Optimizing the strategies to perform prostate biopsy in MRI-positive patients: a systematic review and network meta-analysis

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Summary

Background Early detection of prostate cancer (PCa) is crucial for better patient outcomes. However, due to over-diagnosis with the current biopsy strategy, there is a need to improve and refine the biopsy strategy. The aim of this study was to thoroughly evaluate existing biopsy schemes for patients with suspicious lesions.

Methods This study conducted a systematic review and network meta-analysis following PRISMA guidelines (from their start until 15 January 2025), evaluating 13 biopsy schemes for detecting PCa in MRI-positive (PIRADS/Likert score 2–5) patients. Data from PubMed, Embase, and Cochrane databases were examined to assess the efficacy of biopsy schemes in detecting clinically significant (csPCa) and clinically insignificant (ciPCa) prostate cancer. This study is registered with PROSPERO (CRD42024551971).

Findings The analysis included 211 studies involving 74,113 individuals. When compared with the combination of systematic biopsy (SB, defined as <20 cores) and targeted biopsy (TB, defined as <6 cores) (SB+TB), ipsilateral SB with TB (ips-SB+TB) and saturation TB did not show statistically significant inferior detection rate of csPCa (ips-SB+TB: RR 0.95, 95% CrI 0.88, 1.02; saturation TB: RR 0.96, 95% CrI 0.91, 1.01). Meanwhile, there was no significant difference in csPCa detection rates for saturation SB+TB, SB+saturation TB compared to SB+TB (saturation SB+TB: RR 1.04, 95% CrI 0.98, 1.11; SB+saturation TB: RR 1.14, 95% CrI 0.999, 1.30). TB and SB alone detected significantly less csPCa than SB+TB (TB: RR 0.86, 95% CrI 0.84, 0.88; SB: RR 0.75, 95% CrI 0.73, 0.77). Saturation SB also did not show significant superiority in detecting csPCa. Additionally, saturation TB and ips-SB+TB also decrease the detection of ciPCa. (ips-SB+TB: RR 0.87, 95% CrI 0.72, 1.04; saturation TB: RR 0.76, 95% CrI 0.65, 0.88).

Interpretation The network meta-analysis reveals that saturation SB+TB and SB+saturation TB have no significant difference in csPCa detection between them and SB+TB. Meanwhile, ips-SB+TB and saturation TB are effective biopsy strategies for MRI-positive PCa patients, offering a more targeted approach for detecting csPCa.

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Research in context

Evidence before this study

Before our research, we searched databases like PubMed, MEDLINE, Embase, and Cochrane Library from their start until January 2025 using relevant search terms on prostate biopsy for MRI-positive patients. Studies had to meet criteria such as PSA >4 ng/mL, MRI-detected lesions, and reporting PCa detection rates. Previous meta-analyses mainly focused on pairwise comparisons of biopsy methods, often excluding emerging strategies like ips-SB+TB and saturation TB. Notably, no prior meta-analysis had systematically compared all current biopsy strategies. Our study is the first to conduct a network meta-analysis on 13 biopsy schemes, offering a comprehensive evaluation of their effectiveness.

Added value of this study

Our study provides novel insights by analyzing 211 studies in a network meta-analysis comparing 13 biopsy strategies. Specifically targeting MRI-positive patients, we reveal that saturation SB+TB and SB+saturation TB, despite high csPCa detection rates, show no significant advantage over standard SB+TB. This challenges the notion that more extensive biopsies are always superior. We also highlight reduced ciPCa detection with ips-SB+TB and saturation TB, addressing overdiagnosis concerns. Our subgroup analyses clarify how biopsy history and TB route influence outcomes, enhancing understanding of strategy performance.

Implications of all the available evidence

Our findings indicate saturation SB+TB and SB+saturation TB perform similarly to SB+TB for csPCa detection, while ips-SB+TB and saturation TB reduce ciPCa detection. These strategies offer balanced accuracy and reduced overdiagnosis. Future research should test these methods in broader populations, refine biopsy protocols, and standardize MRI interpretations to optimize prostate cancer diagnosis.

Introduction

The advent of multiparametric magnetic resonance imaging (mpMRI) and the implementation of the Prostate Imaging Reporting and Data System version 2.1 (PI-RADS v2.1) criteria have revolutionized Prostate cancer (PCa) diagnosis.[1–4] These advances have enhanced the ability to detect and localize PCa, particularly clinically significant PCa (csPCa), resulting in significant improvements in detection rates.[4–7] MRI/ultrasound fusion targeted biopsy (TB) has further refined the diagnostic accuracy, enhancing the detection of csPCa while reducing the incidence of clinically insignificant PCa (ciPCa).[6–8] The combined use of systematic prostate biopsy (SB) and TB (SB+TB) has emerged as a standard biopsy scheme. This approach leverages the benefits of both techniques, leading to a higher detection rate of PCa overall.[6,8,9] However, this combined approach also presents several challenges. Firstly, it incurs increased biopsy expenses due to the more biopsy cores and operations.[5,10,11] Secondly, the combination of SB and TB has resulted in a higher detection of ciPCa, potentially leading to subsequent overtreatment among patients with low-grade PCa.[5,10,11] Furthermore, the higher number of biopsies performed in this combined approach has been associated with an increased incidence of complications, such as hematuria and urinary retention.[12]

In recent years, the concept of regional biopsy (RB) has been proposed and has gained increasing attention.[10,13–22] This biopsy scheme includes ipsilateral SB (ips-SB) combined with TB (ips-SB+TB), saturation TB and other biopsy schemes with the objective of maintaining high detection efficiency of csPCa and minimizing the biopsy cores targeting inaccuracies and grade migration. Furthermore, the European Association of Urology (EAU) guidelines for 2024 have also undergone a change in recommendation. Previously, the guidelines advised performing SB+TB when MRI findings were positive (i.e., PI-RADS $\geq$ 3). However, the updated guidelines now advise performing TB with perilesional sampling when MRI findings are positive (i.e., PI-RADS $\geq$ 4). These transformations highlight the importance of refining and optimizing the current biopsy schemes.

Therefore, the aim of this study is to compare existing strategies for prostate biopsy in MRI-positive patients and to identify the optimal and most promising strategies for prostate biopsy.

Methods

The meta-analysis was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, as well as the extension statement for network meta-analyses.[23,24] And the work has been reported in line with AMSTAR (Assessing the methodological quality of systematic reviews).[25] The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (Registration no: CRD42024551971).

Data source, search strategy and inclusion/exclusion criteria

The data source and search strategy employed in the network meta-analysis are as follows: The PubMed, MEDLINE, Embase, and Cochrane databases were searched for relevant data. The publication date was set from the beginning of this investigation up until January 2025. A comprehensive search was conducted across all relevant fields (Supplementary Material).

The inclusion criteria were shown as followed: (1) Patients with elevated levels of prostate-specific antigen

(PSA) (>4 ng/mL), whether or not they have had a previous biopsy underwent MRI; (2) At least one MRI lesion was detected; (3) more than one type of prostate biopsy schemes were performed in the same patient or in different groups with comparable baseline characteristics; (4) The required data pertaining to the detection rate of PCa, csPCa or ciPCa could be extracted from both the paper and its Supplementary Materials. The exclusion criteria were: (1) Studies written in a language other than English, meeting abstracts, and reviews were not included. (2) Phantom and animal studies were also excluded.

Data extraction and quality assessment

Two researchers independently reviewed the titles and abstracts to select the potential articles comprehensively. Subsequently, the full texts were carefully read and suitable articles were selected. Data extraction mainly included basic information included in the study, including the first author, journal, and time of publication; the baseline characteristics of the individuals; the relevant details of the biopsy; the biopsy patterns; the threshold of the suspicious lesion and definition of the csPCa; and the detection rate of PCa (including csPCa and ciPCa).

The research utilized the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) and QUADAS-C. QUADAS-2 encompasses four distinct areas: patient selection, index test, reference standard, and flow and timing. For each of these areas, a bias risk evaluation was performed, while the first three domains were also subject to applicability concerns.[26,27] Meanwhile, QUADAS-C serves as an augmentation of QUADAS-2.

Any discrepancies were resolved by consensus or, if necessary, consultation with a third reviewer.

Statistical analysis

We conducted a Bayesian network meta-analysis utilizing R (version 4.3.2) and the "GeMTC" package. The assessment of model inconsistency (a discrepancy arising when the direct evidence from individual studies comparing biopsy schemes differs from the indirect evidence derived from the entire network of multiple studies) was based on the node-splitting method (mtc.nodesplit function), and a Bayesian p-value threshold of <0.05 was set to indicate significant inconsistency. Heterogeneity was evaluated using the I^2 test, with $I^2 > 50\%$ indicating substantial heterogeneity. Additionally, the mtc.anohe function was implemented to test the heterogeneity hypothesis.

For sensitivity analysis, we excluded the studies that enrolled a small number of the patients with PIRADS/Likert ≤ 2. In addition, we compared the results of the fixed and random effects of the model. And given the substantial number of studies and potential inconsistencies and bias risks among them. We opted for a random-effects model, even though the calculated I^2 statistic fell below 50%. Model convergence was verified through Gelman-Rubin-Brooks plots, as well as Trace and Density Plots.

Subsequently, the detection rate was analyzed using the risk ratio (RR) and its 95% credible interval (CrI), derived from Markov chain Monte Carlo methods. The rank probabilities (This probability-based ranking is like grading candidates by expected test performance, helping infer sampling method superiority) were then calculated to establish the hierarchical ranking of each sampling method. Furthermore, the surface under the cumulative ranking curve (SUCRA, an aggregate metric indicating the likelihood of a biopsy scheme ranking highly in all comparisons; a higher value means better overall detection efficacy) was computed to compare the detection efficacy of different biopsy schemes. The "netmeta" package was employed to examine publication bias of all the studies through Thompson's Test and the visual assessment of a funnel plot. Finally, meta regression analyses and subgroup analyses were performed, taking into account history of prostate biopsy, route of TB, the thresholds for suspicious lesions and the definitions of csPCa.

Role of the funding source

The study's funder had no role in study design, data collection, analysis, interpretation, or report writing.

Results

Search results and study characteristics

A total of 4787 relevant studies were identified. After excluding duplicate articles and screening the literature, 211 studies were included in the final analysis. The study selection process is shown in the flowchart in Fig. 1. A total of 74,113 individuals were included in the study. The detailed characteristics of the included records are presented in Supplementary Table for Characteristics of the studies. The analysis included 13 types of prostate biopsy schemes. 208 studies assessed targeted biopsy (TB), 166 assessed systematic biopsy (SB), 177 assessed SB combined with TB (SB+TB), 24 assessed saturation TB, 20 assessed saturation SB, 3 assessed ipsilateral SB (ips-SB), 4 assessed contralateral SB (con-SB), 13 assessed ips-SB combined with TB (ips-SB+TB), 11 assessed con-SB combined with TB (con-SB+TB), 25 assessed saturation SB combined with TB (saturation SB+TB), 2 assessed non-targeted SB combined with TB (non-targeted SB+TB), 1 assessed adjacent sextant SB combined with TB (adjacent sextant SB), and 5 assessed SB combined with saturation TB (SB+saturation TB) (Supplementary Figure S1). Systematic biopsy (SB) was defined as ≤20 cores SB; Saturation SB were defined as >20 cores SB; Targeted biopsy (TB) was defined as <6 cores TB; Saturation TB was defined as ≥6 cores TB with or without perilesional

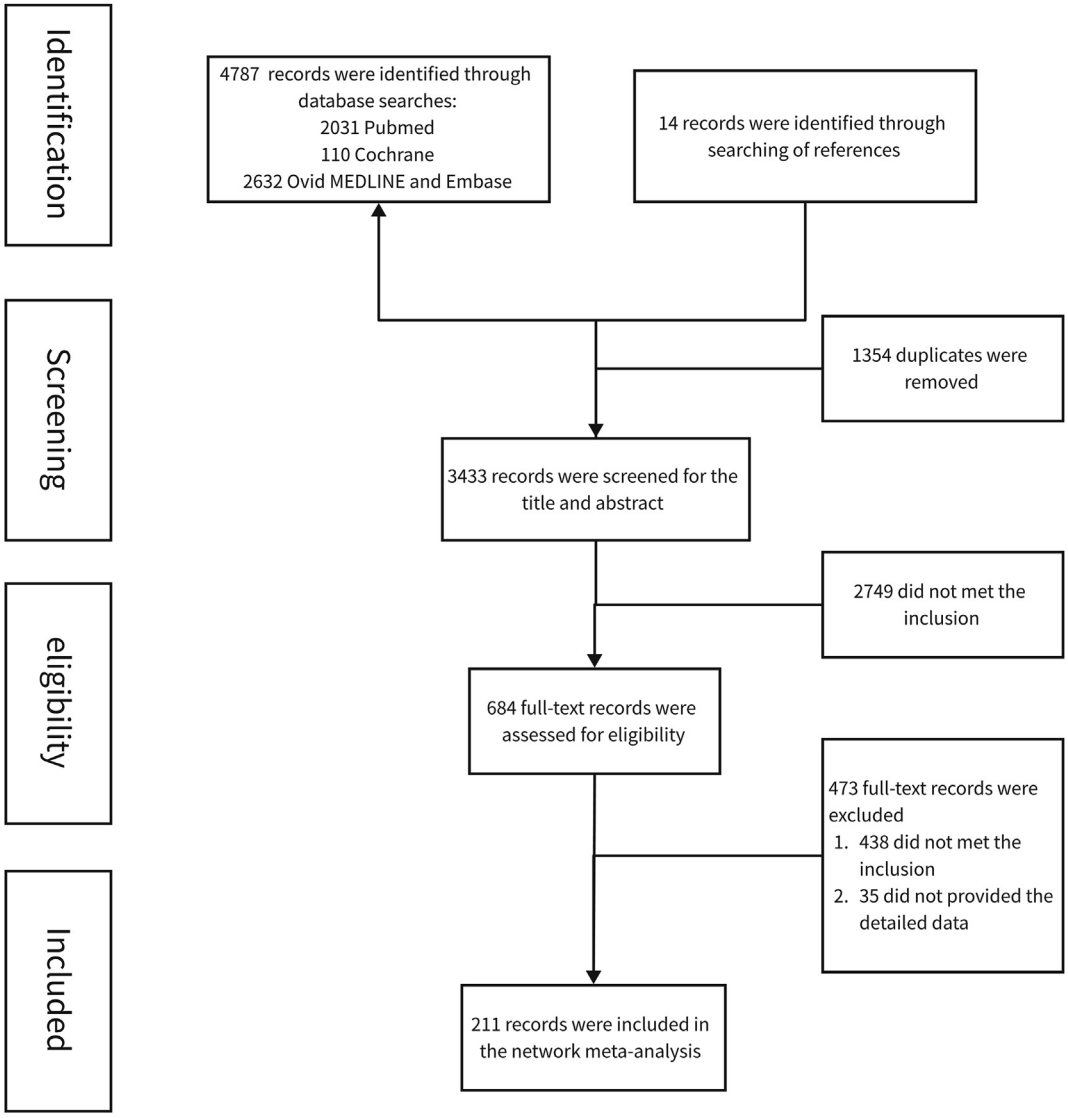

Fig. 1: Flow diagram of the search and inclusion process. The study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.

cores; ipsilateral SB (ips-SB) was defined as the SB only performed on the same side of the Index lesion. Contralateral SB (con-SB) was defined as the SB only performed on the opposite side of the Index lesion (Table 1).

Quality assessment

The assessment of bias for studies are illustrated in Supplementary Figure S2.

Evidence network

In terms of detection rate of PCa, csPCa, and ciPCa, different biopsy schemes were used by a relatively large number of patients. The network structure diagrams, presenting the direct association between different sampling methods, were displayed in Fig. 2.

Inconsistency and heterogeneity test

The node-splitting method and its Bayesian p value were employed to ascertain the discrepancy in the detection rate. No significant discrepancy or qualitative difference was identified in the outcomes of PCa ($p > 0.05$). Nevertheless, when it comes to csPCa and ciPCa, a significant inconsistency was identified in the comparisons of SB+TB vs. saturation SB+TB ($p = 0.032$) and SB vs. saturation TB ($p = 0.016$) for csPCa, and SB+TB vs. SB ($p = 0.014$) and SB+TB vs. con-SB ($p = 0.012$), whereas no significant inconsistency was observed in the remaining comparisons

Biopsy schemes	Definitions	Number of the relevant studies
TB	Defined as <6 cores TB	208
SB	Defined as ≤20 cores	166
SB+TB	Defined as TB combined with SB+TB	177
Saturation TB	Defined as ≥6 cores TB with or without perilesional cores	24
Saturation SB	Defined as >20 cores SB	20
ips-SB	Defined as the SB only performed on the same side of the Index lesion	3
con-SB	Defined as the SB only performed on the opposite side of the Index lesion	4
ips-SB+TB	Defined as ips-SB combined with TB	13
con-SB+TB	Defined as con-SB combined with TB	11
Saturation SB+TB	Defined as saturation SB combined with TB	25
Non-targeted SB+TB	Defined as SB at the non-targeted sector combined with TB	2
adjacent sextant SB	Defined as SB adjacent to the index lesion	1
SB+saturation TB	Defined as SB combined with saturation TB	5

TB, Targeted biopsy; SB, Systematic biopsy.

Table 1: **Summary of the biopsy schemes.**

(Supplementary Figures S3–S5). In addition, the Gelman-Rubin-Brooks plots and Trace and Density Plots were showed in (Supplementary Figures S6–S11). The results showed that the convergence diagnostics across the comparisons of PCa, csPCa, and ciPCa, and indicate that the models have converged well, providing reliable parameter estimates.

The overall model heterogeneity I^2 for PCa, csPCa, and ciPCa was 12%, 8%, and 0%, respectively, indicating low heterogeneity in this study. The analysis of heterogeneity (ANOHE) was performed and the results are shown in the (Supplementary Figures S12–S14).

PCa detection rate

In pairwise meta-analysis (a statistical approach that combines data from multiple studies directly comparing two specific interventions), the detection rate of PCa was significantly lower for TB or SB alone compared to the SB+TB (TB: RR 0.83, 95% CrI 0.82, 0.85; SB: RR 0.83, 95% CrI 0.81, 0.85). Nevertheless, saturation SB+TB and SB+saturation TB had no significant difference in detecting PCa compared with SB+TB (saturation SB+TB: RR 1.0, 95% CrI 0.95, 1.2; SB+saturation TB: RR 1.0, 95% CrI 0.84, 1.3). However, the detection rates of overall PCa were relatively lower for ips-SB+TB and saturation TB than for SB+TB (ips-SB+TB: RR 0.93, 95% CrI 0.86, 1.0; saturation TB: RR 0.94, 95% CrI 0.89, 1.0) (Supplementary Figure S12).

In network meta-analysis (a comprehensive statistical method that integrates both direct and indirect evidence from a network of studies comparing multiple interventions), TB or SB alone still showed significantly lower PCa detection compared to the SB+TB (TB: RR 0.83, 95% CrI 0.81, 0.84; SB: RR 0.82, 95% CrI 0.80, 0.84). Moreover, saturation SB+TB and SB+saturation TB demonstrated no significant difference in detecting PCa compared to SB+TB (saturation SB+TB: RR 1.03, 95% CrI 0.98, 1.09; SB+saturation TB: RR 1.05, 95% CrI 0.94, 1.17). It is notable that ips-SB+TB and saturation TB detected a relatively less PCa than SB+TB (ips-SB+TB: RR 0.94, 95% CrI 0.88, 1.00; saturation TB: RR 0.92, 95% CrI 0.88, 0.97) (Fig. 3 and Supplementary Table S1).

The SUCRA results indicate that the detection rates were highest for SB+saturation TB (0.938), followed by saturation SB+TB (0.926), SB+TB (0.838), and ips-SB+TB (0.607), and the rest of the rankings are detailed in Table 2.

csPCa detection rate

In pairwise meta-analysis, the detection of csPCa was significantly lower when using TB or SB alone compared to SB+TB (TB: RR 0.86, 95% CrI 0.84, 0.88; SB: RR 0.76, 95% CrI 0.74, 0.77). While, there was no significant difference in csPCa detection rates for saturation SB+TB, SB+saturation TB compared to SB+TB (saturation SB+TB: RR 1.4, 95% CrI 0.99, 1.8; SB+saturation TB: RR 1.2, 95% CrI 1.0, 1.4). Nevertheless, there was no significant difference in csPCa detection between ips-SB+TB and SB+TB (ips-SB+TB: RR 0.97, 95% CrI 0.89, 1.1), or between saturation TB and SB+TB (saturation TB: RR 0.98, 95% CrI 0.92, 1.0) (Supplementary Figure S13).

In the network meta-analysis, there was no significant difference in csPCa detection rates for saturation SB+TB, SB+saturation TB, ips-SB+TB, and saturation TB compared to SB+TB (saturation SB+TB: RR 1.0, 95% CrI 0.98, 1.11; SB+saturation TB: RR 1.1, 95% CrI 0.999, 1.3; ips-SB+TB: RR 0.95, 95% CrI 0.88, 1.02; saturation TB: RR 0.96, 95% CrI 0.91, 1.01). And TB and SB alone detected significantly less csPCa than SB+TB (TB: RR 0.86, 95% CrI 0.84, 0.88; SB: RR 0.75, 95% CrI 0.73, 0.77) (Fig. 3 and Supplementary Table S2).

The SUCRA results indicate that the detection rates were highest for SB+saturation TB (0.987), followed by

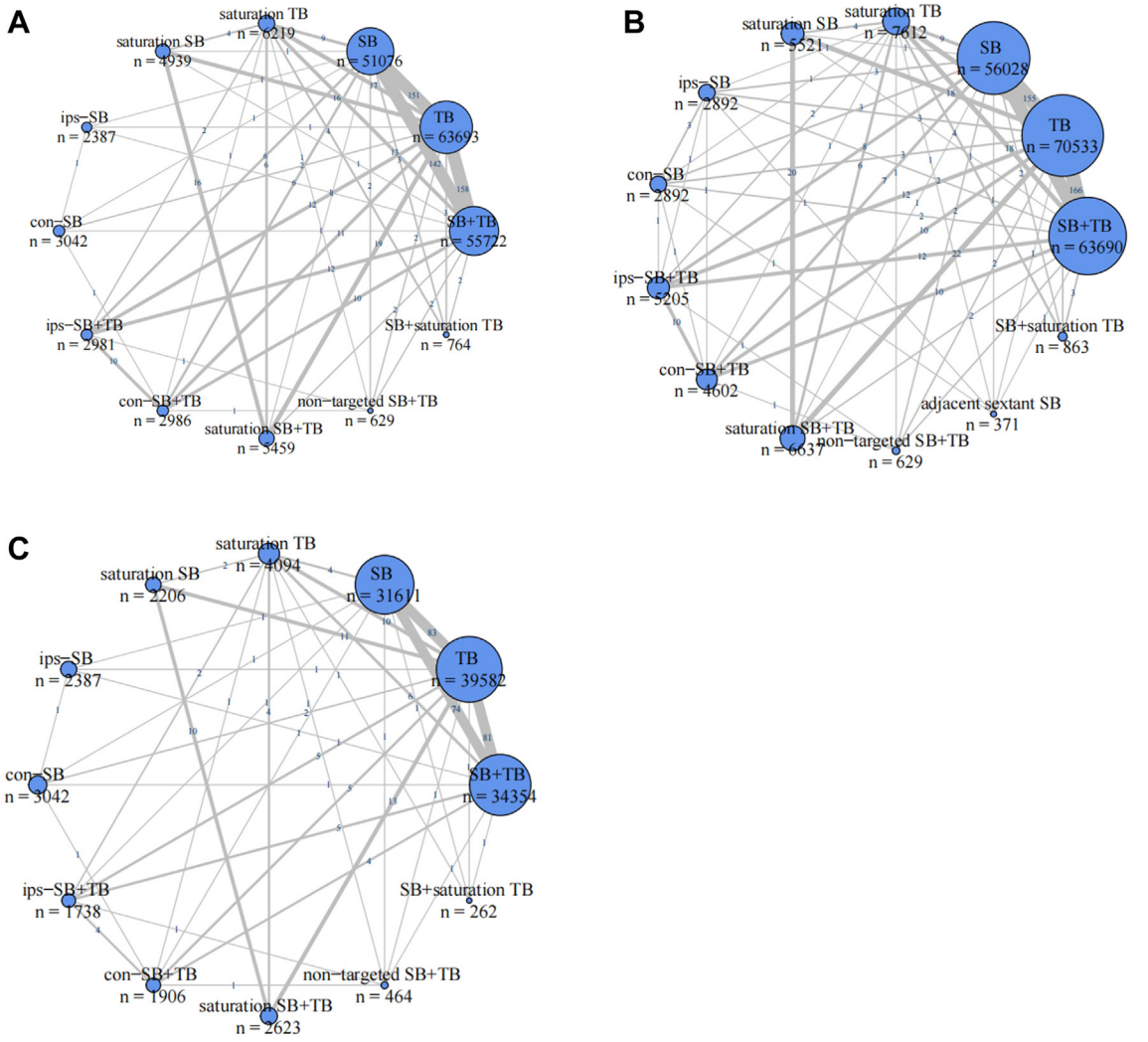

Fig. 2: Network of included studies. A. Analysis of csPCa, B. Analysis of PCa, C. Analysis of ciPCa. (Systematic biopsy (SB) was defined as ≤20 cores SB; Saturation SB were defined as >20 cores SB; Targeted biopsy (TB) was defined as <6 cores TB; Saturation TB was defined as ≥6 cores TB with or without perilesional cores; ipsilateral SB (ips-SB) was defined as the SB only performed on the same side of the Index lesion. Contralateral SB (con-SB) was defined as the SB only performed on the opposite side of the Index lesion.) In Figure 2, the "n" value on each circle represents the number of included patients, and the numbers on the lines connecting the circles denote the number of relevant studies between the corresponding biopsy types.

saturation SB+TB (0.909), SB+TB (0.825), and then saturation TB (0.698), ips-SB+TB (0.672), and the rest of the rankings are detailed in Table 2.

ciPCa detection rate

In pairwise meta-analysis, TB alone detected significantly less ciPCa, compared with SB+TB (RR: 0.68, 95% CrI 0.63, 0.72). Additionally, ips-SB+TB and saturation TB showed a relatively lower detection rate for ciPCa (ips-SB+TB: RR 0.91, 95% CrI 0.72, 1.0; saturation TB: RR 0.88, 95% CrI 0.70, 1.1). Furthermore, SB+saturation TB detected the most of detection rates for ciPCa (RR 1.6, 95% CrI 0.70, 3.7) (Supplementary Figure S14).

In the network meta-analysis, compared with SB+TB, TB alone exhibited significantly less ciPCa detection rate (RR: 0.66, 95% CrI 0.62, 0.70). In addition, ips-SB+TB and saturation TB also demonstrated a comparatively lower detection rate for ciPCa (ips-SB+TB: RR 0.87, 95% CrI 0.72, 1.0; saturation TB: RR 0.76, 95% CrI 0.65, 0.88). While, SB+saturation TB and saturation SB+TB have the highest detection rates for ciPCa (SB+saturation TB: RR 1.54, 95% CrI 0.86, 2.7; saturation SB+TB: RR 1.16, 95% CrI 0.97, 1.39) (Fig. 3 and Supplementary Table S3).

The SUCRA results indicate that the detection rates were highest for SB+saturation TB (0.956), saturation

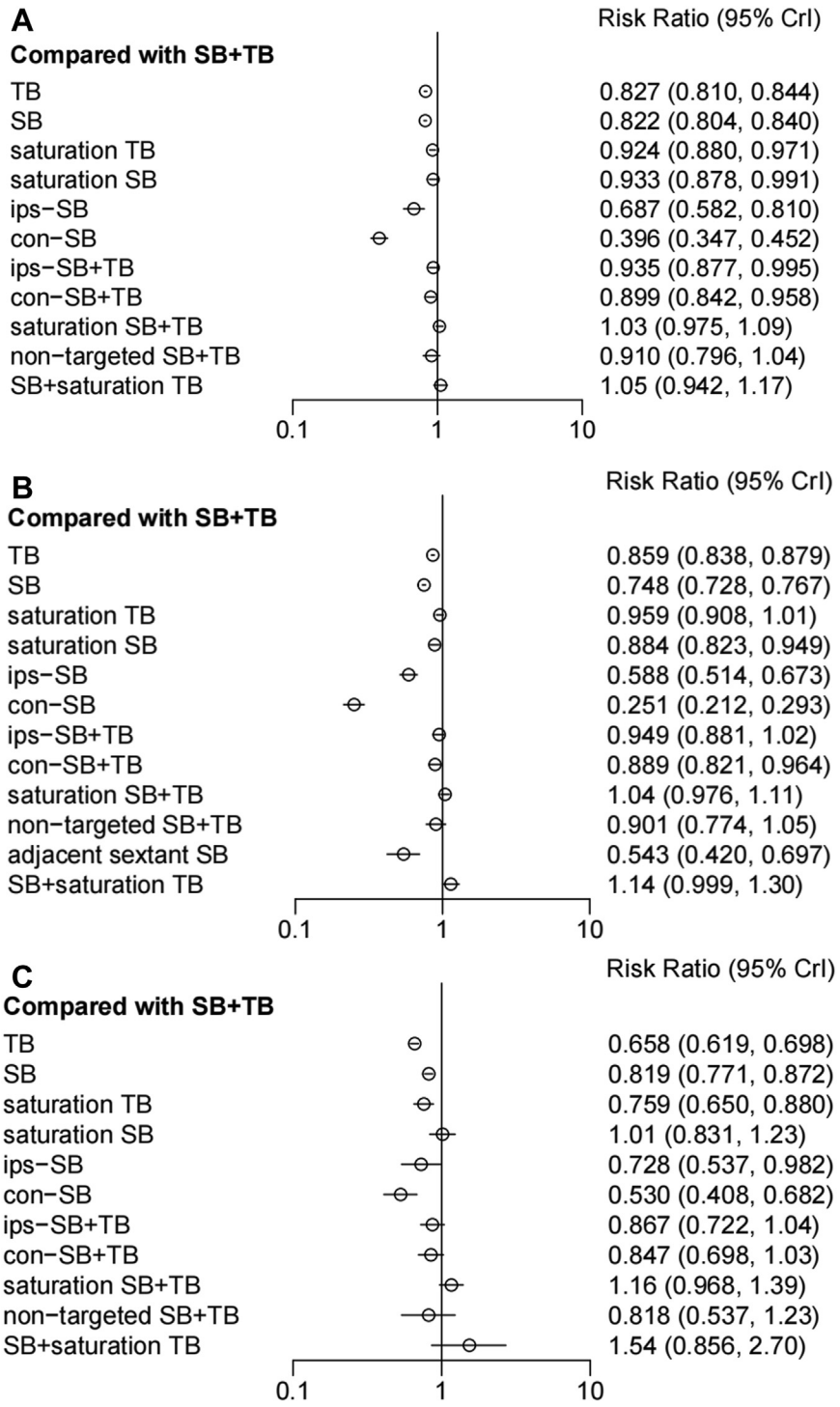

Fig. 3: Forest plot comparing the detection rate A. Analysis of PCa, B. Analysis of csPCa, C. Analysis of ciPCa.

SB+TB (0.906), SB+TB (0.753), followed by saturation SB (0.752), and the rest of the rankings are detailed in Table 2.

Regression analysis and subgroup analysis

In regression analyses, the effects of the four potential sources of heterogeneity on the detection rates for

	PCa		csPCa		ciPCa	
	Biopsy schemes	Cumulative probability	Biopsy schemes	Cumulative probability	Biopsy schemes	Cumulative probability
1	SB+saturation TB	0.938	SB+saturation TB	0.987	SB+saturation TB	0.956
2	Saturation SB+TB	0.926	Saturation SB+TB	0.909	Saturation SB+TB	0.906
3	SB+TB	0.838	SB+TB	0.825	SB+TB	0.753
4	ips-SB+TB	0.607	Saturation TB	0.698	Saturation SB	0.752
5	Saturation SB	0.595	ips-SB+TB	0.672	ips-SB+TB	0.533
6	Saturation TB	0.560	Non-targeted SB+TB	0.542	con-SB+TB	0.492
7	Non-targeted SB+TB	0.520	con-SB+TB	0.495	Non-targeted SB+TB	0.444
8	con-SB+TB	0.457	Saturation SB	0.481	SB	0.436
9	TB	0.252	TB	0.390	Saturation TB	0.308
10	SB	0.215	SB	0.250	ips-SB	0.280
11	ips-SB	0.094	ips-SB	0.143	TB	0.127
12	con-SB	0.000	Adjacent sextant SB	0.108	con-SB	0.012
13			con-SB	0		

Systematic biopsy (SB) was defined as ≤20 cores SB; Saturation SB was defined as >20 cores SB; Targeted biopsy (TB) was defined as <6 cores TB; Saturation TB was defined as ≥6 cores TB with or without perilesional cores; ipsilateral SB (ips-SB) was defined as the SB only performed on the same side of the Index lesion. Contralateral SB (con-SB) was defined as the SB only performed on the opposite side of the Index lesion.

Table 2: **Ranking probability of different biopsy schemes.**

different biopsy strategies were not statistically significant (Supplementary Tables S4–S7).

The subgroup analysis of the network meta-analysis showed that in most subgroups the results were consistent with the overall results, confirming the relative ranking of prostate biopsy methods in terms of prostate cancer detection rates. The best performing methods were consistently the most effective in all subgroups. However, there were discrepancies in the rankings in some specific subgroups (Supplementary Figures S15–S18 and Supplementary Tables S8–S11).

Publication bias

The bias estimates of the analyses of PCa, csPCa, and ciPCa were 0.49 ($p < 0.001$), 0.49 ($p < 0.001$), and 0.02 ($p = 0.13$), respectively. The funnel plots are presented in the Supplementary Figure S19.

Sensitivity analysis

Sensitivity analysis was performed by excluding the studies that enrolled patients with PIRADS/Likert ≤ 2. The results showed excellent consistency with previous studies and lower heterogeneity (csPCa: $I^2 = 1\%$, ciPCa: $I^2 = 0\%$) (Supplementary Figures S20–S28).

Discussion

In this study, we examined 13 types of prostate biopsy schemes applied to patients with suspicious MRI lesions. The results indicated that performing TB or SB alone significantly underestimates csPCa compared to the current standard biopsy scheme (SB+TB), which is consistent with previous studies.[8,28,29] Furthermore, saturation SB+TB and saturation TB+SB were demonstrated to have the highest detection rate for csPCa, though without significant statistical difference with SB+TB. In addition, ips-SB+TB and saturation TB appeared to be the two promising biopsy schemes with non-inferior detection rates of csPCa compared to SB+TB. Both schemes reduce the ciPCa detection rate and avoid unnecessary cores. Furthermore, the saturation biopsy modes including saturation SB, saturation SB+TB, and saturation TB+SB did not show obvious superiority in detecting csPCa compared to SB+TB, which aligns with a previous study showing that having more than 12 cores in SB does not significantly increase cancer detection rates.[30] However, there was an increase in the detection of ciPCa, which may lead to overdiagnosis and overtreatment. The other biopsy schemes con-SB+TB and non-targeted SB+TB, adjacent sextant SB, ips-SB, and con-SB, did not demonstrate the desired PCa detection efficacy and therefore should not be considered as potential alternative schemes.

Notably, in the subgroup analyses, except for some subgroups, where the results are unstable due to the number of studies, the SUCRA ranking of the saturation TB declines significantly in the subgroups that included suspicious lesion with PIRADS/Likert < 3 or applying institutional protocols. These results suggested that saturation TB should be applied with caution in the patients with PIRADS/Likert < 3 lesion or other definition standards.

Previous studies have suggested that MRI/US TB elevates the detection of csPCa while decreasing the detection of ciPCa.[6–8,31] Omitting SB and relying solely on TB would miss a considerable number of patients with csPCa, and SB+TB leads to a higher detection rate of PCa demonstrating the significant added value of both biopsy methods.[6,8,9,31,32] However, with the introduction of the "penumbra" concept, which refers to

biopsy cores taken in the area surrounding an MRI lesion, in recent years, more and more studies have begun to evaluated the added value of SB in order to avoid unnecessary number of biopsy cores and over-diagnosis of PCa.[13,33,34] Some recent studies have emphasized the minimal value of con-SB in terms of cancer detection and upgrading rates.[10,14,15,17,35,36] Zambon et al. revealed that the added value of con-SB was 1.9% (2/103), 3.1% (5/163), and 0% (0/105) for PI-RADS 3, PI-RADS 4, and PI-RADS 5 lesions.[15] Bourgeno et al. recruited 4841 consecutive patients to assess the additional benefit of side-specific SB in csPCa detection, and the added values for detecting csPCa were 5.8%, 4.2%, and 2.8% for SB, ips-SB and con-SB, respectively.[35] Only 35 (1.5%) patients had csPCa on con-SB exclusively. These, studies provide the feasibility of ips-SB+TB as the potential alternative to SB+TB.

In addition, Brisbane et al. indicated that 90% of biopsy cores containing csPCa were located within a 1 cm circumferential area, with variations based on MRI grading score.[34] And Raman et al. discovered that conducting MRI-targeted and perilesional biopsies within a 2 cm circumferential area detected 98% of csPCa, requiring 3.7 fewer biopsy cores per patient compared to SB+TB.[33] Furthermore, Lee et al. found that overlap cores within the suspicious lesion increased the likelihood of detecting csPCa nearly twofold compared to the perilesional cores, regardless of the PI-RADS score assigned. The inclusion of both overlapping and perilesional cores improved the diagnostic accuracy of targeted biopsy for identifying csPCa without increasing the risk of detecting ciPCa.[19] These studies highlighted the importance of conducting perilesional biopsies for suspicious lesions, with saturation TB being one of the prominent approaches in this regard.

However, several studies have indicated that the significant false negative rate of mpMRI, along with inconsistent interpretation of suspicious MRI lesions and lack of standardized biopsy protocols, could impede the successful adoption and widespread use of RB.[6,36–38] This situation may lead to the underdiagnosis of patients with csPCa. Few biopsy models have been developed to assist physicians in identifying patients who could avoid additional SB. Nakanishi et al. proposed that patients with unilateral intraprostatic lesions and any of three predictive variables (age ≥75 years, PI-RADS score ≥ 4, and PSAD ≥ 0.3) were at higher risk of having contralateral csPCa and would benefit from performing SB+TB.[39] Noujeim et al. introduced a model categorizing patients into 'low risk' (PI-RADS 3), 'intermediate risk' (PI-RADS 4 or PI-RADS 5 and PSAD < 0.15), and 'high risk' (PI-RADS 5 and PSAD ≥ 0.15) for detecting csPCa in biopsies taken more than 10 mm away from the MRI lesion.[40] While more widely accepted and validated models need to be proposed and further researched.[35,41]

To the best of our knowledge, this study represents the first network meta-analysis to comprehensively examined the current biopsy schemes for MRI-positive patients. However, it should be noted that this study also had some limitations. Firstly, the studies focused on the ips-SB+TB mainly included patients with unilateral suspicious lesions. Consequently, the efficacy of ips-SB+TB in the broader population of patients with suspicious lesions requires further investigation. Secondly, the asymmetric funnel plot revealed a publication bias in the NMA analysis of detection rates, which may have affected the final results. This may be attributed to the inclusion of disparate populations in the included studies, as well as to the varying biopsy criteria and protocols employed. Thirdly, only one randomized controlled trial was included in this study, with the remainder comprising cohort studies, this may introduce potential bias. Fourthly, the potential bias may be introduced by inconsistency in MRI interpretation across studies, variability in biopsy procedures (e.g., biopsy route, targeted biopsy fusion technique, etc.) and different demographic characteristics (e.g., PSA, prostate volume, etc.), these factors represent a significant challenge in the interpretation of the results. However, except for some factors (e.g., prostate volume, PSA) that could not be analyzed in the study, others, such as different biopsy route, targeted biopsy fusion technique, have been shown in subsequent studies to have a non-significant effect on the PCa detection rate.[42–44] We also performed meta regression and subgroup analyses for some crucial factors. Nonetheless, the degree of heterogeneity across studies was minimal and result were consistent in most subgroups. Fifthly, whether a patient has a first biopsy or not affects the PCa detection rate, and there is a lack of research on RB in patients with repeated biopsies. However, even in studies where repeat biopsy represents the primary population, RB still results in patient benefit and biopsy history does not affect the added value of SB for patients.[15,17,35] Finally, pathological review may play an important role in detecting csPCa, since the majority of the studies did not include pathological results from prostatectomy, it is not possible to make a comparison the pathological consistency of RB and prostatectomy.[45]

In conclusion, the network meta-analysis reveals that, while saturation SB+TB and SB+saturation TB have the highest detection rates for csPCa, there is no significant difference in csPCa detection between them and SB+TB. Meanwhile, ips-SB+TB and saturation TB are effective biopsy strategies for MRI-positive PCa patients. These two approaches not only show non-inferior csPCa detection rates relative to SB+TB but also reduce the detection of ciPCa, offering a more targeted approach for detecting csPCa.

Contributors

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Data sharing statement

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

Declaration of interests

The authors have stated that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103164.

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