



**FIND Scientific Forum
on Recent Advances in TB Diagnostics**

**IGRAs for the diagnosis of LTBI:
are they relevant
in TB endemic settings?**

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McGill



Explosion of IGRA literature!

- 300+ publications
- 25+ review articles; 10+ guidelines
- 2 meetings exclusively focused on IGRAs
- 3rd meeting in 2009 in Croatia



CHEST Translating Basic Research Into Clinical Practice

Diagnosing Tuberculosis Infection in the 21st Century*

New Tools To Tackle an Old Enemy

Utility of the antigen-specific interferon- γ assay for the management of tuberculosis

Keertan Dheda^{a,b}, Zarir F. Udawadia^c, Jim F. Huggett^a, Margaret A. Johnson^b and Graham A.W. Rook^a



Diagnosis of latent *Mycobacterium tuberculosis* infection: is the demise of the Mantoux test imminent?

James S Rothe¹ and Peter Andersen

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 Drobniowski and A Lalvani

Annals of Internal Medicine

ARTICLE

Meta-analysis: New Tests for the Diagnosis of Latent Tuberculosis Infection: Areas of Uncertainty and Recommendations for Research

Dick Menzies, MD, MSc; Madhukar Pal, MD, PhD; and George Comstock, MD, DrPH



QuantiFERON-TB Gold: state of the art for the diagnosis of tuberculosis infection?

Tom G Connell¹, Molebogeng X Rangaka, Nigel Curtis and Robert J Wilkinson

Pulmonary Perspective

An Update on the Diagnosis of Tuberculosis Infection

Luca Richeldi

Respiratory Disease Clinic, Department of Oncology, Hematology, and Respiratory Disease, University of Modena and Reggio Emilia, Modena, Italy

Advantages and drawbacks of in vitro Interferon- γ /T cell assays compared to the Mantoux test for the diagnosis of tuberculosis

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What do we know about IGRA performance in general and is there a difference between high vs. low incidence countries?

Annals of Internal Medicine

ARTICLE

Meta-analysis: New Tests for the Diagnosis of Latent Tuberculosis Infection: Areas of Uncertainty and Recommendations for Research

Dick Menzies, MD, MSc; Madhukar Pai, MD, PhD; and George Comstock, MD, DrPH

Background: Until recently, the tuberculin skin test was the only test for detecting latent tuberculosis (TB) infection, but 2 *ex vivo* interferon- γ release assays (IGRAs) are now commercially licensed.

Purpose: To estimate sensitivity, specificity, and reproducibility of IGRAs (commercial or research versions of QuantiFERON [QFT] and Elispot) for diagnosing latent TB infection in healthy and immune-suppressed persons.

Data Sources: The authors searched MEDLINE and reviewed citations of all original articles and reviews for studies published in English.

Study Selection: Studies had evaluated IGRAs using *Mycobacterium tuberculosis*-specific antigens (RD1 antigens) and overnight (16- to 24-h) incubation times. Reference standards had to be clearly defined without knowledge of test results.

Data Extraction and Quality Assessment: Specific criteria for quality assessment were developed for sensitivity, specificity, and reproducibility.

Data Synthesis: When newly diagnosed active TB was used as a surrogate for latent TB infection, sensitivity of all tests was suboptimal, although it was higher with Elispot. No test distinguishes active TB from latent TB. Sensitivity of the tuberculin skin test and IGRAs was similar in persons who were categorized into clinical

gradients of exposure. Pooled specificity was 97.7% (95% CI, 96% to 99%) and 92.5% (CI, 86% to 99%) for QFT and for Elispot, respectively. Both assays were more specific than the tuberculin skin test in samples vaccinated with bacille Calmette-Guérin. Elispot was more sensitive than the tuberculin skin test in 3 studies of immune-compromised samples. Discordant tuberculin skin test and IGRA reactions were frequent and largely unexplained, although some may be related to varied definitions of positive test results. Reversion of IGRA results from positive to negative was common in 2 studies in which it was assessed.

Limitations: Most studies used cross-sectional designs with the inherent limitation of no gold standard for latent TB infection, and most involved small samples with a widely varying likelihood of true-positive and false-positive test results. There is insufficient evidence on IGRA performance in children, immune-compromised persons, and the elderly.

Conclusions: New IGRAs show considerable promise and have excellent specificity. Additional studies are needed to better define their performance in high-risk populations and in serial testing. Longitudinal studies are needed to define the predictive value of IGRAs.

Ann Intern Med. 2007;146:340-354.
For author affiliations, see end of text.

www.annals.org

Annals of Internal Medicine

REVIEW

Systematic Review: T-Cell–based Assays for the Diagnosis of Latent Tuberculosis Infection: An Update

Madhukar Pai, MD, PhD; Alice Zwerling, MSc; and Dick Menzies, MD, MSc

Background: Interferon- γ -release assays (IGRAs) are alternatives to the tuberculin skin test (TST). A recent meta-analysis showed that IGRAs have high specificity, even among populations that have received bacille Calmette-Guérin (BCG) vaccination. Sensitivity was suboptimal for TST and IGRAs.

Purpose: To incorporate new evidence into an updated meta-analysis on the sensitivity and specificity of IGRAs.

Data Sources: PubMed was searched through 31 March 2008, and citations of all original articles, guidelines, and reviews for studies published in English were reviewed.

Study Selection: Studies that evaluated QuantiFERON-TB Gold, QuantiFERON-TB Gold In-Tube (both from Cellestis, Victoria, Australia), and T-SPOT.TB (Oxford Immunotec, Oxford, United Kingdom) or its precommercial ELISpot version, when data on the commercial version were lacking. For assessing sensitivity, the study sample had to have microbiologically confirmed active tuberculosis. For assessing specificity, the sample had to comprise healthy, low-risk individuals without known exposure to tuberculosis. Studies with fewer than 10 participants and those that included only immunocompromised participants were excluded.

Data Extraction: One reviewer abstracted data on participant characteristics, test characteristics, and test performance from 38 studies; these data were double-checked by a second reviewer. The original investigators were contacted for additional information when necessary.

Data Synthesis: A fixed-effects meta-analysis with correction for overdispersion was done to pool data within prespecified subgroups. The pooled sensitivity was 78% (95% CI, 73% to 82%) for QuantiFERON-TB Gold, 70% (CI, 63% to 78%) for QuantiFERON-TB Gold In-Tube, and 90% (CI, 86% to 93%) for T-SPOT.TB. The pooled specificity for both QuantiFERON tests was 99% among non-BCG-vaccinated participants (CI, 98% to 100%) and 96% (CI, 94% to 98%) among BCG-vaccinated participants. The pooled specificity of T-SPOT.TB (including its precommercial ELISpot version) was 93% (CI, 86% to 100%). Tuberculin skin test results were heterogeneous, but specificity in non-BCG-vaccinated participants was consistently high (97% [CI, 95% to 99%]).

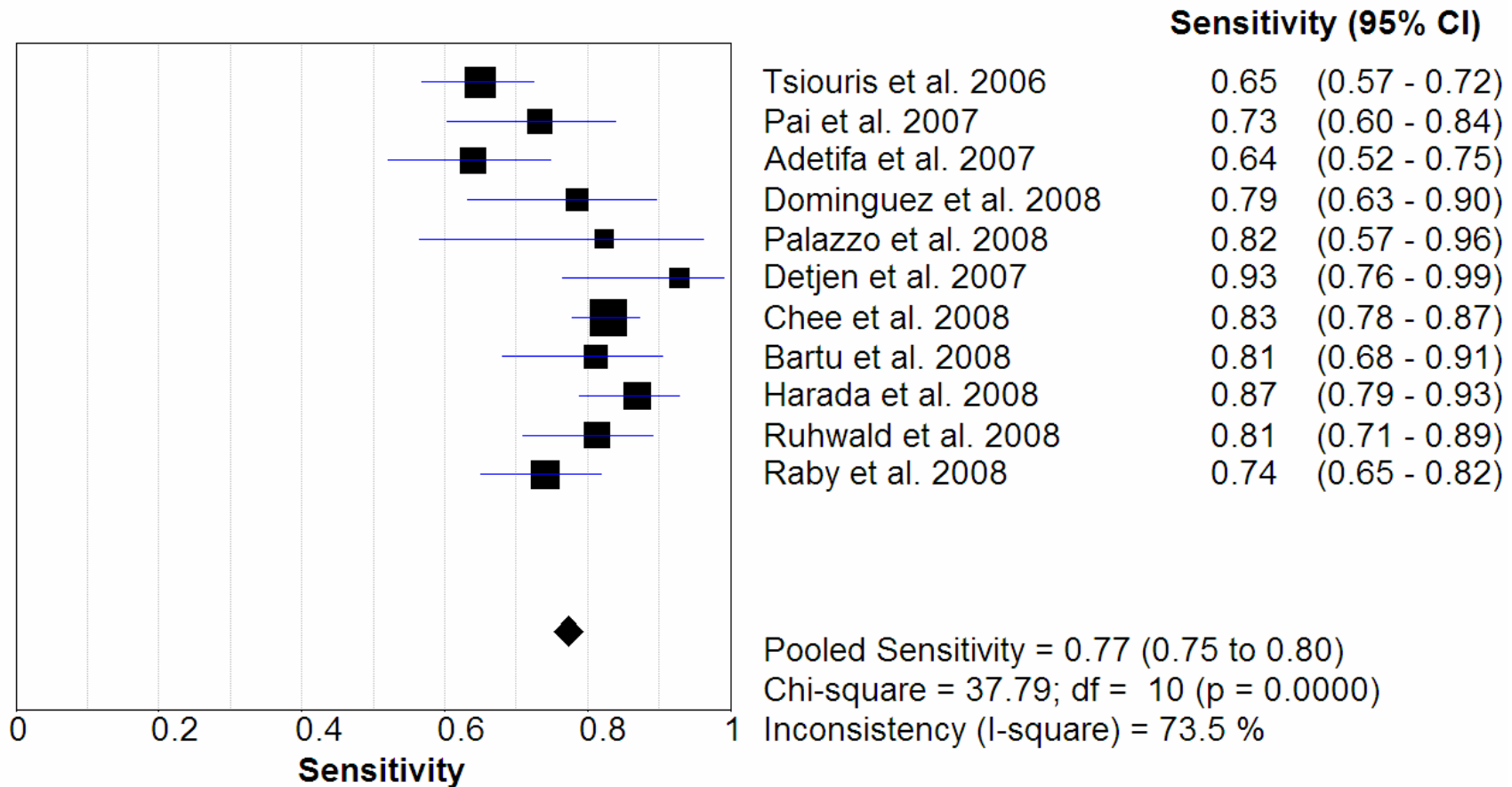
Limitation: Most studies were small and had limitations, including no gold standard for diagnosing latent tuberculosis and variable TST methods and cutoff values. Data on the specificity of the commercial T-SPOT.TB assay were limited.

Conclusion: The IGRAs, especially QuantiFERON-TB Gold and QuantiFERON-TB Gold In-Tube, have excellent specificity that is unaffected by BCG vaccination. Tuberculin skin test specificity is high in non-BCG-vaccinated populations but low and variable in BCG-vaccinated populations. Sensitivity of IGRAs and TST is not consistent across tests and populations, but T-SPOT.TB appears to be more sensitive than both QuantiFERON tests and TST.

Ann Intern Med. 2008;149.
For author affiliations, see end of text.

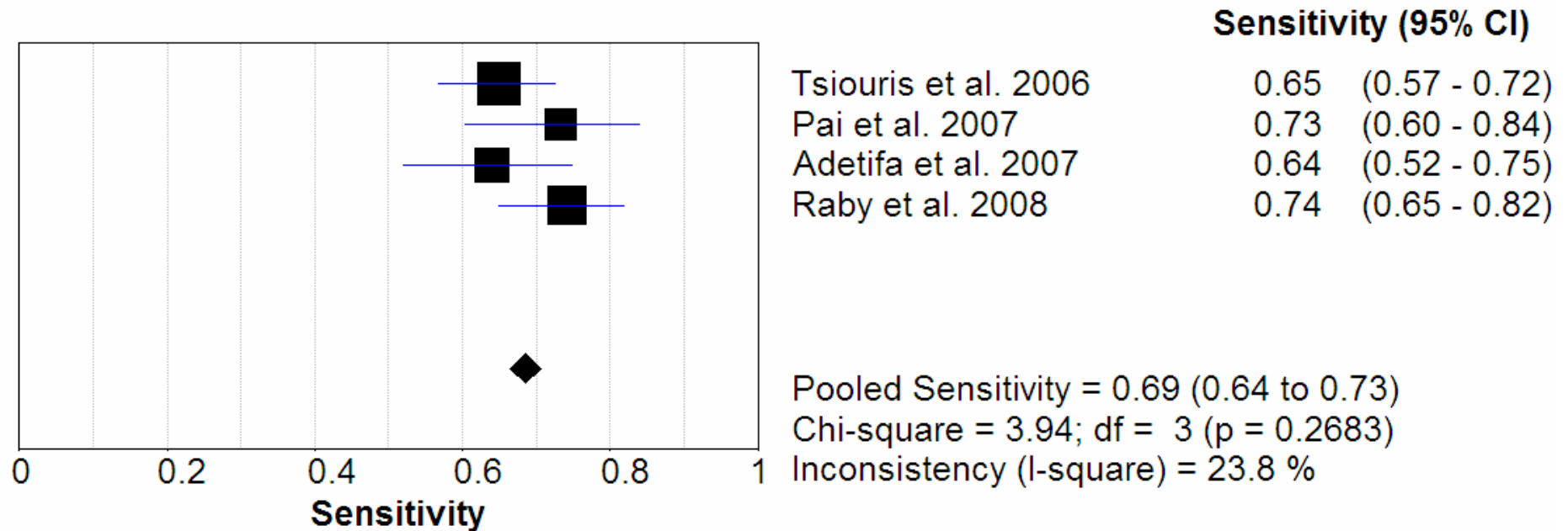
www.annals.org

Sensitivity of QFT-Gold In Tube [All settings]



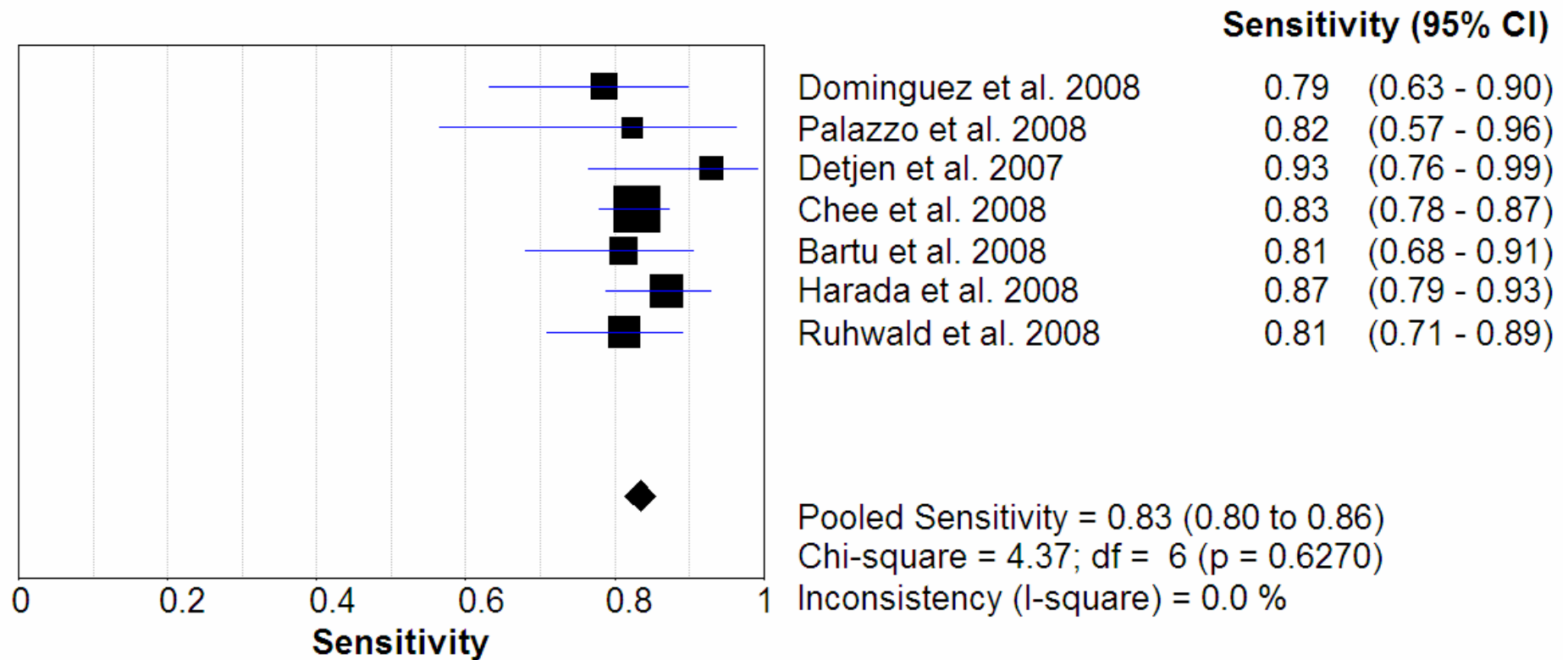
Pooled sens = 77%

Sensitivity of QFT-Gold In Tube [high incidence settings]



Pooled sens = ~70%

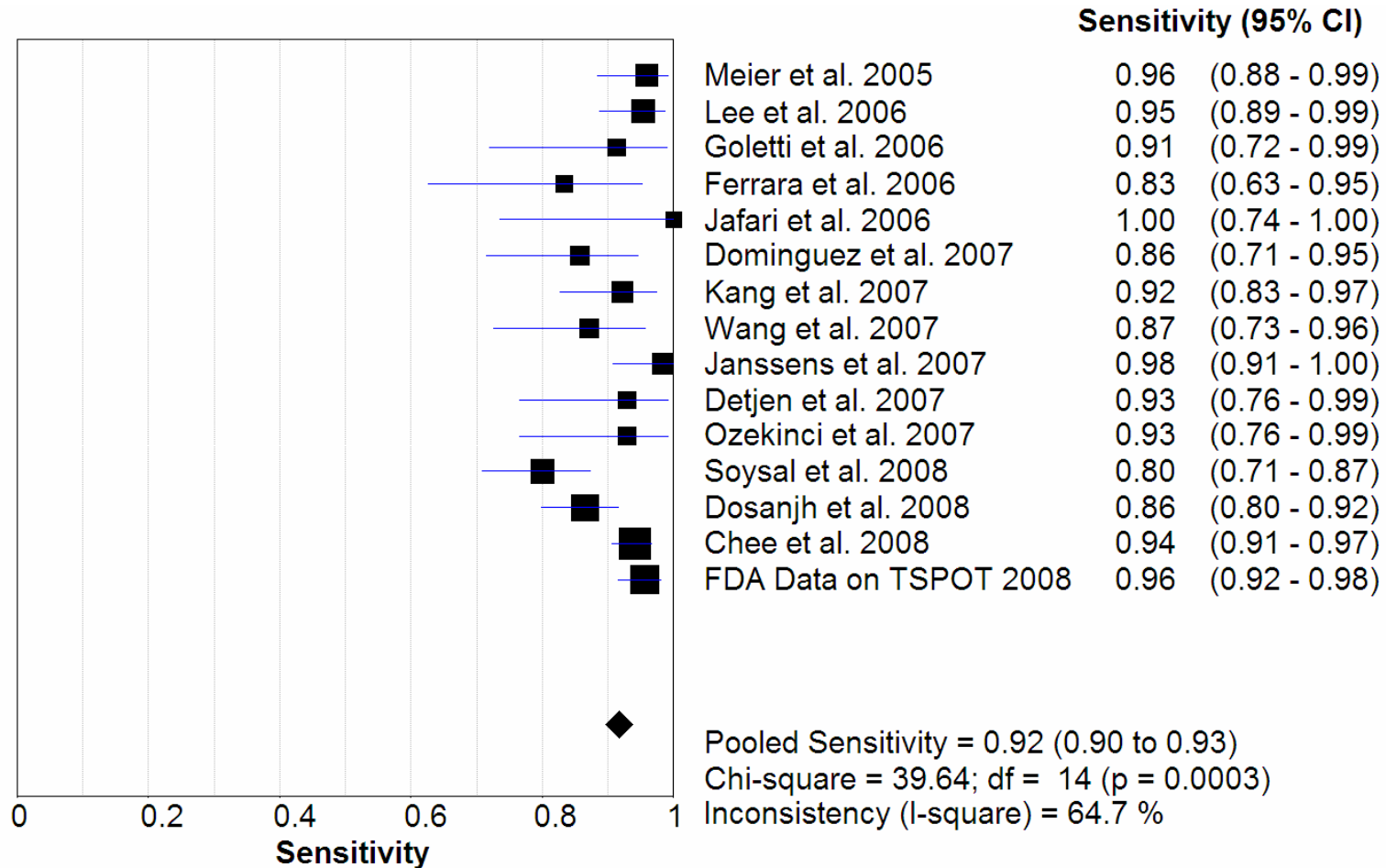
Sensitivity of QFT-Gold In Tube [low incidence settings]



Pooled sens = 83%

Sensitivity of T-SPOT.TB

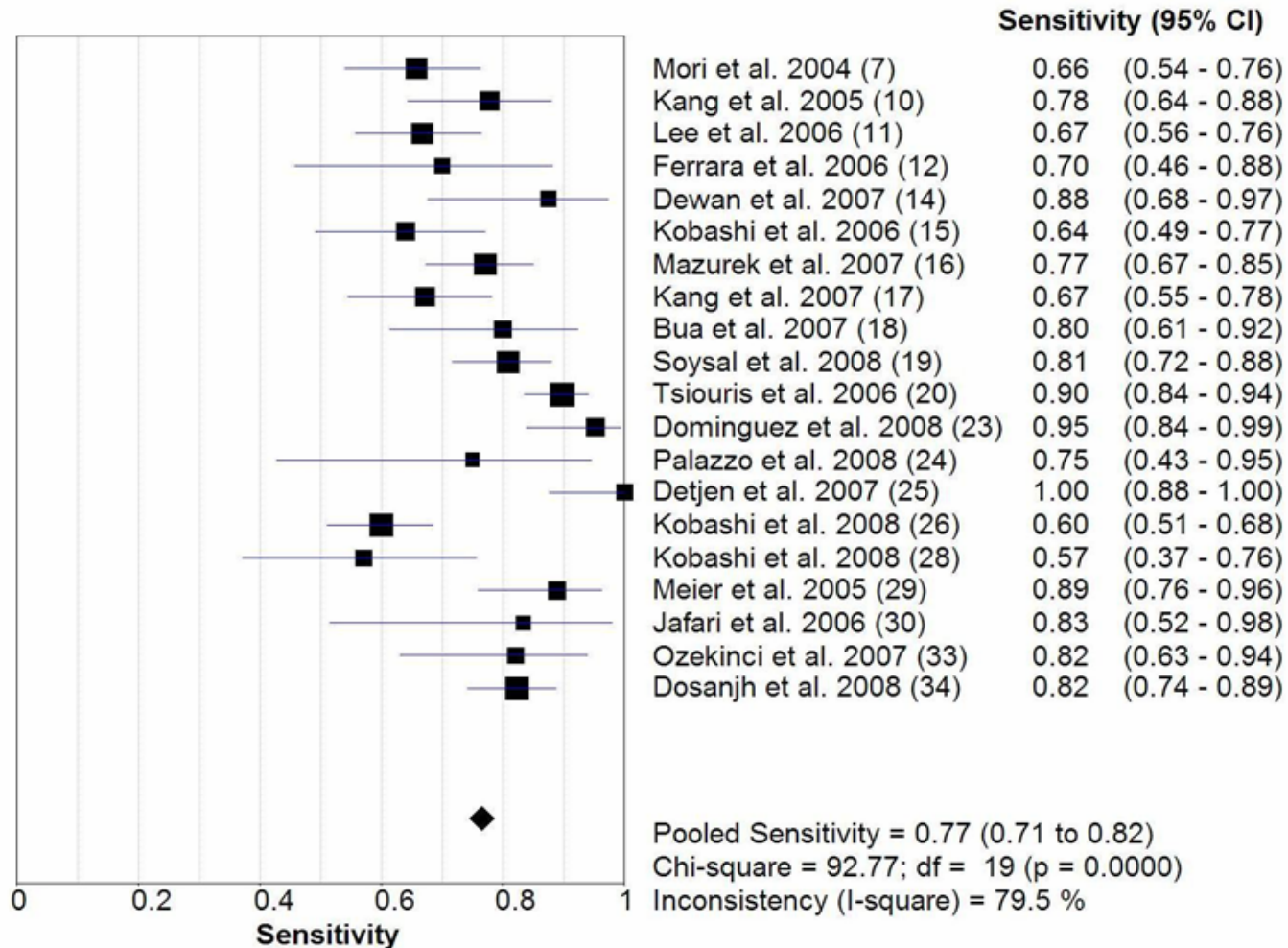
[all settings; mostly low incidence]



Pooled sens = 92%

Sensitivity of TST [all settings]

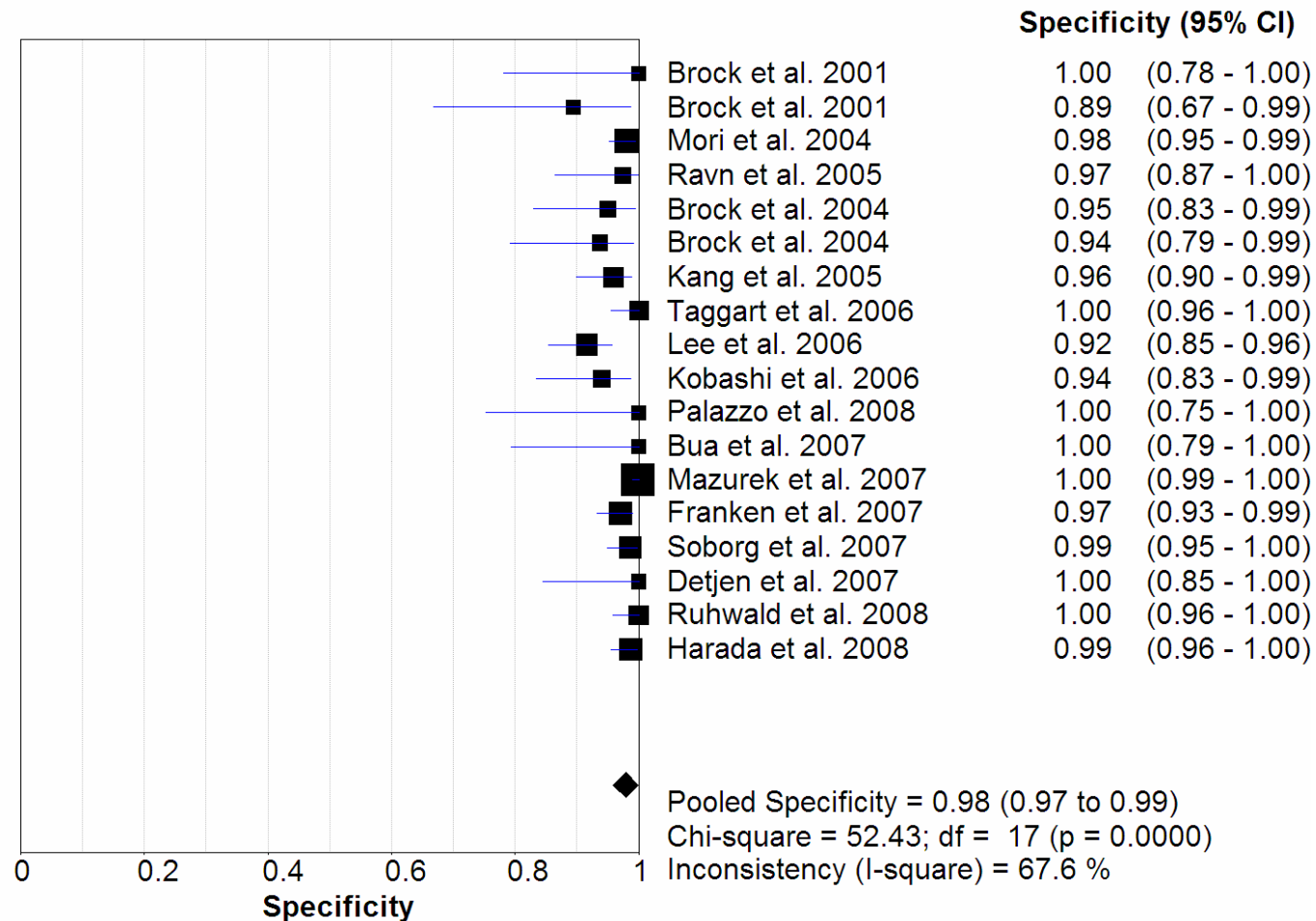
A. TST sensitivity [N=20 studies]



Pooled sens = 77%

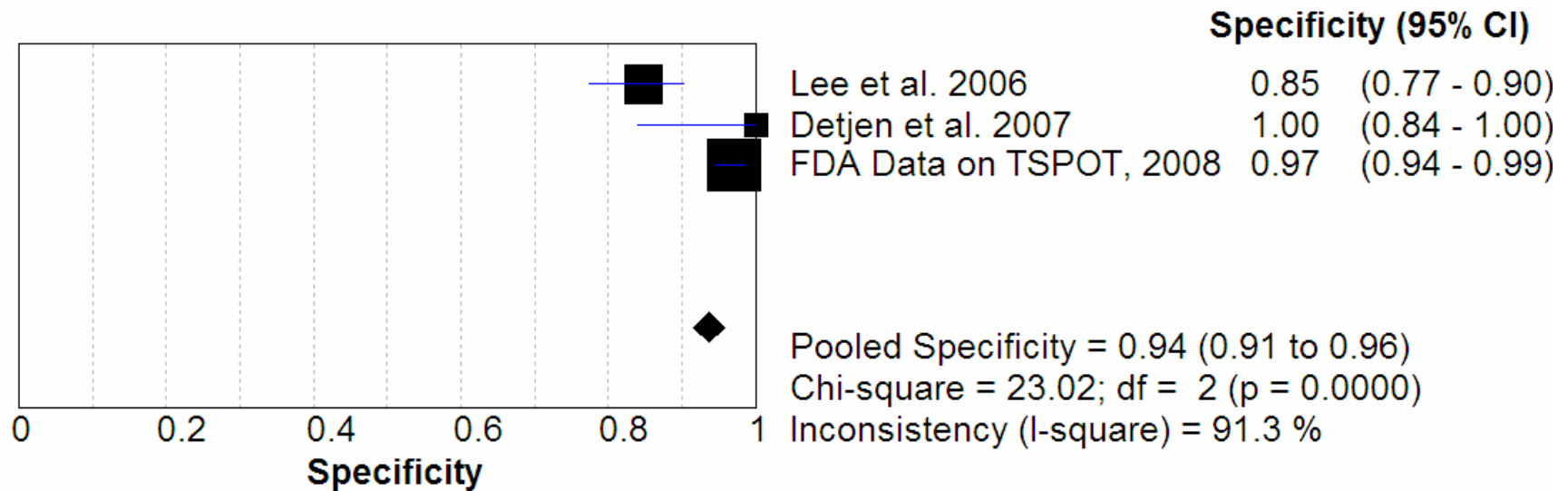
Specificity of QFT

(BCG vaccinated and not vaccinated; low incidence)



Pooled spec = 98%

Specificity of T-SPOT.TB (BCG vaccinated and not vaccinated; low incidence)



Pooled spec = 94%

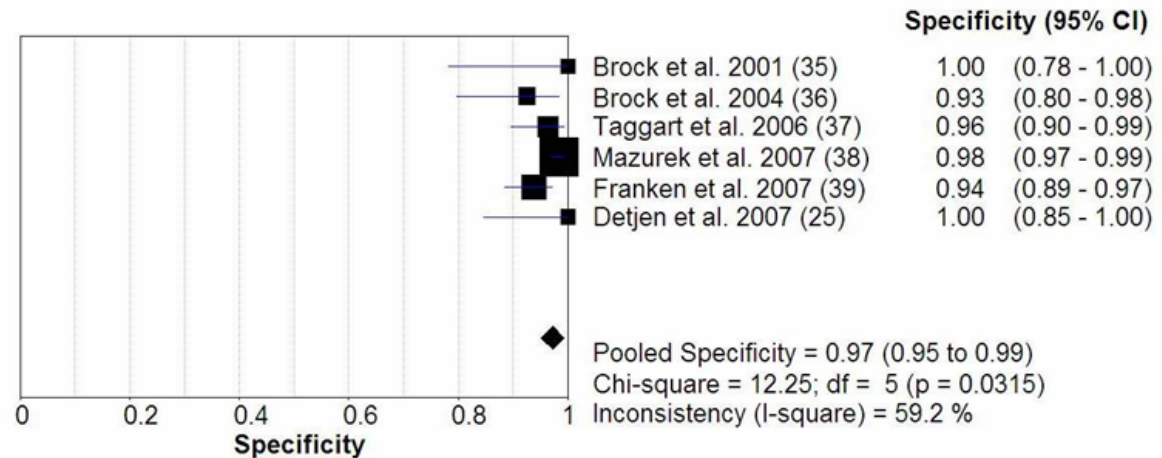
Specificity of TST

[low incidence]

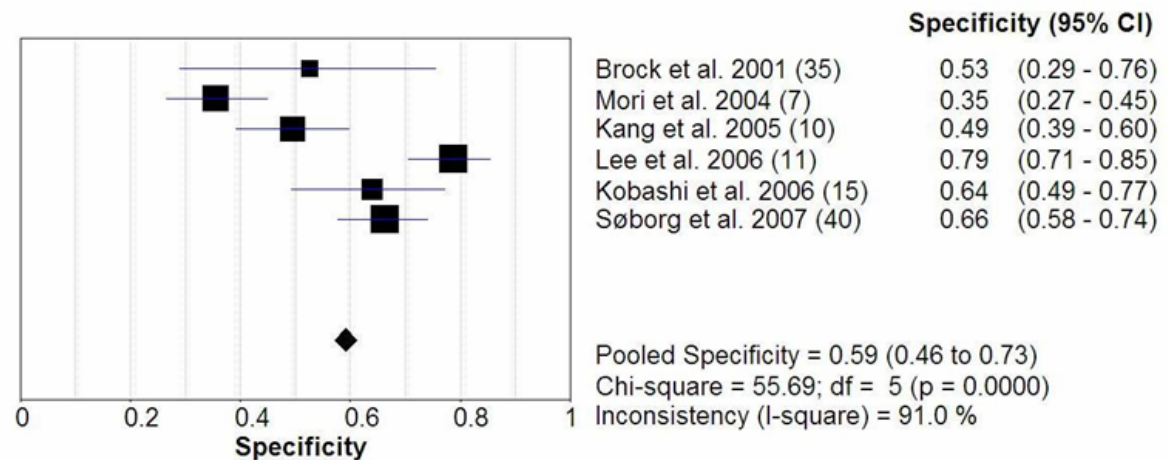
>95% in BCG non-vaccinated

~60% in BCG vaccinated

B. TST specificity in BCG non-vaccinated populations [N= 6 studies]



C. TST specificity in BCG vaccinated populations [N= 6 studies]



Summary of Sens and Spec

- TST specificity is high in BCG non-vaccinated; but low and variable in BCG vaccinated
- IGRAs (especially QFT) have very high specificity
 - IGRA specificity is higher than TST
 - IGRAs are not affected by BCG vaccination
 - Data on commercial T-SPOT.TB are relatively limited
- Sensitivity of IGRAs and TST is not consistent across tests and populations
 - QFT is as sensitive as TST
 - QFT sensitivity may be lower high incidence countries
 - HIV, advanced TB, malnutrition or other factors?
 - T-SPOT.TB appears to be more sensitive than QFT and TST

Effect of BCG on TST results

INT J TUBERC LUNG DIS 10(11):1192–1204
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REVIEW ARTICLE

False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria?

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- Analysis of 24 studies with N = 240,243 subjects
- When BCG is given in infancy, 6% false-positive TST results due to BCG
- When BCG is given after infancy, 40% false-positive TST results due to BCG

Most high endemic countries vaccinate at birth and do not repeat BCG; TST specificity is therefore fairly high

World Atlas of BCG Policies and Practices (Beta)



Authors: Alice Zwerling, Marcel Behr, Timothy Brewer, Dick Menzies & Madhukar Pai
Affiliations: McGill University & McGill University Health Center Montreal Quebec, Canada
Supported in part by the Public Health Agency of Canada

WWW.BCGATLAS.ORG

[Home](#) | [Query](#) | [References](#) | [Questionnaire](#) | [Contact Us](#)

The following tool is a World Atlas of BCG Policies and Practices.

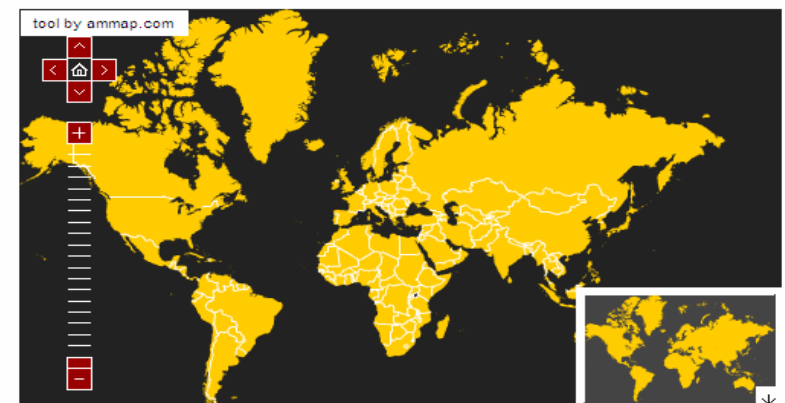
Currently the atlas includes information for over 140 countries from around the world. We have endeavoured to collect data on each country's current and past Bacille Calmette-Guerin (BCG) vaccination policies and practices.

As you know, variations in BCG vaccination practices impact the interpretation of TB diagnostics, such as the widely used Tuberculin Skin Test (TST). The World Atlas of BCG Policies and Practices will help clinicians in your country and around the world make better diagnostic decisions concerning TB infection. We have made the data available, for use as a searchable online tool for physicians and researchers alike.

If information for your country is missing, we encourage you to complete a [very short questionnaire](#) (should take only about 5 minutes to complete) concerning your country's BCG vaccination policy. The questionnaire is available on the website as a word form document. Please take the time to complete the questionnaire and contribute to the creation of a valuable resource for physicians and patients in your country.

India

Country: India
Code: IND
Region: South Asia
Income group (World Bank): Low income
Category: A, B or C: A
First BCG_who: birth
Second BCG_who:
Third BCG_who:
Fourth BCG_who:
Current BCG vaccination?: Yes
Q2: A, B, C: A
Which year was vaccination introduced?: 1948
Year BCG stopped: N/A
Age of 1st BCG?: At birth
Multiple BCG?: No
Age BCG #2: N/A
Age BCG #3: N/A
Age of BCG #4: N/A
Multiple BCG in the past?: No
Age Past BCG #2: N/A
Age past BCG #3: N/A
Year booster BCG stopped: N/A
BCG Strain: BCGVL Chennai strain, BCG laboratory Guindy, Chennai, India
TST done post BCG?: No
BCG coverage year: 2006
BCG coverage: 99
Year of changes: 1948: BCG intro as pilot project, 1949: Immunization program in schools, 51-59 Mass immunization campaigns
Explain changes: 1978: extended program of immunization to be given at birth or within 1st mo, 1985: universal immunization program BCG vaccine policy continued as earlier
Special groups: No
Explain: N/A
Summary : A



Alice Zwerling et al.

Funded by: Public Health Agency of Canada

Contact and outbreak studies

- IGRAs correlate well with surrogate markers of exposure in contact and outbreak settings, but not necessarily better than TST in all populations
- Correlation between IGRA and exposure is better than TST in low incidence settings
- This is not evident in high incidence countries
 - In high incidence countries, TST appears to correlate quite well with markers of exposure
 - ?Because TST detects a cumulative exposure measure

Exposure gradient studies in low incidence countries

17

Enhanced contact tracing and spatial tracking of *Mycobacterium tuberculosis* infection by enumeration of antigen-specific T cells

ARTICLES

Ajit Lalvani, Ansar A Pathan, Helen Durkan, Katalin A Wilkinson, Adam Whelan, Jonathan J Deeks, Will Mohammed Latif, Geoffrey Pasvol, Adrian V S Hill

Comparison of T-cell-based assay with tuberculin skin test for diagnosis of *Mycobacterium tuberculosis* infection in a school tuberculosis outbreak

Comparison of Tuberculin Skin Test and New Specific Blood Test in Tuberculosis Contacts

Inger Brock, Lydia Alvarez, Gerry Bryant, Sue Waller, Peter Andersen, Philip Monk, Ajit Lalvani

Inger Brock, Karin Weldingh, Troels Lillebaek, Frank Follmann, and Peter Andersen

Department of Infectious Disease Immunology, Statens Serum Institute; and International Reference Laboratory, Statens Serum Institute, Copenhagen, Denmark

T Cell-Based Tracking of Multidrug Resistant Tuberculosis Infection after Brief Exposure

Luca Richeldi, Katie Ewer, Monica Losi, Barbara M. Bergamini, Pietro Roversi, Jonathan Deeks, Leonardo M. Fabbri, and Ajit Lalvani

Research

Open Access

Tuberculosis contact investigation with a new, specific blood test in a low-incidence population containing a high proportion of BCG-vaccinated persons

R Diel^{*1}, A Nienhaus², C Lange³, K Meywald-Walter⁴, M Forßbohm⁵ and T Schaberg⁶

Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital; Centre for Statistics in Medicine, Health Sciences, Oxford, United Kingdom; Respiratory Disease and Pediatric Clinics, University of Modena and Reggio Emilia; Ospedaliera Policlinico di Modena, Modena, Italy

Enzyme-linked Immunospot and Tuberculin Skin Testing to Detect Latent Tuberculosis Infection

Homayoun Shams^{*}, Stephen E. Wels^{*}, Peter Klucar, Ajit Lalvani, Patrick K. Moonan, Janice M. Pogoda, Katie Ewer, and Peter F. Barnes

Contact tracing using a new T-cell-based test: better correlation with tuberculosis exposure than the tuberculin skin test

J-P. Zellweger,^{*} A. Zellweger,[†] S. Ansermet,[†] B. de Senardens,[‡] P. Wrighton-Smith[§]

^{*} TB Dispensary, University Medical Policlinic, Lausanne, [†] BBR-LTC Laboratories, Lausanne, [‡] Fondation 'Le Mont-sur-Lausanne, Switzerland; [§] Oxford Immunotec, Oxford, United Kingdom

Department of Infectious Disease Control, and Departments of Microbiology and Immunology and Medicine, Texas Health Center at Tyler, Tyler; Department of Internal Medicine, University of North Texas Health Science Center, Dallas; Nuffield Department of Clinical Medicine, University of Oxford, and John Radcliffe Hospital, Oxford, United Kingdom; University of California, San Francisco, California

Comparison of Two Interferon- γ Assays and Tuberculin Skin Test for Tracing Tuberculosis Contacts

Sandra M. Arend¹, Steven F. T. Thijssen², Ellane M. S. Leyten¹, John J. M. Bouwman², Willeke P. J. Franken¹, Ben F. P. J. Koster³, Frank G. J. Cobelens^{4,5}, Arend-Jan van Houte^{2,6}, and Ailko W. J. Bossink^{7,8}

Exposure gradient studies in high incidence countries

Large-Scale Evaluation of Enzyme-Linked Immunospot Assay and Skin Test for Diagnosis of *Mycobacterium tuberculosis* Infection against a Gradient of Exposure in The Gambia

Philip C. Hill,¹ Roger H. Brookes,¹ Annette Fox,¹ Katherine Fielding,² David J. Jeffries,¹ Moses D. Lugos,¹ Patrick K. Owiafe,¹ Simon A. Donkor,¹ Abdulrahman S. Hammond,¹ Richard A. Adegbola,¹ and Keith P. W. J. McAdam¹

Comparison of Enzyme-Linked Immunospot Assay and Tuberculin Skin Test in Healthy Children Exposed to *Mycobacterium tuberculosis*

Philip C. Hill, MPH, FRACP^a, Roger H. Brookes, PhD^a, Ifedayo M.O. Adetifa, MB, BS, FWACP^a, Annette Fox, PhD^a, Dolly Jackson-Sillah, MB, BS, MSc^a, Moses D. Lugos, FIMLS^a, Simon A. Donkor, BSc^a, Roger J. Marshall, PhD^b, Stephen R.C. Howie, MBChB, FRACP^c, Tuman Corrah, PhD, FRCP^a, David J. Jeffries, PhD^a, Richard A. Adegbola, PhD, FRCPath^a, Keith P.W.J. McAdam, FRCP^d

Surprisingly High Specificity of the PPD Skin Test for *M. tuberculosis* Infection from Recent Exposure in The Gambia

Philip C. Hill^a, Roger H. Brookes, Annette Fox, Dolly Jackson-Sillah, Moses D. Lugos, David J. Jeffries, Simon A. Donkor, Richard A. Adegbola, Keith P. W. J. McAdam

Risk for Tuberculosis among Children

Philip C. Hill^{a,*}, Lovett Lawson,^{a,†} S. Bertel Squire,^{a,*} Brian Coulter,^{a,*} Pernille Ravn,[‡] Inger Brock,[‡] C. Anthony Hart,[§] and Luis E. Cuevas^{a,*}

BMC Infectious Diseases



Open Access

Research article

Comparison of two interferon gamma release assays in the diagnosis of *Mycobacterium tuberculosis* infection and disease in The Gambia

Ifedayo MO Adetifa^{*}, Moses D Lugos, Abdulrahman Hammond, David Jeffries, Simon Donkor, Richard A Adegbola and Philip C Hill

Longitudinal and serial testing studies

- Longitudinal studies are few, but suggest:
 - IGRAs may be more dynamic than TST
 - Conversions and reversions are common among contacts and HCWs in high incidence settings
 - No consensus on how to define conversions and reversions
 - Depending on cut-offs used for conversion, annual rate of conversions will vary between IGRA and TST
 - Prognosis of conversions and reversions is unknown

Predictive value of IGRAs

JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2002, p. 704–706
0095-1137/02/\$04.00+0 DOI: 10.1128/JCM.40.2.704-706.2002
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Immune Responses to the *Mycobacterium tuberculosis*-Specific Antigen ESAT-6 Signal Subclinical Infection among Contacts of Tuberculosis Patients

T. Mark Doherty,^{1*} Abebech Demissie,² Joseph Olobo,² Dawit Wolday,³ Sven Britton,⁴
Tewodros Eguale,⁵ Pernille Ravn,⁶ and Peter Andersen¹

Department of Tuberculosis Immunology, Statens Serum Institute,¹ and Hvidovre Hospital,⁶ Copenhagen, Denmark; Armauer Hansen Research Institute,² Black Lion Hospital,³ and Hossana Regional Hospital, Ministry of Health,⁵ Hossana, Ethiopia; and Karolinska Institute, Stockholm, Sweden⁴

High Incidence

Predictive Value of a Whole Blood IFN- γ Assay for the Development of Active Tuberculosis Disease after Recent Infection with *Mycobacterium tuberculosis*

Roland Diel¹, Robert Loddenkemper², Karen Meywald-Walter³, Stefan Niemann⁴, and Albert Nienhaus⁵

¹School of Public Health, University of Düsseldorf, Düsseldorf, Germany; ²German Central Committee against Tuberculosis, Lungenklinik Heckeshorn, HELIOS, Klinikum Emil von Behring, Berlin, Germany; ³Public Health Department Hamburg-Mitte, Hamburg, Germany; ⁴National Reference Center for Mycobacteria, Research Center Borstel, Borstel, Germany; and ⁵Institution for Statutory Accident Insurance and Prevention in the Health and Welfare Services, Hamburg, Germany

OPEN ACCESS Freely available online



Low Incidence

Incidence of Tuberculosis and the Predictive Value of ELISPOT and Mantoux Tests in Gambian Case Contacts

Philip C. Hill¹, Dolly J. Jackson-Sillah, Annette Fox, Roger H. Brookes, Bouke C. de Jong, Moses D. Lugos, Ifedayo M. Adetifa, Simon A. Donkor, Alex M. Aiken, Stephen R. Howie, Tumani Corrah, Keith P. McAdam, Richard A. Adegbola

Bacterial Diseases Programme, Medical Research Council (MRC) Laboratories, Banjul, The Gambia

What are the key unresolved issues?

- What is the predictive value of IGRAs for the development of active TB? **Will this vary by high vs. low incidence setting?**
- Will treatment of IGRA positive subjects reduce the future probability of active TB?
- What is the interpretation of IGRA conversions and reversions? **Are conversions and reversions more likely in high incidence settings?**
- **What is the exact role of IGRAs in high incidence countries?**

FIND's Work on IGRAs

- Global Plan to Stop TB: by 2012, a test that will accurately identify people with LTBI and those at high risk of progression to active disease
- As active TB case rates decrease, LTBI Dx and Rx will become important to eliminate TB by 2050
- Even in resource-limited settings, high-risk populations may benefit from IPT (immunocompromised, children, and contacts of infectious TB cases)
 - if IGRAs are shown to be more predictive of active TB than the TST, then they may have a big impact
- IGRAs show great promise as research tools.
 - IGRAs now provide a second window into the biology and epidemiology of LTBI

FIND's Work on IGRAs



Stop TB Partnership

Workshop on

T-Cell Based Diagnosis of Latent Tuberculosis Infection in Resource-Limited Settings

Co-organized by FIND and WHO on Behalf of the Stop TB Working Group on New Diagnostics

Dates: 16-17 March 2006

Venue: Ramada Park Hotel, Geneva, Switzerland

W T-cell assays for the diagnosis of latent tuberculosis infection: moving the research agenda forward

Madhukar Pai, Keertan Dheda, Jane Cunningham, Fabio Scano, Richard O'Brien

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428-438
Published Online
April 17, 2007
DOI: 10.1016/S1473-
3099(07)70086-5

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(K Dheda MD); Division of

For nearly a century, the tuberculin skin test was the only tool available for the detection of latent tuberculosis infection. A recent breakthrough has been the development of T-cell-based interferon- γ release assays. Current evidence suggests interferon- γ release assays have higher specificity than the tuberculin skin test, better correlation with surrogate markers of exposure to *Mycobacterium tuberculosis* in low-incidence settings, and less cross-reactivity as a result of BCG vaccination compared with the tuberculin skin test. The body of literature supporting the use of interferon- γ release assays has rapidly expanded. However, several unresolved and unexplained issues remain. To address these issues, a group of experts met in Geneva, Switzerland, in March, 2006, to discuss the research evidence on T-cell-based assays, their clinical usefulness, limitations, and directions for future research, with a specific focus on resource-limited and high HIV prevalence settings. On the basis of 2 days of discussions, a comprehensive research agenda was generated, which will propel the field forward by stimulating focused high-impact research and encourage the investment of resources needed to tackle priority research questions, especially in resource-limited settings. Ultimately, if adequately financed, the research findings will inform appropriate use of novel latent tuberculosis infection diagnostics in global tuberculosis control.

Pai et al. *Lancet Infect Dis* 2007

Rethinking the Epidemiology of Tuberculosis Infection

The First Global Symposium on Interferon- γ Assays

FEBRUARY 21-22, 2007

SHERATON VANCOUVER WALL CENTRE HOTEL

VANCOUVER, BC CANADA



2nd *Global Symposium on IGRAs*
Putting Interferon-gamma Release Assays into Practice
May 30–June 1, 2009
Dubrovnik, Croatia



<http://www.igrasymposium.com/>

FIND evaluation projects on QFT-Gold In Tube

- **CREATE-ZAMSTAR**: household contact study in Zambia and South Africa that will generate data on predictive value for active TB [~2000 enrolled in SA alone]
- **AERAS-SATVI**: Neonatal cohort in South Africa, to assess the value of QFT-G in diagnosing active TB among neonates and infants [~400 infants recruited]
- **AERAS-SJRI**: Neonatal cohort in India, to assess the value of QFT-G in diagnosing active TB among neonates and infants [~200 infants recruited]
- **Pediatric IGRA studies in South Africa** [>300 kids recruited]
 - Stellenbosch University, Univ of Bergen, Case Western Reserve University [supported by NUFU, NIH, Thrasher]
 - Johns Hopkins University, Chris Hani Baragwanath Hospital, Univ of Wiswatersrand
- **IGRAs in HIV+**: IGRAs in a RCT of ART vs. ART+IPT in Cape Town, South Africa [UCT] [~400 participants recruited]
- **IGRAs in US-bound immigrants** from Viet Nam [CDC Atlanta]

Monitoring progress on QuantiFERON evaluation studies in South Africa



FIND team at the Desmond Tutu TB Center, Tygerberg, South Africa

These studies will provide useful data on the key question of predictive value of IGRAs (interferongamma release assays) among high-risk populations such as contacts, children and HIV-infected persons, address the issue of whether QFT-G can contribute to the diagnosis of TB in infants, and assess the utility of IGRAs among young children with TB/HIV co-infection in a high endemic, resource-limited setting.

During a recent site visit, the FIND team (Rick O'Brien, Madhu Pai and Heidi Albert) visited several study sites, including the Desmond Tutu TB Center (DTTC) based at Stellenbosch University, Tygerberg, South Africa. Under the leadership of Dr. Nulda Beyers, the DTTC is enrolling patients into the CREATE ZAMSTAR project, a large-scale household contact study in Zambia and South Africa <http://www.tbhiv.create.org/Studies/ZAMSTAR.htm>. As part of a ZAMSTAR QGIT sub-study, this project will recruit over 5000 TB cases and contacts and

determine the predictive value of QGIT in a high risk population.

FIND staff visit the Desmond Tutu TB Center at Stellenbosch University, Cape Town, to monitor progress on QuantiFERON evaluation studies October 2007

Led by Rick O'Brien, Head of Product Evaluation at FIND, and Madhukar Pai (FIND Consultant for LTBI diagnostics), FIND is supporting several field studies to evaluate the utility and applicability of the QuantiFERON-TB Gold In-Tube (QGIT) assay for the diagnosis of LTBI in HIV-infected persons and in adult and childhood contacts of TB patients, as well as for active TB in young children and neonates. These projects are ongoing in South Africa, Zambia and India.

➤ [More](#)



Dr. Madhukar Pai, Dr. Rick O'Brien, and Dr. Heidi Albert