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Diagnostic accuracy of Truenat and Xpert for diagnosing pulmonary tuberculosis using mycobacterial culture as the reference standard: a systematic review and meta-analysis

Anas Afandi[1], Andiesta Asriyah Mariam Saman[1], Aryati[2*], Puspa Wardhani[2]

[1]Basic Medical Science, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia.
[2]Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia.

ARTICLE INFO

ORCID of all authors

Anas Afandi: https://orcid.org/0009-0001-0707-0672
Andiesta Asriyah Mariam Saman: https://orcid.org/0009-0002-8322-7544
Aryati: https://orcid.org/0000-0002-9383-6354
Puspa Wardhani: https://orcid.org/0000-0003-2202-8090

Correspondence

Aryati
Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia.
Email: aryati@fk.unair.ac.id

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ABSTRACT

Background: Rapid molecular assays are important for improving the timely diagnosis of pulmonary tuberculosis. Truenat and Xpert include several assay variants with diagnostic performance that may vary across populations, testing procedures, and clinical settings.

Objectives: This systematic review and meta-analysis aimed to summarize the diagnostic accuracy of Truenat and Xpert assays for detecting pulmonary tuberculosis using mycobacterial culture as the reference standard, and to compare the pooled diagnostic performance of Truenat versus Xpert.

Materials and methods: PubMed, Scopus, ScienceDirect, SpringerLink, and ProQuest were searched from database inception to 29 September 2026. Eligible studies evaluated at least one Truenat assay and one Xpert assay within the same participant cohort or paired specimen set and provided sufficient data to construct separate 2×2 contingency tables against mycobacterial culture. Pooled sensitivity and specificity with 95% confidence intervals (CIs) were estimated using bivariate random-effects models. Assay-variant subgroup analyses were conducted, and methodological quality was assessed using an adapted QUADAS-2 framework.

Results: Thirteen studies comprising 14 independent cohorts were included. The primary analyses included 14 Truenat and 14 Xpert datasets. Truenat had a pooled sensitivity of 0.87 (95% CI, 0.83–0.90) and specificity of 0.94 (95% CI, 0.89-0.97), with a bivariate I^2 of 64.2%. Xpert had a pooled sensitivity of 0.92 (95% CI, 0.88-0.95) and specificity of 0.97 (95% CI, 0.93-0.99), with a bivariate I^2 of 74.1%. Subgroup estimates were broadly similar across the variants within each platform. Risk-of-bias concerns were most frequent in the flow and timing domain. No formal statistical comparison was performed between the two platforms.

Conclusion: Both Truenat and Xpert demonstrated high pooled diagnostic accuracy for pulmonary tuberculosis. Xpert produced numerically higher pooled sensitivity and specificity, but the separate platform-specific analyses did not establish its superiority over Truenat. The heterogeneity observed in both analyses indicates that assay performance may vary across study populations and testing conditions. Platform selection should therefore consider diagnostic accuracy together with operational feasibility, infrastructure requirements, and the intended testing setting.

Introduction

Tuberculosis (TB) remains a major global health burden. According to the World Health Organization (WHO) Global Tuberculosis Report 2025, an estimated 10.7 million people developed TB and 1.23 million died from the disease in 2024.[1] In the same year, 8.3 million people were newly diagnosed with TB and accessed treatment, representing approximately 78% of those estimated to have developed the disease.[1] This diagnostic gap underscores the need for timely diagnosis and broader access to WHO-recommended rapid molecular tests for people being evaluated for pulmonary TB.[2]

Mycobacterial culture is commonly used as the microbiological reference standard in diagnostic accuracy studies of pulmonary TB.[3] Culture may require several weeks to produce a result, limiting its usefulness for timely clinical decisions.[3] A negative culture result does not necessarily exclude TB, particularly when bacillary burden is low or specimen quality and processing affect organism recovery.[4] These limitations should be considered when interpreting the accuracy of molecular assays against culture.

Nucleic acid amplification tests can detect *Mycobacterium tuberculosis* complex DNA directly from sputum within hours.[3] Xpert MTB/RIF and Xpert MTB/RIF Ultra use the GeneXpert platform and are among the molecular assays recommended for initial testing for pulmonary TB.[2,3] Molecular detection does not establish bacillary viability. A molecular-positive/culture-negative result may therefore reflect residual DNA after previous TB treatment or failure of viable organisms to grow in culture.[4,5] Conversely, molecular assays may produce false-negative results when the specimen contains a low bacillary burden. Interpretation of discordant results requires consideration of the limitations of both the index test and culture, together with the patient's clinical findings and TB treatment history.[4,5]

Truenat MTB and Truenat MTB Plus use chip-based assays and portable, battery-capable equipment to detect *M. tuberculosis* complex DNA in sputum.[3] These operational characteristics can support testing in peripheral laboratories with limited infrastructure.[3] WHO recommends Truenat MTB and Truenat MTB Plus as options for initial testing for pulmonary TB, followed by Truenat MTB-RIF Dx when rifampicin-resistance testing is required.[2] Published diagnostic evaluations have included different Truenat variants, testing workflows, patient populations, and clinical settings, which may contribute to variation in reported accuracy.

Differences in assay variants, study populations, specimen procedures, and reference culture methods complicate the interpretation of pooled estimates across unrelated sets of studies.

To improve comparability, this systematic review and meta-analysis included studies that evaluated at least one eligible Truenat assay and one eligible Xpert assay within the respective study cohorts, using mycobacterial culture as the reference standard. The

sensitivity and specificity of the two platforms were synthesized in separate meta-analyses. Differences between the pooled estimates were described without a formal statistical comparison or inference of superiority between platforms.

Materials and methods

Protocol and reporting standards

This systematic review and meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) guideline.[6] The study selection process was presented using a PRISMA 2020 flow diagram.[7] The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420261373894.

Eligibility criteria

Studies were eligible if they 1) enrolled adolescents or adults undergoing initial diagnostic evaluation for suspected pulmonary tuberculosis, 2) evaluated at least one eligible Truenat assay and at least one eligible Xpert assay within the same participant cohort or paired specimen set, 3) evaluated both index tests against solid or liquid mycobacterial culture, or a combination of both, 4) reported sufficient data to construct separate 2×2 contingency tables for Truenat versus culture and Xpert versus culture, 5) used sputum specimens, either alone or combined with a respiratory swab, 6) used a prospective or retrospective cohort, cross-sectional diagnostic accuracy, or other head-to-head comparative diagnostic accuracy design, and 7) were available as full-text peer-reviewed articles or preprints in English.

Studies were excluded if they 1) evaluated only Truenat or only Xpert, 2) evaluated Truenat and Xpert in different or non-overlapping participant groups, 3) evaluated extrapulmonary tuberculosis exclusively or did not report pulmonary tuberculosis data separately, 4) used non-sputum specimens exclusively, including tongue or oral swabs, 5) focused exclusively on rifampicin or other drug-resistance detection, 6) assessed treatment response or treatment monitoring rather than initial diagnosis, 7) used only a non-culture reference standard or did not report separately extractable culture-based results, or 8) did not provide sufficient data to construct a 2×2 table for either index test. Pediatric-only studies, conventional case-control studies, reviews, systematic reviews, meta-analyses, editorials, letters, case reports, case series, protocols, guidelines, animal studies, analytical studies using contrived specimens, and conference abstracts without extractable full data were also excluded. For duplicate reports or studies with overlapping populations, the most complete peer-reviewed report was retained. Complementary reports containing unique eligible data were linked and treated as a single study.

Information sources and search strategy

A systematic literature search was conducted in PubMed, Scopus, ScienceDirect, SpringerLink, and ProQuest from database inception to 29 September 2026. The search combined terms related to pulmonary tuberculosis, Truenat, Xpert, diagnostic accuracy, and mycobacterial culture. The Truenat and Xpert concepts were combined using the Boolean operator AND to identify studies evaluating both test platforms, while synonyms within each concept were combined using OR. Search terms included “tuberculosis,” “pulmonary tuberculosis,” “Mycobacterium tuberculosis,” “Truenat,” “Truenat MTB,” “Truenat MTB Plus,” “Truenat MTB Ultima,” “Xpert,” “GeneXpert,” “Xpert MTB/RIF,” “Xpert MTB/RIF Ultra,” “diagnostic accuracy,” “diagnostic performance,” “sensitivity,” “specificity,” “culture,” “MGIT,” and “Löwenstein–Jensen.” Search syntax was adapted to the requirements of each database. Searches were restricted to English-language reports, and filters for articles or research articles were applied where available. No publication-year restriction was imposed. Additional eligible studies were identified by manually searching relevant websites, preprint servers, and the reference lists of eligible reports. The complete database-specific search strategies and numbers of records retrieved are provided in Table 1.

Table 1. Search Strategy.

Database	Search strategy	Records retrieved
ProQuest	((“pulmonary tuberculosis” **OR** tuberculos* **OR** “Mycobacterium tuberculosis”) **AND** (Truenat **OR** “Truenat MTB” **OR** “Truenat MTB Plus” **OR** “Truenat MTB Ultima”) **AND** (Xpert **OR** GeneXpert **OR** “Xpert MTB/RIF” **OR** “Xpert MTB RIF” **OR** “Xpert MTB/RIF Ultra” **OR** “Xpert MTB RIF Ultra” **OR** “Xpert Ultra” **OR** “GeneXpert MTB/RIF” **OR** “GeneXpert MTB/RIF Ultra”) **AND** (“diagnostic accuracy” **OR** “diagnostic performance” **OR** sensitiv* **OR** specificit*) **AND** (cultur* **OR** “mycobacterial culture” **OR** MGIT **OR** “Mycobacteria Growth Indicator Tube” **OR** “BACTEC MGIT 960” **OR** “Lowenstein-Jensen” **OR** “Löwenstein-Jensen” **OR** “solid culture” **OR** “liquid culture”)) Document type: Article; Language: English (Search date: **29 September 2026**)	176
SpringerLink	((“pulmonary tuberculosis” **OR** tuberculos* **OR** “Mycobacterium tuberculosis”) **AND** (Truenat **OR** “Truenat MTB” **OR** “Truenat MTB Plus” **OR** “Truenat MTB Ultima”) **AND** (Xpert **OR** GeneXpert **OR** “Xpert MTB/RIF” **OR** “Xpert MTB RIF” **OR** “Xpert MTB/RIF Ultra” **OR** “Xpert MTB RIF Ultra” **OR** “Xpert Ultra” **OR** “GeneXpert MTB/RIF” **OR** “GeneXpert MTB/RIF Ultra”) **AND** (“diagnostic accuracy” **OR** “diagnostic performance” **OR** sensitiv* **OR** specificit*) **AND** (cultur* **OR** “mycobacterial culture” **OR** MGIT **OR** “Mycobacteria Growth Indicator Tube” **OR** “BACTEC MGIT 960” **OR** “Lowenstein-Jensen” **OR** “Löwenstein-Jensen” **OR** “solid culture” **OR** “liquid culture”)) Content type: Article, Research article; Language: English (Search date: **29 September 2026**)	84
Scopus	TITLE-ABS-KEY ((“pulmonary tuberculosis” **OR** tuberculos* **OR** “Mycobacterium tuberculosis”) **AND** (Truenat **OR** “Truenat MTB” **OR** “Truenat MTB Plus” **OR** “Truenat MTB Ultima”) **AND** (Xpert **OR** GeneXpert **OR** “Xpert MTB/RIF” **OR** “Xpert MTB RIF” **OR** “Xpert MTB/RIF Ultra” **OR** “Xpert MTB RIF Ultra” **OR** “Xpert Ultra” **OR** “GeneXpert MTB/RIF” **OR** “GeneXpert MTB/RIF Ultra”) **AND** (“diagnostic accuracy” **OR** “diagnostic performance” **OR** sensitiv* **OR** specificit*) **AND** (cultur* **OR** “mycobacterial culture” **OR** MGIT **OR** “Mycobacteria Growth Indicator Tube” **OR** “BACTEC MGIT 960” **OR** “Lowenstein-Jensen” **OR** “Löwenstein-Jensen” **OR** “solid culture” **OR** “liquid culture”)) **AND** (LIMIT-TO (DOCTYPE , “ar”)) **AND** (LIMIT-TO (LANGUAGE , “English”)) (Search date: **29 September 2026**)	35
ScienceDirect	tuberculosis **AND** Truenat **AND** (Xpert **OR** GeneXpert) **AND** (“diagnostic accuracy” **OR** sensitivity **OR** specificity) **AND** (culture **OR** MGIT) Article type: Research articles; Language: English (Search date: **29 September 2026**)	65
PubMed	(“Tuberculosis, Pulmonary”[Mesh] **OR** “pulmonary tuberculosis”[tiab] **OR** tuberculos*[tiab] **OR** “Mycobacterium tuberculosis”[tiab]) **AND** (Truenat[tiab] **OR** “Truenat MTB”[tiab] **OR** “Truenat MTB Plus”[tiab] **OR** “Truenat MTB Ultima”[tiab]) **AND** (Xpert[tiab] **OR** GeneXpert[tiab] **OR** “Xpert MTB/RIF”[tiab] **OR** “Xpert MTB RIF”[tiab] **OR** “Xpert MTB/RIF Ultra”[tiab] **OR** “Xpert MTB RIF Ultra”[tiab] **OR** “Xpert Ultra”[tiab] **OR** “GeneXpert MTB/RIF”[tiab] **OR** “GeneXpert MTB/RIF Ultra”[tiab]) **AND** (“Sensitivity and Specificity”[Mesh] **OR** “diagnostic accuracy”[tiab] **OR** “diagnostic performance”[tiab] **OR** sensitiv*[tiab] **OR** specificit*[tiab]) **AND** (cultur*[tiab] **OR** “mycobacterial culture”[tiab] **OR** MGIT[tiab] **OR** “Mycobacteria Growth Indicator Tube”[tiab] **OR** “BACTEC MGIT 960”[tiab] **OR** “Lowenstein-Jensen”[tiab] **OR** “Löwenstein-Jensen”[tiab] **OR** “solid culture”[tiab] **OR** “liquid culture”[tiab]) Language: English (Search date: **29 September 2026**)	32

Study selection

Records identified through database and manual searches were combined, and duplicate records were removed. Two reviewers (AA and AS) independently screened titles and abstracts against the eligibility criteria. The same reviewers then independently assessed the full texts of potentially eligible reports and recorded the reasons for exclusion. Any disagreements were resolved through discussion and consensus.

Data extraction

Two reviewers (AA and AS) independently extracted data using a standardized form. Extracted variables included first author, publication year, country, study design, clinical setting, specimen type, sample size, index test and assay variant, reference standard, and the numbers of true positives (TP), false positives (FP), true negatives (TN), and false negatives (FN). When a study did not report a complete 2×2 contingency table, these counts were reconstructed when the reported diagnostic accuracy estimates and corresponding denominators provided sufficient information. Data for Truenat and Xpert were extracted separately against mycobacterial culture. When a study evaluated more than one eligible assay variant, each variant was initially extracted as a separate assay-specific test arm. Non-overlapping participant cohorts reported within the same study were also extracted separately. Disagreements in the extracted data were resolved through discussion and consensus.

Index tests and reference standards

The index tests were molecular assays from the Truenat and Xpert platforms for detecting pulmonary tuberculosis. Eligible Truenat assays included Truenat MTB, Truenat MTB Plus, and Truenat MTB Ultima, including its multiplex configuration when used for MTB detection. Eligible Xpert assays included Xpert MTB/RIF and Xpert MTB/RIF Ultra. The specific assay variant evaluated in each study was recorded separately. For platform-level analyses, eligible Truenat variants were classified as Truenat assays and eligible Xpert variants were classified as Xpert assays. When multiple assay variants from the same platform were evaluated within the same participant cohort, only the most recent eligible variant was included in the primary platform-level analysis to avoid double-counting participants. The alternative variants were retained for variant-specific subgroup and sensitivity analyses.

The reference standard was mycobacterial culture, including solid culture using Löwenstein-Jensen medium, liquid culture using the Mycobacteria Growth Indicator Tube (MGIT), or a combination of both methods. When a study reported diagnostic accuracy against more than one reference standard, only data calculated against mycobacterial culture were extracted and analyzed. Studies using only non-culture reference standards, including smear microscopy, molecular tests, clinical diagnosis, or composite reference standards without separately extractable culture-based results, were excluded.

Risk of bias assessment

The methodological quality of the included studies was assessed independently by two reviewers (AA and AS) using an adapted Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) framework. Risk of bias was evaluated across four domains: patient selection, index test, reference standard, and flow and timing. Each domain was classified as low risk, high risk, or no information based on the QUADAS-2 signaling questions and the information reported in each study. A rating of no information was assigned when the study report did not provide sufficient information to permit a risk-of-bias judgment. Disagreements were resolved through discussion and consensus.

Statistical analysis

Separate meta-analyses were conducted for Truenat and Xpert assays, with mycobacterial culture as the reference standard. True-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) counts were used to calculate study-level sensitivity and specificity. Primary pooled sensitivity and specificity with 95% confidence intervals (CIs) were jointly estimated using a bivariate random-effects model in Meta-DiSc 2.0. Separate univariate random-effects models were used to generate forest plots and pooled univariate estimates for sensitivity and specificity. The bivariate estimates were used as the primary summary measures, whereas the univariate estimates were presented in the forest plots for visual description.

Each independent participant cohort contributed one Truenat estimate and one Xpert estimate to the primary platform-level analyses. When multiple assay variants from the same platform were evaluated in the same participant cohort, only the most recent eligible variant was included in the primary analysis to avoid double-counting participants. Alternative variants were retained for variant-specific subgroup analyses. Non-overlapping participant cohorts reported within the same study were analyzed separately.

Receiver operating characteristic (ROC) plots were used to display the study-level pairs of sensitivity and specificity. Summary receiver operating characteristic (SROC) curves derived from the bivariate model, including confidence and prediction regions, were used to summarize diagnostic performance across studies. Heterogeneity was summarized separately for sensitivity and specificity using univariate I^2 statistics and jointly using the bivariate I^2 statistic. Subgroup analyses were conducted according to the specific Truenat and Xpert assay variants. Pooled estimates for the two platforms were presented separately and interpreted descriptively because no formal statistical test of superiority between Truenat and Xpert was performed.

Results

Study selection

Database searches identified 392 records. After 89 duplicate records were removed, 303 database records underwent title and abstract screening, of which 287 were excluded. Sixteen reports identified through database searches and one additional report identified through manual searching were assessed for eligibility in full text. Four reports were excluded, resulting in 13 studies being included in the systematic review and meta-analysis. The study selection process is presented in Figure 1.

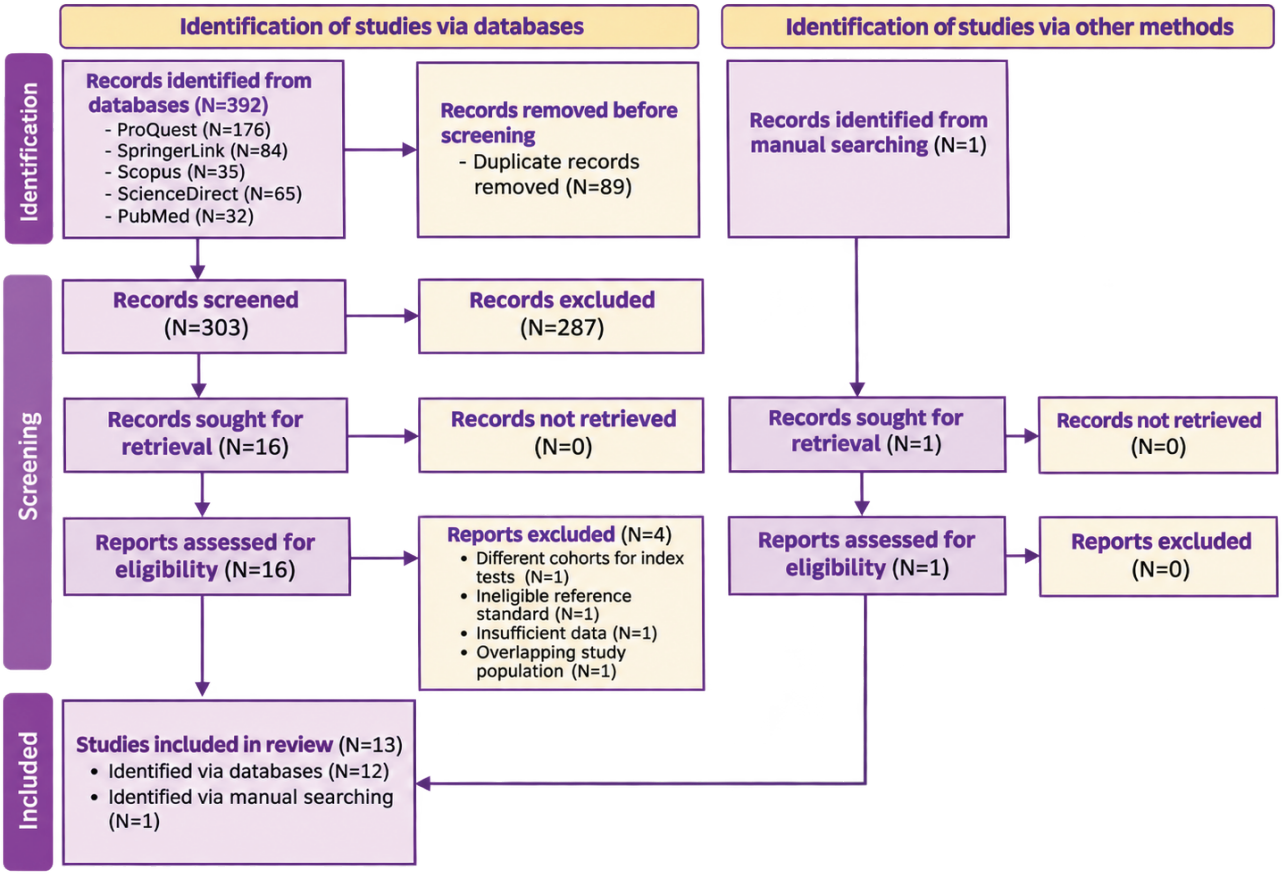


Figure 1. The study selection process.

Study characteristics

Thirteen studies conducted across nine countries were included. Most used prospective or cross-sectional diagnostic accuracy designs, while one used a retrospective design. All studies evaluated at least one eligible Truenat assay and one eligible Xpert assay against mycobacterial culture within the same participant cohort. The reference standards included solid Löwenstein-Jensen culture, liquid MGIT culture, or a combination of both. Penn-Nicholson *et al.*[10] reported two geographically distinct cohorts, resulting in 14 independent participant cohorts across the 13 studies. Across all extracted assay variants, the studies contributed 17 Truenat and 14 Xpert assay-specific 2×2 tables. Most assays were evaluated using sputum specimens. In Steadman *et al.*,[17] Truenat MTB Ultima was evaluated using sputum swabs prepared from collected sputum, while Tootla *et al.*[20] evaluated the Truenat MTB Ultima/COVID-19 multiplex assay using a combined sputum and nasopharyngeal-swab specimen. Xpert MTB/RIF Ultra was performed directly on sputum in both studies.

The analyzed sample size represented the number of participants or specimens contributing to each assay-specific 2×2 table rather than the total number enrolled. Differences in sample size between assays reflected the availability of valid index-test and culture results and study-specific exclusions. Gomathi *et al.*[9] reported specimen-level data, with some participants contributing more than one specimen. Penn-Nicholson *et al.*[10] and Abdulgader *et al.*[14] evaluated multiple Truenat variants in overlapping participant groups. To avoid including dependent datasets in the same platform-level analysis, only the latest-generation eligible Truenat variant from each independent cohort was included in the primary analysis. Consequently, the primary platform-level analyses included 14 Truenat and 14 Xpert datasets. Additional data-reconstruction procedures and discrepancies between extracted counts and reported accuracy estimates are described in the notes accompanying Table 2. Detailed study characteristics are presented in Table 2.

Table 2. Characteristics of included studies.

Author, year	Country	Study design	Reference standard	Index test	Specimen type	N analyzed	TP	FP	TN	FN
Nikam, 2014	India	Retrospective	Liquid MGIT culture	Truenat MTB	Sputum	274	142	58	65	9
				Xpert MTB/RIF	Sputum	274	135	59	64	16
Gomathi, 2020	India	Cross-sectional multicentre	Löwenstein–Jensen and MGIT 960 cultures	Truenat MTB	Sputum	2623	831	441	1241	110
				Xpert MTB/RIF	Sputum	2623	750	222	1460	191
Penn-Nicholson, 2021 (a)	India, Ethiopia, and Papua New Guinea	Prospective multicentre	Löwenstein–Jensen and MGIT cultures	Truenat MTB	Sputum	1162	208	25	884	45
				Truenat MTB Plus	Sputum	1162	222	43	866	31
				Xpert MTB/RIF	Sputum	1162	217	27	882	36
Penn-Nicholson, 2021 (b)	Peru			Truenat MTB	Sputum	378	67	2	283	26
				Truenat MTB Plus	Sputum	378	73	7	278	20
				Xpert MTB/RIF Ultra	Sputum	378	88	8	277	5
Ngangue, 2022	Cameroon	Prospective multisite	Löwenstein–Jensen and MGIT cultures	Truenat MTB Plus	Sputum	945	228	31	663	23
				Xpert MTB/RIF	Sputum	945	227	10	684	24
Barik, 2024	India	Cross-sectional	Liquid MGIT culture	Truenat MTB	Sputum	392	22	4	358	8
				Xpert MTB/RIF	Sputum	392	28	0	362	2
Ssengooba, 2024	Uganda	Cross-sectional	Löwenstein–Jensen and/or MGIT cultures	Truenat MTB	Sputum	242	59	10	159	14
				Xpert MTB/RIF Ultra	Sputum	238	65	15	153	5
Abdulgader, 2025	South Africa	Prospective	MGIT 960 culture	Truenat MTB Ultima	Sputum	447	148	43	240	16
				Truenat MTB Plus	Sputum	412	136	12	239	25
				Xpert MTB/RIF Ultra	Sputum	498	161	16	307	14
Melo, 2025	Brazil	Prospective multicentre	MGIT culture	Truenat MTB Plus	Sputum	277	80	1	166	30
				Xpert MTB/RIF Ultra	Sputum	276	87	1	164	24
Muthaiah, 2025	India	Prospective	MGIT culture	Truenat MTB	Sputum	350	275	5	50	20
				Xpert MTB/RIF	Sputum	350	294	2	50	4
Steadman, 2025	India, Uganda, and Vietnam	Prospective cross-sectional multi-country	MGIT 960 culture	Truenat MTB Ultima	Sputum swab	180	44	3	129	4
				Xpert MTB/RIF Ultra	Sputum	175	47	2	126	0

Table 2. Characteristics of included studies (continued).

Author, year	Country	Study design	Reference standard	Index test	Specimen type	N analyzed	TP	FP	TN	FN
Mehta, 2026	India	Prospective	MGIT 960 culture	Truenat MTB Plus	Sputum	51	32	0	15	4
				Xpert MTB/RIF	Sputum	51	30	0	15	6
Sidiq, 2026	India	Prospective cross-sectional	BACTEC MGIT 960 culture	Truenat MTB Plus	Sputum	596	86	50	453	7
				Xpert MTB/RIF Ultra	Sputum	633	96	24	511	2
Tootla, 2026	Uganda, Peru, South Africa, India	Prospective multicentre	Löwenstein–Jensen and MGIT cultures	Truenat MTB Ultima	Sputum + nasopharyngeal swab	1906	347	49	1438	72
				Xpert MTB/RIF Ultra	Sputum	1906	387	56	1431	32

Note: TP: true positive, FP: false positive, TN: true negative, FN: false negative.

Risk of bias assessment

Risk-of-bias concerns were most frequent in the flow and timing domain, in which nine studies were rated as high risk, two as low risk, and two as having insufficient information. In the patient selection domain, four studies were rated as high risk, seven as low risk, and two as having insufficient information. The index test domain was rated as low risk in 12 studies and high risk in one study. For the reference standard domain, eight studies were rated as low risk, and five had insufficient information, with none rated as high risk. Study-level judgments and the distribution of ratings across domains are presented in Figure 2.

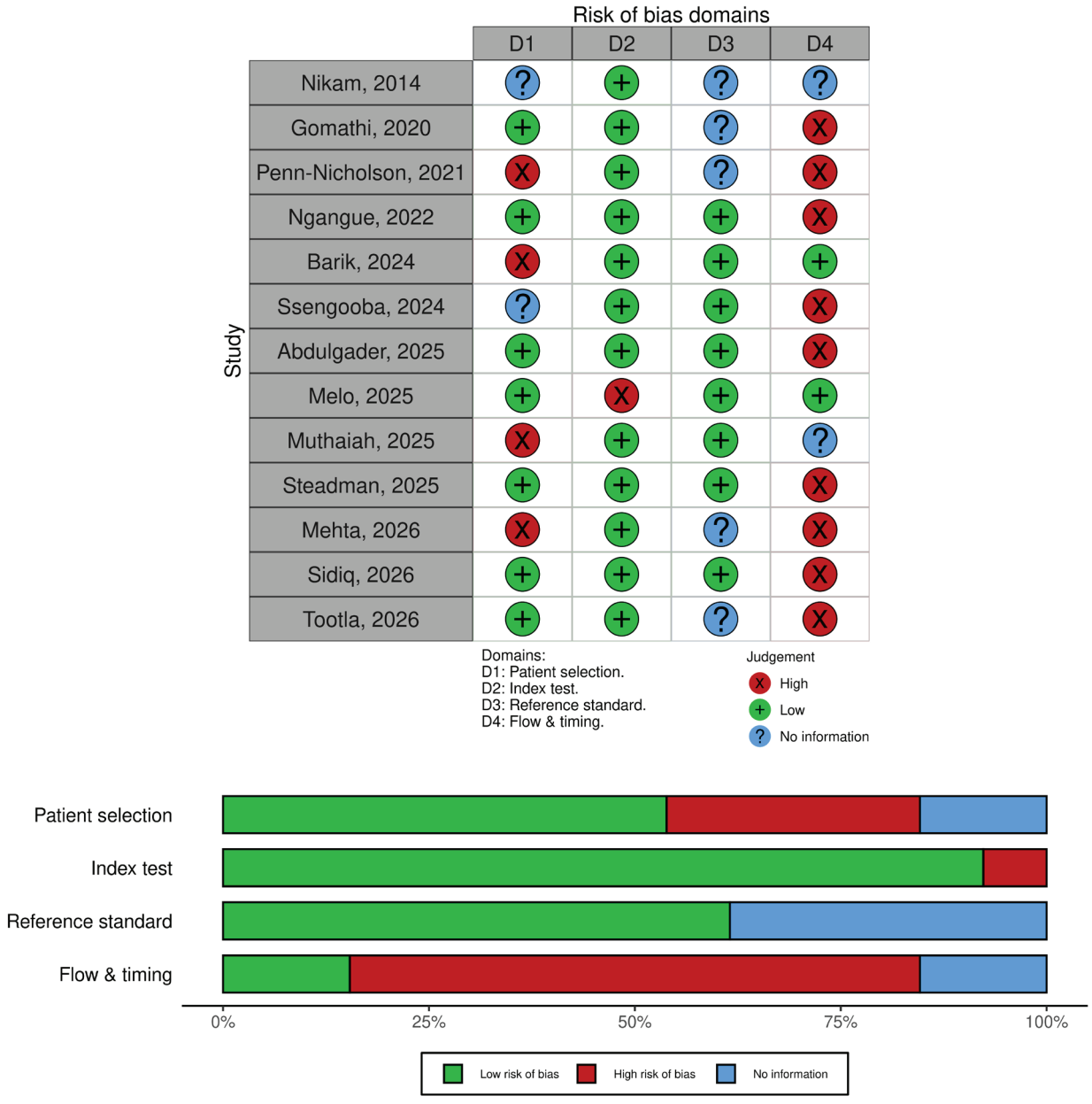


Figure 2. Risk-of-bias assessment. A: study-level judgments, B: distribution across QUADAS-2 domains.

Diagnostic accuracy of Truenat for diagnosing pulmonary tuberculosis

Thirteen studies, comprising 14 independent cohorts, contributed 14 datasets to the meta-analysis of Truenat assays using mycobacterial culture as the reference standard. Penn-Nicholson *et al.* contributed two datasets from geographically distinct and non-overlapping cohorts.[10] To avoid double-counting participants evaluated using multiple Truenat variants, Truenat MTB Plus was selected from both Penn-Nicholson cohorts, while Truenat MTB Ultima was selected from Abdulgader *et al*.[14] Sensitivity estimates across the datasets ranged from 0.73 to 0.94, while specificity estimates ranged from 0.53 to 1.00. The univariate random-effects models yielded a pooled sensitivity of 0.88 (95% CI, 0.84-0.90) and a pooled specificity of 0.95 (95% CI, 0.89-0.97) (Figures 3A and 3B).

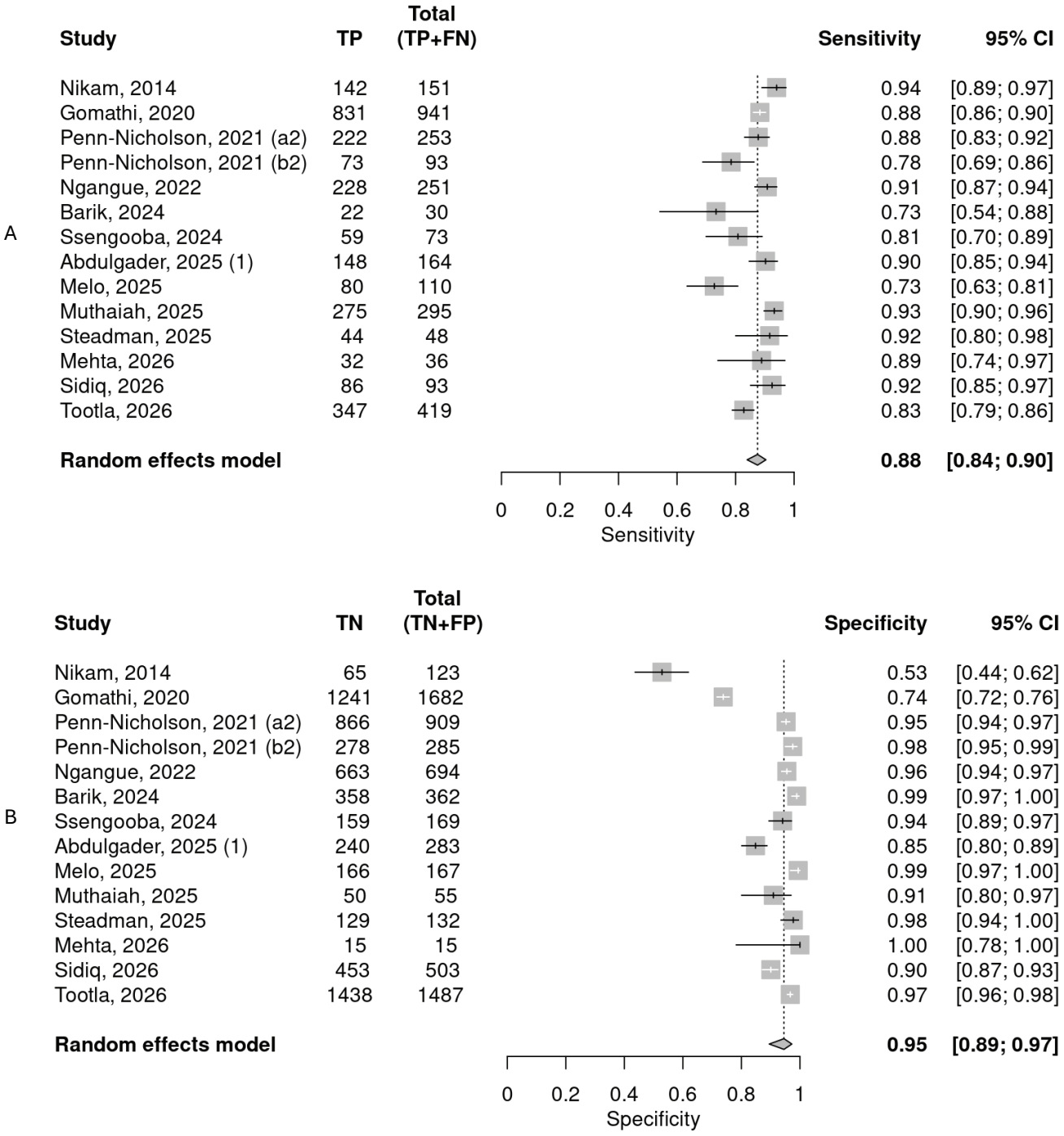
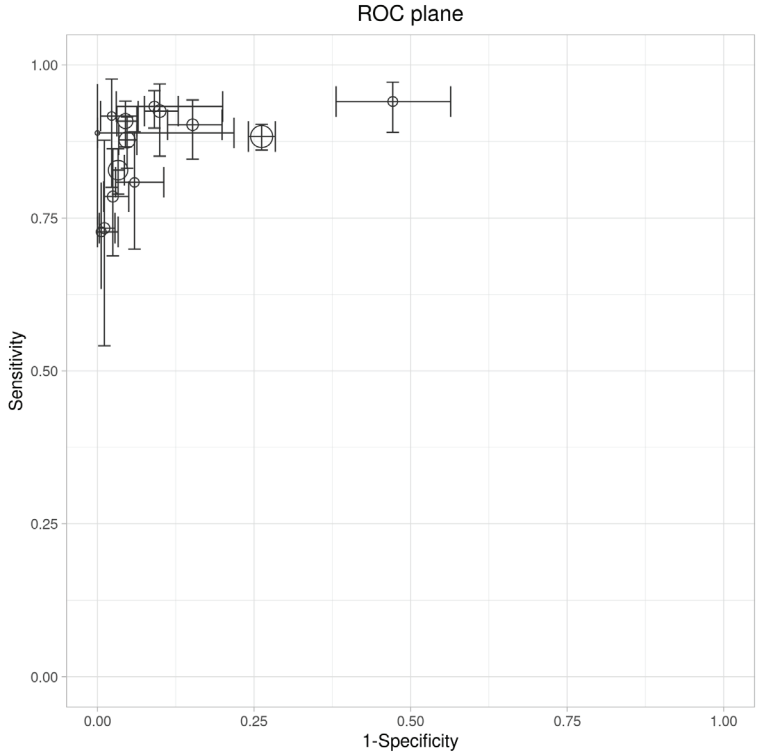


Figure 3. Forest plots of Truenat assays against mycobacterial culture. A: sensitivity, B: specificity.

The bivariate random-effects model yielded a pooled sensitivity of 0.87 (95% CI, 0.83-0.90) and a pooled specificity of 0.94 (95% CI, 0.89-0.97). The bivariate I^2 was 64.2%, indicating heterogeneity in diagnostic performance across datasets. Most estimates were concentrated in the upper-left region of the ROC plane, although variation in sensitivity and false-positive rates was observed (Figure 4A). The SROC curve and its summary point are presented in Figure 4B. The wider prediction ellipse relative to the confidence ellipse indicated greater uncertainty in the expected diagnostic performance across different populations, settings, and assay variants. The pooled diagnostic odds ratio was 113.89 (95% CI, 65.53-197.96), with a positive likelihood ratio of 15.62 (95% CI, 8.20-29.76) and a negative likelihood ratio of 0.14 (95% CI, 0.11-0.17).

A



B

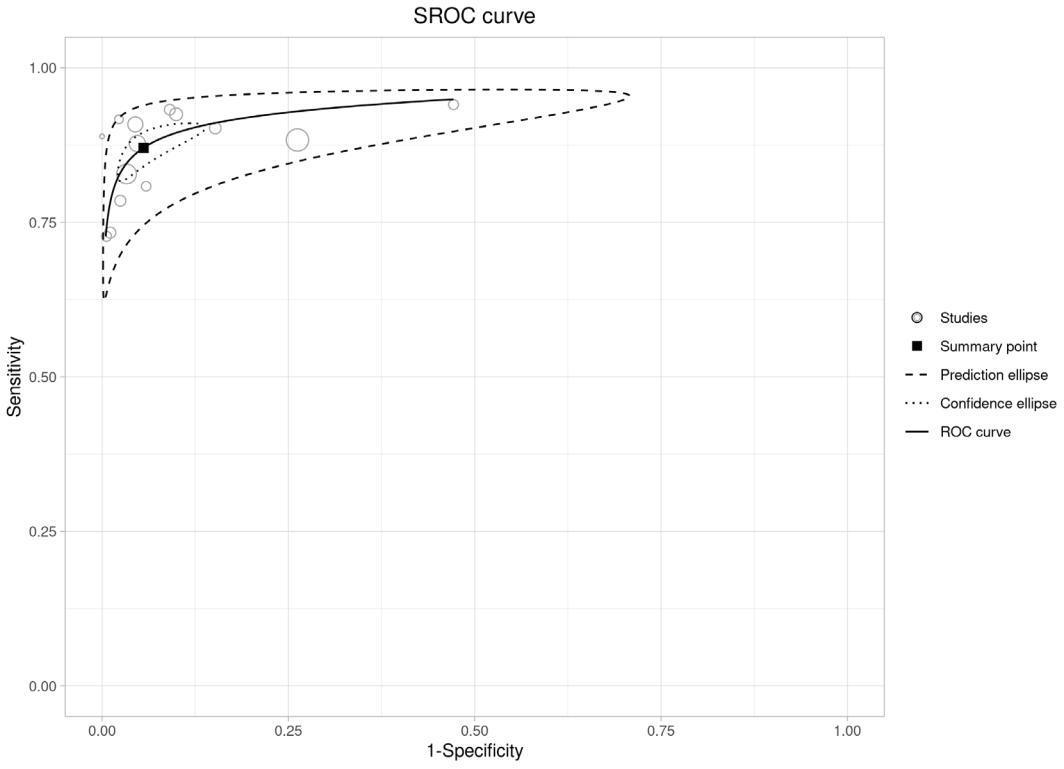


Figure 4. ROC plane (A) and SROC curve (A) of Truenat assays against mycobacterial culture.

Diagnostic accuracy of Xpert for diagnosing pulmonary tuberculosis

Thirteen studies, comprising 14 independent cohorts, contributed 14 datasets to the meta-analysis of Xpert assays using mycobacterial culture as the reference standard. Penn-Nicholson *et al*. contributed two datasets from geographically distinct and non-overlapping cohorts evaluated using Xpert MTB/RIF and Xpert MTB/RIF Ultra. Sensitivity estimates across the datasets ranged from 0.78 to 1.00, while specificity estimates ranged from 0.52 to 1.00.[10] The univariate random-effects models yielded a pooled sensitivity of 0.92 (95% CI, 0.88-0.95) and a pooled specificity of 0.97 (95% CI, 0.93-0.99) (Figures 5a and 5b).

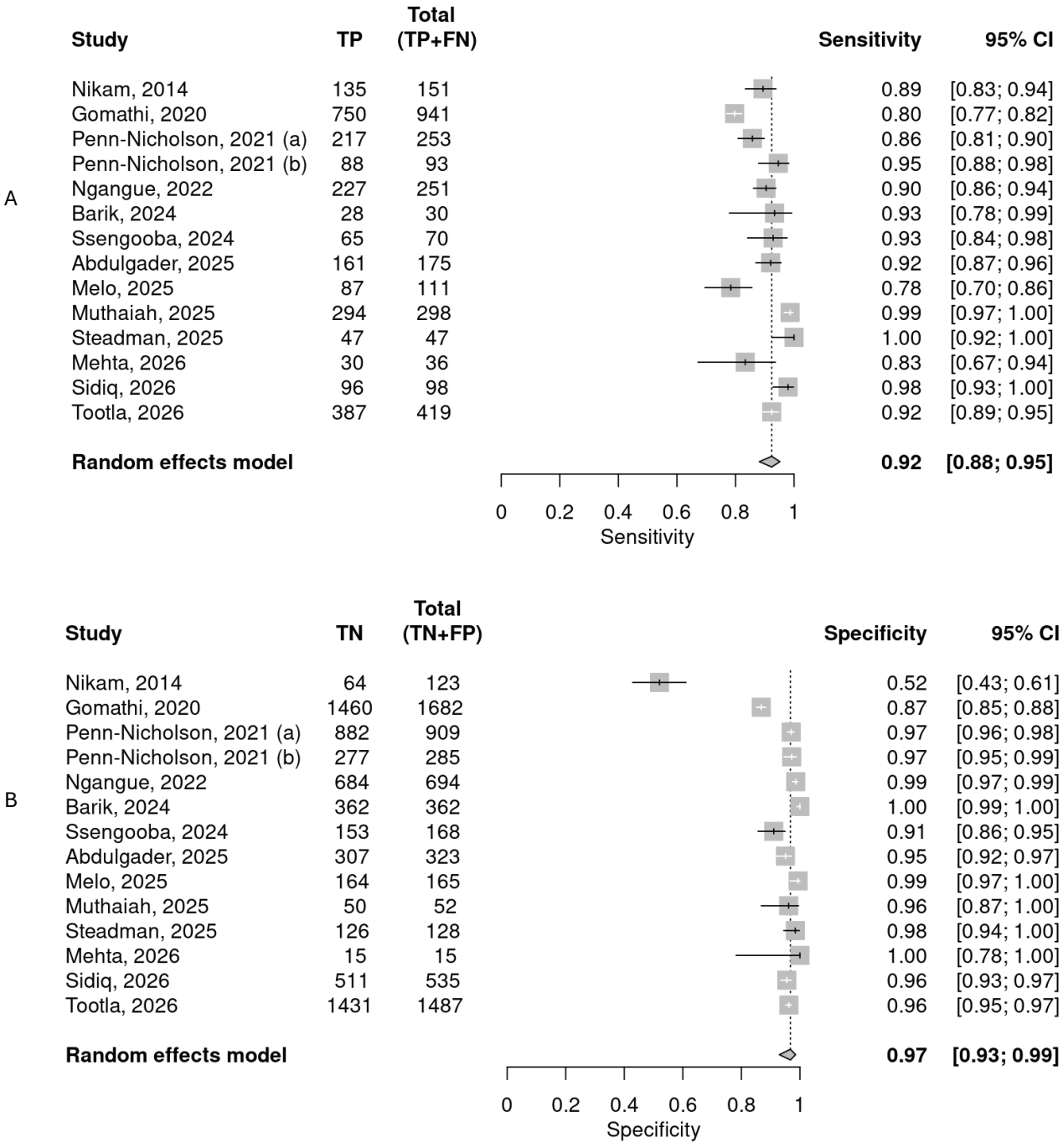
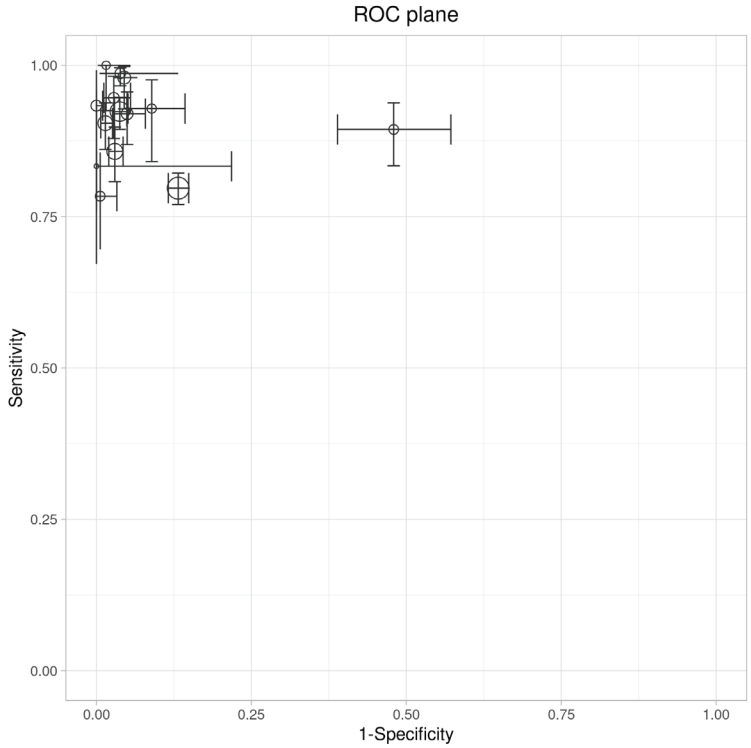


Figure 5. Forest plots of Xpert assays against mycobacterial culture. A: sensitivity, B: specificity.

The bivariate random-effects model yielded a pooled sensitivity of 0.92 (95% CI, 0.88-0.95) and a pooled specificity of 0.97 (95% CI, 0.93-0.99). The bivariate I^2 was 74.1%, indicating heterogeneity in diagnostic performance across datasets. Most estimates were concentrated in the upper-left region of the ROC plane, although one dataset showed a markedly higher false-positive rate (Figure 6A). The SROC curve and its summary point are presented in Figure 6B. The prediction ellipse was considerably wider than the confidence ellipse, indicating greater uncertainty in the expected diagnostic performance across different populations, settings, and Xpert variants. The pooled diagnostic odds ratio was 360.18 (95% CI, 136.64-949.43), with a positive likelihood ratio of 28.31 (95% CI, 13.06-61.39) and a negative likelihood ratio of 0.08 (95% CI, 0.05-0.12).

A



B

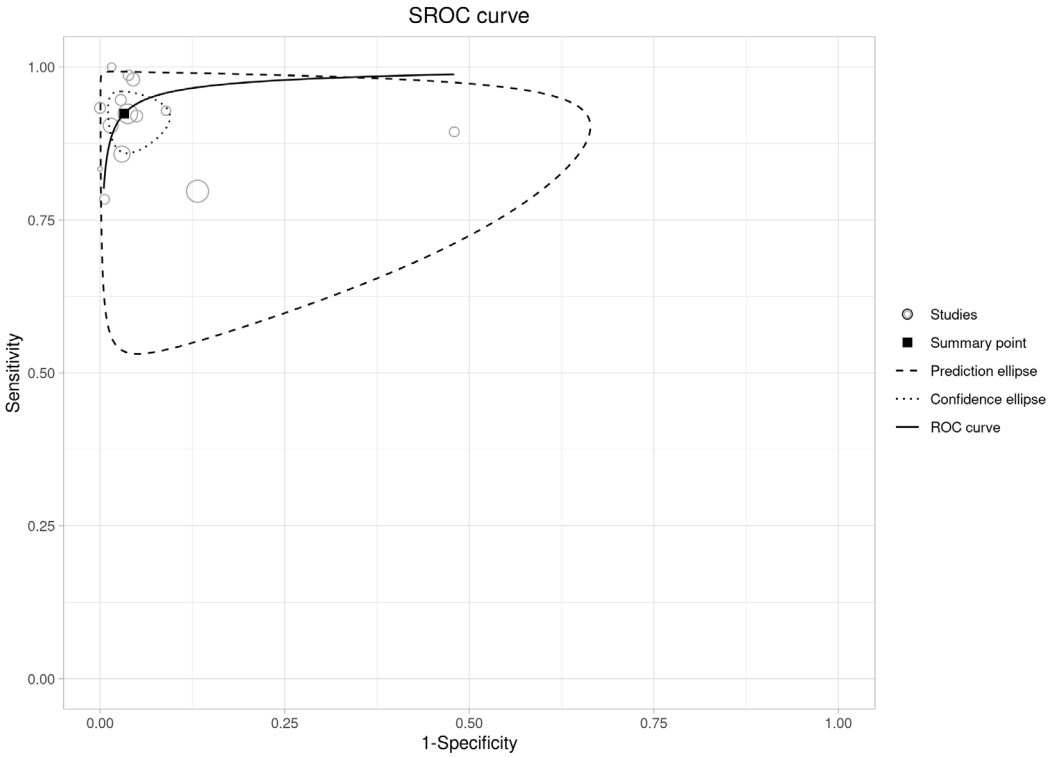


Figure 6. ROC plane (A) and SROC curve (B) of Xpert assays against mycobacterial culture.

Diagnostic accuracy by assay variant

Subgroup analyses were conducted according to assay variant. Truenat MTB, evaluated in six studies, had a pooled sensitivity of 86% (95% CI, 79%-91%) and specificity of 94% (95% CI, 82%-98%). Truenat MTB Plus, evaluated in six studies, yielded a pooled sensitivity of 86% (95% CI, 81%-90%) and specificity of 96% (95% CI, 93%-98%). Truenat MTB Ultima, evaluated in three studies, had a pooled sensitivity of 87% (95% CI, 81%-92%) and specificity of 95% (95% CI, 87%-98%). Xpert MTB/RIF, evaluated in seven studies, had a pooled sensitivity of 91% (95% CI, 83%-95%) and specificity of 97% (95% CI, 86%-100%). Xpert MTB/RIF Ultra, also evaluated in seven studies, yielded a pooled sensitivity of 94% (95% CI, 88%-97%) and specificity of 96% (95% CI, 94%-98%). No formal statistical comparisons were performed among assay variants. The subgroup results are presented in Table 3.

Studies evaluating multiple assay variants could contribute to more than one subgroup. N analyzed represents the cumulative number of participants included in each subgroup analysis.

Table 3. Pooled diagnostic accuracy of Truenat and Xpert according to assay variant.

Index tests	**Assay variant**	**Studies** (N analyzed)	**Pooled sensitivity** (%) (95% CI)	**Pooled specificity** (%) (95% CI)
Truenat	Truenat MTB	6 (5,421)	86 (79-91)	94 (82-98)
	Truenat MTB Plus	6 (3,821)	86 (81-90)	96 (93-98)
	Truenat MTB Ultima	3 (2,533)	87 (81-92)	95 (87-98)
Xpert	Xpert MTB/RIF	7 (5,797)	91 (83-95)	97 (86-100)
	Xpert MTB/RIF Ultra	7 (4,104)	94 (88-97)	96 (94-98)

Note: Studies evaluating multiple assay variants could contribute to more than one subgroup. N analyzed: cumulative number of participants included in each subgroup analysis.

Discussion

This systematic review and meta-analysis found high diagnostic accuracy for both Truenat and Xpert assays when evaluated against mycobacterial culture. The bivariate model yielded a pooled sensitivity of 0.87 and specificity of 0.94 for Truenat, compared with 0.92 and 0.97 for Xpert. Although the point estimates were numerically higher for Xpert, the platform-specific estimates were generated from separate meta-analyses and no formal statistical comparison was performed. These findings therefore do not establish the superiority of either platform. Substantial heterogeneity was observed for both Truenat and Xpert, with bivariate I^2 values of 64.2% and 74.1%, respectively, indicating that diagnostic performance varied across the included study conditions.

The numerically higher sensitivity observed for Xpert may partly reflect the inclusion of Xpert MTB/RIF Ultra datasets. A prospective multicentre study found that Xpert Ultra increased sensitivity compared with Xpert MTB/RIF, particularly among participants with smear-negative or HIV-associated tuberculosis, although this improvement was accompanied by a modest reduction in specificity.[21] The Truenat estimates combined different assay generations and testing workflows. Penn-Nicholson *et al.*[10] reported variation in sensitivity between Truenat MTB and Truenat MTB Plus, while Abdulgader *et al.*[14] identified unsuccessful results and reagent-lot variation during the evaluation of Truenat MTB Plus and Truenat MTB Ultima. These findings suggest that differences in pooled performance may reflect assay generation, participant characteristics, specimen bacillary burden, and operational factors rather than an inherent difference between the two platforms alone.

Subgroup analyses showed relatively narrow differences in pooled accuracy among the assay variants. Sensitivity estimates for Truenat MTB, Truenat MTB Plus, and Truenat MTB Ultima ranged from 86% to 87%, while specificity ranged from 94% to 96%. Xpert MTB/RIF Ultra had a numerically higher sensitivity than Xpert MTB/RIF, at 94% and 91%, respectively, whereas their specificity estimates were similar. The confidence intervals overlapped, and no formal statistical comparisons were performed among assay variants. These subgroup findings should therefore be interpreted descriptively, particularly because each estimate was based on only three to seven studies and studies evaluating multiple variants could contribute data to more than one subgroup.

The observed heterogeneity was likely influenced by differences in study populations, specimen characteristics, culture methods, and testing procedures. Several studies enrolled substantial proportions of participants with HIV infection, previous tuberculosis, or smear-negative disease, all of which may influence bacillary burden and molecular test sensitivity. Ngangue *et al.*[11] and Melo *et al.*[15] reported lower sensitivity in smear-negative participants or people living with HIV than in their overall study populations. Specimen procedures also differed, as Steadman *et al.*[17] evaluated Truenat using swabs prepared from sputum, while Tootla *et al.*[20] used a combined sputum and nasopharyngeal-swab specimen. The notably lower specificity estimates reported by Nikam *et al.*[8] and Gomathi *et al.*[9] for both platforms further indicate that study-level characteristics and

data structure may have contributed to the between-study variability. These sources of heterogeneity limit the extent to which the pooled estimates can be generalized uniformly across clinical settings.

Mycobacterial culture remains an important microbiological reference standard, but its sensitivity depends on bacillary burden, organism viability, specimen quality, transport conditions, and laboratory processing.[3] Molecular-positive/culture-negative results may therefore arise when viable bacilli are not recovered by culture or when molecular assays detect DNA from non-viable organisms. The latter is particularly relevant among individuals with previous tuberculosis treatment. Theron *et al*.[5] demonstrated that Xpert-positive/culture-negative results could persist after successful treatment and may represent residual mycobacterial DNA rather than active disease. Classification of every molecular-positive/culture-negative result as a false positive may consequently underestimate the apparent specificity of molecular assays. Discordant results should be interpreted alongside treatment history, clinical findings, radiological evidence, and additional microbiological results.

Operational considerations are also important when selecting a molecular testing platform. Xpert uses a largely automated cartridge-based workflow and has been widely incorporated into established tuberculosis diagnostic networks.[2,3] Truenat uses portable, battery-capable instruments and can support testing in decentralized settings where laboratory infrastructure or reliable electricity is limited.[3,22] These potential advantages do not eliminate implementation requirements, including operator training, quality assurance, reagent supply, equipment maintenance, biosafety procedures, and referral pathways for confirmatory testing.[22] Platform selection should therefore consider local testing volume, infrastructure, workforce capacity, expected turnaround time, and access to downstream treatment services in addition to diagnostic accuracy.

Limitations

Several limitations should be acknowledged. The number of studies contributing to each assay-variant subgroup was limited, and no formal statistical comparison was performed between the platforms or among assay variants. Substantial heterogeneity remained, and the available data were insufficient for a reliable meta-regression exploring its sources. Several studies had a high risk of bias in the patient selection or flow and timing domains, while information required to assess some domains was unavailable. Some 2×2 tables were reconstructed from reported results, and unresolved discrepancies were identified between tabulated counts and published accuracy estimates in several studies. Differences in assay-specific valid results also meant that Truenat and Xpert were not always evaluated in identical analytical populations. The inclusion of English-language reports only and one non-peer-reviewed preprint may further limit the completeness and certainty of the evidence.

Practical implications

This review has several strengths. All included studies reported results for both Truenat and Xpert within the respective study cohorts and evaluated the assays against mycobacterial culture. The use of a consistent reference-standard framework reduced variability arising from fundamentally different comparator definitions. Multiple Truenat variants evaluated in overlapping participant groups were also handled by selecting one variant per independent cohort for the primary platform-level analysis, thereby avoiding double-counting dependent datasets. The use of a bivariate random-effects model accounted for the relationship between sensitivity and specificity, while subgroup analyses provided descriptive estimates for individual assay variants.

Conclusion

Both Truenat and Xpert demonstrated high pooled diagnostic accuracy for pulmonary tuberculosis when evaluated against mycobacterial culture. Xpert produced numerically higher pooled sensitivity and specificity, but the separate platform-specific analyses and absence of a formal comparative test precluded conclusions regarding statistical differences or superiority between the platforms. The substantial heterogeneity observed in both analyses indicates that diagnostic performance may vary across populations, settings, assay variants, and testing procedures. Platform selection should therefore consider diagnostic accuracy together with operational feasibility, infrastructure requirements, accessibility, and the intended testing setting.

Ethical Approval

This study is a systematic review and meta-analysis based on previously published data. Ethical approval and informed consent were not required.

Declaration of generative AI and AI-assisted technologies

During the preparation of this work, the authors used ChatGPT (OpenAI) to improve grammatical structure and language readability. Covidence was used to facilitate the systematic review process, including duplicate removal and screening of titles and abstracts and full-text articles. Data extraction was performed manually by the authors using Microsoft Excel. ChatGPT was not used for data extraction or data analysis. After using ChatGPT, the authors reviewed and edited the content as necessary and take full responsibility for the content of the published article.

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Conflict of Interest

The authors declare no conflict of interest.

CRediT authorship contribution statement

Anas Afandi: conceptualization, methodology, investigation, data curation, formal analysis, validation, visualization, writing-original draft, review and editing; **Andiesta Asriyah Mariam Saman:** methodology, investigation, data curation, formal analysis, validation, visualization, writing-original draft, review and editing; **Aryati:** supervision, validation, project administration, writing-review and editing; **Puspa Wardhani:** supervision, validation, writing-review and editing. All authors reviewed and approved the final version of the manuscript.

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