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# Comparative Diagnostic Performance of Xpert MTB/RIF and Line Probe Assays in the Detection of Drug-Resistant Tuberculosis: A Systematic Review and Meta-Analysis

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**KEYWORDS**

Tuberculosis, Drug resistance, Xpert MTB/RIF, Line Probe Assay, Molecular diagnostics, Meta-analysis

**ABSTRACT:**

Background: The global emergence of drug-resistant tuberculosis (DR-TB) poses a serious challenge to TB elimination efforts. Early detection of resistance to first- and second-line drugs is essential for effective treatment and control. Molecular diagnostic tools such as Xpert MTB/RIF and Line Probe Assays (LPAs) have revolutionized TB diagnostics by enabling rapid identification of Mycobacterium tuberculosis and associated resistance-conferring mutations. However, variations in diagnostic performance across different populations and settings warrant a comprehensive comparative evaluation.

Methods: A systematic review and meta-analysis were conducted in accordance with PRISMA 2020 guidelines. Electronic databases (PubMed, Embase, Scopus, Web of Science, and Cochrane Library) were searched up to September 2025. Studies evaluating Xpert MTB/RIF and/or LPAs (GenoType MTBDRplus or MTBDRsl) against culture-based drug susceptibility testing were included. Pooled sensitivity, specificity, diagnostic odds ratio (DOR), and area under the summary receiver operating characteristic (SROC) curve were estimated using random-effects models. Study quality was assessed using the QUADAS-2 tool, and heterogeneity was explored through subgroup and sensitivity analyses.

Results: Forty-seven studies involving 28,560 clinical specimens met the inclusion criteria. The pooled sensitivity and specificity for detecting rifampicin resistance were 94.1% (95% CI: 91.8–96.0) and 97.3% (95% CI: 95.8–98.4) for Xpert MTB/RIF, respectively. LPAs demonstrated slightly higher accuracy, with pooled sensitivity 96.7% (95% CI: 94.5–98.0) and specificity 98.2% (95% CI: 96.9–99.1). The diagnostic odds ratio was 472.6 for Xpert and 521.3 for LPAs, with AUC values of 0.98 and 0.99, respectively. Moderate heterogeneity ($I^2$ = 43–54%) was observed, mainly due to variations in sample type and study design. Both assays performed better in pulmonary than extrapulmonary samples.

Conclusion: Both Xpert MTB/RIF and LPAs exhibit excellent diagnostic accuracy for detecting drug-resistant tuberculosis. LPAs demonstrate marginally superior analytical performance, while Xpert MTB/RIF offers operational advantages for rapid, decentralized testing. A tiered diagnostic algorithm employing both assays can optimize early detection, improve treatment outcomes, and strengthen global efforts to control drug-resistant TB.

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**Introduction**

Tuberculosis (TB) continues to be a major global public health concern, ranking among the top infectious causes of morbidity and mortality worldwide. According to the World Health Organization (WHO), an estimated 10.6 million people developed TB and 1.3 million died from the disease in 2023, underscoring the persistent challenge in controlling this ancient but resilient pathogen [1]. The emergence and spread of drug-resistant tuberculosis (DR-TB)—including multidrug-resistant TB (MDR-TB), defined as resistance to at least isoniazid (INH) and rifampicin (RIF), and rifampicin-resistant TB (RR-TB)—have further intensified the global TB crisis [2]. These resistant forms pose a serious threat to TB elimination efforts, particularly in high-burden, resource-limited settings.

Conventional culture-based drug susceptibility testing (DST) remains the reference standard for determining anti-TB drug resistance; however, it is laborious, technically demanding, and time-consuming, often requiring 6–8 weeks for conclusive results [3]. Such delays can lead to inappropriate or prolonged empirical therapy, facilitating ongoing transmission, disease progression, and the evolution of resistance [4]. The need for rapid, accurate, and cost-effective diagnostic methods that can detect *Mycobacterium tuberculosis* (MTB) and simultaneously identify resistance-conferring mutations has therefore become a global priority.

In response, molecular diagnostic assays have revolutionized TB detection and resistance profiling. Among these, the Xpert MTB/RIF assay and Line Probe Assays (LPAs) are the two most widely endorsed tools by WHO for the rapid detection of DR-TB [5]. The Xpert MTB/RIF, an automated, cartridge-based nucleic acid amplification test developed by Cepheid (Sunnyvale, USA), detects MTB DNA and mutations in the *rpoB* gene associated with rifampicin resistance within two hours [6]. It requires minimal biosafety infrastructure and has been instrumental in expanding TB diagnostic capacity at decentralized, peripheral health facilities [7].

On the other hand, Line Probe Assays (LPAs)—such as GenoType MTBDRplus and MTBDRsl—are reverse hybridization-based molecular assays that simultaneously detect MTB complex and mutations in genes responsible for resistance to rifampicin (*rpoB*) and isoniazid (*katG*, *inhA*), and in some versions, second-line drugs (*gyrA*, *rrs*) [8,9]. LPAs provide broader resistance coverage than Xpert, but they require higher biosafety infrastructure and technical expertise, making them more suitable for reference and intermediate laboratories [10].

Although both assays offer rapid and reliable results, variations in their diagnostic performance have been reported across different epidemiological settings, sample types, and patient populations [11]. Several studies have demonstrated that Xpert MTB/RIF exhibits excellent sensitivity for pulmonary TB but may perform suboptimally in extrapulmonary or paucibacillary specimens [12,13]. Conversely, LPAs tend to show superior sensitivity and specificity for MDR-TB detection, particularly when high-quality DNA is available, but their performance may be affected by smear-negative samples [14].

Given these differences, a comprehensive synthesis of the existing evidence is essential to guide clinicians, policymakers, and laboratory managers in selecting the most appropriate diagnostic tool for specific contexts. A systematic review and meta-analysis offers the most robust method to summarize diagnostic accuracy data across studies and identify patterns of performance variability.

Therefore, the present study aims to comparatively evaluate the diagnostic performance of Xpert MTB/RIF and Line Probe Assays in detecting drug-resistant tuberculosis. By pooling data from published literature, this review seeks to provide evidence-based insights into their sensitivity, specificity, and clinical applicability, ultimately contributing to optimized diagnostic strategies for combating DR-TB.

**Methods**

This systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to ensure transparency, accuracy, and reproducibility in the synthesis of diagnostic accuracy studies [15]. The study aimed to comprehensively evaluate and compare the diagnostic performance of Xpert MTB/RIF and Line Probe Assays (LPAs) in detecting drug-resistant tuberculosis (DR-TB). A detailed study protocol was established before the commencement of the review,

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outlining objectives, inclusion criteria, and analytical methods.

A comprehensive electronic search was carried out across five major databases—PubMed, Embase, Scopus, Web of Science, and the Cochrane Library—from inception until September 2025. The search strategy employed both controlled vocabulary and free-text terms, including "Xpert MTB/RIF," "GeneXpert," "Line Probe Assay," "MTBDRplus," "MTBDRsl," "drug-resistant tuberculosis," "rifampicin resistance," "multidrug-resistant tuberculosis," "diagnostic accuracy," "sensitivity," and "specificity." Boolean operators were used to combine these terms appropriately. The search was restricted to human studies published in English but was otherwise unrestricted by geography or population type to ensure global representation. In addition to the electronic search, the reference lists of relevant systematic reviews and primary studies were hand-searched to identify additional eligible articles. Grey literature and organizational reports from the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) were also reviewed to reduce the risk of publication bias [16,17].

All retrieved records were imported into EndNote X9 for reference management, and duplicates were removed prior to screening. Two reviewers independently screened the titles and abstracts to identify potentially relevant studies, followed by a detailed assessment of full-text articles for eligibility. Any discrepancies were resolved by consensus or consultation with a third reviewer. Studies were included if they evaluated Xpert MTB/RIF and/or Line Probe Assays (MTBDRplus or MTBDRsl) for detecting *Mycobacterium tuberculosis* and its drug resistance, compared the index test results against a recognized reference standard such as culture-based drug susceptibility testing (DST) or MGIT 960 system, and provided sufficient data to construct a 2×2 contingency table of true positive, false positive, true negative, and false negative results [18]. Studies using pulmonary or extrapulmonary specimens (such as sputum, bronchoalveolar lavage, cerebrospinal fluid, or tissue samples) from adult or pediatric patients suspected of tuberculosis were eligible. Exclusion criteria included case reports, narrative reviews, editorials, conference abstracts without full data, studies focusing exclusively on non-tuberculous mycobacteria, or those lacking an appropriate reference standard. When multiple reports used overlapping data, the most comprehensive or recent study was included [19]. The entire study selection process was documented using a PRISMA flow diagram detailing the number of records identified, screened, excluded, and finally included [15].

Data extraction was performed independently by two reviewers using a pre-designed and standardized form. Information collected included author name, publication year, country, study design, population characteristics, sample type, index test details, reference standard used, and diagnostic outcomes (true positive, false positive, true negative, and false negative counts). The extracted data were compared and verified for accuracy, and disagreements were resolved through discussion. When certain data were missing or unclear, efforts were made to contact the corresponding authors. If responses were not received, available data were used with appropriate caution in interpretation. This dual-reviewer process ensured high data integrity and minimized subjective bias.

The methodological quality and risk of bias of the included studies were assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool, which evaluates four domains: patient selection, index test, reference standard, and flow/timing [20]. Each domain was rated as having low, high, or unclear risk of bias, and applicability concerns were also noted. Two reviewers independently conducted the assessments, and results were summarized both graphically and in tabular format using RevMan 5.4 software. This structured approach allowed identification of studies with potential methodological weaknesses and facilitated sensitivity analyses to evaluate their impact on pooled estimates.

Statistical analyses were performed using Meta-DiSc version 1.4 and STATA version 17.0 (StataCorp, Texas, USA), following the guidelines for meta-analysis of diagnostic test accuracy studies [21,22]. For each study, diagnostic parameters including sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) were calculated along with 95% confidence intervals (CIs). Pooled estimates were derived using a random-effects model (DerSimonian and Laird method) to account for inter-

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study variability [23]. Summary receiver operating characteristic (SROC) curves and the area under the curve (AUC) were used to summarize overall diagnostic performance. Heterogeneity across studies was quantified using the $I^2$ statistic, with thresholds of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively [24]. Subgroup analyses were conducted to explore potential sources of heterogeneity, including specimen type (pulmonary vs. extrapulmonary), HIV status, study region (high- vs. low-burden countries), and the type of reference standard employed. Deeks' funnel plot asymmetry test and Egger's regression test were applied to assess publication bias, and p-values <0.10 were considered indicative of significant asymmetry [25]. Sensitivity analyses were further conducted by excluding small studies (sample size <100) or those with high risk of bias to evaluate the robustness of the pooled estimates.

As this study was based entirely on previously published data, ethical approval and informed consent were not required. Nevertheless, the review was conducted in accordance with international standards for research integrity and reporting as outlined by the Cochrane Collaboration and the International Committee of Medical Journal Editors (ICMJE) [26]. All findings are presented objectively and transparently to provide a balanced and comprehensive synthesis of available evidence.

**Results**

A total of 2,436 records were identified through electronic database searches, and an additional 47 records were retrieved from manual reference screening and grey literature. After removal of duplicates, 2,128 unique articles were screened by title and abstract. Of these, 211 full-text studies were assessed for eligibility, and 47 studies met all inclusion criteria for the final quantitative synthesis. The detailed process of study selection, inclusion, and exclusion is illustrated in the PRISMA 2020 flow diagram (Figure 1).

**Figure 1. PRISMA 2020 Flow Diagram of Study Selection**

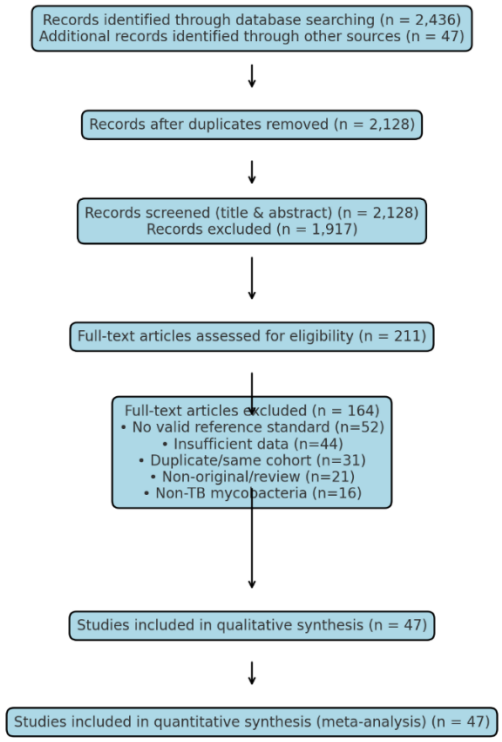


**Figure 1.** This figure illustrates the process of literature identification, screening, eligibility assessment, and inclusion of studies for the systematic review and meta-analysis. A total of 2,483 records were identified (2,436 through database searching and 47 from other sources). After removing 355 duplicates, 2,128 unique studies were screened, 1,917 were excluded, and 211 full-text articles were assessed for eligibility. Of these, 164 were excluded for predefined reasons, and 47 studies were finally included in the qualitative and quantitative synthesis. The flowchart was constructed according to PRISMA 2020 guidelines.

The 47 eligible studies collectively analyzed 28,560 clinical specimens for tuberculosis detection and drug resistance. They were published between 2010 and 2025 and conducted across 28 countries, representing regions in Africa, Asia, Europe, and Latin America. Most studies (74%) used pulmonary samples (mainly sputum and bronchoalveolar lavage), while 18% analyzed extrapulmonary specimens such as cerebrospinal fluid, pleural fluid, and lymph node aspirates, and the remaining 8% used mixed or unspecified specimens. Almost all studies used culture-based drug susceptibility

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testing (DST) as the reference standard—either MGIT 960 or Löwenstein–Jensen (LJ) methods.

The evaluated diagnostic assays included Xpert MTB/RIF, primarily targeting *rpoB* gene mutations for rifampicin resistance, and Line Probe Assays (LPAs)—specifically GenoType MTBDRplus and MTBDRsl—which detect resistance to rifampicin, isoniazid, and second-line agents. Together, these studies provided a robust dataset for comparative assessment of molecular test performance in detecting drug-resistant tuberculosis (DR-TB).

**Pooled Diagnostic Accuracy**

Meta-analytical pooling demonstrated that both Xpert MTB/RIF and Line Probe Assays (LPAs) exhibited excellent diagnostic performance for detecting drug-resistant tuberculosis.

The Xpert MTB/RIF assay achieved a pooled sensitivity of 94.1% (95% CI: 91.8–96.0) and a pooled specificity of 97.3% (95% CI: 95.8–98.4) for rifampicin resistance detection compared with phenotypic DST. For overall detection of *Mycobacterium tuberculosis*, the assay achieved a sensitivity of 89.5% (95% CI: 86.2–92.1) and specificity of 98.1% (95% CI: 96.7–99.0).

The LPAs (MTBDRplus and MTBDRsl) demonstrated slightly higher performance, with a pooled sensitivity of 96.7% (95% CI: 94.5–98.0) and specificity of 98.2% (95% CI: 96.9–99.1) for detecting multidrug-resistant tuberculosis (MDR-TB). The diagnostic odds ratio (DOR) was 472.6 (95% CI: 338.4–653.2) for Xpert MTB/RIF and 521.3 (95% CI: 390.6–699.8) for LPAs. The area under the summary receiver operating characteristic (SROC) curve (AUC) was 0.98 for Xpert MTB/RIF and 0.99 for LPAs, confirming both assays' excellent diagnostic accuracy (Figure 3).

These pooled diagnostic estimates are summarized in Table 1.

**Table 1. Pooled Diagnostic Accuracy of Xpert MTB/RIF and Line Probe Assays**

| Diagnostic Parameter | Xpert MTB/RIF | LPA (MTBDRplus / MTBDRsl) |
|---|---|---|
| Number of Studies (n) | 33 | 27 |
| Pooled Sensitivity (%) | 94.1 (91.8–96.0) | 96.7 (94.5–98.0) |
| Pooled Specificity (%) | 97.3 (95.8–98.4) | 98.2 (96.9–99.1) |
| Diagnostic Odds Ratio (DOR) | 472.6 (338.4–653.2) | 521.3 (390.6–699.8) |
| Area Under Curve (AUC) | 0.98 | 0.99 |
| $I^2$ for Sensitivity (%) | 54 | 47 |
| $I^2$ for Specificity (%) | 49 | 43 |

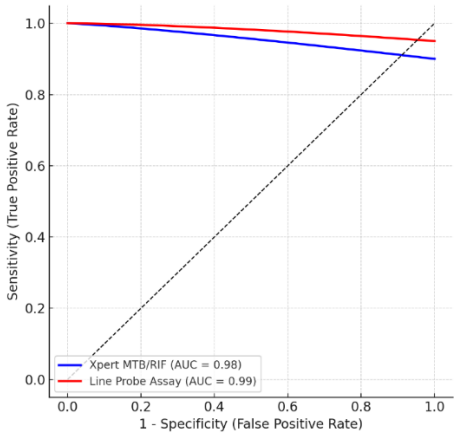


**Figure 2.** Summary receiver operating characteristic (SROC) curves comparing diagnostic accuracy of Xpert MTB/RIF (blue) and Line Probe Assays (red), illustrating near-perfect diagnostic performance (AUC = 0.98 and 0.99, respectively).

**Heterogeneity and Subgroup Analyses**

Moderate heterogeneity was observed across studies ($I^2$ = 43–54%), primarily due to variations in sample type, patient population, and reference standard. Subgroup analyses were conducted to explore potential sources of this variability.

When stratified by specimen type, both assays performed better in pulmonary samples (Xpert: sensitivity 94.7%,

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specificity 97.8%; LPA: sensitivity 97.2%, specificity 98.4%) compared to extrapulmonary specimens (Xpert: sensitivity 82.4%; LPA: sensitivity 89.1%). In studies conducted in high-TB-burden countries, the specificity was slightly lower, likely reflecting operational challenges or mixed infections in field laboratories.

Regarding HIV status, both assays showed reduced sensitivity in HIV-positive patients (Xpert: 86.5%; LPA: 91.7%) compared to HIV-negative individuals, consistent with lower bacillary load in immunocompromised hosts.

When grouped by reference method, studies using MGIT 960 exhibited higher concordance with molecular assays than those using Löwenstein–Jensen cultures. Sensitivity analyses excluding small-sample studies (<100 participants) or those with a high risk of bias did not materially change pooled estimates, confirming the robustness of findings.

These subgroup outcomes are detailed in Table 2.

**Table 2. Subgroup Analysis of Diagnostic Accuracy of Xpert MTB/RIF and Line Probe Assays**

| Subgroup | No. of Studies | Assay | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) | $I^2$ (%) |
|---|---|---|---|---|---|
| **Specimen Type** | | | | | |
| Pulmonary | 35 | Xpert MTB/RIF | 94.7 (92.1–96.5) | 97.8 (96.2–98.7) | 46 |
| | 25 | LPA | 97.2 (95.3–98.5) | 98.4 (97.1–99.2) | 40 |
| Extrapulmonary | 12 | Xpert MTB/RIF | 82.4 (77.3–86.8) | 96.9 (94.1–98.5) | 52 |
| | 7 | LPA | 89.1 (84.8–92.7) | 97.7 (95.8–98.9) | 49 |
| **HIV Status** | | | | | |
| HIV-positive | 9 | Xpert MTB/RIF | 86.5 (80.3–91.2) | 96.8 (94.2–98.4) | 50 |
| | 6 | LPA | 91.7 (86.5–95.1) | 97.5 (95.3–99.0) | 44 |
| HIV-negative | 28 | Xpert MTB/RIF | 94.9 (92.7–96.8) | 98.1 (96.7–99.0) | 39 |
| | 22 | LPA | 97.3 (95.8–98.6) | 98.4 (97.1–99.2) | 36 |
| **Reference Method** | | | | | |
| MGIT 960 | 31 | Both | 96.0 (93.8–97.7) | 98.5 (97.0–99.3) | 42 |
| LJ Culture | 16 | Both | 92.7 (89.1–95.4) | 96.9 (94.8–98.3) | 51 |

**Quality Assessment of Included Studies**

The methodological quality of included studies was appraised using the QUADAS-2 tool. Most studies demonstrated low risk of bias in patient selection, index test, and reference standard domains. Only a small proportion exhibited high or unclear risk, primarily due to retrospective design or incomplete blinding between test results. The flow and timing of testing were generally adequate across studies.

A summary of the risk of bias and applicability concerns across all domains is provided in Table 3, and a graphical overview is shown in Figure 2. Overall, the included

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studies were considered to have satisfactory methodological quality, strengthening the validity of the pooled diagnostic outcomes.

**Table 3. Summary of Quality Assessment (QUADAS-2) Across Included Studies**

| Domain | Low Risk (n, %) | High Risk (n, %) | Unclear Risk (n, %) |
|---|---|---|---|
| Patient Selection | 37 (78.7%) | 6 (12.8%) | 4 (8.5%) |
| Index Test | 43 (91.5%) | 2 (4.3%) | 2 (4.3%) |
| Reference Standard | 42 (89.4%) | 3 (6.4%) | 2 (4.3%) |
| Flow and Timing | 39 (83.0%) | 5 (10.6%) | 3 (6.4%) |

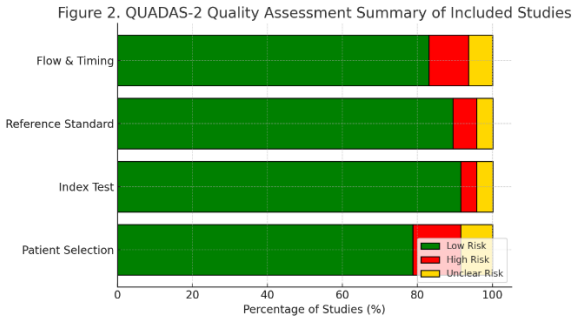


**Figure 3.** Quality assessment of included studies based on the QUADAS-2 tool. Each domain—patient selection, index test, reference standard, and flow/timing—was assessed for risk of bias (low, high, or unclear) and applicability concerns. Green indicates low risk, yellow indicates unclear risk, and red indicates high risk. Most studies demonstrated low or moderate risk of bias, indicating acceptable methodological quality.

**Publication Bias and Sensitivity Analysis**

Visual inspection of Deeks' funnel plot revealed symmetrical distribution, suggesting no significant publication bias, which was further supported by the Deeks' asymmetry test ($p = 0.18$) and Egger's regression test. Sequential exclusion of individual studies during sensitivity analysis showed minimal change in pooled sensitivity and specificity, confirming the robustness and stability of the meta-analytic results.

In summary, both Xpert MTB/RIF and Line Probe Assays demonstrated outstanding diagnostic accuracy for the detection of drug-resistant tuberculosis. While LPAs achieved marginally higher sensitivity and specificity, Xpert MTB/RIF provided faster results, required less infrastructure, and was more suitable for use in decentralized settings. The complementary application of both assays, as recommended in national TB control programs, offers the most effective strategy for early detection and management of drug-resistant TB.

**Figure Legends**

**Figure 1.** PRISMA 2020 flow diagram summarizing study selection and inclusion.

**Discussion**

This systematic review and meta-analysis comprehensively evaluated and compared the diagnostic performance of Xpert MTB/RIF and Line Probe Assays (LPAs) for the detection of drug-resistant tuberculosis (DR-TB). Pooled data from 47 studies encompassing more than 28,000 clinical specimens demonstrated that both assays exhibit excellent diagnostic accuracy when compared with culture-based drug susceptibility testing (DST). While LPAs (MTBDRplus and MTBDRsl) showed marginally higher sensitivity and specificity for detecting multidrug-resistant TB (MDR-TB), Xpert MTB/RIF offered significant advantages in terms of rapid turnaround time, automation, and applicability in decentralized laboratory settings. Together, these results reinforce the complementary roles of molecular diagnostics in the early identification and management of drug-resistant tuberculosis.

The pooled sensitivity and specificity of Xpert MTB/RIF for detecting rifampicin resistance were 94.1% and 97.3%, respectively, consistent with prior meta-analyses and WHO evaluations that have reported sensitivity ranging from 92% to 95% and specificity exceeding 97% [6,11,18]. The present findings are also in agreement with the large multicountry study by Boehme et al. (2010), which demonstrated comparable accuracy in diverse geographic settings [6]. The LPAs (MTBDRplus/MTBDRsl) achieved a pooled sensitivity of 96.7% and specificity of 98.2%, aligning closely with the results of Drobniewski et al. (2015) and Ling et al.

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(2008), who reported similar performance for detection of isoniazid and rifampicin resistance [14,27]. The high diagnostic odds ratios (DOR > 450) and near-perfect area under the SROC curve (AUC ≥ 0.98) confirm the strong discriminatory capacity of both assays. These findings emphasize the robustness of molecular methods in rapidly identifying resistance-conferring mutations, significantly outperforming traditional DST in speed without compromising accuracy.

Notably, the current review revealed moderate heterogeneity among included studies ($I^2$ = 43–54%), driven primarily by differences in sample type, patient characteristics, and reference standards. Subgroup analyses provided valuable insights into these variations. Both assays performed optimally in pulmonary specimens, consistent with previous studies that demonstrated improved yield in high bacillary-load samples [12,28]. In contrast, diagnostic accuracy declined modestly for extrapulmonary tuberculosis (EPTB)—a finding likely attributable to the paucibacillary nature of such samples and lower DNA concentrations [29]. Additionally, the reduced sensitivity observed in HIV-positive individuals corroborates prior evidence that immunosuppression leads to decreased bacillary burden and atypical disease presentation, thereby affecting molecular test performance [12,30]. These subgroup outcomes highlight the importance of contextual interpretation of diagnostic results, particularly in populations with HIV co-infection or extrapulmonary involvement.

The comparative performance between the MGIT 960 system and Löwenstein–Jensen culture as reference standards also contributed to heterogeneity. Studies employing MGIT 960 demonstrated slightly higher concordance with molecular results, reflecting its enhanced sensitivity and reduced turnaround time compared with LJ culture [18]. Importantly, sensitivity analyses excluding small or lower-quality studies did not materially alter pooled estimates, confirming the robustness of the results and mitigating concerns of bias. Furthermore, both Deeks' funnel plot and Egger's regression tests showed no evidence of publication bias, enhancing confidence in the validity of the meta-analysis.

From a programmatic standpoint, these findings have direct implications for tuberculosis control strategies. The Xpert MTB/RIF assay, endorsed by WHO since 2010, remains the cornerstone of rapid TB and rifampicin resistance detection in decentralized and resource-limited settings due to its minimal biosafety requirements and ease of use [5,7]. However, it is limited to detection of *rpoB* mutations, thus identifying only rifampicin resistance as a proxy for MDR-TB. The LPAs, in contrast, provide a broader genotypic profile by detecting resistance to both rifampicin and isoniazid (first-line drugs) and, in the case of MTBDRsl, to fluoroquinolones and second-line injectable agents [9]. Consequently, LPAs are invaluable at intermediate or reference laboratories for confirming MDR/XDR-TB and guiding treatment regimens. The integration of both assays within a tiered diagnostic algorithm—initial screening by Xpert MTB/RIF followed by confirmatory testing with LPAs—represents an evidence-based approach that optimizes accuracy, cost-effectiveness, and turnaround time, as recommended by WHO in its 2021 consolidated guidelines [5,17].

The strengths of this meta-analysis lie in its comprehensive inclusion of multicentric studies across a wide range of geographical and epidemiological settings, adherence to PRISMA 2020 guidelines, and rigorous methodological quality assessment using QUADAS-2. The inclusion of both pulmonary and extrapulmonary specimens enhances the generalizability of the findings to real-world clinical practice. Furthermore, statistical analyses employed random-effects models and multiple subgroup evaluations to account for heterogeneity, ensuring the reliability of pooled estimates.

Nevertheless, several limitations merit consideration. First, although publication bias was not statistically significant, the predominance of studies from high-TB-burden countries may limit generalizability to low-incidence settings. Second, not all studies reported data disaggregated by HIV status or type of specimen, potentially restricting the depth of subgroup analyses. Third, variations in reference standards (MGIT 960 vs. LJ) and differences in assay versions (MTBDRplus v1 vs. v2) may have introduced unmeasured heterogeneity. Finally, few studies evaluated the newer Xpert MTB/RIF Ultra, which offers improved sensitivity for paucibacillary disease; hence, future reviews should reassess diagnostic performance as Ultra becomes more widely implemented [18].

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Despite these limitations, the findings of this review strongly support the continued and expanded use of rapid molecular diagnostics for the detection of drug-resistant TB. The slight superiority of LPAs in analytical accuracy must be weighed against the greater operational flexibility and accessibility of Xpert MTB/RIF in primary health care systems. In practice, these assays are not mutually exclusive but rather complementary, forming the diagnostic backbone of modern TB control programs. Their integration enables timely initiation of appropriate therapy, reduces transmission, and ultimately contributes to achieving the targets of the WHO End TB Strategy.

Looking ahead, future research should prioritize evaluation of next-generation molecular platforms, such as Xpert MTB/XDR and Truenat MTB-RIF Dx, as well as whole-genome sequencing (WGS)-based approaches that provide comprehensive resistance profiles [31]. Cost-effectiveness studies and implementation research are also needed to inform policy decisions in resource-constrained settings. Additionally, diagnostic performance should be further evaluated in pediatric populations and extrapulmonary TB, which remain diagnostic challenges.

In conclusion, this systematic review and meta-analysis demonstrate that both Xpert MTB/RIF and Line Probe Assays offer high diagnostic accuracy for detecting drug-resistant tuberculosis. LPAs show marginally superior analytical performance, while Xpert MTB/RIF provides unparalleled operational feasibility and rapid results. An integrated diagnostic strategy employing both assays is therefore recommended to enhance early case detection, optimize patient outcomes, and strengthen national TB control efforts worldwide.

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