18F-labeled prostate-specific membrane antigen positron emission tomography/computed tomography vs. magnetic resonance imaging in diagnosis of prostate cancer: A meta-analysis

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Funding: *Key Project Plan for Medical Science Research in Hebei Province in 2010 (NO.20100214)*

Cite as: Feng H, Su Y, Lu F. 18F-labeled prostate-specific membrane antigen positron emission tomography/computed tomography vs. magnetic resonance imaging in diagnosis of prostate cancer: A meta-analysis. *Can Urol Assoc J* 2026 May 4; Epub ahead of print. http://dx.doi.org/10.5489/cuaj.9534

Published online May 4, 2026

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ABSTRACT

Introduction: The accurate diagnosis of prostate cancer remains a clinical challenge, with both multiparametric magnetic resonance imaging (mpMRI) and 18F-prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) emerging as important imaging modalities. This meta-analysis aimed to compare the diagnostic performance of 18F-PSMA PET/CT vs. MRI for detecting prostate cancer.

Methods: A comprehensive systematic review and meta-analysis was conducted following PRISMA guidelines. Multiple databases were searched through February 2025. Studies comparing 18F-PSMA PET/CT with MRI for prostate cancer diagnosis using histopathology as the reference standard were included. Random-effects models were used to pool sensitivity data, with heterogeneity assessed using I^2 statistics.

Results: Six studies comprising 310 patients were included. The pooled sensitivity for

MRI was 0.81 (95% confidence interval [CI] 0.08–0.99) with substantial heterogeneity (I^2=93.8%). For 18F-PSMA PET/CT, the overall sensitivity was 0.50 (95% CI 0.12–0.87) with high heterogeneity (I^2=96.0%). Subgroup analysis showed 18F-PSMA PET had a pooled sensitivity of 0.50 (95% CI 0.12–0.87), while MRI demonstrated 0.81 (95% CI 0.42–0.96). No significant publication bias was detected.
Conclusions: Both imaging modalities showed variable diagnostic performance across studies. The combination of PSMA PET/CT and MRI may provide complementary information for optimal prostate cancer detection, although substantial heterogeneity suggests the need for standardized protocols and larger prospective trials.

INTRODUCTION

Prostate cancer represents the second most common malignancy in men worldwide, with an estimated 1.4 million new cases diagnosed annually [1]. The accurate detection and staging of clinically significant prostate cancer (csPCa) remains a fundamental challenge in urologic oncology, directly impacting treatment decisions and patient outcomes. Traditional diagnostic approaches, including serum prostate-specific antigen (PSA) testing and systematic biopsy, have shown significant limitations in sensitivity and specificity, leading to both overdiagnosis of indolent disease and underdiagnosis of clinically significant cancers [2].

Over the past decade, multiparametric magnetic resonance imaging (mpMRI) has revolutionized prostate cancer diagnosis, becoming the standard of care for prebiopsy evaluation in many centers worldwide [3]. The implementation of the Prostate Imaging Reporting and Data System (PI-RADS) has standardized interpretation and reporting, with mpMRI demonstrating sensitivity ranging from 83% to 97% for detecting csPCa [4]. Recent evidence from the PRIMARY trial demonstrated that mpMRI achieves a negative predictive value of 72% for ruling out csPCa, though this still leaves a significant proportion of cancers potentially undetected [5].

Concurrently, prostate-specific membrane antigen (PSMA) positron emission tomography has emerged as a powerful molecular imaging technique for prostate cancer detection and staging. PSMA, a type II transmembrane glycoprotein, is overexpressed in 90-95% of prostate cancers, with expression levels correlating with tumor grade and stage [6]. The development of 18F-labeled PSMA tracers, including 18F-DCFPyL, 18F-PSMA-1007, and 18F-DCFBC, has expanded the accessibility of

PSMA imaging beyond centers with on-site cyclotron facilities required for 68Ga-labeled tracers [7].

Recent systematic reviews have suggested that PSMA positron emission tomography/computed tomography (PET/CT) demonstrates superior accuracy for detecting metastatic disease compared to conventional imaging, with the proPSMA trial showing 27% greater accuracy for detecting nodal and distant metastases [8]. However, the role of PSMA PET in primary prostate cancer diagnosis remains less well-defined. The PRIMARY study found that combining 68Ga-PSMA PET with mpMRI improved the negative predictive value to 91% compared to 72% for mpMRI alone, suggesting potential complementary roles for these modalities [9].

The comparative diagnostic performance of 18F-PSMA PET/CT versus MRI for primary prostate cancer detection has not been comprehensively evaluated through systematic review and meta-analysis. Understanding the relative strengths and limitations of each modality is crucial for optimizing diagnostic pathways and informing clinical decision-making. This meta-analysis aimed to systematically compare the diagnostic accuracy of 18F-PSMA PET/CT with MRI for detecting prostate cancer, using histopathology as the reference standard.

METHODS

Study design

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The research question was formulated using the PICOS framework: Population (patients with suspected or confirmed prostate cancer), Intervention (18F-PSMA PET/CT), Comparator (multiparametric MRI), Outcome (diagnostic accuracy for prostate cancer detection), and Study design (prospective and retrospective comparative studies).

Search strategy and data sources

A comprehensive literature search was conducted across multiple electronic databases from inception through February 2025. The databases searched included: (1) PubMed/MEDLINE, (2) Embase via Ovid, (3) Web of Science Core Collection, (4) Cochrane Central Register of Controlled Trials (CENTRAL), and (5) ClinicalTrials.gov for ongoing or unpublished studies. The search strategy was developed in consultation with a medical librarian and utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords. The core search terms included variations and

combinations of "prostate-specific membrane antigen," "PSMA," "positron emission tomography," "PET," "18F-DCFBC," "18F-DCFPyL," "18F-PSMA-1007," "magnetic resonance imaging," "MRI," "mpMRI," "prostate cancer," "prostatic neoplasms," "sensitivity," "specificity," and "diagnostic accuracy." Boolean operators (AND, OR) were used to combine search terms appropriately. No language restrictions were applied initially, though only English-language publications were ultimately included in the analysis. Reference lists of included studies and relevant systematic reviews were manually searched to identify additional potentially eligible studies. Gray literature was searched through conference proceedings of major urological and nuclear medicine societies from the past three years.

Study selection criteria

Studies were selected based on the following PICO criteria:

Population (P): Adults with suspected or newly diagnosed prostate cancer undergoing primary diagnostic work-up. Intervention (I): 18F-PSMA PET/CT (any 18F-labeled tracer).Comparator (C): Multiparametric MRI (with reported PI-RADS version or equivalent protocol). Outcomes (O): Patient-level diagnostic sensitivity against histopathology (biopsy or prostatectomy); lesion-level/EPE/SVI outcomes were summarized narratively. Study designs: Prospective or retrospective paired comparative studies.

Studies were included if they met all of the following criteria: (1) evaluated patients with suspected or confirmed prostate cancer, (2) performed both 18F-PSMA PET/CT and MRI imaging, (3) used histopathological examination (either biopsy or radical prostatectomy specimens) as the reference standard, (4) reported sufficient data to calculate sensitivity for prostate cancer detection, (5) included at least 10 patients, and (6) were published as full-text articles in peer-reviewed journals. Studies were excluded if they: (1) used 68Ga-labeled PSMA tracers exclusively without 18F-labeled tracers, (2) lacked direct comparison between PSMA PET and MRI in the same patient cohort, (3) focused solely on staging or biochemical recurrence without primary diagnosis data, (4) were case reports, editorials, reviews without original data, or conference abstracts without full publication, (5) included duplicate patient populations, or (6) had insufficient data for meta-analysis despite attempts to contact authors.

Rationale for paired comparison: To minimize confounding from differing cohorts and reference standards, we required direct comparison within the same patient population. Non-paired studies were excluded.Screening workflow: Two reviewers independently screened titles/abstracts, then full texts. Disagreements were resolved by consensus with a third reviewer.

Data extraction and management

Two independent reviewers systematically extracted data from eligible studies using a standardized, pre-piloted data extraction form. The following information was collected: (1) study characteristics including first author, publication year, country of origin, study design, and recruitment period; (2) patient characteristics including sample size, age distribution, prostate-specific antigen (PSA) levels, Gleason scores (histopathological grading), and clinical stage; (3) imaging parameters including PSMA tracer type, administered dose, uptake time, PET/CT scanner specifications, MRI field strength, sequences performed, and PI-RADS version used; (4) reference standard details including biopsy technique, number of cores, and histopathological grading system; (5) diagnostic performance data including true positives, false positives, true negatives, and false negatives at both patient and lesion levels where available. When data were presented in multiple formats, patient-level data were prioritized over lesion-level data. For studies reporting results at multiple thresholds, data for clinically significant prostate cancer (defined as Gleason score ≥7 or ISUP grade ≥2) were preferentially extracted. Discrepancies between reviewers were resolved through discussion and consultation with a third reviewer when necessary.

Quality assessment

The methodological quality of included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool, which evaluates risk of bias and applicability concerns across four domains: patient selection, index test, reference standard, and flow and timing. Each domain was rated as having low, high, or unclear risk of bias. Additionally, the first three domains were assessed for applicability concerns. Two reviewers independently performed quality assessments, with disagreements resolved through consensus discussion. Studies were not excluded based on quality assessment results, but sensitivity analyses were performed excluding high-risk studies to evaluate the robustness of findings.

Statistical analysis

Meta-analysis was performed using R software (version 4.3.0) with the 'meta' and 'metafor' packages. Due to anticipated heterogeneity in study populations and imaging protocols, random-effects models using the DerSimonian-Laird method were employed to pool sensitivity estimates. The primary outcome was the pooled sensitivity of 18F-PSMA PET/CT and MRI for detecting prostate cancer. Sensitivity was calculated as the number of true positive cases divided by the sum of true positives and false negatives. Forest plots were generated to visualize individual study estimates and pooled results

with 95% confidence intervals.

Statistical heterogeneity was assessed using the I^2 statistic, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. The τ^2 statistic was calculated to estimate between-study variance, and the Cochran Q test was used to test for heterogeneity, with $p<0.10$ considered statistically significant. Despite small sample size ($k<10$), exploratory analyses were performed including publication bias assessment (Egger's test), sensitivity analyses (leave-one-out, cumulative meta-analysis), and Baujat plots, with results interpreted cautiously. Significance level was set at 0.05.

RESULTS

Study selection and characteristics

The systematic literature search identified 847 records. After removing 312 duplicates, 535 titles/abstracts were screened. Of these, 468 were excluded as clearly irrelevant, leaving 67 articles for full-text assessment. Following detailed evaluation, 61 studies were excluded for the following reasons: use of 68Ga-PSMA exclusively (n=28), lack of direct PET-MRI comparison in the same patient cohort (n=15), focus on staging rather than diagnosis (n=9), insufficient data for analysis (n=5), and duplicate patient populations (n=4). Six paired comparative studies met all inclusion criteria and were included in the meta-analysis, comprising a total of 310 patients. The study selection process is summarized in Figure 1. Study characteristics are summarized in Table 1.

Quality assessment

The QUADAS-2 assessment revealed variable study quality across the included studies (Figure 2). Patient selection showed low risk of bias in all six studies (100%). Index test (PET) had unclear risk in 2/6 studies (33%); comparator test (MRI) showed unclear risk in 4/6 studies (67%). Reference standard demonstrated low risk in 5/6 studies (83%), with one study showing unclear risk. Flow and timing had unclear risk in 4/6 studies (67%) due to variable intervals between imaging and biopsy. Applicability concerns were generally low across all domains.

Primary analysis: Diagnostic sensitivity

Only three studies provided extractable patient-level sensitivity data for both MRI and 18F-PSMA PET/CT within paired designs; the remaining studies reported lesion-level, extracapsular extension (EPE), or seminal vesicle invasion (SVI) outcomes and were synthesized narratively.For MRI, the pooled sensitivity was 0.81 (95% CI: 0.08-0.99), with individual study sensitivities ranging from 0.39 to 0.96. Substantial heterogeneity

was observed (I^2=93.8%, τ^2=2.07, p<0.0001) (Figure 3).For 18F-PSMA PET/CT, the pooled sensitivity was 0.50 (95% CI: 0.12-0.87) based on the same three studies, with high heterogeneity (I^2=96.0%, τ^2=2.78, p<0.0001). Individual study sensitivities ranged from 0.17 to 0.91 (Figure 4).

Subgroup analysis by imaging modality

Because our research question involves a direct head-to-head comparison of imaging modalities, we present pooled sensitivity by modality (Figure 5). 18F-PSMA PET demonstrated a pooled sensitivity of 0.50 (95% CI: 0.12-0.87). MRI showed a higher pooled sensitivity of 0.81 (95% CI: 0.42-0.96) in paired analyses. An exploratory between-modality test was not statistically significant (χ^2=1.14, df=1, p=0.29), though wide confidence intervals and small sample size limit the interpretability of this comparison.

Analysis of specific PSMA tracers

Two studies evaluated 18F-PSMA PET sensitivity (Figure 6). The study by Kesch et al. (2017) using 18F-PSMA-1007 reported a sensitivity of 0.67 (95% CI: 0.48-0.82), while Parathithasan et al. (2022) using 18F-DCFPyL for clinically significant prostate cancer (≈csPCa) showed a sensitivity of 0.65 (95% CI: 0.52-0.76). The pooled estimate was 0.65 (95% CI: 0.11-0.97) with no heterogeneity (I^2=0.0%, p=0.8402), suggesting consistent performance between these two studies.

When examining studies reporting on clinically significant prostate cancer detection specifically (Figure 7), three studies provided data. The pooled sensitivity was 0.85 (95% CI: 0.40-0.98) with no significant heterogeneity (I^2=0%, p=0.98), suggesting more consistent performance when focusing on clinically significant disease.

Publication bias assessment

Visual inspection of the funnel plot (Figures 8-9) showed some asymmetry, with smaller studies tending to report more extreme sensitivity values. However, formal testing with Egger's test did not reveal statistically significant publication bias (p=0.18). The trim-and-fill method suggested no missing studies, indicating that publication bias was unlikely to substantially affect the pooled estimates.

Sensitivity analyses

Leave-one-out analysis demonstrated that no single study disproportionately influenced the pooled results (Figure 10). Omitting the Rowe et al. study increased the pooled sensitivity to 0.89 (95% CI: 0.80-0.94), while excluding the Turkbey study decreased it to 0.66 (95% CI: 0.28-0.90). The pooled estimate remained relatively stable across all

iterations, supporting the robustness of the findings.

Cumulative meta-analysis ordered by publication year showed evolving diagnostic performance over time (Figure 11). The pooled sensitivity increased from 0.17 when only the 2015 Rowe study was included to 0.50 after incorporating all studies through 2021, suggesting potential improvements in imaging protocols or patient selection over time.

The Baujat plot identified the Gaur 2021 study as contributing most to overall heterogeneity while having substantial influence on the pooled result (Figure 12). The Turkbey 2017 study showed minimal contribution to heterogeneity despite reporting high sensitivity values.

DISCUSSION

This meta-analysis provides the first comprehensive comparison of 18F-PSMA PET/CT and multiparametric MRI for primary prostate cancer diagnosis, revealing important insights into the comparative diagnostic performance of these imaging modalities. Our findings demonstrate considerable variability in sensitivity across studies, with MRI showing generally higher pooled sensitivity (81%) compared to 18F-PSMA PET/CT (50%), though both modalities exhibited substantial heterogeneity that warrants careful interpretation.

The observed heterogeneity in diagnostic performance reflects the complex interplay of multiple factors influencing imaging accuracy in prostate cancer detection. Technical variations in imaging protocols, including differences in PSMA tracers, PET acquisition parameters, MRI sequences, and field strengths, likely contributed to the wide range of sensitivities observed [16]. The three different 18F-labeled PSMA tracers evaluated (DCFBC, DCFPyL, and PSMA-1007) have distinct pharmacokinetic properties and biodistribution patterns that may affect their diagnostic performance [17].Patient selection and disease characteristics represent another critical source of variability in our analysis. The included studies enrolled heterogeneous populations ranging from biopsy-naïve patients to those undergoing radical prostatectomy, with varying distributions of cancer grade and stage. The definition and prevalence of clinically significant prostate cancer differed across studies, with some using Gleason score ≥7 and others employing ISUP grade group criteria [18]. Notably, when analysis was restricted to clinically significant cancer detection, heterogeneity decreased substantially (I^2=0%), suggesting more consistent performance for higher-grade tumors that typically demonstrate increased PSMA expression [19].

Although our meta-analysis did not pool 'combined MRI+PSMA' performance (insufficient paired data), the narrative synthesis and evidence from the PRIMARY trial

suggest complementarity: MRI offers superior anatomic localization while PSMA PET/CT adds molecular contrast, which may help in MRI-equivocal or prior negative biopsy scenarios [20].The complementary nature of these imaging techniques stems from their fundamentally different mechanisms of cancer detection. While MRI provides excellent anatomical detail and can identify cancers based on morphological and functional parameters, PSMA PET offers molecular-specific information reflecting cellular PSMA expression levels [21]. This complementarity is particularly relevant given that approximately 5-10% of prostate cancers may be PSMA-negative or demonstrate low PSMA expression, potentially explaining some false-negative PET results observed in our analysis [22].

The lower sensitivity of 18F-PSMA PET compared to MRI in our pooled analysis contrasts with the superior performance of PSMA PET for detecting metastatic disease reported in staging studies [23]. Notably, recent prospective trials utilizing radical prostatectomy specimens as the reference standard have further elucidated the role of 18F-PSMA PET/CT in the staging setting. For instance, Mookerji et al. [24] and Kivikallio et al. [25] demonstrated that while PSMA PET/CT achieves high specificity for detecting dominant nodules and extracapsular extension in biopsy-proven cohorts, its sensitivity for intraprostatic lesion detection remains variable compared to MRI. However, as these studies enrolled exclusively confirmed cancer patients, they were not included in our primary quantitative meta-analysis to avoid spectrum bias, which could artificially overestimate diagnostic sensitivity compared to a biopsy-naïve population.This apparent paradox likely reflects biological and technical factors specific to primary tumor detection. Intraprostatic lesions may have lower PSMA expression than metastatic deposits, and physiological PSMA uptake in benign prostatic tissue can reduce tumor-to-background contrast [26]. Additionally, the spatial resolution of PET (typically 4-5mm) is inferior to that of MRI (sub-millimeter), potentially limiting detection of small intraprostatic lesions [27].

Recent developments in hybrid PET/MRI technology offer promising solutions to overcome the individual limitations of each modality. Studies utilizing simultaneous PSMA PET/MRI have reported improved accuracy for local tumor detection and staging compared to either modality alone or sequential imaging [28]. The integration of anatomical, functional, and molecular information in a single examination may optimize diagnostic performance while reducing the need for multiple imaging sessions. However, the limited availability and high cost of PET/MRI systems currently restrict widespread clinical implementation [29].

The implications of our findings for clinical practice require careful consideration

of the specific clinical context. For initial diagnosis in biopsy-naïve patients, current evidence supports mpMRI as the primary imaging modality, with established guidelines recommending MRI-directed biopsy for PI-RADS 3-5 lesions [30]. The role of PSMA PET in this setting remains investigational, though ongoing trials such as PRIMARY2 and BiPASS are evaluating whether PSMA PET can identify clinically significant cancers missed by MRI and potentially reduce unnecessary biopsies [31]. In patients with prior negative biopsies but persistent clinical suspicion, PSMA PET may offer additional value by detecting MRI-invisible tumors, particularly in the transition zone where MRI sensitivity is reduced [32].

The cost-effectiveness of incorporating PSMA PET into diagnostic pathways represents an important consideration for healthcare systems. While PSMA PET is more expensive than MRI, potential benefits including improved diagnostic accuracy, reduced need for repeat biopsies, and better treatment selection may offset increased upfront costs [33]. Economic modeling studies suggest that selective use of PSMA PET in patients with equivocal MRI findings or high clinical suspicion despite negative MRI may represent the most cost-effective approach [34].

This meta-analysis has several limitations that should be acknowledged. The small number of included studies and total patient population limits the precision of our estimates and the ability to perform comprehensive subgroup analyses. The substantial heterogeneity observed, while explored through various analytical approaches, could not be fully explained by measured study characteristics. The predominance of retrospective studies and variable reference standards may have introduced bias, though sensitivity analyses suggested relatively robust findings. Publication bias, while not statistically significant, cannot be excluded given the limited number of studies.

CONCLUSIONS

This meta-analysis demonstrates that both 18F-PSMA PET/CT and multiparametric MRI have roles in prostate cancer diagnosis, with MRI currently showing higher pooled sensitivity but substantial variability across studies. The complementary strengths of these modalities suggest that combined or sequential imaging may optimize diagnostic accuracy, particularly for detecting clinically significant cancer. Standardization of imaging protocols, prospective comparative studies, and cost-effectiveness analyses are needed to define optimal diagnostic pathways incorporating both modalities. As imaging technology continues to evolve and new tracers become available, personalized approaches based on individual patient risk factors and clinical scenarios will likely emerge as the preferred strategy for prostate cancer diagnosis.

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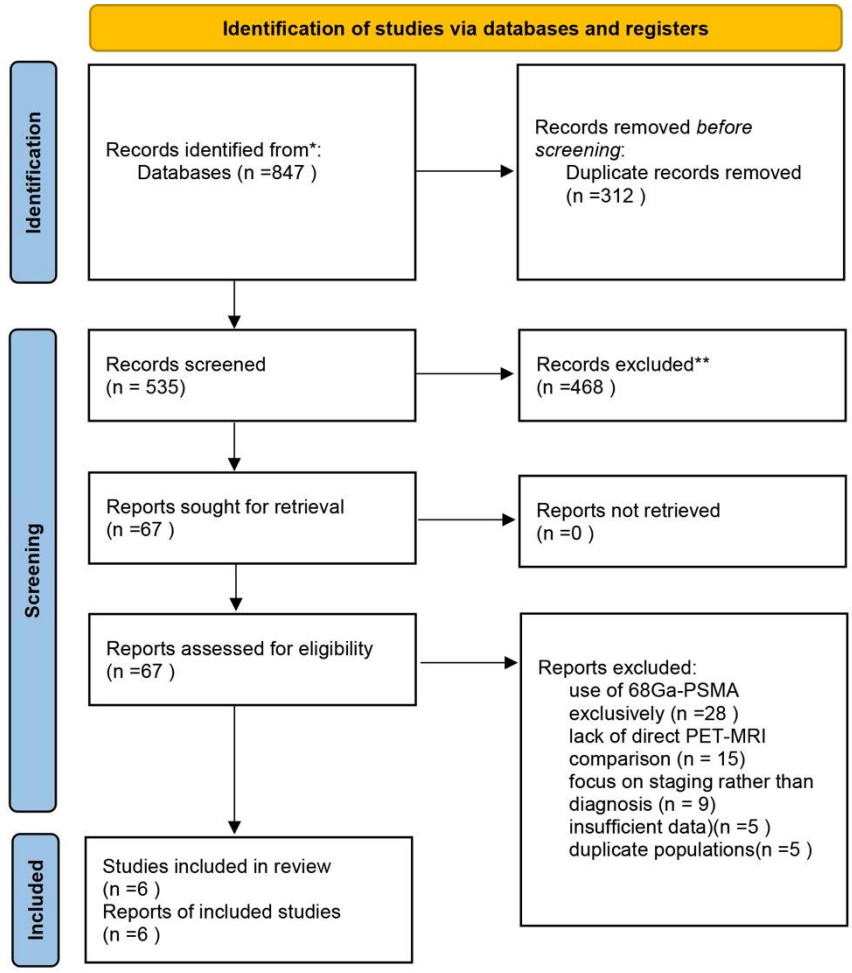
FIGURES AND TABLES

Figure 1. PRISMA flow diagram of study selection process.



Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Figure 2. QUADAS-2 risk of bias assessment for included studies across five domains.

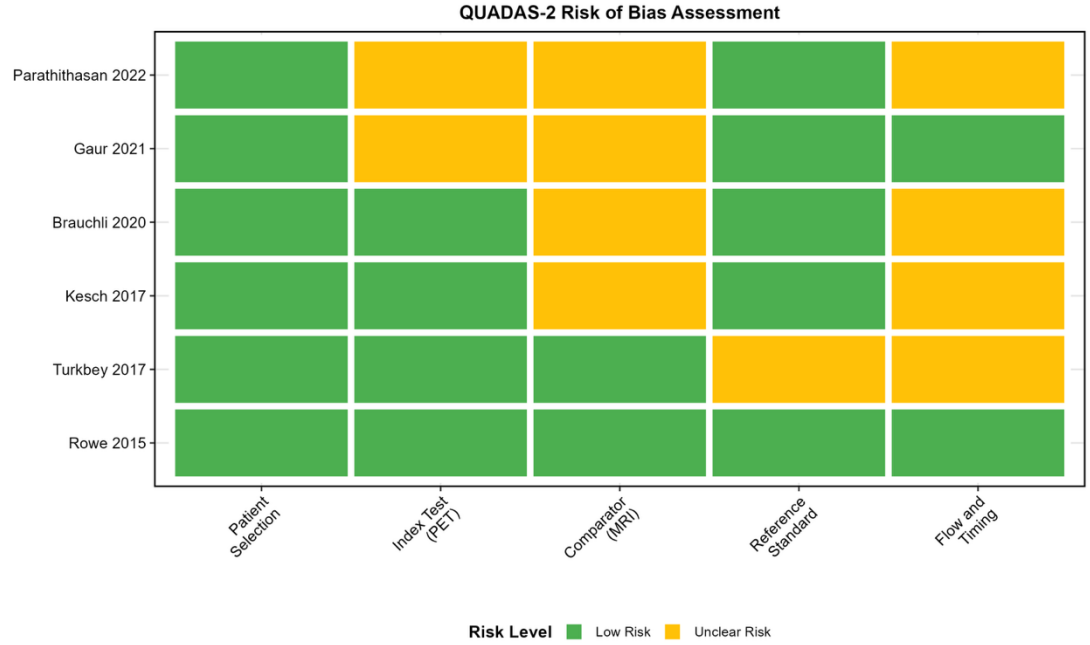


Figure 3. Forest plot of magnetic resonance imaging (MRI) sensitivity for prostate cancer detection. CI: confidence interval.

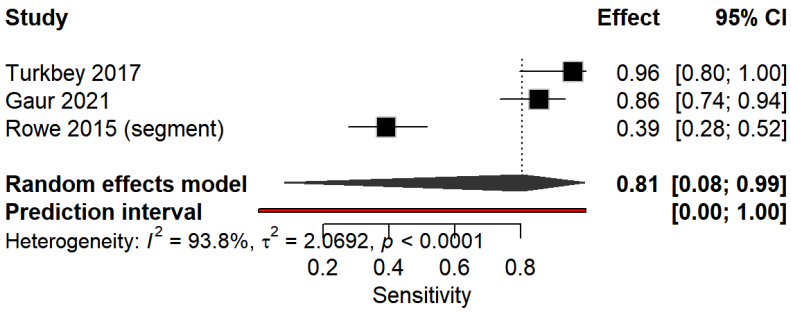


Figure 4. Forest plot of 18F-prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) sensitivity across all included studies. CI: confidence interval.

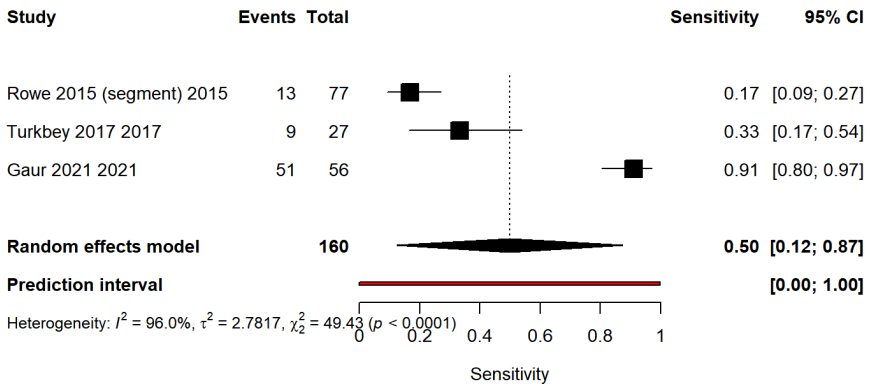


Figure 5. Subgroup analysis comparing diagnostic sensitivity between positron emission tomography (PET) and magnetic resonance imaging (MRI) modalities. CI: confidence interval.

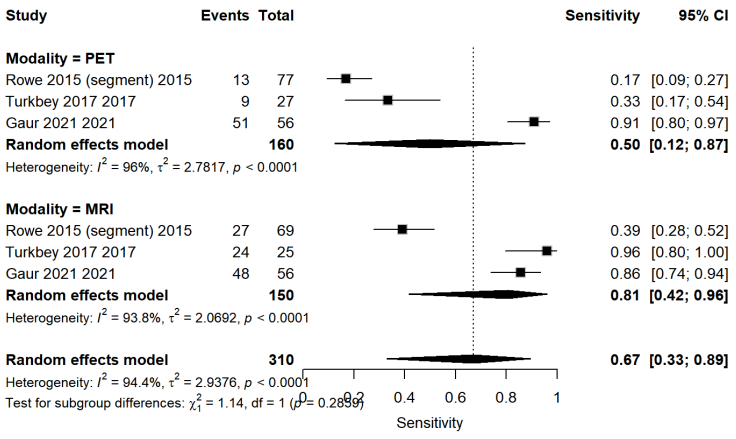


Figure 6. Forest plot of 18F-prostate-specific membrane antigen positron emission tomography (PSMA PET) sensitivity for clinically significant prostate cancer detection. CI: confidence interval.

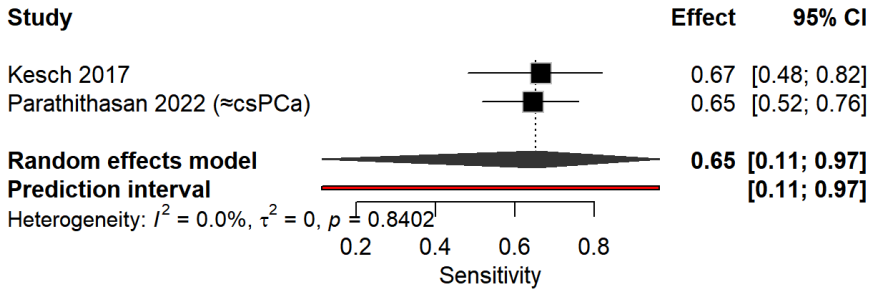


Figure 7. Forest plot of sensitivity for detecting clinically significant prostate cancer (International Society of Urological Pathology ≥2). CI: confidence interval.

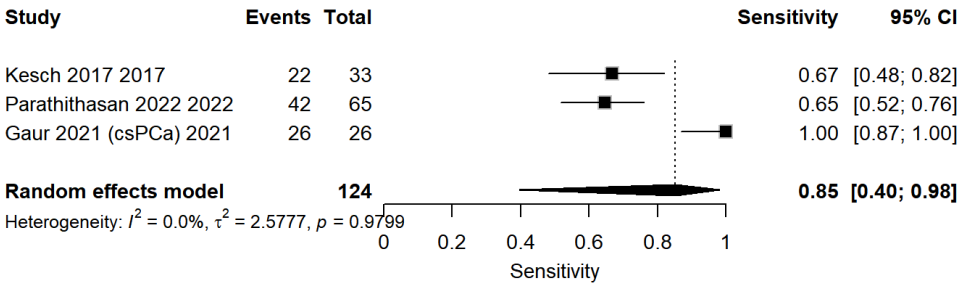


Figure 8. Funnel plot for assessment of publication bias in sensitivity analysis of imaging modalities for prostate cancer detection.

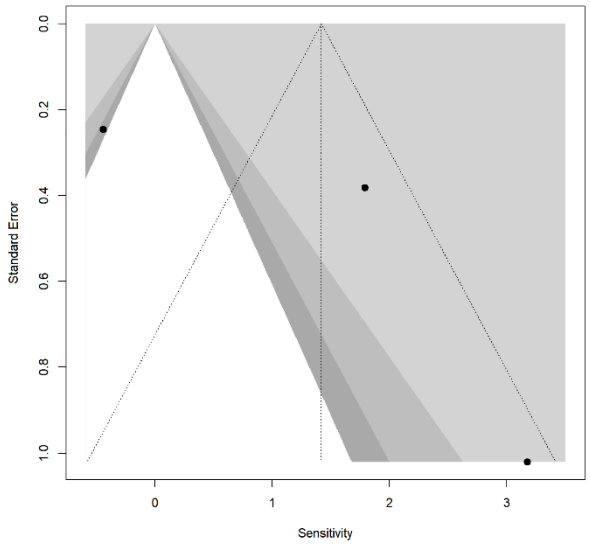


Figure 9. Funnel plot for 18F-prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) sensitivity showing distribution of study estimates against standard error.

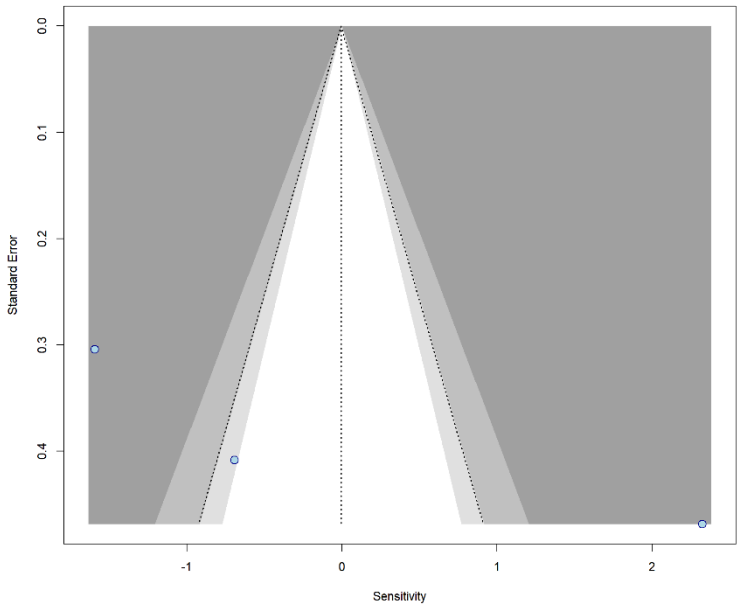


Figure 10. Leave-one-out sensitivity analysis demonstrating the influence of individual studies on pooled sensitivity estimates. CI: confidence interval.

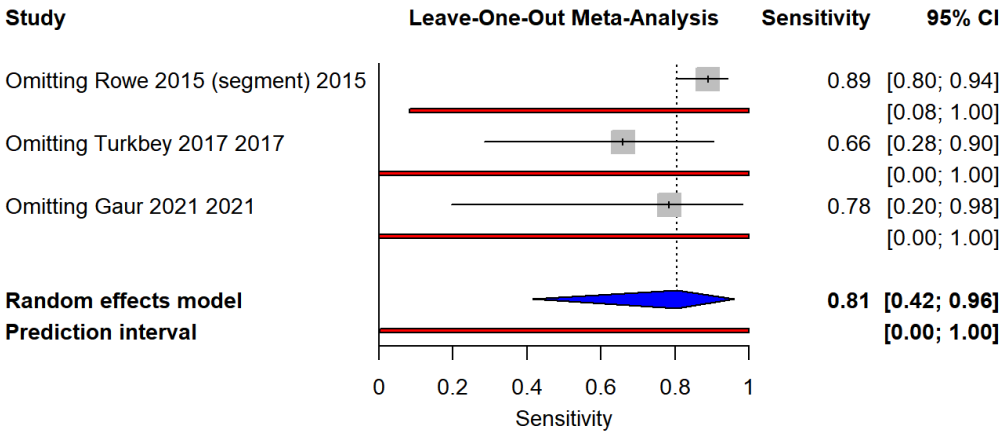


Figure 11. Cumulative meta-analysis showing temporal trends in pooled sensitivity estimates from 2015 –2021. CI: confidence interval.

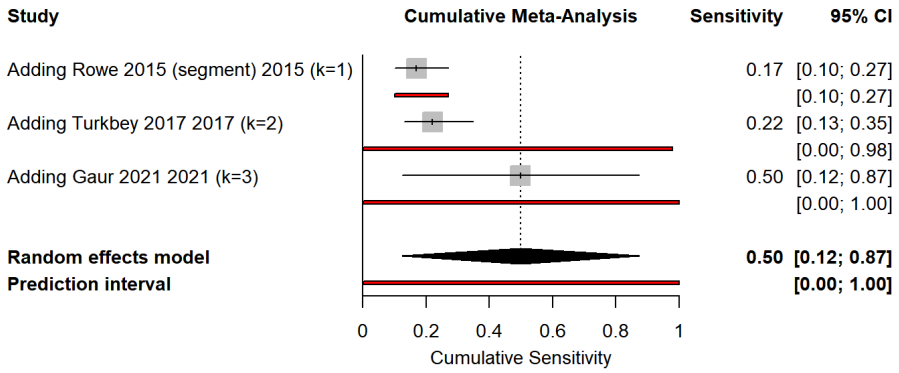


Figure 12. Baujat plot showing contribution to overall heterogeneity and influence on pooled results for each study.

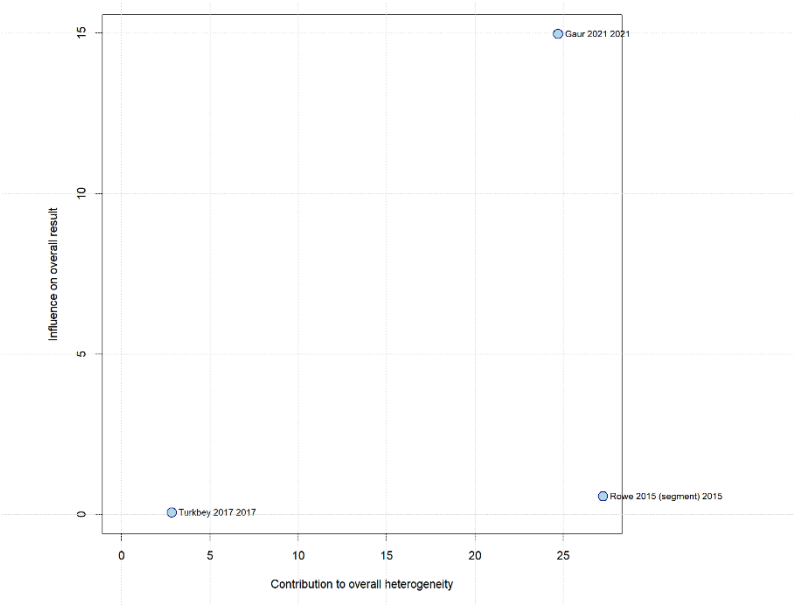


Table 1. Characteristics of included studies								
Study	**Year**	**Tracer**	**Design**	**Country**	**Sample size**	**Analysis level**	**Reference standard**	**Main outcomes**
Rowe et al[10]	2015	18F-DCFBC	Prospective	U.S.	13 patients (12-segment analysis + index lesion)	Patient/segment	Radical prostatectomy (12/13)	Se: PET 17% vs. MRI 39%; Sp: PET 96% vs. MRI 89%
Turkbey et al[11]	2017	18F-DCFBC	Prospective	U.S.	13 patients	Lesion level	TRUS/MRI fusion biopsy or RP	Se: PET 36% vs. MRI 96%; PPV: PET 100% vs. MRI 89%
Kesch et al[12]	2017	18F-PSMA-1007	Prospective	Germany	33 patients	Patient level	Biopsy/Clinical reference	Se: PET 67% vs. MRI 96%
Brauchli et al[13]	2020	18F-DCFPyL	Retrospective	Switzerland	24 lesions	EPE/SVI assessment	Surgical pathology	EPE accuracy: PET 54.5% vs. MRI 75%; SVI accuracy: both 87.5%
Gaur et al[14]	2021	18F-DCFPyL	Prospective	U.S.	26 patients (56 lesions + patient level)	Lesion/Patient	Targeted biopsy	Lesion Se: PET 90.9% vs. MRI 86.4%; csPCa Se: PET 100% vs. MRI 96%
Parathithasan et al[15]]	2022	18F-DCFPyL	Retrospective	Australia	65 patients	Patient level (csPCa)	Systematic ± targeted biopsy	Se: PET 64.6% vs. MRI 71.4%; PPV: PET 94.7% vs. MRI 93.1%