

# Major changes with reduced harms in prostate cancer diagnosis and management

**Mark Frydenberg**

**SINCE THE 1990s**, when prostate-specific antigen (PSA)-based prostate cancer testing was introduced, the majority of guidelines have counselled against PSA testing; however, major changes have occurred that have changed the benefit-harm balance firmly in favour of benefit.

Randomised controlled trials, such as the European Randomized study of Screening for Prostate Cancer (ERSPC) and its Göteborg arm, have demonstrated significant benefits in favour of screening. The Göteborg trial, with 22 years of follow up, demonstrated a 41% relative risk reduction of dying from prostate cancer.<sup>1</sup> Having demonstrated that there is a benefit to survival from screening men of the correct age group, namely those with a greater than seven- to 10-year life expectancy, the challenge now was to reduce the harms of screening and treatment.

Multiparametric magnetic resonance imaging (mpMRI) of the prostate has profoundly changed how prostate cancer is diagnosed as it is now used and funded as a triage test to determine if a patient requires a biopsy or can be safely reassured. A standardised reporting system, the prostate imaging – reporting and data system (PI-RADS), is now routinely used, with scores between 1 and 5 demonstrating increasing risk of prostate cancer being present (a positive predictive value of PI-RADS 3 = 13%, PI-RADS 4 = 40% and PI-RADS 5 = 69%). The European Association of Urology recommends biopsy in patients with PI-RADS  $\geq 3$ , and suggests omitting biopsy in those with less suspicious magnetic

resonance imaging (MRI) features.<sup>2</sup> Several randomised controlled trials, such as PROMIS and PRECISION, have demonstrated the role of MRI in the diagnostic pathway, with improved sensitivity compared with transrectal ultrasound (TRUS)-guided biopsies (87% versus 60%) for the detection of clinically significant disease and 27% avoided the biopsy altogether.<sup>3,4</sup> In addition, prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) can also improve the detection of higher grade disease with evidence that the standardised uptake value in the primary lesion correlates with tumour grade. This, in combination with mpMRI of the prostate, improves sensitivity and the negative predictive value of detection of clinically significant disease,<sup>5</sup> which is also strongly supported by the results of the PRIMARY trial.<sup>6</sup>

Having now ensured that only men at risk of clinically significant cancers are biopsied, the challenge was to make that process safer. The major advantage of transperineal biopsies (TPB) has been the significant reduction in biopsy-related sepsis that is associated with the TRUS-guided approach (0–0.7% with TPB compared with 0.5–6.9% with TRUS).<sup>7</sup> Once diagnosed, staging of high-risk cancers is also vastly improved using PSMA PET/CT with a landmark Australian trial (proPSMA) clearly demonstrating the improved accuracy of PET/CT compared with standard care, namely CT of the abdomen and pelvis and a nuclear bone scan (92% versus 65%), with the results changing the management in 27% of men.<sup>8</sup>

Last, there has been a massive shift away from definitive treatment to

active surveillance for low-risk prostate cancer and even some small lower-risk, intermediate-risk disease. The risk of prostate cancer death is very low (1%) in trials regardless of whether patients were treated with surgery, radiotherapy or observation,<sup>9,10</sup> with significant improvements in quality of life associated with avoiding the potentially debilitating side effects of surgery or radiotherapy. An experimental but emerging treatment option is focal therapy for patients with unifocal prostate cancer proven on MRI, PSMA PET/CT and biopsy, whereby the tumour is ablated by an energy source (eg irreversible electroporation, high-intensity focused ultrasound, brachytherapy seeds, interstitial laser or cryotherapy) with early results showing promising cancer ablation rates in the treatment zones with a reduced risk of side effects.<sup>11</sup> While experimental, this does demonstrate that urologists around the world are determined to reduce morbidity where possible for all prostate cancer patients.

The tide has turned in prostate cancer diagnosis and treatment with the advent of these new technologies. The 2016 National Health and Medical Research Council-endorsed guidelines are currently being reviewed, and we all eagerly await the outcome of this review and the revised recommendations.

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