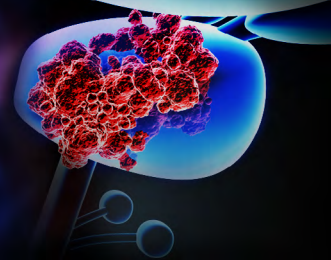


# Prostate Cancer Research Review™



Making Education Easy

Issue 81 - 2024

## In this issue:

- > <sup>18</sup>F-piflufolastat to diagnose prostate cancer
- > Four-year results of screening for prostate cancer with PSA and MRI
- > Prostate virtual high-dose-rate brachytherapy boost
- > PSCA-CAR T-cell therapy for mCRPC
- > <sup>177</sup>Lu-PSMA-617 for progressive mCRPC
- > Intestinal microbiota prediction of radiotherapy-induced acute GI toxicity
- > Long-term outcomes using protocol-directed AS
- > Nomogram to re-define disease stage and risk
- > Artificial intelligence vs radiologists for MRI prostate cancer detection
- > High-dose vitamin D to attenuate ADT-induced bone loss

## Abbreviations used in this issue:

**ADT** = androgen deprivation therapy; **AS** = active surveillance;  
**AUC** = area under the receiver operating curve; **CI** = confidence interval;  
**CT** = computed tomography; **EAU** = European Association of Urology;  
**EBRT** = external beam radiotherapy; **FDG** = fludeoxyglucose;  
**GI** = gastrointestinal; **HR** = hazard ratio;  
**mCRPC** = metastatic castration-resistant prostate cancer;  
**mHSPC** = metastatic hormone-sensitive prostate cancer;  
**mpMRI** = multiparametric magnetic resonance imaging;  
**NCCN** = National Comprehensive Cancer Network; **OS** = overall survival;  
**PET** = positron emission tomography; **PSA** = prostate-specific antigen;  
**PSCA** = prostate stem cell antigen; **PSMA** = prostate-specific membrane antigen;  
**RANKL** = receptor activator of NF-kappaB ligand.



## Welcome to Issue 81 of Prostate Cancer Research Review.

In the PEDAL trial, MRI was superior to PSMA for the diagnosis of prostate cancer, although there was no difference in ability to diagnose clinically significant prostate cancer. Five-year results from the phase II PROMETHEUS trial show that a gantry-based "virtual" high-dose-rate brachytherapy boost followed by conventionally fractionated EBRT in men with prostate cancer is associated with low rates of progression and acceptable toxicity. We conclude this issue with a study showing that high-dose vitamin D supplementation for 24 weeks in men with prostate cancer receiving ADT is associated with significantly reduced hip and femoral neck BMD loss, especially for those with low baseline serum 25-hydroxyvitamin D levels.

I hope you find the research in this issue useful to you in your practice and I look forward to your comments and feedback.

Kind Regards,

**Professor Niall Corcoran**

[niall.corcoran@researchreview.com.au](mailto:niall.corcoran@researchreview.com.au)

## Fluorine-18-labelled prostate-specific membrane antigen positron emission tomography/computed tomography or magnetic resonance imaging to diagnose and localise prostate cancer. A prospective single-arm paired comparison (PEDAL)

**Authors:** Wong L-M et al.

**Summary:** This prospective, multicentre, single-arm, phase III trial assessed the diagnostic accuracy of <sup>18</sup>F-piflufolastat (<sup>18</sup>F-DCFPyL) PSMA-PET/CT versus mpMRI (Prostate Imaging Reporting and Data System [PIRADS] score 3-5) for the detection of prostate cancer confirmed by targeted and systematic biopsy in 236 patients. Of 236 patients receiving mpMRI and PSMA-PET/CT, 184 (76.7%) had a biopsy, with 73 patients having benign biopsies, 27 patients having International Society of Urological Pathology grade group (GG) 1 tumours, and 84 having GG ≥2 tumours (clinically significant prostate cancer). Diagnostic accuracy of mpMRI was higher (AUC 0.76; 95% CI 0.69-0.82) than PSMA-PET/CT (AUC 0.63; 95% CI 0.56-0.70, p = 0.03), as was the diagnostic accuracy of mpMRI for detecting clinically significant prostate cancer (AUC 0.72; 95% CI 0.67-0.78), which was higher than PSMA-PET/CT (AUC 0.62; 95% CI 0.55-0.69), but not statistically significant. Combination PSMA-PET/CT and mpMRI had excellent sensitivity (98.8%; 95% CI 93.5-100) and negative predictive value (96%; 95% CI 79.6-99.9) over mpMRI alone (86.9% and 80.7%; p = 0.01). Overall, 32 (13.6%) patients had metastatic disease, and they tended to be older (68.4 vs 65.1 years; p = 0.023), with higher median PSA (9.6 vs 6.2 ng/mL; p < 0.001) and an abnormal prostate on digital rectal examination (DRE; 78.2% vs 44.1%; p < 0.001).

**Comment:** This single-arm study from Australia and New Zealand investigated the comparative performance of mpMRI and PSMA-PET/CT to diagnose and localise prostate cancer in patients presenting with an elevated PSA/abnormal DRE. Overall, MRI performed better than PSMA-PET/CT for local tumour detection consistent with previous studies, although the combination had greater sensitivity and negative predictive value over MRI alone. This suggests PSMA-PET/CT has a role in determining which patients with a negative MRI but suspicious clinical parameters need to proceed to a biopsy. The maximum standardised uptake value (SUV<sub>max</sub>) for a positive lesion was >7 based on the authors previously published pilot data, somewhat lower than that derived from the PRIMARY study, although this is likely to only increase the measured sensitivity at a cost of loss of specificity.

**Reference:** *Eur Urol Oncol.* 2024;7(5):1015-1023

[Abstract](#)



2024  
**COSA**  
ASM

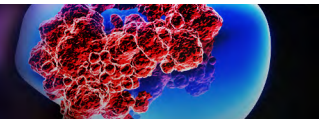


**COSA's**  
51st Annual  
Scientific Meeting

**GOLD COAST**  
Convention  
and Exhibition  
Centre

**13 - 15**  
November  
2024

Bridging gaps,  
building progress,  
breaking down  
disparities



## Results after four years of screening for prostate cancer with PSA and MRI

**Authors:** Hugosson J et al.

**Summary:** This report provides a 4-year follow-up on a Swedish population-based trial of PSA screening in men with a PSA of  $\geq 3$  ng/mL who underwent systematic biopsy and MRI-targeted biopsy ( $n = 6578$ ) versus MRI-targeted biopsy only ( $n = 6575$ ). At a median of 3.9 years (26,000 person-years), prostate cancer was identified in 185 (2.8%) MRI-targeted biopsy and 298 (4.5%) systematic biopsy recipients. Relative risk (RR) of detecting clinically insignificant cancer was 0.43 (95% CI: 0.32-0.57;  $p < 0.001$ ) for MRI-targeted versus systematic biopsy and was lower at repeat screening than during the first screening (RR 0.25 vs 0.49); clinically significant prostate cancer had an RR of 0.84 (95% CI 0.66-1.07). Advanced or high-risk cancers were detected in 15 MRI-targeted biopsy recipients and 23 systematic biopsy recipients (RR 0.65; 95% CI 0.34-1.24). There were a total of five severe adverse events identified (3 with systematic biopsy and 2 with MRI-targeted biopsy).

**Comment:** PSA-based population screening for prostate cancer leads to both high rates of negative biopsies and diagnosis of indolent tumours, which has limited widespread adoption. This large RCT from Sweden compared two different approaches, both incorporating prostate MRI; performing a systematic biopsy in all cases with an elevated PSA regardless of MRI findings, with additional targeted cores taken in cases of a suspicious lesion versus taking targeted cores only from a suspicious lesion if present, or systematic biopsies in patients with no MRI lesion but a compelling clinical indication. The latter strategy reduced both the number of biopsies and the number of indolent tumours diagnosed by over half, with a similar number of 'clinically significant' cancers identified. Certainly an improvement, but whether it is better than the 'case finding' practice in Australia (which mirrors the latter approach) is unclear.

**Reference:** *N Engl J Med.* 2024;391(12):1083-1095

[Abstract](#)

## Prostate virtual high-dose-rate brachytherapy boost: 5-year results from the PROMETHEUS prospective multicentre trial

**Authors:** Wegener E et al.

**Summary:** The multicentre, single-arm, phase II PROMETHEUS trial assessed the use of stereotactic body radiotherapy (SBRT) or "virtual" high-dose-rate brachytherapy boost (19-20 Gy in two fractions) followed by conventionally fractionated external beam radiotherapy (EBRT; 46 Gy in 23 fractions) or standard EBRT (36 Gy in 12 fractions) in 151 patients (median age of 69 years) with prostate cancer (74% intermediate risk, 26% high risk). After a median follow-up of 60 months, the 5-year biochemical/clinical relapse-free rate was 94.1% (95% CI 90-98) with a local control rate of 98.7%. The acute grade 2 gastrointestinal (GI) toxicity rate was 6.1% and genitourinary (GU) toxicity rate was 23.2%, with no acute grade 3 toxicity. After 60 months, late grade  $\geq 2$  GI toxicity prevalence was 1.7% (95% CI 0.3-6.5) and late grade  $\geq 2$  GU toxicity prevalence was 3.3% (95% CI 1.1-8.8). Quality of life (QoL; Expanded Prostate Cancer Index Composite-26 questionnaire) improved in urinary obstructive and hormonal domains, was stable in bowel domains, and deteriorated in sexual and urinary incontinence domains.

**Comment:** The ASCEND-RT trial previously showed that a low-dose brachytherapy boost improves time to progression in men with intermediate- and high-risk disease undergoing EBRT. The NSW/QLD run PROMETHEUS trial investigated if a similar oncological benefit can be obtained using a 'virtual brachytherapy' boost using SBRT of 19-20 Gy in 2 fractions one week apart, followed by conventionally fractionated EBRT up to 36 or 46 Gy. At 5 years the rate of progression was low with acceptable toxicity, noting that all patients received a rectal spacer prior to treatment. This schedule is currently being compared with SBRT monotherapy (40 Gy in 5 fractions given on alternating days) in the ongoing NINJA study (Trans-Tasman Radiation Oncology Group; TROG).

**Reference:** *Eur Urol Oncol.* 2024;7(5):1042-1050

[Abstract](#)

## PSCA-CAR T cell therapy in metastatic castration-resistant prostate cancer: A phase 1 trial

**Authors:** Dorff TB et al.

**Summary:** This first-in-human phase I study examined prostate stem cell antigen (PSCA)-directed chimeric antigen receptor (CAR) T cells (100 million CAR T cells without lymphodepletion [LD]), followed by incorporation of LD in 14 men with mCRPC. No dose-limiting toxicities (DLTs) occurred at dose level 1 (DL1), but a DLT of grade 3 cystitis occurred at DL2, so a new cohort used a reduced LD regimen plus 100 million CAR T cells (DL3). There were no DLTs in DL3. Overall, 5 patients experienced cytokine release syndrome of grade 1 or 2. PSA decreases ( $>30\%$ ) occurred in 4 patients, along with radiographic improvements. In a subgroup of patients, dynamic changes suggesting activation of peripheral blood endogenous and CAR T cell subsets, T cell receptor diversity and changes in the tumour immune microenvironment occurred. There was limited persistence of CAR T cells beyond 28 days.

**Comment:** CAR T cells are patient-derived T cells which have been genetically modified to express receptors to antigens found on tumour cells. They frequently incorporate co-stimulatory domains which enhance T-cell activation and tumour cell kill, with a number being FDA-approved for haematological malignancies. Solid tumours however have proven less tractable to CAR T cells, possibly due to issues with tumour penetration. This phase I study investigated the efficacy of CAR T cells engineered with an antibody against PSCA in a cohort of heavily pre-treated mCRPC patients with PSCA expressing tumours. Although there were some signs of efficacy (PSA response, radiographic improvement), these were generally short-lived, as the cells were cleared quite quickly from the circulation. Encouraging, but still a fair amount of optimisation required.

**Reference:** *Nat Med.* 2024;30(6):1636-1644

[Abstract](#)

## <sup>177</sup>Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): A phase 3, randomised, controlled trial

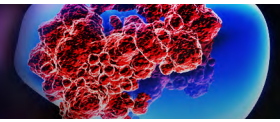
**Authors:** Morris MJ et al.

**Summary:** This multinational, randomised, controlled phase III trial assessed the efficacy of <sup>177</sup>Lutitium-PSMA-617 (4 GBq every 6 weeks for 6 cycles) or a change of androgen receptor pathway inhibitor (ARPI) to abiraterone or enzalutamide, in 468 patients with taxane-naive mCRPC. Overall, 134 (57%) ARPI change patients crossed over to <sup>177</sup>Lu-PSMA-617. At a median of 7.26 months, median radiographic progression-free survival (rPFS) was 9.30 months (95% CI 6.77-not estimable) with <sup>177</sup>Lu-PSMA-617 versus 5.55 months (95% CI 4.04-5.95) with ARPI change (HR 0.41; 95% CI 0.29-0.56;  $p < 0.0001$ ). At a median of 24.11 months, median rPFS was 11.60 months (95% CI 9.30-14.19) with <sup>177</sup>Lu-PSMA-617 versus 5.59 months (95% CI 4.21-5.95) with ARPI change (HR 0.49; 95% CI 0.39-0.61). The incidence of grade 3-5 adverse events was lower with <sup>177</sup>Lu-PSMA-617 than ARPI change (36% vs 48%).

**Comment:** Accumulating evidence supports the use of <sup>177</sup>Lu-PSMA after docetaxel in the mCRPC setting (VISION etc.), but what about as a second-line therapy before taxanes? This is addressed in this open-label randomised controlled trial, which randomised patients progressing on an ARPI to either a change in ARPI or up to 6 cycles of <sup>177</sup>Lu-PSMA-617. Patients were not selected based on the concordance of FDG/PSMA-PET imaging as is common in Australian trials, but all lesions of a certain size, depending on anatomical location, had to be PSMA-PET avid. Given that responses to second-line ARPI have been generally poor due to cross-resistance, it is perhaps predictable that the primary endpoint of improvement in rPFS was readily met. This has not translated yet into a difference in OS in this third interim analysis, presumably due to the high cross-over rate (78%) of patients with radiological progression in the ARPI group. Docetaxel may have been a better comparator to give clearer guidance on treatment sequencing.

**Reference:** *Lancet* 2024;404(10459):1227-1239

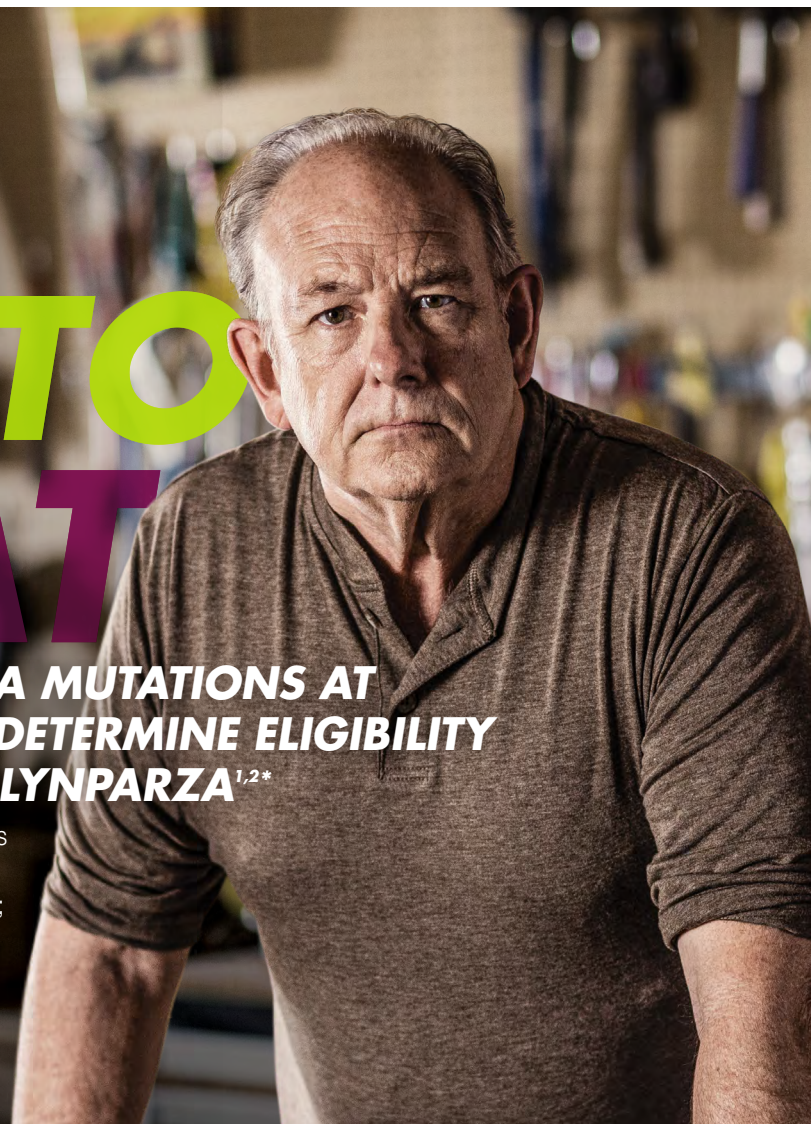
[Abstract](#)



# TEST TO TREAT

**TUMOUR TEST FOR BRCA MUTATIONS AT mCRPC DIAGNOSIS TO DETERMINE ELIGIBILITY FOR LIFE-PROLONGING LYNPARZA<sup>1,2\*</sup>**

\*LYNPARZA prolonged overall survival by 5.7 months vs NHA retreatment in BRCA-mutated mCRPC post-NHA (median 20.1 vs 14.4 months; HR 0.63; 95% CI 0.42, 0.95; p-value not reported)<sup>1</sup>



**The 1st and only PARPi for BRCA-mutated mCRPC<sup>1</sup>**

Find out more about tumour BRCA testing in mCRPC

**Lynparza<sup>®</sup>**  
olaparib  
tablets

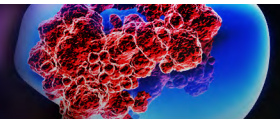
**PBS Listed:** Authority Required. Refer to PBS Schedule for full information.

PLEASE [CLICK HERE](#) TO REVIEW FULL PRODUCT INFORMATION BEFORE PRESCRIBING.  
FURTHER INFORMATION AVAILABLE ON REQUEST FROM ASTRAZENECA ON 1800 805 342.

BRCA: BReast CAncer; CI: confidence interval; HR: hazard ratio; mCRPC: metastatic castration-resistant prostate cancer; NHA: novel hormonal agent; PARPi: poly (ADP-ribose) polymerase inhibitor. "BRCA-mutated" refers to patients with a mutation in BRCA1 or BRCA2. **References:** 1. LYNPARZA<sup>®</sup> (olaparib) Tablets Product Information. 2. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer: NCCN Evidence Blocks.™ Version 4.2023 - September 7, 2023. LYNPARZA<sup>®</sup> is a registered trademark of the AstraZeneca group of companies. Registered user AstraZeneca Pty. Ltd. ABN 54 009 682 311. 66 Talavera Road, Macquarie Park, NSW 2113. www.astrazeneca.com.au. For Medical Information enquiries or to report an adverse event or product quality complaint: Telephone 1800 805 342 or via <https://contactazmedical.astrazeneca.com>.

AU-18205 LYNP0169/EMBC Date of preparation: November 2023.

AstraZeneca



## Intestinal microbiota composition is predictive of radiotherapy-induced acute gastrointestinal toxicity in prostate cancer patients

**Authors:** Iacovacci J et al.

**Summary:** The MicroLearner observational cohort examined the role of intestinal microbiota in the development of radiotherapy-induced GI toxicity in 136 (discovery) and 79 (validation) prostate cancer patients with an average Common Terminology Criteria for Adverse Events grade >1.3. Core bacterial composition suggested a cluster of patients enriched for toxicity, with a toxicity rate of 60%. Internal and external validation cohorts identified a high-risk microbiota composition that predicted risk of toxicity based on relative abundance of *Faecalibacterium*, *Bacteroides*, *Parabacteroides*, *Alistipes*, *Prevotella* and *Phascolarctobacterium*.

**Comment:** Increasing clinical studies suggest that the composition of the colonic microbiome plays a causative role in the development and progression of several inflammatory intestinal conditions. This interesting prospective cohort study investigated the association of faecal bacterial species with the severity of GI toxicity in patients undergoing EBRT in the primary or salvage setting. The risk of toxicity was linked with the relative abundance of specific bacterial genera, suggesting pre-treatment testing could be used to identify patients at higher risk of bowel complications. These patients could then potentially have their microbiomes altered through probiotics or faecal transfer to reduce this risk. Lucky radiation oncologists.

**Reference:** *EBioMedicine* 2024;106:105246

[Abstract](#)

## Long-term outcomes in patients using protocol-directed active surveillance for prostate cancer

**Authors:** Newcomb LF et al.

**Summary:** The North American, multicentre, prospective, protocol-directed, Canary Prostate Active Surveillance Study (PASS) sought to identify long-term oncological outcomes in a cohort of 2155 patients (median age 63 years, 83% White, 90% grade group 1 cancer, median PSA 5.2 ng/mL). After 10 years, incidence of biopsy grade reclassification was 43% (95% CI 40-45) and treatment incidence was 49% (95% CI 47-52), with treatment in 425 patients after confirmatory biopsy (median 1.5 years after diagnosis) and 396 patients after subsequent surveillance biopsies (median 4.6 years after diagnosis); 5-year recurrence rate of 11% (95% CI 7-15) and 8% (95% CI 5-11). Metastatic cancer progression occurred in 21 participants and 3 prostate cancer-related deaths occurred. Estimated 10-year rate of metastasis was 1.4% (95% CI 0.7-2) and rate of prostate cancer-specific mortality was 0.1% (95% CI 0-0.4); overall mortality was 5.1% (95% CI 3.8-6.4).

**Comment:** Medium-term results from the Canary PASS study, a prospective observation cohort study of active surveillance in patients with low- (83%) and intermediate- (17%) risk prostate cancer across 10 sites in North America. The active surveillance protocol consisted of regular PSA tests (every 3-6 months) as well as early confirmatory and interval biopsies every 2 years. The headline result is that almost half the cohort remained progression and treatment free at 10 years, which is useful for patient counselling. The most common indication for treatment was tumour upgrading, which may have been avoided with better sampling at diagnosis, as only half the patients had a prostate MRI and most had limited core, transrectal biopsies. Ten patients developed M1 disease, the majority of whom had disease upgraded on an early re-biopsy suggesting initial misclassification.

**Reference:** *JAMA*. 2024;331(24):2084-2093

[Abstract](#)

## Combining PSMA-PET and PROMISE to re-define disease stage and risk in patients with prostate cancer: A multicentre retrospective study

**Authors:** Karpinski MJ et al.

**Summary:** This multicentre, retrospective study compared the prognostic value of standard clinical nomograms versus PSMA-PET by Prostate Cancer Molecular Imaging Standardized Evaluation (PROMISE) criteria (PPP) quantitative and visual nomograms based on a large prostate cancer dataset including 2414 patients (1110 development dataset, 502 internal validation cohort, 802 external validation cohort), including 901 (37%) patients who had died by data cut-off (median follow-up 52.9 months). Predictors identified for the quantitative PPP nomogram were locoregional lymph node metastases, distant metastases, tumour volume, and tumour mean standardised uptake value. Predictors identified for the visual PPP nomogram were distant metastases and total tumour lesion count. In internal and external validation analyses, C-indices were 0.80 (95% CI 0.77-0.84) and 0.77 (0.75-0.78) for the quantitative PPP nomogram, and 0.78 (0.75-0.82) and 0.77 (0.75-0.78) for the visual PPP nomogram. The quantitative PPP nomogram was superior to a STARCAP (International Staging Collaboration for Cancer of the Prostate) risk score for patients at initial staging (AUC 0.73 vs 0.54;  $p = 0.018$ ), EAU risk score at biochemical recurrence (AUC 0.69 vs 0.52;  $p < 0.0001$ ), and NCCN pan-stage risk score (AUC 0.81 vs 0.74;  $p < 0.0001$ ) for OS prediction, but did not differ from the Gafita et al., nomogram for mHSPC (AUC 0.76 vs 0.72) and mCRPC (AUC 0.67 vs 0.75). The visual nomogram was superior to EAU risk score at biochemical recurrence (AUC 0.64 vs 0.52;  $p = 0.0004$ ) and NCCN pan-stage risk score (AUC 0.79 vs 0.73;  $p < 0.0001$ ), but was no different to the STARCAP risk score for initial staging (AUC 0.56 vs 0.53) and the Gafita et al., nomogram for mHSPC (AUC 0.74 vs 0.72) and mCRPC (0.71 vs 0.75).

**Comment:** This German study proposes a prognostic model for OS in patients with prostate cancer across the disease spectrum based on PSMA-metrics, both qualitative and quantitative, and claims to outperform existing clinical calculators. The study concept is quite elegant, but the inclusion of all disease stages skews the relative importance of some variables when both early disease (where OS is very high) and mCRPC (where OS is much lower) are included. An example of this is the presence of a positive extra-pelvic lymph node metastasis, which has 5-6-fold the weight in the nomogram for predicting death than bony or visceral metastases! The comparisons are methodologically weak, with data required for the other calculators missing in half of all patients, and use an endpoint for which they were not developed. Bit of a mess really.

**Reference:** *Lancet Oncol.* 2024;25(9):1188-1201

[Abstract](#)

## Earn CPD

**Royal Australasian College of Physicians (RACP)** MyCPD participants can claim the time spent reading and evaluating research reviews as CPD in the online [MyCPD program](#). Please contact [MyCPD@racp.edu.au](mailto:MyCPD@racp.edu.au) for any assistance.

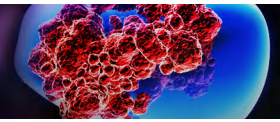
**Royal Australian & New Zealand College of Radiologists (RANZCR)** members can claim reading related to their practice as a CPD activity under the category 'journal reading and web based no certificate \*reflection required'. [More info.](#)

## Kindly Supported by

Australian Prostate Centre 

 ANZUP  
Cancer Trials Group Limited

RESEARCH REVIEW™ Australia's Leader in Specialist Publications



## Artificial intelligence and radiologists in prostate cancer detection on MRI (PI-CAI): An international, paired, non-inferiority, confirmatory study

**Authors:** Saha A et al.

**Summary:** This multinational, paired, non-inferiority, confirmatory study compared the performance of artificial intelligence (AI) systems with 62 experienced radiologists for detection of clinically significant prostate cancer on MRI based on 9207 training cases and 1000 test cases (2440 cases with histologically confirmed Gleason grade group  $\geq 2$  tumours). In 400 paired MRI test cases, the AI system had a non-inferior (margin of 0.05) and superior AUC of 0.91 (95% CI 0.87-0.94;  $p < 0.0001$ ) versus the radiologists using Prostate Imaging-Reporting and Data System version 2.1 (PI-RADS 2.1; AUC 0.86; 0.83-0.89). At the mean PI-RADS  $\geq 3$  operating point, AI identified 6.8% more Gleason grade group  $\geq 2$  cases at the same specificity (57.7%; 95% CI 51.6-63.3), and 50.4% fewer false-positive results (20.0% fewer cases) with Gleason grade group 1 tumours at the same sensitivity (89.4%; 95% CI 85.3-92.9). In 1000 testing cases comparing AI with radiology readings during multidisciplinary practice, non-inferiority was not confirmed, because the AI system had lower specificity (68.9%; 95% CI 65.3-72.4 vs 69.0%; 95% CI 65.5-72.5) at the same sensitivity (96.1%; 95% CI 94.0-98.2) as the PI-RADS  $\geq 3$  operating point.

**Comment:** The robots are coming for all our jobs, but it looks like radiology will be the first to fall. In this study the authors trained an AI algorithm to detect grade group  $\geq 2$  prostate cancer using data from over 10,000 prostate biparametric MRIs. They then compared its performance to the pooled results of 62 experienced radiologists using the PI-RADS 2.1 system, using both biparametric and multiparametric sequences. Overall, the AI algorithm was superior to the pooled results of the human readers, with greater sensitivity across all PI-RADS groups with the same specificity and was non-inferior to calls made in multidisciplinary routine practice. Although it is unlikely to completely replace human oversight, given the speed of output (5-10 mins) it could certainly speed up reporting.

**Reference:** *Lancet Oncol.* 2024;25(7):879-887

[Abstract](#)

## High-dose vitamin D to attenuate bone loss in patients with prostate cancer on androgen deprivation therapy: A phase 2 RCT

**Authors:** Peppone LJ et al.

**Summary:** This 24-week, randomised, placebo-controlled, phase II trial assessed the effect of high-dose weekly vitamin D (50,000 IU/week) on ADT-induced bone loss assessed by dual-energy x-ray absorptiometry (DEXA) in men with prostate cancer receiving ADT (all patients received 600 IU/day vitamin D and 1000 mg/day calcium). High-dose recipients ( $n = 29$ ) lost 1.5% bone mineral density (BMD) at the total hip versus 4.1% ( $p = 0.03$ ) in low-dose recipients ( $n = 30$ ) and 1.7% BMD at the femoral neck versus 4.4% ( $p = 0.06$ ). Stratified analyses suggested that among those with baseline 25-hydroxyvitamin D level  $< 27$  ng/mL, the total hip BMD loss was 2.3% versus 7.1% ( $p < 0.01$ ). High-dose recipients had changes in parathyroid hormone ( $p < 0.01$ ), osteoprotegerin ( $p < 0.01$ ), and N-terminal ( $p < 0.01$ ) and C-terminal ( $p < 0.01$ ) telopeptide of type 1 collagen.

**Comment:** Patients on ADT are at risk of accelerated bone loss and routinely advised to take calcium and vitamin D supplements as well as engaging in an exercise program. In this phase II study, patients on ADT for less than 6 months were randomised to either high-dose vitamin D combined with standard daily supplementation or standard daily supplementation plus placebo. After 24 weeks, patients randomised to high-dose treatment showed significantly improved preservation of BMD on DEXA scan, particularly in patients with low baseline vitamin D. This certainly warrants longer-term study, as it may ultimately prevent the development of osteopenia and the need for bisphosphonates/RANKL inhibitors with all their attendant side effects.

**Reference:** *Cancer* 2024;130(14):2538-2551

[Abstract](#)



## Prostate Cancer Research Review™

### Independent commentary by Professor Niall Corcoran.

Professor Niall Corcoran is a urological surgeon and translational scientist based in Melbourne. He is Head of the Urology Unit at Western Health and a visiting surgeon at Royal Melbourne and Frankston Hospitals. His group in the University of Melbourne Centre for Cancer Research investigates molecular drivers of prostate cancer metastases and treatment resistance.

cpdhome | AMA

CERTIFIED  
LEARNING PROVIDER  
2024

Follow us at:



### Earn CPD

**Nursing and Midwifery Board of Australia (NMBA)** Journal reading and watching videos (including Research Reviews) may be considered a self-directed activity set out in the [NMBA Registration Standard: Continuing Professional Development](#). One hour of active learning will equal one hour of CPD. Details at [NMBA CPD page](#).

### Earn CPD

**CPD Home.** Subscribers can claim the time spent reading and evaluating research reviews as an Educational Activity: Professional Reading in the CPD Tracker. Please [Contact Us](#) for support.

**Australian Research Review subscribers can claim CPD/CME points** for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our [CPD page](#).

Research Reviews are prepared with an independent commentary from relevant specialists. To become a reviewer please email [geoff@researchreview.com.au](mailto:geoff@researchreview.com.au).

Research Review Australia Pty Ltd is an independent Australian publisher. Research Review receives funding from a variety of sources including Government depts., health product companies, insurers and other organisations with an interest in health. Journal content is created independently of sponsor companies with assistance from leading local specialists. **Privacy Policy:** Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time. **Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Research Review publications are intended for Australian health professionals.

