



Overview

- WHO recommendations on the use of serological tests
- Review of the evidence
 - Background
 - Serological tests: An updated systematic review and meta-analysis
 - Cost effectiveness model of serological tests in India

WHO issues a strong recommendation against the use of serological tests

- WHO Expert Group recommended that serological tests should not be used in individuals suspected of active pulmonary or extrapulmonary TB, irrespective of their HIV status (22 July 2010)
- The WHO Strategic and Technical Advisory Group for TB (STAG-TB, highest policy making body for TB at WHO) endorsed the Expert Group recommendations (27 September 2010) <u>http://www.who.int/tb/advisory_bodies/stag_tb_report_20</u> <u>10.pdf</u>
- A negative WHO policy on TB serology is expected in early 2011





WHO/TDR Laboratory-based...2008

- Rapid test result (< 15 mins)</p>
- Simple 1 or 2 steps, minimal training and no equipment
- Easy to interpret card or strip format with visual readout
- Gold standard culture plus clinical follow-up
- Archived specimens



	Manufacturer	Rapid Test	Sensitivity % (95% CI)	Specificity % (95% CI)
1	ABP Diagnostics	Focus Sure Check TB	8 (4-11)	95 (92-99)
2	Advanced Diagnostics	Tuberculosis Rapid Test	40 (33-46)	53 (45-61)
3	American Bionostica	Rapid Test for TB	20 (15-26)	80 (73-86)
4	Ameritek dBest	One Step TB Test	34 (27-40)	68 (61-76)
5	BioMedical Products Corp	TB Rapid Screen Test	49 (42-56)	57 (49-65)
6	Chembio	TB Stat-Pak II	32 (25-38)	83 (76-89)
7	CTK Biotech TB Antibody	Onsite Rapid Screening Test	27 (21-33)	69 (62-77)
8	Hema Diagnostic	Rapid 1-2-3 TB Test	36 (29-42)	72 (65-80)
9	Laboratorio Silanes	TB-Instantest	38 (31-44)	70 (62-77)
10	Millenium Biotechnology	Immuno-Sure TB Plus	2 (0-5)	99 (97-100)
11	Minerva Biotech	V Scan	21 (16-27)	89 (84-94)
12	Mossman Associates	MycoDot	36 (30-42)	87 (81-92)
13	Pacific Biotech	Bioline TB	19 (14-25)	95 (91-98)
14	Premier Medical Corporation	First Response Rapid TB	21 (16-27)	95 (92-99)
15	Princeton BioMeditech	BioSign M tuberculosis	1 (0-2)	99 (97-100)
16	Span Diagnostics	TB Spot ver 2.0	38 (32-45)	78 (71-85)
17	Standard Diagnostics	SD Rapid TB	21 (15-26)	96 (93-99)
18	UniMED International Inc	FirstSign MTB Card Test	60 (53-66)	58 (50-66)
19	Veda Lab	TB Rapid Test	13 (8-17)	98 (96-100)





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Based on a survey of more than 80 Indian laboratories, some preliminary estimates

• About 50 large and medium *private labs* alone are doing over 60,000 tests per month

• ~1.5 million TB serological (ELISA) tests every year

• @ \$10 per test**, the market is worth <u>at least</u> \$15 million (this is <u>highly</u> conservative)

**The cost is actually ~\$10 per antibody (e.g. IgG). Testing for all 3 antibodies (IgG, IgA, IgM) is often done at cost of ~\$30 per patient; for simplicity, we have used \$10 per patient, a conservative estimate (RNTCP annual budget ~ \$65 million)

Pai et al. Unpublished

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Commercial serological tests, framing the question

Population - adults and children with and without HIV infection suspected of active TB, all countries
 Intervention - commercial serological test
 Comparison - no test/smear microscopy
 Outcomes - sensitivity and specificity

Reference standard - culture (either solid or liquid) Excluded studies published before 1990 and studies with < 10 TB cases

Results - Pulmonary TB















Head-to-head comparison SDHO and smear microscopy, HIV-infected individuals

Test	Sensitivity % (95% Cl)	Specificity (95% CI)
SDHO (Saint-Sauveur des Monts, Canada)	16 (5, 34)	90 (74, 98)
Smear microscopy	68 (49, 83)	100 (89,100)

- 55 HIV-infected pulmonary TB suspects, hospitalized and outpatient
- 31 culture-confirmed TB cases
- Median age 31
- Central African Republic

Kassa-Kelembho et al. Clin Vaccine Immunol. 2006 June; 13(6): 702-3

Discussion

The sensitivity and specificity estimates in the meta-analysis are likely to be overly optimistic for at least two reasons:

- 1. study quality generally suffered from lack of a representative patient spectrum and could have resulted in inflated estimates of test accuracy
- 2. publication bias was possible because studies with poor performance were unlikely to be unpublished





Dowdy DW, Steingart KR; Pai M

Hypothetical "Study Population"

- ▶ 1.5 million TB suspects
 - Conservative estimate of annual number of serologic tests in India
- 1 in 7 actually have TB
 - Estimate from FIND, comparable to other studies
- Among TB patients, 53% are "highly infectious"
 - Would be diagnosed with 2 sputum smears in ideal lab
- ▶ 5% HIV prevalence
 - 10% with access to ART (UNAIDS 2009); does not affect model results
- Accuracy estimates obtained from the systematic review

Dowdy et al., 2010 submitted manuscript

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)iagnostic Test	Cost (US\$)	Additional TB Cases Treated	Additional False-Positive Cases Treated	Secondary Cases Averted
putum smear microscopy	\$11.9 million	44,000	36,000	443,000
putum smear + TB culture	\$45.0 million	71,000	48,000	555,000
erologicaltesting	\$47.5 million	58,000	157,000	411,000
Rapid molecular testing	\$52.8 million	86,000	12,000	629,000

In conclusion

- Published data on commercial serological tests for the diagnosis of active TB inconsistent and imprecise estimates of sensitivity and specificity
- Modeling study in a hypothetical cohort of 1.5 million adult Indian TB suspects suggests that serological testing for active TB is both more costly and less effective than sputum smear microscopy

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