Table 1. Findings from Systematic Reviews on TB Diagnostic Tests

Diagnostic Test [References]	Number of Reviews	Disease/Site	Major Findings/Results of Systematic Reviews
Diagnosis of active TB			
Sputum smear microscopy [20,31,32]	3	Pulmonary TB	• Fluorescence microscopy is on average 10% more sensitive than conventional microscopy. Specificity of both fluorescence and conventional microscopy is similar. • Centrifugation and overnight sedimentation, preceded with any of several chemical methods (including bleach), is more sensitive than direct microscopy; specificity is unaffected by sputum processing methods. • When serial sputum specimens are examined, the mean incremental yield and/or increase in sensitivity from examination of 3rd sputum specimen ranges between 2% and 5%.
NAATs [9,10,11,14,18,23,24,28]	8	Pulmonary and extrapulmonary TB	• NAATs have high specificity and positive predictive value. NAATs, however, have relatively lower (and highly variable) sensitivity and negative predictive value for all forms of TB, especially in smear-negative and extrapulmonary disease. • In-house ("home-brew") NAATs produce highly inconsistent results as compared to commercial, standardized NAATs.
Commercial serological antibody detection tests [10,29,30]	3	Pulmonary and extrapulmonary TB	• Serological tests for both pulmonary and extrapulmonary TB produce highly inconsistent estimates of sensitivity and specificity; none of the assays perform well enough to replace microscopy.
ADA [12,13,17,27,33]	5	TB pleuritis, pericarditis, peritonitis	• Measurement of ADA levels in pleural, pericardial, and ascitic fluid has high sensitivity and specificity for extrapulmonary TB.
IFN-γ [13,15]	2	TB pleuritis	• Pleural fluid IFN-γ determination is a sensitive and specific test for the diagnosis of TB pleuritis.
Phage amplification assays [16]	1	Pulmonary TB	• Phage-based assays have high specificity but lower and variable sensitivity. • Their performance characteristics are similar to sputum microscopy.
Automated liquid cultures [10]	1	Pulmonary TB	• Automated liquid cultures are more sensitive than solid cultures. • Time to detection is more rapid than solid cultures.
Diagnosis of latent TB infection			
TST [34,35]	2	Latent TB infection	• Individuals who receive BCG vaccination are more likely to have a positive TST; the effect of BCG on TST results is less after 15 years; positive TST with indurations of >15 mm are more likely to be the result of TB infection than of BCG vaccination. • The effect on TST of BCG received in infancy is minimal, especially 10 years after vaccination. BCG received after infancy produces more frequent, more persistent, and larger TST reactions. • Non-tuberculous mycobacterial (NTM) infection is not a clinically important cause of false-positive TST, except in populations with a high prevalence of NTM sensitization and a very low prevalence of TB infection.
T cell–based IGRAs [21,26,37]	3	Latent TB infection	• IGRAs have excellent specificity (higher than the TST), and are unaffected by prior BCG vaccination.
Diagnosis of drug-resistant TB			
Phage amplification assays [25]	1	Rapid detection of rifampicin resistance	• When used on culture isolates, phage assays have high sensitivity, but variable and lower specificity. • In contrast, evidence is lacking on the accuracy of these assays when they are directly applied to sputum specimens.
Line probe assays: INNO-LiPA Rif. TB (LiPA) [22] and GenoType MTBDR assays [38]	2	Rapid detection of rifampicin resistance	• LiPA is a highly sensitive and specific test for the detection of rifampicin resistance in culture isolates, with relatively lower sensitivity when used directly on clinical specimens. •The GenoType MTBDR assays have excellent sensitivity and specificity for rifampicin resistance even when directly used on clinical specimens.
Colorimetric redox-indicator methods [19] and nitrate reductase assays [36]	2	Rapid detection of rifampicin and isoniazid resistance	• Colorimetric methods and nitrate reductase assays are highly sensitive and specific for the rapid detection of rifampicin and isoniazid resistance in culture isolates.

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