Table 1. Overview of selected current and future diagnostic tests for tuberculosis

Test method	Stage of development	Cost	Turnaround time	Complexity	Distinction between LTBI and active TB	Advantages	Disadvantages
Immune-based							
Tuberculin skin test	In clinical use	Low	48 to 72 hours	Low	No	No laboratory required, minimal training required, widely used in TB control programs, large amount of data on performance and positive predictive value	Limited specificity, subjectivity of reading test results, risk of supply shortages of test substance, potential boosting phenomenon with repeated testing, false-negative test results in immunodeficient and immunosuppressed patients, need for patient to return for reading within 48-72 hour window, potential discomfort (including rarely skin ulceration)
C-Tb test	In clinical trials (Statens Serum Institut)	Unknown	Likely 48 to 72 hours	Low	No	No laboratory required, minimal training required, likely greater specificity than TST	Subjectivity of reading test results, need for patient to return for reading within 48-72 hour window, performance characteristics (i.e. sensitivity and specificity) currently uncertain
Interferon-gamma release assays	In clinical use	High	> 1 day	Moderate	No	Likely greater specificity than TST, result available after single visit	Requires laboratory, false-negative test results in immuno-deficient and immunosuppressed patients, poor reproducibility, potentially lower sensitivity than TST in children, worse performance in children, indeterminate results more common in children, limited data on positive predictive value for the development of active TB (particularly in children)
Unstimulated interferon-gamma-based assays	In development for commercial use (IRISA-TB assay)	Unknown	< 2 hours	Low - Moderate	Only for active TB	Has potential for use in certain forms of extrapulmonary TB (TB pleuritis, pericarditis, meningitis and ascites)	Requires laboratory, currently limited data available, requires invasive procedure to obtain sample, performance characteristics (i.e. sensitivity and specificity) currently uncertain, likely limited specificity based on test principle
M. tuberculosis-specific cytokine-based assays	Research	Moderate	Variable (hours to days)	Moderate	Potentially	Performed on blood samples, likely high specificity, result interpretation operator-independent	Require laboratory, currently limited data (considerable variation in the methods used by different investigators)
M. tuberculosis-specific polyfunctional T cell assays	Research	High	Variable (hours to days)	High	Potentially	Performed on blood samples, likely high specificity	Requires laboratory, expensive equipment and considerable expertise (both in performing assays and in interpreting results)
T cell activation marker assays	Research	High	Unknown	High	Potentially	Performed on blood samples, likely high specificity	Requires laboratory, expensive equipment and considerable expertise (both in performing assays and in interpreting results)
Antibody-based (serological) assays	Commercially available (multiple products)	Low - Moderate	Minutes to few hours	Low - Moderate	No	Performed on blood samples, potential use as point-of-care tests	Currently available commercial products have inadequate performance characteristics; WHO therefore advised against their use, but encourages the development of more robust antibody-based assays. Novel multiplexed assays are currently in development.
Antigen-based							
Lipoarabinomannan (LAM)-based assays	Commercially available (Alere Determine TB LAM Ag)	Low - Moderate	Minutes to few hours	Low - Moderate	Only for active TB	Available as lateral-flow point-of-care test (and as ELISA), no laboratory instruments required, test sample (urine) easily obtained	Poor sensitivity (typically ≤50%-60%, marginally better performance in HIV-positive patients with low CD4 count) – therefore only has potential to be used as rule-in test (combined with other methods), worse performance in children, potential for false-positive results in non-tuberculous mycobacterial diseases
Other urinary TB antigen-based tests	Research	Unknown	Unknown	Unknown	Only for active TB	Test sample (urine) easily obtained	Cannot detect LTBI, performance characteristics (i.e. sensitivity and specificity) currently uncertain

Enzyme-based & VOC-based							
Adenosine deaminase (ADA)-based assays	Research	Unknown	Minutes to few hours	Unknown	Only for active TB	Has potential for use in certain forms of extrapulmonary TB (TB pleuritis, pericarditis, meningitis and ascites)	Limited data, requires invasive procedure to obtain sample, poor sensitivity (typically ≤50%-70%, depending on the site of TB disease)
β-lactamase-based assays	Research / in development for commercial use (TB REaD POC assay)	Unknown	< 1 hour (estimated)	Low - Moderate	Only for active TB	Aimed at peripheral care level, automated battery-powered reader in development	Requires sputum, qualitative analysis only, performance characteristics (i.e. sensitivity and specificity) currently uncertain
TB-specific volatile organic compounds (VOC)	Research	Unknown	Unknown (potentially minutes)	Low - Moderate	Only for active TB	Test sample (breath) easily obtained, potential for use as point-of-care test (handheld device in development)	Likely requires expensive instruments, difficulties with standardising conditions for sampling, likely to perform worse in paucibacillary disease / children with pulmonary TB, unable to diagnose extrapulmonary TB, performance characteristics (i.e. sensitivity and specificity) currently uncertain
Nucleic acid-based							
Line probe assays	In clinical use (multiple products)	Moderate	Hours	Low - Moderate	Only for active TB	Can be used on isolates or sputum, detect *M. tuberculosis* complex and resistance genes (type and number of genes vary between products)	Require laboratory (require DNA extraction and thermocycler), require trained personnel, labour-intensive, prone to contamination, only moderate sensitivity in smear-negative sputum samples, lower sensitivity than culture
Xpert MTB/RIF assay	In clinical use	High	2 hours (excluding transport and sample preparation)	Low	Only for active TB	High specificity, can be performed with minimal training, low risk of operator acquiring TB by generation of aerosols	Requires laboratory (with continuous power supply and air-conditioning), lower sensitivity than culture (particularly in children), does not detect drug-resistances other than rifampicin-resistance, generates significant amount of biohazard waste
Other PCR-based assays	Commercially available or in clinical use (multiple products)	High	Hours	Low - High	Only for active TB	High specificity, intermediate to fast turnaround time	Require laboratory, lower sensitivity than culture (particularly in children)
Microarray-based assays	Multiple products at development stage or available for research use	Moderate - High	Unknown (likely hours)	Moderate - High	Uncertain	Detect *M. tuberculosis* complex and resistance genes (type and number of genes vary between products)	Require laboratory, labour-intensive, performance characteristics (i.e. sensitivity and specificity) currently uncertain

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