Journal of Associated Medical Sciences 2026; 59(3): 151-167

JAMS
Journal of Associated Medical Sciences

Scopus Indexed & Thai-Journal Citation Index Centre (TCI)

Journal of Associated Medical Sciences

Journal homepage: https://www.tci-thaijo.org/index.php/bulletinAMS/index



Diagnostic accuracy of urine AlereLAM and FujiLAM assays for diagnosing active tuberculosis in people living with HIV: A systematic review and meta-analysis

Andiesta Asriyah Mariam Saman[1], Puspa Wardhani[2,3,4,5*], Aryati[2,3,4], Lukman Nur Rahman[1]

[1]*Master Program of 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.*
[3]*Department of Clinical Pathology, Dr. Soetomo General Academic Hospital, Surabaya, East Java, Indonesia.*
[4]*Institute of Tropical Disease, Universitas Airlangga, Surabaya, East Java, Indonesia.*
[5]*Postgraduate School, Universitas Airlangga, Surabaya, East Java, Indonesia.*

ARTICLE INFO

Article history:
Received 5 February 2026
Accepted as revised 10 May 2026
Available online 23 June 2026

Keywords:
Tuberculosis, people living with HIV, urine lipoarabinomannan, AlereLAM, FujiLAM, diagnostic accuracy

ABSTRACT

Background: People living with HIV (PLHIV) remain at high risk of active tuberculosis (TB), yet diagnosis is often challenging due to difficulty obtaining sputum and reduced sensitivity of conventional tests. Urine-based lipoarabinomannan (LAM) assays offer a rapid, non-sputum diagnostic approach. The more recent Fujifilm SILVAMP TB LAM (FujiLAM) may provide better diagnostic performance than the extensively used Alere Determine TB-LAM (AlereLAM).

Objectives: To evaluate the diagnostic accuracy of urine AlereLAM and FujiLAM for diagnosing active TB in PLHIV, and to compare the pooled diagnostic performance of AlereLAM versus FujiLAM.

Materials and methods: We conducted a systematic review and a meta-analysis of diagnostic test accuracy in accordance with PRISMA-DTA guidelines. PubMed, Scopus, and SpringerLink were searched for studies published between 2016 and 2025. Eligible studies enrolled PLHIV evaluated for suspected active TB and assessed urine AlereLAM and/or FujiLAM against microbiological reference standards (MRS) and/or composite reference standards (CRS), with MRS prioritized. Diagnostic 2×2 data were extracted or reconstructed. Pooled sensitivity, specificity, likelihood ratios, and diagnostic odds ratios were estimated using a bivariate random-effects model, with separate analyses for AlereLAM and FujiLAM.

Results: Twenty-five diagnostic accuracy studies were included. AlereLAM demonstrated a pooled sensitivity of 0.364 (95% CI 0.272-0.467) and specificity of 0.928 (95% CI 0.875-0.960). In contrast, FujiLAM showed a substantially higher pooled sensitivity of 0.642 (95% CI 0.567-0.711) while maintaining a high specificity of 0.901 (95% CI 0.872-0.924). FujiLAM yielded a higher diagnostic odds ratio (16.34 vs 7.38), a higher positive likelihood ratio (6.49 vs 5.06), and a lower negative likelihood ratio (0.40 vs 0.69) than AlereLAM. Summary receiver operating characteristic (SROC) analyses demonstrated superior overall diagnostic accuracy for FujiLAM.

Conclusion: Urine FujiLAM showed markedly higher sensitivity than AlereLAM while maintaining high specificity for diagnosing active TB in PLHIV. These findings suggest that next-generation urine LAM assays may substantially improve TB case detection in this high-risk population, particularly in settings where sputum-based diagnostics are limited.

*** Corresponding contributor.**
Author's Address: *Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia.*
E-mail address: puspa-w-2@fk.unair.ac.id
doi: 10.66285/JAMS.2026.089
E-ISSN: 2539-6056

Introduction

Tuberculosis (TB) remains a major global public health problem and the leading cause of death from a single infectious agent worldwide, with an estimated 10.7 million incident cases and 1.23 million deaths reported in 2024.[1] The burden of TB is highly concentrated in high-burden countries, accounting for 87% of global cases, and is driven by key determinants such as poverty, undernutrition, diabetes, smoking, and HIV infection.[1] HIV infection markedly increases the risk of progression from TB infection to active disease and contributes substantially to TB-related mortality.[1] Globally, approximately 150,000 TB deaths occur among people living with HIV (PLHIV), highlighting the urgent need for improved strategies for early and accurate TB diagnosis in this vulnerable population.[1] Rapid and accurate diagnosis is a cornerstone of effective TB care and control.[2,3] Global coverage is still inadequate despite the introduction of WHO-recommended rapid diagnostic tests (RDTs), such as lateral flow urine lipoarabinomannan (LF-LAM) assays, to enhance TB detection. In 2024, WRDs were used as the initial diagnostic test in only 54% of newly diagnosed TB cases, with marked regional and country-level disparities, highlighting persistent gaps in access to rapid TB diagnostics, particularly in high-burden and HIV-affected settings.[1,3] Diagnostic challenges are particularly pronounced among PLHIV, in whom TB frequently presents with smear-negative or extrapulmonary disease and low mycobacterial burden, substantially reducing the sensitivity of conventional sputum-based diagnostic methods.[4] Urine-based LF-LAM assays have therefore emerged as a promising point-of-care, non-sputum diagnostic approach for TB in PLHIV, especially among those with advanced immunosuppression. However, evidence on diagnostic accuracy and optimal use remains heterogeneous.[2,3]

Lipoarabinomannan (LAM) is a lipopolysaccharide component of the *Mycobacterium tuberculosis* cell wall that can be released into the bloodstream and subsequently detected in urine during active TB disease.[4] Detection of urinary LAM is biologically plausible, particularly among PLHIV, in whom disseminated disease, higher mycobacterial burden, and increased glomerular permeability are more common.[2,4] Unlike sputum-based diagnostics, urine-based LF-LAM assays do not depend on sputum production. They can be performed at the point of care, making them particularly attractive for severely ill or immunocompromised patients and for use in resource-limited settings.[2]

Alere Determine TB LAM Ag (AlereLAM) is currently the only commercially available LF-LAM assay.[2] It has been incorporated into WHO recommendations for selected subgroups of PLHIV, although its diagnostic sensitivity is recognized to be suboptimal and variable across clinical settings.[2] It is a point-of-care lateral flow assay that provides qualitative results interpreted visually using a reference card with graded intensity bands.[2]

More recently, Fujifilm SILVAMP TB LAM (FujiLAM) has been developed as a next-generation urine-based LF-LAM assay.[2,11] This assay incorporates high-affinity monoclonal antibodies and a silver amplification step, which enhances signal detection and enables identification of lower concentrations of LAM.[11] In contrast to AlereLAM, which is based on conventional lateral flow immunoassay technology using polyclonal antibodies, these features may contribute to differences in analytical performance.[11] Results from FujiLAM are also interpreted visually.[2,11]

In practical use, both assays are rapid, non-sputum-based, and suitable for point-of-care settings. FujiLAM has been reported to show higher sensitivity than AlereLAM while maintaining high specificity, which may be particularly relevant in PLHIV, in whom early and accurate detection of active tuberculosis remains challenging. Despite these promising characteristics, evidence on the diagnostic accuracy of both assays remains heterogeneous, reflecting differences in study populations, disease severity, reference standards, and clinical settings. This heterogeneity underscores the need for a systematic review and meta-analysis to comprehensively synthesize and compare their diagnostic performance. Therefore, this systematic review and diagnostic test accuracy meta-analysis aimed to summarize and compare the diagnostic accuracy of urine AlereLAM and FujiLAM assays for diagnosing active tuberculosis in people living with HIV.

Materials and methods

Protocol and reporting standards

This systematic review and diagnostic test accuracy (DTA) meta-analysis was conducted in accordance with a prespecified protocol. The reporting of this review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Diagnostic Test Accuracy (PRISMA-DTA) statement.[5] The study selection process is presented in a PRISMA flow diagram. The protocol has been registered in the PROSPERO database (CRD420261294478).

Information source and search strategy

A systematic literature search was conducted to identify studies evaluating the diagnostic accuracy of urine lipoarabinomannan assays for diagnosing active TB among PLHIV. Data were gathered from PubMed, Scopus, and SpringerLink by searching for key terms related to urine lipoarabinomannan assays and tuberculosis, including Fujifilm SILVAMP TB LAM (FujiLAM), SILVAMP-LAM, Determine TB-LAM (AlereLAM), lipoarabinomannan, and *Mycobacterium tuberculosis* or tuberculosis. Searches were limited to studies published in English between 2016 and 2025. The last search was conducted on 9 January 2026. The complete search strategies are provided in the Supplementary.

Eligibility criteria

We included full-text English-language studies enrolling PLHIV evaluated for suspected active TB. The index tests were urine Alere Determine TB-LAM (AlereLAM) and/or Fujifilm SILVAMP TB LAM (FujiLAM). Reference standards included microbiological reference standards (MRS) and/or composite reference standards (CRS). Studies were required to provide diagnostic 2×2 data or sufficient information to reconstruct these data. Eligible study designs included cohort, cross-sectional diagnostic accuracy, and case-control studies.

We restricted the search to studies published between 1 January 2016 and 31 December 2025 to reflect contemporary evidence on urine LAM assays. This time frame was selected because recent studies more accurately reflect current diagnostic technologies, including the development and evaluation of newer-generation assays such as FujiLAM, and align with evolving WHO recommendations on the use of LAM-based diagnostics in people living with HIV.

We excluded non-human studies, studies using non-urine specimens or non-eligible index tests, studies with inadequate reference standards, and publications without extractable 2×2 data. Review articles, meta-analyses, case reports or case series, editorials, commentaries, and conference abstracts were also excluded.

Study selection

All records retrieved from database searches were independently screened by two reviewers (AS, LR) against the eligibility criteria. Titles and abstracts were screened first, followed by full-text assessment of potentially relevant articles. Any disagreements were resolved by consensus. The final set of included studies was determined after full-text review.

Data extraction

Data were extracted independently by two reviewers (AS, LR) using a standardized extraction form. Extracted variables included study characteristics (author, year, country, setting, and design), participant characteristics, index test details (AlereLAM and/or FujiLAM), reference standards (MRS or CRS), and diagnostic 2×2 outcomes. For each study, true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN) were extracted or reconstructed from reported sensitivity and specificity with denominators when required. In studies enrolling participants with and without HIV infection, data extraction was restricted to the HIV-positive subgroup. Any discrepancies were resolved by consensus.

Index tests and reference standards

The study population comprised PLHIV evaluated for suspected active TB in inpatient and/or outpatient settings. The index tests were urine AlereLAM and FujiLAM. Diagnostic performance was assessed against MRS and/or CRS, with MRS prioritized when both were available. MRS was defined as mycobacterial culture and/or nucleic acid amplification tests (NAAT), such as Xpert MTB/RIF or Xpert Ultra, performed on sputum and/or other clinical specimens. CRS was defined as microbiological evidence and/or compatible histopathology or cytology and/or guideline-based clinical diagnosis supported by imaging findings and treatment response.

Quality assessment

The methodological quality of included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. Two reviewers (AS, LR) independently evaluated risk of bias across four domains: patient selection, index test, reference standard, and flow and timing. Applicability concerns were assessed for the first three domains. Any discrepancies were resolved by consensus. Risk of bias assessments were summarized and visualized using the Robvis web application (https://mcguinlu.shinyapps.io/robvis/).

Statistical analysis

Diagnostic accuracy data were summarized using 2×2 contingency tables, including TP, FP, FN, and TN. A diagnostic test accuracy meta-analysis was conducted using the MetaDiSc2 web application. Pooled sensitivity and specificity with 95% confidence intervals were estimated using a bivariate random-effects model. Results were presented in tabular form, and forest plots of sensitivity and specificity were generated for individual studies. When both MRS and CRS were reported, MRS-based estimates were preferentially included in the meta-analysis. Overall test performance was visualized using receiver operating characteristic (ROC) plane plots and summary receiver operating characteristic (SROC) curves, including confidence and prediction regions.

Results

Study selection

The systematic search identified 157 records, including 65 from Scopus, 57 from PubMed, and 35 from SpringerLink. After removal of 51 duplicate records, 106 studies were screened by title and abstract, of which 73 were excluded for not meeting the inclusion criteria. The remaining 33 studies were subsequently assessed in full text for eligibility. Eight studies were excluded after full-text review for insufficient data on diagnostic accuracy (N=4), inappropriate study populations (N=3), or incorrect sample types (N=1). Ultimately, 25 studies fulfilled all eligibility criteria and were included in the systematic review and diagnostic test accuracy meta-analysis. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

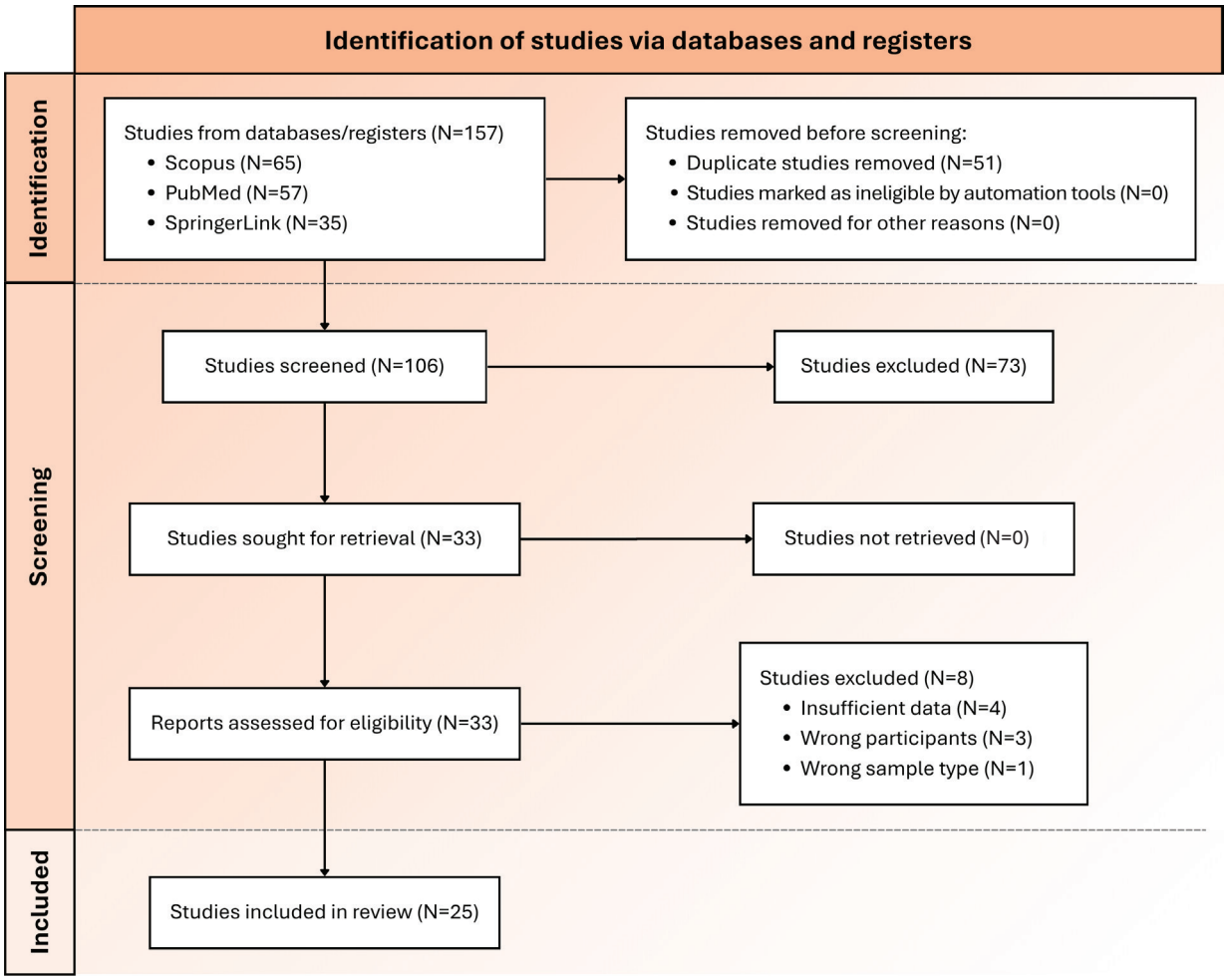

Figure 1. *PRISMA flow diagram.*

Study characteristics

A total of 25 studies on diagnostic accuracy were included. Six studies evaluated both AlereLAM and FujiLAM, 11 evaluated AlereLAM only, and 9 evaluated FujiLAM only. One FujiLAM-only study reported separate diagnostic accuracy results for fresh and stored urine samples, which were extracted as distinct datasets for analysis. All studies provided extractable or constructible 2×2 diagnostic accuracy data and included inpatient and/or outpatient populations (Table 1).

Table 1. Characteristics of all studies included.

Author, year	Country	Study design	Setting	Median age	Sex (male%)	TB type	Reference standard	Sample size	Median CD4 (cells/µL)	Index test (s)	TP	FP	TN	FN
Hanifa *et al.* 2016	South Africa	Prospective	OP	39 (32-45)	39.2	PTB	MRS	404	111 (56–161)	AlereLAM	3	5	363	37
Lawn *et al.* 2017	South Africa	Prospective	IP	36,1 (28.9-42.4)	39.3	PTB, EPTB	MRS	413	149 (55-312)	AlereLAM	53	3	274	86
Sahle *et al.* 2017	Ethiopia	Cross-sectional	OP	30 (23-45)	56	PTB	MRS	21	NR	AlereLAM	5	0	12	4
Boyles *et al.* 2018	South Africa	Prospective	IP	36.2 (29.7-42.1)	33.7	PTB, EPTB	MRS	332	107 (38-118)	AlereLAM	60	11	152	109
LaCourse *et al.* 2018	Kenya	Prospective	IP	24 (13-58)	54.6	PTB	MRS	129	NR	AlereLAM	3	11	111	4
Broger *et al.* 2019	South Africa	Prospective	IP	35 (30-42)	46	PTB, EPTB	MRS	968	86 (33-190)	AlereLAM	268	18	350	332
										FujiLAM	455	33	335	145
Songkhla *et al.* 2019	Thailand	Prospective	IP, OP	39 (32-48)	62.5	PTB, EPTB	MRS	280	33 (12-68)	AlereLAM	54	50	158	18
Andama *et al.* 2020	Uganda	Cross-sectional	OP	32 (25-39)	70	PTB	MRS	116	NR	AlereLAM	10	1	51	54
Bjerrum *et al.* 2020	Ghana	Prospective	IP, OP	38 (31-45)	66.5	PTB, EPTB	MRS	450	152 (44-349)	AlereLAM	35	17	367	31
										FujiLAM	49	41	343	17
Esmail *et al.* 2020	South Africa, Tanzania, Zambia, Zimbabwe	Post-hoc	IP	36 (18-75)	52.4	PTB, EPTB	MRS	561	99.5 (IQR NR)	AlereLAM	68	45	110	338
Garcia *et al.* 2020	Guatemala	Prospective	IP, OP	36 (IQR NR)	74.5	PTB, EPTB	CRS	292	NR	AlereLAM	37	30	202	22
Comella-Del-Barrio *et al.* 2021	Nigeria	Cross-sectional	OP	NR	46.6	PTB	MRS	70	NR	FujiLAM	7	4	56	3
Muyoyeta *et al.* 2021	Zambia	Cross-sectional	OP	37 (28-43)	58.9	PTB	MRS	68	NR	FujiLAM	9	6	50	3

Table 1. Characteristics of all studies included. (continue).

Author, year	Country	Study design	Setting	Median age	Sex (male%)	TB type	Reference standard	Sample size	Median CD4 (cells/μL)	Index test (s)	TP	FP	TN	FN
Nicol *et al.* 2021	South Africa	Prospective	IP	3.8 (1.8-7.4)	54	PTB	MRS	40	NR	AlereLAM	9	8	7	16
										FujiLAM	15	1	14	10
Nkereuwem *et al.* 2021	Gambia, Mali, Nigeria, Tanzania	Cross-sectional	OP	5.6 (2.3-9.3)	54	PTB	MRS	61	NR	AlereLAM	5	9	37	10
										FujiLAM	8	11	35	7
Bjerrum *et al.* 2022	Ghana	Prospective	IP, OP	38 (31-45)	34	PTB, EPTB	MRS	389	176 (52-361)	FujiLAM	29	34	312	14
											30	38	308	13
Indirawati *et al.* 2022	Indonesia	Cross-sectional	IP	NR	82.2	EPTB	MRS	62	44.5 (IQR NR)	FujiLAM	12	12	34	4
Huerga *et al.* 2023	Kenya, Mozambique, South Africa, Uganda	Prospective	OP	41 (33-50)	47.7	PTB, EPTB	MRS	1106	NR	AlereLAM	46	133	859	68
										FujiLAM	68	135	857	46
Reeve *et al.* 2024	South Africa	Cross-sectional	OP	32 (26-39)	41	PTB	MRS	732	299 (170-483)	AlereLAM	14	7	628	83
Székely *et al.* 2024	Malawi, South Africa, Tanzania, Thailand, Uganda, Vietnam, Zambia,	Prospective	IP, OP	40 (IQR NR)	48	PTB, EPTB	MRS	1637	369 (IQR NR)	FujiLAM	160	197	1137	134
Sossen *et al.* 2024	Malawi, South Africa, Tanzania, Thailand, Uganda, Vietnam Zambia	Prospective	IP, OP	40 (33-48)	47.7	PTB, EPTB	MRS	1602	374 (138-630)	AlereLAM	78	129	1219	176

Table 1. Characteristics of all studies included (continue).

Author, year	Country	Study design	Setting	Median age	Sex (male%)	TB type	Reference standard	Sample size	Median CD4 (cells/μL)	Index test (s)	TP	FP	TN	FN
Adzemovic *et al.* 2025	Uganda	Prospective	OP	NR	51	EPTB	MRS	388	NR	FujiLAM	25	16	326	21
Chikamatsu *et al.* 2025	Malawi, South Africa, Tanzania, Thailand, Vietnam, Zambia,	Laboratory-based	NR	NR	NR	PTB, EPTB	MRS	158	NR	AlereLAM	39	6	75	32
										FujiLAM	55	6	80	14
Ellis *et al.*, 2025	Uganda	Prospective	IP	NR	54	PTB, EPTB	MRS	435	34 (11-96)	FujiLAM	36	19	309	71
Tytarenko *et al.* 2025	Nigeria	Retrospective	OP	NR	43.3	PTB	MRS	63	NR	FujiLAM	4	1	55	3
Huerga *et al.* 2023	Kenya, Mozambique, South Africa, Uganda	Prospective	OP	41 (33-50)	47.7	PTB, EPTB	MRS	1106	NR	AlereLAM	46	133	859	68
										FujiLAM	68	135	857	46
Reeve *et al.* 2024	South Africa	Cross-sectional	OP	32 (26-39)	41	PTB	MRS	732	299 (170-483)	AlereLAM	14	7	628	83
Székely *et al.* 2024	Malawi, South Africa, Tanzania, Thailand, Uganda, Vietnam, Zambia,	Prospective	IP, OP	40 (IQR NR)	48	PTB, EPTB	MRS	1637	369 (IQR NR)	FujiLAM	160	197	1137	134

Note: *TP: true positive, FP: false positive, TN: true negative, FN: false negative, IP: inpatient, OP: outpatient, PTB: pulmonary tuberculosis, EPTB: extrapulmonary tuberculosis, MRS: microbiological reference standard, CRS: composite reference standard, NR: not reported.*

Quality assessment

Most included studies were judged to be at low risk of bias across the QUADAS-2 domains (supplementary). Low risk was predominantly observed in the patient selection, index test, and reference standard domains. A small number of studies showed high risk, some concerns, or unclear risk, mainly related to non-consecutive sampling, case-control study designs, insufficient reporting of index test procedures, or the use of composite reference standards. In the flow and timing domain, most studies were assessed as low risk, although a few raised concerns due to incomplete verification or participant exclusions. Overall, most studies were classified as low risk of bias, with only a limited number rated as having some concerns or high risk.

Diagnostic accuracy of AlereLAM

The diagnostic accuracy of urine AlereLAM for detecting active TB in PLHIV was evaluated across the included studies. Individual study estimates demonstrated substantial variability in sensitivity, whereas specificity was consistently high across studies (Figure 2). In the meta-analysis, AlereLAM showed a pooled sensitivity of 0.364 (95% CI 0.272-0.467) and a pooled specificity of 0.928 (95% CI 0.875-0.960). The pooled positive likelihood ratio (LR+) was 5.06 (95% CI 2.95-8.68), while the negative likelihood ratio (LR-) was 0.69 (95% CI 0.59-0.79), with a diagnostic odds ratio (DOR) of 7.38 (95% CI 3.99-13.65). Between-study heterogeneity was substantial, with an I^2 of 91.8% for sensitivity and 93.0% for specificity. The SROC curve is shown in Figure 3, with the summary operating point reflecting these pooled estimates.

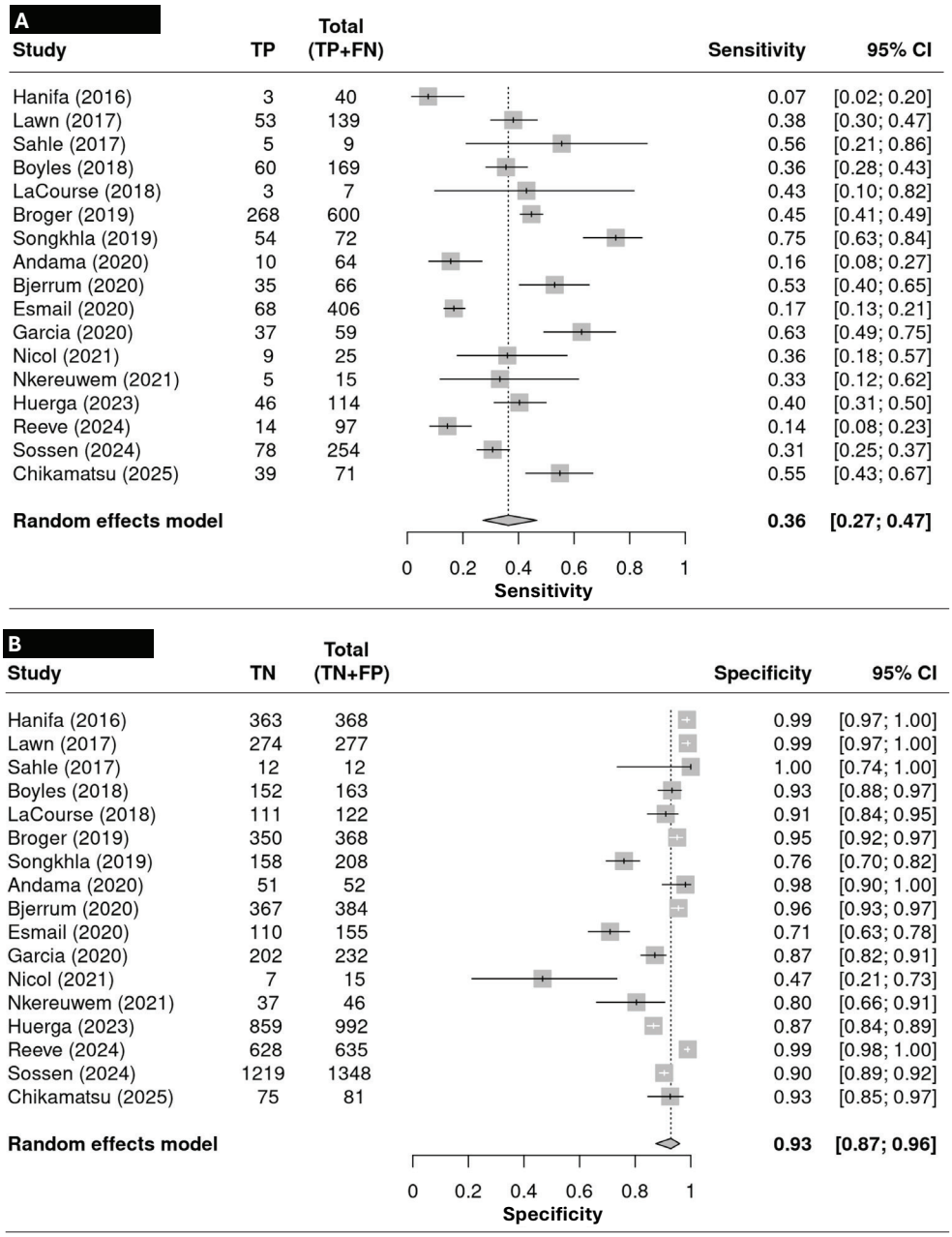

Figure 2. *Forest plots of the sensitivity and specificity of AlereLAM for the diagnosis of active TB in PLHIV.*

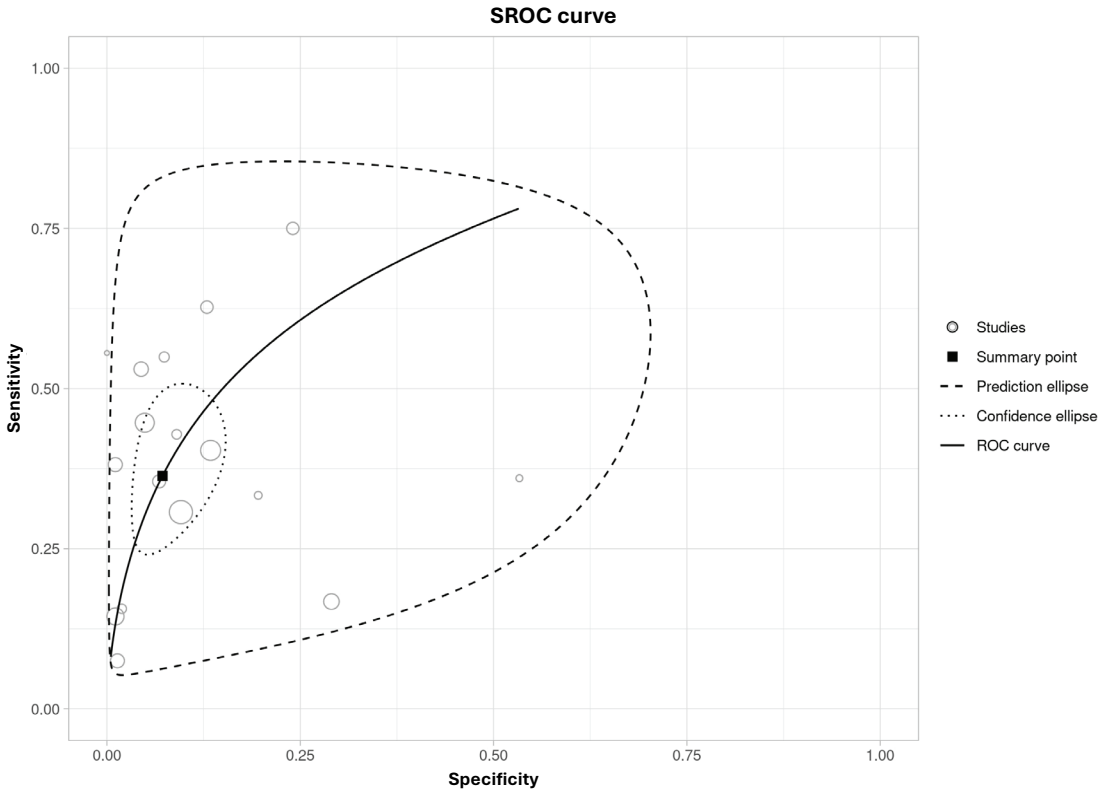

Figure 3. *Summary receiver operating characteristic (SROC) curve of AlereLAM for the diagnosis of active TB in PLHIV.*

Diagnostic accuracy of FujiLAM

The diagnostic accuracy of urine FujiLAM for detecting active TB in PLHIV was assessed across the included studies. FujiLAM demonstrated high sensitivity and specificity, with substantial variability across studies (Figure 4). In the meta-analysis, FujiLAM showed a pooled sensitivity of 0.642 (95% CI 0.567-0.711) and a pooled specificity of 0.901 (95% CI 0.872-0.924). The pooled LR+ was 6.49 (95% CI 4.99-8.43), and the LR- was 0.40 (95% CI 0.33-0.48), corresponding to a DOR of 16.34 (95% CI 11.13-23.98). Between-study heterogeneity was substantial, with an I^2 of 86% for sensitivity and 79% for specificity. The SROC curve (Figure 5) illustrates FujiLAM's overall diagnostic performance, with a summary operating point reflecting the pooled estimates.

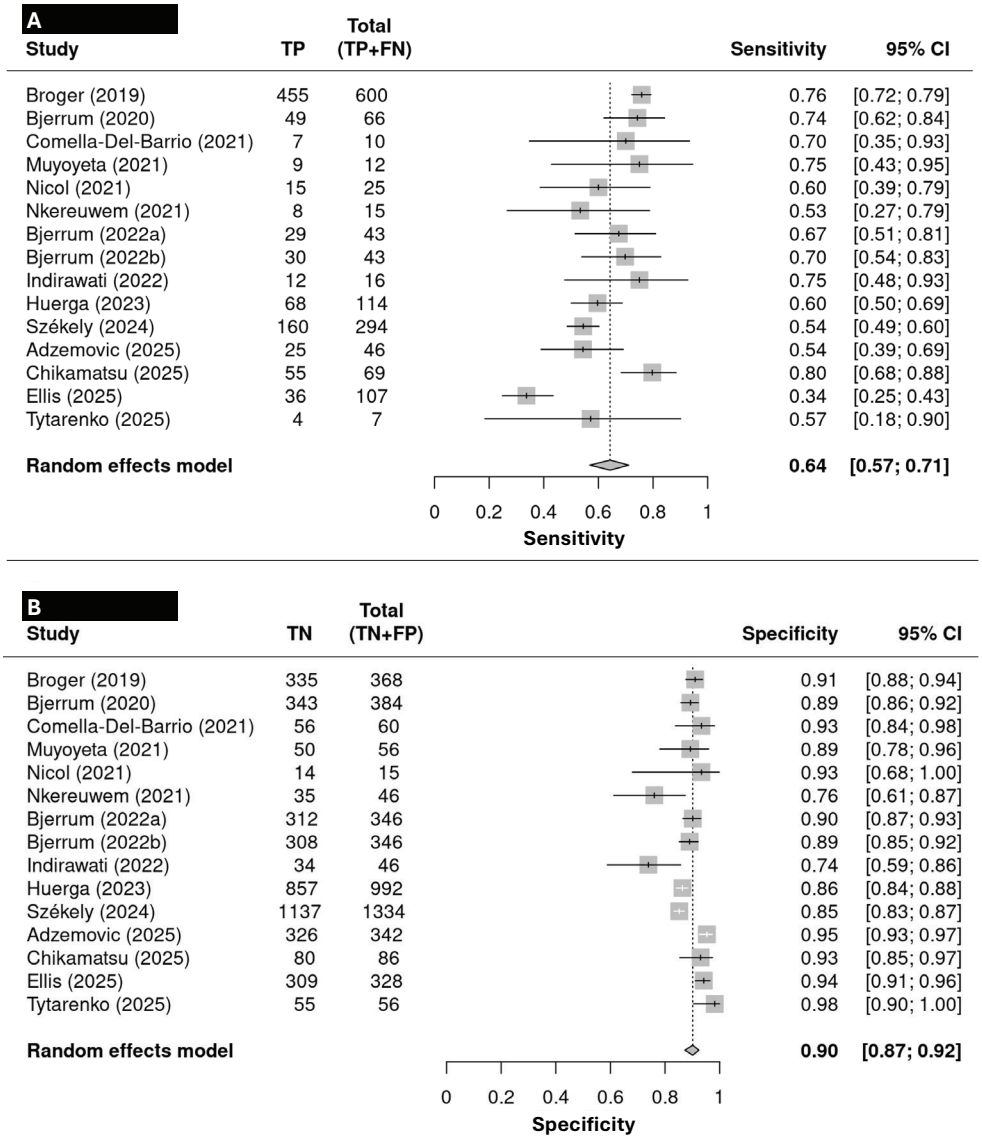

Figure 4. *Forest plots of sensitivity and specificity of FujiLAM for the diagnosis of active TB in PLHIV.*

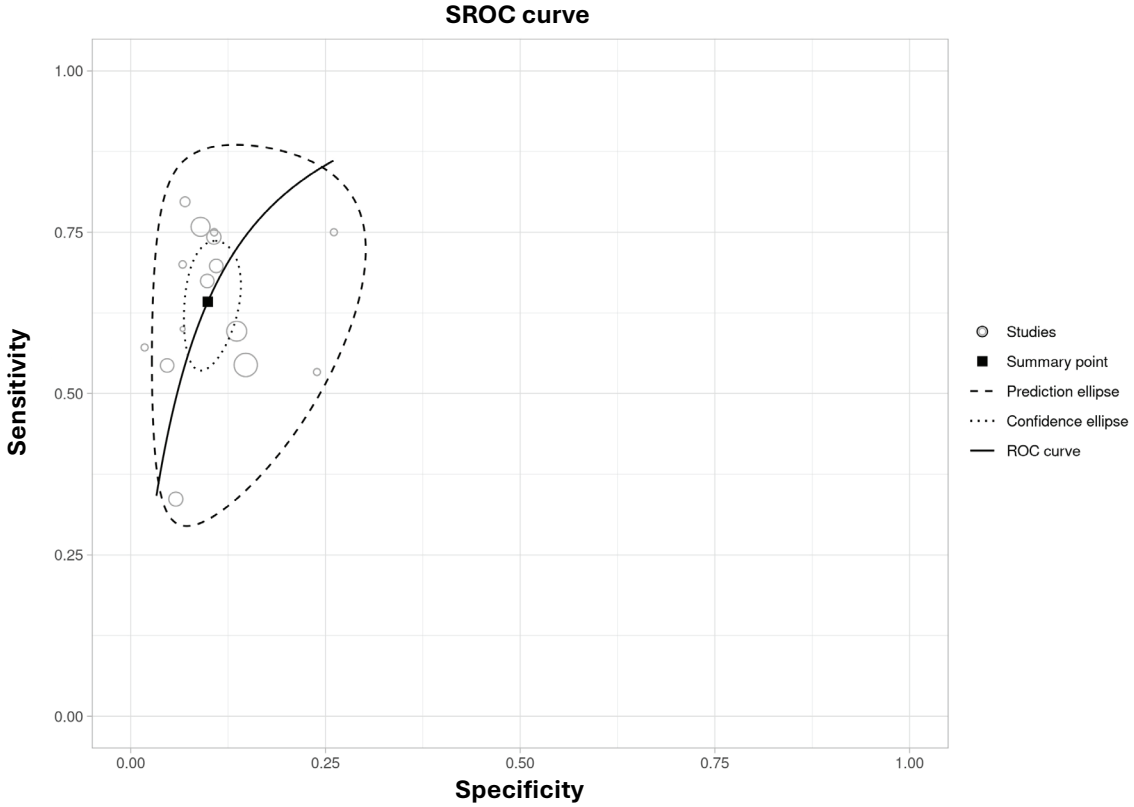

Figure 5. *Summary receiver operating characteristic (SROC) curve of FujiLAM for the diagnosis of active TB in PLHIV.*

Comparison of diagnostic accuracy between AlereLAM and FujiLAM

A comparative analysis of urine AlereLAM and FujiLAM demonstrated clear differences in diagnostic performance among PLHIV evaluated for suspected active TB. Overall, FujiLAM showed substantially higher pooled sensitivity than AlereLAM (0.642 vs 0.364), while maintaining comparably high specificity (0.901 vs 0.928). Consistent with these findings, FujiLAM yielded a higher DOR (16.34 vs 7.38), a higher LR+ (6.49 vs 5.06), and a lower LR- (0.40 vs 0.69) compared with AlereLAM. On the ROC plane, the summary operating point for FujiLAM was positioned closer to the upper-left corner than that for AlereLAM, indicating improved overall diagnostic accuracy (Figure 6). While both assays demonstrated between-study heterogeneity, variability appeared less pronounced for FujiLAM, as indicated by narrower confidence and prediction regions on the SROC curve.

Subgroup analyses were conducted to compare the diagnostic performance of AlereLAM and FujiLAM across CD4 strata and clinical settings. Pooled sensitivity and specificity estimates were summarized for each assay where two or more studies were available (Table 2). Across CD4 strata, FujiLAM consistently demonstrated higher pooled sensitivity than AlereLAM, while pooled specificity remained high for both assays. The difference in sensitivity between assays was most pronounced at lower CD4 counts (<100 cells/μL), whereas specificity showed minimal variation across CD4 strata. Similar patterns were observed across clinical settings, with FujiLAM showing higher pooled sensitivity than AlereLAM in both inpatient and outpatient settings, while pooled specificity remained comparable between assays.

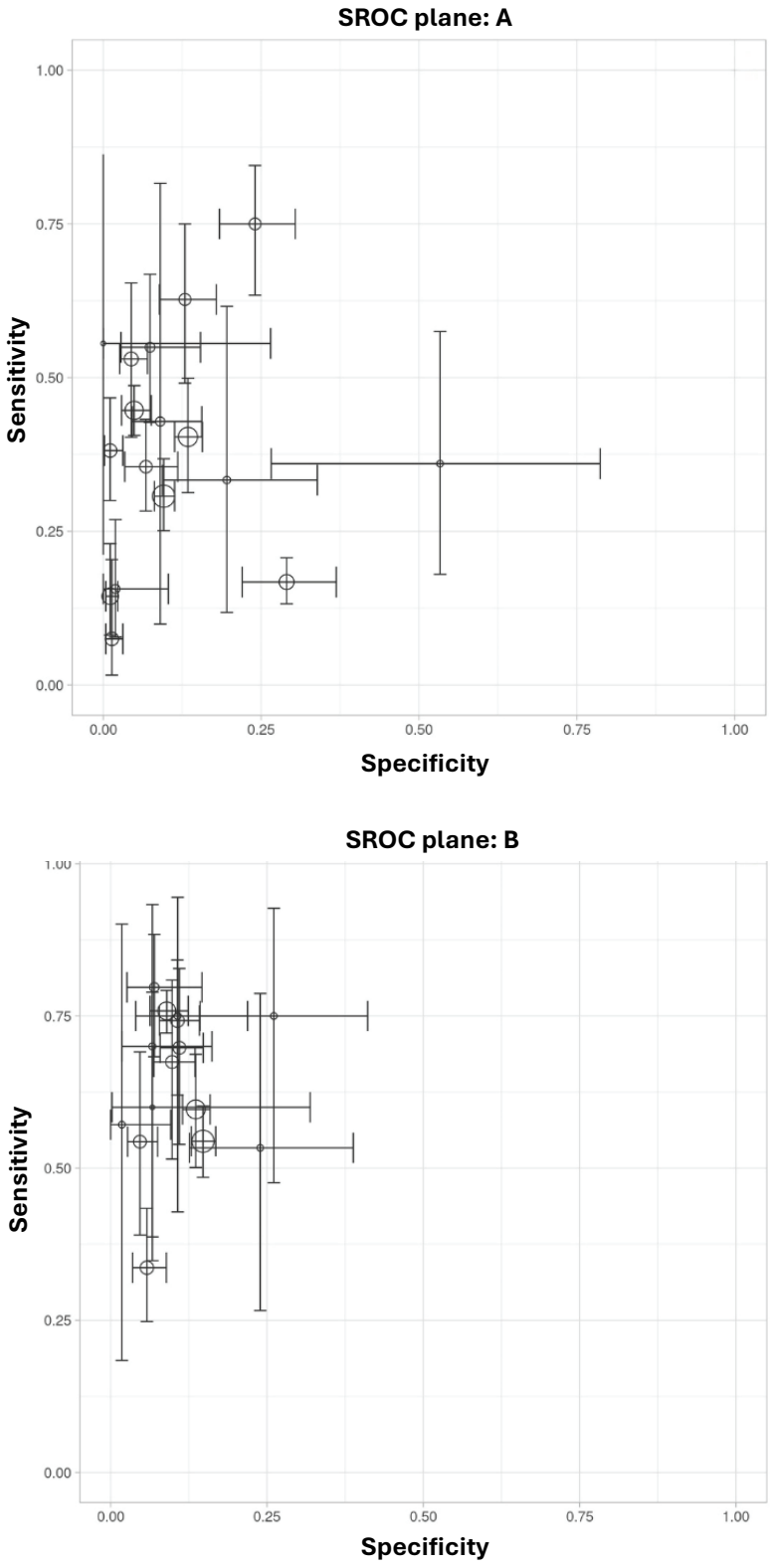

Figure 6. *Comparison of AlereLAM and FujiLAM diagnostic accuracy on the SROC plane.*

Table 2. Subgroup analysis of pooled sensitivity and specificity of AlereLAM and FujiLAM assays by CD4 count and clinical setting among people living with HIV.

Variables	Sub groups	AlereLAM			FujiLAM		
		Studies (total samples)	Pooled sensitivity (%) (95% CI)	Pooled specificity (%) (95% CI)	Studies (total samples)	Pooled sensitivity (%) (95% CI)	Pooled specificity (%) (95% CI)
Median CD4 count (cells/μL)	<100	3 (1809)	44 (18-73)	84 (65-94)	3 (1465)	62 (37-82)	89 (79-95)
	100-200	4 (1600)	32 (16-52)	97 (94-99)	2 (839)	71 (63-78)	89 (88-91)
	>200	2 (2334)	22 (13-36)	97 (85-99)	1 (1637)	NA	NA
By settings	IP	6 (2443)	34 (25-44)	90 (74-97)	4 (1505)	61 (42-78)	90 (81-95)
	OP	6 (2440)	23 (13-38)	97 (90-99)	6 (1756)	59 (52-66)	91 (85-95)

Note: *For subgroups including a single study, pooled estimates are not applicable (NA), and values represent results from the individual study.*

Discussion

This systematic review and diagnostic test accuracy meta-analysis evaluated and compared the performance of urine-based LAM assays (AlereLAM and FujiLAM) for the diagnosis of active TB among people living with HIV. Across the included studies, FujiLAM demonstrated higher pooled sensitivity than AlereLAM, while pooled specificity remained high for both assays. AlereLAM showed modest pooled sensitivity but high specificity, indicating that positive test results are more informative than negative results, consistent with its established role as a rule-in assay, particularly in individuals with advanced HIV disease.

The pooled sensitivity of FujiLAM was higher than that of AlereLAM, with correspondingly higher diagnostic odds ratios and more favorable likelihood ratios. The improved diagnostic performance of FujiLAM is biologically plausible, given its use of a high-affinity monoclonal antibody and silver amplification technology, which may enable detection of lower urinary LAM concentrations.[8,13] Between-study heterogeneity was observed for both assays and may reflect differences in patient populations, CD4 cell counts, clinical settings, and reference standards. Despite higher pooled sensitivity, FujiLAM's negative predictive value remains insufficient to exclude TB when used in isolation.

Current World Health Organization policy recommendations conditionally endorse the use of urine-based LAM assays, particularly among PLHIV with advanced immunosuppression[2]. Within this context, the pooled diagnostic accuracy estimates presented in this review provide updated evidence on the performance of both AlereLAM and FujiLAM in relation to existing policy guidance. The World Health Organization target product profiles for tuberculosis diagnostics emphasize the need for non-sputum-based tests with improved sensitivity in this population.[2,3] Overall, urine LAM assays should be interpreted as part of a comprehensive diagnostic approach that includes microbiological testing and clinical assessment, consistent with their positioning as adjunctive tools within TB diagnostic algorithms for PLHIV.[4]

Limitations

This systematic review and meta-analysis of diagnostic test accuracy have several limitations. Firstly, substantial between-study heterogeneity was observed for both AlereLAM and FujiLAM, likely reflecting differences in study populations, clinical settings, disease severity, and reference standards, which may limit the precision of pooled estimates. Secondly, the use of composite reference standards in some studies may have introduced misclassification bias, particularly where microbiological confirmation was incomplete. Thirdly, inclusion of case-control study designs may have led to spectrum bias and potential overestimation of diagnostic accuracy, and incomplete reporting in some studies limited consistent subgroup analyses. Fourthly, restricting to English-language publications may have introduced language bias, and the relatively small number of studies evaluating FujiLAM may affect the robustness of the pooled estimates. Finally, this review focused on diagnostic accuracy outcomes and did not assess downstream clinical or public health impacts, which should be addressed in future prospective and implementation studies.

Conclusion

In this systematic review and diagnostic test accuracy meta-analysis, the AlereLAM and FujiLAM urine assays demonstrated high pooled specificity for diagnosing active tuberculosis among PLHIV. The pooled sensitivity of FujiLAM was higher than that of AlereLAM, while specificity estimates were comparable between the two assays.

Ethical approval

Ethical approval was not required for this systematic review and meta-analysis because it used data from previously published studies.

Funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare no conflicts of interest.

CRediT authorship contribution statement

Andiesta Asriyah Mariam Saman: conceptualization, data curation, formal analysis, methodology, visualization, writing: original draft, review and edit; **Puspa Wardhani:** methodology, supervision, validation, writing: review and edit; **Aryati:** methodology, supervision, validation, writing: review and edit; **Lukman Nur Rahman:** data curation, formal analysis, writing: review and edit.

Acknowledgements

The authors acknowledge the contributions of the original studies included in this review, which provided the data for this analysis.

References

[1] World Health Organization. Global tuberculosis report 2025. Geneva: World Health Organization; 2025.

[2] World Health Organization. Lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis of active tuberculosis in people living with HIV: policy update 2019. Geneva: World Health Organization; 2019.

[3] World Health Organization. Target product profiles for tuberculosis diagnosis and detection of drug resistance. Geneva: World Health Organization; 2024.

[4] Yang Q, Han J, Shen J, Peng X, Zhou L, Yin X. Diagnosis and treatment of tuberculosis in adults with HIV. Medicine (Baltimore). 2022; 101(35): e30405. doi: 10.1097/MD.0000000000030405.

[5] Salameh JP, Bossuyt PM, McGrath TA, et al. Preferred reporting items for systematic review and meta-analysis of diagnostic test accuracy studies (PRISMA-DTA): explanation, elaboration, and checklist. BMJ. 2020; 370: m2632. doi: 10.1136/bmj.m2632.

[6] Andama A, Jaganath D, Crowder R, et al. Accuracy and incremental yield of urine Xpert MTB/RIF Ultra versus Determine TB-LAM for diagnosis of pulmonary tuberculosis. Diagn Microbiol Infect Dis. 2020; 96(1): 114892. doi: 10.1016/j.diagmicrobio.2019.114892.

[7] Adzemovic T, Nalintya E, Fieberg A, et al. Diagnostic accuracy of the updated FujiLAM II assay to detect tuberculosis in outpatients with advanced HIV disease. Clin Infect Dis. 2025; 81(4): e137-e142. doi: 10.1093/cid/ciaf079.

[8] Bjerrum S, Ahsberg J, Szekely R, et al. Diagnostic accuracy of urine lipoarabinomannan testing in early morning urine versus spot urine for diagnosis of tuberculosis among people with HIV. Microbiol Spectr. 2022; 10(2): e0020822. doi: 10.1128/spectrum.00208-22.

[9] Bjerrum S, Broger T, Szekely R, et al. Diagnostic accuracy of a novel and rapid lipoarabinomannan test for diagnosing tuberculosis among people with human immunodeficiency virus. Open Forum Infect Dis. 2019; 7(1): ofz530. doi: 10.1093/ofid/ofz530.

[10] Boyles TH, Griesel R, Stewart A, Mendelson M, Maartens G. Incremental yield and cost of urine Determine TB-LAM and sputum induction in seriously ill adults with HIV. Int J Infect Dis. 2018; 75: 67-73. doi: 10.1016/j.ijid.2018.08.005.

[11] Broger T, Sossen B, du Toit E, Kerkhoff AD, Schutz C, Ivanova Reipold E, et al. Novel lipoarabinomannan point-of-care tuberculosis test for people with HIV: a diagnostic accuracy study. Lancet Infect Dis. 2019; 19(8): 852-61. doi: 10.1016/S1473-3099(19)30001-5.

[12] Chikamatsu K, Shimomura Y, Osugi A, Mitarai S. Assessing the accuracy of the updated Fujifilm SILVAMP TB LAM II assay between lot numbers. IJTLD Open. 2025; 2(2): 96-100. doi: 10.5588/ijtldopen.24.0449.

[13] Comella-del-Barrio P, Bimba JS, Adelakun R, Kontogianni K, Molina-Moya B, Osazuwa O, et al. Fujifilm SILVAMP TB-LAM for the diagnosis of tuberculosis in Nigerian adults. J Clin Med. 2021; 10(11): 2514. doi: 10.3390/jcm10112514.

[14] Ellis J, Dai B, Kabahubya M, Hale G, Mande E, Katende G, et al. Diagnostic accuracy of the re-engineered urinary FujiLAM2 assay among hospitalized adults with advanced HIV disease. AIDS. 2025; 39(10): 1334-43. doi: 10.1097/QAD.0000000000004213.

[15] Friedrich R, Rappold E, Bogdan C, Held J. Comparative analysis of the Wako β-glucan test and the Fungitell assay for diagnosis of candidemia and Pneumocystis jirovecii pneumonia. J Clin Microbiol. 2018; 56(9): e00499-18. doi: 10.1128/JCM.00499-18.

[16] Garcia JI, Melendez J, Alvarez R, Mejia-Chew C, Kelley HV, Sidiki S, et al. Accuracy of the tuberculosis point-of-care Alere Determine lipoarabinomannan antigen diagnostic test using α-mannosidase-treated and untreated urine in people living with HIV in Guatemala. AIDS Res Ther. 2020; 17(1): 60. doi: 10.1186/s12981-020-00318-8.

[17] Hanifa Y, Fielding KL, Chihota VN, Adonis L, Charalambous S, Karstaedt A, et al. Diagnostic accuracy of lateral flow urine LAM assay for tuberculosis screening of adults with advanced immunosuppression attending routine HIV care in South Africa. PLoS One. 2016; 11(6): e0156866. doi: 10.1371/journal.pone.0156866.

[18] Huerga H, Bastard M, Lubega AV, Akinyi M, Antabak NT, Ohler L, et al. Novel FujiLAM assay

to detect tuberculosis in HIV-positive ambulatory patients in four African countries: a diagnostic accuracy study. Lancet Glob Health. 2023; 11(1): e126-e135. doi: 10.1016/S2214-109X(22)00463-6.

[19] Indirawati NN, Yunihastuti E, Yulianti M, Nasir UZ, Wulandari D, Rinaldi I. Lateral flow urine lipoarabinomannan assay for extrapulmonary tuberculosis diagnosis in HIV-positive adults. Int J Infect Dis. 2022; 122: 415-9. doi: 10.1016/j.ijid.2022.06.007.

[20] Lacourse SM, Pavlinac PB, Cranmer LM, Njuguna IN, Mugo C, Gatimu J, et al. Stool Xpert MTB/RIF and urine lipoarabinomannan for the diagnosis of tuberculosis in hospitalized HIV-infected children. AIDS. 2018; 32(1): 69-78. doi: 10.1097/QAD.0000000000001662.

[21] Lawn SD, Kerkhoff AD, Burton R, Schutz C, Boulle A, Vogt M, et al. Diagnostic accuracy, incremental yield, and prognostic value of Determine TB-LAM for routine diagnostic testing for tuberculosis in HIV-infected patients requiring acute hospital admission in South Africa. BMC Med. 2017; 15(1): 67. doi: 10.1186/s12916-017-0822-8.

[22] Muyoyeta M, Kerkhoff AD, Chilukutu L, Moreau E, Schumacher SG, Ruhwald M. Diagnostic accuracy of a novel point-of-care urine lipoarabinomannan assay for the detection of tuberculosis among adult outpatients in Zambia. Eur Respir J. 2021; 58(5): 2003999. doi: 10.1183/13993003.03999-2020.

[23] Nicol MP, Schumacher SG, Workman L, Broger T, Baard C, Prins M, et al. Accuracy of a novel urine test, Fujifilm SILVAMP tuberculosis lipo-arabinomannan, for the diagnosis of pulmonary tuberculosis in children. Clin Infect Dis. 2021; 72(9): e280-e288. doi: 10.1093/cid/ciaa1052.

[24] Nkereuwem E, Togun T, Gomez MP, Szekely R, Mace A, Jobe D, et al. Comparing accuracy of lipoarabinomannan urine tests for diagnosis of pulmonary tuberculosis in children from four African countries: a cross-sectional study. Lancet Infect Dis. 2021; 21(3): 376-84. doi: 10.1016/S1473-3099(20)30598-3.

[25] Reeve BWP, Ndlangalavu G, Mishra H, Palmer Z, Tshivhula H, Rockman L, et al. Point-of-care C-reactive protein and Xpert MTB/RIF Ultra for tuberculosis screening and diagnosis in unselected antiretroviral therapy initiators: a prospective cross-sectional diagnostic accuracy study. Lancet Glob Health. 2024; 12(5): e793-e803. doi: 10.1016/S2214-109X(24)00052-4.

[26] Sahle SN, Asress DT, Tullu KD, Weldemariam AG, Tola HH, Awas YA, et al. Performance of point-of-care urine test in diagnosing tuberculosis suspects with and without HIV infection in selected peripheral health settings of Addis Ababa, Ethiopia. BMC Res Notes. 2017; 10(1): 1-6. doi: 10.1186/s13104-017-2404-4.

[27] Songkhla MN, Tantipong H, Tongsai S, Angkasekwinai N. Lateral flow urine lipoarabinomannan assay for diagnosis of active tuberculosis in adults with human immunodeficiency virus infection: a prospective cohort study. Open Forum Infect Dis. 2019; 6(4): ofz132. doi: 10.1093/ofid/ofz132.

[28] Sossen B, Szekely R, Mukoka M, Muyoyeta M, Nakabugo E, Hella J, et al. Urine Xpert Ultra for the diagnosis of tuberculosis in people living with HIV: a prospective multicentre diagnostic accuracy study. Lancet Glob Health. 2024; 12(12): e2024-e2034. doi: 10.1016/S2214-109X(24)00357-7.

[29] Szekely R, Sossen B, Mukoka M, Muyoyeta M, Nakabugo E, Hella J, et al. Prospective multicentre accuracy evaluation of the Fujifilm SILVAMP TB LAM test for the diagnosis of tuberculosis in people living with HIV demonstrates lot-to-lot variability. PLoS One. 2024; 19(5): e0303846. doi: 10.1371/journal.pone.0303846.

[30] Tytarenko N, Bimba JS, Vulcano D, Comella-del-Barrio P, Osazuwa O, Creswell J, et al. Diagnostic performance of second-generation Fujifilm SILVAMP TB LAM in Nigerian adults with presumptive tuberculosis. J Clin Med. 2025; 14(21): 7524. doi: 10.3390/jcm14217524.

Supplementary
Search strategy for systematic review and diagnostic test accuracy meta-analysis

Search period:

1. Studies published from 1 January 2016 to 31 December 2025.
2. The last search was conducted on 9 January 2026.

Language restriction:

Searches were limited to English-language publications.

Search concepts:

The search strategy was developed using combinations of controlled vocabulary terms and free-text keywords covering the following concepts:

1. Tuberculosis
2. Human immunodeficiency virus (HIV)
3. Urine lipoarabinomannan (LAM) assays, including:
    a. Alere Determine TB-LAM (AlereLAM)
    b. Fujifilm SILVAMP TB LAM (FujiLAM)

Table S1. Search strategy and results for systematic review and diagnostic test accuracy meta-analysis.

Databases	Boolean search strategy	Search result
PubMed	((“Tuberculosis”[Mesh] OR tuberculosis[tiab] OR TB[tiab]) AND (“HIV Infections”[Mesh] OR HIV[tiab] OR “human immunodeficiency virus”[tiab] OR PLHIV[tiab]) AND ((“Lipoarabinomannan”[tiab] OR LAM[tiab]) AND (urine[tiab] OR urinary[tiab])) AND (“Determine TB LAM”[tiab] OR AlereLAM[tiab] OR “Alere Determine TB LAM”[tiab] OR FujiLAM[tiab] OR “Fujifilm SILVAMP TB LAM”[tiab] OR SILVAMP[tiab]) AND (diagnos*[tiab] OR sensitiv*[tiab] OR specific*[tiab] OR accuracy[tiab] OR ROC[tiab]))	57
SCOPUS	TITLE-ABS-KEY ((tuberculosis OR TB) AND (HIV OR “human immunodeficiency virus” OR PLHIV OR “people living with HIV”) AND (urine OR urinary) AND (“lipoarabinomannan” OR LAM) AND (“Determine TB LAM” OR AlereLAM OR FujiLAM OR “Fujifilm SILVAMP TB LAM” OR “SILVAMP TB LAM” OR SILVAMP) AND (diagnos* OR sensitiv* OR specific* OR accuracy OR ROC OR “diagnostic accuracy”))	65
SpringerLink	(“FujiLAM” OR “Fujifilm SILVAMP TB LAM” OR “SILVAMP TB LAM” OR SILVAMP OR “Determine TB LAM” OR AlereLAM OR “Alere Determine TB LAM”) AND (tuberculosis OR TB) AND (HIV OR “human immunodeficiency virus” OR PLHIV) AND (urine OR urinary) AND (LAM OR lipoarabinomannan)	35

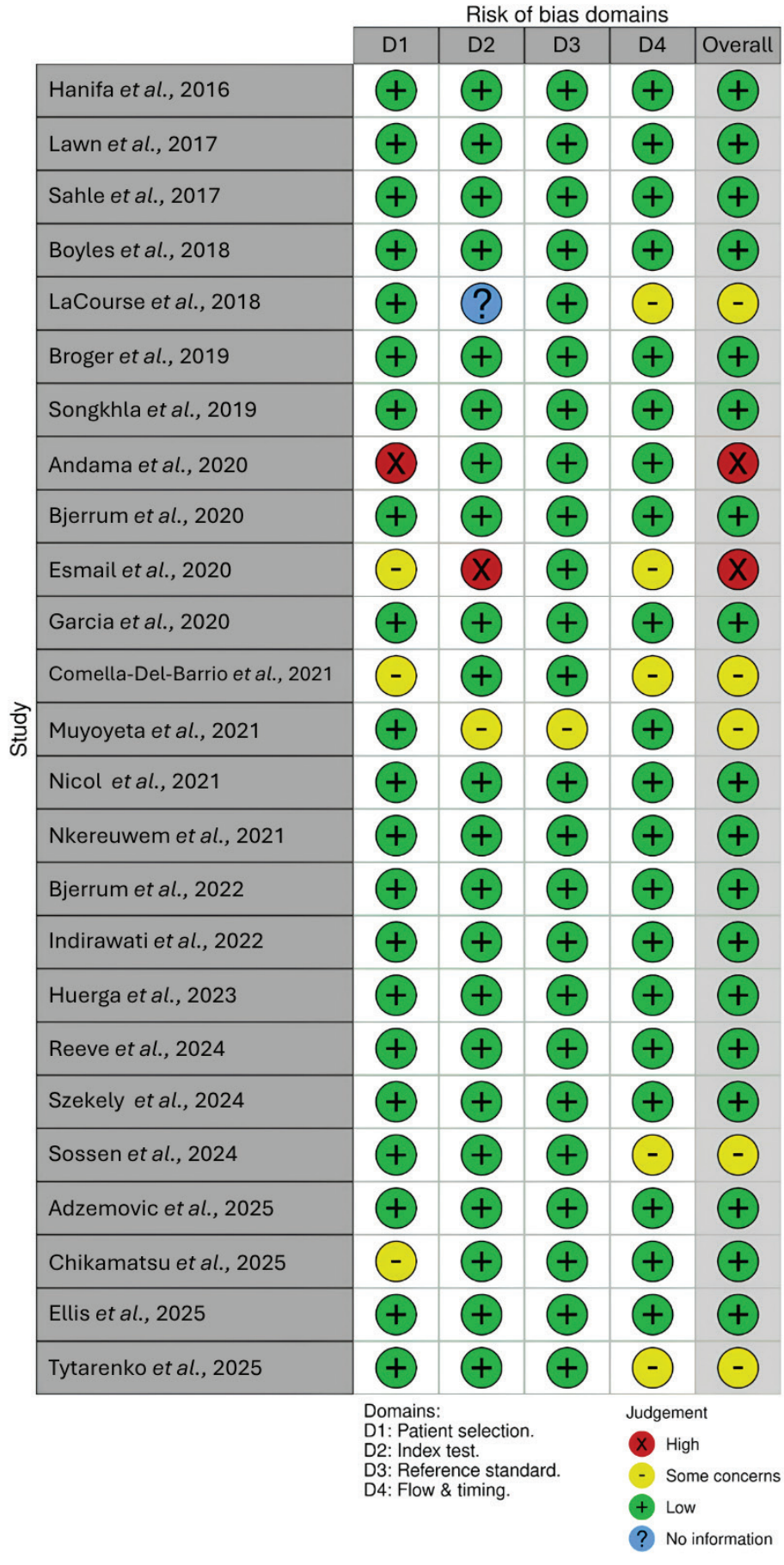

Figure S1. *QUADAS-2 risk of bias assessment of included studie.*