

Review

The PSA test for prostate cancer screening: an abridged Cochrane review

Juan V. A. Franco¹ , Eu Chang Hwang² , Jae Hung Jung^{3,4}, Octavio Vaimberg⁵ , Dragan Ilic⁶ , Anne Cleves⁷ and Philipp Dahm^{8,9} 

¹Cochrane Evidence Synthesis Unit Germany/UK – Düsseldorf Subunit, Centre for Health and Society, Institute of General Practice, Heinrich Heine University Düsseldorf, Düsseldorf, Germany, ²Department of Urology, Chonnam National University Medical School, Chonnam National University Hwasun Hospital, Hwasun, ³Department of Urology, Yonsei University Wonju College of Medicine, Wonju, ⁴Center of Evidence-Based Medicine, Institute of Convergence Science, Yonsei University, Seoul, South Korea, ⁵School of Medicine, Universidad del Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, ⁶Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia, ⁷Velindre NHS Trust, Library Services, Cardiff University, Cardiff, UK, ⁸Urology Section, Minneapolis VA Health Care System, and ⁹Department of Urology, University of Minnesota, Minneapolis, MN, USA

J.V.A.F. and E.C.H. joint first authors.

Objectives

To assess the effects of prostate cancer screening compared to no screening in men with no prior diagnosis of prostate cancer.

Methods

This systematic review represents an update of a prior Cochrane review from 2013, searching multiple databases up to November 2025. We included randomised controlled trials (RCTs) of prostate cancer screening vs no screening. We used standard Cochrane methods, including rating the certainty of the evidence following a Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.

Results

Six RCTs (789 086 participants; follow-up 3.2–23 years) were included: five evaluated prostate-specific antigen (PSA)-alone screening; one evaluated PSA combined with a kallikrein panel and magnetic resonance imaging (MRI) (ProScreen). Results are based on the certainty of evidence for each outcome and are therefore mainly derived from a sensitivity analysis by risk of bias, using the European Randomised Study of Screening for Prostate Cancer (ERSPC) trial: screening likely results in a reduction in prostate cancer-specific mortality (sensitivity analysis from ERSPC: risk ratio [RR] 0.87, 95% confidence interval [CI] 0.80–0.95; one study, 162 236 participants; moderate-certainty evidence; minimal clinically important difference [MCID]: one per 1000 participants). Assuming a baseline risk of 16 prostate-cancer-related deaths per 1000, this corresponds to two fewer (95% CI three fewer to one fewer) per 1000. Based on the analysis that included all eligible trials, screening may reduce overall mortality, although the CI includes the possibility of little to no effect (RR 0.99, 95% CI 0.97–1.00; $I^2 = 22\%$; four studies, 675 121 participants; low-certainty evidence; MCID: one per 1000 participants). Assuming a baseline risk of 491 deaths from any cause per 1000, this corresponds to five fewer (95% CI 15 fewer to 0 fewer) per 1000. Screening may result in little to no difference in adverse events (RR 1.32, 95% CI 0.48–3.65; low certainty) or quality of life. In the ProScreen trial (60 745 participants, 3.2-year follow-up), combined screening probably has little to no effect on overall detection (RR 1.85, 95% CI 1.56–2.19; moderate certainty), localised detection (RR 1.88, 95% CI 1.55–2.27; moderate certainty), or advanced detection (RR 1.78, 95% CI 1.19–2.66; moderate certainty). Mortality data are not yet mature.

Conclusions

Screening likely reduces prostate cancer-specific mortality and may reduce overall mortality. It may have little to no effect on adverse events (as measured by intervention-related mortality). Study limitations, inconsistency, and imprecision reduced our confidence in the effect estimates. Interpretation of these findings is highly sensitive to the choice of MCID. Emerging

alternatives, such as screening with a kallikrein panel and MRI, may have little to no effect on diagnoses of prostate cancer, but the results on mortality are not yet known.

Keywords

prostate-specific antigen (PSA), systematic review, screening, Grading of Recommendations, Assessment, Development, and Evaluation (GRADE), Meta-analysis

Introduction

Prostate cancer is one of the most common malignancies globally. According to the International Agency for Research on Cancer's GLOBOCAN database, ~1.5 million new cases and 396 000 deaths occurred worldwide in 2022, making it the second most commonly diagnosed cancer and the fifth leading cause of cancer death among men [1]. Incidence and mortality vary substantially by region: Northern Europe has the highest estimated incidence (82.8 per 100 000 men) and Southern Africa the highest mortality (29.7 per 100 000 men), while South-Central Asia has the lowest rates for both [2].

Established risk factors include increasing age (most diagnoses occur in men aged >50 years), first-degree family history [3], and ethnicity, with Black men at higher risk [4,5]. Mutations in *BRCA* genes, *HOXB13 G84E*, *ATM*, and common single-nucleotide polymorphisms across multiple chromosomal regions are also increasingly recognised [6–8]. When combined into a polygenic risk score, these genetic variants may help identify men at higher risk who could benefit from early detection [9].

Prostate-specific antigen (PSA) is a serine protease secreted exclusively by prostatic epithelial cells; small quantities are measurable in blood serum. Elevated or rapidly rising PSA levels prompt further diagnostic evaluation, which now commonly includes multiparametric MRI to stratify risk and guide biopsy [10,11]. PSA testing is widely used to detect prostate cancer at an asymptomatic, earlier stage, with the goal of providing treatment with curative intent and reducing mortality [12]. However, PSA testing also carries potential harms: psychological stress, false-positive results, invasive follow-up tests and their complications (e.g., sepsis from biopsy), overdiagnosis of indolent disease, and downstream treatment-related morbidity including urinary, bowel, and erectile dysfunction [13].

Several randomised trials have evaluated PSA-based screening vs no screening, with conflicting results [14–19], and major guideline bodies—including the United States Preventive Services Task Force (USPSTF) [20], American Cancer Society [21], AUA [22], the UK's National Institute for Health and Care Excellence [23], and the European Association of Urology (EAU) [4] – hold differing recommendations. The 2013 version of this Cochrane review, which pooled five trials with 341 342 participants, found no significant reduction in

prostate cancer-specific or all-cause mortality from PSA screening [13]. Since then, extended follow-up data have become available from several included trials [16–18], and two new trials have been published [19,24], warranting this update. The objective of this review was to assess the effects of prostate cancer screening compared to no screening in men with no prior diagnosis of prostate cancer.

Methods

We conducted and reported this systematic review according to the Methodological Expectations of Cochrane Intervention Reviews (MECIR) standards and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 [25–27]. The underlying protocol was published in 2004 [28].

Eligibility Criteria

We included randomised controlled trials (RCTs) and cluster-randomised trials comparing PSA-based prostate cancer screening (PSA alone, or PSA combined with DRE or adjuvant markers such as kallikrein) to no screening. We excluded crossover trials, pseudo-randomised trials (including the Norrköping study [15] excluded for its pseudo-RCT design), and studies enrolling men with a prior prostate cancer diagnosis. There were no language or publication-status restrictions. All men enrolled in prostate cancer screening studies were eligible, with no exclusions based on age, ethnicity, or LUTS.

Critical outcomes were prostate cancer-specific mortality and overall mortality. Important outcomes were adverse events (mortality due to diagnostic biopsy or prostate cancer treatment), quality of life, prostate cancer diagnosis overall, and prostate cancer diagnosis by stage (localised [Stage I–II], advanced [Stage III–IV], and metastatic). Minimal clinically important differences (MCIDs) were set at: one per 1000 for prostate cancer-specific and overall mortality; 10 per 1000 for overall and localised or advanced prostate cancer diagnosis; five per 1000 for metastatic diagnosis; and 0.09–0.10 on the Short form six dimensions (SF-6D) for quality of life.

Search Methods

We searched the Medical Literature Analysis and Retrieval System Online (MEDLINE), the Excerpta Medica dataBASE (EMBASE), Cochrane Central Register of Controlled Trials

(CENTRAL), and additional databases and trial registers from inception to 19 November 2025, with no language restrictions. Full search strategies are reported in Appendix S1. We also searched reference lists of included trials, conference proceedings of the AUA, EAU, and American Society of Clinical Oncology (ASCO) (2014–2018; more recent years captured electronically), and contacted trial authors to identify any additional relevant studies.

Study Selection and Data Extraction

Two authors (E.C.H. and J.F.) independently screened all records using Covidence; discrepancies were resolved by a third author (P.D.). Two of five authors (D.I., J.F., E.C.H., O.V., J.H.J.) independently extracted data using a dedicated form. We report study characteristics in Table 1.

Risk of Bias Assessment

Two authors (J.H.J., E.C.H., or P.D.) independently assessed risk of bias using the Cochrane Collaboration's original tool [29], evaluating sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, adherence, and contamination. Disagreements were resolved by consensus or by a third author (D.I.).

Statistical Analysis and Synthesis

We pooled data using a random-effects model with the Mantel–Haenszel method for dichotomous outcomes and the inverse-variance method for continuous outcomes, using Review Manager (RevMan). We report outcomes as risk ratios (RRs) or incidence rate ratios (IRRs) with 95% CIs. We quantified heterogeneity using the I^2 statistic. We conducted a prespecified sensitivity analysis restricted to the European Randomised Study of Screening for Prostate Cancer (ERSPC) trial (International Standard Randomised Controlled Trial Number: ISRCTN49127736), the sole trial assessed as having the lowest risk of bias. We also analysed the ProScreen trial (ClinicalTrials.gov identifier: NCT03423303) separately because it evaluated a combined PSA, kallikrein panel, and MRI screening strategy not directly comparable to PSA alone. Subgroup and sensitivity analyses, handling of missing data, and heterogeneity exploration followed Cochrane Handbook guidance [30]. We were unable to construct funnel plots due to the small number of studies per analysis.

Certainty of Evidence

We assessed the certainty of evidence for each outcome using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach, rating evidence as high, moderate, low, or very low using GRADEpro Guideline

Development Tool (GDT) software. We applied a minimally contextualised approach to imprecision using the prespecified MCIDs above.

Results

Of 16 260 citations identified in our most recent search (19 November 2025), we selected 226 for full-text review. The updated review includes six RCTs: ERSPC (including individual sites), the Prostate, Lung, Colorectal, and Ovarian cancer screening trial (PLCO), Quebec, Stockholm, Cluster randomised trial of PSA testing for Prostate cancer (CAP), and ProScreen—reported across 193 publications (PRISMA flow diagram, Fig. 1). The six RCTs randomised a total of 789 086 participants. In the meta-analyses, the five trials comparing PSA-alone screening to no screening contributed 721 612 participants, and the ProScreen trial, which evaluated a combined PSA, kallikrein panel, and MRI strategy, contributed 60 745 participants. Follow-up ranged from 11 to 23 years across trials. Participants were predominantly men aged 45–74 years from European and North American populations. Two trials are ongoing (GÖTEBORG-2 2022 [ISRCTN94604465] [31]; China Randomized Study of Screening for Prostate Cancer [ChiCTR2500102254] [32]).

The effects of PSA-based screening compared to no screening are summarised in Table 2 (PSA-based screening) and Table 3 (ProScreen). Table 2 is a selected-estimates summary: for each outcome it presents the estimate with the higher GRADE certainty from either the primary all-studies analysis or the ERSPC sensitivity analysis (see the Table 2 footnote for the selection rule). Both analyses are reported in full below.

Risk of Bias

The results of our risk of bias assessment are summarised in Fig. 2. Low adherence in the CAP, ERSPC, PLCO, and Quebec studies and control-arm contamination through opportunistic PSA testing in several trials were notable issues. The ERSPC trial was judged as having an overall lower risk of bias.

Screening Based on PSA (Alone) Versus no Screening — All Studies

Prostate cancer-specific mortality: screening may reduce prostate cancer-specific mortality (RR 0.91, 95% CI 0.85–0.99; five studies, 721 607 participants; low-certainty evidence; MCID one per 1000).

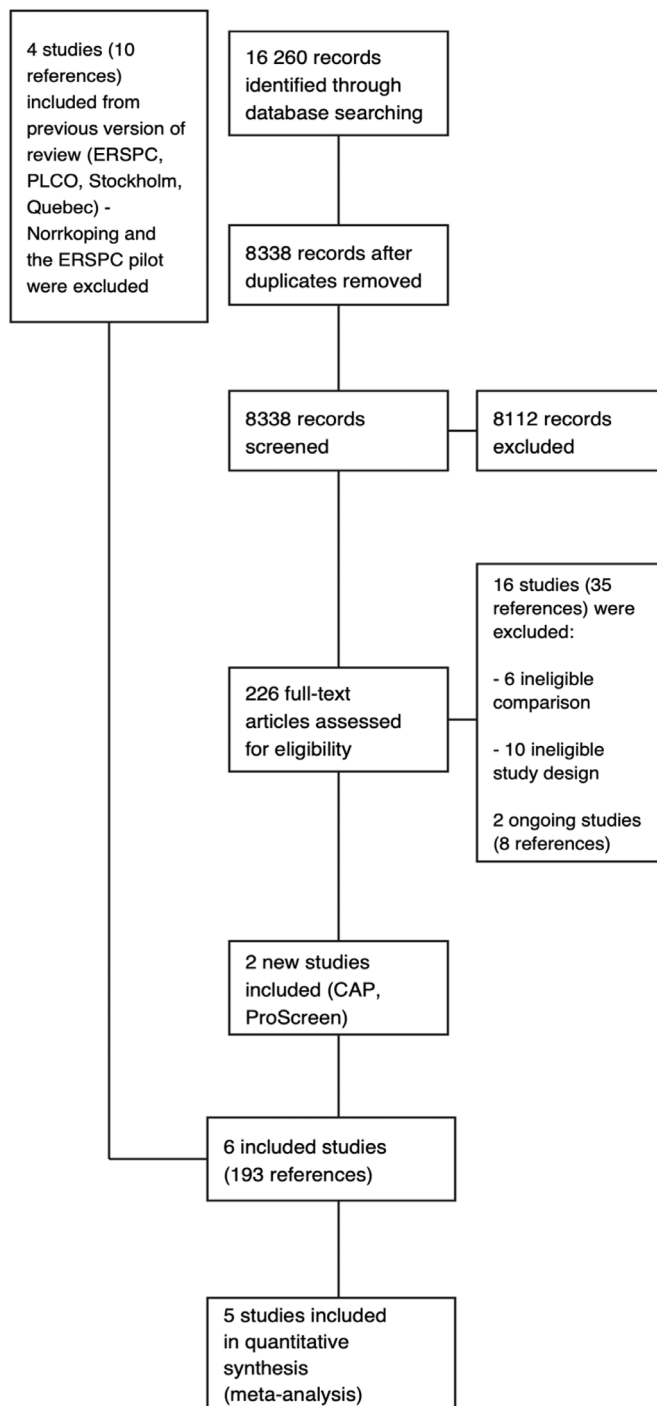
Overall mortality: screening may reduce overall mortality, although the CI includes the possibility of little to no effect (RR 0.99, 95% CI 0.97–1.00; four studies, 675 121 participants; low-certainty evidence; MCID one per 1000).

Table 1 Overview of studies included in synthesis (study characteristics, intervention, and comparisons).

Study name	Trial period (year to year)	Setting/country	Description of participants	Intervention(s) and comparator(s)	Duration of intervention (duration of follow-up), years	Age, years, median	Outcomes in the summary of findings tables
CAP	2002–2021	UK	All men aged 50–69 years in each of the randomised primary care practices	Screening	15	58.5	PCa mortality, overall mortality, adverse events, PCa diagnosis, localised and advanced PCa diagnosis
ERSPC	1993–	Multicentre across: Belgium, Finland, France, Italy, the Netherlands, Spain, Sweden, Switzerland (Portugal withdrew from the study in October 2000)	Men aged 50–74 years from participating sites	No screening Screening	23	58.6 60.2 (core group)	PCa mortality, overall mortality, PCa diagnosis, localised and advanced PCa diagnosis, metastatic PCa diagnosis
ERSPC (Antwerp) Belgium	1992–	Belgium	Men aged 55–74 years	No screening Screening	13	60.2 (core group) 63.0	
ERSPC Finland	1996–	Finland	Men aged 55–67 years without a previous diagnosis of PCa	No screening Screening	12	63.0 58.7	
ERSPC France	2000– (Tarn); 2003– (Herault)	France	Men aged 50–74 years	No screening Screening	7.5 and 6.4	58.7 61.7 (Tarn) 62.6 (Herault)	
ERSPC Italy	1996–	Italy	Men aged 55–70 years	No screening Screening		61.7 (Tarn) 62.6 (Herault)	
ERSPC (Rotterdam) The Netherlands	1993–	The Netherlands	Men aged 54–74 years	Screening	12.6	61.8	
ERSPC Spain	1996–	Spain	Men aged 45–70 years with a life expectancy >10 years	No screening Screening	13	61.8 63.2	
ERSPC (Göteborg) Sweden	1994–	Sweden	Men aged 50–65 years without a current diagnosis of PCa	No screening Screening	21.1	63.2 56.9	
ERSPC (Aargau) Switzerland	1998–	Switzerland	Men aged 55–70 years	No screening Screening	18	57.1 56.4	
Stockholm	1988–2008	Sweden	Men aged 55–70 years without a previous history of PCa	No screening Screening	12.2	56.4 60.5	
Quebec	1988–2004	Canada	Men aged 45–80 years	No screening Screening	20	60.7 62.4	PCa mortality, overall mortality, PCa diagnosis
PLCO	1993–	USA	Men aged 55–74 years	No screening Screening	11	62.5 NR	PCa mortality
ProScreen	2018–	Finland	Men aged 50–63 years, without a previous diagnosis of PCa	No screening Screening*	15	NR NR (reported as age category)	PCa mortality, overall mortality, PCa diagnosis, localised and advanced PCa diagnosis, metastatic PCa diagnosis
				No screening	3.2 [†]	NR (reported as age category) 57.3	PCa diagnosis in general, localised and advanced

NR, not reported; PCa, prostate cancer. *Screening using a stepwise approach with a kallikrein panel and MRI for those with elevated PSA test.

[†]Expected follow-up: 15 years.

Fig. 1 The PRISMA flow diagram.

Adverse events (mortality due to diagnostic biopsy or prostate cancer treatment): screening may result in little to no difference in adverse events (RR 1.32, 95% CI 0.48–3.65; one study, 408 721 participants; low-certainty evidence; MCID one per 1000).

Quality of life (SF-6D, 0–1, higher = better): screening may result in little to no difference in quality of life (one study,

969 participants; low-certainty evidence; MCID 0.09–0.10). No effect estimate was calculable.

Prostate cancer diagnosis overall: screening may increase prostate cancer diagnoses (RR 1.13, 95% CI 1.02–1.25; four studies, 675 121 participants; low-certainty evidence; MCID 10 per 1000).

Localised (Stage I–II) prostate cancer diagnosis: screening may increase localised prostate cancer diagnoses, although the CI includes the possibility of little to no effect and the evidence is very uncertain (RR 1.27, 95% CI 0.84–1.92; three studies, 647 640 participants; very low-certainty evidence; MCID 10 per 1000).

Advanced (Stage III–IV) prostate cancer diagnosis: screening likely results in little to no difference in advanced prostate cancer diagnoses (RR 0.89, 95% CI 0.88–0.91; three studies, 647 640 participants; moderate-certainty evidence; MCID 10 per 1000).

Metastatic prostate cancer diagnosis: screening may result in little to no difference in metastatic prostate cancer diagnoses (RR 0.73, 95% CI 0.56–0.94; two studies, 238 919 participants; low-certainty evidence; MCID five per 1000).

Screening Based on PSA (Alone) – Sensitivity Analysis (ERSPC Trial, 23-Year Follow-Up)

Prostate cancer-specific mortality: screening likely reduces prostate cancer-specific mortality (RR 0.87, 95% CI 0.80–0.95; one study, 162 236 participants; moderate-certainty evidence; MCID one per 1000).

Overall mortality: the effect of screening on overall mortality is very uncertain (RR 1.00, 95% CI 0.98–1.02; one study, 162 236 participants; very low-certainty evidence; MCID one per 1000).

Quality of life (SF-6D): screening may result in little to no difference in quality of life (one study, 969 participants; low-certainty evidence; MCID 0.09–0.10).

Prostate cancer diagnosis overall: screening likely increases prostate cancer diagnoses (RR 1.30, 95% CI 1.27–1.34; one study, 162 241 participants; moderate-certainty evidence; MCID 10 per 1000).

Localised (Stage I–II) prostate cancer diagnosis: screening likely increases localised prostate cancer diagnoses (RR 1.53, 95% CI 1.48–1.59; one study, 162 236 participants; moderate-certainty evidence; MCID 10 per 1000).

Advanced (Stage III–IV) prostate cancer diagnosis: screening likely reduces advanced prostate cancer diagnoses (RR 0.90, 95% CI 0.85–0.95; one study, 162 236 participants; moderate-certainty evidence; MCID 10 per 1000).

Metastatic prostate cancer diagnosis: screening may reduce metastatic prostate cancer diagnoses (RR 0.65, 95% CI 0.59–0.71; one study, 162 236 participants; low-certainty evidence; MCID five per 1000).

Table 2 Summary of findings: selected estimates for prostate-specific antigen (PSA)-based screening compared to no screening for men at risk of prostate cancer.

Outcomes	Anticipated absolute effects ^a (95% CI)		RR (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no screening	Risk with PSA-based screening				
Prostate cancer-specific mortality (minimal clinically important difference (MCID) one per 1000) follow-up: 23 years [†]	16 per 1000 [‡]	14 per 1000 (13–15)	RR 0.87 (0.80–0.95)	162 236 (1 RCT)	Moderate [§]	Screening likely reduces prostate cancer-specific mortality. [Sensitivity analysis]
Overall mortality (MCID one per 1000) follow-up: range 15 years to 23 years	491 per 1000 [‡]	486 per 1000 (476–491)	RR 0.99 (0.97–1.00)	675 121 (4 RCTs)	Low ^{¶,***}	Screening may reduce overall mortality although the confidence interval includes the possibility of little to no effect. [Primary analysis]
Adverse events (mortality due to diagnostic biopsy or prostate cancer treatment) (MCID one per 1000) assessed with: mortality due to diagnostic biopsy or prostate cancer treatment	3 per 100 000 ^{††}	4 per 100 000 (1–11)	RR 1.32 (0.48–3.65)	408 721 (1 RCT)	Low ^{‡‡,§§}	Screening may result in little to no difference in adverse events. [Primary analysis]
Quality of life (MCID 0.09–0.10) assessed with: SF-6D (range 0–1, higher values indicate higher quality of life) follow-up: 5 years	—	—	—	969 (1 RCT)	Low ^{¶¶}	Screening may result in little to no difference in quality of life. [Primary analysis]
Prostate cancer diagnosis (MCID 10 per 1000) assessed with: biopsy follow-up: 23 years ^{***}	120 per 1000 [‡]	156 per 1000 (152–161)	RR 1.30 (1.27–1.34)	162 241 (1 RCT)	Moderate [§]	Screening likely results in an increase in prostate cancer diagnoses. [Sensitivity analysis]
Localised (Stage I and II) prostate cancer diagnosis (MCID 10 per 1000) assessed with: biopsy, CT, or MRI follow-up: 23 years ^{***}	64 per 1000 [‡]	98 per 1000 (95–102)	RR 1.53 (1.48–1.59)	162 236 (1 RCT)	Moderate [§]	Screening likely results in an increase in localised (stage I and II) prostate cancer diagnoses. [Sensitivity analysis]
Advanced (Stage III and IV) prostate cancer diagnosis (MCID 10 per 1000) assessed with: biopsy, CT, or MRI follow-up: range 15–23 years	31 per 1000 [‡]	28 per 1000 (27–28)	RR 0.89 (0.88–0.91)	647 640 (3 RCTs)	Moderate [§]	Screening likely results in little to no difference in advanced (stage III and IV) prostate cancer diagnoses. [Primary analysis]
Metastatic prostate cancer diagnosis (MCID five per 1000) assessed with: biopsy, CT, or MRI follow-up: range 16–23 years	13 per 1000 [‡]	9 per 1000 (7–12)	RR 0.73 (0.56–0.94)	238 919 (2 RCTs)	Low ^{¶,†††,‡‡‡}	Screening may result in little to no difference in metastatic prostate cancer diagnoses. [Primary analysis]

GRADE Working Group grades of evidence. High certainty: we are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: we are moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: our confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect. Very low certainty: we have very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of the effect. For each outcome, Table 2 shows the estimate with the higher GRADE certainty, selected from either the primary all-studies analysis or the ERSPC sensitivity analysis; where GRADE certainty was equal, the primary all-studies analysis was retained. The source analysis for each outcome is indicated in the Comments column. ^aThe risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). [†]The MCID: absolute change of 0.1% or one per 1000 participants. [‡]The control rate was extracted from the 23-year follow-up of the ERSPC trial. [§]Downgraded one level due to high risk of bias: although the ERSPC study is at lower risk of bias, which was considered when conducting this sensitivity analysis, it has an overall high risk of bias. [¶]Downgraded one level due to high risk of bias: all studies had an overall high risk of bias. ^{**}Downgraded one level due to imprecision: the confidence interval crosses the MCID (one per 1000). ^{††}The control rate was extracted from the 15-year follow-up of the CAP trial. ^{‡‡}Downgraded one level due to high risk of bias: the included study was at an overall high risk of bias. ^{§§}Downgraded one level due to indirectness: these data represent only part of the spectrum of possible adverse events (including non-fatal sepsis, among others). ^{¶¶}Downgraded two levels due to study limitations: lack of allocation concealment, attrition bias, and the exclusion of men with a diagnosis of prostate cancer from this analysis. ^{***}The MCID: absolute change of 1% or 10 per 1000 participants. ^{†††}Downgraded one level for inconsistency (high I^2 value reflects clinically important heterogeneity). ^{‡‡‡}We did not downgrade further for imprecision, as we assumed the apparent imprecision resulted from inconsistency, for which we downgraded the evidence.

Table 3 Summary of findings for screening (with PSA, kallikrein, and MRI) compared to no screening for men at risk of prostate cancer.

Outcomes	Anticipated absolute effects* (95% CI)		RR (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no screening	Risk with screening (with PSA, kallikrein, and MRI)				
Prostate cancer diagnosis (MCID 10 per 1000) assessed with: biopsy and MRI follow-up: median 3.2 years	8 per 1000	14 per 1000 (12–17)	RR 1.85 (1.56–2.19)	60 745 (1 RCT)	Moderate ⁺	Screening likely results in little to no difference in prostate cancer diagnoses
Localised prostate cancer diagnosis (T1–T2 N0/Nx M0/Mx) (MCID 10 per 1000) assessed with: biopsy and MRI follow-up: 3.2 years	6 per 1000	11 per 1000 (9–14)	RR 1.88 (1.55–2.27)	60 745 (1 RCT)	Moderate ⁺	Screening likely results in little to no difference in localised prostate cancer diagnoses
Advanced prostate cancer diagnosis (T3–T4 N1 M0/Mx, TX NX M1) (MCID 10 per 1000) assessed with: biopsy and MRI follow-up: 3.2 years	1 per 1000	3 per 1000 (2–4)	RR 1.78 (1.19–2.66)	60 745 (1 RCT)	Moderate ⁺	Screening likely results in little to no difference in advanced prostate cancer diagnoses

GRADE Working Group grades of evidence. High certainty: we are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: we are moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: our confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect. Very low certainty: we have very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of the effect. *The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). ⁺Downgraded one level due to risk of bias: the included study was at a high risk of bias.

Screening Based on PSA, Kallikrein Panel, and MRI Versus no Screening (ProScreen)

Based on moderate-certainty evidence from the ProScreen RCT (60 745 participants; median follow-up of 3.2 years), screening using PSA, a kallikrein panel, and MRI probably has little to no effect on the overall detection of prostate cancer (RR 1.85, 95% CI 1.56–2.19; Table 3). Absolute rates were eight per 1000 in the control group vs 14 per 1000 in the screening group, representing a difference below the predefined clinical threshold of 10 per 1000. Similarly, screening had little to no effect on the detection of localised disease (RR 1.88, 95% CI 1.55–2.27) or advanced stages (RR 1.78, 95% CI 1.19–2.66; Table 3). Mortality and long-term adverse events have not yet been reported.

Overall, certainty of evidence ranged from moderate to very low. The most common reasons for downgrading were study limitations (predominantly performance bias and inadequate allocation concealment), imprecision, and inconsistency across trials.

Discussion

This updated Cochrane review synthesises evidence from six RCTs randomising 789 086 participants, five comparing

PSA-based screening to no screening (721 612 participants in the analyses; up to 23 years of follow-up) and one comparing a combined PSA, kallikrein panel, and MRI strategy to no screening (60 745 participants; ProScreen) and represents the most comprehensive body of evidence on prostate cancer screening to date.

Summary of Main Results

Across all five PSA-screening RCTs, low-certainty evidence suggests that PSA-based screening may reduce prostate cancer-specific mortality (RR 0.91) and may marginally reduce overall mortality (RR 0.99), although the CI for overall mortality includes no effect. The sensitivity analysis restricted to the ERSPC RCT, the only trial assessed as having lower risk of bias, with 23 years of follow-up, strengthens confidence in the mortality benefit: screening probably reduces prostate cancer-specific mortality (RR 0.87, moderate certainty). At the same time, screening increases the detection of prostate cancer overall and of localised disease, while the incidence of advanced disease appears reduced and metastatic diagnosis may also be reduced with longer follow-up. Adverse events and quality of life appear largely unaffected, although evidence is limited to single studies and of low certainty. The emerging ProScreen strategy (PSA, kallikrein, and MRI)

Fig. 2 Risk of bias summary: review authors' judgements about each risk of bias item for each included trial (blank cells indicate that the trial did not measure that particular outcome).

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias): Subjective outcomes	Blinding of outcome assessment (detection bias): Objective outcomes	Incomplete outcome data (attrition bias): Prostate cancer-specific mortality	Incomplete outcome data (attrition bias): Overall mortality	Incomplete outcome data (attrition bias): Adverse events (Mortality due to diagnostic biopsy or prostate cancer treatment)	Incomplete outcome data (attrition bias): Quality of life	Incomplete outcome data (attrition bias): Prostate cancer diagnosis	Incomplete outcome data (attrition bias): Localized (stage I and stage II) prostate cancer diagnosis	Incomplete outcome data (attrition bias): Advanced (stage III and IV) prostate cancer diagnosis	Incomplete outcome data (attrition bias): Metastatic prostate cancer diagnosis	Selective reporting (reporting bias)	Adherence	Contamination	Other bias
CAP	+	-	+	+	+	+	+	?		+	+	+		+	-	-	+
ERSPC	+	+	-	+	+	+	+			+	?	?	+	+	-	?	-
ERSPC (Aargau) Switzerland	+	+	-	+	+	+	+			+	+	+		+	+	?	-
ERSPC (Antwerp) Belgium	?	?	-	+	+	?	?			+	-	-		+	+	?	-
ERSPC (Göteborg) Sweden	+	+	-	+	+	+	+			+	+	+		+	?	?	-
ERSPC (Rotterdam) The Netherlands	?	?	-	+	+	?	?			+	+	+		+	+	-	-
ERSPC Finland	+	+	-	+	+	+	+	-		+	+	+		+	?	-	+
ERSPC France	?	?	-	+	+	?	?			+	-	-		+	-	-	+
ERSPC Italy	?	?	-	+	+	+	+				-	-		+	?	-	-
ERSPC Spain	+	+	-	+	+	+	+			+	-	-		+	+	-	-
PLCO	+	+	-	+	+	+	+			+	+	+	+	+	-	-	-
ProScreen	+	+	-	+	+					+	?	?		+	+	?	?
Quebec	+	?	-	?	+	+	?			+				?	-	-	-
Stockholm	?	?	-	?	+	+	+			+	?	?		?	?	?	+

probably has little to no effect on cancer detection rates at short follow-up; mortality data are not yet available.

Limitations of the Evidence

Certainty ranged from moderate to very low. The principal reasons for downgrading were study limitations, particularly performance bias (blinding is inherently impossible in screening trials), variable allocation concealment, and adherence and contamination issues in the CAP, PLCO, and Quebec studies, as well as imprecision and inconsistency across trials. Overdiagnosis and overtreatment, among the most clinically consequential harms of PSA screening, are not directly captured by the outcomes included in the trials and would require formal modelling to quantify [20,33,34]. Adverse events data were available from only one trial (CAP), and quality of life from a subset of participants in a single ERSPC site.

Comparison with Other Reviews

The 2013 version of this review concluded that PSA screening conferred no significant reduction in prostate cancer-specific or overall mortality [13], a conclusion substantially different from the present findings, primarily because extended long-term follow-up data from the ERSPC (now 23 years) were not then available. Our findings are directionally consistent with the Rahal et al. [35] living review, which reported a mortality RR of 0.78 (95% CI 0.65–0.94) favouring screening. The Fenton et al. [20] review informing the USPSTF did not include ERSPC long-term follow-up or the CAP trial. The German Institute for Quality and Efficiency in Health Care (IQWiG) report, which applied stricter exclusion criteria and excluded CAP, found an indication of benefit for disease-specific mortality and metastases but concluded that potential benefits did not outweigh harms [36]. The UK National Screening Committee recently concluded that population-based PSA screening remains not recommended, while acknowledging that risk-stratified approaches incorporating MRI or the Stockholm3 model may offer improved diagnostic accuracy [37].

Implications for Clinical Practice

Prostate-specific antigen-based screening likely reduces prostate cancer-specific mortality, but the absolute benefit is small, and the number of men diagnosed with prostate cancer—and thus exposed to potential overdiagnosis and overtreatment—increases markedly. Assessing the trade-offs between benefits and harms in the context of individual patient values, resource use, equity, and feasibility is beyond the scope of this review and is the domain of evidence-based guideline developers [20,38]. One point that appears uncontroversial across major guidelines is the importance of shared decision-making, ideally supported by a validated

decision aid [39–41], for asymptomatic men considering PSA testing [22,23,38,42,43].

Conclusion

Prostate-specific antigen-based prostate cancer screening may reduce prostate cancer-specific mortality and overall mortality based on low-certainty evidence across five RCTs; the effect on prostate cancer-specific mortality is probably real based on moderate-certainty evidence from the ERSPC trial at 23 years. However, the absolute mortality benefit is small, and screening substantially increases the detection of localised prostate cancer, raising concerns about overdiagnosis and overtreatment that are incompletely captured by available trial data. Emerging strategies combining PSA with kallikrein panels and MRI probably have little to no effect on overall cancer detection at short follow-up; longer-term mortality outcomes are awaited.

For clinical practice, shared decision-making supported by a validated decision aid is essential for any asymptomatic man considering PSA testing. For research, continued active follow-up of ongoing pivotal trials (ERSPC [44], CAP, the Prostate Cancer Intervention Versus Observation Trial [PIVOT] [45], Prostate testing for cancer and Treatment [ProtecT] [46]), strong support for the ProScreen trial [24], and future trials enrolling representative numbers of Black men and other under-represented populations are priorities. Investigation of polygenic risk scores [9] and novel biomarker strategies in large population-based trials is also warranted before their entry into routine care.

Disclosure of Interests

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

- 1 Bray F, Laversanne M, Sung H et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; 74: 229–63
- 2 Schafer E, Laversanne M, Sung H et al. Recent patterns and trends in global prostate cancer incidence and mortality: an update. *Eur Urol* 2025; 87: 302–13
- 3 Johns L, Houlston R. A systematic review and meta-analysis of familial prostate cancer risk. *BJU Int* 2003; 91: 789–94
- 4 Cornford P, Tilki D, Van den Bergh R et al. EAU - EANM - ESTRO ESUR - ISUP - SIOG Guidelines on Prostate Cancer. Available at: <https://uroweb.org/guidelines/prostate-cancer>. Accessed prior to 7 April 2026.
- 5 Eastham J, Auffenberg G, Barocas D et al. Clinically localized prostate cancer: AUA/ASTRO guideline, part I: introduction, risk assessment, staging, and risk-based management. *J Urol* 2022; 208: 10–8
- 6 Castro E, Goh C, Leongamornlert D et al. Effect of BRCA mutations on metastatic relapse and cause-specific survival after radical treatment for localised prostate cancer. *Eur Urol* 2015; 68: 186–93
- 7 Pritchard C, Mateo J, Walsh M et al. Inherited DNA-repair gene mutations in men with metastatic prostate cancer. *N Engl J Med* 2016; 375: 443–53
- 8 Zheng S, Sun J, Wiklund F et al. Cumulative association of five genetic variants with prostate cancer. *N Engl J Med* 2008; 358: 910–9
- 9 McHugh J, Bancroft E, Saunders E et al. Assessment of a polygenic risk score in screening for prostate cancer. *N Engl J Med* 2025; 392: 1406–17
- 10 Drost F, Osses D, Nieboer D et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. *Cochrane Database Syst Rev* 2019; 4: CD012663
- 11 Dahm P. Future of screening for prostate cancer. *BMJ* 2017; 358: j4200
- 12 Vickers A. Prostate cancer screening: time to question how to optimize the ratio of benefits and harms. *Ann Intern Med* 2017; 167: 509–10
- 13 Ilic D, Neuberger M, Djulbegovic M et al. Screening for prostate cancer. *Cochrane Database Syst Rev* 2013; CD004720. <https://doi.org/10.1002/14651858.CD004720.pub3>
- 14 Labrie F, Candas B, Cusan L et al. Screening decreases prostate cancer mortality: 11-year follow-up of the 1988 Quebec prospective randomized controlled trial. *Prostate* 2004; 59: 311–8
- 15 Sandblom G, Varenhorst E, Rosell J, Lofman O, Carlsson P. Randomised prostate cancer screening trial: 20-year follow-up. *BMJ* 2011; 342: d1539
- 16 Andriole G, Crawford E, Buys S et al. Prostate cancer screening in the randomized prostate, lung, colorectal, and ovarian cancer screening trial: mortality results after 13 years of follow-up. *J Natl Cancer Inst* 2012; 104: 125–32
- 17 Schröder F, Hugosson J, Roobol M et al. Screening and prostate cancer mortality: results of the European randomised study of screening for prostate cancer (ERSPC) at 13 years of follow-up. *Lancet* 2014; 384: 2027–35
- 18 Lundgren P, Kjellman A, Norming U, Lundgren PO, Gustafsson O. Long-term outcome of a single intervention population based prostate cancer screening study. *J Urol* 2018; 200: 82–8
- 19 Martin R, Donovan J, Turner E et al. Effect of a low-intensity PSA-based screening intervention on prostate cancer mortality: the CAP randomized clinical trial. *JAMA* 2018; 319: 883–95
- 20 Fenton J, Weyrich M, Durbin S et al. Prostate-specific antigen-based screening for prostate cancer: evidence report and systematic review for the US preventive services task force. *JAMA* 2018; 319: 1914–31
- 21 Smith R, Andrews K, Brooks D et al. Cancer screening in the United States, 2018: a review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin* 2018; 68: 297–316
- 22 Wei J, Barocas D, Carlsson S et al. Early detection of prostate cancer: AUA/SUO guideline part I: prostate cancer screening. *J Urol* 2023; 210: 46–53
- 23 NG131: Prostate cancer: diagnosis and management; updated 2021. Available at: <https://www.nice.org.uk/guidance/ng131>. Accessed prior to 8 April 2026.
- 24 Auvinen A, Tammela TL, Mirtti T et al. Prostate cancer screening with PSA, kallikrein panel, and MRI: the ProScreen randomized trial. *JAMA* 2024; 331: 1452–9
- 25 Page M, McKenzie J, Bossuyt P et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; 372: n71
- 26 Page M, Moher D, Bossuyt P et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021; 372: n160
- 27 Higgins J, Lasserson T, Thomas J et al. *Methodological Expectations of Cochrane Intervention Reviews*. London: Cochrane, 2016
- 28 Ilic D, Green S, O'Connor D et al. Screening for prostatic cancer. *Cochrane Database Syst Rev* 2004; CD004720. <https://doi.org/10.1002/14651858.CD004720>
- 29 Higgins P, Altman D. Chapter 8: assessing risk of bias in included studies. In Higgins JP, Churchill R, Chandler J, Cumpston MS eds, *Cochrane Handbook for Systematic Reviews of Interventions Version 5.2.0 (updated June 2017)*. London: Cochrane, 2017. Available at: <https://www.cochrane.org/authors/handbooks-and-manuals/handbook/archive/v520>.
- 30 Higgins J, Thomas J, Chandler J et al. *Cochrane Handbook for Systematic Reviews of Interventions*. Hoboken, NJ: John Wiley & Sons, 2019
- 31 Hugosson J, Månsson M, Wallström J et al. Prostate cancer screening with PSA and MRI followed by targeted biopsy only. *N Engl J Med* 2022; 387: 2126–37
- 32 China Randomized Study of Screening for Prostate Cancer. Available at: <https://www.chictr.org.cn/showproj.html?proj=255823>. Accessed 28 January 2026.
- 33 Gulati R, Gore J, Etzioni R. Comparative effectiveness of alternative prostate-specific antigen-based prostate cancer screening strategies: model estimates of potential benefits and harms. *Ann Intern Med* 2013; 158: 145–53
- 34 Tikkinen K, Dahm P, Lytvyn L et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a clinical practice guideline. *BMJ* 2018; 362: k3581
- 35 Rahal A, Badgett R, Hoffman R. Screening coverage needed to reduce mortality from prostate cancer: a living systematic review. *PLoS One* 2016; 11: e0153417
- 36 Prostate cancer screening with a PSA test: IQWiG Reports – Commission No. S19-01. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK558459/>. Accessed June 2020.
- 37 Screening for prostate cancer: external review against programme appraisal criteria for the UK National Screening Committee. 2020. Available at: <https://view-health-screening-recommendations.service.gov.uk/prostate-cancer/>. Accessed 05 May 2025.
- 38 Grossman D, Curry S, Owens D et al. Screening for prostate cancer. *JAMA* 2018; 319: 1901
- 39 Riikonen J, Guyatt G, Kilpeläinen T et al. Decision aids for prostate cancer screening choice: a systematic review and meta-analysis. *JAMA Intern Med* 2019; 179: 1072–82
- 40 Stacey D, Légaré F, Lewis K et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2017; CD001431. <https://doi.org/10.1002/14651858.CD001431.pub6>
- 41 Agoritsas T, Heen A, Brandt L et al. Decision aids that really promote shared decision making: the pace quickens. *BMJ* 2015; 350: g7624
- 42 Mottet N, Bellmunt J, Bolla M et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. *Eur Urol* 2017; 71: 618–29
- 43 S3 Guideline: Prostate cancer—Long version 8.1. Available at: <https://hubeitlinienprogramm-onkologie.de/leitlinie/prostatakarzinom>. Accessed prior to 7 April 2026.

- 44 Hugosson J, Roobol M, Mansson M et al. A 16-yr follow-up of the European randomized study of screening for prostate cancer. *Eur Urol* 2019; 76: 43–51
- 45 Wilt T, Vo T, Langsetmo L et al. Radical prostatectomy or observation for clinically localized prostate cancer: extended follow-up of the prostate cancer intervention versus observation trial (PIVOT). *Eur Urol* 2020; 77: 713–24
- 46 Hamdy F, Donovan J, Lane J et al. Fifteen-year outcomes after monitoring, surgery, or radiotherapy for prostate cancer. *N Engl J Med* 2023; 388: 1547–58

Correspondence: Philipp Dahm, Urology Section, Minneapolis Veterans Affairs Medical Center, One Veterans Drive, Minneapolis, MN 55417, USA. e-mail: pdahm@umn.edu

Abbreviations: CAP, Cluster randomised trial of PSA testing for Prostate cancer; EAU, European Association of Urology; ERSPC, European Randomised Study of Screening for

Prostate Cancer; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; ISRCTN, International Standard Randomised Controlled Trial Number; MCID, minimal clinically important difference; PLCO, Prostate, Lung, Colorectal, and Ovarian cancer screening trial; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomised controlled trial; RR, risk ratio; SF-6D, Short form six dimensions; USPSTF, United States Preventive Services Task Force.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Search strategies.