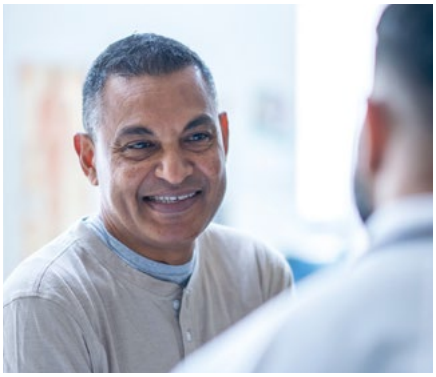
Shared decision making in prostate cancer screening

An update



CPD

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POPULATION SCREENING of low-risk asymptomatic men for prostate cancer with prostate-specific antigen (PSA) testing remains controversial, and mass screening programs have not been implemented. In Australia, if a patient enquires about prostate cancer screening, The Royal Australian College of General Practitioners (RACGP) and the Urological Society of Australia and New Zealand (USANZ) recommend shared decision making, taking into consideration the benefits and harms of, and alternatives for, PSA testing before an informed choice is made.[1–3] Recent 16-year follow-up data from the landmark European Randomized study of Screening for Prostate Cancer (ERSPC) and developments in the diagnosis of prostate cancer with multiparametric magnetic resonance imaging (MRI) provide evolved viewpoints.[4–6] In this article, the authors aim to highlight these advances for primary care physicians to facilitate the shared decision-making process.

The ERSPC was the largest study on prostate cancer screening and pivotal in informing worldwide guidelines, with results previously reported at nine-, 11- and 13-year follow up.[4] This landmark multicentre randomised trial in eight European countries included 162,389 men aged between 55 and 69 years. PSA testing was used as the primary screening test, with most centres incorporating a four-year screening interval (range: 2–7 years) followed by systematic prostate biopsies for patients with elevated PSA. The 16-year follow-up results showed that the relative risk reduction in prostate cancer mortality remained at 20%, while the absolute risk reduction in prostate cancer mortality from screening continued to increase. The excess incidence of prostate cancer in the screening group remained at 41% when compared with the control group. Interestingly, the number needed to screen (NNS) to prevent a case of prostate cancer decreased from 1947 at nine years to 570 at 16-year follow up (Table 1). Similarly, the number of excess cases needed to diagnose (NND) to prevent a case of prostate cancer decreased from 76 at nine years to 18 at 16 years. As the natural history of prostate cancer is long, it is important to interpret results from shorter follow-up periods with caution. Most men with curable prostate cancer who are treated conservatively do not die within the first decade after diagnosis.[7] As the median follow-up time since diagnosis in the ERSPC is 8.8 years in the screened arm and only 5.4 years in the control arm, it can be expected that the benefit of PSA screening will not plateau but should continue to improve with further maturity of this study. This was supported by Shoag et al (2020), who modelled the ERSPC results to 25-year follow up and predicted that the estimated NNS and NND to prevent a case of prostate cancer will decrease to 385 and 11 respectively.[8] These results show that prolonged follow-up time alone has already resulted in a trend of continually decreasing NNS and NND, which might affect the shared decision-making process.[4,8]

Traditionally, patients with an elevated PSA level or suspicion of prostate cancer from digital rectal examination would proceed to a transrectal ultrasound (TRUS)-guided prostate biopsy. However, PSA screening has led to concerns of overdiagnosis (detection of clinically insignificant cancers) and overtreatment, along with possible complications from biopsies. As a result of these concerns, technological advances in the past decade resulted in the development of a diagnostic pathway in which a multiparametric MRI is initially performed and subsequent targeted biopsies are only attempted in the presence of radiologically suspicious cancer, compared with traditional random sampling occurring from TRUS biopsies, which can lead to incorrect staging or biopsy-related

sepsis.[9] Patients are usually graded using the prostate imaging – reporting and data system version 2 (PI-RADS v2) and given a score of 1 to 5, with patients with a score of 3 or greater proceeding to biopsy.[5,6] The PRECISION study showed that in 500 patients with elevated PSA levels, the MRI pathway was non-inferior and indeed superior to standard biopsy for diagnosing clinically significant cancers (38% vs 26%), with fewer patients identified with clinically insignificant cancers (9% vs 22%).[6] Importantly, 28% of patients avoided a biopsy because of a negative MRI. The use of the MRI pathway in screening was investigated in the STHLM3-MRI trial in 2021.[5] Of 12,750 patients enrolled, the MRI pathway resulted in a higher diagnosis rate of clinically significant cancers (21% vs 18%) and lower diagnosis rate for clinically insignificant cancers (4% vs 12%). Similarly, more patients avoided a biopsy in the MRI pathway (absolute difference between groups 36% [95% confidence interval: 32, 41]) despite improved outcomes.

The MRI pathway has now been incorporated in multiple worldwide guidelines.[10,11] These are summarised in Table 2, with the common recommendation being an initial MRI followed by a targeted biopsy if the PI-RADS score is ≥3. While the MRI pathway has clearly improved issues within PSA screening regarding overdiagnosis, it is also likely that it has been a factor in addressing concerns of overtreatment, with the increased uptake of active surveillance or watchful waiting. The Prostate Cancer Outcomes Registry – Australia and New Zealand report from 2020 collated data from 72% of all men diagnosed with prostate cancer in 2018 and identified that 71% of men diagnosed with low-risk prostate cancer in Australia and New Zealand were initially managed with active surveillance or watchful waiting, increasing from 54% in 2015. As such, the criticism of overtreatment might be becoming outdated.[12]

Improved image detection of clinically significant prostate cancer does not end at multiparametric MRI. The road forward will likely incorporate prostate-specific membrane antigen (PSMA) positron emission tomography (PET) scans, which detect cell surface PSMA present on prostate cancer. The use of these scans in conjunction with MRI for the detection of prostate cancer was investigated in the Australian multicentre prospective PRIMARY trial published in 2021.[13] Combination MRI and PSMA PET increased the negative predictive value from 72% to 91% and the sensitivity of diagnosing clinically significant prostate cancer from 83% to 97% when compared with MRI alone. PSMA PET scans appear particularly useful in identifying clinically significant prostate cancer in patients with PI-RADS 2–3 lesions on MRI.[13]

Long-term follow-up data from the ERSPC continue to offer evolving insights on prostate cancer screening. The MRI pathway has resulted in improved diagnosis of clinically significant cancers with subsequent reduction in overdiagnosis and fewer biopsies. Effective shared decision making between

Table 1. European Randomised study of Screening for Prostate Cancer (ERSPC): Number needed to screen or number needed to diagnose to prevent one prostate cancer death

Years of follow up	Nine[4]*	11[4]*	13[4]*	16[4]*	25[8]†
Number needed to screen	1,947	962	742	570	385
Number needed to diagnose	76	34	26	18	11

**Years nine, 11, 13 and 16 from ERSPC trial findings[4]*
†Year 25 modelled from ERSPC trial data[7]

Table 2. Summary of international guidelines incorporating magnetic resonance imaging prior to biopsy for suspected prostate cancer

Guideline	Year	Recommendation
European Association of Urology/European Association of Nuclear Medicine/European Society for Radiotherapy and Oncology/European Society of Urogenital Radiology/International Society of Geriatric Oncology[10]	2020	In patients who are biopsy naive – perform multiparametric MRI before prostate biopsy. If radiological PI-RADS score ≥3, perform combined targeted and systematic biopsy. If radiological PI-RADS score <3 and clinical suspicion is low, omit biopsy on the basis of shared decision making with the patient.
United Kingdom National Institute for Health and Care Excellence[11]	2019	Offer a multiparametric MRI as first-line investigation to patients suspected of clinically localised prostate cancer. If the radiological Likert/PI-RADS score is ≥3, proceed to an MRI-targeted biopsy. Consider omitting prostate biopsy in patients with multiparametric MRI Likert/PI-RADS score <3 but only after discussing the risks and benefits with the person and reaching a shared decision.

MRI, magnetic resonance imaging; PI-RADS, prostate imaging – reporting and data system

general practitioners and patients requires knowledge of recent advances, which continue to influence the risk–benefit equation for prostate cancer screening.

Key points

- Prostate cancer has a long natural history, and the 16-year follow-up data from the ERSPC continue to show improvements in NNS and NND to prevent a death from prostate cancer.
- Multiparametric MRI followed by a targeted prostate biopsy if PI-RADS score is ≥3 is superior to standard biopsy for detecting clinically significant cancers, allows men to avoid unnecessary biopsies and reduces the number of clinically insignificant cancers detected on biopsy (reduction in overdiagnosis).
- The majority of low-risk prostate cancer in Australia and New Zealand is now treated with active surveillance or watchful waiting (reduction in overtreatment).
- Combination MRI and PSMA PET scanning increases the negative predictive value and sensitivity of diagnosing clinically significant prostate cancer when compared with MRI alone.

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