10.3390/jpm14010084
https://uroweb.org/praise-u

One of the other drivers for the renewed interest in screening has been the advent and utility of MRI scanning and targeted biopsies as a means of identifying clinically significant prostate cancer while reducing overdetection of low-risk disease. On the back of this a £42 million research program, the TRANSFORM study, was announced in the UK in 2023, with funding from the charity Prostate Cancer UK and from the UK Government. Although there is no published protocol at the time of writing, as was reported in World News in January, the study should commence recruitment in the autumn of 2024, and further details are awaited.

https://bjui-journals.onlinelibrary.wiley.com/doi/epdf/10.1111/bju.16262?af=R

 

MRI © istock.com/thelinke

## The Lancet Commission on Prostate Cancer

A final driver for the increased interest in early diagnosis and screening is demographic change. The recent Lancet Commission on prostate cancer suggested that the number of new cases of prostate cancer diagnosed globally will rise from 1.4 million per annum in 2020 to 2.9 million per annum by 2040 [10]. This will be driven by changing age profiles and by improved life expectancy. Given that, especially in low and middle income countries, many cases of prostate cancer are diagnosed late in their course, there is an urgent need to explore ways of early diagnosis and screening in such countries.

The crucial issue in all this is to ascertain whether this renewed interest in prostate cancer screening, together with the enhanced technology offered by MRI scanning, can change the fundamental difficulties that we have with screening for and managing early prostate cancer, namely our continued ability to understand what a clinically significant prostate cancer looks like. Given the relatively slow progression of early prostate cancer, it is likely to be several years before we are able to answer that question.

https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(24)00651-2.pdf

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