Commercial serological tests for the diagnosis of active TB: The evidence is reviewed

Karen R Steingart, MD, MPH
New Diagnostics Working Group
Lille, 26 October, 2011
karenst@uw.edu

CURRY INTERNATIONAL TUBERCULOSIS CENTER

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Disclosure

- I have no financial disclosures to declare
- I have published previous systematic reviews on serological tests
- I serve as Coordinator of the Evidence Synthesis & Policy subgroup of Stop TB Partnership's New Diagnostics Working Group

Overview

- Background
- The evidence is reviewed
  - Updated systematic review and meta-analysis
  - WHO/TDR evaluation of rapid tests
  - Economic and epidemiological impact of serologic testing for active TB in India
- WHO policy statement on serological tests
- Response to the new policy

Background - definitions

- Antigen – any molecule that can bind specifically to an antibody (the name comes from the ability to **gen**erate **anti**body)
- Antibody - a protein that binds specifically to a particular substance, its antigen; all antibody molecules belong to a family of proteins called immunoglobulins
- **Serological tests for TB - tests (such as ELISA, immunochromatographic tests) on a sample of blood serum that detect the humoral immune (antibody) responses to *M. tuberculosis antigens***
- Do not confuse serological tests with IGRAs that measure the T-cell-based interferon-gamma response to *M. tuberculosis* antigens

Janeway, Immunobiology, 6th edition

Background - advantages

- Serological tests could be developed into point-of-care tests
- Serological tests provide rapid results
  - ELISA, within hours
  - immunochromatographic assay, within minutes
- For children, a blood test may be more practical than sputum microscopy
- For patients suspected of extrapulmonary TB, a blood test, if accurate, could replace more invasive tests

Package inserts claim high accuracy

SD STANDARD DIAGNOSTICS, INC.
156-68 Hagal-dong, Giheung-gu, Yongin-si, Kyonggi-do, Korea
Tel : 82-31-899-9700 Fax : 82-31-899-9740 http://www.standardia.com

2) Comparison SD Rapid TB vs. a commercial anti-TB ELISA
The SD Rapid TB have tested with positive and negative clinical samples tested by a leading commercial ELISA test. The result shows that the SD Rapid TB is very accurate to other commercial ELISA test.

		A Commertial PHA		Total Results
		Positive	Negative	
A commercial anti-M.tuberculosis ELISA kit	Positive	112	2	114
	Negative	1	350	351
Total Results		113	352	465

In a comparison of the SD Rapid TB versus a leading commercial ELISA test, results gave sensitivity of 98.2% (112/114), a specificity of 99.7 % (350/351), and a total agreement of 99.35% (462/465).

Sensitivity = 98%
Specificity = 100%

TASHIMA Inc.

PERFOMANCE CHARACTERISTICS:

Sensitivity : Sera were collected from patients under anti TB treatment. Results of sputum examination were not available. Among 75 sera collected, samples were positive by the TB onsite Rapid screening Test Thus, the test sensitivity is 93%.

Specificity : In 53 sera derived from Northern America, all the samples were negative.

Sensitivity = 93%
Specificity = 100%

Serological tests for TB have not been found to perform well in previous systematic reviews

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Commercial Serological Antibody Detection Tests for the Diagnosis of Pulmonary Tuberculosis: A Systematic Review

Karen R. Steingart[1,2], Megan Henry[3], Suman Laal[4,5,6], Philip C. Hopewell[1,2], Andrew Ramsay[7], Dick Menzies[8,9], Jane Cunningham[7], Karin Weldingh[10], Madhukar Pai[8,9*]

Health Technology Assessment 2007; Vol. 11: No. 3

A systematic review of rapid diagnostic tests for the detection of tuberculosis infection

J Dinnes, J Deeks, H Kunst, A Gibson, E Cummins, N Waugh, F Drobniewski and A Lalvani

A systematic review of commercial serological antibody detection tests for the diagnosis of extrapulmonary tuberculosis

Karen R Steingart, Megan Henry, Suman Laal, Philip C Hopewell, Andrew Ramsay, Dick Menzies, Jane Cunningham, Karin Weldingh, Madhukar Pai

Thorax 2007;**62**:911–918. doi: 10.1136/thx.2006.075754

CLINICAL AND VACCINE IMMUNOLOGY, Feb. 2009, p. 260–276 Vol. 16, No. 2
1556-6811/09/$08.00+0 doi:10.1128/CVI.00355-08

Performance of Purified Antigens for Serodiagnosis of Pulmonary Tuberculosis: a Meta-Analysis▽†

Karen R. Steingart,[1]* Nandini Dendukuri,[2] Megan Henry,[3]‡ Ian Schiller,[2] Payam Nahid,[4] Philip C. Hopewell,[1,4] Andrew Ramsay,[5] Madhukar Pai,[2] and Suman Laal[6,7,8]

Deeply troubling…

- Serological tests are being used widely in a majority of high TB burden countries

- "*Our survey also confirms the previous observation that companies in western countries (e.g. France, UK, USA, Germany, Australia) are exporting inaccurate and unreliable TB diagnostics to poor countries, while not approving the same tests for domestic use.*" Grenier, Eur Respir J, 2011, in press

In 2010, WHO convened a process to develop recommendations about commercial serological tests

- **Commissioned an updated systematic review and a decision-analysis model**
- **Convened an Expert Group to assess the evidence base**
- **Used the GRADE approach to rate the quality of evidence and determine the strength of recommendations**

www.gradeworkinggroup.org

OPEN ACCESS Freely available online PLoS MEDICINE

Commercial Serological Tests for the Diagnosis of Active Pulmonary and Extrapulmonary Tuberculosis: An Updated Systematic Review and Meta-Analysis

Karen R. Steingart[1], Laura L. Flores[2,3], Nandini Dendukuri[4], Ian Schiller[4], Suman Laal[5,6,7], Andrew Ramsay[8], Philip C. Hopewell[2,3], Madhukar Pai[4]*

- **Objective: To obtain summary estimates of the diagnostic accuracy of commercial serological tests for the diagnosis of pulmonary and extrapulmonary TB**

- **Participants: adults and children, all coutries**
- **Reference standards**
  - **Pulmonary TB: Culture, solid or liquid**
  - **Extrapulmonary TB: Smear, culture, histopathology**

Methods

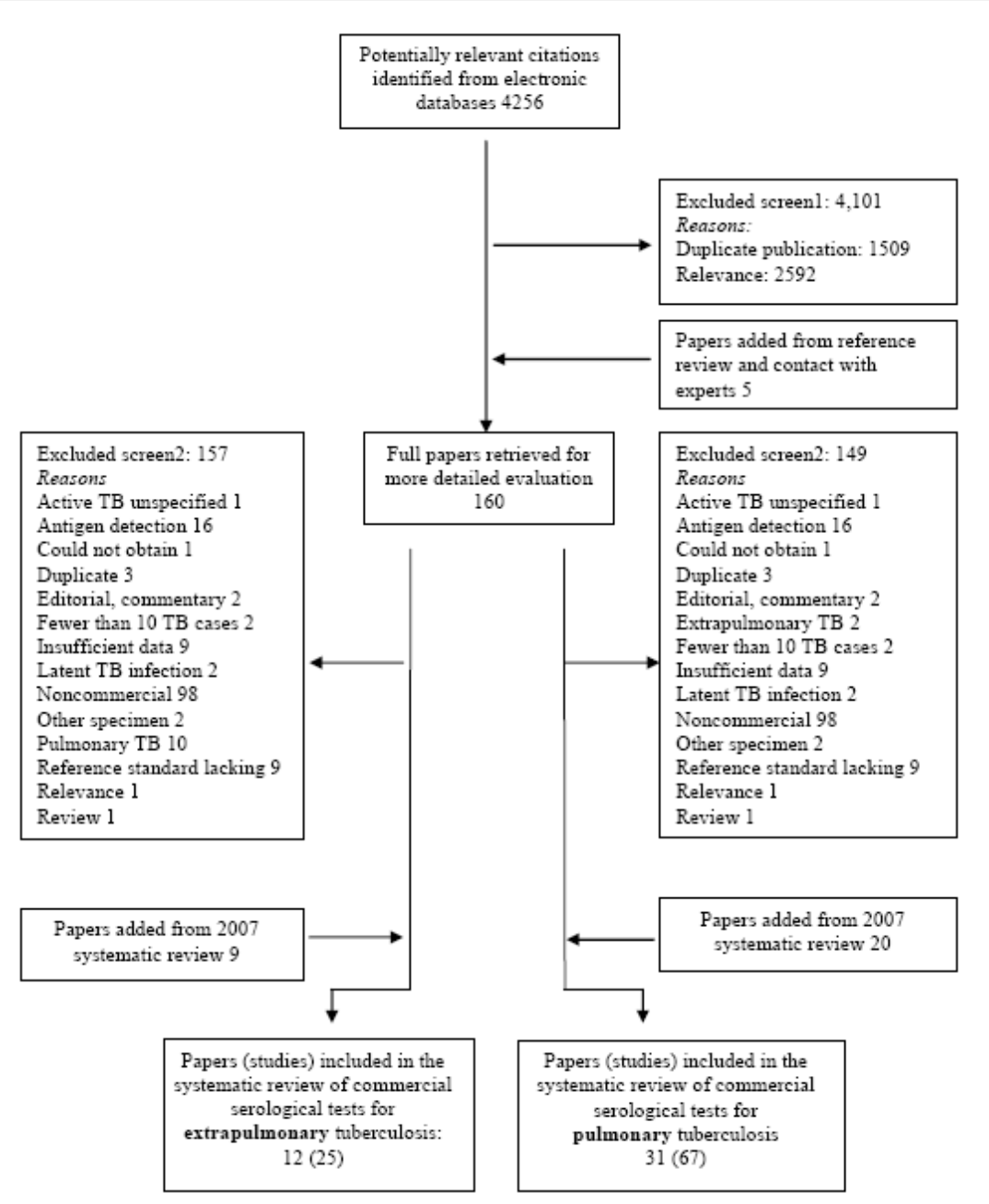
- Two independent reviewers
- Updated literature search from previous systematic reviews, all languages
- QUADAS to appraise methodological quality
- Prespecified subgroups by test, smear, HIV
- Meta-analysis by hierarchical SROC random effects model
- The GRADE approach to determine quality of the body of evidence

PRISMA Diagram

- 4256 citations
- 160 full-text papers

- PTB: 31 papers
  original review (20)
  update (11)

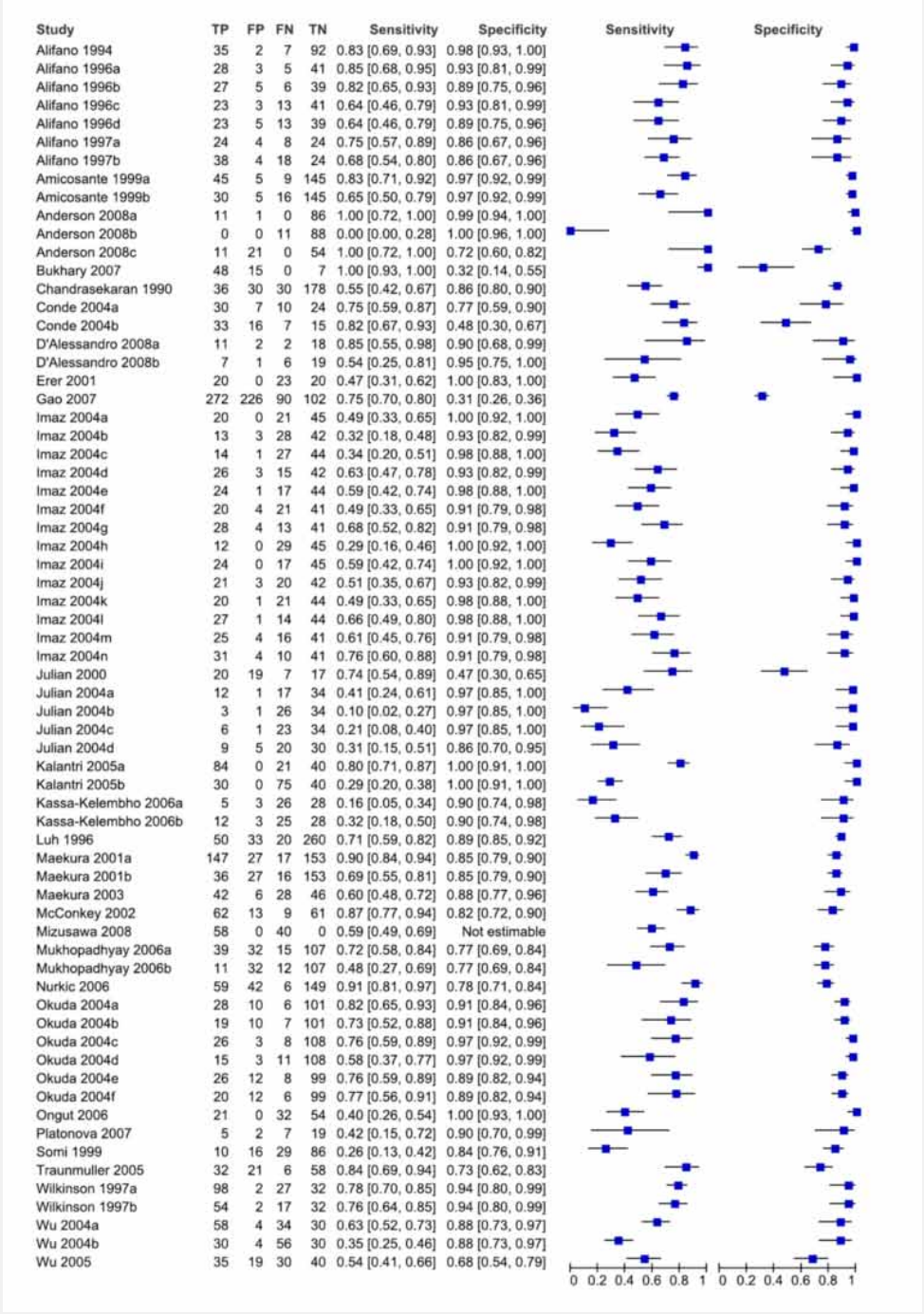
- EPTB: 12 papers
  original review (9)
  update (3)



Characteristics of included studies

- **Pulmonary TB:** 67 studies (5147 participants); 48% studies from low and middle-income countries
- anda-TB (IgG, IgA, and IgM) was the test most frequently evaluated (16 studies, 24%)

- **Extrapulmonary TB:** 25 studies (1809 participants); 40% from low and middle-income countries
- anda-TB (IgG, IgA, and IgM) was the test most frequently evaluated (17 studies, 68%)

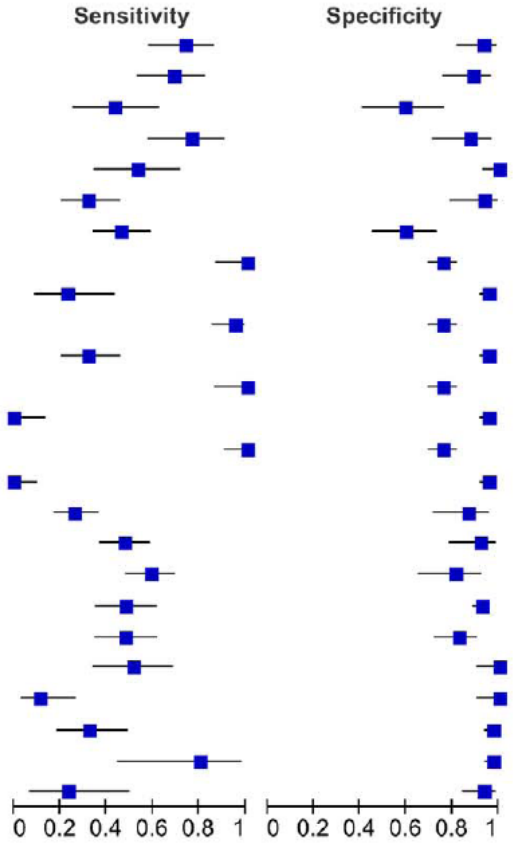


Pulmonary TB

Sensitivity range: 0 to 100%

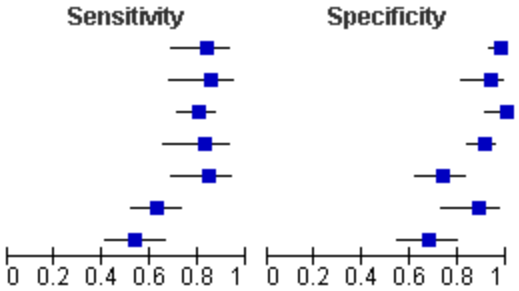
Specificity range: 31 to 100%

Study	TP	FP	FN	TN	Sensitivity	Specificity
Alifano 1998a	31	3	11	41	0.74 [0.58, 0.86]	0.93 [0.81, 0.99]
Alifano 1998b	29	5	13	39	0.69 [0.53, 0.82]	0.89 [0.75, 0.96]
Banerjee 2003a	13	13	17	19	0.43 [0.25, 0.63]	0.59 [0.41, 0.76]
Banerjee 2003b	23	4	7	28	0.77 [0.58, 0.90]	0.88 [0.71, 0.96]
Caminero 1993	16	0	14	48	0.53 [0.34, 0.72]	1.00 [0.93, 1.00]
Caminero 1994	18	2	38	29	0.32 [0.20, 0.46]	0.94 [0.79, 0.99]
Chierakul 2001	31	21	36	31	0.46 [0.34, 0.59]	0.60 [0.45, 0.73]
Gevaudan 1992a	26	47	0	147	1.00 [0.87, 1.00]	0.76 [0.69, 0.82]
Gevaudan 1992b	6	9	20	185	0.23 [0.09, 0.44]	0.95 [0.91, 0.98]
Gevaudan 1992c	53	47	3	147	0.95 [0.85, 0.99]	0.76 [0.69, 0.82]
Gevaudan 1992d	18	9	38	185	0.32 [0.20, 0.46]	0.95 [0.91, 0.98]
Gevaudan 1992e	25	47	0	147	1.00 [0.86, 1.00]	0.76 [0.69, 0.82]
Gevaudan 1992f	0	9	25	185	0.00 [0.00, 0.14]	0.95 [0.91, 0.98]
Gevaudan 1992g	34	47	0	147	1.00 [0.90, 1.00]	0.76 [0.69, 0.82]
Gevaudan 1992h	0	9	34	185	0.00 [0.00, 0.10]	0.95 [0.91, 0.98]
Kunter 2003a	23	5	65	32	0.26 [0.17, 0.37]	0.86 [0.71, 0.95]
Kunter 2003b	42	3	46	34	0.48 [0.37, 0.59]	0.92 [0.78, 0.98]
Kunter 2003c	52	7	36	30	0.59 [0.48, 0.69]	0.81 [0.65, 0.92]
Luh 1996	28	17	30	207	0.48 [0.35, 0.62]	0.92 [0.88, 0.96]
McConkey 2002	27	13	29	61	0.48 [0.35, 0.62]	0.82 [0.72, 0.90]
Nsanze 1997a	18	0	17	35	0.51 [0.34, 0.69]	1.00 [0.90, 1.00]
Nsanze 1997b	4	0	31	35	0.11 [0.03, 0.27]	1.00 [0.90, 1.00]
Ratanasuwan 1997a	13	4	27	149	0.33 [0.19, 0.49]	0.97 [0.93, 0.99]
Ratanasuwan 1997b	8	4	2	151	0.80 [0.44, 0.97]	0.97 [0.94, 0.99]
Senol 2007	4	4	13	56	0.24 [0.07, 0.50]	0.93 [0.84, 0.98]



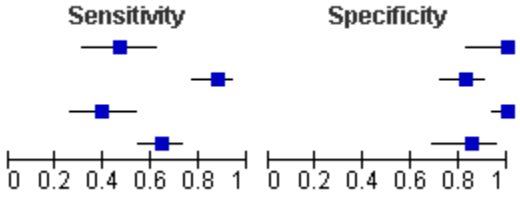
Extrapulmonary TB
Sensitivity range: 0 to 100%
Specificity range: 59 to 100%

Study	TP	FP	FN	TN	Sensitivity	Specificity
Alifano 1994	35	2	7	92	0.83 [0.69, 0.93]	0.98 [0.93, 1.00]
Alifano 1996 (a)	28	3	5	41	0.85 [0.68, 0.95]	0.93 [0.81, 0.99]
Kalantri 2005 (a)	84	0	21	40	0.80 [0.71, 0.87]	1.00 [0.91, 1.00]
Okuda 2004 (a)	28	10	6	101	0.82 [0.65, 0.93]	0.91 [0.84, 0.96]
Traunmuller 2005	32	21	6	58	0.84 [0.69, 0.94]	0.73 [0.62, 0.83]
Wu 2004 (a)	58	4	34	30	0.63 [0.52, 0.73]	0.88 [0.73, 0.97]
Wu 2005	35	19	30	40	0.54 [0.41, 0.66]	0.68 [0.54, 0.79]



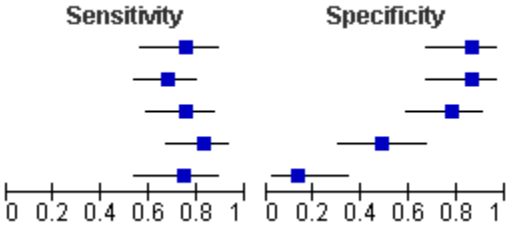
andaTB IgG, smear +

Study	TP	FP	FN	TN	Sensitivity	Specificity
Erer 2001	20	0	23	20	0.47 [0.31, 0.62]	1.00 [0.83, 1.00]
McConkey 2002	62	13	9	61	0.87 [0.77, 0.94]	0.82 [0.72, 0.90]
Ongut 2006	21	0	32	54	0.40 [0.26, 0.54]	1.00 [0.93, 1.00]
Perkins 2003	77	5	43	29	0.64 [0.55, 0.73]	0.85 [0.69, 0.95]



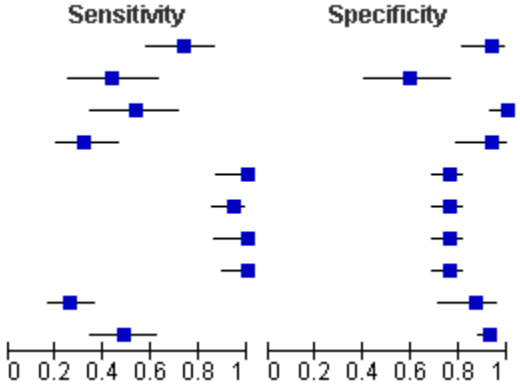
ICT

Study	TP	FP	FN	TN	Sensitivity	Specificity
Alifano 1997 (a)	24	4	8	24	0.75 [0.57, 0.89]	0.86 [0.67, 0.96]
Alifano 1997 (b)	38	4	18	24	0.68 [0.54, 0.80]	0.86 [0.67, 0.96]
Conde 2004 (a)	30	7	10	24	0.75 [0.59, 0.87]	0.77 [0.59, 0.90]
Conde 2004 (b)	33	16	7	15	0.82 [0.67, 0.93]	0.48 [0.30, 0.67]
Julian 2000	20	19	7	3	0.74 [0.54, 0.89]	0.14 [0.03, 0.35]



TB-EIA

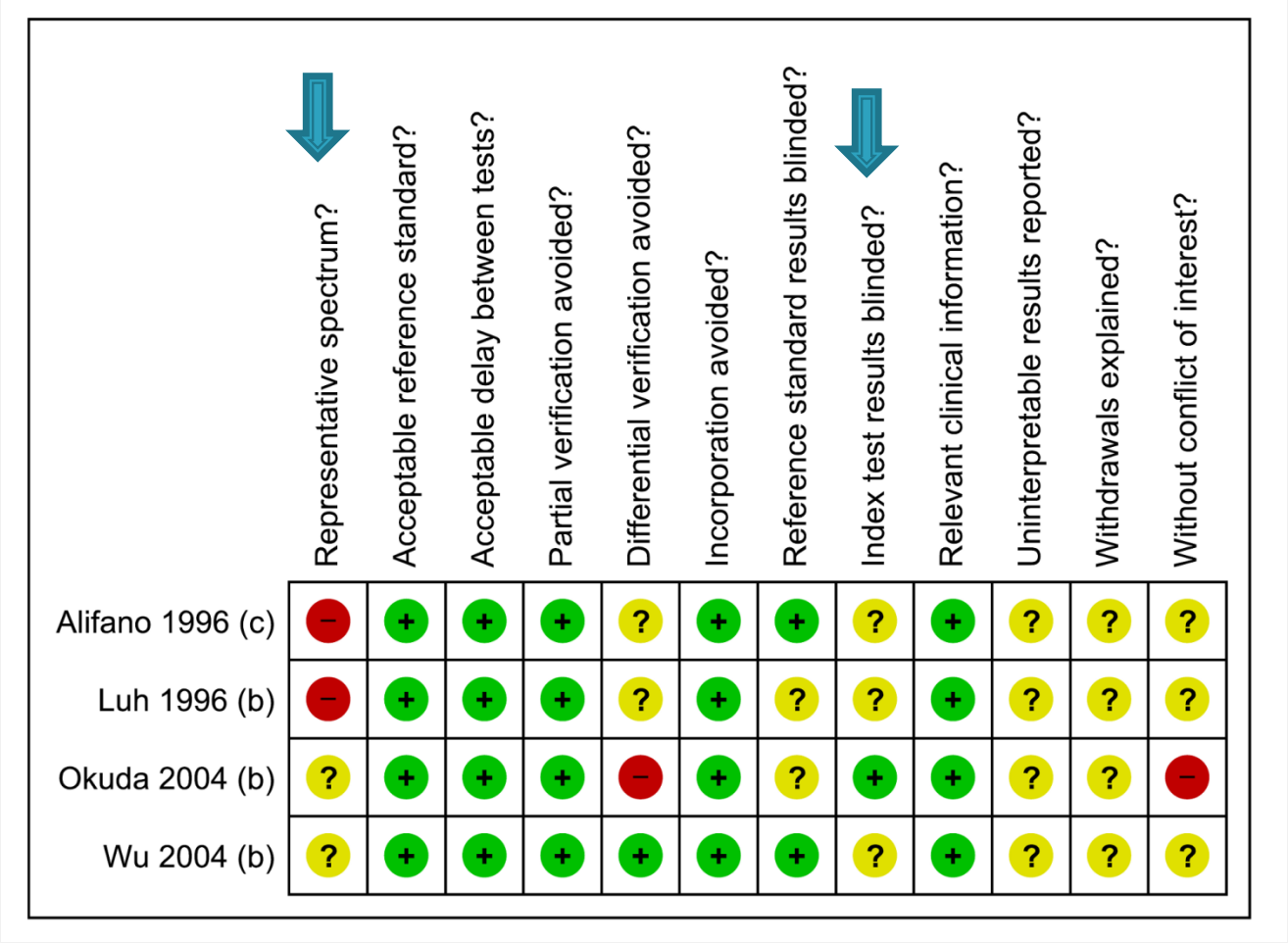
Study	TP	FP	FN	TN	Sensitivity	Specificity
Alifano 1998b	31	3	11	41	0.74 [0.58, 0.86]	0.93 [0.81, 0.99]
Banerjee 2003a	13	13	17	19	0.43 [0.25, 0.63]	0.59 [0.41, 0.76]
Caminero 1993	16	0	14	48	0.53 [0.34, 0.72]	1.00 [0.93, 1.00]
Caminero 1994	18	2	38	29	0.32 [0.20, 0.46]	0.94 [0.79, 0.99]
Gevaudan 1992b	26	47	0	147	1.00 [0.87, 1.00]	0.76 [0.69, 0.82]
Gevaudan 1992f	53	47	3	147	0.95 [0.85, 0.99]	0.76 [0.69, 0.82]
Gevaudan 1992j	25	47	0	147	1.00 [0.86, 1.00]	0.76 [0.69, 0.82]
Gevaudan 1992n	34	47	0	147	1.00 [0.90, 1.00]	0.76 [0.69, 0.82]
Kunter 2003a	23	5	65	32	0.26 [0.17, 0.37]	0.86 [0.71, 0.95]
Luh 1996	28	17	30	207	0.48 [0.35, 0.62]	0.92 [0.88, 0.96]



andaTB IgG, Extrapulmonary TB

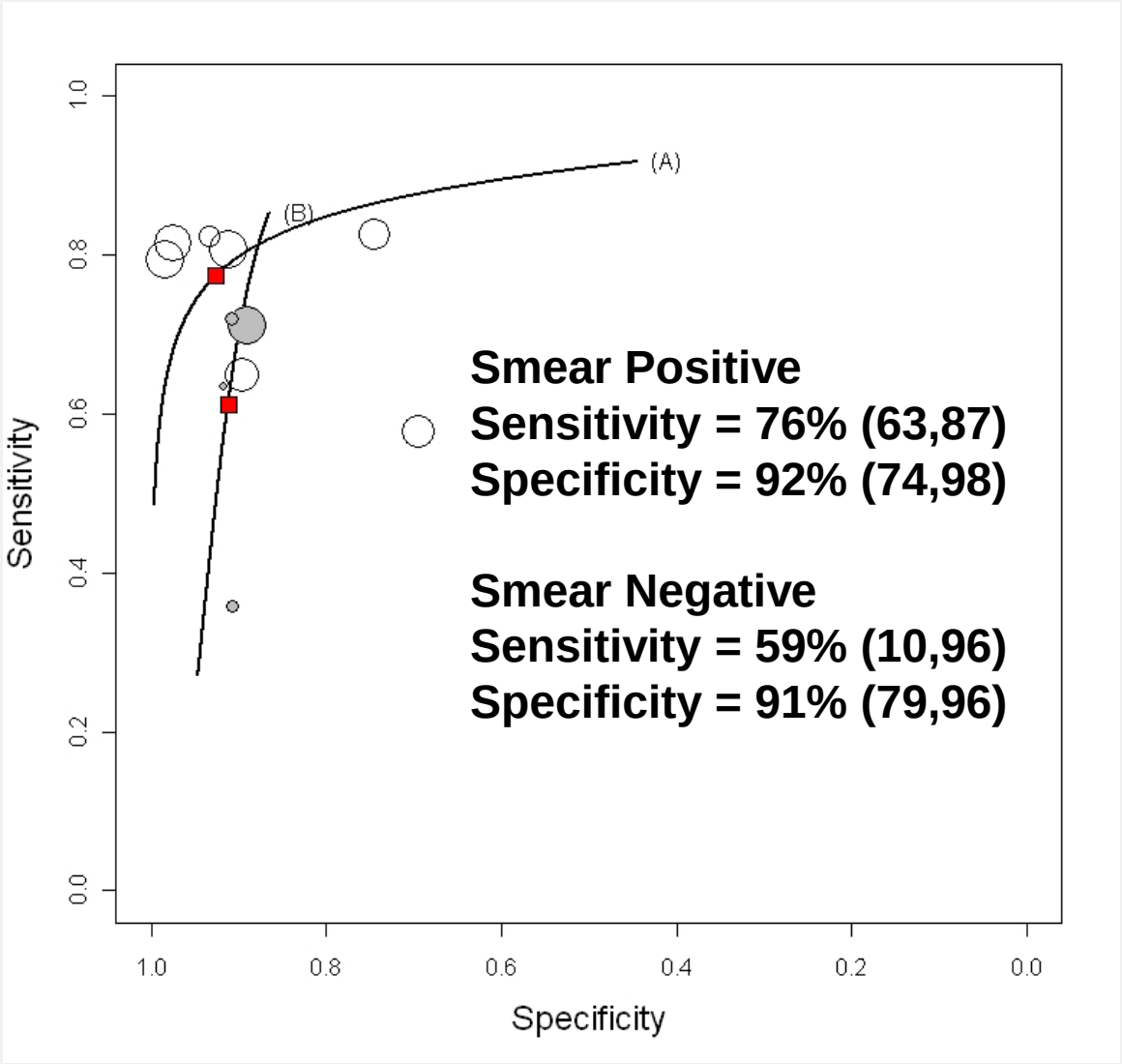

anda-tb
REF 311909
IgA
192
MYCOBACTERIA
A60 ELISA KIT
IVD
anda Biologicals
CE
anda-tb
REF 311917
IgM
192
MYCOBACTERIA
A60 ELISA KIT
IVD
anda Biologicals
CE
anda-tb
REF 311914
IgG
192
MYCOBACTERIA
A60 ELISA KIT
IVD
Diagnostic kit for the quantitative determination of anti-mycobacteria antibodies in human serum.
Trousse diagnostique pour la détermination quantitative des anticorps humains anti-mycobactéria.
anda Biologicals
CE
ELISA test for the determination of anti-mycobacterial antibodies
Test ELISA pour la détermination des anticorps anti-mycobactérie
192 Determinations / 192 Déterminations
REF 311914
KIT COMPONENTS
anda-tb IgG
IVD
Anda Biologicals S.A
F-67000 STRASBOURG
Ltd., Mumbai
Import Licence:
NCD-476/2009

Methodological quality summary with QUADAS, anda-TB IgG, smear-negative patients



Steingart et al. PLoS Med 2011

Summary HSROC plots for anda-TB IgG: (A) smear-positive and (B) smear-negative pulmonary TB patients



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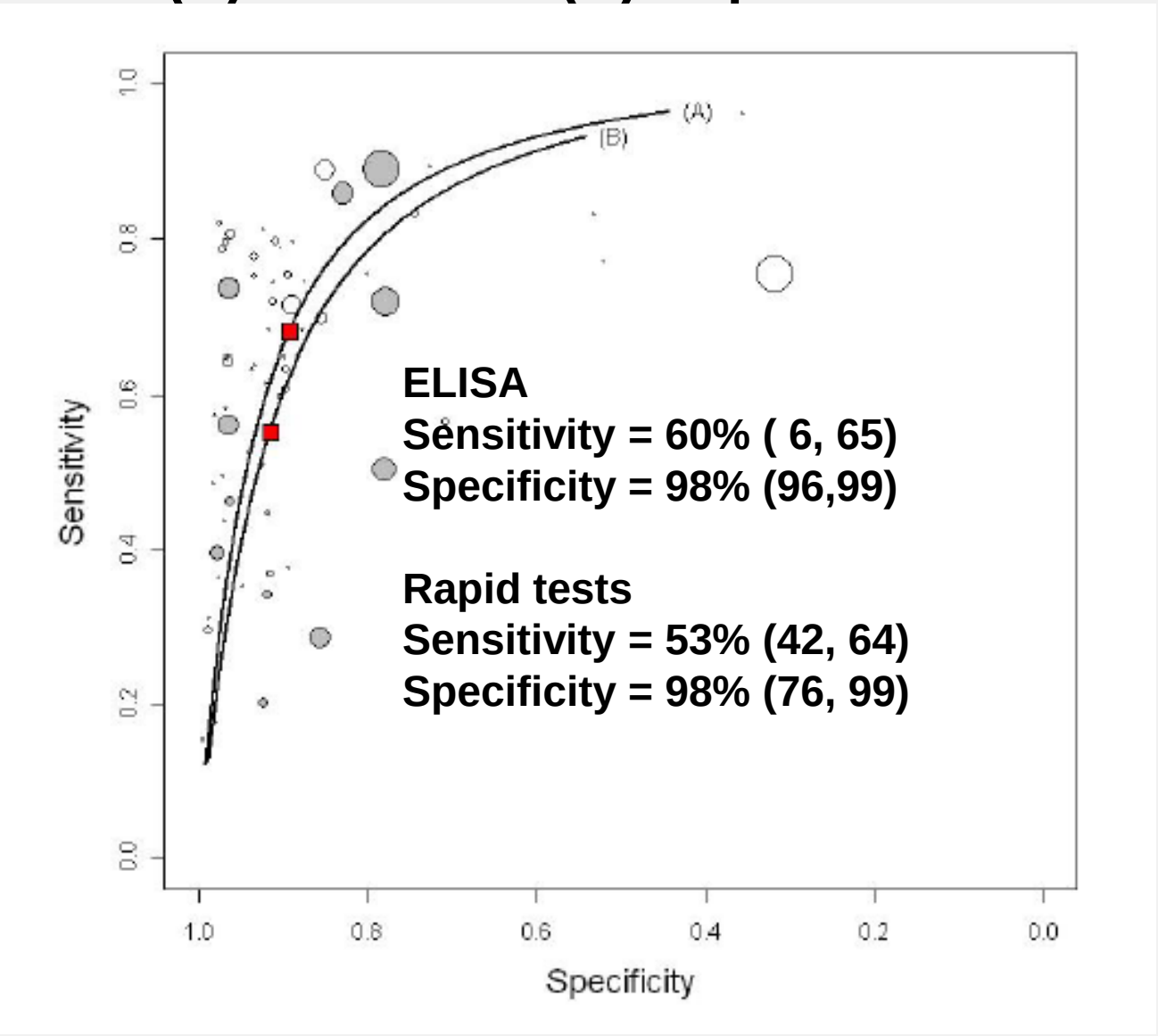
HROC plots by assay technique
(A) ELISA and (B) Rapid tests



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

Test	Sensitivity % (95% CI)	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 individuals suspected of having pulmonary TB, inpatient 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

Quality of evidence can be decreased by 5 factors

1. Study limitations (QUADAS criteria)
2. Inconsistency (unexplained heterogeneity)
3. Indirectness
4. Imprecision (width of confidence intervals)
5. Publication bias

GRADE Evidence Profile

Table 3. GRADE Evidence Profile: should commercial serological tests be used as a replacement test for conventional tests such as smear microscopy in patients of any age suspected of having pulmonary tuberculosis?

Outcome	Number of Studies (Participants)	Study Design	Limitations	Indirectness	Inconsistency	Imprecision	Publication Bias	Final Quality	Effect per 1,000[a]	Importance[b]
True Positives	67 (5,147)	Cross-sectional and case-control	Very serious[c] (−2)	No serious indirectness[d]	Very serious[e] (−2)	Serious[f]	Likely[g]	Very low ⊕◯◯◯	Prevalence 10%: 64; prevalence 30%: 192	Critical
True Negatives	67 (5,147)	Cross-sectional and case-control	Very serious[c] (−2)	No serious indirectness[d]	Very serious[e] (−2)	Serious[f]	Likely[g]	Very low ⊕◯◯◯	Prevalence 10%: 819; prevalence 30%: 637	Critical
False Positives	67 (5,147)	Cross-sectional and case-control	Very serious[c] (−2)	No serious indirectness[d]	Very serious[e] (−2)	Serious[f]	Likely[g]	Very low ⊕◯◯◯	Prevalence 10%: 81; prevalence 30%: 63	Critical
False Negatives	67 (5,147)	Cross-sectional and case-control	Very serious[c] (−2)	No serious indirectness[d]	Very serious[e] (−2)	Serious[f]	Likely[g]	Very low ⊕◯◯◯	Prevalence 10%: 36; prevalence 30%: 108	Critical

Based on sample size = 8,318, sensitivity median = 64%, specificity median = 91%.

[a]What do these results mean given 10% or 30% prevalence among individuals being screened for TB?

[b]Outcomes were ranked by their relative importance as critical, important, or of limited importance. Ranking helped to focus attention on those outcomes that were considered most important.

[c]The majority of studies lacked a representative patient population and were not blinded.

[d]Although diagnostic accuracy is considered a surrogate for patient-important outcomes, we did not downgrade.

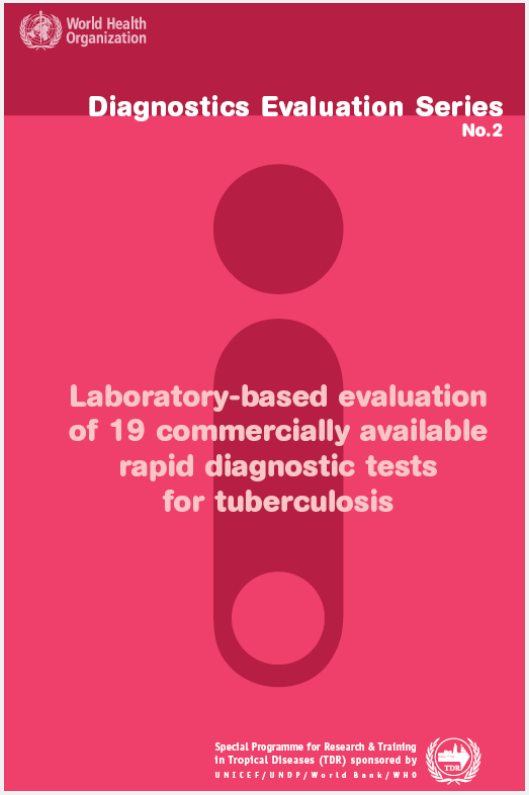
Steingart et al. PLoS Med 2011

GRADE defines quality as *confidence* in the estimates of effect

Special Programme for Research & Training in Tropical Diseases (TDR) sponsored by UNICEF/UNDP/ World Bank/ WHO

- **Objective: To compare performance and reproducibility of rapid MTB-specific antibody detection tests using archived serum samples from the WHO/TDR TB Specimen Bank**

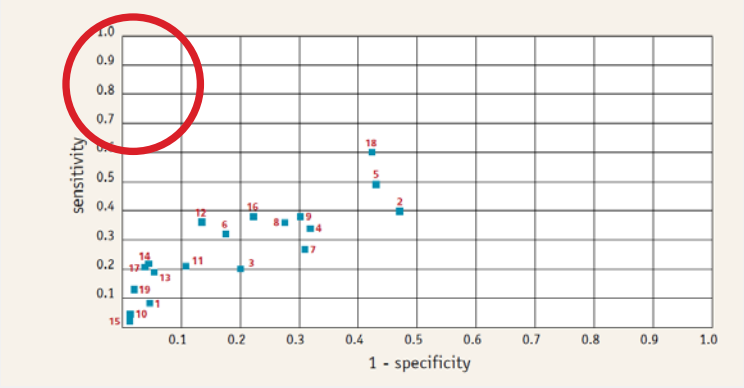
- **Reference standard: culture and clinical follow-up**



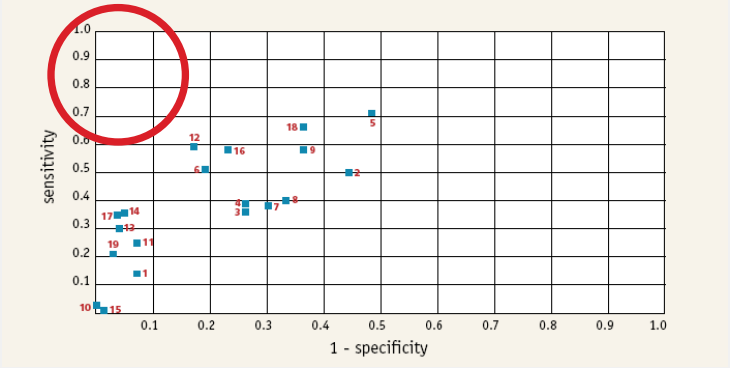
Methods

- **Rapid test - result < 15 minutes**
- **Simple - 1 or 2 steps, minimal training and no equipment**
- **Easy to interpret - card or strip format with visual readout**
- **Archived specimens from Uganda, The Gambia, Canada, Tanzania, Brazil, and Spain**
- **ROC plots**

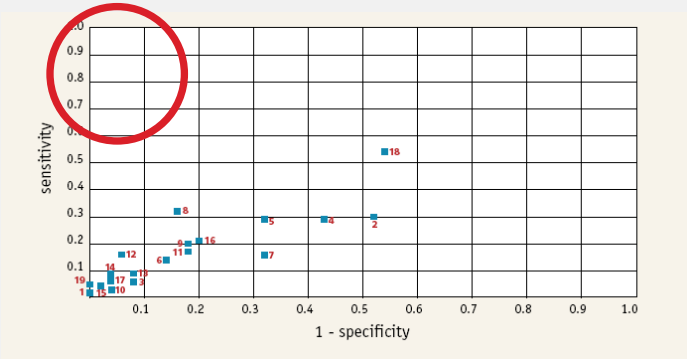
WHO/TDR Laboratory-based evaluation



All samples, n = 355



HIV negative samples , n = 198



HIV positive samples, n = 157

Sensitivity = 1 to 60%
Specificity =53 to 99%

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Serological Testing Versus Other Strategies for Diagnosis of Active Tuberculosis in India: A Cost-Effectiveness Analysis

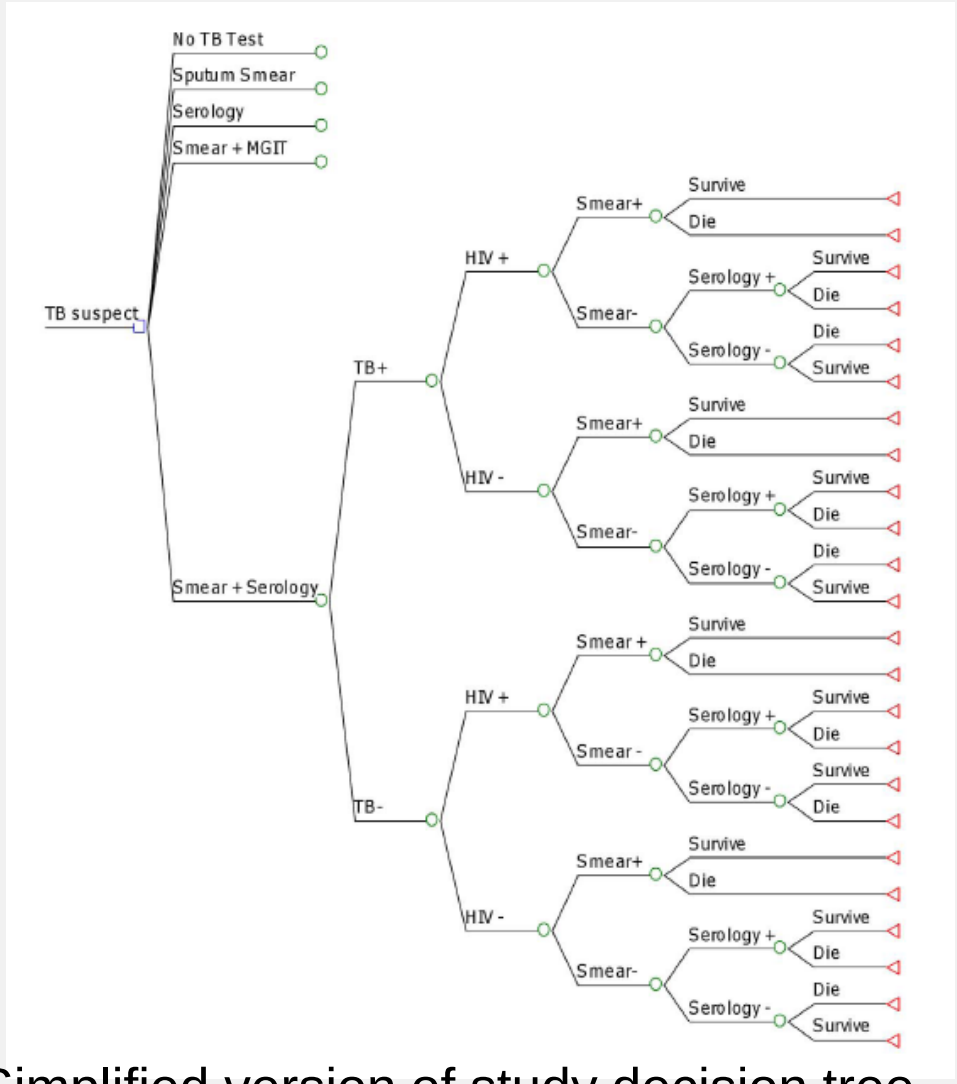
David W. Dowdy[1], Karen R. Steingart[2], Madhukar Pai[3]*

1 Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America, 2 Department of Health Services, University of Washington School of Public Health, Seattle, Washington, United States of America, 3 Department of Epidemiology, Biostatistics, and Occupational Health, McGill University& Montreal Chest Institute, Montreal, Canada

Objective: to estimate costs and effectiveness of sputum microscopy (US$3.62 for two smears), microscopy plus automated liquid culture (MGIT, US$20/test), and serological testing (anda-tb ELISA, US$20/test)

Hypothetical study population

- 1.5 million TB suspects
- 1/7 with TB
- 53% TB patients are highly infectious
- 5% HIV prevalence
- 10% with access to ART
- Accuracy estimates from the updated systematic review



Simplified version of study decision tree

Dowdy D et al. PLoS Med 2011

Table 3. Cost-effectiveness of diagnostic strategies for 1.5 million persons with suspected active TB in India.

Diagnostic Test	Cost (US$)	Additional TB Cases Treated	Additional False-Positive Cases Treated	Secondary Cases Averted	DALYs Averted	Incremental DALYs Averted	Incremental Cost per DALY Averted (US$)
Performed alone, relative to no microbiological testing							
Sputum smear microscopy	11.9 million	44,000	36,000	443,000	623,000	623,000	19
anda-TB serology	47.5 million	58,000	157,000	411,000	520,000	(Dominated)	(Dominated)
Performed on smear-negative specimens only, relative to sputum smear alone							
MGIT culture	27.6 million	26,000	12,000	112,000	130,000	130,000	213
anda-TB serology	39.0 million	24,000	152,000	112,000	110,000	(Dominated)	(Dominated)

doi:10.1371/journal.pmed.1001074.t003

Compared with no testing

- **Sputum smear: additional 44,000 TB cases, 36,000 false positives (FPs)**
- **Serology as replacement test: additional 58,000 TB cases,157,000 FPs**
- **Smear estimated to avert 102,000 more DALY*s, 32,000 more secondary cases than serology, at ~ 1/4 the incremental cost**

*DALY, disability-adjusted life year

Dowdy et al. PLoS Med 2011

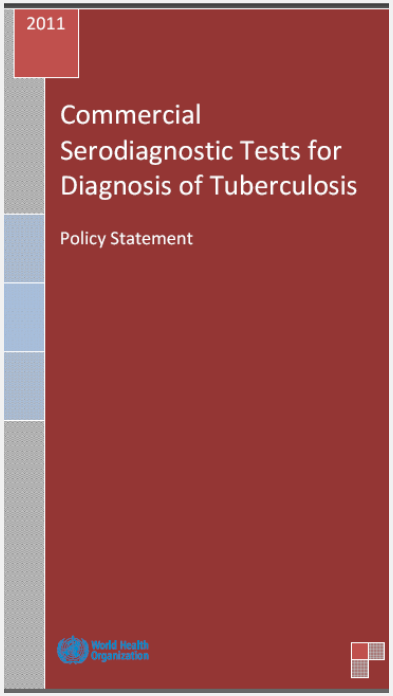
GRADE determinants of strength of recommendation

Factor
Balance between desirable and undesirable effects
Quality of evidence
Values and preferences
Costs (resource allocation)

Guyatt GH et al. BMJ 2008

- Commercial serological tests provide inconsistent and imprecise findings resulting in highly variable values for sensitivity and specificity…high proportions of false-positive and false-negative results adversely impact patient safety. Overall data quality was graded as very low and **it is strongly recommended that these tests not be used for the diagnosis of pulmonary and extra-pulmonary TB.**

- Targeted further research to identify new/alternative point-of-care tests for TB diagnosis and/or serological tests with improved accuracy is strongly encouraged.



- World Health Organization (2011) Policy Statement: Commercial serodiagnostic tests for diagnosis of tuberculosis. WHO, Geneva, Switzerland. WHO/HTM/TB/2011.5. Available: http://whqlibdoc.who.int/publications/2011/9789241502054_eng.pdf

Reactions to the WHO policy against the use of TB serological tests

"Responses from governments of high-burden countries have been overwhelmingly positive," Karin Weyer, WHO Stop TB Department. Morris K, The Lancet Infect Dis 2011

The (Indian) Union Health Ministry has asked all state tuberculosis (TB) officers to endorse the recommendations of the World Health Organization (WHO), urging countries to ban "unapproved" blood tests to diagnose the disease
http://www.indianexpress.com/news/tb-battle-states-told-to-follow-who-guideli/820721/

"These tests were discouraged from use almost 20 years ago globally but 10 out of 18 types of strips are still in use in the private sector in Kenya today," Ms Lucy Chesire, one of the two Kenyan TB experts involved in a WHO study of the problem
http://www.nation.co.ke/News/TB+tests+done+at+private+clinics+not+accurate/-/1056/1207098/-/item/0/-/nxponp/-/index.html

References

1. Dinnes J et al. *A systematic review of rapid diagnostic tests for the detection of tuberculosis infection.* Health Technol Assess, 2007. 11(3): p. 1-196.

2. Dowdy DW et al. Serological Testing Versus Other Strategies for Diagnosis of Active Tuberculosis in India: A Cost-Effectiveness Analysis. PLoS Med, 2011. 8(8): e1001074. doi:10.1371/journal.pmed.1001074

3.Schünemann HJ et al. *Grading quality of evidence and strength of recommendations for diagnostic tests and strategies.* BMJ, 2008. 336(7653): p. 1106-10.

4. Special Programme for Research and Training in Tropical Diseases. Laboratory-based evaluation of 19 commercially available rapid diagnostic tests for tuberculosis. 2008. Geneva: World Health Organization.

5. Steingart KR et al., *Performance of purified antigens for serodiagnosis of pulmonary tuberculosis: a meta-analysis.* Clin Vaccine Immunol, 2009. 16(2): p. 260-76.

6. Steingart KR et al., *Commercial serological antibody detection tests for the diagnosis of pulmonary tuberculosis: a systematic review.* PLoS Med, 2007. 4(6): p. e202.

7. Steingart KR et al. *A systematic review of commercial serological antibody detection tests for the diagnosis of extrapulmonary tuberculosis.* Thorax, 2007. 62(10): p. 911-8.

8. Steingart KR et al. Extrapulmonary Tuberculosis: An Updated Systematic Review and Meta-Analysis. PLoS Med 8(8): e1001062. doi:10.1371/journal.pmed.1001062

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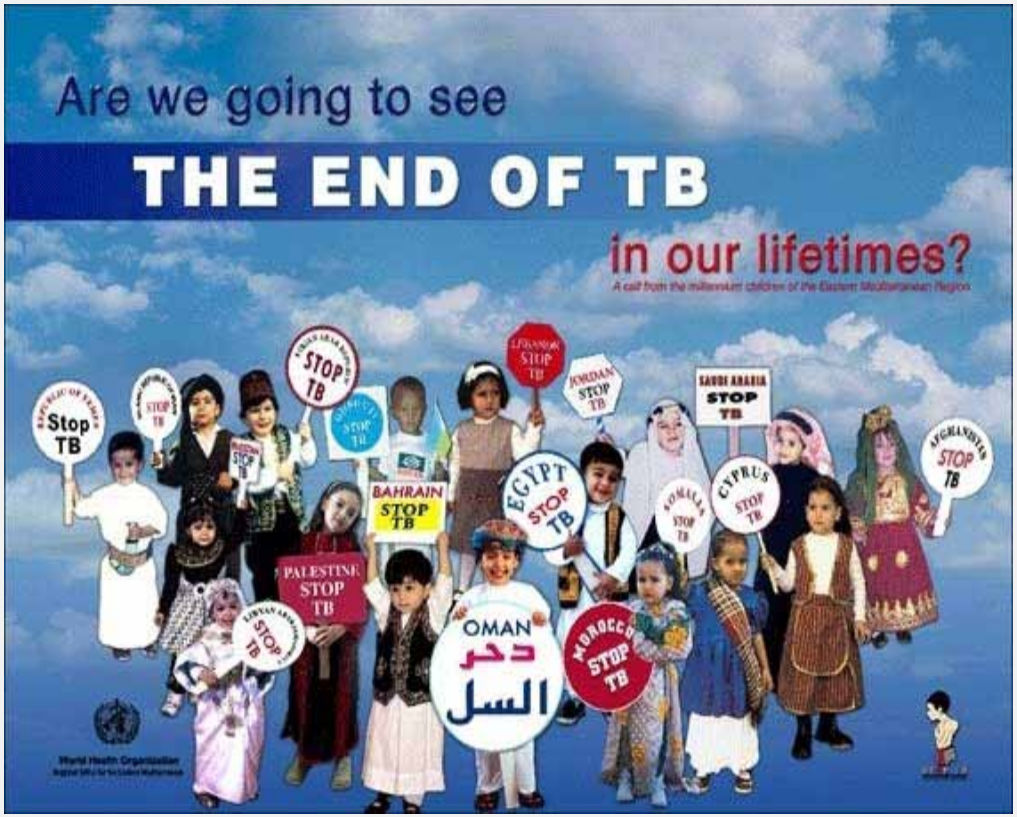
Merci!


Are we going to see
THE END OF TB
in our lifetimes?
A call from the millennium children of the Eastern Mediterranean Region
Stop TB
STOP TB
BAHRAIN STOP TB
EGYPT STOP TB
PALESTINE STOP TB
OMAN دحر السل
MOROCCO STOP TB
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CYPRUS STOP TB
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