Children

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Adetifa 2010[105]
Country: Gambia
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community-based
Number of centres: NR
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Medical Research Council (MRC) labs UK

Aim of the study

To compare TSPOT, QFT-GIT, and TST for diagnosis of LTBI in Gambian childhood contacts of TB patients

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: NR
Total N of recruited patients: 285
Inclusion criteria: Household contacts (< 16 yrs) of newly diagnosed TB index cases
Exclusion criteria: History of treatment for active TB, TB diagnosis within 1 month of recruitment
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 215 (for TST) and 245 (for IGRAs)
Methods of active TB diagnosis (if applicable): Sputum smears and mycobacterial cultures examined using standard methods
Outcomes (study-based) list: Agreement; associations of test results with risk factors; combining two tests to explore gains in sensitivity and loss in specificity
Characteristics of participants (total study sample)
Mean (range or SD) Age (years): NR
Women (n [%]): 145 [51]
Race/ethnicity (n [%]):NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 127/199 [59.1]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): HIV positive (3 [1.1])
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	NR	72	143	2	215
IGRA	NR	71	144	0	215

(TSPOT):					
TST (≥10mm):	NR	57	158	0	215
Test 3 (specify):	NA	NA	NA	NA	NA
Total N of patients with valid results for both IGRA and TST: 215 for all three tests					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group – sleep proximity					
Non-exposed	Different house (reference group)				
Exposed 1 **(specify):**	Same house – different room				
Exposed 2 **(specify):**	Same house – same room				
Exposed 3 **(specify):**	NA				
Exposed 4 **(specify):**	NA				
Tests					
	Assay used, methodology, timing for test measurement, manufacturer		**Cut-off values/thresholds Definition of test+**		**Other information**
IGRA (TSPOT)	Carried out according to manufacturer's instructions. The spot unit counting performed using ELISPOT reader (AID GmbH, Strassburg, Germany)		Where the negative control had 0-5 spots, a positive result was defined as ≥6 spots in either the ESAT-6 or CFP-10 panel after subtracting the number of spots in the negative control panel In case of >6 spots in negative control panel, ESAT-6 or CFP-10 panel had to contain at least twice the number of spots in negative control panel to obtain a positive result		NA
IGRA (QFT-GIT)	Carried out according to manufacturer's instructions. IFN gamma levels measured using Dynex ELISA reader ver. 6.0 (Dynex Technologies, West Sussex, UK)		Positive result was defined as ≥0.35 IU/ml		NA
TST (≥10mm)	Carried out with 2 TU (PPD RT23, Statens Serum Institut, Copenhagen, Denmark) immediately after blood samples' completion. Indurations were recorded at 48-72 hours		≥10mm threshold for positivity		NA
Association between test results and incidence of active TB (if applicable)					

IGRA				TST			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)							
IGRA (QFT-GIT)				**TST (≥10mm)**			
	Sleep proximity		Total		Sleep proximity		Total
	Same house – same room	Different house			Same house – same room	Different house	
IGRA +	14	19	33	TST +	15	10	25
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	215	Total	NR	NR	215

Test performance parameters	
IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
Same house same room vs. Different house OR (crude; for T^+ reported) = 3.20 (95% CI: 1.20, 9.10)	**Same house same room vs. Different house** OR (crude; for T^+ reported) = 10.10 (95% CI: 3.20, 32.10)
Same house same room vs. Different house OR (regression-based; reported) = 4.00 (95%	**Same house same room vs. Different house** OR (regression-based; reported) = 15.00 (95% CI: 4.70, 47.20)

CI: 1.40, 11.40) List of covariates: age, sex, ethnic group	List of covariates: age, sex, ethnic group
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 0.58 (0.28, 0.90)
Ratio of ORs (regression-based; reported) = 0.52 (0.29, 0.91)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				**TST (≥10mm)**			
	Sleep proximity		Total		Sleep proximity		Total
	Same house – different room	Different house			Same house – different room	Different house	
IGRA +	39	18	57	TST +	32	10	42
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	215	Total	NR	NR	215

Test performance parameters

IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
Same house different room vs. Different house OR (crude; for T^+ reported) = 2.00 (95% CI: 0.80, 5.10)	**Same house different room vs. Different house** OR (crude; for T^+ reported) = 2.40 (95% CI: 1.00, 5.80)
Same house different room vs. Different house OR (regression-based; reported) = 2.60 (95% CI: 0.90, 7.10) List of covariates: age, sex, ethnic group	**Same house different room vs. Different house** OR (regression-based; reported) = 2.90 (95% CI: 1.30, 6.70) List of covariates: age, sex, ethnic group
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 0.83(0.43, 1.60)
Ratio of ORs (regression-based; reported) = 0.90(0.46, 1.76)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				**TST (≥10mm)**			
	Sleep proximity		Total		Sleep proximity		Total
	Same house – same room	Different house			Same house – same room	Different house	
IGRA +	14	18	32	TST +	15	10	25
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeter	NR	NR	NR	Indetermina	NR	NR	NR

minate				te			
Total	NR	NR	215	Total	NR	NR	215

Test performance parameters	
IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
Same house same room vs. Different house OR (crude; for T^+ reported) = 5.30 (95% CI: 1.50, 18.50)	**Same house same room vs. Different house** OR (crude; for T^+ reported) = 10.10 (95% CI: 3.20, 32.10)
Same house same room vs. Different house OR (regression-based; reported) = 6.60 (95% CI: 1.70, 25.20) List of covariates: age, sex, ethnic group	**Same house same room vs. Different house** OR (regression-based; reported) = 15.00 (95% CI: 4.70, 47.20) List of covariates: age, sex, ethnic group
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 0.52(0.22, 1.25)
Ratio of ORs (regression-based; reported) = 0.44(0.18, 1.09)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				TST (≥10mm)			
	Sleep proximity		Total		Sleep proximity		Total
	Same house – same room	Different house			Same house – same room	Different house	
IGRA +	14	18	32	TST +	15	10	25
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	215	Total	NR	NR	215

Test performance parameters	
IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
Same house same room vs. Different house OR (crude; for T^+ reported) = 5.30 (95% CI: 1.50, 18.50)	**Same house same room vs. Different house** OR (crude; for T^+ reported) = 10.10 (95% CI: 3.20, 32.10)
Same house same room vs. Different house OR (regression-based; reported) = 6.60 (95% CI: 1.70, 25.20) List of covariates: age, sex, ethnic group	**Same house same room vs. Different house** OR (regression-based; reported) = 15.00 (95% CI: 4.70, 47.20) List of covariates: age, sex, ethnic group
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA							
Ratio of OR (crude; for T^+ reported) = 0.52 (0.22, 1.25)							
Ratio of ORs (regression-based; reported) = 0.44 (0.18, 1.09)							
Other reported measure = NA							
Association between test results and BCG status (if applicable)							
IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR
Test performance parameters							
IGRA				**TST**			
DOR (for T^+ calculated)$_{IGRA}$ = NR				DOR (for T+ calculated)$_{TST}$ = NR			
OR (crude; for T^+ reported)$_{QFT}$ = 1.10 (95% CI: 0.60, 2.00) OR (crude; for T^+ reported)$_{TSPOT}$ = 1.10 (95% CI: 0.61, 2.09)				OR (crude; for T+ reported) = 0.89 (95% CI: 0.50, 1.70)			
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates:				OR (regression-based; reported) $_{TST}$ = NR List of covariates:			
Other reported measure = NR				Other reported measure = NR			
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**							
Total sample: **QFT-GIT**							
	TST (≥10mm) +			TST -			Total
IGRA (QFT-GIT) +	43			29			72
IGRA (QFT-GIT) -	14			129			143
Indeterminate	NR			NR			2
Total							217
Description							
Sample definition (e.g., total, if stratified by BCG or condition – specify): total – QFT-GIT							
TST + threshold: ≥10mm							
Parameters							
Kappa = 0.52 (95% CI: 0.39, 0.65)							
% concordance = 80.00% (95% CI: 74.15, 84.8)							
% discordance = 20.00% (95% CI: 15.2, 25.85)							
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**							
Total sample : TSPOT							
	TST (≥10mm) +			TST -			Total
IGRA (TSPOT) +	43			28			71
IGRA (TSPOT) -	14			130			144
Indeterminate	0			0			0

Total	57	158	215
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Total -TSPOT			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.53 (95% CI: 0.40, 0.66)			
% concordance = 80.47% (95% CI: 74.65, 85.21)			
% discordance = 19.53% (95% CI: 14.79, 25.35)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
TST was most responsive of the 3 tests; none of the tests was affected by prior BCG vaccination
Reviewers:
Similar moderate agreement between TSPOT vs. TST and QFT vs. TST; TSPOT and TST were more strongly correlated with sleep proximity than QFT; none of the tests was influenced by BCG vaccination
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Cruz 2011[106]
Country: US
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Pediatric tuberculosis clinics
Number of centres: 3
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Cellestis, Ltd, Oxford Immunotec, Inc

Aim of the study

To compare the performance of 1 IGRA, the T-SPOT.TB assay with the tuberculin skin test (TST) in children with different epidemiologic risk factors for tuberculosis

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: 2005 to 2006
Total N of recruited patients: NR
Inclusion criteria: Children (aged 1 month to 18 years) with LTBI or tuberculosis disease and children uninfected with tuberculosis
Exclusion criteria: Children on any tuberculosis medication for 2 or more months were not eligible for enrollment
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 215 (22 did not have valid results)
Total N of patients with valid results for both IGRA and TST: 193 (of these, 30 had diagnosis of TB)
Methods of active TB diagnosis (if applicable): Children with tuberculosis disease was subcategorized as those with confirmed or clinically diagnosed tuberculosis. Children with confirmed tuberculosis had a positive culture or polymerase chain reaction result for Mycobacterium tuberculosis. Clinically diagnosed case subjects were defined as children without positive mycobacterial culture results who had radiographic or clinical findings consistent with tuberculosis and at least 1 or more of the following: (1) exposure to a known tuberculosis case; (2) a positive TST result (≥5 mm); or (3) histopathologic findings compatible with tuberculosis (eg, caseating granulomas)
and the exclusion of reasonable alternative diagnoses
Outcomes (study-based) list: Agreement, exposure-based
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median 8.6 (range: 1 mo to 18 yrs)
Women (n [%]): 94 [51]
Race/ethnicity (n [%]): Hispanic 115 [62.5], Non-Hispanic black 36 [19.6], Non-Hispanic white 19 [10.3], Asian 6 [3]
Geographic origin (n[%]): Low prevalence regions (US/UK) (121 [65.7])
BCG vaccination (n [%]): 68 [37]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): None
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NA
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results

					available)
IGRA (TSPOT):	185 (30 TB pts not counted)	94	69	22	163
TST (≥15mm):	185 (30 TB pts not counted)	94	69	22	163
Test 3 (specify)	NA	NA	NA	NA	NA
Total N of patients with valid results for both IGRA and TST: 163					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group					
Non-exposed	No contact with an identifiable source case				
Exposed 1 **(specify):**	contact with an identifiable source case				
Exposed 2 **(specify):**	NA				
Exposed 3 **(specify):**	NA				
Exposed 4 **(specify):**	NA				
Tests					
	Assay used, methodology, timing for test measurement, manufacturer		**Cut-off values/thresholds Definition of test+**		**Other information**
IGRA (TSPOT)	The commercially available T-SPOT.TB assay (Oxford Immunotec, Oxford, United Kingdom) was performed within 5 hours of specimen collection in the laboratory of 1 of the investigators (per manufacturer instructions. Briefly, this assay used 2 M tuberculosis–specific antigens, early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP10), to stimulate interferon-production in washed and enumerated peripheral blood mononuclear cells; 8 mL of blood was drawn from children 10 years old or older and 4 mL from children younger than 10 years. Peripheral blood mononuclear cells were counted to ensure that a standardized cell number was added in the assay to control for low T-cell volumes. General T-cell reactivity was confirmed by a positive mitogen control (phytohemagglutinin). A negative control was used to identify nonspecific cell activation		Spots were counted manually by using a microscope and confirmed by using an automated plate counter by the manufacturer. Assays with 8 or more spots were considered positive, and assays with less than 5 spots were considered negative. Borderline results (5–7 spots) were excluded from concordance analyses but were analyzed separately. A subgroup analysis was performed for specimens with 6 to 7 spots, because these specimens are sometimes considered positive internationally.		NA

TST (≥15mm)	Trained clinic or health department personnel placed and interpreted Mantoux tests. Transverse induration was measured at 48 to 72 hours and interpreted according to the American Thoracic Society criteria	TSTs were considered positive for all children who had results of 15 mm or more, 10 mm or more for children with chronic medical problems or exposure to people at high risk, and 5 mm or more for children with suspected disease or who were immunocompromised or children with identifiable source cases	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				**TST≥15mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR

OR (regression-based; reported) = 4.41 [95% CI: 1.78, 10.94]) List of covariates: NR	OR (regression-based; reported) = 0.48 [95% CI: 0.26, 0.91] List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = 9.19 (95% CI: 5.23, 16.3)
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = 4.77 [95% CI: 2.29, 9.95]
OR (regression-based; reported) $_{IGRA}$ = 0.69 [95% CI: 0.37, 1.31] List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 4.32 [95% CI: 1.02, 18.35] List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total
TST + threshold: ≥15mm

Parameters

Kappa = NR
% concordance = NR
% discordance = NR

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
T-SPOT.TB was more specific than the TST for children who were immunized with BCG. Contact with a source case was associated with T-SPOT.TB result but not TST
Reviewers:
BCG influenced TST but not TSPOT in terms of false positives; TSPOT performed better than TST in terms of the association with exposure (contact with TB case)
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Kasambira 2011[107]
Country: South Africa
Study design: Retrospective cohort/cross-sectional study (with limited follow-up of 6 months)
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community based
Number of centres: 3
Total length of follow up (if applicable): 6 months
Funding (government/private/manufacturer/other - specify)**:** The United States Agency for International Development

Aim of the study

To determine and compare the prevalence of M. tuberculosis infection as assessed by TST and by QFT-GIT. Secondary objectives were to assess agreement between the two test methods and identify factors associated with various patterns of test results

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: October 2006 and December 2009
Total N of recruited patients: NR
Inclusion criteria: Children aged 6-16 years whose parents/guardians were TB index cases aged ⩾18 years, with diagnosis of pulmonary TB within the preceding 3 months, willingness to have the child undergo study testing and provision of informed consent
Exclusion criteria: Children's prior diagnosis or treatment of active or latent TB.
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 270
Total N of patients with valid results for both IGRA and TST: 254
Methods of active TB diagnosis (if applicable): Microbiological tests, histopathology, clinician diagnosis or a combination of these. Performance of diagnostic testing for adult TB suspects was not a component of this study, and diagnoses of pulmonary TB in the adult index cases were made by non-study clinicians. The study team reviewed medical records and interviewed adult index cases to corroborate the diagnosis
Outcomes (study-based) list: LTBI prevalence, agreement, association of test positivity with different index case- and child-related baseline factors
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median 6 [3–9]
Women (n [%]): 141 [52]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 257 [95]
History of anti-TB treatment (n [%]): None
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): NR
Clinical examination (yes/no): Yes
Morbidity (n [%]): HIV 14 [5]
Co-morbidity (n [%]): NA
Type of during-study treatment (n [%]): Active TB treatment 37 [19%] and LTBI treatment 19 [10%]

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (GIT):	270	79	172	19	251

TST (⩾5 mm):	270	71	183	16	254
Test 3 (specify)	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 254

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group –

	Adult index case type of TB diagnosis	**Adult index case smear grade**	**Exposure to index case during the day**
Non-exposed	Smear-positive TB	Negative	Minority of day (< 6 h)
Exposed 1 **(specify):**	Smear-negative, culture-positive TB	Scanty	Majority of day (> 7 h)
Exposed 2 **(specify):**	Clinical TB	1+	NA
Exposed 3 **(specify):**	NA	2+	NA
Exposed 4 **(specify):**	NA	3+	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	All children underwent QFT-GIT testing 5–30 min after TST placement. Blood was drawn from the right arm. QFT-GIT testing was performed according to the manufacturer's instructions, and included nil control, mitogen control and TB antigen tubes. Assays were conducted in a single laboratory at the study site by the same trained technician. Average interval between blood collection and initiation of incubation was 8.3 min (median 5, range 2–60, interquartile range 3–10). Following stimulation and centrifugation, harvested plasma specimens were stored at 4°C for up to 28 days prior to ELISA testing	Results were calculated and interpreted by the assay software as positive, negative or indeterminate	NA
TST⩾5 mm	the Mantoux method using Tuberculin purified protein derivative (PPD) RT-23 (2 units, Statens Serum Institut, Copenhagen, Denmark) was injected subcutaneously into the left forearm and the test was read 48–96 h later	An induration of ⩾5 mm was considered a positive test during the study	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA

PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA

Ratio of incidence density rate ratios = NA

Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)

	Exposure level		Total
	High/Yes	Low/No	
IGRA +	46	32	78
IGRA -	108	81	189
Indeterminate	0	0	0
Total	154	113	267

TST (≥5mm)

	Exposure level		Total
	High/Yes	Low/No	
TST +	42	29	71
TST -	99	81	180
Indeterminate	0	0	0
Total	141	110	251

Test performance parameters

IGRA	TST
Exposure to index case during the day (see 2 x 2 above) Sensitivity = 46/154 = 29.87% (95% CI: 23.2, 37.52)	**Exposure to index case during the day (see 2 x 2 above)** Sensitivity = 42/141 = 29.79% (95% CI: 22.86, 37.79)
Exposure to index case during the day (see 2 x 2 above) Specificity = 81/113 = 71.68% (95% CI: 62.77, 79.17)	**Exposure to index case during the day (see 2 x 2 above)** Specificity = 81/110 = 73.64% (95% CI: 64.71, 80.97)
Exposure to index case during the day (see 2 x 2 above) PPV = 46/78 = 58.97% (95% CI: 47.89, 69.22)	**Exposure to index case during the day (see 2 x 2 above)** PPV = 42/71 = 59.15% (95% CI: 47.54, 69.83)
Exposure to index case during the day (see 2 x 2 above) NPV = 81/189 = 42.86% (95% CI: 36.01, 49.99)	**Exposure to index case during the day (see 2 x 2 above)** NPV = 45.00% (95% CI: 37.91, 52.30)
DOR (for T^+ calculated) = not calculated	DOR (for T^+ calculated) = not calculated
OR (crude; for T^+ reported) = <u>Adult index case type of TB diagnosis</u> Smear-positive TB: 1.00 (reference group) Smear-negative, culture-positive TB: 0.18 (95% CI: 0.05, 0.70) Clinical TB: 0.81 (95% CI: 0.45, 1.50) <u>Adult index case smear grade</u> Negative: 1.00 (reference group) Scanty: 0.3 (95% CI: 0.05, 1.60) 1+: 1.50 (95% CI: 0.70, 3.60) 2+: 1.50 (95% CI: 0.50, 4.90) 3+: 3.20 (95% CI: 1.40, 7.40)	OR (crude; for T^+ reported) = <u>Adult index case type of TB diagnosis</u> Smear-positive TB: 1.00 (reference group) Smear-negative, culture-positive TB: 0.17 (95% CI: 0.05, 0.60) Clinical TB: 0.46 (95% CI: 0.24, 0.89) <u>Adult index case smear grade</u> Negative: 1.00 (reference group) Scanty: NR 1+: 2.81 (95% CI: 1.20, 6.70) 2+: 2.90 (95% CI: 0.80, 10.60) 3+: 4.10 (95% CI: 1.50, 11.10)

Exposure to index case during the day Minority of day (< 6 h) – 1.00 reference group Majority of day (> 7 h): 1.1 (95% CI: 0.63, 1.80)	Exposure to index case during the day Minority of day (< 6 h) – 1.00 reference group Majority of day (> 7 h): 1.20 (95% CI: 0.67, 2.10)
OR (regression-based; reported) = Adult index case type of TB diagnosis Smear-positive TB: 1.00 (reference group) Smear-negative, culture-positive TB: 0.84 (95% CI: 0.09, 7.80) Clinical TB: 3.90 (95% CI: 0.67, 23.5) Adult index case smear grade Negative: 1.00 (reference group) Scanty: NR 1+: 5.50 (95% CI: 0.89, 34.70) 2+: 8.70 (95% CI: 1.20, 62.00) 3+: 11.40 (95% CI: 1.80, 72.00) Exposure to index case during the day Minority of day (< 6 h) – 1.00 reference group Majority of day (> 7 h): 1.30 (95% CI: 0.69, 2.30) List of covariates: NR	OR (regression-based; reported) = Adult index case type of TB diagnosis Smear-positive TB: 1.00 (reference group) Smear-negative, culture-positive TB: 2.70 (95% CI: 0.56, 13.0) Clinical TB: NR Adult index case smear grade Negative: 1.00 (reference group) Scanty: NR 1+: 7.90 (95% CI: 1.50, 41.00) 2+: 15.70 (95% CI: 2.60, 92.0) 3+: 11.70 (95% CI: 2.20, 62.00) Exposure to index case during the day Minority of day (< 6 h) – 1.00 reference group Majority of day (> 7 h): 1.10 (95% CI: 0.58, 2.10) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NR
Ratio of OR (crude; for T^+ reported) = 0.78 (95% CI: 0.40, 1.52) [Adult index case smear grade: 3+ vs. negative]
Ratio of ORs (regression-based; reported) = 0.97 (95% CI: 0.27, 3.47) [Adult index case smear grade: 3+ vs. negative]
Ratio of OR (crude; for T^+ reported) = 0.92 (0.62, 1.36) [Exposure to index case during the day (>7 h)]
Ratio of ORs (regression-based; reported) = 1.18 (0.75, 1.85) [Exposure to index case during the day (>7 h)]
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (specify)				**TST (specify)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	75	2	77	TST +	68	2	70
IGRA -	182	3	185	TST -	175	2	177
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	257	5	262	Total	243	4	247

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 0.61 (95% CI: 0.10, 3.77)	DOR (for T+ calculated)$_{TST}$ = 0.38 (95% CI: 0.05, 2.81)
OR (crude; for T^+ reported) = 0.62 (95% CI: 0.08, 4.76) reference group flipped (yes vs. no)	OR (crude; for T+ reported) = 0.38 (95% CI: 0.05, 2.85) reference group flipped (yes vs. no)
OR (regression-based; reported)$_{IGRA}$ = 0.83 (95% CI: 0.08, 8.33) reference group flipped (yes vs. no)	OR (regression-based; reported)$_{TST}$ = 0.52 (95% CI: 0.06, 4.00) reference group flipped (yes vs. no)

List of covariates: NR		List of covariates:	
Other reported measure = NR		Other reported measure = NR	
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST + (≥5mm)	TST -	Total
IGRA (QFT-GIT) +	56	19	75
IGRA -	12	149	161
Indeterminate	3	15	18
Total	71	183	254
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥5mm			
Parameters			
Kappa = 0.68 (95% CI: 0.56, 0.81) indeterminate excluded			
% concordance = 205/236 = 86.86% (95% CI: 81.96, 90.59) ; indeterminate excluded			
% discordance = 31/236 = 13.14% (95% CI: 9.41, 18.04) indeterminate excluded			
Stratification (≥10mm)):			
	TST +(≥10mm)	TST -	Total
IGRA +	48	27	75
IGRA -	7	154	161
Indeterminate	2	16	18
Total	57	197	254
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.64 (95% CI: 0.51, 0.76)			
% concordance = 202/236 = 85.59% (95% CI: 80.54, 89.5)			
% discordance = 34/236 = 14.41% (95% CI: 10.5, 19.46)			
Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Other outcomes			
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**		**Health related quality of life mean score (SD) (specify)**
IGRA:	NR		NR
TST:	NR		NR
Test 3 (specify):	NR		NR
Conclusions			
Authors:			
Prevalence of M. tuberculosis infection in paediatric contacts was high regardless of the diagnostic			

method used. TST should not be excluded for the detection of paediatric M. tuberculosis infection in this setting, but QFT-GIT may be a feasible alternative in children aged ⩾2 years
Reviewers:
Similar performance of TST and IGRA for exposure DORs; BCG did not affect TST or IGRA positivity differentially; TST threshold did not influence the agreement between the two tests
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Data extraction sheet for included primary study reports

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Laniado-Laborin 2014[148]
Country: Mexico
Study design: Cross-sectional/retrospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify): Tuberculosis (TB) clinic
Number of centres: one
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify): NR

Aim of the study

To compare the prevalence of LTBI between paediatric contacts of drug-resistant cases and drug susceptible cases

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: From August 2011 to June 2013
Total N of recruited patients: NR
Inclusion criteria: Family contacts of culture–proven cases age ≤16 years
Exclusion criteria: Subjects with a history of TB, a previous diagnosis of LTBI or the administration of TST in the past year
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 173
Total N of patients with valid results for both IGRA and TST: 172
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: concordance between TST and QFT-GIT test, association between exposure and test results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): drug susceptible (7.79 SD4.28); drug resistant (7.36 SD4.46)
Women (n [%]): 86/173 [50.0%]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 164 [95%]
History of anti-TB treatment (n [%]): None
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NA
Co-morbidity (n [%]): NA
Type of during-study treatment (n [%]): 77/173 [44.5%] contacts of multidrug susceptible index cases were treated for LTBI with INH or rifampicin (RMP). 96/173 [55.5%] contacts of multidrug resistant cases did not receive treatment for LTBI

Number of patients tested

	Total N (tested)	**Total N (test+)**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results available)**
IGRA (QFT-GIT):	173	71	101	1	172
TST (≥5mm):	173	136	36	1	172

Total N of patients with valid results for both IGRA and TST: 172

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – various definitions (see below)	
Non-exposed	NR
Exposed 1 **(specify):**	Exposure to source
Exposed 2 **(specify):**	Hours/day exposure
Exposed 3 (**specify):**	Cohabitants, n
Exposed 4 (**specify):**	Rooms, n

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QuantiFERON Gold In-Tube assay (QFT-GIT) (QIAGEN Inc., Valencia, CA, USA) Each participant had 73 ml of blood drawn which was performed according to the manufacturer's instructions	QFT-GIT result was considered positive if the interferon-gamma response to TB antigens minus the negative control was ≥0.35 IU/ml and also >25% of the negative control, negative if these criteria were not met and indeterminate if either the negative control had a result of >8 IU/ml or the positive control had a result of <0.5 IU/ml	
TST(≥5mm)	TST (5 tuberculin units purified protein derivative [PPD]; Tubersol, Sanofi Pasteur Lt, Toronto, ON, Canada) was performed using the Mantoux method. An intradermal injection of 0.1 ml PPD was administered to the volar surface of the forearm. The transverse diameter of induration was recorded in mm 48 h after administration	An induration of ≥5 mm was considered positive, as every subject was a close contact of a culture-proven case	

Association between test results and incidence of active TB (if applicable)

IGRA				**TST (>5mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA
NPV= NA	NPV= NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA-GIT				TST≥5mm			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = Exposure to source: 0.91 (95% CI 0.57, 1.45) Hours/day exposure: 1.03 (95% CI 0.96, 1.10) # of cohabitants: 0.91 (95% CI 0.79, 1.05) # of rooms: 1.12 (95% CI 0.77, 1.61) List of covariates: age, sex, history of BCG vaccination, intensity of exposure, exposure time of the contacts to a source case, exposure to a drug-susceptible case, and exposure to a drug-resistant case	OR (regression-based; reported) = Exposure to source: NR (p=NR; NS) Hours/day exposure: NR (p=NR; NS) # of cohabitants: NR (p=NR; NS) # of rooms: NR (p=NR; NS) List of covariates: age, sex, history of BCG vaccination, intensity of exposure, exposure time of the contacts to a source case, exposure to a drug-susceptible case, and exposure to a drug-resistant case
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				TST			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA

OR (regression-based; reported) $_{IGRA}$ = NA List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +≥5mm	TST -	Total
IGRA +	69	2	71
IGRA -	67	34	101
indeterminate	NR	NR	1
Total	136	36	172

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥ 5mm

Parameters

Kappa = 0.27 (95% CI: 0.17, 0.38)

% concordance = [69+34]/172 = 59.88% (95% CI: 52.42, 66.92)

% discordance = 69/172 = 40.12% (95% CI: 33.08, 47.58)

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA

TST + threshold: NA

Parameters

Kappa = NA

% concordance = NA

% discordance = NA

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA

TST + threshold: NA

Parameters

Kappa = NA

% concordance = NA

% discordance = NA

Conclusions

Authors:

The only variables predictive of a positive QFT-GIT were older age and TST positivity. Logistic regression analysis with TST as a dependent variable had similar results, with a positive QFT-GIT test as the only predictor of a positive TST (results not shown).

The main finding in our study is that overall prevalence of LTBI in paediatric contacts in our region is high, and not significantly different among contacts of drug-susceptible and those of drug resistant patients

Reviewers:
There was no associations between exposure to TB and GIT test results; likewise for TST (but no results reported); inconclusive results; between test agreement was poor
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Mahomed 2011b[108]
Country: South Africa
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** High schools
Number of centres: 11
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** The Aeras Global TB Vaccine Foundation and the Gates Grand Challenge 6 and Gates Grand Challenge 12 grants for QuantiFERON testing

Aim of the study

To determine the prevalence of and predictive factors associated with latent TB infection in adolescents

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children (adolescents in a high TB burden area)

Participants

Recruitment dates: NA
Total N of recruited patients: 6363 enrolled, 5244 enrolled for analysis
Inclusion criteria: All adolescents aged 12-18 years
Exclusion criteria: Diagnosed with active TB
Total N of excluded patients: 13 (an indeterminate QFT results), 639 (TST was not performed with past TB), 22 (TST was not performed with current TB, 22 (diagnosed with active TB)
Total N of patients tested with both IGRA and TST: 5244
Total N of patients with valid results for both IGRA and TST: 5244
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: TST and QFT results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 12-18 years
Women (n [%]): 2842 [54.2]
Race/ethnicity (n [%]): Indian/White (410 [7.8]); Mixed race (3839 [73.2]); Black (995 [19.0])
Geographic origin (n[%]): NR
BCG vaccination (n [%]): No (46 [0.9]); yes (4917 [93.8]); unknown (281 [5.4])
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): No
Clinical examination (yes/no): No
Morbidity (n [%]): NR
Co-morbidity (n [%]): Chronic allergy related condition e.g. asthma, hay fever, eczema yes (53 [1.0]); No (5191 [99.0])
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	Unclear	2669	2562	13	5244
TST (≥5mm):	Unclear	2894	2350	0	5244
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 5244

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NR

Exposed 1 **(specify):**	Current or prior TB household contact
Exposed 2 **(specify):**	BCG scar
Exposed 3 **(specify):**	BCG reported as being given
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA	QuantiFERON- TB Gold In-Tube (QFT-GIT, Cellestis, Carnegie, Victoria, Australia)	A result was considered positive if the QFT-GIT was ≥ 0.35 IU	NA
TST	Mantoux method on either forearm, using 2 tuberculin units of RT23 (Statens Serum Institut, Copenhagen, Denmark). Induration at the TST site was read 48-96 hours later with a ruler or a caliper, by trained personnel	A result was considered positive if induration ≥ 5mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (current or prior TB household contact)

IGRA (QFT-GIT)				**TST≥ 5mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	888	1781	2669	TST +	950	1944	2894
IGRA -	444	2118	2562	TST -	382	1968	2350
Indeterminate	0	13	13	Indeterminat	0	0	0

			(excluded)	e			
Total	1332	3912	5244	Total	1332	3912	5244

Test performance parameters	
IGRA	**TST**
Sensitivity = 888/1332 = 66.67%, 95% CI (64.09, 69.15)	Sensitivity = 950/1332 = 71.32%, 95% CI (68.83, 73.69)
Specificity = 2118/3899 = 54.32%, 95% CI (52.75, 55.88)	Specificity = 1968/3912 = 50.31%, 95% CI (48.74, 51.87)
PPV = 888/2669 = 33.27%, 95% CI (31.51, 35.08)	PPV = 950/2894 = 32.83%, 95% CI (31.14, 34.56)
NPV = 2118/2562 = 82.67%, 95% CI (81.16, 84.09)	NPV = 1968/2350 = 83.74%, 95% CI (82.2, 85.18)
DOR (for T^+ calculated) = 2.38, 95% CI (2.09, 2.71)	DOR (for T^+ calculated) = 2.52, 95% CI (2.20, 2.88)
OR (crude; for T^+ reported) = 2.40, 95% CI (2.11, 2.74)	OR (crude; for T^+ reported) = 2.52, 95% CI (2.20, 2.88)
OR (regression-based; reported) = 1.90, 95% CI (1.70, 2.20) List of covariates: NR	OR (regression-based; reported) = 2.00 (1.70, 2.30) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T+ calculated) = 0.94 (95% CI: 0.86, 1.04)
Ratio of OR (crude; for T+ reported) = 0.94 (95% CI: 0.86, 1.04)
Ratio of ORs (regression-based; reported) = 0.95 (95% CI: 0.86, 1.05)
Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (QFT-GIT)				**TST (≥ 5mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	2064	1490	3554	Total	2064	1490	3554

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = 0.99, 95% CI (0.86, 1.12)	OR (crude; for T+ reported) = 1.16, 95% CI (1.0, 1.33)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates:	OR (regression-based; reported) $_{TST}$ = NR List of covariates:
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample ≥ 5mm			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description
Sample definition (e.g., total, if stratified by BCG or condition – specify): total
TST + threshold: ≥ 5mm

Parameters

Kappa = 0.70, 95% CI: 0.68, 0.71			
% concordance = 84.8% (95% CI NR)			
% discordance = NR			
Total sample (≥ 10mm)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥ 10mm			
Parameters			
Kappa = 0.63, 95% CI: 0.61, 0.65			
% concordance = 81.4% (95% CI NR)			
% discordance = NR			
Total sample (≥ 15mm)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify):			
TST + threshold: ≥ 15mm			
Parameters			
Kappa = 0.30, 95% CI: 0.27, 0.32			
% concordance = 64.3% (95% CI NR)			
% discordance = NR			
Other outcomes			
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**		**Health related quality of life mean score (SD) (specify)**
IGRA:	NR		NR
TST:	NR		NR
Test 3 (specify):	NR		NR
Conclusions			
Authors:			
The predictive factor profile for both measures was similar			
Reviewers:			
TST was slightly influenced by BCG vaccination, but not IGRA; Both tests performed similarly in detection LTBI; 5mm threshold TST had better agreement than 10 and 15mm			
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation			

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Metin Timur 2014[150]
Country: Turkey
Study design: prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify): community based contact study
Number of centres: NR
Total length of follow up (if applicable): 3 years as outpatients with 3 months intervals
Funding (government/private/manufacturer/other - specify): NR

Aim of the study

To compare QuantiFeron-TB gold in tube test (QFT-GIT) and tuberculin skin test (TST) as a diagnosis of latent tuberculosis infection in the children with Bacille Calmette-Guerin (BCG) vaccine

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: between 2008 and 2011
Total N of recruited patients: NR
Inclusion criteria: children with positive TST results, children without a history of contact with a TB case, active TB case in the household was not detected through the family screening, children having no medical reason for immunosuppression, children who had diagnosed TB disease without a contact with active TB case
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 81
Total N of patients with valid results for both IGRA and TST: 81
Methods of active TB diagnosis (if applicable): LTBI as defined both TST and QFT-GIT test positive in a children who had no abnormality on the chest x-ray. Active TB disease was defined both TST and QFT-GIT test positive in a child who had symptoms of TB disease and/or abnormal findings on chest radiograph, CT or proven M. tuberculosis culture, PCR or histo- pathological examination.
Outcomes (study-based) list: diagnosis of prevalent TB, incidence of active TB
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 94.8 ±51.9 months (range: 6-193)
Women (n [%]): 33 [40.7%]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): one BCG scar (69 [85.2%]; two BCG scars (12 [14.8%]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): None
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NA
Co-morbidity (n [%]): acute appendicitis (1 [1.2%])
Type of during-study treatment (n [%]): no treatment (n=69 children with TST^+/QFT^- results); isoniazid (n=8 children with TST^+/QFT^+ results but no symptoms – assumed with LTBI); isoniazid, rifampicin and pyrazinamide (n=4 children with TST^+/QFT^+ results with symptoms –with TB)

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	81	12	69	0	81

TST (≥15mm):	81	81	0	0	81
Total N of patients with valid results for both IGRA and TST: 81					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group					
Non-exposed	NA				
Exposed 1 **(specify)**:	NA				
Exposed 2 **(specify)**:	NA				
Exposed 3 **(specify)**:	NA				
Exposed 4 **(specify)**:	NA				

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Peripheral blood samples were taken in the laboratory, where they were processed by trained physicians and performed according to manufacturer's instructions. For each child, total 3 mL whole blood was taken, then blood was collected in three special tubes: gray- (negative control, ''nil''), red- (test tube), and purple-cap (positive control; mitogen-coated) tubes. Test tube is specially designed for blood collection which is coated with M. tuberculosis-specific antigens (ESAT-6, CFP-10, and a portion of TB 7.7). Once blood was collected it is essential to provide adequate shaking for antigens to dissolve. They were incubated at 37°C for 16 to 24 hours and centrifugation at 3000 g for 15 minutes, then plasma was separated. The amount of IFN-γ was measured by using the QFT ELISA	A positive result was defined if the difference in the IFN-γ levels between the test tube and negative control is greater than or equal to 0.35 IU/mL and is greater than 25% of the nil value. Also for determinate results, nil control must be < 8.0 IU/mL	
TST(≥15mm)	All children underwent a TST with 5 TU of purified protein derivative, according to intradermal Mantoux method	When interpreting a TST result, the widest diameter of induration, not erythema, was measured in millimetres after 72 hours by trained physician or nurses. TST was considered as positive if an induration was ≥ 15mm, regardless of BCG vaccination scar numbers	

Association between test results and incidence of active TB (if applicable)							
IGRA-GIT				**TST (≥15mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	0	0	0	TST +	0	69	69
IGRA -	0	69	69	TST -	0	0	0
indeterminate	0	0	0	indeterminate	0	0	0
Total	0	69	69	Total	0	69	69

Test performance parameters	
IGRA-GIT	**TST≥15mm**
Sensitivity = NA	Sensitivity = NA
Specificity = 69/69 = 100% (95% CI: NR)	Specificity = 0/69 = 0.0% (95% CI: NR)
PPV= NA	PPV = 0/69=0.0% (95% CI: NR)
NPV= 69/69 = 100% (95% CI: NR)	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = 0/69 = 0.0% (95% CI: NR)
Cumulative Incidence $_{IGRA-}$ = 0/69 = 0.0% (95% CI: NR)	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios= NA
Other reported measure= NA

Association between test results and levels of TB exposure (if applicable)							
IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA
NPV= NA	NPV= NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				TST			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$= NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA
OR (regression-based; reported) $_{IGRA}$= NA List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			

% concordance = NA
% discordance = NA
Conclusions
Authors:
Study suggests that confirmation of positive TST results with QFT- GIT test may enhance the accuracy of diagnosing both active TB and LTBI, particularly among BCG vaccinated children. The correct diagnosis of LTBI prevents unnecessary treatment and treatment complications
Reviewers:
None of the 69 children with TST positive results and QFT-GIT negative results developed active TB, indicating better specificity of QFT-GIT vs. TST (100% vs. 0%)
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Pavic 2011[109]
Country: Croatia
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Children hospital and general hospital
Number of centres: 2
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** None

Aim of the study

To evaluate an IGRA for diagnosis of LTBI in BCG –vaccinated children up to 5 years of age, with documented exposure to active TB

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Younger children with history of exposure to active TB

Participants

Recruitment dates: Between January 2008 and December 2009
Total N of recruited patients: 142
Inclusion criteria: Pediatric patients' ≤5 years of age and a documented exposure (close or distant contact) to a case of active TB. Close contact (household contact with aggregate exposure to a patient with active TB of not < 40 hours in closed room and distant contact (occasional or unclear exposure time of <40 hours during the presumed period of infectiousness)
Exclusion criteria: Children >5 years, immunocompromised children, inadequate blood sampling and diagnosis of active TB
Total N of excluded patients: 1 (diagnosed with pneumonia**:** data were not included in further statistical analysis)
Total N of patients tested with both IGRA and TST: 142
Total N of patients with valid results for both IGRA and TST: 141
Methods of active TB diagnosis (if applicable): Induration of ≥10mm
Outcomes (study-based) list: Test results, impact of age and on results of IGRA and level of agreement between IGRA and TST results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 29 ± 16 months
Women (n [%]): 57 [40.1]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 142 [100]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): NR
Co-morbidity (n [%]): Pneumonia 1 [0.7]
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	142	18	123	1	141
TST (≥10mm):	142	24	118	0	142
Test 3 (specify)	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 142

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	Distant contact was defined as occasional or unclear exposure time or < 40 hours during the presumed period of infectiousness.
Exposed 1 **(specify):**	Close contact was defined as household contact with aggregate exposure to a patient with active TB ≥40 hours in closed rooms
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-GIT (Cellestis Limited, Chadstone, Australia)	≥ 0.35 IU/mL as recommended by the manufacturer.	Blood samples for QFT-GIT were drawn under standardized condition in our hospital at the same day as TST. The test was considered indeterminate if the value of the positive-control well was less than 0.5 IU/mL, and/or nil negative control was more than 8 IU/L
TST≥ 10 mm	Two tuberculin units of standardized purified protein derivative solution (Tuberculin PPD RT 23, Statens Serum Institute, Copenhagen, Denmark) injected into the volar aspect of the forearm and transverse induration and was measured by a trained healthcare worker 68 to 72 hours later	Induration ≥ 10 mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (close contact)

IGRA (QFT-GIT)				TST≥ 10 mm			
	Exposure level		Total		Exposure level		Total
	Close	Distant			Close	Distant	
IGRA +	17	1	18	TST +	23	1	24
IGRA -	70	53	123	TST -	64	54	118
Indeterminate	0	1	1 (excluded)	Indeterminate	0	0	0
Total	87	54	141	Total	87	55	142

Test performance parameters

IGRA	TST
Sensitivity = 17/87 = 19.54%, 95% (12.57, 29.08)	Sensitivity = 23/87 = 26.44%, 95% (18.31, 36.56)
Specificity = 53/54 = 98.15%, 95% (90.23, 99.67)	Specificity = 54/55 = 98.18%, 95% (90.39, 99.68)
PPV = 17/18 = 94.44%, 95% (74.24, 99.01)	PPV = 23/24 = 95.83%, 95% CI (79.76, 99.26)
NPV = 53/123 = 43.09%, 95% (34.68, 51.92)	NPV = 54/118 = 45.76%, 95% CI (37.05, 54.74)
DOR (for T^+ calculated) = 12.87, 95% CI (1.66, 99.80)	DOR (for T^+ calculated) = 19.41, 95% CI (2.53, 148.40)
OR (crude; for T^+ reported) = 1.66, 95% CI (0.92, 3.35) error	OR (crude; for T^+ reported) = 1.75, 95% CI (0.92, 3.35) error
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 0.66 (95% CI: 0.15, 2.89)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (QFT)				TST (>10 mm)			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA (TSPOT/QFT)	TST (>5 mm)
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = NR	DOR $_{TST}$ (for T+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = NR OR (regression-based; reported)$_{TSPOT}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)

This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition			
Total sample			
	TST +	TST -	Total
IGRA +	14	4	18
IGRA -	11	112	123
Indeterminate	0	1	1 (excluded)
Total	25	116	141
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Total			
TST + threshold: ≥10 mm in duration			
Parameters			
Kappa = 0.59, 95% CI (0.42, 0.75)			
% concordance = 126/141 = 89.36%, 95% CI (83.19, 93.45)			
% discordance = 15/141 = 10.64%, 95% CI (6.554, 16.81)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Authors concluded that in a high-risk population of children ≤ 5 years, both the TST and IGRA should be performed and a positive result on either test a suggestive of LTBI
Reviewers:
Tests performed similarly well in identifying LTBI by association with the active TB exposure

Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Perez-Porcuna 2014[151]
Country: Brazil
Study design: Cross-sectional/retrospective
Study setting (e.g., outbreak investigation, community-based - specify): community-based
Number of centres: 2
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify): the Brazilian National Counsel of Technological and Scientific Development (CNPq), the Foundation of Research Support of the State of Amazonas (FAPEAM), and the University of Barcelona. Cellestis Ltd. donated QuantiFERON test kits. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

Aim of the study

To evaluate the response of the IGRA QuantiFERON-TB Gold In-Tube (QFT) and TST tests in young children with recent exposure to an index case

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: from March 2009 to February 2010
Total N of recruited patients: 140
Inclusion criteria: children from 0–6 years of age with recent contact with an adult symptomatic TB index case within the last 12 months
Exclusion criteria: Subjects receiving treatment or prophylaxis for TB
Total N of excluded patients: 3
Total N of patients tested with both IGRA and TST: 135
Total N of patients with valid results for both IGRA and TST: 116
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: between-test agreement, discordance, concordance, associations between different factors and test results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 46 (28.0; 64.5) months
Women (n [%]): 74 (54.8%)
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 118 (90.8%)
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NA
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	135	36	80	19	116
TST: ≥ 10mm	135	47	88	0	135

Total N of patients with valid results for both IGRA and TST: 116

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – Time of exposure to the index case

Non-exposed	NA		
Exposed **(specify)**:	# months measured as continuous covariate		
Definition of exposure group – mycobacterium tuberculosis contact (MTC) score: 0-15			
Non-exposed	NA		
Exposed **(specify)**:	MTC score measured as continuous covariate. The score is composed of infectivity of the index case (0–4), the duration of exposure hours per day (0–4), the relationship to the index case (0–4) and the type of exposure (0–3)		
Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA [QFT-GIT]	The QFT (Cellestis, Carnegie, Australia) was carried out and interpreted according to the manufacturer's instructions was considered indeterminate if there was excessive IFN-c production with the negative control tube $8.0 IU/mL	The result was positive (QFT+) if the net value of IFN-c to the TB antigens (after subtracting the negative control) was ≥0.35 U/mL and ≥25% of the value of the negative control, independently of the response of the mitogen. The result was negative if the net value of the IFN-c was <0.35 IU/mL and mitogen response was sufficient (≥0.50 IU/mL). The result was indeterminate if there was excessive IFN-c production with the negative control tube ≥8.0 IU/mL (indeterminate hypereactive) or with insufficient net mitogen response <0.50 IU/mL plus insufficient net response of the TB antigen < 0.35 IU/mL (indeterminate hyporeactive) When the QFT result was indeterminate the test was repeated to confirm the result	Experienced laboratory technicians who were unaware of the data of the study subjects
TST≥ 10mm	The TST was performed with an intradermic injection of 2 tuberculin units (TU) of PPD RT23 (Statens Serum Institut,	≥ 10mm positivity threshold according to the protocols of the WHO	Experienced laboratory technicians who were unaware of the data of the study subjects

	Copenhagen, Denmark) and read 72 hours thereafter	≥ 5-9 mm weak reaction ≥ 10mm strong reaction	

Association between test results and incidence of active TB (if applicable)							
IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)							
IGRA (QFT-GIT)				**TST (≥10mm)**			
	Exposure level (# of months of exposure to the index case)		Total		Exposure level (# of months of exposure to the index case)		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated)= NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported)= NR (p=0.024) OR is associated with one unit increase in # of exposure months	OR (crude; for T^+ reported) = NR (p<0.001) OR is associated with one unit increase in # of exposure months
OR (regression-based; reported) = NR (p = 0.537); OR is associated with one unit increase in # of exposure months List of covariates: NR	OR (regression-based; reported) = 1.15 (95% CI 1.04, 1.27; p = 0.009) OR is associated with one unit increase in # of exposure months

	List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				TST (≥10mm)			
	Exposure level (MTC score)		Total		Exposure level (MTC score)		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA
NPV= NA	NPV= NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NR (p = 0.021) OR is associated with one unit increase in MTC score	OR (crude; for T^+ reported) = NR (p<0.001) OR is associated with one unit increase in # MTC score
OR (regression-based; reported) = 1.16 (95% CI 1.01, 1.33; p = 0.035); OR is associated with one unit increase in MTC score List of covariates: NR	OR (regression-based; reported) = 1.29 (95% CI 1.08, 1.54; p = 0.005) OR is associated with one unit increase in MTC score List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = 0.90 (95% CI: 0.80, 1.01)
Other reported measure= NA

Association between test results and BCG status (if applicable)

IGRA (GIT)				TST (10mm)			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	35	1	36	TST +	37	2	39
IGRA -	72	8	80	TST -	70	7	77
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	107	9	116	Total	107	9	116

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{IGRA}$ = 3.89 (95% CI: 0.46, 32.33)	DOR (for T+ calculated)$_{TST}$ = 1.85 (95% CI: 0.36, 9.36)
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{IGRA}$ = NR List of covariates:	OR (regression-based; reported)$_{TST}$ = NR List of covariates:
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition			
Total sample			
	TST + (≥10mm)	TST -	Total
IGRA +	21	15	36
IGRA -	18	62	80
indeterminate	8	11	19
Total	47	88	135
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.35 (95% CI: 0.16, 0.53) p<0.001			
% concordance = [21+62]/116=71.55 (95% CI: 62.75, 78.97)			
% discordance = [18+15]/116 = 28.44 (95% CI: 21.03, 37.25)			
Stratification (specify group 1):			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Conclusions			
Authors:			
We observed that the results of both tests were related to the intensity of exposure, although, as previously reported, the TST was more strongly influenced by exposure than QFT. Another factor we observed was that TST+ results were related to a greater time of exposure while the same was not observed for QFT. Likewise, we did not observe any association between the TST results and the presence of a BCG scar. Analysis of our data supports the contention that QFT probably undergoes more rapid conversion (step from negative to positive) after primary infection than the TST and would explain most of the discordant test results in this group			
Reviewers:			
Both the TST and QFT were associated with the intensity of exposure (MTC score) with only the TST being significantly associated with the time of exposure (regression-based analyses). Concordance			

between the TST and QFT (excluding the indeterminate cases) was fair (Kappa = 0.35); presence of BCG scar did not significantly influence the odds of TST or IGRA
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Rutherford 2012a[110] and Rutherford 2012b[111] (same study but plus neighborhood contacts; agreement analysis)
Country: Indonesia
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Out-patient-based clinic
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** NR

Aim of the study

aimed to quantify M. tuberculosis infection in children living with a smear-positive adult TB case and identify risk factors for TST and QFT-GIT positivity

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: NR
Total N of recruited patients: 320
Inclusion criteria: Child contacts living for more than 3 months with newly diagnosed TB cases (index case) who were smear and chest X-ray (CXR) positive
Exclusion criteria: Child contacts who had received a diagnosis of TB disease within the past year or who were aged <6 months were excluded (the latter due to known poor parental acceptability of blood collection)
Total N of excluded patients: 16 (active TB)
Total N of patients tested with both IGRA and TST: 304
Total N of patients with valid results for both IGRA and TST: 288
Methods of active TB diagnosis (if applicable): Active TB was defined by CXR findings consistent with TB according to the consultants
Outcomes (study-based) list: Association of test positivity with exposure factors (Rutherford 2012a), agreement (Rutherford 2012b)
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median [IQR] 58 [31–81] months
Women (n [%]): 152 [50.7]
Race/ethnicity (n [%]): Sundanese (284 [93.7]), Other (19 [6.3])
Geographic origin (n[%]): NR
BCG vaccination (n [%]): With scar (221 [73.2]), unknown BCG status (30 [9.9])
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes (Children who were symptomatic and test-negative (on either IGRA or TST) were referred to the children's clinic for further assessment according
to clinic policy
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	304	152	138	14	290
TST (≥10mm):	304	145	157	2	302
Test 3 (specify):	NA	NA	NA	NA	NA
Total N of patients with valid results for both IGRA and TST: 288					

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group – Characteristics of TB case smear positivity	
Non-exposed	Scanty and 1+
Exposed 1 **(specify):**	2+
Exposed 2 **(specify):**	3+
Definition of exposure group – Relationship to child	
Non-exposed	Other
Exposed 1 **(specify):**	Aunt/uncle
Exposed 2 **(specify):**	Parent
Definition of exposure group – Sleeping proximity to child	
Non-exposed	Different room
Exposed 1 **(specify):**	Same room
Exposed 2 **(specify):**	Same bed
Definition of exposure group – Time spent with child (# hrs/day)	
Non-exposed	< 2
Exposed 1 **(specify):**	2 - 8
Exposed 2 **(specify):**	> 8

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	For QFT-GIT, 3 ml of venous blood was collected into a syringe; 1 ml was immediately transferred to each of the QFT-GIT tubes (nil, mitogen and antigen). The tubes were vigorously hand-shaken and placed in an incubator within 3 h. Incubated samples were centrifuged and stored at 4°C for up to 1 month. The QFT-GIT assay was conducted and interpreted according to the manufacturer's instructions using specific software	NR	NA
TST (≥10mm)	TST was performed by the study nurse following blood collection using two tuberculin units of purified protein derivative (PPD; RT23 Biofarma®, Bandung, Indonesia). Induration was measured 48–72 h after administration and confirmed by the study doctor	An induration of ⩾10 mm was considered positive	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA

Ratio of incidence density rate ratios = NA

Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)					**TST (≥10mm)**				
	Exposure level characteristics of TB case Smear positivity			Total		Exposure level characteristics of TB case Smear positivity			Total
	3+	2+	Scanty/1+			3+	2+	Scanty/1+	
IGRA +	75	36	40	152	TST +	78	34	33	145
IGRA -	45	34	59	138	TST -	48	38	71	157
Indeterminate	NR	NR	NR	14 (excluded)	Indeterminate	NR	NR	NR	2 (excluded)
Total	120	70	99	290	Total	126	72	104	302

Test performance parameters

IGRA	**TST**
Trend in ORs across the gradient of exposure (p = 0.001) Scanty/1+: OR (crude; reported) = 1.00 (reference group) 2+: OR (crude; reported) = 1.56 (95% CI: 0.78, 3.11) 3+: OR (crude; reported) = 2.43 (95% CI: 1.21, 4.86) **3+ vs. scanty/1+** Sensitivity = 75/120 = 62.5% (95% CI: 53.58, 70.65) Specificity = 59/99 = 59.6% (95% CI: 49.75, 68.73) PPV = 75/115 = 65.22% (95% CI: 56.15, 73.3) NPV = 59/104 = 56.73% (95% CI: 47.14, 65.85) DOR (for T^+ calculated) = 2.46 (95% CI: 1.42, 4.24) OR (crude; for T^+ reported) = 2.43 (95% CI: 1.21, 4.86) OR (regression-based; reported) = 2.28 (95% CI: 1.06, 4.90) List of covariates: TB case's relationship to child, marital status of household head Other reported measure = NR	Trend in ORs across the gradient of exposure (p = 0.000) Scanty/1+: OR (crude; reported) = 1.00 (reference group) 2+: OR (crude; reported) = 1.80 (95% CI: 0.89, 3.63) 3+: OR (crude; reported) = 3.35 (95% CI: 1.81, 6.21) **3+ vs. scanty/1+** Sensitivity = 78/126 = 61.9% (95% CI: 53.19, 69.91) Specificity = 71/104 = 68.27% (95% CI: 58.81, 76.43) PPV = 78/111 = 70.27% (95% CI: 61.21, 77.98) NPV = 71/119 = 59.66% (95% CI: 50.68, 68.04) DOR (for T^+ calculated) = 3.50 (95% CI: 2.02, 6.04) OR (crude; for T^+ reported) = 3.35 (95% CI: 1.81, 6.21) OR (regression-based; reported) = 2.93 (95% CI: 1.59, 5.39) List of covariates: TB case's relationship to child Other reported measure = NR

Comparison between tests (IGRA vs. TST)

3+ vs. scanty/1+
Ratio of DORs (for T^+ calculated) = 0.70 (95% CI: 0.47, 1.04)

3+ vs. scanty/1+
Ratio of OR (crude; for T^+ reported) = 0.73 (95% CI: 0.45, 1.17)

3+ vs. scanty/1+
Ratio of ORs (regression-based; reported) = 0.78(95% CI: 0.47, 1.28)

Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)			**TST (≥10mm)**		
	Exposure level	Total		Exposure level	Total

	relationship to child					relationship to child			
	parent	Aunt or uncle	Other			parent	Aunt or uncle	Other	
IGRA +	134	8	10	152	TST +	128	9	8	145
IGRA -	85	19	34	138	TST -	101	19	37	157
Indeterminate	NR	NR	NR	14 (excluded)	Indeterminate	NR	NR	NR	2 (excluded)
Total	219	27	44	290	Total	229	28	45	302

Test performance parameters

IGRA	**TST**
Trend in ORs across the gradient of exposure (p = 0.000) Other: OR (crude; reported) = 1.00 (reference group) Aunt/uncle: OR (crude; reported) = 1.51 (95% CI: 0.44, 5.17) Parent: OR (crude; reported) = 5.61 (95% CI: 2.40, 13.12) **Parent vs. Other** Sensitivity = 134/219 = 61.19% (95% CI: 54.59, 67.4) Specificity = 34/44 = 77.27% (95% CI: 63.01, 87.16) PPV = 134/144 = 93.06% (95% CI: 87.69, 96.18) NPV = 34/119 = 28.57% (95% CI: 21.22, 37.26) DOR (for T^+ calculated) = 5.36 (95% CI: 2.52, 11.41) OR (crude; for T^+ reported) = 5.61 (95% CI: 2.40, 13.12) OR (regression-based; reported) = 4.30 (95% CI: 1.48, 12.45) List of covariates: marital status of household head, smear positivity of household head Other reported measure = NR	Trend in ORs across the gradient of exposure (p = 0.000) Other: OR (crude; reported) = 1.00 (reference group) Aunt/uncle: OR (crude; reported) = 2.31 (95% CI: 0.77, 6.79) Parent: OR (crude; reported) = 5.85 (95% CI: 2.56, 13.38) **Parent vs. Other** Sensitivity = 128/229 = 55.9% (95% CI: 49.42, 62.18) Specificity = 37/45 = 82.22% (95% CI: 68.67, 90.71) PPV = 128/136 = 94.12% (95% CI: 88.82, 96.99) NPV = 37/138 = 26.81% (95% CI: 20.12, 34.76) DOR (for T^+ calculated) = 5.86 (95% CI: 2.61, 13.14) OR (crude; for T^+ reported) = 5.85 (95% CI: 2.56, 13.38) OR (regression-based; reported) = 7.04 (95% CI: 2.23, 22.28) List of covariates: marital status and smear positivity of household head Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Parent vs. Other
Ratio of DORs (for T^+ calculated) = 0.91 (95% CI: 0.52, 1.61)

Parent vs. Other
Ratio of OR (crude; for T^+ reported) = 0.96 (95% CI: 0.52, 1.75)

Parent vs. Other
Ratio of ORs (regression-based; reported) = 0.61 (95% CI: 0.27, 1.36)

Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)					**TST (≥10mm)**				
	Exposure level Sleeping proximity to child			Total		Exposure level Sleeping proximity to child			Total
	Same bed	Same room	Different room			Same bed	Same room	Different room	
IGRA +	93	15	43	152	TST +	85	13	47	145
IGRA -	64	12	62	138	TST -	80	15	62	157

Indeterminate	NR	NR	NR	14 (excluded)	Indeterminate	NR	NR	NR	2 (excluded)
Total	157	27	105	290	Total	165	28	109	302

Test performance parameters

IGRA	**TST**
Trend in ORs across the gradient of exposure (p = 0.006) Different room: OR (crude; reported) = 1.00 (reference group) Same room: OR (crude; reported) = 1.87 (95% CI: 0.70, 5.02) Same bed: OR (crude; reported) = 2.01 (95% CI: 1.12, 3.61) **Same bed vs. different room** Sensitivity = 93/157 = 59.24% (95% CI: 51.42, 66.61) Specificity = 62/105 = 59.05% (95% CI: 49.48, 67.97) PPV = 93/136 = 68.38% (95% CI: 60.15, 75.6) NPV = 62/126 = 49.21% (95% CI: 40.63, 57.83) DOR (for T^+ calculated) = 2.09 (95% CI: 1.26 , 3.46) OR (crude; for T^+ reported) = 2.01 (95% CI: 1.12, 3.61) OR (regression-based; reported) = 1.45 (95% CI: 0.70, 2.99) List of covariates: case's relationship to child, age of child, smear positivity Other reported measure = NR	Trend in ORs across the gradient of exposure (p = 0.186) Different room: OR (crude; reported) = 1.00 (reference group) Same room: OR (crude; reported) = 1.21 (95% CI: 0.41, 3.53) Same bed: OR (crude; reported) = 1.35 (95% CI: 0.79, 2.32) **Same bed vs. different room** Sensitivity = 85/165 = 51.52% (95% CI: 43.94, 59.02) Specificity = 62/109 = 56.88% (95% CI: 47.51, 65.79) PPV = 85/132 = 64.39% (95% CI: 55.92, 72.05) NPV = 62/142 = 43.66% (95% CI: 35.78, 51.88) DOR (for T^+ calculated) = 1.40 (95% CI: 0.86, 2.28) OR (crude; for T^+ reported) = 1.35 (95% CI: 0.79, 2.32) OR (regression-based; reported) = NR List of covariates: NA Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Same bed vs. different room Ratio of DORs (for T^+ calculated) = 1.49 (95% CI: 1.04, 2.14)
Same bed vs. different room Ratio of OR (crude; for T^+ reported) = 1.47 (95% CI: 1.05, 2.16)
Same bed vs. different room Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)					**TST (≥10mm)**				
	Exposure level Time spent with child h/day			Total		Exposure level Time spent with child h/day			Total
	>8	2-8	<2			>8	2-8	<2	
IGRA +	78	46	27	152	TST +	75	42	28	145
IGRA -	72	46	20	138	TST -	83	54	20	157
Indeterminate	NR	NR	NR	14 (excluded)	Indeterminate	NR	NR	NR	2 (excluded)
Total	150	92	47	290	Total	158	96	48	302

Test performance parameters

IGRA	**TST**
Trend in ORs across the gradient of exposure (p = 0.948) <2 h: OR (crude; reported) = 1.00 (reference group) 2-8 h: OR (crude; reported) = 0.78 (95% CI: 0.33, 1.80) >8 h: OR (crude; reported) = 0.83 (95% CI: 0.38, 1.79)	Trend in ORs across the gradient of exposure (p = 0.494) <2 h: OR (crude; reported) = 1.00 (reference group) 2-8 h: OR (crude; reported) = 0.55 (95% CI: 0.24, 1.24)

>8 vs. <2 Sensitivity = 78/150 = 52.00% (95% CI: 44.06, 59.85) Specificity = 20/47 = 42.55% (95% CI: 29.51, 56.72) PPV = 78/105 = 74.29% (95% CI: 65.17, 81.68) NPV = 20/92 = 21.74% (95% CI: 14.54, 31.21) DOR (for T^+ calculated) = 0.80 (95% CI: 0.41, 1.55) OR (crude; for T^+ reported) = 0.83 (95% CI: 0.38, 1.79) OR (regression-based; reported) = NR List of covariates: NA Other reported measure = NR	>8 h: OR (crude; reported) = 0.64 (95% CI: 0.31, 1.36) **>8 vs. <2** Sensitivity = 75/158 = 47.47% (95% CI: 39.83, 55.22) Specificity = 20/48 = 41.67% (95% CI: 28.85, 55.72) PPV = 75/103 = 72.82% (95% CI: 63.52, 80.47) NPV = 20/103 = 19.42% (95% CI: 12.94, 28.1) DOR (for T^+ calculated) = 0.64 (95% CI: 0.33, 1.24) OR (crude; for T^+ reported) = 0.64 (95% CI: 0.31, 1.36) OR (regression-based; reported) = NR List of covariates: NA Other reported measure = NR

Comparison between tests (IGRA vs. TST)

>8 vs. <2
Ratio of DORs (for T^+ calculated) = 1.25 (95% CI: 0.77, 2.02)

>8 vs. <2
Ratio of OR (crude; for T^+ reported) = 1.30 (95% CI: 0.75, 2.24)

>8 vs. <2
Ratio of ORs (regression-based; reported) = NA

Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	104	34	138	TST +	105	29	134
IGRA -	105	17	122	TST -	116	22	138
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	209	51	260	Total	221	51	272

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 0.49 (95% CI: 0.26, 0.94)	DOR (for T+ calculated)$_{TST}$ = 0.68 (95% CI: 0.37, 1.27)
OR (crude; for T^+ reported) = 0.51 (95% CI: 0.26, 1.00)	OR (crude; for T+ reported) = 0.68 (95% CI: 0.35, 1.35)
OR (regression-based; reported)$_{IGRA}$ = 0.60 (95% CI: 0.26, 1.38) List of covariates: TB case's relationship to child, marital status of household head	OR (regression-based; reported)$_{TST}$ = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

From Rutherford 2012b	TST +	TST -	Total
IGRA +	121	35	156
IGRA -	22	114	136
Indeterminate	1 (excluded)	6 (excluded)	7 (excluded)
Total	143	149	292

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total (household contacts of TB cases)

TST + threshold: ≥10mm

Parameters

Kappa = 0.61 (95% CI: 0.49, 0.72)			
% concordance = 235/292 = 80.48% (95% CI: 75.55, 84.62)			
% discordance = 57/292 = 19.52% (95% CI: 15.38, 24.45)			
Stratification (specify group 1):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 1):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 1):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			

% concordance = NR		
% discordance = NR		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
In this setting, M. tuberculosis infection by either test was high in children living with a smear-positive TB case. Test positivity was driven by high index case infectivity levels and intimacy of exposure (if the index case was the child contact's parent). Child contacts whose parent was the index case were over four times as likely to be positive by both or either tests. High increased risk of M. tuberculosis infection when the index case is the parent, particularly the mother, has been reported elsewhere. Both the TST and QFT-GIT responded as expected to most hypothesised risk factors, and neither test performed significantly better than the other along any of the gradients		
Reviewers:		
IGRA and TST performed well showing similar strong associations with a) characteristics of TB case smear positivity and b) relationship to child. IGRA did better than TST for sleeping proximity. Neither test showed association with time spent with child. None of the tests was influenced by BCG status		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Talbot 2012[112]
Country: US
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** College health setting
Number of centres: 1
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Oxford Immunotec

Aim of the study

To test the specificity of the tuberculin skin test and the T-SPOT.TB assay among students at low risk for TB exposure

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children (student at low risk for TB exposure)

Participants

Recruitment dates: NA
Total N of recruited patients: 184
Inclusion criteria: Students with history of exposure to TB
Exclusion criteria: NR
Total N of excluded patients: 4 (procedural errors at the laboratory)
Total N of patients tested with both IGRA and TST: 180
Total N of patients with valid results for both IGRA and TST: 143
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Test results, specificity test
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median age 20 [17-47]
Women (n [%]): 97 [53.9]
Race/ethnicity (n [%]): US-born (165 [91.7]); White (135 [75])
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 7 [3.9]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): NR
Clinical examination (yes/no): NR
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	**Total N (test+)**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results available)**
IGRA (T-SPOT.TB):	180	5	138	15	143
TST (> 15mm):	180	6	137	22	143
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 143

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	Low-TB exposure risk group
Exposed 1 **(specify):**	Non-low-TB exposure risk (any history of exposure to TB through country of birth, residence, or visits>3 weeks to high–TB burden areas [>40 cases/100,000

	population], or occupational exposure)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA (T-SPOT.TB)	Blood was tested for LTBI by using T-SPOT.TB according to the manufacturer's instructions for use. Peripheral blood mononuclear cells (PBMCs) were harvested by Ficoll density gradient centrifugation, washed, counted, and plated at 2.5 × 105 cells per well into a membrane-bottomed plate coated with anti-interferon-γ antibody. PBMCs from each study participant were incubated overnight in the presence of the provided TB antigens ESAT-6 and CFP-10, along with controls (positive mitogen control and a nil control). The PBMCs producing interferon-γ were revealed as spots by incubation with an enzyme-conjugated secondary antibody for interferon-γ and a color-producing enzyme substrate. Spots were counted, and clinical results recorded according to the approved algorithm in the package insert where, compared to the nil control, 8 spots and above is positive and 4 spots and below is negative	Results with spot counts of 5–7 are regarded as borderline, and results with a low mitogen response or a high nil control response are indeterminate	NA
TST> 15mm	TSTs were administered by trained professionals who used the Mantoux method intradermally according to published guidelines	A TST was considered positive if there was an induration > 15mm for students with no risk factors for TB exposure	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (TB exposure risk group)

IGRA (T-SPOT.TB)				TST≥15mm			
	Exposure level		Total		Exposure level		Total
	Non-low	Low			Non-low	Low	
IGRA (T-SPOT.TB) +	NR	0	NR	TST +	NR	2	NR
IGRA (T-SPOT.TB) -	NR	124	NR	TST -	NR	122	NR
Indeterminate	NR	NR	0	Indeterminate	NR	NR	0
Total	NR	124	NR	Total	NR	124	NR

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = 124/124 = 100.00% (95% CI: 97, 100.00)	Specificity = 122/124 = 98.39% (95% CI: 94.31, 99.56)
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				TST (>15 mm)			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = NR	DOR $_{TST}$ (for T+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = NR OR (regression-based; reported)$_{TSPOT}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample			
	TST +	TST -	Total
IGRA +	4	1	5
IGRA -	2	136	138
Indeterminate	0	0	0
Total	6	137	143
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Total			
TST + threshold: >15mm induration			
Parameters			
Kappa = 0.71, 95% CI (0.55, 0.88)			
% concordance = 140/143 = 97.9%, 95% CI (94.01, 99.28)			
% discordance = 3/143 = 2.01%, 95% CI (0.72, 5.99)			
Other outcomes			
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**		**Health related quality of life mean score (SD) (specify)**
IGRA:	NR		NR
TST:	NR		NR
Test 3 (specify):	NR		NR
Conclusions			
Authors:			
The authors concluded that T-SPOT.TB specificity in a low-TB incidence, largely immunocompetent, non-BCG-vaccinated population, is high. Further research is required to inform on the policy decisions for LTBI screening			
Reviewers:			
TBSPOT specificity was slightly higher than that of TST			
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation			

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Tieu 2014[154]
Country: Thailand
Study design: cross-sectional/retrospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify): community-based
Number of centres: 3
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify): This study was funded by a competitive, investigator-initiated research grant from Tibotec REACH Initiative. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

Aim of the study

To compare the performances of the IGRAs (T-Spot.TB, QuantiFERON-TB Gold In-tube) and TST at two different cut-off thresholds (10 mm and 15 mm) in Thai children who had recent exposure to an adult index case with TB

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: Between September 2009 and December 2011
Total N of recruited patients: 137 [TB exposed]
Inclusion criteria: Children between the ages of 2 months and 16 years with recent exposure (defined as having lived with and/or having had close contact with) to adults with active pulmonary TB (confirmed by
positive AFB stain, PCR for TB, or TB culture), with or without extra-pulmonary TB manifestations
Exclusion criteria: Children's caregivers refused study participation, if they were receiving anti-TB medications for TB disease (including isoniazid [INH] for latent TB), or if they had recently been diagnosed with active TB
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 137
Total N of patients with valid results for both IGRA and TST: 136
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: between test agreement, association between prior exposure and test results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 7.6 (4.3)
Women (n [%]): 67 (49.3)
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 132 (96.4)
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): None [for TB exposed]

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	136	40	96	0	136
TST:≥10mm	136	88	48	0	136

TST:≥15mm	136	48	88	0	136
TSPOT	136	36	100	0	136

Total N of patients with valid results for both IGRA and TST: 136

Levels/groups of exposure to TB in increasing order (if applicable):

1. Definition of exposure group – TB contact score (range 6-19)	
Non-exposed	TB contact score (8-10)
Exposed 1 **(specify)**:	TB contact score (11-12)
Exposed 2 **(specify)**:	TB contact score (13-14)
Exposed 3 **(specify)**:	TB contact score (15-16)
2. Definition of exposure group – TB contact score (range 6-19)	
Non-exposed	TB contact score (8-12)
Exposed 1 **(specify)**:	TB contact score (≥13)
3. Definition of exposure group – relationship to TB index case	
Non-exposed	Relative other contact in household with TB
Exposed 1 **(specify)**:	Second caregiver in household with TB
Exposed 2 **(specify)**:	Primary caregiver in household with TB
4. Definition of exposure group – Duration of average contact per day with TB index case	
Non-exposed	0-7 hours
Exposed 1 **(specify)**:	≥8 hours
5. Definition of exposure group – Duration of contact with TB index case in last 12 months	
Non-exposed	≤7 months
Exposed 1 **(specify)**:	>7 months
6. Definition of exposure group – Index TB case history	
Non-exposed	Sputum acid fast smear negative
Exposed 1 **(specify)**:	Sputum acid fast smear positive

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	The children had whole blood and peripheral blood mononuclear cells collection for the interferon-gamma release assay (QFNGIT) The blood samples were sent on the same day of collection to the laboratory for testing according to the manufacturers' instructions using positive and negative controls	Results were reported as positive, negative, or indeterminate according to the manufacturers' guidelines Positive cutoff values for the tests were defined using the manufacturers' standard guidelines	Study investigators, site coordinators, and clinicians were blinded to the results of the IGRAs until the study had completed enrollment and 9-month follow-up
TST≥10mm TST≥15mm	At the baseline visit, the children had a TST (0.1 ml solution or 10 international units of tuberculin purified protein derivative) implanted on the forearm followed by result reading by trained health care personnel in 48–72 hours, in accordance with Thai	The size of TST induration was determined by measuring the maximum width (or transverse diameter) of an indurated lesion; test positivity was defined at ≥10mm or ≥15mm	

	national guidelines		
T-SPOT.TB	The children had whole blood and peripheral blood mononuclear cells collection for the interferon-gamma release assay (TSPOT). The blood samples were sent on the same day of collection to the laboratory for testing according to the manufacturers' instructions using positive and negative controls	Results were reported as positive, negative, or indeterminate Positive cutoff values were defined using the manufacturers' standard guidelines	

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA

NPV= NA	NPV= NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = **TB contact score (range 6-19)** Score 8-10 (reference/non-exposed): 1.0 Score 11-12: 2.00 (95% CI: 0.38, 10.61) Score 13-14: 3.64 (95% CI: 0.75,17.77) Score 15-16: 7.50 (95% CI: 1.35, 41.71) **TB contact score (range 6-19)** Score 8-12 (reference/non-exposed): 1.0 Score ≥13: 4.04 (95% CI: 1.81, 8.99) **Relationship to TB index case** Relative other contact (reference/non-exposed): 1.0 Second caregiver: 3.95 (95% CI: 1.50, 10.43) Primary caregiver: 3.25 (95% CI: 1.36, 7.77) **Duration of average contact per day with TB index case** 0-7 hours (reference/non-exposed): 1.0 ≥8 hours: 1.75 (95% CI: 0.78, 4.00) **Duration of contact with TB index case in last 12 months** ≤7 months (reference/non-exposed): 1.0 >7 months: 1.96 (95% CI: 0.99, 3.84) **Index TB case history** Sputum acid fast smear negative (reference/non-exposed): 1.0 Sputum acid fast smear positive: 0.97 (95% CI: 0.27, 3.33)	OR (crude; for T^+ reported) = **TB contact score (range 6-19)** Score 8-10 (reference/non-exposed): 1.0 Score 11-12: 3.97 (95% CI: 1.19, 13.28) Score 13-14: 4.40 (95% CI: 1.38, 14.08) Score 15-16: 7.33 (95% CI: 1.67,32.21) **TB contact score (range 6-19)** Score 8-12 (reference/non-exposed): 1.0 Score ≥13: 2.59 (95% CI: 1.28, 5.23) **Relationship to TB index case** Relative other contact (reference/non-exposed): 1.0 Second caregiver: 0.87 (95% CI: 0.34, 2.23) Primary caregiver: 1.44 (95% CI: 0.61, 3.41) **Duration of average contact per day with TB index case** 0-7 hours (reference/non-exposed): 1.0 ≥8 hours: 2.27 (95% CI: 1.08, 4.76) **Duration of contact with TB index case in last 12 months** ≤7 months (reference/non-exposed): 1.0 >7 months: 2.04 (95% CI: 1.00, 4.16) **Index TB case history** Sputum acid fast smear negative (reference/non-exposed): 1.0 Sputum acid fast smear positive: 2.38 (95% CI: 0.49, 11.11)
OR (regression-based; reported) = **TB contact score (range 6-19)** Score 8-10 (reference/non-exposed): 1.0 Score 11-12: NR Score 13-14: NR Score 15-16: NR **TB contact score (range 6-19)** Score 8-12 (reference/non-exposed): 1.0 Score ≥13: 1.98 (95% CI: 0.64, 6.11) **Relationship to TB index case** Relative other contact (reference/non-exposed): 1.0 Second caregiver: 3.95 (95% CI: 1.25, 12.52) Primary caregiver: 4.07 (95% CI: 1.38, 11.99) **Duration of average contact per day with TB index case** 0-7 hours (reference/non-exposed): 1.0 ≥8 hours: NR	OR (regression-based; reported) = **TB contact score (range 6-19)** Score 8-10 (reference/non-exposed): 1.0 Score 11-12: NR Score 13-14: NR Score 15-16: NR **TB contact score (range 6-19)** Score 8-12 (reference/non-exposed): 1.0 Score ≥13: 2.21 (95% CI: 0.99, 4.98) **Relationship to TB index case** Relative other contact (reference/non-exposed): 1.0 Second caregiver: NR Primary caregiver: NR **Duration of average contact per day with TB index case** 0-7 hours (reference/non-exposed): 1.0

Duration of contact with TB index case in last 12 months ≤7 months (reference/non-exposed): 1.0 >7 months: 1.47 (95% CI: 0.62, 3.44) **Index TB case history** Sputum acid fast smear negative (reference/non-exposed): 1.0 Sputum acid fast smear positive: NR List of covariates: NR	≥8 hours: 1.61 (95% CI: 0.68, 3.84) **Duration of contact with TB index case in last 12 months** ≤7 months (reference/non-exposed): 1.0 >7 months: NR **Index TB case history** Sputum acid fast smear negative (reference/non-exposed): 1.0 Sputum acid fast smear positive: NR List of covariates: NR
Other reported measure = NR	Other reported measure =NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated)=NA

Ratio of OR (crude; for T^+ reported)= TB contact score: 13+ vs. 8-12 [GIT vs. TST-10mm]=1.56 (95% CI: 0.91, 2.69)
Ratio of OR (crude; for T+ reported)=TB contact score: 13+ vs. 8-12 [GIT vs. TST-15mm]=1.84 (95% CI: 1.07, 3.18)

Ratio of ORs (regression-based; reported)=TB contact score: 13+ vs. 8-12 [GIT vs. TST-10mm]= 0.90 (95% CI: 0.44, 1.82)
Ratio of ORs (regression-based; reported)=TB contact score: 13+ vs. 8-12 [GIT vs. TST-15mm]=2.39 (95% CI: 1.15, 4.93)

Other reported measure= NR

Association between test results and BCG status (if applicable)

IGRA (specify)				**TST (specify)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$= NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST ≥10mm	TST -	Total
IGRA [QFT-GIT] +	36	2	38
IGRA -	51	42	93
indeterminate	NR	NR	NR
Total	87	44	131

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥10mm

Parameters

Kappa = 0.29 (95% CI 0.18, 0.40)

% concordance = [36+42]/131=59.54% (95% CI: 50.98, 67.56)

% discordance = 53/131=40.46% (95% CI: 32.44, 49.02)			
Between-test agreement, concordance, and discordance (if applicable) This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition			
Total sample			
	TST ≥15mm	TST -	Total
IGRA [QFT-GIT] +	29	9	38
IGRA -	18	75	93
indeterminate	NR	NR	NR
Total	47	84	131
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥15mm			
Parameters			
Kappa = 0.53 (95% CI 0.38, 0.69)			
% concordance = [29+75]/131=79.39% (95% CI 71.67, 85.43)			
% discordance = 27/131=20.61% (95% CI 14.57, 28.33)			
Between-test agreement, concordance, and discordance (if applicable) This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition			
Total sample			
	TST ≥10mm	TST -	Total
IGRA [TSPOT] +	32	3	35
IGRA -	55	41	96
indeterminate	NR	NR	NR
Total	87	44	131
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.23 (95% CI 0.12, 0.34)			
% concordance = [32+41]/131=55.73% (95% CI 47.18, 63.95)			
% discordance = 58/131=44.27% (95% CI 36.05, 52.82)			
Between-test agreement, concordance, and discordance (if applicable) This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition			
Total sample			
	TST ≥15mm	TST -	Total
IGRA [TSPOT] +	27	8	35
IGRA -	20	76	96
indeterminate	NR	NR	NR
Total	47	84	131
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥15mm			
Parameters			
Kappa = 0.51 (95% CI 0.35, 0.66)			
% concordance = [27+76]/131 = 78.63% (95% CI 70.84, 84.78)			
% discordance = 28/131 = 21.37% (95% CI 15.22, 29.16)			
Stratification (specify group 1):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Conclusions			
Authors:			
Both QFNGIT and T-Spot.TB performed well in our generally healthy Thai pediatric study population with recent exposure to adults with active pulmonary TB, with no indeterminate or equivocal/borderline results. No significant differences were found between the performances of the IGRAs and TST at the two cut-offs with increasing TB exposure. Concordance for positive IGRAs and TST ranged from 42–46% for TST≥10 mm and 62–67% for TST≥15 mm. On multivariable analyses, exposure to household secondary caregiver with TB was associated with positive QFNGIT. Higher TB contact score was associated with positive T-Spot.TB.			
Reviewers:			
QFT and TSPOT had similar concordance with TST (at both thresholds); however, this concordance was higher when TST threshold was 15mm (vs. 10mm). On average, TSPOT and QFT performed similarly better in relation to TST, especially compared to TST 15mm			
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation			

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Tsolia 2010[113]
Country: Greece
Study design: Retrospective cohort/cross sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** TB clinic
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** The Bienmoyo Foundation

Aim of the study

To evaluate and compare the performance of the QFT-GIT assay and the TST among children with active TB or possible latent TB infection in a low endemicity setting.

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: 1st January 2007 to 31st December 2003
Total N of recruited patients: 295
Inclusion criteria: Adolescents ≤ 15 years
Exclusion criteria: NR
Total N of excluded patients: 9 (refusal, lost specimen, sample processing delay)
Total N of patients tested with both IGRA and TST:
Total N of patients with valid results for both IGRA and TST: 286 (total sample including active TB patients)
Methods of active TB diagnosis (if applicable): Based on CDC criteria and MTB isolation from culture
Outcomes (study-based) list: Agreement; association between test results and risk factors
Characteristics of participants (total study sample)
Mean (range or SD) age (years): NR
Women (n [%]): NR
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	99 (patients in contact with adult TB)	32	63	4	95
TST (≥ 5mm):	99 (patients in contact with adult TB)	55	44	0	99
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 95 (patients in contact with adult TB)

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group - Contact with an adult TB	
Non-exposed	Non-household occasional contact
Exposed 1 **(specify):**	Non-household regular contact
Exposed 2 **(specify):**	Household contact
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-GIT (Cellestis Limited, Carnegie, Victoria, Australia)	> 10 IU/mL	Indeterminate results on the QFT-GIT were excluded from the analysis
TST ≥ 5mm or ≥10mm	Purified protein derivative (PPD) RT23 (Statens Serum Institut, Copenhagen, Denmark)	≥ 10mm for BCG immunized children ≥ 5mm for non-BCG immunized children	NA

Association between test results and incidence of active TB (if applicable)							
IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (Type of contact with TB case)							
IGRA (QFT-GIT)				TST≥5mm			
	Exposure level		Total		Exposure level		Total
	Non-household regular	Non-household occasional			Non-household regular	Non-household occasional	
IGRA +	9	1	10	TST +	18	7	25
IGRA -	18	10	28	TST -	10	4	14
Indeterminate	1	0	1	Indeterminate	0	0	0
Total	28	11	39	Total	28	11	39

Test performance parameters	
IGRA	TST
Sensitivity = 9/27 = 33.33% (95% CI: 18.64, 52.18)	Sensitivity = 18/28 = 64.29% (95% CI: 45.83, 79.29)
Specificity = 10/11 = 90.91% (95% CI: 62.26, 98.38)	Specificity = 4/11 = 36.36% (95% CI: 15.17, 64.62)
PPV = 9/10 = 90.00% (95% CI: 59.58, 98.21)	PPV = 18/25 = 72.00% (95% CI: 52.42, 85.72)
NPV = 10/28 = 35.71% (95% CI: 20.71, 54.17)	NPV = 4/14 = 28.57% (95% CI: 11.72, 54.65)
DOR (for T^+ calculated) = 5.00 (95% CI: 0.55, 45.39)	DOR (for T^+ calculated) = 1.03 (95% CI: 0.24, 4.39)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 4.85 (95% CI: 1.26, 18.69)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and levels of TB exposure (Type of contact with TB case)							
IGRA (QFT-GIT)				TST≥5mm			
	Exposure level		Total		Exposure level		Total
	Household	Non-household occasional			Household	Non-household occasional	
IGRA +	22	1	23	TST +	30	7	37
IGRA -	35	10	45	TST -	30	4	34
Indeterminate	3	0	3	Indeterminate	0	0	0
Total	60	11	71	Total	60	11	71

Test performance parameters	
IGRA	TST
Sensitivity = 22/57 = 38.6% (95% CI: 27.06, 51.57)	Sensitivity = 30/60 = 50.00% (95% CI: 37.73, 62.27)
Specificity = 10/11 = 90.91% (95% CI: 62.26, 98.38)	Specificity = 4/11 = 36.36% (95% CI: 15.17, 64.62)
PPV = 22/23 = 95.65% (95% CI: 79.01, 99.23)	PPV = 30/37 = 81.08% (95% CI: 65.79, 90.52)
NPV = 10/45 = 22.22% (95% CI: 12.54, 36.27)	NPV = 4/34 = 11.76% (95% CI: 4.67, 26.62)
DOR (for T^+ calculated) = 6.28 (95% CI: 0.75, 52.56)	DOR (for T^+ calculated) = 0.57 (95% CI: 0.15, 2.15)

OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 11.02 (95% CI: 3.07, 39.60)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST≥5mm**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{QFT}$ = NR	DOR $_{TST}$ (for T+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = 0.19, 95% CI (0.06, 0.60) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 20.34, 95% CI (5.60, 73.89) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	29	3	32
IGRA -	24	39	63
Indeterminate	2	2	4
Total	55	44	99

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total
TST + threshold: ≥5 mm

Parameters

Kappa = 0.45, 95% CI (0.27, 0.63)
% concordance = 68/95 = 71.58%, 95% CI (61.81, 79.67)
% discordance = 27/95 = 28.42%, 95% CI (20.33, 38.19)

Stratification (BCG vaccinated)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	43

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated
TST + threshold: ≥10 mm

Parameters

Kappa = 0.13 (p = 0.06)
% concordance = 20/43 = 46.50% (95% CI NR)

% discordance = NR			
Stratification (non-BCG vaccinated)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	52
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated			
TST + threshold: ≥5 mm			
Parameters			
Kappa = 0.91 (p = 0.06)			
% concordance = 50/52 = 96.20% (95% CI NR)			
% discordance = NR			
Stratification (Household contact)			
	TST +	TST -	Total
IGRA +	20	2	22
IGRA -	8	27	35
Indeterminate	2	1	3
Total	30	30	60
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Household contact with TB case			
TST + threshold: ≥5 mm			
Parameters			
Kappa = 0.65, 95% CI (0.39, 0.90)			
% concordance = 47/53 = 82.46%, 95% CI (70.63, 90.18)			
% discordance = 10/53 = 17.54%, 95% CI (9.81, 29.37)			
Stratification (Non-household regular contact)			
	TST +	TST -	Total
IGRA +	8	1	9
IGRA -	10	8	18
Indeterminate	0	1	1
Total	18	10	28
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Non-household regular contact with TB case			
TST + threshold: ≥5 mm			
Parameters			
Kappa = 0.27, 95% CI (-0.03, 0.56)			
% concordance = 16/27 = 59.26%, 95% CI (40.73, 75.49)			
% discordance = 11/27 = 40.74%, 95% CI (24.51, 59.27)			
Stratification (Non-household occasional contact)			
	TST +	TST -	Total
IGRA +	1	0	1
IGRA -	6	4	10
Indeterminate	0	0	0
Total	7	4	11
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify):			
TST + threshold:			
Parameters			
Kappa = 0.11, 95% CI (-0.15, 0.37)			

% concordance = 5/11 = 45.45%, 95% CI (21.27, 71.99)		
% discordance = 6/11 = 54.55%, 95% CI (28.01, 78.73)		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
QFT may improve the diagnosis of LTBI especially in BCG vaccinated children		
Reviewers:		
There was a better agreement in BCG non-immunized vs. BCG immunized children; QFT suggested strong associations with TB contact exposure but they were NS; TST was not associated with exposure (contact with TB); odds of TST positivity (unlike QFT-GIT) was greater in BCG vaccinated vs. not vaccinated		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Diel 2011[102]
Country: Germany
Study design: Prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community based contact study
Number of centres: Multi-center (NR)
Total length of follow up (if applicable): 2-4 yrs
Funding (government/private/manufacturer/other - specify)**:** NR (None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript)

Aim of the study

To compare the QuantiFERONTB Gold in-tube assay (QFT) with the tuberculin skin test (TST) in close contacts of patients with TB and evaluate progression to active TB for up to 4 years

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children (close contacts of smear-positive index cases)

Participants

Recruitment dates: May 2005 to April 2010
Total N of recruited patients: 141
Inclusion criteria: Close contacts of smear-positive and subsequently culture-confirmed source MTB index cases; aggregate exposure time of the contact in the 3 months before the diagnosis of respective index case (presumed
period of infectiousness > 40 hours indoors with shared air)
Exclusion criteria: Contacts with an exposure time of < 40 hours to the source
Total N of excluded patients: 15
Total N of patients tested with both IGRA and TST: 126
Total N of patients with valid results for both IGRA and TST: 106
Methods of active TB diagnosis (if applicable): CXR (and computerized tomography), identification of AFB in sputum samples by bronchoscopy or lavage of gastric secretions, conventional culture of M. tuberculosis, nucleic acid amplification assays and/or histopathology, assessment of preceding clinical suspicion of TB. In culture-negative cases, and given a CXR consistent with TB, subsequent clinical and radiographic response to multidrug therapy over an appropriate time course (1–3 mo) was considered sufficient to confirm the diagnosis of TB
Outcomes (study-based) list: Incidence of active TB, predictive values of IGRA and TST
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 10.4 (4.3) years
Women (n [%]): NR
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): Germany (84 [66.7])
BCG vaccination (n [%]): 45 [35.7]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): 6/104 [5.7]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): anti TB chemoprophylaxis (2/106 [1.8])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)

IGRA (QFT-GIT):	126	23	83	NR	106
TST (>5mm):	126	40	66	NR	106
TST (>10mm):	126	20	86	NR	106

Total N of patients with valid results for both IGRA and TST: 104 (2 patients receiving chemoprophylaxis excluded)

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NR
Exposed 1 **(specify):**	NR
Exposed 2 **(specify):**	NR
Exposed 3 **(specify):**	NR
Exposed 4 **(specify):**	NR

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Performed according to the manufacturer's instructions (Cellestis Ltd, Carnegie, Australia) The maximal level of IFN-g accurately detected by the QFT ELISA is 10 IU/ml, and thus values greater than this are reported as 10 IU/ml	IFN-g of 0.35 IU/ml or greater	Assessors of the TST were blinded to QFT results and vice versa. Induration was read by trained and well-experienced public health nurses. If there was a borderline result (e.g., 5 mm exactly), a second reading was performed by a different nurse to verify this result. If there was disagreement, a third nurse read the TST and the consensus result used
TST	Administered by the Mantoux method; 0.1 ml of Tuberculin-10-GT (Chiron Behring, Marburg, Germany; bioequivalent to 5 units of the international purified protein derivative-Seifert [PPD-S] standard), and subsequently 0.1 ml (2 tuberculin units) of purified protein derivative RT23 (Statens Serum Institute, Copenhagen, Denmark), which is equivalent to Tuberculin-10-GT (Chiron Behring)	TST reaction was scored as positive at > 5mm or > 10mm	

Association between test results and incidence of active TB (if applicable)

IGRA				**TST (>5mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	6	15	21	TST +	6	34	40
IGRA -	0	83	83	TST -	0	64	64
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	6	98	104	Total	6	98	104

Test performance parameters

IGRA	**TST**
Sensitivity = 6/6 = 100% (95% CI: 60.97, 100)	Sensitivity = 6/6 = 100% (95% CI: 60.97, 100)
Specificity = 83/98 = 84.69% (95% CI: 76.27, 90.5)	Specificity = 64/98 = 65.31% (95% CI: 55.47, 73.99)
PPV = 6/21 = 28.57% (95% CI: 13.81, 49.96)	PPV = 6/40 = 15.00% (95% CI: 7.06, 29.07)
NPV = 83/83 = 100% (95% CI: 95.58, 100)	NPV = 64/64 = 100% (95% CI: 94.34, 100)

Cumulative Incidence $_{IGRA+}$ = 6/21 = 28.57% (95% CI: 13.81, 49.96)	Cumulative Incidence $_{TST+}$ = 6/40 = 15.00% (95% CI: 7.06, 29.07)
Cumulative Incidence $_{IGRA-}$ = 0/83 = 1.20% (95% CI: 0.03, 6.53)	Cumulative Incidence $_{TST-}$ = 0/64 = 1.55% (95% CI: 0.04, 8.4)
Cumulative Incidence Ratio $_{IGRA}$ = 23.7% (95% CI: 2.57, 110.3)	Cumulative Incidence Ratio $_{TST}$ = 9.6% (95% CI: 1.08, 448.2)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = 2.47(95% CI: 0.40, 15.12)
Ratio of incidence density rate ratios = NR
Other reported measure = NR

Association between test results and incidence of active TB (if applicable)

IGRA				**TST (>10mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	6	15	21	TST +	4	36	40
IGRA -	0	83	83	TST -	2	62	64
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	6	98	104	Total	6	98	104

Test performance parameters

IGRA	**TST**
Sensitivity = 6/6 = 100% (95% CI: 60.97, 100)	Sensitivity = 4/6 = 66.67% (95% CI: 30.00, 90.32)
Specificity = 83/98 = 84.69% (95% CI: 76.27, 90.5)	Specificity = 62/98 = 63.27% (95% CI: 53.39, 72.14)
PPV = 6/21 = 28.57% (95% CI: 13.81, 49.96)	PPV = 4/40 = 10% (95% CI: 3.96, 23.05)
NPV = 83/83 = 100% (95% CI: 95.58, 100)	NPV = 62/64 = 96.88% (95% CI: 89.3, 99.14)
Cumulative Incidence $_{IGRA+}$ = 6/21 = 28.57% (95% CI: 13.81, 49.96)	Cumulative Incidence $_{TST+}$ = 4/40 = 10.00% (95% CI: 3.958, 23.05)
Cumulative Incidence $_{IGRA-}$ = 0/83 = 1.20% (95% CI: 0.03, 6.53)	Cumulative Incidence $_{TST-}$ = 2/64 = 3.12% (95% CI: 0.22, 11.33
Cumulative Incidence Ratio $_{IGRA}$ = 23.7% (95% CI: 2.57, 110.3)	Cumulative Incidence Ratio $_{TST}$ = 3.20% (95% CI: 0.61, 16.67)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = 7.41(95% CI: 2.06, 26.57)
Ratio of incidence density rate ratios = NR
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				TST			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA
OR (regression-based; reported) $_{IGRA}$ = NA List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify):
TST + threshold: NR

Parameters

Kappa = NR
% concordance = NR
% discordance = NR

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Results suggest that QFT is more reliable than the TST for identifying those who will soon progress to active TB, especially in children
Reviewers:
Overall, QFT performed better (sensitivity, specificity, predictive values) than TST in identifying LTBI by predicting the occurrence of active TB
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Tara Gurung
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Mahomed 2011a[103]
Country: South Africa
Study design: Longitudinal cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** High school (TB vaccine trial site in the town of Worcester (and surrounding villages) (high burden of TB)
Number of centres: 11
Total length of follow up (if applicable): 3.8 years
Funding (government/private/manufacturer/other - specify)**:** The Aeras Global TB Vaccine Foundation with some support from the Gates Grand Challenge 6 and Gates Grand Challenge 12 grants for the QuantiFERON testing.

Aim of the study

To compare the predictive value of a baseline tuberculin skin test (TST) with that of the QuantiFERON TB Gold (In-tube) assay (QFT) for subsequent microbiologically confirmed TB disease among adolescents.

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Adolescents from high burden TB area

Participants

Recruitment dates: From 2005 to 2006
Total N of recruited patients: 6,363
Inclusion criteria: adolescents aged 12 to 18 years
Exclusion criteria: NR
Total N of excluded patients: 1,119 (those with prior or current TB, indeterminate QFT results, or missing QFT or TST results)
Total N of patients tested with both IGRA and TST: 5,244
Total N of patients with valid results for both IGRA and TST: 5,244
Methods of active TB diagnosis (if applicable): Two sputum samples for smear microscopy on two separate occasions. If any single sputum was smear positive, a mycobacterial culture, chest x-ray, and HIV test were performed
Outcomes (study-based) list: Test results, concordance between TST and QTB, TB disease incidence rate
Characteristics of participants (total study sample)
Mean (range or SD) age (years): NR
Women (n [%]): 2842 [54.2]
Race/ethnicity (n [%]): Black (995 [19.0]); Mixed race (3839 [73.2]); Indian/white (410 [7.8])
BCG vaccination (n [%]): Yes (4917 [93.8]; Unknown (281 [5.4])
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): 52 [1.0]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (specify): QFT-GIT	5244	2669	2575	NR	5244
TST≥5mm:	5244	2894	2350	NR	5244

Test 3 (specify)	NR	NR	NR	NR	NR
Total N of patients with valid results for both IGRA and TST: 5244					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group					
Non-exposed	NA				
Exposed 1 **(specify):**	NA				
Exposed 2 **(specify):**	NA				
Exposed 3 **(specify):**	NA				
Exposed 4 **(specify):**	NA				

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA	QFT-GIT, In-tube method, (Cellestis Limited, Carnegie, Victoria, Australia)	≥ 0.35 IU/mL	NA
TST	Mantoux method on either forearm, using 2 tuberculin units of RT23, induration was read 48-96 hours later with a ruler or caliper by trained personnel, (Statens Serum Institut, Denmark)	≥ 5mm	People with a recent household contact, TB related symptoms, a positive TST ≥10 mm induration or a positive QFT were referred for two sputum smears. If results of either or both were sputum positive for acid fast bacilli, the sputum were cultured, and a chest x-ray and HIV test were undertaken.

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-GIT)				**TST≥5mm**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	39	2630	2669	TST +	40	2854	2894
IGRA -	13	2562	2575	TST -	12	2338	2350
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	52	5192	5244	Total	52	5192	5244

Test performance parameters

IGRA	**TST**
Sensitivity = 39/52 = 75.00%, 95% CI (61.79, 84.77)	Sensitivity = 40/52 = 76.92%, 95% CI (63.87, 86.28)
Specificity = 2562/5192 = 49.35%, 95% CI (47.99, 50.71)	Specificity = 2338/5192 = 45.03%, 95% CI (43.68, 46.39)
PPV = 39/2669 = 1.46%, 95% CI (1.07, 1.99)	PPV = 40/2894 = 1.38%, 95% CI (1.02, 1.88)
NPV = 2562/2575 = 99.50%, 95% CI (99.14, 99.7)	NPV = 2338/2350 = 99.49%, 95% CI (99.11, 99.71)
Cumulative Incidence $_{IGRA+}$ = 39/2669 = 1.46%, 95% CI (1.07, 1.99)	Cumulative Incidence $_{TST+}$ = 40/2894 = 1.38%, 95% CI (1.02, 1.87)
Cumulative Incidence $_{IGRA-}$ = 13/2575 = 0.50%,	Cumulative Incidence $_{TST-}$ = 12/2350 = 0.51%,

95% CI (0.28, 0.87)	95% CI (0.28, 0.90)
Cumulative Incidence Ratio $_{IGRA}$ = 2.89, 95% CI (1.55, 5.40)	Cumulative Incidence Ratio $_{TST}$ = 2.71 (95% CI: 1.42, 5.14)
Incidence density rate $_{IGRA+}$ = 0.64 per 100 person years, 95% CI (0.45, 0.87)	Incidence density rate $_{TST+}$ = 0.60 per 100 person years, 95% CI (0.43, 0.82)
Incidence density rate $_{IGRA-}$ = 0.22 per 100 person years, 95% CI (0.12, 0.38)	Incidence density rate $_{TST-}$ = 0.22 per 100 person years, 95% CI (0.11, 0.39)
Incidence density rate ratio $_{IGRA}$ = 2.92, 95% CI (1.58, 5.67)	Incidence density rate ratio $_{TST}$ = 2.73, 95% CI (1.45, 5.42)

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence = 1.07, (95% CI: 0.68, 1.68)
Ratio of incidence density rate ratios = 1.07, (95% CI: 0.67, 1.71)
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA				TST			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	2383	286	2669
IGRA -	511	2064	2575
Indeterminate	0	0	0
Total	2894	2350	5244

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total
TST + threshold: ≥5 mm induration

Parameters

Kappa = 0.69 95% CI, (0.66, 0.72)
% concordance = 4447/5244 = 84.80%, 95% CI (83.80, 85.75)
% discordance = 797/5244 = 15.20%, 95% CI (14.25, 16.20)

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Based on the findings from this study, these authors concluded/demonstrated that TST and QFT-GIT are equally predictive of progression to active TB in a cohort of adolescents in a high TB burden population. They further stated that their results do not support that QFT-GIT is more superior to TST in its predictive value
Reviewers:
Authors reported that Isoniazid prevention therapy is not standard care for people with LTBI except for children under the age of five years old. TST and QFT-GIT are equally predictive of progression to active TB in a cohort of adolescents in a high TB burden population
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Tara Gurung
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Noorbakhsh 2011[104]
Country: Iran
Study design: Cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Pulmonary and infectious diseases department of Rasul hospital in Tehran
Number of centres: 1
Total length of follow up (if applicable): 1 year
Funding (government/private/manufacturer/other - specify)**:** Research Centre of Paediatric Infectious Diseases, Iran University of Medical Sciences.

Aim of the study

To detect the agreement between TST and QTB in young household contacts (aged < 20 years) of cases of proven active pulmonary TB in a BCG-vaccinated population in Tehran, Islamic Republic of Iran, and to compare subjects progressing to TB with non-progressive subjects

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: 2006-2008
Total N of recruited patients: NR
Inclusion criteria: all young (< 20 years old) close or household contacts of people (as any person who had lived with the index case for more than 3 months) with confirmed active pulmonary TB and previous BCG vaccination received at birth. The subjects were invited to our research centre for clinical and laboratory follow-up
Exclusion criteria: Household contacts were excluded if they had been treated for TB in the past year or had a known immunodeficiency state on history or clinical signs (malignancy, corticosteroid therapy, HIV, etc.).
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 58
Methods of active TB diagnosis (if applicable): Person diagnosed by an internist in the pulmonary and infectious ward of Rasht hospital. The index cases were confirmed by positive culture for M. tuberculosis or sputum smear-positive TB
Outcomes (study-based) list: Test results, concordance between TST and QTB, progression to TB disease
Characteristics of participants (total study sample)
Mean (range or SD) age (years): NR
Women (n [%]): 34 [57.6]
Race/ethnicity (n [%]): NR
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): 10 [16.9]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)

IGRA (QFT-G):	NR	18	41	NR	59
TST (≥ 10mm):	NR	8	50	1	58
Test 3 (specify)	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 48

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NR
Exposed 1 **(specify):**	NR
Exposed 2 **(specify):**	NR
Exposed 3 **(specify):**	NR
Exposed 4 **(specify):**	NR

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-G)	For the QTB fresh blood samples from all of the participants were processed on site according to the manufacturer's instruction (Gold Quantiferon-TB, Cellestis). First, 1 mL of heparinized whole blood was incubated with aliquots of antigen-free control and antigens for 16–24 hours at 37 °C in a carbon dioxide incubator. After overnight incubation, 200 µL plasma was removed from each well and the concentration of IFN-γ was determined using the assay kits	Not reported	NA
TST (≥ 10mm)	For the TST a test dose (0.1 mL) of 5 tuberculin units of purified protein derivative solution (Pasteur Institute, Tehran) was injected intradermally into the volar aspect of the forearm with a 26–27 gauge needle by trained field worker. The induration diameter of the raised, blanched weal (not the erythema) was read after 48–72 hours	A reactive TST was an induration diameter of ≥ 10mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-G)				**TST≥ 10mm**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	10	8	18	TST +	3	5	8
IGRA -	0	41	41	TST -	7	43	50
Indeterminate	NR	NR	NR	Indeterminate	0	1	1
Total	10	49	59	Total	10	49	59

Test performance parameters

IGRA	**TST**
Sensitivity = 10/10 = 100.00%, 95% CI (72.25, 100.00)	Sensitivity = 3/10 = 30.00%, 95% CI (10.78, 60.32)
Specificity = 41/49 = 83.67%, 95% CI (70.96, 91.49)	Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)
PPV = 10/18 = 55.56%, 95% CI (33.72, 75.44)	PPV = 3/8 = 37.50%, 95% CI (13.68, 69.43)

NPV = 41/41 = 100%, 95% CI (91.43, 100)	NPV = 43/50 = 86.00%, 95% CI (73.81, 93.05)
Cumulative Incidence $_{IGRA+}$ = 10/18 = 55.56%, 95% CI (33.72, 75.44)	Cumulative Incidence $_{TST+}$ = 3/8 = 37.5%, 95% CI (13.49, 69.62)
Cumulative Incidence $_{IGRA-}$ = 0/41 = 2.41% (95% CI: 0.06, 12.9)	Cumulative Incidence $_{TST-}$ = 7/50 = 14.00%, 95% CI (6.63, 26.50)
Cumulative Incidence Ratio $_{IGRA}$ = 22.78% (95% CI: 2.75, 101.1)	Cumulative Incidence Ratio $_{TST}$ = 2.68% (95% CI: 0.86, 8.27)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence = 8.50% (95% CI: 2.87, 25.17)
Ratio of incidence density rate ratios = NR
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA				TST			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	NR	NR	18
IGRA -	NR	NR	41
Indeterminate	NR	NR	NR
Total	8	51	59

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total
TST + threshold: ≥10mm

Parameters

Kappa = NR
% concordance = NR
% discordance = NR

Stratification (non-progressive)			
	TST +	TST -	Total
IGRA +	39	4	43
IGRA -	2	3	5
Indeterminate	0	0	0
Total	41	7	48
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): 49 children who did not progress to active TB			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.43 (95% CI: 0.15, 0.70)			
% concordance = 42/48 = 87.60% (95% CI:75.3, 94.14)			
% discordance = 6/48 = 12.5% (95% CI: 5.85, 24.70)			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
From this study, the authors demonstrated that QTB assay can reflect recent rather than remote TB infections compared with TST in an adolescent population who had previously received BCG vaccination
Reviewers:
QFT performed better than TST in detecting LTBI by predicting development of active TB
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Song 2014[152]
Country: South Korea
Study design: prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify): community-based
Number of centres: 1 (children sampled from 45 schools)
Total length of follow up (if applicable): 24 months
Funding (government/private/manufacturer/other - specify): This research was supported by a fund (2008-E00226-00, 2009-E46002-00, 2010-E46003-00, 2011-E46006-00, and 2012-E46001-00) by Research of Korea
Centers for Disease Control and Prevention. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

Aim of the study

To determine the agreement between IGRA (QFT-GIT) and TST and identify the relationships between the results of these tests and the development of active tuberculosis in middle and high school students in close contact with tuberculosis patients in South Korea

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Children

Participants

Recruitment dates: Between 2008 and 2012
Total N of recruited patients: 3,202
Inclusion criteria: Close contacts of identified smear-positive tuberculosis cases with normal chest X-ray aged 11–19 years
Exclusion criteria: Participants showing (1) abnormal findings in simple chest radiographs, (2) they had taken immunosuppressive agents or anticancer drugs earlier, and (3) they had been treated with antituberculous drugs or chemoprophylaxis earlier
Total N of excluded patients: 220 (at baseline)
Total N of patients tested with both IGRA and TST: 2,982
Total N of patients with valid results for both IGRA and TST: 2,966
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: between test agreement, incidence of active TB
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 15.1 (1.3)
Women (n [%]): 1,356 (45.5)
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 1,818 (61.0)
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): 23/2,982 (0.77)
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): 5/215 [2.32] (isoniazid)

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	2982	317	2649	16	2966
TST≥10mm	2982	663	2319	0	2982
TST≥15mm	2982	231	2751	0	2982

Test 3 (specify)					
Total N of patients with valid results for both IGRA and TST: 2,966					
Levels/groups of exposure to TB in increasing order (if applicable): NA					
Definition of exposure group –					
Non-exposed	NA				
Exposed 1 **(specify)**:	NA				
Exposed 2 **(specify)**:	NA				
Exposed 3 **(specify)**:	NA				
Exposed 4 **(specify)**:	NA				
Tests					

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA –[QFT-GIT]	QFT Gold In-Tube (Cellestis Inc, Valencia, CA) tests were performed according to the manufacturer's instructions. Briefly, whole blood was collected by venipuncture from each subject at the date of injection of PPD and incubated for 16–24 hours in 3 separate conditions: 1) a mixture of 3 TB antigens from RD1 and RD11 (ESAT-6, CFP-10, and TB7.7); 2) a mitogen as a positive control; and 3) a mock stimulation as a negative control (nil). Following the stimulations, 150 mL of the supernatant was harvested from each tube. Then, 50 mL of each supernatant was used to determine its interferon gamma (IFN-c) concentration by the ELISA	A QuantiFERON value of 0.35 international units or more was deemed positive according to manufacturer's instructions	To eliminate the possibility of false-positive IGRA results due to PPD reagents, blood samples were collected before PPD injection
TST≥10mm	Intradermal injection (0.1 ml) of 2 tuberculin units of purified protein derivative (RT 23; Statens Serum Institute, Copenhagen, Denmark) into the anterior surface of the forearm with a disposable syringe and a	The maximal transverse size of induration was read 48–72 hours later with a ruler or a caliper by a research nurse ≥10mm ≥15mm	

	27-gauge needle by using the Mantoux technique		

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-GIT)				TST≥10mm			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	11	306	317	TST +	13	650	663
IGRA -	12	2637	2649	TST -	10	2309	2319
indeterminate	NR	NR	16	indeterminate	0	0	0
Total	23	2943	2966	Total	23	2959	2982

Test performance parameters

IGRA	TST
Sensitivity = 11/23=47.83% (95% CI: 29.24, 67.04)	Sensitivity =13/23=56.52% (95% CI: 36.81, 74.37)
Specificity = 2637/2943=89.6% (95% CI: 88.45, 90.65)	Specificity = 2309/2959=78.03% (95% CI: 76.51, 79.49)
PPV= 11/317=3.47% (95% CI: 1.94, 6.10)	PPV= 13/663=1.96% (95% CI: 1.14, 3.32)
NPV= 2637/2649=99.55% (95% CI: 99.21, 99.74)	NPV= 2309/2319=99.57% (95% CI: 99.21, 99.77)
Cumulative Incidence $_{IGRA+}$ = 11/317=3.47% (95% CI: 1.87, 6.17)	Cumulative Incidence $_{TST+}$ = 13/663=1.96% (95% CI: 1.11, 3.36)
Cumulative Incidence $_{IGRA-}$ = 12/2649=0.45% (95% CI: 0.24, 0.79)	Cumulative Incidence $_{TST-}$ = 10/2319=0.43% (95% CI: 0.22, 0.80)
Cumulative Incidence Ratio $_{IGRA}$ =7.66 (95% CI: 3.41, 17.21)	Cumulative Incidence Ratio $_{TST}$ =4.55 (95% CI: 2.00, 10.32)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$= NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$= NR
Other reported measure $_{IGRA}$ =OR=7.90 (95% CI: 3.46, 18.06)	Other reported measure $_{TST}$ = OR=4.62 (95% CI: 2.02, 10.58)

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios=1.68 (95% CI: 0.94, 3.03)
Ratio of incidence density rate ratios=NA
Other reported measure= OR = 1.71 (95% CI: 0.94, 3.11)

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-GIT)				TST≥15mm			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	11	306	317	TST +	13	218	231
IGRA -	12	2637	2649	TST -	10	2741	2751
indeterminate	NR	NR	16	indeterminate	0	0	0
Total	23	2943	2966	Total	23	2959	2982

Test performance parameters

IGRA	TST
Sensitivity = 11/23=47.83% (95% CI: 29.24, 67.04)	Sensitivity =13/23=56.52% (95% CI: 36.81, 74.37)
Specificity = 2637/2943=89.6% (95% CI: 88.45, 90.65)	Specificity = 2741/2959=92.63% (95% CI: 91.64, 93.52)
PPV= 11/317=3.47% (95% CI: 1.94, 6.10)	PPV= 13/231=5.62% (95% CI: 3.31, 9.38)
NPV= 2637/2649=99.55% (95% CI: 99.21, 99.74)	NPV= 2741/2751=99.64% (95% CI: 99.33, 99.80)

Cumulative Incidence IGRA+ = 11/317=3.47% (95% CI: 1.87, 6.17)	Cumulative Incidence $_{TST+}$ = 13/231=5.62% (95% CI: 3.23, 9.47)
Cumulative Incidence IGRA- = 12/2649=0.45% (95% CI: 0.24, 0.79)	Cumulative Incidence $_{TST-}$ = 10/2741=0.36% (95% CI: 0.18, 0.67)
Cumulative Incidence Ratio IGRA =7.66 (95% CI: 3.41, 17.21)	Cumulative Incidence Ratio $_{TST}$ =15.48 (95% CI: 6.86, 34.92)
Incidence density rate IGRA+ = NR	Incidence density rate $_{TST+}$= NR
Incidence density rate IGRA- = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio IGRA = NR	Incidence density rate ratio $_{TST}$= NR
Other reported measure IGRA =OR=7.90 (95% CI: 3.46, 18.06)	Other reported measure $_{TST}$ = OR=16.35 (95% CI: 7.08, 37.71)

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios=0.49 (95% CI: 0.28, 0.89)
Ratio of incidence density rate ratios=NA
Other reported measure= 0.48 (95% CI: 0.27, 0.88)

Association between test results and levels of TB exposure (if applicable)

IGRA (specify)				**TST (specify)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (specify)				**TST (specify)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA
OR (regression-based; reported) $_{IGRA}$ = NA List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA List of covariates: NA

Other reported measure = NA	Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST ≥10mm	TST -	Total
IGRA +	231	86	317
IGRA -	430	2,219	2,649
indeterminate	2	14	16
Total	663	2,319	2982

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥10mm

Parameters

Kappa = 0.38 (95% CI: 0.342, 0.424)

% concordance = [231+2,219]/2,966 = 82.6% (95% CI: 81.2, 83.92)

% discordance = [430+86]/2,966 = 17.4% (95% CI: 16.08, 18.80)

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST ≥15mm	TST -	Total
IGRA +	163	154	317
IGRA -	68	2,581	2,649
indeterminate	0	16	16
Total	231	2,751	2,982

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥15mm

Parameters

Kappa = 0.55 (95% CI: 0.50, 0.61)

% concordance = [163+2581]/2,966 = 92.52% (95% CI: 91.51, 93.41)

% discordance = [68+154]/2,966 = 7.48% (95% CI: 6.59, 8.48)

Stratification (specify group 1):

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA

TST + threshold: NA

Parameters

Kappa = NA

% concordance = NA

% discordance = NA

Stratification (specify group 2):

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA

TST + threshold: NA

Parameters
Kappa = NA
% concordance = NA
% discordance = NA
Conclusions
Authors:
TST at 15 mm had a higher OR for the development of active tuberculosis compared to TST 10mm and QFT-GIT. The agreement between TST and QFT was better when TST had 15 mm threshold
Reviewers:
Children testing positive on both tests had a greater risk of developing active TB; TST at 15mm performed better in diagnosing LTBI compared to TST 10mm or QFT-GIT; TST 15mm agreed with QFT GIT better than TST 10 mm
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation

Immunocompromised

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Ahmadinejad 2013[120]
Country: Iran
Study design: Cross sectional/retrospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Tertiary care teaching hospital
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Tehran University of Medical Sciences and Health Services grant

Aim of the study

To compare the QFT and TST in diagnosis of LTBI in solid organ transplant (SOT) candidates (kidney, liver, lung)

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (SOT candidates**:** kidney, liver, lung)

Participants

Recruitment dates: March 2008 through September 2011
Total N of recruited patients: 187
Inclusion criteria: SOT candidates who were referred to the transplant clinic
Exclusion criteria: (i) failure to return to the clinic for reading the results of TST within 5 days of the initial intradermal injection, or (ii) unwillingness to continue the study at any stage
Total N of excluded patients: 23 (dropouts)
Total N of patients tested with both IGRA and TST: 164
Total N of patients with valid results for both IGRA and TST:TST (n = 164), IGRA (n = 159)
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Agreement/disagreement, association between test results and exposure to active TB
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 39.9 (12.7) yrs
Women (n [%]): 76 [46.3]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 151 [92.1]
History of anti-TB treatment (n [%]): 1/164 [0.6]
Total incidence of active TB (n [%]): 1/164 [0.6]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): End-stage renal disease (64 [39.0]), chronic hepatic failure (97 [59.2]), Pulmonary failure (3 [1.8])
Co-morbidity (n [%]): NA
Type of during-study treatment (n [%]): Patients with positive TST received chemoprophylaxis with 300 mg isoniazid for 9 months; immunosuppressive medication (24 [14.6])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	164	33	126	5	159
TST:	164	26	138	0	164
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 164	
Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	No history of exposure to active TB
Exposed 1 **(specify):**	Exposure history to active TB
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA (QFT-GIT)	QuantiFERON-TB Gold In-Tube test (QFT-GiT) Blood sample of 3 mL was obtained, and 1 mL was added to each of the 3 tubes designated as the nil, mitogen, and antigen tubes. After vigorous shaking of the tubes, they were sent to the laboratory up to 6 h after acquisition The tubes were reshaken and incubated for 24 h at 37°C. Then the samples were centrifuged at 2000–3000 RCF rate for 15 min, and the resulting plasma samples were kept at >70°C for the measurement of interferon-gamma (IFN-c) with enzyme-linked immunosorbant assay (ELISA)	NR	For prevention of potential boosting effect of TST on QFT, blood sampling and purified protein derivative (PPD) injection were done simultaneously for all patients
TST	0.1 mL from 5 tuberculin units of PPD solution was injected intradermally 2–4 inches (~5–10 cm) lower than the elbow, with an angle of about 5–15 degrees, and the induration size was measured after 48–72h	If the induration is ≥10 mm in largest diameter, the test was considered positive	

Association between test results and incidence of active TB (if applicable)

IGRA				TST			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA

Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA

Ratio of incidence density rate ratios = NA

Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	0	33	33	TST +	0	26	26
IGRA -	5	121	126	TST -	5	133	138
Indeterminate	0	5	5	Indeterminate	0	0	0
Total	5	159	164	Total	5	159	164

Test performance parameters

IGRA	**TST**
Sensitivity = 0/5 = 0.00%	Sensitivity = 0/5 = 0.00%
Indeterminate excluded Specificity = 121/154 = 78.57% (95% CI: 71.44, 84.32) **Indeterminate included** Specificity = 126/159 = 79.25% (95% CI: 72.29, 84.82)	Specificity = 133/159 = 83.65% (95% CI: 77.12, 88.59)
PPV = 0/33 = 0.00%	PPV = 0/26 = 0.00%
Indeterminate excluded NPV = 121/126 = 96.03% (95% CI: 91.05, 98.29) **Indeterminate included** NPV = 126/131 = 96.18% (95% CI: 91.38, 98.36)	NPV = 133/138 = 96.38% (95% CI: 91.8, 98.44)
DOR (for T^+ calculated) = 0.00	DOR (for T^+ calculated) = 0.00
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates:	OR (regression-based; reported) = NR List of covariates:
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA

Ratio of OR (crude; for T^+ reported) = NR

Ratio of ORs (regression-based; reported) = NR

Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	28	5	33	TST +	23	3	26
IGRA -	118	8	126	TST -	128	10	138
Indeterminate	5	0	5	Indeterminate	0	0	0
Total	151	13	164	Total	151	13	164

Test performance parameters

IGRA	**TST**

DOR (for T^+ calculated)$_{IGRA}$ = 0.38 (95% CI: 0.11, 1.24)	DOR (for T+ calculated)$_{TST}$ = 0.60 (95% CI: 0.15, 2.34)
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	13	20	33
IGRA -	12	114	126
Indeterminate	1	4	5
Total	26	138	164

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥10mm

Parameters

Indeterminate excluded
Kappa = 0.32 (95% CI: 0.17, 0.48)
Indeterminate included
Kappa = 0.32 (95% CI: 0.17, 0.47)

Indeterminate excluded
% concordance = 127/159 = 79.87% (95% CI: 72.97, 85.37)
Indeterminate included
% concordance = 131/164 = 79.88% (95% CI: 73.09, 85.3)

% discordance = 20.13% (95% CI: 14.63, 27.03)

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
Considering the fair overall agreement between the 2 tests, and greater ease of the QFT from the patient's point of view, QFT is recommended for detection of LTBI in SOT candidates		
Reviewers:		
The tests performed similarly in relation to construct of validity (exposure to active TB) in terms of sensitivity (low), specificity (high), DOR (low), and NPV (high); agreement between the tests was fair (0.32); neither test was influenced by BCG status		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Al Jahdali 2013[121]
Country: Saudi Arabia
Study design: retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** outpatient hemodialysis unit hospital-based
Number of centres: one
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** No funding sources

Aim of the study

To compare the performance of the QTF-GIT test and the TST for detecting LTBI among hemodialysis patients and to investigate the agreement between these 2 tests in the detection of tuberculosis infection in a population showing an intermediate TB prevalence

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (hemodialysis patients)

Participants

Recruitment dates: August to December 2010
Total N of recruited patients: 215
Inclusion criteria: Hemodialysis patients
Exclusion criteria: NR
Total N of excluded patients: 15 (active TB)
Total N of patients tested with both IGRA and TST: 215
Total N of patients with valid results for both IGRA and TST: 200
Methods of active TB diagnosis (if applicable): positive tuberculosis culture or biopsy showing granuloma and good response to anti-tuberculosis therapy
Outcomes (study-based) list: test result association with construct of validity (high likelihood of LTBI) and between-test agreement
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 58.42 (17.65) yrs
Women (n [%]):103 [51.5]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 28 [14.0]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Hemodialysis patients
Co-morbidity (n [%]): diabetic nephropathy (127 [63.5]), kidney transplant failed (21 [10.5]), NR (52 [26.0])
Type of during-study treatment (n [%]): Immunosuppressant in the last 12mo (2 [1.0])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	NR	65	135	NR	200
TST (≥10mm):	NR	26	174	NR	200
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 200

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group - High likelihood of LTBI	
Non-exposed	No high likelihood of LTBI
Exposed 1 **(specify):**	High likelihood of LTBI (contact with TB case, abnormal chest X-ray, DM, immunosuppressant in the last 12 M, failed kidney transplant or BMI≤20)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA	Test was performed according to the manufacturer's instructions. One ml of whole blood was collected in each of 3 separate test tubes: 1 containing no antigen (nil control), 1 with a mitogen (phytohemagglutinin, positive control) and 1 with TB antigens (ESAT-6, CFP-10 and TB7.7). The 3 tubes were incubated overnight for 18-20 h at 37 ◦C. Following incubation, the tubes were centrifuged, and the plasma was removed from each tube and frozen at −20 ◦C. Measurement of IFN-γ via ELISA was subsequently performed in batch testing	A value of 0.35 IU/ml or more for the relationship ([IFN-γ in the TB antigen tube] − [IFN-γ in the negative control tube]) was considered to be a positive result. If the IFN- γ level was <0.35 IU/ml in the TB antigen tube and the mitogen control was positive (≥0.5 IU/ml), the test was recorded as negative	IGRA blood was collected before the administration of the TST
TST	The TST employed in this study was Tubersol —Tuberculin Purified Protein Derivative (Mantoux), 5 TU per 0.1 ml, test manufactured by Sanofi Pasteur Limited, Toronto, Ontario, Canada. A trained and experienced public health nurse performed all TSTs. Five tuberculin units (0.1 ml) of the purified protein derivative (PPD) were administered via intradermal injection on the volar surface of the forearm that did not have the arteriovenous vessel. The responses were read within 72 h by the same nurse, usually during the next regularly scheduled HD visit	An induration of 10mm or more in transverse diameter was used as the threshold to classify the test results as positive for LTBI. Patients with an induration of less than 10mm upon initial testing were considered to be negative and were administered a second TST within 3—6 weeks to elicit a potential booster response. The results obtained from the 2-step testing were used in all further analyses. The TST was considered to be positive if either the 1st or 2nd test showed a response of 10mm or more	NA

Association between test results and incidence of active TB (if applicable)

IGRA				TST			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA

IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	51	14	65	TST +	19	7	26
IGRA -	103	32	135	TST -	135	39	174
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	154	46	200	Total	154	46	200

Test performance parameters	
IGRA	**TST**
Sensitivity = 51/154 = 33.12% (95% CI: 26.00, 41.00)	Sensitivity = 19/154 = 12.34% (95% CI: 8.04, 18.47)
Specificity = 32/46 = 69.57% (95% CI: 55.19, 80.92)	Specificity = 39/46 = 84.78% (95% CI: 71.78, 92.43)
PPV = 51/65 = 78.46% (95% CI: 67.03, 86.71)	PPV = 19/26 = 73.08% (95% CI: 53.92, 86.3)
NPV = 32/135 = 23.70% (95% CI: 17.32, 31.54)	NPV = 39/174 = 22.41% (95% CI: 16.85, 29.17)
DOR (for T+ calculated) = 1.13 (95% CI: 0.55, 2.31)	DOR (for T^+ calculated) = 0.78 (95% CI: 0.31, 2.00)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates:	OR (regression-based; reported) = NR List of covariates:
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 1.45 (95% CI: 0.79, 2.64)
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = NR
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR

IGRA -	NR	NR	NR	TST -	NR	NR	NR
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample			
	TST +	TST -	Total
IGRA +	21	44	65
IGRA -	5	130	135
indeterminate	NR	NR	NR
Total	26	174	200
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.34 (95% CI: 0.22, 0.45)			
% concordance = 151/200 = 75.50% (95% CI: 69.10, 80.94)			
% discordance = 49/200 = 24.5% (95% CI: 19.06, 30.90)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if	**Adverse events n/N (%)**	**Health related quality**

applicable)	(specify)	of life mean score (SD) (specify)
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
The discriminatory ability of the QTF-G test is superior to that of the TST. The QTFG test was more sensitive but less specific than the TST in predicting LTBI		
Reviewers:		
There was fair agreement between the tests (k = 0.34); In general, QFT-GIT performed better than TST in terms of sensitivity; specificity was higher for TST vs. QFT-GIT		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Ates 2009[122]
Country: Turkey
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Outpatient hemodialysis hospital centers
Number of centres: 5
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Grant from University of Dicle

Aim of the study

To assess the efficacy of QTF-GIT test for detection of LTBI and determine the degree of agreement between the results of TST and QTFGIT tests in hemodialysis patients

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (hemodialysis patients)

Participants

Recruitment dates: March 15 and April 15 of 2008
Total N of recruited patients: 290
Inclusion criteria: Hemodialysis patients 18 yrs or older
Exclusion criteria: The patients diagnosed with active tuberculosis and receiving treatment for the last 12 months, or taking immunosuppressive medicine or younger than 18 years old were excluded from the present study
Total N of excluded patients: 15 (rejected tests, improper blood sampling, and unsuccessful phlebotomy)
Total N of patients tested with both IGRA and TST: 275
Total N of patients with valid results for both IGRA and TST: 230
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Agreement, risk factors for positive test
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 51.9 (16.2) yrs
Women (n [%]):137 [50.0]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 134 [48.72]
History of anti-TB treatment (n [%]): 17 [7.4%]
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): hemodialysis
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	275	115	131	29	246
TST (≥10mm):	275	92	167	16	259
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 230

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group

Non-exposed	No Tuberculosis exposure
Exposed 1 **(specify):**	Tuberculosis exposure
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA	The QTF-GIT test was performed in two steps. Whole blood was collected first into each of the QTF-GIT blood collection tubes, consisting of a nil control tube, a tuberculosis antigen tube, and a mitogen tube. The tubes were incubated at 37^{o}C as soon as possible. After a 16-20 hours incubation period, the tubes were centrifuged and the plasma was removed and frozen at -70oC until the ELISA was performed. The ELISA for IFN-g was performed according to manufacturer's specifications and the ELISA readout was analyzed using the QTF-GIT analysis software	According to the QTF-GIT analysis software results were recorded as positive, negative and indeterminate. The whole blood was drawn just before hemodialysis	Observers were blinded to the results of the TST
TST	TST were administered and its results were interpreted in relation to American Thoracic Society Guidelines (1). Briefly, a trained nurse performed one-step tuberculin skin test using the Mantoux technique through the injection of 0.1 ml (5 tuberculin units) of purified protein derivative (PPD; Tween 80, BB-NCIPD Ltd, Sofia, Bulgaria) into the volar surface of the forearm	A skilled nurse measured the transverse axis of indurations with a flexible ruler, and an experienced physician verified all the results. A positive TST result was defined as an induration diameter of 10 mm or larger	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA

Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST≥10mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	10	105	115	TST +	5	87	92
IGRA -	7	124	131	TST -	12	155	167
Indeterminate	NR	NR	29	Indeterminate	NR	NR	16
Total			275	Total			275

Test performance parameters

IGRA	**TST**
Sensitivity = 10/17 = 58.82% (95% CI: 36.01, 78.39)	Sensitivity = 5/17 = 29.41% (95% CI: 13.28, 53.13)
Specificity = 124/229 = 54.15% (95% CI: 47.68, 60.48)	Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)
PPV = 10/115 = 8.69% (95% CI: 4.792, 15.27)	PPV = 5/92 = 5.43% (95% CI: 2.34, 12.10)
NPV = 124/131 = 94.66% (95% CI: 89.38, 97.39)	NPV = 155/167 = 92.81% (95% CI: 87.86, 95.84)
DOR (for T^+ calculated) = 1.68 (95% CI: 0.62, 4.58)	DOR (for T^+ calculated) = 0.74 (95% CI: 0.25, 2.17)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 1.30 (0.43, 3.91) List of covariates: NR	OR (regression-based; reported) = 0.49 (0.17, 1.45) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 2.27 (95% CI: 1.07, 4.81)
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = 2.65 (95% CI: 1.21, 5.82)
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	57	58	115	TST +	45	47	92
IGRA -	61	70	131	TST -	88	79	167
Indeterminate	NR	NR	29	Indeterminate	NR	NR	16
Total			275	Total			275

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 1.13 (95% CI: 0.68, 1.86)	DOR (for T+ calculated)$_{TST}$ = 0.85 (95% CI: 0.51, 1.43)
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = 1.14 (95% CI: 0.68, 1.92) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 0.87 (95% CI: 0.50, 1.51) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)

This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition			
Total sample			
	TST +	TST -	Total
IGRA +	58	49	107
IGRA -	25	98	123
indeterminate	NR	NR	29
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.34 (95% CI: 0.21, 0.47)			
% concordance = 156/230 = 67.83% (95% CI: 61.54, 73.53)			
% discordance = 74/230 = 32.17% (95% CI: 26.47, 38.46)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
QTF-GIT is more sensitive than TST in the detection of LTBI among renal dialysis patients; both QTF-GIT and TST results were not correlated with contact to the patients with tuberculosis; we observed no association among the results of both TST & QTF-GIT and BCG vaccination status; agreement between tests was fair (k = 0.34)

Reviewers:
See above
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details
First author surname year of publication: Casas 2011a[123] **Country:** Spain **Study design:** Retrospective cohort/cross-sectional study **Study setting** (e.g., outbreak investigation, community-based - specify)**:** Outpatient clinics **Number of centres:** 4 **Total length of follow up (if applicable):** NA **Funding** (government/private/manufacturer/other - specify)**:** The first author received research grant from the University Barcelona (October 2006–January 2010). This study was supported by the Ministerio de Sanidad y Consumo, Instituto de Salud Carlos III-FEDER, Spanish Network for the Research in Infectious Diseases (REIPI RD06/0008)
Aim of the study
To assess the prevalence of LTBI obtained by the whole blood-based QFT-GIT and TST in patients with IMID, and second, to determine whether QFT-GIT performs in the same way as in healthy people
Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)
Immunocompromised people (immune-mediated inflammatory diseases [IMID] before anti–TNF-α therapy)
Participants
Recruitment dates: NR **Total N of recruited patients:** 323 **Inclusion criteria:** Patients with immune-mediated inflammatory diseases (IMID) before anti–TNF-α therapy **Exclusion criteria:** NR **Total N of excluded patients:** n = 9 (no IMID: n = 2 and problems with QFT-GIT plasma sample storage: n = 7) **Total N of patients tested with both IGRA and TST:** 323 **Total N of patients with valid results for both IGRA and TST:** 314 (214 IMID and 100 healthy controls) **Methods of active TB diagnosis (if applicable):** NR **Outcomes (study-based) list:** Associations between test positivity and risk factors of LTBI, BCG status, type of treatment; agreement; influence of risk factors on indeterminate results **Characteristics of participants (total study sample)** Mean (range or SD) age (years): 49.1 (12.9) Women (n [%]): 109 [50.9] Race/ethnicity (n [%]): NR Geographic origin (n[%]): Born in a high TB incidence country (16 [7.5]) BCG vaccination (n [%]): 56 [26.2] History of anti-TB treatment (n [%]): NR Total incidence of active TB (n [%]): NA Chest radiography (yes/no): NR Clinical examination (yes/no): NR Morbidity (n [%]): Rheumatoid arthritis (91 [42.5]); Cutaneous psoriasis (57 [26.6]); Spondylarthropathies (29 [13.6]); Psoriatic arthropathy (21 [9.8]); Inflammatory bowel disease (14 [6.5]); Others (2 [0.9]) Co-morbidity (n [%]): NR Type of during-study treatment (n [%]): Immunosuppressive treatment (163 [76.2]); Corticosteroids (91 [42.5]); Methotrexate (91 [42.5]); Leflunomide (36 [16.8]); Cyclosporine A (22 [10.3]); azathioprine/efalizumab (13 [6.1])
Number of patients tested

	Total N	**Total**	**Total N**	**Total N**	**Total N**

	(tested)	N (test+)	(test-)	(indeterminate)	(test results available)
IGRA (QFT-GIT):	214	45	157	12	214
TST (≥5 mm):	214	52	162	0	214
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 214

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group - risk factors for TB infection	
Non-exposed	No risk factors for TB infection
Exposed 1 **(specify):**	Risk factors for TB infection (birth or residence for ≥6 months in a high TB incidence country, TB contact, prior prison stay, intravenous drug abuse, health care worker, abnormal chest X-ray, and history of past TB)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QuantiFERON®-TB Gold in-Tube test samples were collected just before TST was performed (Nil, TB-antigens [ESAT-6, CFP-10 and TB-7.7] and phytohemagglutinin [PHA] tubes). All plasma samples were stored and analyzed in the Mycobacterial Laboratory (Clinical Microbiology Department) in accordance with the manufacturer's instructions	According to manufacturer QFT-GIT results could be positive, negative, or indeterminate depending on the IFN-γ production. Plasma samples with indeterminate results were retested	NA
TST	TST was performed according to the Mantoux method using 2 U of tuberculin RT-23 (Statens Serum Institute, Copenhagen, Denmark)	TST was administered and read by experienced staff following the standard protocol (in the left forearm and transverse diameter measurement). Any induration of ≥5 mm at 48–72 h was considered as positive	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA

Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥5mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	45	TST +	NR	NR	52
IGRA -	NR	NR	157	TST -	NR	NR	162
indeterminate	NR	NR	12	indeterminate	0	0	0
Total	NR	NR	214	Total	NR	NR	214

Test performance parameters

IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = 2.50 (95% CI: 1.20, 5.10)	OR (crude; for T^+ reported) = 2.80 (95% CI: 1.40, 5.50)
OR (regression-based; reported) = 2.90 (95% CI: 1.30, 6.30) List of covariates: age, gender, BCG vaccination, and immunosuppressive treatment	OR (regression-based; reported) = 2.90 (95% CI: 1.40, 6.00) List of covariates: age, gender, BCG vaccination, and immunosuppressive treatment
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 0.89 (95% CI: 0.54, 1.48)
Ratio of ORs (regression-based; reported) = 1.00 (95% CI: 0.58, 1.73)
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST (≥5mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	45	TST +	NR	NR	52
IGRA -	NR	NR	157	TST -	NR	NR	162
indeterminate	NR	NR	12	indeterminate	0	0	0
Total	NR	NR	214	Total	NR	NR	214

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = 1.20 (95% CI: 0.50, 3.20)	OR (crude; for T+ reported) = 1.70 (95% CI: 0.90, 3.40)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = 1.50 (95% CI: 0.70, 3.40)

	List of covariates: age, gender, risk factors for TB, and immunosuppressive treatment
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	32	13	45
IGRA -	19	138	157
indeterminate	1 (excluded)	11 (excluded)	12 (excluded)
Total	51	151	202
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total (IMID n = 202)			
TST + threshold: ≥5mm			
Parameters			
Kappa = 0.56 (95% CI: 0.42, 0.70)			
% concordance = 170/202 = 84.16% (95% CI: 78.49, 88.55)			
% discordance = 32/202 = 15.84% (95% CI: 11.45, 21.51)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		

Reviewers:
Association between immunosuppression therapy and TST positivity (adjusted OR, 0.50, 95% CI 0.24, 1.04; P = 0.07) was lower compared with that for QFT-GIT positivity (adjusted OR 0.53, 95% CI 0.24, 1.19); similar results in corticosteroid users (OR for TST was lower than OR for QFT); immunosuppression therapy was a predictor of indeterminate results (OR 4.87, 95% CI 1.05, 22.60); agreement was 0.56; there was no association between test positivity (for QFT or TST) and BCG status (no influence of BCG status on test positivity); TST and QFT had a similar association with risk of LTBI (risk factor for TB)
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details
First author surname year of publication: Casas 2011b[124] **Country:** Spain **Study design:** Retrospective/cross-sectional study **Study setting** (e.g., outbreak investigation, community-based - specify)**:** hospital-based **Number of centres:** one **Total length of follow up (if applicable):** NA **Funding** (government/private/manufacturer/other - specify) grants from the Spanish Ministry for Health and Consumer Affairs and the Carlos III Health Institute through the Fund for Health Investigations (PI070810, 2007-2010) and from the Carlos III Health Institute and Spanish Federation for Rare Diseases through the Spanish Network for Research in Infectious Diseases; research grant from the University of Barcelona
Aim of the study
To compare the performance of the TST and the QuantiFERON-TB Gold In-Tube (QFT-IT) test (a commercially available, whole blood–based IGRA) in detecting latent TB infection in patients with end-stage liver disease (ESLD) requiring liver transplant (LT)
Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)
Immunocompromised people: ESLD patients requiring LT
Participants
Recruitment dates: From July 2008 to July 2010 **Total N of recruited patients:** 110 **Inclusion criteria:** All patients with ESLD who were being considered for LT were invited to participate in the study **Exclusion criteria:** Patients younger than 18 years, patients with a previous history of TB, patients who had recently been tested with the TST, and patients with known immunosuppressive conditions **Total N of excluded patients:** 15 (previous TB infection, HIV, dropouts, anti-TNF-alpha agents, incomplete IGRA results) **Total N of patients tested with both IGRA and TST:** 95 **Total N of patients with valid results for both IGRA and TST:** 95 **Methods of active TB diagnosis (if applicable):** all patients underwent a chest x-ray examination; the findings were defined as normal or abnormal according to the presence or absence of lesions suggestive of past TB **Outcomes (study-based) list:** associations between test positivity and risk factors of LTBI, BCG status, agreement **Characteristics of participants (total study sample)** Mean (range or SD) age (years): 56.4 (7.6) Women (n [%]): 23 [24.2] Race/ethnicity (n [%]): Spanish (89 [93.7]) Geographic origin (n[%]): Born or residing in a country with a high TB burden (6 [6.3]) BCG vaccination (n [%]): 30 [31.6] History of anti-TB treatment (n [%]): None Total incidence of active TB (n [%]): NA Chest radiography (yes/no): Yes Clinical examination (yes/no): NR Morbidity (n [%]): Cirrhosis (52 [54.7]), hepatocellular carcinoma (35 [36.8]), and other hepatopathies (8 [8.4]) Co-morbidity (n [%]): Diabetes mellitus 28 [29.5], chronic pulmonary obstructive disease 3 (3.2), renal failure 12 [12.6] Type of during-study treatment (n [%]): NR
Number of patients tested

	Total N	**Total**	**Total N**	**Total N**	**Total N**

	(tested)	N (test+)	(test-)	(indeterminate)	(test results available)
IGRA (QFT-GIT):	95	42	51	2	95
TST (2 step; ≥5mm):	95	44	51	0	95
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 95

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group - risk factors for TB	
Non-exposed	No risk factors for TB
Exposed 1 **(specify):**	Risk factors for TB (previous contact with TB, abnormal chest x-rays, birth or prolonged residence in a country with a high TB burden, alcoholism, drug abuse, a previous stay in prison, and involvement with health care)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	The QFT-IT test was performed in accordance with the manufacturer's instructions. Briefly, 3 tubes with 1 mL of whole blood were filled for each patient**:** a tube with no antigens (the nil tube), a tube with M. tuberculosis–specific antigens, and a tube with phytohemagglutinin (the mitogen tube). The blood samples were stored and analyzed at the Mycobacterial Laboratory. The blood samples for QFT-IT testing were collected immediately before the TST was performed	Results were scored as positive [interferon-c level ≥0.35 IU/mL (the M. tuberculosis–specific antigen tube minus the nil tube)], negative [interferon-c level < 0.35 IU/mL (the M. tuberculosis–specific antigen tube minus the nil tube)], or indeterminate [interferon-c level < 0.5 (the mitogen tube minus the nil tube) or > 8.0 IU/mL (the nil tube)] according to the production of interferon-c. Plasma samples with indeterminate results were retested	NA
TST (2 step; ≥ 5 mm)	The TST was performed in the left forearm according to the Mantoux method with purified protein derivative RT-23 (2 U/0.1 mL; Statens Serum Institute, Copenhagen, Denmark). In all cases, the TST was administered and evaluated by experienced staff. If the result for the first test was negative, the test was administered again 7 to 10 days later (the 2-step TST), and that result was considered definitive	Any induration ≥ 5 mm at 48 to 72 hours was considered a positive result in accordance with the national transplant guidelines	NA

Association between test results and incidence of active TB (if applicable)

IGRA			**TST**		
	Incidence	Total		Incidence of	Total

	of active TB				active TB		
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (2 step; ≥ 5 mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	27	15	42	TST +	30	14	44
IGRA -	33	20	53	TST -	30	21	51
Indeterminate	NR	NR	2 (excluded)	Indeterminate	0	0	0
Total	60	35	95	Total	60	35	95

Test performance parameters	
IGRA	**TST**
Sensitivity = 27/60 = 45.00% (95% CI: 33.09, 57.51)	Sensitivity = 30/60 = 50.00% (95% CI: 37.73, 62.27)
Specificity = 20/35 = 57.14% (95% CI: 40.86, 72.02)	Specificity = 21/35 = 60.00% (95% CI: 43.57, 74.45)
PPV = 27/42 = 64.29% (95% CI: 49.17, 77.01)	PPV = 30/44 = 68.18% (95% CI: 53.44, 80.00)
NPV = 20/53 = 37.74% (95% CI: 25.94, 51.19)	NPV = 21/51 = 41.18% (95% CI: 28.75, 54.83)
DOR (for T^+ calculated) = 1.01 (95% CI: 0.47, 2.52)	DOR (for T^+ calculated) = 1.50 (95% CI: 0.64, 3.49)
OR (crude; for T^+ reported) = 1.66 (95% CI: 0.66, 3.33)	OR (crude; for T^+ reported) = 1.25 (95% CI: 0.50, 2.50)
OR (regression-based; reported) = 1.50 (95% CI: 0.50, 4.10) List of covariates: age, sex, albumin, BCG status, Model for End-Stage Liver Disease (MELD) score	OR (regression-based; reported) = 1.80 (95% CI: 0.60, 5.10) List of covariates: age, sex, albumin, BCG status, Model for End-Stage Liver Disease (MELD) score
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 0.67 (95% CI: 0.37, 1.24)

Ratio of OR (crude; for T^+ reported) = 1.33 (95% CI: 0.74, 2.38)							
Ratio of ORs (regression-based; reported) = 0.83 (95% CI: 0.39, 1.79)							
Other reported measure = NR							
Association between test results and BCG status (if applicable)							
IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	11	31	42	TST +	13	31	44
IGRA -	19	34	53	TST -	17	34	51
Indeterminate	NR	NR	2 (excluded)	Indeterminate	0	0	0
Total	30	65	95	Total	30	65	95
Test performance parameters							
IGRA				**TST**			
DOR (for T^+ calculated)$_{IGRA}$ = 0.63 (95% CI: 0.26, 1.54)				DOR (for T+ calculated)$_{TST}$ = 0.83 (95% CI: 0.35, 2.00)			
OR (crude; for T^+ reported) = 0.62 (95% CI: 0.26, 1.42)				OR (crude; for T+ reported) = 0.83 (95% CI: 0.35, 2.00)			
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA				OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA			
Other reported measure = NR				Other reported measure = NR			
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**							
Total sample							
	TST +		TST -			Total	
IGRA +	33		9			42	
IGRA -	11		42			53	
Indeterminate	NR		NR			2 (excluded)	
Total	44		51			95	
Description							
Sample definition (e.g., total, if stratified by BCG or condition – specify): total							
TST + threshold: ≥ 5 mm							
Parameters							
Kappa = 0.57 (95% CI: 0.37, 0.77)							
% concordance = 75/95 = 78.95% (95% CI: 69.71, 85.94)							
% discordance = 20/95 = 36.36% (95% CI: 24.93, 49.58)							
Stratification (specify group 1)							
	TST +		TST -			Total	
IGRA +	NR		NR			NR	
IGRA -	NR		NR			NR	
Indeterminate	NR		NR			NR	
Total	NR		NR			NR	
Description							
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR							
TST + threshold NR							
Parameters							
Kappa = NR							
% concordance = NR							
% discordance = NR							
Stratification (specify group 2)							
	TST +		TST -			Total	
IGRA +	NR		NR			NR	
IGRA -	NR		NR			NR	

Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Other outcomes			
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**		**Health related quality of life mean score (SD) (specify)**
IGRA:	NR		NR
TST:	NR		NR
Test 3 (specify):	NR		NR
Conclusions			
Authors:			
We conclude that the QFT-IT test and the TST detect latent TB infection at similar rates in patients with ESLD who require LT, but the QFT-IT test performs better in patients with more severe liver disease			
Reviewers:			
No difference in performance of the two tests irrespective of disease severity; however, in patients with more severe disease (MELD =>18), the QFT positivity rates were higher (OR = 0.20, 95% CI: 0.04, 0.70) compared to TST positivity rates (OR = 0.80, 95% CI: 0.20, 2.80)			
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation			

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Chkhartishvili 2013[125]
Country: Georgia
Study design: Retrospective/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** National referral institution for HIV diagnosis, treatment and care
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** the U.S. Civilian Research and Development Foundation (CRDF) award; the NIH/FIC through the Emory AIDS International Training and Research Program award and the Emory-Georgia Tuberculosis Research Training Program award

Aim of the study

To assess the performance of two commercially available IGRAs (QuantiFERON-TB Gold in Tube [QFT-GIT] and TSPOT. TB [TSPOT]) compared to the TST for the diagnosis of LTBI in HIV-infected patients, and to identify risk factors for LTBI in effort to improve the TB prevention and care among HIV patients

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people: HIV patients

Participants

Recruitment dates: November 2009 and June 2011
Total N of recruited patients: NR
Inclusion criteria: Age ≥18 years old, confirmed HIV infection, and ability to provide written informed consent
Exclusion criteria: Patients with a history of active TB disease
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 240 (QFT, TST), 238 (TSPOT)
Total N of patients with valid results for both IGRA and TST: 237 (QFT), 238 (TST), 218 (TSPOT)
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Agreement, test positivity and risk factor association
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median 38.0 (range 32.8-43.8)
Women (n [%]): 81 [33.75]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 219 [94%]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): NR
Clinical examination (yes/no): NR
Morbidity (n [%]): HIV
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT)	240	70	167	3	237
IGRA (TSPOT)	240	56	162	22	218

TST (≥ 5 mm)	240	41	195	4	236

Total N of patients with valid results for both IGRA and TST: 240	
Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group - Household Member treated for TB	
Non-exposed	No household member treated for TB
Exposed 1 **(specify):**	Household member treated for TB
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Each participant had approximately 12 ml of blood drawn, which was performed according to the manufacturer's instructions	the QFT-GIT result was considered positive if the interferon-gamma response to TB antigens minus the negative control was ≥ 0.35 IU/ml and also > 25% of the negative control; negative if these criteria were not met; and indeterminate if either the negative control had a result of > 8 IU/ml or the positive control had a result of < 0.5 IU/ml	Blood was drawn for the IGRAs prior to the placement of the TST
IGRA (TSPOT)	Each participant had approximately 12 ml of blood drawn, which was performed according to the manufacturer's instructions	For TSPOT 250,000 peripheral blood mononuclear cells (PBMCs) were isolated and plated per well: a nil control, a positive control containing phytohemagglutinin and TB specific antigens (CFP-10 and ESAT-6). Spot forming units were counted using AID Eli-Spot Reader System (Autoimmun Diagnostika, Germany). The test result was considered reactive if the response to either CFP-10 or ESAT-6 minus the nil control was ≥ 6 spot forming cells, or twice the nil control. The result was considered indeterminate if nil control spot count was > 10 spot forming cells or if the reading in the positive control was < 20 spot forming cells	Blood was drawn for the IGRAs prior to the placement of the TST
TST	The TST was performed using the Mantoux method. An intradermal injection of 0.1 ml purified protein derivative was administered into the volar surface of the forearm. The transverse diameter of induration was recorded in millimeters 48–72 hours after administration	An induration of ≥ 5 mm of induration was considered positive	

Association between test results and incidence of active TB (if applicable)

IGRA				TST			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)							
IGRA (QFT-GIT)				**TST ≥ 5 mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	70	TST +	NR	NR	41
IGRA -	NR	NR	167	TST -	NR	NR	195
Indeterminate	NR	NR	3	Indeterminate	NR	NR	4
Total	13	227	240	Total	13	227	240

Test performance parameters	
IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = 0.43 (95% CI: 0.09, 1.97)	OR (crude; for T^+ reported) = 1.48 (95% CI: 0.39, 5.62)
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 0.29 (95% CI: 0.10, 0.82)
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)					
IGRA (TSPOT)			**TST ≥ 5 mm**		
	Exposure level	Total		Exposure level	Total

	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	56	TST +	NR	NR	41
IGRA -	NR	NR	162	TST -	NR	NR	195
Indeterminate	NR	NR	22	Indeterminate	NR	NR	4
Total	13	227	240	Total	13	227	240

Test performance parameters	
IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = 1.48 (95% CI: 0.44, 5.00)	OR (crude; for T^+ reported) = 1.48 (95% CI: 0.39, 5.62)
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 1.00 (95% CI: 0.40, 2.51)
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)							
IGRA (QFT-GIT)				**TST ≥ 5 mm**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	70	TST +	NR	NR	41
IGRA -	NR	NR	167	TST -	NR	NR	195
Indeterminate	NR	NR	3	Indeterminate	NR	NR	4
Total	173	67	240	Total	173	67	240

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = 1.41 (95% CI: 0.38, 5.29)	OR (crude; for T+ reported) = 2.55 (95% CI: 0.32, 20.18)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (TSPOT)				**TST ≥ 5 mm**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	56	TST +	NR	NR	41
IGRA -	NR	NR	162	TST -	NR	NR	195
Indeterminate	NR	NR	22	Indeterminate	NR	NR	4
Total	173	67	240	Total	173	67	240

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = 1.78 (95% CI: 0.38, 8.28)	OR (crude; for T+ reported) = 2.55 (95% CI: 0.32, 20.18)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA

Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + (≥ 5 mm)	TST -	Total
IGRA (QFT-GIT) +	25	44	69
IGRA (QFT-GIT) -	16	148	164
Indeterminate	0	3	3
Total	41	195	236

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): QFT-GIT (total)

TST + threshold: ≥ 5 mm

Parameters

Kappa = 0.30 (95% CI: 0.17, 0.42) calculated – indeterminate excluded
Kappa = 0.29 (95% CI: 0.16, 0.42) reported

% concordance = 173/233 = 74.25% (95% CI: 68.27, 79.44) calculated– indeterminate excluded

% discordance = 60/233 = 25.75% (95% CI: 20.56, 31.73) calculated– indeterminate excluded

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + (≥ 5 mm)	TST -	Total
IGRA (TSPOT) +	20	36	56
IGRA (TSPOT) -	18	143	161
Indeterminate	3	16	19
Total	41	195	236

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): TSPOT (total)

TST + threshold: =>5mm

Parameters

Kappa = 0.27 (95% CI: 0.14, 0.40) calculated – indeterminate excluded
Kappa = 0.22 (95% CI: 0.07, 0.29) reported

% concordance = 163/217 = 75.12% (95% CI: 68.96, 80.4) calculated– indeterminate excluded

% discordance = 54/217 = 24.88% (95% CI: 19.6, 31.04) calculated– indeterminate excluded

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR		
TST + threshold: NR		
Parameters		
Kappa = NR		
% concordance = NR		
% discordance = NR		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
There was very poor agreement among all tests. This lack of agreement makes it difficult to know which test is superior and most appropriate for LTBI testing among HIV-infected patients; Multivariate analysis did not identify one specific population subgroup at higher risk of LTBI		
Reviewers:		
There were no differences in the association between the test results for QFT (or TSPOT) vs. TST and risk of LTBI (exposure measured as household member treated for TB); BCG vaccination status did not appear to influence test positivity for either of the tests; agreement measured with kappa was fair		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Chung 2010a[126]
Country: Korea
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Medical Centre
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** funding from the Gil Medical Centre

Aim of the study

Two IGRAs (QFT-GIT and TSPOT) were simultaneously compared with the TST for their diagnostic efficacy for latent TB infection in Korea, an intermediate TB-burden country

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people - haemodialysis patients with end stage renal disease (ESRD)

Participants

Recruitment dates: 1 March to 30 April 2008
Total N of recruited patients: NR
Inclusion criteria: Hemodialysis patients with ESRD
Exclusion criteria: Those patients who had taken empirical anti-TB medications and patients taking anti-TB medication for active TB infection
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 167 (total), 146 (review-relevant population), 21 (patients with a cured TB infection)
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list:
Characteristics of participants (total study sample): n = 167
Mean (range or SD) age (years): 54.1 (14.4)
Women (n [%]): 71 [42.5]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 111 [67.3]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): ESRD due to Diabetes mellitus (67 [40.1]), Hypertension (18 [10.8]), Glomerulonephritis (12 [7.2]), Others (11 [6.6]), Unknown (59 [35.3])
Co-morbidity (n [%]): History of cancer (12 [7.2]), Cardiac disease (46 [27.5]), Cerebrovascular accident (13 [7.8]), History of TB infection (21 [12.6])
Type of during-study treatment (n [%]): Immunosuppressant medication (9 [5.4])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	NR	56	90	NR (for n = 146)	146
IGRA (TSPOT):	NR	83	63	NR (for n = 146)	146
TST ≥10 mm:	NR	32	114	NR (for n = 146)	146

Total N of patients with valid results for both IGRA and TST: 146

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – High vs. low risk	
Non-exposed	Low risk

Exposed 1 **(specify):**	The high-risk group for latent TB infection consisted of patients with a history of close contact with TB patients, old TB lesions on CXR, or a history of TB infection
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA (QFT-GIT)	Whole blood was extracted just before dialysis for the two IFN-c tests. The QFT-G was performed according to the manufacturer's instructions (Cellestis Ltd., Carnegie, Victoria, Australia)	Results of each test were classified as positive, negative or indeterminate, as previously described	NA
IGRA (TSPOT)	The TSPOT was also performed according to the manufacturer's instructions (Oxford Immunotec, Oxford, UK)	Results of each test were classified as positive, negative or indeterminate, as previously described	NA
TST	Within a week after the IGRAs, 2-TU of purified protein derivative RT23 (Statens Serum Institute, Copenhagen, Denmark) was intradermally injected on the volar side of the forearm contralateral to the patient's vascular access. Two physicians, blind to the patients' clinical information, measured the main diameter of the induration after 48 h independently	The positive criterion was ≥10 mm size of the mean values of two measurements	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)							
Ratio of cumulative incidence ratios = NA							
Ratio of incidence density rate ratios = NA							
Other reported measure = NA							
Association between test results and levels of TB exposure (if applicable)							
IGRA (QFT-GIT)				**TST≥10mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	9	47	56	TST +	2	30	32
IGRA -	8	82	90	TST -	15	99	114
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	17	129	146	Total	17	129	146
Test performance parameters (based on 146 patients; 21 with previous TB excluded)							
IGRA				**TST**			
Sensitivity = 9/17 = 52.94% (95% CI: 30.96, 73.84)				Sensitivity = 2/17 = 11.76% (95% CI: 3.28, 34.34)			
Specificity = 82/129 = 63.57% (95% CI: 54.98, 71.37)				Specificity = 99/129 = 76.74% (95% CI: 68.75, 83.20)			
PPV = 9/56 = 16.07% (95% CI: 8.69, 27.81)				PPV = 2/32 = 6.25% (95% CI: 1.73, 20.15)			
NPV = 82/90 = 91.11% (95% CI: 83.43, 95.43)				NPV = 99/114 = 86.84% (95% CI: 79.42, 91.86)			
DOR (for T^+ calculated) = 1.96 (95% CI: 0.71, 5.43)				DOR (for T^+ calculated) = 0.44 (95% CI: 0.09, 2.03)			
OR (crude; for T^+ reported) = NA (reported only for total sample of 167 patients that included 21 previous TB patients)				OR (crude; for T^+ reported) = NA (reported only for total sample of 167 patients that included 21 previous TB patients)			
OR (regression-based; reported) = NA (reported only for total sample of 167 patients that included 21 previous TB patients) List of covariates: NA				OR (regression-based; reported) = (reported only for total sample of 167 patients that included 21 previous TB patients) List of covariates: NA			
Other reported measure = NR				Other reported measure = NR			
Comparison between tests (IGRA vs. TST)							
Ratio of DORs (for T^+ calculated) = 4.45 (95% CI: 1.72, 11.51)							
Ratio of OR (crude; for T^+ reported) = NA							
Ratio of ORs (regression-based; reported) = NA							
Other reported measure = NA							
Association between test results and levels of TB exposure (if applicable)							
IGRA (TSPOT)				**TST≥10mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	8	75	83	TST +	2	30	32
IGRA -	9	54	63	TST -	15	99	114
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	17	129	146	Total	17	129	146
Test performance parameters (based on 146 patients; 21 with previous TB excluded)							
IGRA				**TST**			
Sensitivity = 8/17 = 47.06% (95% CI: 26.16, 69.04)				Sensitivity = 2/17 = 11.76% (95% CI: 3.28, 34.34)			
Specificity = 54/129 = 41.86% (95% CI: 33.70, 50.49)				Specificity = 99/129 = 76.74% (95% CI: 68.75, 83.20)			
PPV = 8/83 = 9.64% (95% CI: 4.96, 17.88)				PPV = 2/32 = 6.25% (95% CI: 1.73, 20.15)			
NPV = 54/63 = 85.71% (95% CI: 75.03, 92.30)				NPV = 99/114 = 86.84% (95% CI: 79.42, 91.86)			
DOR (for T^+ calculated) = 0.64 (95% CI: 0.23, 1.76)				DOR (for T^+ calculated) = 0.44 (95% CI: 0.09, 2.03)			

OR (crude; for T^+ reported) = NA (reported only for total sample of 167 patients that included 21 previous TB patients)	OR (crude; for T^+ reported) = NA (reported only for total sample of 167 patients that included 21 previous TB patients)
OR (regression-based; reported) = NA (reported only for total sample of 167 patients that included 21 previous TB patients) List of covariates: NA	OR (regression-based; reported) = (reported only for total sample of 167 patients that included 21 previous TB patients) List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 1.45 (95% CI: 0.56, 3.76)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (QFT-G)				**TST ≥10mm**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	47	TST +	NR	NR	30
IGRA -	NR	NR	82	TST -	NR	NR	99
Indeterminate	NR	NR		Indeterminate	NR	NR	
Total	NR	NR	129	Total	NR	NR	129

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NA (reported only for 129 low risk patients that also included 21 previous TB patients)	OR (crude; for T+ reported) = NA (reported only for 129 low risk patients that also included 21 previous TB patients)
OR (regression-based; reported) $_{IGRA}$ = NA (reported only for 129 low risk patients that also included 21 previous TB patients) List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA (reported only for 129 low risk patients that also included 21 previous TB patients) List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	75	TST +	NR	NR	30
IGRA -	NR	NR	54	TST -	NR	NR	99
Indeterminate	NR	NR		Indeterminate	NR	NR	
Total	NR	NR	129	Total	NR	NR	129

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NA (reported only for 129 low risk patients that also included 21 previous TB patients)	OR (crude; for T+ reported) = NA (reported only for 129 low risk patients that also included 21 previous TB patients)
OR (regression-based; reported) $_{IGRA}$ = NA (reported only for 129 low risk patients that also included 21 previous TB patients) List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA (reported only for 129 low risk patients that also included 21 previous TB patients) List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total of 167			
TST + threshold: =>10mm			
Parameters			
Kappa = NA (reported only for total 167 patient sample that included 21 patients with previous TB)			
% concordance = NA			
% discordance = NA			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Previous BCG vaccination increased the TST-positive rate in the low-risk group (OR 4.438), whereas it affected neither QFT nor TSPOT. The QFT was associated with the high-risk group (OR 2.578), whereas the TST and TSPOT were not. The frequency of indeterminate results was higher for the QFT (12.6%) compared with the TSPOT (4.8%). In conclusion, the IGRAs can be useful for the diagnosis of latent TB infection in haemodialysis patients
Reviewers:

The only relevant data available in this study was for the association between test positivity and exposure groups (n = 146; which excluded 21 patients with previous TB). All the other analyses (agreement, BCG status influence) were based on a total sample of 167 patients that included 21 patients with previously cured TB QFT performed better than TST and TSPOT (in DORs) due its higher sensitivity relative to the other tests; TST had better specificity than the two IGRAs
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Costantino 2013[127]
Country: France
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Rheumatology Department of Nancy University Hospital
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** NR

Aim of the study

To compare TST and IGRA results in screening for LTBI in a large population of patients with chronic inflammatory
arthritis requiring biologic treatment and to investigate predictive factors of results of these 2 tests, with special
attention for indeterminate IGRA results

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people: chronic inflammatory arthritis before anti TNF treatment

Participants

Recruitment dates: Between 2005 and 2009
Total N of recruited patients: NR
Inclusion criteria: Patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA)requiring TNF antagonists (first-line therapy or switch)
Exclusion criteria: Patients with previous antituberculous chemoprophylaxis
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 563
Total N of patients with valid results for both IGRA and TST: IGRA (n = 475), TST (n = 514)
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Association between test positivity and conventional risk factors (CRF) of LTBI; agreement; association between test positivity and patient characteristics
Characteristics of participants (total study sample)
Mean (range or SD) age (years)**:** 51.0 (39.0–59.0)
Women (n [%]): 321 [57.0]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): Birth in endemic zone of TB (52 [9.2])
BCG vaccination (n [%]): 439 [78.0]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Rheumatoid arthritis (293 [52.0]), spondyloarthritis (270 [48.0])
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): DMARD (277 [49.2]), Corticosteroids (254 [45.1]), NSAID (255 [45.4])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	563	122	353	88	475
TST (≥ 5 mm):	563	196	318	49	514

Test 3 (specify):	NA	NA	NA	NA	NA
Total N of patients with valid results for both IGRA and TST: 563					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group - conventional risk factors (CRF) of LTBI					
Non-exposed	No CRF of LTBI				
Exposed 1 **(specify)**:	CRF of LTBI: history of active TB treated before 1970 or not treated for at least 6 months including 2 months with a combination of rifampicine and pyrazinamide, close contact with a patient with active TB, and chest radiograph suggestive of previous TB infection				
Exposed 2 **(specify):**	NA				
Exposed 3 **(specify):**	NA				
Exposed 4 **(specify):**	NA				

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (TSPOT)	T-SPOT.TB assays were performed according to the manufacturer's instructions	Assays were considered indeterminate if the negative control (cell suspension in medium alone) spot count yielded more than 10 spots (referred to hereafter as a high nil control) or if the positive control (cell suspension stimulated with phytohemagglutinin) spot count yielded fewer than 20 spots (low positive control). For determinate tests, T-SPOT.TB assays were interpreted according to the manufacturer's recommendations by subtracting the spot count of the negative control from the highest spot count between panels A (TB-specific antigen ESAT-6) and B (TB-specific antigen CFP-10). A test was considered positive if this difference was equal to, or higher than, 6 spots; otherwise, the test was considered negative	To avoid any potential boosting effect of TST on IGRA results, all T-SPOT.TB assays were performed before initiating TST
TST ≥ 5 mm	The TST was performed with 5 tuberculin units corresponding to 0.1 ml of purified protein derivative (Tubertest, Sanofi Pasteur MSD, SNC) according to the Mantoux method. Tuberculin was injected intradermally in the forearm, and 72 h later the diameter of skin induration was recorded	An induration diameter of 5 mm or more was considered a positive test	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA

Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				TST ≥ 5 mm			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	23	99	122	TST +	31	165	196
IGRA -	25	328	353	TST -	18	300	318
Indeterminate	16	72	88	Indeterminate	15	34	49
Total	64	499	563	Total	64	499	563

Test performance parameters	
IGRA	**TST**
Indeterminate included Sensitivity = 23/64 = 35.94% (95% CI: 25.29, 48.18) **Indeterminate excluded** Sensitivity = 23/48 = 47.92% (95% CI: 34.47, 61.67)	**Indeterminate included** Sensitivity = 31/64 = 48.44% (95% CI: 36.63, 60.42) **Indeterminate excluded** Sensitivity = 31/49 = 63.27% (95% CI: 49.27, 75.34)
Indeterminate included Specificity = 400/499 = 80.16% (95% CI: 76.44, 83.42) **Indeterminate excluded** Specificity = 328/427 = 76.81% (95% CI: 72.58, 80.57)	**Indeterminate included** Specificity = 334/499 = 66.93% (95% CI: 62.69, 70.92) **Indeterminate excluded** Specificity = 300/465 = 64.52% (95% CI: 60.06, 68.73)
PPV = 23/122 = 18.85% (95% CI: 12.9, 26.70)	PPV = 31/196 = 15.82% (11.37, 21.58)
Indeterminate included NPV = 400/441 = 90.70% (95% CI: 87.63, 93.07) **Indeterminate excluded** NPV = 328/353 = 92.92% (95% CI: 89.75, 95.16)	**Indeterminate included** NPV = 334/367 = 91.01% (95% CI: 87.64, 93.53) **Indeterminate excluded** NPV = 300/318 = 94.34% (95% CI: 91.23, 96.39)
Indeterminate included DOR (for T^+ calculated) = 2.26 (95% CI: 1.30, 3.95) **Indeterminate excluded**	**Indeterminate included** DOR (for T^+ calculated) = 1.90 (95% CI: 1.12, 3.21) **Indeterminate excluded**

DOR (for T+ calculated) = 3.05 (95% CI: 1.65, 5.60)	DOR (for T+ calculated) = 3.13 (95% CI: 1.70, 5.77)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 2.70 (95% CI: 1.49, 4.89) List of covariates: NR	OR (regression-based; reported) = 1.95 (95% CI: 1.13, 3.36) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 0.97 (95% CI: 0.63, 1.51)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = 1.38 (95% CI: 0.92, 2.09)
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				**TST ≥ 5 mm**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	80	NR	122	TST +	162	NR	196
IGRA -	NR	NR	353	TST -	NR	NR	318
Indeterminate	NR	NR	88	Indeterminate	NR	NR	49
Total	439	124	563	Total	439	124	563

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = 0.39 (95% CI: 0.24, 0.62) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR (p = 0.11, NS) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + ≥ 5 mm	TST -	Total
IGRA (TSPOT) +	59	51	110
IGRA (TSPOT) -	114	220	334
Indeterminate			
Total	173	271	444

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total
TST + threshold: ≥ 5 mm

Parameters

Kappa = 0.16 (95% CI: 0.07, 0.25)
% concordance = 279/444 = 62.84% (95% CI: 58.25, 67.2)
% discordance = 165/444 = 37.16% (95% CI: 32.8, 41.75)

Stratification (BCG vaccinated)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated
TST + threshold: ≥ 5 mm

Parameters

Kappa = 0.15 (95% CI: NA)			
% concordance = NA			
% discordance = NA			
Stratification (BCG not vaccinated)			
	TST +	TST -	Total
IGRA (TSPOT) +	NR	NR	NR
IGRA (TSPOT) -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG not vaccinated			
TST + threshold: ≥ 5 mm			
Parameters			
Kappa = 0.22 (95% CI: NA)			
% concordance = NA			
% discordance = NA			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
It is confirmed that there is poor agreement between TST and IGRA results, especially in a population largely vaccinated by BCG. The results suggest that IGRA should be included in the strategy to identify LTBI in patients with chronic inflammatory diseases before starting anti-TNF therapy. The data indicate that replacement of TST by IGRA in the screening would have led to a 27% reduction of antibiotics prophylaxis introduction
Reviewers:
T-SPOT.TB was less influenced by BCG than TST; specificity and DOR of T-SPOT.TB was higher than those of TST; sensitivity of TST was slightly higher than that of T-SPOT.TB; kappa for agreement was low, especially for BCG-vaccinated patients
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Hadaya 2013[128]
Country: Switzerland
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Geneva University Hospital
Number of centres: NR
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Ligue Pulmonaire Genevoise, a non-profit organisation

Aim of the study

To compare the diagnostic performance of the TST and two IGRAs (T-SPOT.TB and QuantiFERON Gold In-Tube [QGIT]) in renal transplant recipients (RTRs) under stable immunosuppression

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people - renal transplant recipients (RTRs)

Participants

Recruitment dates: November 2009 and December 2011
Total N of recruited patients: 205
Inclusion criteria: > 18 years, being able to provide informed consent, having had a renal transplant at least 12 months before inclusion, and having a stable immunosuppression.
Exclusion criteria: treatment for acute rejection within the preceding 3 months and signs or symptoms of acute infection
Total N of excluded patients: 5 (indeterminate IGRAs)
Total N of patients tested with both IGRA and TST: 205
Total N of patients with valid results for both IGRA and TST: 200
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Agreement; association of test results with the risk of LTBI
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 59.0 (13.2)
Women (n [%]): 84 (42.0)
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): High incidence of TB in country of origin (24 [12.0])
BCG vaccination (n [%]): 155 [77.5]
History of anti-TB treatment (n [%]): Active therapy (9 [4.5]), LTBI treatment (12 [6.0])
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Renal transplant recipients
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Prednisone (88 [44.0]), Tacrolimus, (127 [63.5]), Cyclosporine (41 [20.5]) Mycophenolate mofetil (159 [79.5]), Azathioprine (17 [8.5]), Sirolimus (12 [6.0])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	205	47	155	3	202
IGRA (TSPOT):	205	41	162	2	203
TST (≥5 mm):	205	9	191	0	200

Total N of patients with valid results for both IGRA and TST: 200

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group- Composite outcome 2 (risk for LTBI)	
Non-exposed	No risk for LTBI

Exposed 1 **(specify):**	Risk for LTBI**:** Chest X-ray suggestive of prior infection (calcified granuloma or adenopathy, suggestive fibrotic scars) and/or close contact with TB patient
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Blood samplings for determination of M. tuberculosis-specific QGIT (Cellestis) were processed, and scored according to the manufacturer's recommendations. Peripheral venous blood samples were processed by our laboratory within 3 hr	According to the manufacturer's recommendations	Blood samplings for determination of M. tuberculosis-specific QGIT (Cellestis) and interferon-F-secreting T cells (T-SPOT.TB (Oxford Immunotec) were performed simultaneously
IGRA (TSPOT)	Blood samplings for determination of M. tuberculosis-specific interferon-F-secreting T cells (T-SPOT.TB (Oxford Immunotec) were processed, and scored according to the manufacturer's recommendations. Peripheral venous blood samples were processed by our laboratory within 3 hr	According to the manufacturer's recommendations	NA
TST≥5mm	A TST was performed intradermally, according to the Mantoux technique, using two units of purified protein derivative (RT-23; Statens Serum Institute, Copenhagen, Denmark), which is the biological equivalent of five units of US purified protein derivative	Results of TST were considered positive if the transverse diameter, measured 48 to 72 hr after injection, was ≥ 5 mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA

Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = Na	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST≥5mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	14 (calculated)	28 (calculated)	42 (calculated)	TST +	3 (calculated)	6 (calculated)	9 (calculated)
IGRA -	28 (calculated)	113 (calculated)	141 (calculated)	TST -	39 (calculated)	135 (calculated)	174 (calculated)
Indeterminate	NR	NR	3 (excluded)	Indeterminate	NR	NR	0
Total	42	141	183	Total	42	141	183

Test performance parameters

IGRA	**TST**
Sensitivity = 33.30% (95% CI: 19.60, 49.50) reported	Sensitivity = 7.10% (95% CI: 1.50, 19.50)
Specificity = 80.10% (95% CI: 72.90, 86.20) reported	Specificity = 95.50% (95% CI: 90.80, 98.20)
PPV = 33.33% (95% CI: 21.01, 48.45) calculated	PPV = 33.33% (95% CI: 12.06, 64.58) calculated
NPV = 81.10% (95% CI: 73.80, 87.00) reported	NPV = 78.40% (95% CI: 71.70, 84.20)
DOR (for T^+ calculated) = 2.01 (95% CI: 0.94, 4.32)	DOR (for T^+ calculated) = 1. 73 (95% CI: 0.41, 7.24)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 1.16 (95% CI: 0.51, 2.66)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				**TST≥5mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	14 (calculated)	20 (calculated)	34 (calculated)	TST +	3 (calculated)	6 (calculated)	9 (calculated)
IGRA -	28 (calculated)	121 (calculated)	149 (calculated)	TST -	39 (calculated)	135 (calculate)	174 (calculated)
Indeterminate	NR	NR	2 (excluded)	Indeterminate	NR	NR	0
Total	42	141	183	Total	42	141	183

Test performance parameters

IGRA	**TST**
Sensitivity = 33.30% (95% CI: 19.60, 49.50)	Sensitivity = 7.10% (95% CI: 1.50, 19.50)
Specificity = 85.50% (95% CI: 78.90, 90.70)	Specificity = 95.50% (95% CI: 90.80, 98.20)
PPV = 41.18% (95% CI: 26.37, 57.78) calculated	PPV = 33.33% (95% CI: 12.06, 64.58) calculated

NPV = 81.90% (95% CI: 75.00, 87.60)	NPV = 78.40% (71.70, 84.20)
DOR (for T^+ calculated) = 3.02 (95% CI: 1.36, 6.71)	DOR (for T^+ calculated) = 1.73 (95% CI: 0.41, 7.24)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 1.75 (95% CI: 0.76, 4.04)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA (QFT-GIT) +	NR	NR	47
IGRA (QFT-GIT) -	NR	NR	153
indeterminate	NR	NR	3 (excluded)
Total	9	191	200

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total (n = 200)
TST + threshold: ≥5mm

Parameters

Kappa = 0.11 (P = 0.010)
% concordance = NR
% discordance = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA (TSPOT) +	NR	NR	41
IGRA (TSPOT) -	NR	NR	159
Indeterminate	NR	NR	2 (excluded)
Total	9	191	200

Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total (n = 200)			
TST + threshold: ≥5mm			
Parameters			
Kappa = 0.09 (P = 0.034)			
% concordance = NR			
% discordance = NR			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Neither the TST nor the IGRAs are sensitive enough in RTRs to exclude a diagnosis of TB or LTBI. Combining IGRAs did not significantly improve sensitivity
Reviewers:
Although low (33.3%), sensitivities of IGRAS were greater than that of TST (7%); agreement between IGRAs and TST was low (kappa = 0.09-0.11)
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Hsia 2012[129]
Country: US
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** NR
Number of centres: 340
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Johnson & Johnson, honoraria from Genentech, Pfizer, Celgene, Corrona, Amgen, Bristol-Myers Squibb, and Janssen

Aim of the study

To evaluate the performance of an interferon- release assay (IGRA) versus the standard tuberculin skin test (TST) as a screening tool for latent tuberculosis (TB) infection prior to the initiation of anti–tumor necrosis factor therapy in patients with autoimmune inflammatory diseases

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis prior to the initiation of anti–tumor necrosis factor therapy)

Participants

Recruitment dates: NR
Total N of recruited patients: 2303
Inclusion criteria: No history of latent/active TB prior to screening (except in GO-AFTER, which allowed the inclusion of patients with a history of latent TB who had been treated within the last 3 years) and having no signs or symptoms of active TB or no recent close contact with anyone with active TB. All patients were required to have a chest radiograph, obtained within 3 months before the first dose of study agent, that showed no evidence of active TB or old inactive TB.
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 2282
Total N of patients with valid results for both IGRA and TST: 2241
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Agreement; exposure-based
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 48.58 (12.6)
Women (n [%]): 1515 [65.7]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): North America (962 [41.8]), Western Europe (440 [19.1]), Eastern Europe (432 [18.8]), Latin America (203 [8.8]), Asia (266 [11.6])
BCG vaccination (n [%]): 788 [34.2]
History of anti-TB treatment (n [%]): 317 [13.8]
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Rheumatoid arthritis (1,542 [67.0]), Psoriatic arthritis (405 [17.6]), Ankylosing spondylitis (356 [15.5])
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Methotrexate (571 [24.8]), Corticosteroids (1,000 [43.4])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)

IGRA (QFT-GIT):	2282	160	2081	41	2241
TST (≥5mm):	2282	215	2067	0	2282
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 2241

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – geographic region	
Non-exposed	North America
Exposed 1 **(specify):**	Western Europe
Exposed 2 **(specify):**	Asia
Exposed 3 **(specify):**	Eastern Europe
Exposed 4 **(specify):**	Latin America

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	The QFT-GIT test was the IGRA assay used. For this procedure, standard venipuncture is performed at a single visit to collect blood in tubes that contain the M tuberculosis–specific antigens. The QFT-GIT test also contains an extra antigen, TB7.7 (p4) that was not present in the original version of this IGRA and is thought to improve sensitivity. In addition, this version of the IGRA shortens the manual processing time, since antigens are already present in the tubes. Initial IGRA sample-handling procedures were performed at investigational sites, and a central laboratory performed the enzyme-linked immunosorbent assay–based testing and reported the results for each patient according to the manufacturer's interpretation criteria	According to the manufacturer Positive results were confirmed by duplicate testing of the same sample. Any results initially indeterminate on the IGRA required a second sample to be drawn and tested, and the final results were used to determine study eligibility	NA
TST	The TST was performed according to the Mantoux method, using 5 tuberculin units (TU) of purified protein derivative (PPD) standard or 2 TU of PPD RT-23 (Statens Serum Institut). A trained health-care worker recorded each patient's reaction to the TST at 48–72 hours after placement	The TST was deemed positive for latent TB infection according to the local country guidelines for defining an immunosuppressed host or, in the absence of local guidelines, according to the presence of induration 5 mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**

Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence ratios = NA	
Ratio of incidence density rate ratios = NA	
Other reported measure = NA	

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST≥5 mm**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	160	TST +	NR	NR	215
IGRA -	NR	NR	2081	TST -	NR	NR	2067
Indeterminate	NR	NR	41	Indeterminate	NR	NR	0
Total	Vary by geographic region		2282	Total	Vary by geographic region		2282

Test performance parameters

IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = Western Europe vs. North America: 3.41 (95% CI: 1.99, 5.83) Latin America vs. North America: 3.43 (95% CI: 1.64, 7.19) Eastern Europe vs. North America: 3.58 (95% CI: 1.93, 6.63) Asia vs. North America: 8.48 (95% CI: 4.78, 15.03) List of covariates: baseline methotrexate use, baseline steroid use, disease type, age, and prior BCG vaccination	OR (regression-based; reported) = Western Europe vs. North America: 2.10 (95% CI: 1.30, 3.38) Latin America vs. North America: 1.56 (95% CI: 0.80, 3.05) Eastern Europe vs. North America: 0.95 (95% CI: 0.53, 1.70) Asia vs. North America: 7.47 (95% CI: 4.61, 12.08) List of covariates: : baseline methotrexate use, baseline steroid use, disease type, age, and prior BCG vaccination
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = NA	
Ratio of OR (crude; for T^+ reported) = NA	
Ratio of ORs (regression-based; reported) = Western Europe vs. North America: 1.62 (95% CI: 1.13, 2.34) Latin America vs. North America: = 2.20 (95% CI: 1.32, 3.66)	

Eastern Europe vs. North America: = 3.77 (95% CI: 2.44, 5.81)
Asia vs. North America: = 1.14 (95% CI: 0.77, 1.66)

Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST ≥5 mm**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	71	72	143	TST +	119	62	181
IGRA -	NR	NR	1853	TST -	NR	NR	1848
Indeterminate	9	24	33	Indeterminate	NR	NR	0
Total	781	1248	2029	Total	781	1248	2029

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = 1.00 (95% CI: 0.66, 1.51) List of covariates: baseline methotrexate use, baseline steroid use, disease type, age, and geographic region	OR (regression-based; reported) $_{TST}$ = 2.47 (95% CI: 1.71, 3.55) List of covariates: baseline methotrexate use, baseline steroid use, disease type, age, and geographic region
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	59	101	160
IGRA -	NR	NR	2081
Indeterminate	NR	NR	41
Total	215	2067	2282

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥5 mm

Parameters

Kappa = 0.22 (95% CI: 0.15, 0.27)

% concordance = NR

% discordance = NR

Stratification (specify group 1): BCG-vaccinated

	TST +	TST -	Total
IGRA +	28	43	71
IGRA -	91	619	710
Indeterminate	0 (excluded)	9 (excluded)	9 (excluded)
Total	119	662	781

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated

TST + threshold: ≥5 mm

Parameters

Kappa = 0.20 (95% CI: 0.13, 0.27) calculated

% concordance = 647/781 = 82.84% (95% CI: 80.04, 85.32) calculated

% discordance = 134/781 = 17.16% (95% CI: 14.68, 19.96) calculated

Stratification (specify group 2): BCG non-vaccinated

	TST +	TST -	Total

IGRA +	24	48	72
IGRA -	38	1138	1176
Indeterminate	6 (excluded)	18 (excluded)	24 (excluded)
Total	62	1186	1248
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG non-vaccinated			
TST + threshold: ≥5 mm			
Parameters			
Kappa = 0.32 (95% CI: 0.26, 0.37) calculated			
% concordance = 1162/1248 = 93.11% (95% CI: 91.57, 94.39) calculated			
% discordance = 86/1248 = 6.89% (95% CI: 5.61, 8.43) calculated			
Other outcomes			
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**		**Health related quality of life mean score (SD) (specify)**
IGRA:	NR		NR
TST:	NR		NR
Test 3 (specify):	NR		NR
Conclusions			
Authors:			
Thus, in the absence of a true gold standard test to screen for latent TB infection, results of this large cohort comparison of an IGRA (the QFT-GIT test) and the TST in patients with rheumatic disease suggest that the IGRA provides greater specificity and possibly greater sensitivity than the TST			
Reviewers:			
BCG vaccination influenced TST but not IGRA (indicating better specificity of IGRA); agreement was higher in BCG non-vaccinated vs. vaccinated patients; exposure-based (geographic location) ORs were stronger for IGRA vs. TST, indicating better specificity and/or sensitivity of IGRA vs. TST			
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation			

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Kim 2010[130]
Country: Korea
Study design: Retrospective/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Clinic based
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Korea Research Foundation

Aim of the study

To compare the results of the ELISPOT assay T-SPOT.TB with those of the TST in renal transplant candidates before transplantation in a country with an intermediate TB burden

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (kidney transplant candidates before transplantation)

Participants

Recruitment dates: June 2008 and May 2009
Total N of recruited patients: 213
Inclusion criteria: Kidney transplant adult candidates before transplantation
Exclusion criteria: If abnormal chest radiograph findings were observed, a sputum acid-fast bacilli smear and a computed tomography scan were performed to rule out active pulmonary TB
Total N of excluded patients: 4 (n = 1 refusal, n = 1 active TB, n = 2 cancer)
Total N of patients tested with both IGRA and TST: 209
Total N of patients with valid results for both IGRA and TST: 184
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Agreement, association of test positivity with risk factors, influence of BCG vaccination
Characteristics of participant (total study sample)
Mean (range or SD) age (years): NR
Women (n [%]): NR
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 163 [78.0]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): End-stage renal disease
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Isoniazid for 9 months immediately after renal transplantation (5 [19%])

Number of patients tested

	Total N (tested)	Total N (test +)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	209	65	119	25	184
TST (≥5mm):	209	47	162	0	209
TST (≥10mm):	209	21	188	0	209

Total N of patients with valid results for both IGRA and TST: 209

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – LTBI group

Non-exposed	No LTBI group
Exposed 1 **(specify):**	(i) close contact with a person with pulmonary tuberculosis within the last year, (ii) abnormal chest radiography, (iii) a history of untreated or inadequately treated TB, or (iv) newly acquired infection (recent conversion of the tuberculin skin test to positive status)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (TSPOT)	A peripheral venous blood sample was collected from each patient for the ELISPOT assay for the IFN-g-producing T-cell response (i.e., T-SPOT.TB, Oxford Immunotec, Abingdon, UK). Peripheral blood mononuclear cells (PBMC) were separated from peripheral venous blood within 4 h from sampling, and 2.5 x 10^5 PBMC were plated per well in wells precoated with anti-human IFN-g antibody The PBMC were cultured at 37◦C for 18h, and spots were counted with an automated microscope (ELiSpot04 HR, Autoimmun Diagnostika GmbH, Strassberg, Germany)	We used the criteria for positive, negative, and indeterminate outcomes that were recommended by the manufacturer	All blood samples were collected before TST to avoid the possible boosting effect of TST on the ELISPOT assay
TST (≥5mm or ≥10mm)	The Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm	The positive criterion for TST was ≥10 mm size of induration 48-72 h after injection	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				TST (≥5mm)			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/ No	
IGRA +	10	55	65	TST +	8	39	47
IGRA -	9	110	119	TST -	14	148	162
Indeterminate	3 (excluded)	22 (excluded)	25 (excluded)	Indeterminate	0	0	0
Total	22	187	209	Total	22	187	209

Test performance parameters

IGRA	TST
Sensitivity = 10/19 = 52.63% (95% CI: 31.71, 72.67)	Sensitivity = 8/22 = 36.36% (95% CI: 19.73, 57.05)
Specificity = 110/165 = 66.67% (95% CI: 59.17, 73.41)	Specificity = 148/187 = 79.14% (95% CI: 72.76, 84.35)
PPV = 10/65 = 15.38% (95% CI: 8.57, 26.06)	PPV = 8/47 = 17.02% (95% CI: 8.88, 30.14)
NPV = 110/119 = 92.44% (95% CI: 86.25, 95.97)	NPV = 148/162 = 91.36% (95% CI: 86.02, 94.78)
DOR (for T^+ calculated) = 2.22 (95% CI: 0.85, 5.78)	DOR (for T^+ calculated) = 2.17 (95% CI: 0.85, 5.54)
OR (crude; for T^+ reported) = 2.35 (95% CI: 0.90, 6.12)	OR (crude; for T^+ reported) = 2.17 (95% CI: 0.85, 5.54)
OR (regression-based; reported) = 2.38 (95% CI: 0.87, 6.52) List of covariates: age	OR (regression-based; reported) = 2.11 (95% CI: 0.82, 5.46) List of covariates: age
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 1.02 (95% CI: 0.52, 2.03)
Ratio of OR (crude; for T^+ reported) = 1.08 (95% CI: 0.55, 2.15)
Ratio of ORs (regression-based; reported) = 1.13 (95% CI: 0.56, 2.28)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				TST (≥10mm)			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/ No	
IGRA +	10	55	65	TST +	4	17	21
IGRA -	9	110	119	TST -	18	170	188
Indeterminate	3 (excluded)	22(excluded)	25(excluded)	Indeterminate	0	0	0
Total	22	187	209	Total	22	187	209

Test performance parameters

IGRA	TST
Sensitivity = 10/19 = 52.63% (95% CI: 31.71, 72.67)	Sensitivity = 4/22 = 18.18% (95% CI: 7.31, 38.52)

Specificity = 110/165 = 66.67% (95% CI: 59.17, 73.41)	Specificity = 170/187 = 90.91% (95% CI: 85.92, 94.25)
PPV = 10/65 = 15.38% (95% CI: 8.57, 26.06)	PPV = 4/21 = 19.05% (95% CI: 7.66, 40.00)
NPV = 110/119 = 92.44% (95% CI: 86.25, 95.97)	NPV = 170/188 = 90.43% (95% CI: 85.37, 93.86)
DOR (for T^+ calculated) = 2.22 (95% CI: 0.85, 5.78)	DOR (for T^+ calculated) = 2.22 (95% CI: 0.67, 7.32)
OR (crude; for T^+ reported) = 2.35 (95% CI: 0.90, 6.12)	OR (crude; for T^+ reported) = 2.22 (95% CI: 0.67, 7.32)
OR (regression-based; reported) = 2.38 (95% CI:0.87, 6.52) List of covariates: age	OR (regression-based; reported) = 2.12 (95% CI: 0.60, 7.49) List of covariates: age
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 1.00 (95% CI: 0.46, 2.19)
Ratio of OR (crude; for T^+ reported) = 1.06 (95% CI: 0.48, 2.31)
Ratio of ORs (regression-based; reported) = 1.12 (95% CI: 0.49, 2.56)
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				**TST (≥5mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	48	17	65	TST +	38	9	47
IGRA -	97	22	119	TST -	125	37	162
Indeterminate	18 (excluded)	7 (excluded)	25 (excluded)	Indeterminate	0	0	0
Total	163	46	209	Total	163	46	209

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 0.64 (95% CI: 0.31, 1.32)	DOR (for T+ calculated)$_{TST}$ = 1.25 (95% CI: 0.55, 2.82)
OR (crude; for T^+ reported) = 0.69 (95% CI: 0.36, 1.34)	OR (crude; for T+ reported) = 1.25 (95% CI: 0.55, 2.82)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				**TST (≥10mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	48	17	65	TST +	16	5	21
IGRA -	97	22	119	TST -	147	41	188
Indeterminate	18 (excluded)	7 (excluded)	25 (excluded)	Indeterminate	0	0	0
Total	163	46	209	Total	163	46	209

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 0.64 (95% CI: 0.31, 1.32)	DOR (for T+ calculated)$_{TST}$ = 0.89 (95% CI: 0.30, 2.58)
OR (crude; for T^+ reported) = 0.69 (95% CI: 0.36, 1.34)	OR (crude; for T+ reported) = 0.89 (95% CI: 0.31, 2.58)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA

Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + (≥10mm)	TST -	Total
IGRA (TSPOT) +	15	48	63
IGRA (TSPOT) -	5	116	121
Indeterminate	1 (excluded)	24 (excluded)	25 (excluded)
Total	20	164	184

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥10mm

Parameters

Kappa = 0.23 (95% CI: 0.12, 0.34)

% concordance = 131/184 = 71.2% (95% CI: 64.27, 77.25)

% discordance = 53/184 = 28.8% (95% CI: 22.75, 35.73)

Stratification (BCG vaccinated):

	TST + (≥10mm)	TST -	Total
IGRA (TSPOT) +	10	38	48
IGRA (TSPOT) -	5	92	97
Indeterminate	NR	NR	NR
Total	15	130	145

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated

TST + threshold: ≥10mm

Parameters

Kappa = 0.19 (95% CI: 0.06, 0.31)

% concordance = 102/145 = 70.34% (95% CI: 62.46, 77.18)

% discordance = 43/145 = 29.66% (95% CI: 22.82, 37.54)

Stratification (specify group 2):

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Other outcomes

Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

T-SPOT.TB test was more frequently positive than TST in renal transplant candidates. However, further longitudinal studies are awaited to determine whether the ability of T-SPOT.TB assay to detect

LTBI in renal transplant recipients can better predict the development of TB than can TST after transplantation. Neither univariate nor multivariate analysis showed any association between the clinical risk for LTBI and positivity on TSPOT or TST
Reviewers:
TSPOT had better sensitivity but lower specificity than TST regardless of the two thresholds; the DORs showed similar strength of association with LTBI composite risk factor; BCG status did not influence the test positivity of TST and IGRA differentially, neither did it influence corresponding kappas
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Kim 2013b[131]
Country: Korea
Study design: Retrospective/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Clinic based
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Grant of the Korean Health Technology R&D Project, Ministry for Health, Welfare and Family Affairs, Republic of Korea

Aim of the study

To compare the results of the TST and QFTGIT as methods for screening for LTBI and determined the agreement between the TST and QFT-GIT in renal transplant candidates before transplantation in a country with an intermediate TB burden

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (kidney transplant candidates before transplantation)

Participants

Recruitment dates: May 2010 and February 2012
Total N of recruited patients: NR
Inclusion criteria: Kidney transplant adult candidates before transplantation
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 126
Total N of patients with valid results for both IGRA and TST: 113
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Agreement, association of test positivity with risk factors, influence of BCG vaccination
Characteristics of participant (total study sample)
Mean (range or SD) age (years): 47 (20–69)
Women (n [%]): 55 [43.6]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 115 [91.3]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): End-stage renal disease (100 [79.4]), hemodialysis, (12 [9.5]), PD peritoneal dialysis, no dialysis (14 [11.1])
Co-morbidity (n [%]): Hypertension (60 [47.6]), Diabetes (31 [24.6])
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	126	53	67	6	120
TST (≥10mm):	126	35	91	7	119
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 113

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – LTBI group

Non-exposed	No LTBI group
Exposed 1 **(specify):**	(1) patients with a history of LTBI or active TB; (2) patients with abnormal chest radiograph findings consistent with previously healed TB; and (3) patients with a history of close contact with active pulmonary TB patients within the past year
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QuantiFERON-TB Gold In-Tube test Peripheral venous blood samples were collected from all patients for QFT-GIT assays. We performed the test according to the manufacturer's instructions (Cellestis Ltd., Carnegie, Victoria, Australia). Blood samples were divided into three blood collection tubes (1 mL each): one containing heparin alone (Nil tube, negative control), one with phytohemagglutinin (mitogen tube, positive control), and one with TB-specific antigens (ESAT-6, CFP-10, and TB 7.7). The three tubes were incubated for 20 h at 37◦C. The concentration of IFN-c was measured by the QFT enzymelinked immunosorbent assay. QFT-GIT software provided by the manufacturer was used for calculating the results	A positive QFT-GIT result was defined as IFN-c response of TB antigen minus that of the Nil tube ≥0.35 IU/mL and ≥25 % of the negative control value	NA
TST (≥5mm or ≥10mm)	The TST was performed by injecting a 2-TU dose of PPDRT 23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm, which was in accordance with the Mantoux method	The transverse induration site was measured by a trained nurse in mm after 48–72 h Induration ≥10 mm was defined as a positive TST result	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence ratios = NA	
Ratio of incidence density rate ratios = NA	
Other reported measure = NA	

Association between test results and levels of TB exposure (if applicable)							
IGRA (QFT-GIT)				**TST (≥10mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low /No			High/Yes	Low/ No	
IGRA +	11	42	53	TST +	13	10	23
IGRA -	4	63	67	TST -	2	94	96
Indeterminate	1	5	6 (excluded)	Indeterminate	1	6	7 (excluded)
Total	16	110	126	Total	16	110	126

Test performance parameters	
IGRA	**TST**
Sensitivity = 11/15 = 73.33% (95% CI: 48.05, 89.1)	Sensitivity = 13/15 = 86.67% (95% CI: 62.12, 96.26)
Specificity = 63/105 = 60.00% (95% CI: 50.44, 68.86)	Specificity = 94/104 = 90.38% (95% CI: 83.2, 94.69)
PPV = 11/53 = 20.75% (95% CI: 12.00, 33.46)	PPV = 13/23 = 56.52% (95% CI: 36.81, 74.37)
NPV = 63/67 = 94.03% (95% CI: 85.63, 97.65)	NPV = 94/96 = 97.92% (95% CI: 92.72, 99.43)
DOR (for T^+ calculated) = 4.12 (95% CI: 1.23, 13.82)	DOR (for T^+ calculated) = 61.1 (95% CI: 12.03, 310.4)
OR (crude; for T^+ reported) = 4.13 (95% CI: 1.23, 13.82)	OR (crude; for T^+ reported) = 0.61 (95% CI: 0.13, 2.91) -error
OR (regression-based; reported) = 4.62 (95% CI: 1.15, 18.64) List of covariates: NR	OR (regression-based; reported) = 0.40 (95% CI: 0.07. 2.20) -error List of covariates: NR
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = 0.07 (95% CI: 0.02, 0.19)	
Ratio of OR (crude; for T^+ reported) = NA	
Ratio of ORs (regression-based; reported) = NA	
Other reported measure = NA	
Association between test results and BCG status (if applicable)	
IGRA (QFT-GIT)	**TST (≥10mm)**

	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	50	3	53	TST +	22	1	23
IGRA -	60	7	67	TST -	86	10	96
Indeterminate	5	1	6 (excluded)	Indeterminate	7	0	7 (excluded)
Total	115	11	126	Total	115	11	126

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 1.94 (95% CI: 0.47, 7.91)	DOR (for T^+ calculated)$_{TST}$ = 2.55 (95% CI: 0.32, 21.06)
OR (crude; for T^+ reported) = 1.94 (95% CI: 0.48, 7.91)	OR (crude; for T^+ reported) = 2.56 (95% CI: 0.31, 21.06)
OR (regression-based; reported) $_{IGRA}$ = 2.32 (95% CI: 0.50, 10.66) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 3.32 (95% CI: 0.38, 28.97) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + (≥10mm)	TST -	Total
IGRA (QFT-GIT) +	17	33	50
IGRA (QFT-GIT) -	6	57	63
Indeterminate	0	6	6 (excluded)
Total	23	96	119

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥10mm

Parameters

Kappa = 0.26 (95% CI: 0.10, 0.41)

% concordance = 74/113 = 65.49% (95% CI: 56.34, 73.61)

% discordance = 39/113 = 34.51% (95% CI: 26.39, 43.66)

Stratification (specify group 2):

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Other outcomes

Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
The positive results for QFT-GIT were associated with risk for LTBI, however not for TST (error); agreement between the two tests was fair
Reviewers:
TST better performed than GIT in accuracy measures (sensitivity, PPV, specificity, DOR); BCG did not influence TST and IGRA differentially
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Kim 2013c[132]
Country: Korea
Study design: Retrospective cohort/cross-sectional study (with prospective part)
Study setting (e.g., outbreak investigation, community-based - specify)**:** NR
Number of centres: NA
Total length of follow up (if applicable): Mean 24.6 ±14.4 months
Funding (government/private/manufacturer/other - specify)**:** The Korea health care technology R & D project, ministry for health, welfare and family affair, republic of Korea.

Aim of the study

To compare the QuantiFERON-TB Gold In tube test (QFT-GIT) with the tuberculin skin test (TST) for screening of LTBI in kidney transplant recipients (KTRs)

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Kidney transplant recipients (KTRs)

Participants

Recruitment dates: Between July 2008 and July 2012
Total N of recruited patients: 109
Inclusion criteria: Kidney transplant recipients
Exclusion criteria: NR
Total N of excluded patients: 4 with indeterminate QFT-GIT results (excluded for analysis)
Total N of patients tested with both IGRA and TST: 97
Total N of patients with valid results for both IGRA and TST: 93
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Test results, concordance between TST and QFT-GIT
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 44.7 ±11.5
Women (n [%]): 41 (38)
Race/ethnicity (n [%]): NR
Geographic origin (n[%]):NR
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): 3 [2.8]
Total incidence of active TB (n [%]):1 [0.9]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): Glomerulonephritis (19 [17.4]); hypertensive nephrosclerosis (11 [10.1]); diabetes mellitus (31 [28.4]); Unknown (34 [31.2]); polycystic kidney disease (2 [1.8]); Others (12 [11.0])
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	**Total N (test+)**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results available)**
IGRA (specify): QFT-GIT	106	21	81	4	102
TST≥10mm:	97	12	81	0	93
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 97

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NR

Exposed 1 **(specify):**	History of treated tuberculosis
Exposed 2 **(specify):**	Abnormal chest radiograph
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA	QuantiFERON- Gold In-Tube (QFT-GIT) was performed according to the manufacturer's instructions (Cellestic Ltd, Carnegie, Victoria, Australia)	A positive QFT-GIT was defined as ≥ 0.35 IU/mL and ≥ 25% in the presence of TB-specific antigen minus that of the Nil tude	NA
TST≥10 mm	TST was performed on the volar side of the forearm by injection of a 2 tuberculin unit dose of perified protein derivative RT-23 according to the Mantoux method	The TST was considered positive if the size of the induration was ≥10 mm at 48 to 72 hours after the injection.	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (History of treated tuberculosis)

IGRA (QFT-GIT)				**TST≥10 mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	2	17	19	TST +	NR	NR	12
IGRA -	0	74	74	TST -	NR	NR	81
Indeterminate	NR	NR	4	Indeterminate	NR	NR	0

			(excluded)				
Total	2	91	93	Total	NR	NR	93

Test performance parameters	
IGRA	**TST**
Sensitivity = 2/2 = 100%, 95% CI (34.24, 100)	Sensitivity = NR
Specificity = 74/91 = 81.32%, 95% CI (72.10, 88.00)	Specificity = NR
PPV = 2/19 = 10.53%, 95% CI (2.93, 31.39)	PPV = NR
NPV = 74/74 = 100%, 95% CI (95.06, 100)	NPV = NR
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 9.21, 95% CI (NR) List of covariates: NR	OR (regression-based; reported) = NR (NS) List of covariates:
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = NR
Other reported measure = NR

Association between test results and levels of TB exposure (Abnormal chest radiograph)							
IGRA (QFT-GIT)				**TST TST≥10 mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	3	16	19	TST +	NR	NR	12
IGRA -	1	73	74	TST -	NR	NR	81
Indeterminate	0	0	4 (excluded)	Indeterminate	NR	NR	0
Total	4	89	93	Total	NR	NR	93

Test performance parameters	
IGRA	**TST**
Sensitivity = 3/4 = 75.00%, 95% CI (30.06, 95.44)	Sensitivity = NR
Specificity = 73/89 = 82.02%, 95% CI (72.77, 88.62)	Specificity = NR
PPV = 3/19 = 15.79%, 95% CI (5.52, 37.57)	PPV = NR
NPV = 73/74 = 98.65%, 95% CI (92.73, 99.76)	NPV = NR
DOR (for T^+ calculated) = 13.69, 95% CI (1.33, 140.30)	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 27.95, 95% CI (1.22, 636.62) List of covariates: NR	OR (regression-based; reported) = NR (NS) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = NR
Other reported measure = NR

Association between test results and BCG status (if applicable)					
IGRA (TSPOT/QFT)			**TST (≥10 mm)**		
	BCG status	Total		BCG status	Total

	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA (TSPOT/QFT)	**TST (>5 mm)**
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = NR	DOR $_{TST}$ (for T+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = NR OR (regression-based; reported)$_{TSPOT}$ = NR List of covariates:NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	6	13	19
IGRA -	6	68	74
Indeterminate	0	0	0
Total	12	81	93

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total less Indeterminate results

TST + threshold: ≥10 mm

Parameters

Kappa = 0.27, 95% CI (0.07, 0.46)

% concordance = 74/93 = 79.57%, 95% CI (70.28, 86.51)

% discordance = 19/93 = 20.43%, 95% CI (13.49, 29.72)

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR		
% discordance = NR		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
The authors concluded that there was overall fair agreement between the QFT-GIT and TST. Furthermore, they stated that a superiority of QFT-GIT [and] TST was not demonstrated and this may be a result of the clinical risk factors for LTBI		
Reviewers:		
No TST based ORs data reported		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Kleinert 2012[133]
Country: Germany
Study design: Retrospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Hospital-based
Number of centres: 62
Total length of follow up (if applicable): NA (no prospective follow-up)
Funding (government/private/manufacturer/other - specify)**:** Abbott, Pfizer, Roche and Wyeth, Chugai, Cellestis Ltd, Oxford Immunotec Ltd, Pharmore Ltd, and Roche

Aim of the study

To compare the utility of IGRA and TST in LTBI screening in a large cohort of patients with rheumatic diseases receiving immunosuppressive therapy

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) prior to the initiation of anti-tumour necrosis factor therapy)

Participants

Recruitment dates: NR
Total N of recruited patients: NR
Inclusion criteria: Patients with rheumatic diseases
Exclusion criteria: NR
Total N of excluded patients: None
Total N of patients tested with both IGRA and TST: 1609
Total N of patients with valid results for both IGRA and TST: 1529 (80 had indeterminate IGRA)
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Influence of risk factors on test results, agreement/disagreement (total, by age, sex, and risk factor), association between test and clinical risk factors for LTBI (construct)
Characteristics of participants (total study sample)
Mean (range or SD) age (years): mean age range (50.8-59.5)
Women (n [%]): 937 [61.3]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 204 [13.3]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): 852 [55.7] Rheumatoid arthritis (RA), (294 [19.2]), ankylosing spondylitis (AS) (215 [14.0]), psoriatic arthritis (PsA) (92 [6.0]), undifferentiated spondyloarthropathy (SpA) and (76 [5.0]) various other rheumatologic disorders
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Immunosuppressive therapy (not specified)

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-G):	NR	50	635	NR	685
IGRA (TSPOT):	NR	70	774	NR	844
TST (≥5mm):	1609	173	1356	80 (QFT + TSPOT)	1529

Total N of patients with valid results for both IGRA and TST: 1529

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	None of the compound risk factors (CRF) were present
Exposed 1 **(specify):**	A compound risk factor (CRF) defined as the presence of at least one of these three risk factors: 1) history of prior TB, 2) close contact to a patient with TB, or 3) CXR suggestive of LTBI
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-G)	Quantiferon TB Gold administered in accordance with contemporary guidelines for immunosuppressed patients; IGRAs were mainly based on the two peptide antigens ESAT-6 and CFP-10	NR	All patients received one type of IGRA, either TSPOT.TB or QFT, depending on what was available in the corresponding laboratory
IGRA (TSPOT)	TSPOT.TB (TSPOT) administered in accordance with contemporary guidelines for immunosuppressed patients; IGRAs were mainly based on the two peptide antigens ESAT-6 and CFP-10	The cut-off for TSPOT positivity was ≥6 spots	All patients received one type of IGRA, either TSPOT.TB or QFT, depending on what was available in the corresponding laboratory
TST	NR	TST with a diameter of ≥5 mm skin induration was considered positive	All patients received a TST

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-G)				TST (≥5 mm)			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	9	41	50	TST +	48	125	173
IGRA -	45	590	635	TST -	74	1282	1356
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	54	631	685	Total	122	1407	1529

Test performance parameters

IGRA(QFT-G)	TST (>5 mm)
Sensitivity = 9/54 = 16.67% (95% CI: 9.02, 28.74)	Sensitivity = 48/122 = 39.34% (95% CI: 31.13, 48.21)
Specificity = 590/631 = 93.5% (95% CI: 91.3, 95.17)	Specificity = 1282/1407 = 91.12% (95% CI: 89.52, 92.49)
PPV = 9/50 = 18.00% (95% CI: 9.77, 30.8)	PPV = 48/173 = 27.75% (95% CI: 21.61, 34.85)
NPV = 590/635 = 92.91% (95% CI: 90.65, 94.66)	NPV = 1282/1356 = 94.54% (95% CI: 93.2, 95.63)
DOR (for T^+ calculated) = 2.88 (95% CI: 1.31, 6.29)	DOR (for T^+ calculated) = 6.65 (95% CI: 4.42, 9.99)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 2.63 (95% CI: 1.15, 5.98) List of covariates: NR	OR (regression-based; reported) = 6.20 (95% CI: 4.08, 9.44) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (QFT vs. TST)

Ratio of DORs (for T^+ calculated) = 0.43 (95% CI: 0.28, 0.68)
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = 0.42 (95% CI: 0.26, 0.68)
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				TST (≥5 mm)			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	24	46	70	TST +	48	125	173
IGRA -	44	730	774	TST -	74	1282	1356
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	68	776	844	Total	122	1407	1529

Test performance parameters

IGRA (TSPOT)	TST (≥5 mm)
Sensitivity = 24/68 = 35.29% (95% CI: 25.00, 47.16)	Sensitivity = 48/122 = 39.34% (95% CI: 31.13, 48.21)
Specificity = 730/776 = 94.07% (95% CI: 92.18, 95.53)	Specificity = 1282/1407 = 91.12% (95% CI: 89.52, 92.49)
PPV = 24/70 = 34.29% (95% CI: 24.25, 45.96)	PPV = 48/173 = 27.75% (95% CI: 21.61, 34.85)
NPV = 730/774 = 94.32% (95% CI: 92.45, 95.74)	NPV = 1282/1356 = 94.54% (95% CI: 93.2, 95.63)

DOR (for T^+ calculated) = 8.65 (95% CI: 4.84, 15.46)	DOR (for T+ calculated) = 6.65 (95% CI: 4.42, 9.99)
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) = 8.74 (95% CI: 4.83, 15.82) List of covariates: NR	OR (regression-based; reported) = 6.20 (95% CI: 4.08, 9.44) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 1.30 (95% CI: 0.91, 1.87)
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = 1.41 (95% CI: 0.97, 2.04)
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (TSPOT/QFT)				**TST (≥5 mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	14	106	120	TST +	50	123	173
IGRA -	190	1219	1409	TST -	154	1202	1356
Indeterminate				Indeterminate			
Total	204	1325	1529	Total	204	1325	1529

Test performance parameters

IGRA (TSPOT/QFT)	**TST (≥5 mm)**
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = 0.84 (95% CI: 0.47, 1.51)	DOR $_{TST}$ (for T+ calculated) = 3.17 (95% CI: 2.19, 4.58)
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = 0.43 (95% CI: 0.17, 1.10) OR (regression-based; reported)$_{TSPOT}$ = 1.07 (95% CI: 0.47, 2.43) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 2.95 (95% CI: 2.00, 4.35) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + **(≥5 mm)**	TST -	Total
IGRA (QFT/TSPOT) +	66	54	120
IGRA (QFT/TSPOT) -	107	1302	1409
Indeterminate	NR	NR	NR
Total	173	1356	1529

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total
TST + threshold: >5 mm

Parameters

Kappa = 0.39 (95% CI: 0.34, 0.44)
% concordance = 1368/1529 = 89.47% (95% CI: 87.83, 90.91) between IGRA (QFT/TSPOT) vs. TST % concordance = 87.60% (95% CI: NR) between QFT vs. TST (raw 2 x 2 cell counts: NR) % concordance = 91.10% (95% CI: NR) between TSPOT vs. TST (raw 2 x 2 cell counts: NR)
% discordance = 161/1529 = 10.53% (95% CI: 9.09, 12.17)

Stratification (BCG vaccinated)

	TST +	TST -	Total
IGRA (QFT/TSPOT) +	11	3	14
IGRA (QFT/TSPOT) -	39	152	191
Indeterminate			

Total	50	155	205
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated			
TST + threshold: ≥5 mm			
Parameters			
Kappa = 0.26 (95% CI: 0.15, 0.37)			
% concordance = 163/205 = 79.5% (95% CI: 73.47, 84.47)			
% discordance = 42/205 = 20.49% (95% CI: 15.53, 26.53)			
Stratification (non-BCG vaccinated)			
	TST +	TST -	Total
IGRA (QFT/TSPOT) +	55	51	106
IGRA (QFT/TSPOT) -	68	1150	1218
Indeterminate	NR	NR	NR
Total	123	1201	1324
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): non-BCG vaccinated			
TST + threshold:≥5 mm			
Parameters			
Kappa = 0.43 (95% CI: 0.37, 0.48)			
% concordance = 1205/1324 = 91.01% (95% CI: 89.35, 92.44)			
% discordance = 119/1324 = 8.98% (95% CI: 7.56, 10.65)			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

In patient populations with low rates of TB incidence and BCG vaccination, the use of both TST and IGRA may maximise sensitivity in detecting LTBI but may also reduce specificity; CRF influenced the results for all three of the tests but had less influence on QFT than on the other test systems. By this standard, TSPOT appears to perform better than QFT due to its greater correlation with known LTBI risk factors. Nevertheless, we cannot exclude the possibility that a poorer correlation with clinical risk factors is due to a higher specificity rather than a lower sensitivity. A better understanding of the relative merit of QFT versus TSPOT will require head-to-head tests under real-world conditions

Reviewers:

DOR of TST was higher than DOR for QFT, but it was similar to DOR of TSPOT; BCG influenced TST positivity (odds of TST positivity was higher in BCG vaccinated vs. non-vaccinated; OR>1) but not IGRA positivity (odds of IGRA positivity was the same in BCG vaccinated vs. non-vaccinated; OR = 1); between test agreement was higher in non-vaccinated vs. vaccinated group

Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Laffitte 2009[134]
Country: Switzerland
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Hospital-based
Number of centres: 2
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** NR

Aim of the study

The aim of this study was (i) to determine the frequency of LTBI in a population of patients with psoriasis before anti-TNF treatment, (ii) to compare the TST with T-SPOT.TB for detecting LTBI, and (iii) to evaluate the tolerance and effectiveness of treatment for LTBI under anti-TNF therapy in our patients.

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (patients with psoriasis before anti-TNF treatment)

Participants

Recruitment dates: November 2004 and March 2008
Total N of recruited patients: NR
Inclusion criteria: Patients with moderate to severe psoriasis qualifying for anti-TNF-a therapy
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 50
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Agreement, association between test positivity and selected patient characteristics
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 48 (17–74)
Women (n [%]): 15 [30]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): High TB incidence in country of origin (10 [20])
BCG vaccination (n [%]): 45 (90)
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): None
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): Psoriasis
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): 12 patients treated for LTBI (9 with rifampicin and 3 with isoniazid) before anti TNF

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	NR	10	40	NR	50
TST (≥5mm):	NR	20	30	NR	50
TST (≥10mm):	NR	18	32	NR	50

Total N of patients with valid results for both IGRA and TST: 50

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – probable LTBI	
Non-exposed	No probable LTBI

Exposed 1 **(specify):**	Probable LTBI defined as having a history of definite exposure to a case of active tuberculosis and/or having a chest X-ray suggestive of prior tuberculosis infection (granulomas, calcified adenopathy) and/or originating from a high-incidence country (defined as > 40 cases in 100 000 per year)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (TSPOT)	NR	NR	NA
TST (≥ 5mm or ≥10mm)	NR	The TST was considered positive if the induration diameter was ≥ 5mm or ≥10mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				**TST (≥5mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	8	2	10	TST +	11	9	20
IGRA -	14	26	40	TST -	11	19	30
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR

Total	22	28	50	Total	22	28	50
Test performance parameters							
IGRA				**TST**			
Sensitivity = 8/22 = 36.36% (95% CI: 19.73, 57.05)				Sensitivity = 11/22 = 50.00% (95% CI: 30.72, 69.28)			
Specificity = 26/28 = 92.86% (95% CI: 77.35, 98.02)				Specificity = 19/28 = 67.86% (95% CI: 49.34, 82.07)			
PPV = 8/10 = 80.00% (95% CI: 49.02, 94.33)				PPV = 11/20 = 55.00% (95% CI: 34.21, 74.18)			
NPV = 26/40 = 65.00% (95% CI: 49.51, 77.87)				NPV = 19/30 = 63.33% (95% CI: 45.51, 78.13)			
DOR (for T^+ calculated) = 7.43 (95% CI: 1.38, 39.87)				DOR (for T^+ calculated) = 2.11 (95% CI: 0.67, 6.68)			
OR (crude; for T^+ reported) = 7.43 (95% CI: 1.38, 39.90)				OR (crude; for T^+ reported) = 3.00 (95% CI: 0.93, 9.70)			
OR (regression-based; reported) = NR List of covariates: NA				OR (regression-based; reported) = NR List of covariates: NA			
Other reported measure = NR				Other reported measure = NR			
Comparison between tests (IGRA vs. TST)							
Ratio of DORs (for T^+ calculated) = 3.52 (95% CI: 1.25, 9.96)							
Ratio of OR (crude; for T^+ reported) = 2.48 (95% CI: 0.87, 7.05)							
Ratio of ORs (regression-based; reported) = NA							
Other reported measure = NA							
Association between test results and levels of TB exposure (if applicable)							
IGRA (TSPOT)				**TST (≥10mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	8	2	10	TST +	12	6	18
IGRA -	14	26	40	TST -	10	22	32
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	22	28	50	Total	22	28	50
Test performance parameters							
IGRA				**TST**			
Sensitivity = 8/22 = 36.36% (95% CI: 19.73, 57.05)				Sensitivity = 12/22 = 54.55% (95% CI: 34.66, 73.08)			
Specificity = 26/28 = 92.86% (95% CI: 77.35, 98.02)				Specificity = 22/28 = 78.57% (95% CI: 60.46, 89.79)			
PPV = 8/10 = 80.00% (95% CI: 49.02, 94.33)				PPV = 12/18 = 66.67% (95% CI: 43.75, 83.72)			
NPV = 26/40 = 65.00% (95% CI: 49.51, 77.87)				NPV = 22/32 = 68.75% (95% CI: 51.43, 82.05)			
DOR (for T^+ calculated) = 7.43 (95% CI: 1.38, 39.87)				DOR (for T^+ calculated) = 4.40 (95% CI: 1.28, 15.09)			
OR (crude; for T^+ reported) = 7.43 (95% CI: 1.38, 39.90)				OR (crude; for T^+ reported) = 2.08 (95% CI: 0.64, 6.73)			
OR (regression-based; reported) = NR List of covariates: NA				OR (regression-based; reported) = NR List of covariates: NA			
Other reported measure = NR				Other reported measure = NR			
Comparison between tests (IGRA vs. TST)							
Ratio of DORs (for T^+ calculated) = 1.69 (95% CI: 0.58, 4.89)							
Ratio of OR (crude; for T^+ reported) = 3.57 (95% CI: 1.25, 10.18)							
Ratio of ORs (regression-based; reported) = NA							
Other reported measure = NA							

Association between test results and BCG status (if applicable)							
IGRA (TSPOT)				**TST (≥5mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	9	1	10	TST +	19	1	20
IGRA -	36	4	40	TST -	26	4	30
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	45	5	50	Total	45	5	50
Test performance parameters							
IGRA				**TST**			
DOR (for T^+ calculated)$_{IGRA}$ = 1.00 (95% CI: 0.01, 10.07)				DOR (for T+ calculated)$_{TST}$ = 2.92 (95% CI: 0.30, 28.29)			
OR (crude; for T^+ reported) = NR				OR (crude; for T+ reported) = NR			
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA				OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA			
Other reported measure = NR				Other reported measure = NR			
Association between test results and BCG status (if applicable)							
IGRA (TSPOT)				**TST (≥10mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	9	1	10	TST +	17	1	18
IGRA -	36	4	40	TST -	28	4	32
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	45	5	50	Total	45	5	50
Test performance parameters							
IGRA				**TST**			
DOR (for T^+ calculated)$_{IGRA}$ = 1.00 (95% CI: 0.01, 10.07)				DOR (for T+ calculated)$_{TST}$ = 2.43 (95% CI: 0.25, 23.57)			
OR (crude; for T^+ reported) = NR				OR (crude; for T+ reported) = NR			
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA				OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA			
Other reported measure = NR				Other reported measure = NR			
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**							
Total sample							
	TST (≥5mm) +			TST -			Total
IGRA (TSPOT) +	8			2			10
IGRA (TSPOT) -	12			28			40
Indeterminate	NR			NR			NR
Total	20			30			50
Description							
Sample definition (e.g., total, if stratified by BCG or condition – specify): total							
TST + threshold: ≥5mm							
Parameters							
Kappa = 0.36 (95% CI: 0.12, 0.61) calculated Kappa = 0.33 (CI NR) reported							
% concordance = 36/50 = 72.00% (95% CI: 58.33, 82.53)							
% discordance = 14/50 = 28.00% (95% CI: 17.47, 41.67)							
Stratification (specify group 1):							
	TST +			TST -			Total
IGRA +	NR			NR			NR
IGRA -	NR			NR			NR
Indeterminate	NR			NR			NR

Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

T-SPOT.TB IGRA is strongly associated with the presence of risk factors for LTBI. This association was not found for the TST, and agreement between the T-SPOT.TB and TST was poor, probably because of a high rate of BCG-vaccinated patients (90%) acting as a confounding factor

Reviewers:

T-SPOT.TB IGRA is strongly associated with the presence of risk factors for LTBI (but not TST≥5mm). Strong association was also found for the TST≥10mm. Agreement between the T-SPOT.TB and TST≥5mm was poor. Influence of BCG on test positivity was slightly higher for TST (both thresholds) than TSPOT, but given the small sample and that 90% were BCG vaccinated, there results are inconclusive due to wide CIs

Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Alexander Tsertsvadze

Study details

First author surname year of publication: Maritsi 2011[135]
Country: UK
Study design: Retrospective case study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Pediatric rheumatology centre
Number of centres: One centre
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Authors report that there is no source of funding

Aim of the study

To describe the findings of QTB test when applied to a paediatric rheumatology population and to assess the efficacy of this test versus the methods previously used for the exclusion of TB infection prior to starting anti-TNFα treatment

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (Paediatric Rheumatology prior to Initiation of Infliximab)

Participants

Recruitment dates: NR
Total N of recruited patients: 27
Inclusion criteria: Children on infliximab since 2007
Exclusion criteria: NR
Total N of excluded patients: 4 (no record of the QTB test)
Total N of patients tested with both IGRA and TST: 27
Total N of patients with valid results for both IGRA and TST: 23
Methods of active TB diagnosis (if applicable):
Outcomes (study-based) list: Test results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median age 8.9 years (1.5 to 13 years)
Women (n [%]): 12 (52.1)
Race/ethnicity (n [%]): Caucasian [55%], Afro-Caribbean [19%], Asian [26%]
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 5 [22%]
History of anti-TB treatment (n [%]): 5 [22]
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): No
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Methotrexate (5 [22]), infliximab (23 [100])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	23	1	20	2	23
TST (NR):	14	0	14	0	14
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 23

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – Risk for LTBI

Non-exposed	Low-risk group
Exposed 1 **(specify):**	High-risk group (TB risk evaluation was performed using the questionnaire formulated by the United States Pediatric Tuberculosis Collaborative Group, which was published in 2004 [3])
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Quantiferon-TB gold in-tube (QTB), Cellestis Corp. Australia. The methodology and timing of the test have not been reported.	Not reported	Authors suggested that results for the QTB are reported as positive, negative and indeterminate.
TST	Not reported	Not reported	Not reported

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (high-risk group)

IGRA (GIT)				**TST (NR)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	1	0	1	TST +	0	0	0
IGRA -	2	18	20	TST -	3	11	14
Indeterminate	0	2	2	Indeterminate	NR	NR	9

							(exclude)
Total	3	20	23	Total	3	11	14

Test performance parameters	
IGRA (exclude indeterminate)	**TST (exclude indeterminate)**
Sensitivity = 1/3 = 33.33%, 95% (6.149, 79.23)	Sensitivity = 0/3 = 0.0%, 95% CI (0.0, 56.15)
Specificity = 18/18 = 100.00%, 95% CI (82.41, 100.00)	Specificity = 11/11 = 100.00%, 95% CI (74.12, 100.00)
PPV = 1/1 = 100.00%, 95% CI (20.65, 100.00)	PPV = NA
NPV = 18/20 = 90.00%, 95% CI (69.9, 97.21)	NPV = 11/14 = 78.57%, 95% CI (52.41, 92.43)
DOR (for T^+ calculated) = Undefined	DOR (for T^+ calculated) = Undefined
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NR	Other reported measure = NA

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = NR
Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (TSPOT/QFT)				**TST (NR mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA (TSPOT/QFT)	**TST (NR mm)**
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = NR	DOR $_{TST}$ (for T+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = NR OR (regression-based; reported)$_{TSPOT}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR
Parameters
Kappa = NR
% concordance = NR
% discordance = NR

Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR

IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

The authors concluded that QTB is a useful screening tool for LTBI. Additionally, indeterminate results warrant careful assessment and re-evaluation, but should not preclude from initiation of anti-TNF treatment. Furthermore, the authors suggested that a negative TST in children receiving immunosuppressive treatment is not adequate in excluding LTBI

Reviewers:

Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Mutsvangwa 2010[136]
Country: Zimbabwe
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** NR
Number of centres: NR
Total length of follow up (if applicable): NR
Funding (government/private/manufacturer/other - specify)**:** The Wellcome Trust

Aim of the study

We tested for LTBI using ELISpot and TST, correlated test results with TB exposure in household contacts of TB cases and assessed the impact of HIV co-infection on test results in these contacts

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (HIV positive adult contacts)

Participants

Recruitment dates: February 2002 to November 2004
Total N of recruited patients: NR
Inclusion criteria: All consenting individuals over the age of 10 years living with the TB cases (index case household contacts) and those (household contacts of controls) living with controls (no TB), TB cases were sampled from factories in Harare and controls samples randomly from the same factories
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 73 (HIV positives)
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Agreement, association of test positive results with exposure to TB, degree of TB exposure
Characteristics of participants (total study sample)
Mean (range or SD) age (years): NR
Women (n [%]): 65 [89.0]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): Sub-Saharan Africa
BCG vaccination (n [%]): 63 [86.0]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): NR
Clinical examination (yes/no): NR
Morbidity (n [%]): HIV infected
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	NR	22	51	NR	73
TST (≥10mm):	NR	33	40	NR	73
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 73

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – household contact	
Non-exposed	Contact of index control (no TB)

Exposed 1 **(specify):**	Contact of index TB case
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA
Definition of exposure group – smear status of index cases	
Non-exposed	Smear negative, culture negative
Exposed 1 **(specify):**	Smear negative, culture positive
Exposed 2 **(specify):**	Smear positive, culture positive

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (TSPOT)	Blood was drawn for ELISpot testing before or after the TST was placed. ELISpot assays were carried out as described elsewhere. Duplicate wells contained no antigen (negative control), phytohaemagglutinin (positive control) (ICN Biomedical, Aurora, Ohio, USA) at 5 mg/ml or 13 pairs of duplicate wells each containing one of 13 peptide pools incorporating 5-7 overlapping 15-mer peptides spanning the length of early secretory antigenic target-6 and culture filtrate protein-10, on which T-SPOT.TB is based. The final concentration of each peptide was 10 mg/ml	ELISpot plates were sent to Oxford for automated spot counting (AID, Strassberg, Germany)	Persons performing and reading the assays were blind to all personal identifiers and TST results
TST (two stage; ≥10mm)	A two-step TST protocol was used to provide a suitable baseline for identifying subsequent TST conversions. As recommended by the manufacturer, 2 units of RT-23 PPD (purified protein derivative) in Tween-80 (Statens Serum Institut, Copenhagen, Denmark) were injected intradermally into the forearm and results read at 48-72h. Placement and assessment followed recommended techniques	If the first reaction was <10 mm, then a second TST was placed after 7-14 days. Results were expressed as the greater of the two reactions. Reaction sizes ≥10 mm were considered positive	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA

IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)							
IGRA (TSPOT)				**TST (≥10 mm; two step)**			
	Exposure level		Total		Exposure level		Total
	Index case	Index control			Index case	Index control	
IGRA +	19	3	22	TST +	27	6	33
IGRA -	36	15	51	TST -	28	12	40
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	55	18	73	Total	55	18	73

Test performance parameters	
IGRA	**TST**
Sensitivity = 19/55 = 34.55% (95% CI: 23.36, 47.75)	Sensitivity = 27/55 = 49.09% (95% CI: 36.38, 61.92)
Specificity = 15/18 = 83.33% (95% CI: 60.78, 94.16)	Specificity = 12/18 = 66.67% (95% CI: 43.75, 83.72)
PPV = 19/22 = 86.36% (95% CI: 66.66, 95.25)	PPV = 27/33 = 81.82% (95% CI: 65.61, 91.39)
NPV = 15/51 = 29.41% (95% CI: 18.71, 43.0)	NPV = 12/40 = 30.00% (95% CI: 18.07, 45.43)
DOR (for T^+ calculated) = 2.64 (95% CI: 0.67, 10.27)	DOR (for T^+ calculated) = 1.93 (95% CI: 0.63, 5.87)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 1.37 (95% CI: 0.56, 3.36)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)							
IGRA (TSPOT)				**TST (≥10 mm; two-step)**			
	Exposure level		Total		Exposure level		Total
	High	Low			High	Low	
IGRA +	NR	NR	NR	TST +	NR	NR	NR

IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = Smear $^-$ culture $^-$ = 1.00 (reference group) Smear $^-$ culture $^+$ = 1.60 (95% CI: 0.20, 12.69) Smear $^+$ culture $^+$ = 4.80 (95% CI: 1.05, 21.91)	**OR (crude; for T^+ reported) =** Smear $^-$ culture $^-$ = 1.00 (reference group) Smear $^-$ culture $^+$ = 1.50 (95% CI: 0.24, 9.46) Smear $^+$ culture $^+$ = 3.50 (95% CI: 0.88, 13.93)
OR (regression-based; reported) = Smear $^-$ culture $^-$ = 1.00 (reference group) Smear $^-$ culture $^+$ = 1.87 (95% CI: 0.22, 16.16) Smear $^+$ culture $^+$ = 5.36 (95% CI: 1.11, 25.93) List of covariates: NR	**OR (regression-based; reported) =** Smear $^-$ culture $^-$ = 1.00 (reference group) Smear $^-$ culture $^+$ = 1.09 (95% CI: 0.13, 9.42) Smear $^+$ culture $^+$ = 3.43 (0.76 to 15.52) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 1.37 (95% CI: 0.48, 3.91) [Smear + culture + vs. Smear – culture –]
Ratio of ORs (regression-based; reported) = 1.56 (95% CI: 0.51, 4.76) [Smear + culture + vs. Smear – culture –]
Other reported measure = NA

Association between test results and BCG status (if applicable)							
IGRA (specify)				**TST (specify)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR

Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (contacts with TB index case):			
	TST + (≥ 10mm)	TST -	Total
IGRA (TSPOT) +	15	4	19
IGRA (TSPOT) -	12	24	36
Indeterminate	NR (excluded)	NR (excluded)	NR (excluded)
Total	27	28	55
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): contacts with TB index case			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.41 (95% CI: 0.16, 0.66)			
% concordance = 39/55 = 70.91% (95% CI: 57.86, 81.23)			
% discordance = 16/55 = 29.09% (95% CI: 18.77, 42.14)			
Stratification (contacts with control index):			
	TST + (≥ 10mm)	TST -	Total
IGRA (TSPOT) +	2	1	3
IGRA(TSPOT) -	4	11	15
Indeterminate	NR (excluded)	NR (excluded)	NR (excluded)
Total	6	12	18
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): contacts with control index			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.28 (95% CI: -0.13, 0.70)			
% concordance = 13/18 = 72.22% (95% CI: 49.13, 87.5)			
% discordance = 5/18 = 27.78% (95% CI: 12.5, 50.87)			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Our findings suggest that ELISpot is a more accurate test than TST in HIV-infected persons recently infected with TB in a high-burden setting for both these infections. The increased accuracy of ELISpot testing compared with TST could improve targeting of preventive treatment to HIV-infected recent contacts of TB with LTBI which could further reduce the risk of active TB
Reviewers:
TSPOT performed better than TST in correctly identifying LTBI amongst HIV infected adult contacts due to higher specificity; agreement was higher amongst index case contacts vs. control contacts
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Papay 2011[137]
Country: Austria
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Outpatient clinic
Number of centres: One
Total length of follow up (if applicable): NR
Funding (government/private/manufacturer/other - specify)**:** NR

Aim of the study

To evaluate the impact of IM treatment on results from TST and IGRA in IBD patients before starting therapy with a biologic agent

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Inflammatory bowel disease (IBD) patients

Participants

Recruitment dates: December 2006 to August 2009
Total N of recruited patients: 208
Inclusion criteria: IBD patients
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 208
Total N of patients with valid results for both IGRA and TST: 192
Methods of active TB diagnosis (if applicable):
Outcomes (study-based) list: Test results, concordance of TST and IGRA, risk factor for LTB
Characteristics of participants (total study sample)
Mean (range or SD) age (years): age at screening 36.6 ± 11.3
Women (n [%]): 107 [51.4]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]):NR
BCG vaccination (n [%]): All subjects underwent BCG vaccination during childhood
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): Medically confirmed active TB (1 [0.5])
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): Crohn's disease (152 [73.1]); Ulcerative colitis (56 [26.9])
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Immunotherapy

Number of patients tested

	Total N (tested)	**Total N (test+)**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results available)**
IGRA (QFT-GIT):	192	15	177	0	192
TST:	192	26	166	0	192
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 192

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NR
Exposed 1 **(specify):**	Origin from a high-prevalent country
Exposed 2 **(specify):**	History of contact with active TB
Exposed 3 **(specify):**	Chest x-ray indicative of LTBI

Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA	QFT-GIT, Cellestis, Carnegie, Australia	≥0.35 IU/mL	NA
TST	Tuberculin purified protein derivative (PPD RT23, Staten Serum Institute, Copenhagen, Denmark), Mantoux method	For people with IM, TST was considered positive if the size of the induration was ≥ 5mm. For people without IM but have IBD a positive test result was >10 mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (Presence of risk factors for LTBI)

IGRA (QFT-GIT)				**TST (≥5 mm)**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	9	6	15	TST +	15	11	26
IGRA -	56	121	177	TST -	54	128	182
Indeterminate	4	12	16 (excluded)	Indeterminate	0	0	0
Total	69	139	208	Total	69	139	208

Test performance parameters

IGRA (excluding Indeterminate**)**	**TST**
Sensitivity = 9/65 = 13.85% (95% CI: 7.45, 24.27)	Sensitivity = 15/69 = 21.74% (95% CI: 13.64, 32.82)

Specificity = 121/127 = 95.28% (95% CI: 90.08, 97.82)	Specificity = 128/139 = 92.09% (95% CI: 86.38, 95.52)
PPV = 9/15 = 60.00% (95% CI: 35.75, 80.18)	PPV = 15/26 = 57.69% (95% CI: 38.95, 74.46)
NPV = 121/177 = 68.36% (95% CI: 61.18, 74.76)	NPV = 128/182 = 70.33% (95% CI: 63.33, 76.49)
DOR (for T^+ calculated) = 3.24 (95% CI: 1.10, 9.54)	DOR (for T^+ calculated) = 3.23 (95% CI: 1.39, 7.49)
OR (crude; for T^+ reported) = 3.20 (95% CI: 1.10, 10.10)	OR (crude; for T^+ reported) = 3.20 (95% CI: 1.40, 7.50)
OR (regression-based; reported) = 3.50 (95% CI: 1.20, 11.30) List of covariates: NR	OR (regression-based; reported) = 3.70 (95% CI: 1.50, 9.60) List of covariates: NR
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = 1.00 (95% CI: 0.50, 2.02)	
Ratio of OR (crude; for T^+ reported) = NR	
Ratio of ORs (regression-based; reported) = NR	
Other reported measure = NR	

Association between test results and levels of TB exposure (origin from a high-incidence country)

IGRA (QFT-GIT)				**TST (≥5 mm)**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	4	11	15	TST +	11	15	26
IGRA -	24	153	177	TST -	18	164	182
Indeterminate	1	15	16 (excluded)	Indeterminate	0	0	0
Total	29	179	208	Total	29	179	208

Test performance parameters	
IGRA (excluding indeterminate)	**TST (excluding indeterminate)**
Sensitivity = 4/28 = 14.29%, 95% CI (5.69, 31.49)	Sensitivity = 11/29 = 37.93%, 95% CI (22.69, 56)
Specificity = 153/164 = 93.29%, 95% CI (88.39, 96.21)	Specificity = 164/179 = 91.62%, 95% CI (86.64, 94.86)
PPV = 4/15 = 26.67%, 95% CI (10.9, 51.95)	PPV = 11/26 = 42.31%, 95% CI (25.54, 61.05)
NPV = 153/177 = 86.44%, 95% CI (80.62, 90.72)	NPV = 164/182 = 90.11%, 95% CI (84.91, 93.65)
DOR (for T^+ calculated) = 2.32, 95% CI (0.68, 7.87)	DOR (for T^+ calculated) = 6.68, 95% CI (2.67, 16.73)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = 0.35 (95% CI: 0.16, 0.76)	
Ratio of OR (crude; for T^+ reported) = NR	
Ratio of ORs (regression-based; reported) = NR	
Other reported measure = NR	

Association between test results and levels of TB exposure (history of contact with active TB)

IGRA (QFT-GIT)				**TST(≥5 mm)**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	2	13	15	TST +	4	22	26

IGRA -	8	169	177	TST -	7	175	182
Indeterminate	1	15	16	Indeterminate	0	0	0
Total	11	197	208	Total	11	197	208

Test performance parameters	
IGRA (excluding indeterminate)	**TST (excluding indeterminate)**
Sensitivity = 2/10 = 20.00%, 95% CI (5.668, 50.98)	Sensitivity = 4/11 = 36.36%, 95% CI (15.17, 64.62)
Specificity = 169/182 = 92.86%, 95% CI (88.16, 95.78)	Specificity = 175/197 = 88.83%, 95% CI (83.67, 92.51)
PPV = 2/15 = 13.33%, 95% CI (3.736, 37.88)	PPV = 4/26 = 15.38%, 95% CI (6.15, 33.53)
NPV = 169/177 = 95.48%, 95% CI (91.34, 97.69)	NPV = 175/182 = 96.15%, 95% CI (92.27, 98.12)
DOR (for T^+ calculated) = 3.25, 95% CI (0.62, 16.91)	DOR (for T^+ calculated) = 4.54, 95% CI (1.23, 16.78)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = 0.72 (95% CI: 0.24, 2.10)	
Ratio of OR (crude; for T^+ reported) = NR	
Ratio of ORs (regression-based; reported) = NA	
Other reported measure = NR	

Association between test results and levels of TB exposure (Chest x-ray indicative of LTBI)

IGRA (QFT-GIT)				**TST(≥5 mm)**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	1	14	15	TST +	5	21	26
IGRA -	10	167	177	TST -	6	176	182
Indeterminate	0	16	16 (excluded)	Indeterminate	0	0	0
Total	11	197	208	Total	11	197	208

Test performance parameters	
IGRA (excluding indeterminate)	**TST**
Sensitivity = 1/11 = 9.09%, 95% CI (1.62, 37.74)	Sensitivity = 5/11 = 45.45%, 95% CI (21.27, 71.99)
Specificity = 167/181 = 92.27%, 95% CI (87.44, 95.34)	Specificity = 176/197 = 89.34%, 95% CI (84.25, 92.92)
PPV = 1/15 = 6.66%, 95% CI (1.18, 29.82)	PPV = 5/26 = 19.23%, 95% CI (8.50, 37.88)
NPV = 167/177 = 94.35%, 95% CI (89.91, 96.9)	NPV = 176/182 = 96.7%, 95% CI (93, 98.48)
DOR (for T^+ calculated) = 1.19, 95% CI (0.14, 10.01)	DOR (for T^+ calculated) = 6.98, 95% CI (1.96, 24.87)
OR (crude; for T^+ reported) = 1.20, 95% CI: 0.10, 6.90	OR (crude; for T^+ reported) = 6.30, 95% CI: 1.70, 22.90
OR (regression-based; reported) = 1.10, 95% CI: 0.10, 7.70 List of covariates: NR	OR (regression-based; reported) = 4.90, 95% CI: 1.10, 19.9 List of covariates: NR
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = 0.17 (95% CI: 0.05, 0.61)	
Ratio of OR (crude; for T^+ reported) = 0.19 (95% CI: 0.05, 0.68)	
Ratio of ORs (regression-based; reported) = 0.22 (95% CI: 0.06, 0.85)	
Other reported measure = NR	

Association between test results and levels of TB exposure (IM treatment)							
IGRA (QFT-GIT)				**TST(≥5 mm)**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	7	8	15	TST +	18	8	26
IGRA -	130	47	177	TST -	131	51	182
Indeterminate	12	4	16 (excluded)	Indeterminate	0	0	0
Total	149	59	208	Total	149	59	208

Test performance parameters	
IGRA (excluding indeterminate)	**TST**
DOR (for T^+ calculated) = 0.31 (95% CI: 0.10, 0.92)	DOR (for T^+ calculated) = 0.87 (95% CI: 0.35, 2.14)
OR (crude; for T^+ reported) = 0.30 (95% CI: 0.10, 0.90)	OR (crude; for T^+ reported) = 0.90 (95% CI: 0.40, 2.30)
OR (regression-based; reported) = 0.30 (95% CI: 0.10, 0.90) List of covariates: NR	OR (regression-based; reported) = 0.90 (95% CI: 0.40, 2.60) List of covariates: NR
Other reported measure =	Other reported measure =

Association between test results and BCG status (if applicable)							
IGRA (specify)				**TST (specify)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	157	20	177
IGRA -	9	6	15
Indeterminate	0	0	0
Total	166	26	192
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥5 mm			
Parameters			
Kappa = 0.21, 95% CI (0.07, 0.34)			
% concordance = 163/192 = 84.90%, 95% CI (79.15, 89.27)			
% discordance = 29/192 = 15.10%, 95% CI (10.73, 20.85)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR

Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

These authors demonstrated that there is an association of positive results from TST and IGRA with the presence of risk factors for LTBI. Additionally, their results showed that there is a negative impact of therapy with IM on IGRA results (not on TST). They further concluded that LTBI screening should be undertaken at the diagnosis of IBD, and before treatment for IM

Reviewers:

IGRA positivity rate was lower in patients on IM vs. no IM treatment; TST was not affected by IM treatment

Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details
First author surname year of publication: Ramos 2013[138] **Country:** Spain **Study design:** Retrospective cohort/cross-sectional study **Study setting** (e.g., outbreak investigation, community-based - specify)**:** Outpatient infectious diseases clinic of a university hospital **Number of centres:** NR **Total length of follow up (if applicable):** NA **Funding** (government/private/manufacturer/other - specify)**:** Grants from Conselleria de Sanidad (051/2007), and FIS (PI08/90778)
Aim of the study
To evaluate the performance of QFG compared with the TST for the diagnosis of LTBI in patients with immune-mediated inflammatory disease (IMID) before TNF-a antagonist therapy. Additionally, the impact of immunosuppressive therapy on QFG and TST performance in different IMID was evaluated
Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)
Immunocompromised people (patients with IMID before TNF-a antagonist therapy)
Participants
Recruitment dates: From January 2009 to May 2011 **Total N of recruited patients:** NR **Inclusion criteria:** All adults (age C 15 years) candidates for anti-TNF-a therapy who attended the clinic **Exclusion criteria:** NR **Total N of excluded patients:** NR **Total N of patients tested with both IGRA and TST:** 153 **Total N of patients with valid results for both IGRA and TST:** 152 **Methods of active TB diagnosis (if applicable):** NR **Outcomes (study-based) list:** Agreement; association of test positivity with exposure; influence of immunosuppressive treatment on test positivity and agreement; influence of underlying disease on test positivity **Characteristics of participants (total study sample)** Mean (range or SD) age (years): Median 52 (16–82) Women (n [%]): 73 [47.7] Race/ethnicity (n [%]): NR Geographic origin (n[%]): Born in a TB endemic area (8 [5.2]) BCG vaccination (n [%]): 29 [19] History of anti-TB treatment (n [%]): 5 [3.3] Total incidence of active TB (n [%]): NR Chest radiography (yes/no): Yes Clinical examination (yes/no): NR Morbidity (n [%]): Rheumatoid arthritis (RA) (53 [43.6]), psoriasis/psoriatic arthritis (45 [29.4]), inflammatory bowel diseases (IBD) (25 [16.3]), spondyloarthropathy (SA) (22 [14.4]), severe hidradenitis (3 [2.0]), systemic lupus erythematosus (2 [1.3]), polymyositis (1 [0.6]), sarcoidosis (1 [0.6]), and mixed connective tissue disease (1 [0.6]) Co-morbidity (n [%]): NR Type of during-study treatment (n [%]): Immunosuppressive drug (91 [59.5]), methotrexate (57 [37.3]), corticosteroids (28 [18.3]), leflunomide (21 [13.7]), azathioprine (19 [12.4]), cyclosporine (6 [3.9])

Number of patients tested

	Total N (tested)	Total N	Total N (test-)	Total N (indeterminate)	Total N (test results

		(test+)			**available)**
IGRA (QFT-GIT):	153	15	137	1	152
TST (≥5mm):	153	43	110	0	153
Test 3 (specify):	NA	NA	NA	NA	NA
Total N of patients with valid results for both IGRA and TST: 152					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group – Born in a TB endemic area					
Non-exposed	Not born in a TB endemic area				
Exposed 1 **(specify):**	Born in a TB endemic area				
Definition of exposure group – History of contact with TB patients					
Non-exposed	No contact with TB patients				
Exposed 1 **(specify):**	Contact with TB patients				
Tests					
	Assay used, methodology, timing for test measurement, manufacturer		**Cut-off values/thresholds Definition of test+**		**Other information**
IGRA (QFT-GIT)	For QFG, three aliquots of 1 ml of undiluted heparinized whole blood were collected in three tubes**:** one containing TB antigens (ESAT-6, CFP-10, and TB7.7), a positive control tube containing phytohemagglutinin, and a negative control tube. Blood samples were incubated for 16–20 h at 37◦C. Plasma samples were then harvested for IFN-c quantification by a single-step sandwich-type ELISA The test was performed according to the manufacturer's instructions (Cellestis, Carnegie, Australia)		According to the instructions, the result was considered to be positive if the IFN-c level after stimulation with TB antigens minus negative control was ≥0.35 IU/ml. The test was considered negative if the IFN-c level was <0.35 IU/ml after subtraction of the negative control The test result was considered to be indeterminate if (1) the negative control was ≥8.0 IU/ml or (2) the positive control was <0.5 IU/ml Moreover, the test result was considered to be intermediate if IFN-c level was ≥0.10 IU/ml but <0.35 IU/ml		QFG and TST were performed simultaneously in a blinded fashion
TST(≥5mm)	Study participants were injected with 0.1 ml of tuberculin (2 tuberculin units of PPD) (Tuberculina PPD; Evans 2UT, UCB Pharma, S.A. Madrid, Spain) in accordance with the American Thoracic Society guidelines. The transverse skin induration diameter was measured 48–72h later		TST was deemed positive if the induration diameter was more than 5 mm		QFG and TST were performed simultaneously in a blinded fashion

Association between test results and incidence of active TB (if applicable)							
IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)							
IGRA (QFT-GIT)				**TST (≥5mm)**			
	Exposure level		Total		Exposure level		Total
	Born in TB endemic area	Not born in TB endemic area			Born in TB endemic area	Not born in TB endemic area	
IGRA +	4	11	15	TST +	4	39	43
IGRA -	4	133	137	TST -	4	106	110
Indeterminate	NR (excluded)	NR (excluded)	1 (excluded)	Indeterminate	0	0	0
Total	8	144	152	Total	8	145	153

Test performance parameters	
IGRA	**TST**
Sensitivity = 4/8 = 50.00% (95% CI: 21.52, 78.48)	Sensitivity = 4/8 = 50.00% (95% CI: 21.52, 78.48)
Specificity = 133/144 = 92.36% (95% CI: 86.84, 95.68)	Specificity = 106/145 = 73.1% (95% CI: 65.36, 79.66)
PPV = 4/15 = 26.67% (95% CI: 10.90, 51.95)	PPV = 4/43 = 9.30% (95% CI: 3.67, 21.60)
NPV = 133/137 = 97.08% (95% CI: 92.73, 98.86)	NPV = 106/110 = 96.36% (95% CI: 91.02, 98.58)
DOR (for T^+ calculated) = 12.09 (95% CI: 2.65, 55.07)	DOR (for T^+ calculated) = 2.72 (95% CI: 0.65, 11.40)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 29.30 (95% CI: 4.60, 18.5) error	OR (regression-based; reported) = 3.10 (95% CI: 0.70, 13.70)

List of covariates: age, sex	List of covariates: age, sex
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 4.44 (95% CI: 1.53, 12.89)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥5mm)**			
	Exposure level		Total		Exposure level		Total
	Contact with TB	No contact with TB			Contact with TB	No contact with TB	
IGRA +	3	12	15	TST +	4	39	43
IGRA -	4	133	137	TST -	3	107	110
Indeterminate	NR (excluded)	NR (excluded)	1 (excluded)	Indeterminate	0	0	0
Total	7	145	152	Total	7	146	153

Test performance parameters

IGRA	**TST**
Sensitivity = 3/7 = 42.86% (95% CI: 15.82, 74.95)	Sensitivity = 4/7 = 57.14% (95% CI: 25.05, 84.18)
Specificity = 133/145 = 91.72% (95% CI: 86.09, 95.20)	Specificity = 107/146 = 73.29% (95% CI: 65.58, 79.8)
PPV = 3/15 = 20.00% (95% CI: 7.04, 45.19)	PPV = 4/43 = 9.30% (95% CI: 3.67, 21.6)
NPV = 133/137 = 97.08% (95% CI: 92.73, 98.86)	NPV = 107/110 = 97.27% (95% CI: 92.29, 99.07)
DOR (for T^+ calculated) = 8.31 (95% CI: 1.66, 41.56)	DOR (for T^+ calculated) = 3.66 (95% CI: 0.78, 17.08)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = 8.00 (95% CI: 1.40, 47.00) List of covariates: age, sex	OR (regression-based; reported) = 3.20 (95% CI: 0.70, 15.50) List of covariates: age, sex
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 2.27 (95% CI: 0.73, 7.08)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = 2.50 (95% CI: 0.76, 8.26)
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST (≥5mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	7	8	15	TST +	13	30	43
IGRA -	22	115	137	TST -	16	94	110
Indeterminate	NR (excluded)	NR (excluded)	1 (excluded)	Indeterminate	0	0	0
Total	29	123	152	Total	29	124	153

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = 4.57 (95% CI: 1.50, 13.91)	DOR (for T+ calculated)$_{TST}$ = 2.54 (95% CI: 1.10, 5.89)

OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = 5.10 (95% CI: 1.50, 17.50) List of covariates: Age, sex	OR (regression-based; reported) $_{TST}$ = 2.40 (95% CI: 1.01, 5.80) List of covariates: Age, sex
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + (≥5mm)	TST -	Total
IGRA (QFT-GIT) +	13	2	15
IGRA (QFT-GIT) -	30	107	137
Indeterminate	NR (excluded)	NR (excluded)	1 (excluded)
Total	43	109	152

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥5mm

Parameters

Kappa = 0.35 (95% CI: 0.22, 0.48)

% concordance = 120/152 = 78.95% (95% CI: 71.79, 84.67)

% discordance = 32/152 = 21.05% (95% CI: 15.33, 28.21)

Between-test agreement, concordance, and discordance (if applicable)
Patients not receiving immunosuppressant

Total sample

	TST + (≥5mm)	TST -	Total
IGRA (QFT-GIT) +	11	0	11
IGRA (QFT-GIT) -	10	41	51
Indeterminate	NR (excluded)	NR (excluded)	1 (excluded)
Total	21	41	62

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Patients not receiving immunosuppressant

TST + threshold: ≥5mm

Parameters

Kappa = 0.59 (95% CI: 0.36, 0.82)

% concordance = 52/62 = 83.87% (95% CI: 72.79, 91.00)

% discordance = 10/62 = 16.13% (95% CI: 9.00, 27.21)

Between-test agreement, concordance, and discordance (if applicable)
Patients receiving immunosuppressant

Total sample

	TST + (≥5mm)	TST -	Total
IGRA (QFT-GIT) +	2	2	4
IGRA (QFT-GIT) -	20	66	86
Indeterminate	NR (excluded)	NR (excluded)	1 (excluded)
Total	22	68	90

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Patients receiving immunosuppressant

TST + threshold: ≥5mm

Parameters

Kappa = 0.08 (95% CI: -0.05, 0.22)

% concordance = 68/90 = 75.56% (95% CI: 65.75, 83.27)

% discordance = 22/90 = 24.44% (95% CI: 16.73, 34.25)

Other outcomes

Test and cut-off (if applicable)	Adverse events n/N (%) (specify)	Health related quality of life mean score (SD) (specify)
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

Test positivity odds for QFT was decreased in immunosuppressant recipients vs. those not on immunosuppressant (OR = 0.20, 95% CI: 0.06, 0.80). In contrast, test positivity odds for TST between these groups was similar (OR = 0.70, 95% CI: 0.30, 1.40). Therefore, immunosuppressant therapy impaired preferentially the sensitivity of the QFG test, since the rate of positive results was significantly lower in patients on immunosuppressive therapy

We observed a worse agreement between TST and QFG in patients on immunosuppressive therapy. The TST positive and QFG-negative results in immunosuppressive patients may be explained due to a false positivity of TST related to atypical mycobacteria

In patients with IMID, QFG may have a limited role for screening of LTBI. We found a negative effect of immunosuppressive therapy on QFG performance (sensitivity)

Reviewers:

QFT performed better than TST in correctly identifying LTBI with better specificity (stronger associations with exposures: born in endemic area; contact with TB case); however, QFT test positivity rate (not necessarily sensitivity) was influenced by immunosuppressant therapy, i.e., it was lower in patients on this therapy vs. patients without the therapy. This influence was not observed for TST

BCG vaccination influenced both QFT and TST positivity odds similarly (increased positivity odds in vaccinated vs. not vaccinated for both tests)

Agreement was lower in patients on immunosuppressant therapy vs. without the therapy due to lower specificity of TST vs. QFT

Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; IBD = inflammatory bowel diseases; PPV = positive predictive value; NPV = negative predictive value; RA = rheumatoid arthritis; SA = spondyloarthropathy; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Seyhan 2010[139]
Country: Turkey
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** NR
Number of centres: NR
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** None

Aim of the study

To compare the results of QFT-G with TST for detecting LTBI in hemodialysis patients

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Hemodialysis patients

Participants

Recruitment dates: Between November 2008 and December 2008
Total N of recruited patients: NR
Inclusion criteria: Hemodialysis patients
Exclusion criteria: Suspicion of active TB infection, use of immunosuppressive drugs, and other known immunodeficiency status (human immunodeficiency virus [HIV], malignancy, etc
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 100
Methods of active TB diagnosis (if applicable):
Outcomes (study-based) list: Test results, TST or QFT-G and risk factors, concordance between TST and QFT-G test
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 56.2±15.3
Women (n [%]): 53 [53]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 72 [72]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-G):	100	43	57	0	100
TST (≥10mm):	100	34	66	0	100
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 100

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group-1	
Non-exposed	No prior history of active TB
Exposed 1 **(specify):**	Prior history of active TB
Definition of exposure group-2	
Non-exposed	No previous contact of the patient with TB cases

Exposed 1 **(specify):**	Previous contact of the patient with TB cases (details of any contact with a person having TB, individuals who had household contact with or who had worked in the same rooms as patients with smear-positive pulmonary TB, and elapsed time after the contact)
Definition of exposure group-3	
Non-exposed	No chest radiograph changes consistent with old TB
Exposed 1 **(specify):**	Chest radiograph changes consistent with old TB

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-G, not reported	≥0.35 IU/mL of IFN-γ in the TB antigen tube minus the negative control tube was considered to be a positive test result	Blood was collected before TST placement.
TST≥ 10mm	Mantoux method was performed intradermally on the volar surface of the forearm with 0.1 mL (5TU) of PPD material (Intervax Biologicals, Markham, Ontario, Canada), induration was measured 48-72 hours after TST placement	≥ 10mm induration was considered to be a positive test result	People with an initial induration of less than 10mm were administered a second TST one week later to cause a potential booster response. Results from the two-step testing were used in all further analyses

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA

Other reported measure = NR

Association between test results and levels of TB exposure (Previous TB disease)

IGRA (QFT-GIT)				TST≥ 10mm			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	6	37	43	TST +	3	31	34
IGRA -	2	55	57	TST -	5	61	66
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	8	92	100	Total	8	92	100

Test performance parameters

IGRA	TST
Sensitivity = 6/8 = 75%, 95% CI (40.93, 92.85)	Sensitivity = 3/8 = 37.5%, 95% CI (13.68, 69.43)
Specificity = 55/92 = 59.78%, 95% CI (49.57, 69.22)	Specificity = 61/92 = 66.3%, 95% CI (56.17, 75.14)
PPV = 6/43 = 13.95%, 95% CI (6.556, 27.26)	PPV = 3/34 = 8.824%, 95% CI (3.047, 22.96)
NPV = 55/57 = 96.49%, 95% CI (88.08, 99.03)	NPV = 61/66 = 92.42%, 95% CI (83.46, 96.72)
DOR (for T^+ calculated) = 4.46, 95% CI (0.85, 23.31)	DOR (for T^+ calculated) = 1.18, 95% CI (0.26, 5.26)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR (NS)
OR (regression-based; reported) = 2.06, 95% CI (0.30, 12.80) List of covariates: NR	OR (regression-based; reported) = NR (NS) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 3.78 (95% CI: 1.21, 11.83)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and levels of TB exposure (Previous contact with TB)

IGRA (QFT-GIT)				TST (≥10mm)			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	10	33	43	TST +	6	28	34
IGRA -	3	54	57	TST -	7	59	66
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	13	87	100	Total	13	87	100

Test performance parameters

IGRA	TST
Sensitivity = 10/13 = 76.92%, 95% CI (49.74, 91.82)	Sensitivity = 6/13 = 46.15%, 95% CI (23.21, 70.86)
Specificity = 54/87 = 62.07%, 95% CI (51.57, 71.55)	Specificity = 59/87 = 67.82%, 95% CI (57.43, 76.7)
PPV = 10/43 = 23.26%, 95% CI (13.15, 37.74)	PPV = 6/34 = 17.65%, 95% CI (8.349, 33.51)
NPV = 54/57 = 94.74%, 95% CI (85.63, 98.19)	NPV = 59/66 = 89.39%, 95% CI (79.69, 94.77)
DOR (for T^+ calculated) = 5.45, 95% CI (1.40, 21.27)	DOR (for T^+ calculated) = 1.81, 95% CI (0.55, 5.87)

OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR (NS)
OR (regression-based; reported) = 5.08, 95% CI (1.20, 21.20) List of covariates: NR	OR (regression-based; reported) = NR (NS) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 3.01 (95% CI: 1.20, 7.56)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and levels of TB exposure (Chest X-ray with changes)

IGRA (QFT-GIT)				TST≥10mm			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	11	32	43	TST +	4	30	34
IGRA -	5	52	57	TST -	12	54	66
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	16	84	100	Total	16	84	100

Test performance parameters

IGRA	TST
Sensitivity = 11/16 = 68.75%, 95% CI (44.40, 85.84)	Sensitivity = 4/16 = 25.00%, 95% CI (10.18, 49.50)
Specificity = 52/84 = 61.90%, 95% CI (51.22, 71.55)	Specificity = 54/84 = 64.29%, 95% CI (53.62, 73.70)
PPV = 11/43 = 25.58%, 95% CI (14.93, 40.24)	PPV = 4/34 = 11.76%, 95% CI (4.67, 26.62)
NPV = 52/57 = 91.23%, 95% CI (81.05, 96.19)	NPV = 54/66 = 81.82%, 95% CI (70.85, 89.28)
DOR (for T^+ calculated) = 3.57, 95% CI (1.14, 11.24)	DOR (for T^+ calculated) = 0.60, 95% CI (0.18, 2.02)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR (NS)
OR (regression-based; reported) = 3.06, 95% CI (2.10, 11.90) List of covariates: NR	OR (regression-based; reported) = NR (NS) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 5.95 (95% CI: 2.54, 13.91)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				TST ≥10mm			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	34	9	43	TST +	30	4	34
IGRA -	38	19	57	TST -	42	24	66
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	72	28	100	Total	72	28	100

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{QFT}$ = 1.89 (95% CI: 0.75, 4.73)	DOR $_{TST}$ (for T+ calculated) = 4.28 (95% CI: 1.35, 13.64)

OR (crude; for T^+ reported) = NR (NS)	OR (crude; for T+ reported) = NR (SS)
OR (regression-based; reported)$_{QFT}$ = NR (NS) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 4.10 (1.30, 13.90) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	21	22	43
IGRA -	13	44	57
Indeterminate	0	0	0
Total	34	66	100

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total

TST + threshold: ≥ 10mm

Parameters

Kappa = 0.27, 95% CI (95% CI: 0.07, 0.46)

% concordance = 65/100 = 65.00%, 95% CI (55.25, 73.64)

% discordance = 35/100 = 35.00%, 95% CI (26.36, 44.75)

Stratification (BCG vaccinated)

	TST +	TST -	Total
IGRA +	17	17	34
IGRA -	13	25	38
Indeterminate	0	0	0
Total	30	42	72

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG

TST + threshold: ≥ 10mm

Parameters

Kappa = 0.16, 95% CI (-0.07, 0.39)

% concordance = 42/72 = 58.33%, 95% CI (46.81, 69.01)

% discordance = 30/72 = 41.67%, 95% CI (30.99, 53.19)

Stratification (non-BCG vaccinated)

	TST +	TST -	Total
IGRA +	4	5	9
IGRA -	0	19	19
Indeterminate	0	0	0
Total	4	24	28

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Unvaccinated

TST + threshold: ≥ 10mm

Parameters

Kappa = 0.52, 95% CI (0.19, 0.84)

% concordance = 23/28 = 82.14%, 95% CI (64.41, 92.12)

% discordance = 5/28 = 17.86%, 95% CI (7.878, 35.59)

Other outcomes

Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
These authors concluded that there was poor agreement between TST and QFT-G for LTBI in HD patients. Additionally, unlike the TST, the QFT-G results were significantly related to LTBI risk factors, but not related to the BCG status. They further concluded that QFT-G was a superior to the TST test for detecting LTBI in HD patients
Reviewers:
QFT-GIT performed better than TST in identifying LTBI correctly showing stronger associations between test positivity odds and the exposures. Also, IGRA was not dependent on BCG vaccination unlike TST positivity. Agreement was higher in BCG non vaccinated patients
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Shen 2012[140]
Country: China
Study design: Retrospective study
Study setting (e.g., outbreak investigation, community-based - specify)**:** University hospital
Number of centres: 1
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** None

Aim of the study

To evaluated the diagnostic value of an enzyme-linked immunosorbent spot (ELISPOT) assay measuring interferon-Y in hepatitis C patients with LTBI

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Hepatitis C patients

Participants

Recruitment dates: From January 2009 to December 2010
Total N of recruited patients: NR
Inclusion criteria: Hepatitis patients with (TB exposure group-patients who had history of exposure to TB and did not do clinical diagnosis of TB, with obvious clinical symptoms; non-TB exposure group- patients who had no history of exposure to TB and no clinical symptoms; TB group-patients who were clinically diagnosed with TB and with apparent clinical symptoms)
This review focuses on 70 patients (TB exposure group-patients), n = 31 (suspected LTBI; excluding 9 TB patients) and n = 39 non-exposed patients (no history of exposure to TB and no clinical symptoms)
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 160 (TST and ELISPOT)
Total N of patients with valid results for both IGRA and TST: 160 (TST and ELISPOT)
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Test results, sensitivity and specificity of TST and ELISPOT
Characteristics of participants (total study sample)
Mean (range or SD) age (years): TB exposure group n = 40 (42.9 ± 18.6); No TB exposure group (n = 39) 37.8 ±17.6
Women (n [%]): TB exposure (37 [47]); No TB exposure (17 [45])
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]):NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Hepatitis C
Co-morbidity (n [%]): Heart disease, diabetes, liver cirrhosis, solid tumor, chronic renal failure
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT): ELISPOT	70	26	44	0	70
TST (≥5 mm):	70	34	36	0	70
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST:	
Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	No history of TB exposure and no clinical symptoms (n = 39)
Exposed 1 **(specify):**	History of exposure to tuberculosis (suspected having TB, but no symptoms of TB, n = 31)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (TSPOT)	IFN-γ ELISPOT assay (Beijing Gaoke Life and Technology Inc., China) was performed according to the manufacturer's recommendations	Not stated	NA
TST≥5 mm	TST was performed by intradermal injection (Mantoux method) of 0.1 mL (5U) of PPD according to current recommendations. The induration was measured with a ruler by a trained physician 72 hours after the injection	TST was considered positive when the transverse diameter of induration was ≥5 mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (Suspected TB disease)

IGRA (TSPOT)			**TST≥5mm**		
	Exposure level	Total		Exposure level	Total

	Yes	No			Yes	No	
IGRA +	22	4	26	TST +	19	15	34
IGRA -	9	35	44	TST -	12	24	36
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	31	39	70	Total	31	39	70

Test performance parameters	
IGRA	**TST**
Sensitivity = 22/31 = 70.97%, 95% CI (53.41, 83.9)	Sensitivity = 19/31 = 61.29%, 95% CI (43.82, 76.27)
Specificity = 35/39 = 89.74% (95% CI: 76.42, 95.94)	Specificity = 24/39 = 61.54% (95% CI: 45.9, 75.11)
PPV = 22/26 = 84.62% (95% CI: 66.47, 93.85)	PPV = 19/34 = 55.88% (95% CI: 39.45, 71.12)
NPV = 35/44 = 79.55% (95% CI: 65.5, 88.85)	NPV = 24/36 = 66.67% (95% CI: 50.33, 79.79)
DOR (for T^+ calculated) = 21.39 (95% CI: 5.87, 77.93)	DOR (for T^+ calculated) = 2.53 (95% CI: 0.96, 6.67)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 8.45 (95% CI: 3.71, 19.28)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (TSPOT/QFT)				**TST (>5 mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA (TSPOT/QFT)	**TST (>5 mm)**
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = NR	DOR $_{TST}$ (for T+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported)$_{QFT}$ = NR OR (regression-based; reported)$_{TSPOT}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR
Parameters

Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Based on the results from this study the ELISPOT assay had a high diagnostic sensitivity and a low false positive rate in the diagnosis of LTBI. They concluded that the use of this assay may be effective in diagnosing LTBI in this patient group to prevent LTBI developing into active TB
Reviewers:
IGRA performed better than TST for LTBI identification (on all parameters)
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Souza 2014[153]
Country: Brazil
Study design: cross-sectional/retrospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify): outpatient clinics
Number of centres: 8
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify): This research was supported by Fundacao de Apoio `a Pesquisa do Distrito Federal, FAPDF funded by SUS-PPSUS Grant no. 193.000.353/2010.

Aim of the study

To evaluate the added value of QFT-GIT over the TST for detecting LTBI among persons living with HIV/AIDS (PLWHA); also to explore the factors associated with a positive QFT-GIT and with discordant QFT-GIT/TST results

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised (HIV/AIDS)

Participants

Recruitment dates: between May 2011 and March 2013
Total N of recruited patients: NR
Inclusion criteria: People with HIV/AIDS over 17 years who were not submitted to TST in the previous five weeks
Exclusion criteria: Patients with history of other immunosuppression conditions (severe AIDS-related opportunistic infections, acute viral infections, those submitted to any vaccination in the previous two months, and those using immunosuppressive drugs), patients with present or past active TB and those with a history of a previous positive TST
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 299
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: between test agreement, association between factors and test results (positive, discordant tests)
Characteristics of participants (total study sample)
Mean (range or SD) age (years): median 40 (IQR = 32–46) years
Women (n [%]): 85 [28.3]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 228 [76.0]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): NR
Clinical examination (yes/no): NR
Morbidity (n [%]): HIV/AIDS
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT)	300	14	285	1	299
TST: **≥5mm**	300	10	290	0	300

Test 3 (specify)					

Total N of patients with valid results for both IGRA and TST: 299

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – History of contact with index case

Non-exposed	No
Exposed 1 **(specify)**:	Yes
Exposed 2 **(specify)**:	NR
Exposed 3 **(specify)**:	NR
Exposed 4 **(specify)**:	NR

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-GIT was performed according to the manufacturer's instruction	Positive result was considered if the difference between interferon response to TB antigens and negative control was ≥0.35 UI/mL and interferon response to TB antigens was ≥25% compared to the negative control response QFT-GIT was considered to be indeterminate if the interferon response to the negative control was ≥8UI/mL or <0.5UI/mL compared to the positive control	
TST≥5mm	Participants were submitted to TST using 0.1mL of PPD-RT 23 (2 units of tuberculin)	Injection and reading of induration 72 to 96 hours after injection were performed by a trained HCW Positive result was TST induration was ≥5mm	

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA
NPV= NA	NPV= NA

Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$= NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$= NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				TST (≥5mm)			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	0	13	13	TST +	1	8	9
IGRA -	35	245	280	TST -	34	251	285
indeterminate	NR	NR	1	indeterminate	0	0	0
Total	35	258	293	Total	35	259	294

Test performance parameters

IGRA	TST
Sensitivity = 0/35=0.00% (95% CI: 0.0, 9.89)	Sensitivity = 1/35=2.86% (95% CI: 0.50, 14.53)
Specificity = 245/258=94.96% (95% CI: 91.57, 97.03)	Specificity =251/259=96.91% (95% CI: 94.02, 98.43)
PPV= 0/13=0.00% (95% CI: 0.0, 22.81)	PPV=1/9= 11.11% (95% CI: 1.99, 43.5)
NPV= 245/280=87.5% (95% CI: 83.11, 90.87)	NPV=251/285=88.07% (95% CI: 83.79, 91.34)
DOR (for T^+ calculated)= 0.50 (95% CI: 0.06, 4.24)	DOR (for T^+ calculated)= 0.93 (95% CI: 0.11, 7.61)
OR (crude; for T^+ reported)= 0.49 (95% CI: 0.06, 3.82)	OR (crude; for T^+ reported)= 0.92 (95% CI: 0.11, 7.61)
OR (regression-based; reported)= NR List of covariates: NR	OR (regression-based; reported)= 1.21 (95% CI: 0.13, 11.16) List of covariates: NR
Other reported measure = NR	Other reported measure =NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 0.54 (95% CI: 0.12, 2.49)
Ratio of OR (crude; for T^+ reported) = 0.53 (95% CI: 0.12, 2.42)
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (specify)				TST (specify)			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA
OR (regression-based; reported) $_{IGRA}$ = NA	OR (regression-based; reported) $_{TST}$ = NA

List of covariates: NA	List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +(≥5mm)	TST -	Total
IGRA +	6	8	14
IGRA -	4	281	285
indeterminate	0	1	1
Total	10	289	299

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥5mm

Parameters

Kappa = 0.48 (95% CI: 0.37, 0.59)

% concordance = 287/299 = 96.00% (95% CI: 93.12, 97.69)

% discordance = 12/299 = 4.01% (95% CI: 2.31, 6.88)

Stratification (specify group 1):

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA

TST + threshold: NA

Parameters

Kappa = NA

% concordance = NA

% discordance = NA

Stratification (specify group 2):

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA

TST + threshold: NA

Parameters

Kappa = NA

% concordance = NA

% discordance = NA

Conclusions

Authors:

QFT-GIT alone was more effective to detect LTBI than TST (QFT yielded more positives), assuming that any test is a marker of LTBI

Reviewers:

The authors used invalid assumption of test positivity as a marker of LTBI; the results are inconclusive regarding the strength of association between test positivity and prior exposure to index

case (ORs and 95% CIs are too wide)
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Alexander Tsertsvadze

Study details

First author surname year of publication: Takeda 2011[141]
Country: Japan
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Hospital based
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Ministry of Health, Labor, and Welfare

Aim of the study

To evaluate whether QFT-GIT is useful in detecting LTBI in systemic lupus erythematosus (SLE) patients

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (patients with SLE)

Participants

Recruitment dates: July 2006 to September 2008
Total N of recruited patients: NR
Inclusion criteria: Systemic lupus erythematosus (SLE) patients; non-SLE connective tissue disease (rheumatoid arthritis, myositis, vasculitides, systemicscleroderma, Sjoegren's syndrome, Behcet's disease, adult-onset Still's disease)
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 71 (IGRA) and 43 (TST)
Total N of patients with valid results for both IGRA and TST: NR
Methods of active TB diagnosis (if applicable): Positive culture for MTB or a positive result on a polymerase chain reaction test for MTB DNA in any clinical specimen associated with compatible TB symptoms and radiographic findings
Outcomes (study-based) list: Association of test positivity and risk for LTBI, factors influencing indeterminate QFT results
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 38.3 (15.2)
Women (n [%]): 58 [81.7]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): SLE
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Corticosteroids (37 [52.1]), immunosuppressive drugs (19 [26.8]), prednisolone pulse therapy (2 [2.8]), NSAIDs or no therapy (13 [18.3])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-2G):	71	2	46	23	71
TST (≥10 mm):	43	3	40	0	43
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: Unclear

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	Without risk of LTBI
Exposed 1 **(specify):**	With risk factors for LTBI (history of household TB contact; chest X ray suggestive of previous TB showing nodules, fibrotic scars, calcified granulomas, basal thickening; history of active TB)
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA (QFT-GIT)	Quantiferon-TB Gold (QFT-2G), Cellestis, Carnegie, Australia	≥ 0.35 IU/mL	Negative result if the IFN-γ level in the antigen stimulated wells was <0.35 IU/mL and in the mitogen wells was ≥0.5 IU/mL. Results were considered indeterminate if the IFN-γ level in the antigen stimulated wells was <0.5 IU/mL, or if the IFN-γ level in the antigen-stimulated wells was below half of the level of the negative control was > 0.7 IU/mL
TST≥10 mm	0.1 mL of tuberculin purified protein derivative (PPD) (approximately 3 tuberculin units of PPD-S), Nippon BCG Manufacturing, Tokyo, Japan) into the venral surface of the forearm. The induration was measured 48 hours later	≥10 mm, according to the usual criterion of the TST in Japan	NA

Association between test results and incidence of active TB (if applicable)

IGRA				TST			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA

Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NR

Association between test results and levels of TB exposure (risk for LTBI)

IGRA				TST			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	2	0	2	TST +	1	2	3
IGRA -	16	30	46	TST -	13	27	40
Indeterminate	8	15	23	Indeterminate	0	0	0
Total	26	45	71	Total	14	29	43

Test performance parameters

IGRA	TST
Including indeterminate-as test negative Sensitivity = 2/26 = 7.70% (95% CI: 2.13, 24.14) **Excluding indeterminate** Sensitivity = 2/18 = 11.11% (95% CI: 3.10, 32.80)	Sensitivity = 1/14 = 7.14%, 95% CI (1.27, 31.47)
Including indeterminate-as test negative Specificity = 45/45 = 100.00% (95% CI: 92.13, 100.00) **Excluding indeterminate** Specificity = 30/30 = 100.00% (95% CI: 88.65, 100.00)	Specificity = 27/29 = 93.10%, 95% CI (78.04, 98.09)
PPV = 2/2 = 100.00%, 95% CI (34.24, 100.00)	PPV = 1/3 = 33.33%, 95% CI (6.15, 79.23)
Including indeterminate-as test negative NPV = 45/69 = 65.22% (95% CI: 53.45, 75.38) **Excluding indeterminate** NPV = 30/46 = 65.22% (95% CI: 50.77, 77.32)	NPV = 27/40 = 67.50%, 95% CI (52.02, 79.92)
DOR (for T^+ calculated) = 3.75 (95% CI: 0.31, 44.6)	DOR (for T^+ calculated) = 1.04, 95% CI (0.08, 12.53)
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 3.61 (95% CI: 0.59, 21.99)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (TSPOT/QFT)				TST (>5 mm)			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA (TSPOT/QFT)	**TST (>5 mm)**
DOR (for T^+ calculated)$_{TSPOT/QFT}$ = NA	DOR $_{TST}$ (for T+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA
OR (regression-based; reported)$_{QFT}$ = NA OR (regression-based; reported)$_{TSPOT}$ = NA List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**

IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
The authors concluded that the QFT-2G test may have more potential to assist in the diagnosis of active MTB infection and LTBI than TST in people who have systemic lupus. Additionally, the authors suggested that the results should be taken in caution in this patient group because one-third of the patients had an indeterminate test result, and care should be taken especially for those patients who have parallel or subsequent flares of the disease		
Reviewers:		
The authors did not report on the number of people who had valid results for both the IGRA and TST. TST was done on a subsample of 71 patients		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Vassilopolous 2011[142]
Country: Greece
Study design: Retrospective cohort study/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Outpatient rheumatology clinic of Hippokration general hospital
Number of centres: One
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Supported in part by research grants from the Hellenic Society for Rheumatology and the Special Account for Research Grants (SARG), National and Kapodistrian University of Athens, Athens, Greece

Aim of the study

To compare the latest IGRAs (QFT-GIT and T-SPOT.TB assays) and TST for LTBI diagnosis in rheumatic patients starting anti –TNF treatment

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Rheumatic patients starting anti-TNF therapies

Participants

Recruitment dates: Between September 2008 and September 2010
Total N of recruited patients: 157
Inclusion criteria: Patients with various rheumatic diseases who were seen at the Outpatient Rheumatology Clinic of Hippokration General Hospital (2nd Department of Medicine, Athens University School of Medicine, Athens, Greece) and scheduled for anti-TNF treatment
Exclusion criteria: Patients with active TB, a history of treatment with anti-TB agents, including isoniazid (INH) for LTBI, or a history of previous treatment with anti-TNF agents or other biologics
Total N of excluded patients: 2 (indeterminate QFT-GIT results from the analysis: spondyloarthropathy related to UC on high dose methylprednisolone)
Total N of patients tested with both IGRA and TST: 157
Total N of patients with valid results for both IGRA and TST: 155
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Test results, concordance of agreement between two assays
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 52 ±16
Women (n [%]): 90 [58]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]):NR
BCG vaccination (n [%]): 81 [76]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): NR
Co-morbidity (n [%]): 15 [21.4]
Type of during-study treatment (n [%]): Immunosuppressive therapy (DMARDs/steroids (98 [63]); DMARDs (80 [52]) steroids (66 [43])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	157	32	123	2	155
IGRA (T-SPOT.TB):	157	39	116	2	155

TST (≥ 5mm):	157	58	97	2	155

Total N of patients with valid results for both IGRA and TST: 155

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	No history of previous TB contact
Exposed 1 **(specify):**	History of previous TB contact
Definition of exposure group	
Non-exposed	Chest x-ray without signs suggestive of old TB
Exposed 2 **(specify):**	Chest x-ray suggestive of old TB
Definition of exposure group	
Non-exposed	No risk factor for TB (≥ 1)
Exposed 3 **(specify):**	Any risk factor for TB (≥ 1) including: age >50 years, chest X-ray suggestive of old/healed TB, contact with a person with TB, and birth or residence in a country with a high TB prevalence (non-Greek nationality)

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-GIT was performed according to the manufacturer's instructions	NR	The blood draw for both IGRAs was performed just prior to TST application in order to avoid potential interference with the IGRA results
IGRA (TSPOT)	The T-SPOT.TB assay was performed as previously described	NR	The blood draw for both IGRAs was performed just prior to TST application in order to avoid potential interference with the IGRA results
TST≥ 5mm	Mantoux method of 0.1 mL (2 IU) of purified protein derivative (PPD) RT 23; Statens Serum Institute, Copenhagen, Denmark)	A TST was considered positive when the diameter of transverse induration was ≥ 5mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA

Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA

Ratio of incidence density rate ratios = NA

Other reported measure = NR

Association between test results and levels of TB exposure (TB exposure)

IGRA (T-SPOT.TB)				**TST≥ 5mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	5	34	39	TST +	10	48	58
IGRA -	15	101	116	TST -	10	87	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	20	135	155	Total	20	135	155

Test performance parameters

IGRA	**TST**
Sensitivity = 5/20 = 25.00%, 95% CI (11.19, 46.87)	Sensitivity = 10/20 = 50.00%, 95% CI (29.93, 70.07)
Specificity = 101/135 = 74.81%, 95% CI (66.88, 81.38)	Specificity = 87/135 = 64.44%, 95% CI (56.07, 72.02)
PPV = 5/39 = 12.82%, 95% CI (5.60, 26.71)	PPV = 10/58 = 17.24%, 95% CI (9.64, 28.91)
NPV = 101/116 = 87.07%, 95% CI (79.76, 92.00)	NPV = 87/97 = 89.69%, 95% CI (82.05, 94.3)
DOR (for T^+ calculated) = 0.99, 95% CI (0.33, 2.92)	DOR (for T^+ calculated) = 1.81, 95% CI (0.70, 4.66)
OR (crude; for T^+ reported) = 0.99, 95% CI (NR; p = 0.99)	OR (crude; for T^+ reported) = 1.81, 95% CI (NR; p = 0.22)
OR (regression-based; reported) = 0.89, 95% CI (NR; p = 0.86) List of covariates: NR	OR (regression-based; reported) = 1.73, 95% CI (NR; p = 0.30) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 0.55 (95% CI: 0.26, 1.14)

Ratio of OR (crude; for T^+ reported) = NA

Ratio of ORs (regression-based; reported) = NA

Other reported measure = NR

Association between test results and levels of TB exposure (TB exposure)

IGRA (QFT-GIT)				**TST≥ 5mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	3	29	32	TST +	10	48	58
IGRA -	17	106	123	TST -	10	87	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	20	135	155	Total	20	135	155

Test performance parameters

IGRA	**TST**
Sensitivity = 3/20 = 15.00%, 95% CI (5.23, 36.04)	Sensitivity = 10/20 = 50.00%, 95% CI (29.93, 70.07)
Specificity = 106/135 = 78.52%, 95% CI (70.85, 84.61)	Specificity = 87/135 = 64.44%, 95% CI (56.07, 72.02)

PPV = 3/32 = 9.37%, 95% CI (3.24, 24.22)	PPV = 10/58 = 17.24%, 95% CI (9.64, 28.91)
NPV = 106/123 = 86.18%, 95% CI (78.98, 91.19)	NPV = 87/97 = 89.69%, 95% CI (82.05, 94.3)
DOR (for T^+ calculated) = 0.64, 95% CI (0.17, 2.35)	DOR (for T^+ calculated) = 1.81, 95% CI (0.70, 4.66)
OR (crude; for T^+ reported) = 0.64, 95% CI (NR; p = 0.5)	OR (crude; for T^+ reported) = 1.81, 95% CI (NR; p = 0.22)
OR (regression-based; reported) = 0.55, 95% CI (NR; p = 0.41) List of covariates: NR	OR (regression-based; reported) = 1.73, 95% CI (NR; p = 0.30) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 0.35 (95% CI: 0.15, 0.81)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and levels of TB exposure (Chest x-ray suggestive of old TB)

IGRA (T-SPOT.TB)				**TST≥ 5mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	4	35	39	TST +	9	49	58
IGRA -	10	106	116	TST -	5	92	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	14	141	155	Total	14	141	155

Test performance parameters

IGRA	**TST**
Sensitivity = 4/14 = 28.57%, 95% CI (11.72, 54.65)	Sensitivity = 9/14 = 64.29%, 95% CI (38.76, 83.66)
Specificity = 106/141 = 75.18%, 95% CI (67.44, 81.58)	Specificity = 92/141 = 65.25%, 95% CI (57.08, 72.61)
PPV = 4/39 = 10.26%, 95% CI (4.06, 23.58)	PPV = 9/58 = 15.52%, 95% CI (8.38, 26.93)
NPV = 106/116 = 91.38%, 95% CI (84.86, 95.25)	NPV = 92/97 = 94.85%, 95% CI (88.5, 97.78)
DOR (for T^+ calculated) = 2.21, 95% CI (0.35, 4.10)	DOR (for T^+ calculated) = 3.38, 95% CI (1.07, 10.64)
OR (crude; for T^+ reported) = 2.21, 95% CI (NR; p = 0.76)	OR (crude; for T^+ reported) = 3.38, 95% CI (NR; p = 0.04)
OR (regression-based; reported) = 0.48, 95% CI (NR; p = 0.31) List of covariates: NR	OR (regression-based; reported) = 3.50, 95% CI (NR; p = 0.05) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = 0.65 (95% CI: 0.28, 1.54)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and levels of TB exposure (Chest x-ray suggestive of old TB)

IGRA (QFT-GIT)				**TST≥ 5mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	14	28	32	TST +	9	49	58
IGRA -	10	113	123	TST -	5	92	97
Indeterminate	0	0	0	Indeterminate	0	0	0

Total	24	141	155	Total	14	141	155
Test performance parameters							
IGRA				**TST**			
Sensitivity = 58.33% (95% CI: 38.83, 75.53)				Sensitivity = 9/14 = 64.29%, 95% CI (38.76, 83.66)			
Specificity = 80.14% (95% CI: 72.8, 85.89)				Specificity = 92/141 = 65.25%, 95% CI (57.08, 72.61)			
PPV = 33.33% (95% CI: 21.01, 48.45)				PPV = 9/58 = 15.52%, 95% CI (8.38, 26.93)			
NPV = 91.87% (95% CI: 85.68, 95.52)				NPV = 92/97 = 94.85%, 95% CI (88.5, 97.78)			
DOR (for T^+ calculated) = 5.65 (95% CI: 2.27, 14.05)				DOR (for T^+ calculated) = 3.38, 95% CI (1.07, 10.64)			
OR (crude; for T^+ reported) = 1.61, 95% CI (NR; p = 0.44)				OR (crude; for T^+ reported) = 3.38, 95% CI (NR; p = 0.04)			
OR (regression-based; reported) = 1.29, 95% CI (NR; p = 0.72) List of covariates: NR				OR (regression-based; reported) = 3.50, 95% CI (NR; p = 0.05) List of covariates: NR			
Other reported measure = NR				Other reported measure = NR			
Comparison between tests (IGRA vs. TST)							
Ratio of DORs (for T^+ calculated) = 1.67 (95% CI: 0.79, 3.53)							
Ratio of OR (crude; for T^+ reported) = NA							
Ratio of ORs (regression-based; reported) = NA							
Other reported measure = NR							
Association between test results and levels of TB exposure (any risk factor for TB ≥ 1)							
IGRA (T-SPOT.TB)				**TST≥ 5mm**			
	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	34	5	39	TST +	42	16	58
IGRA -	68	48	116	TST -	60	37	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	102	53	155	Total	102	53	155
Test performance parameters							
IGRA				**TST**			
Sensitivity = 34/102 = 33.33%, 95% CI (24.94, 42.94)				Sensitivity = 42/102 = 41.18%, 95% CI (32.12, 50.88)			
Specificity = 48/53 = 90.57%, 95% (79.75, 95.9)				Specificity = 37/53 = 69.81%, 95% CI (56.46, 80.48)			
PPV = 34/39 = 87.18%, 95% CI (73.29, 94.4)				PPV = 42/58 = 72.41%, 95% CI (59.80, 82.25)			
NPV = 48/116 = 41.38%, 95% CI (32.83, 50.48)				NPV = 37/97 = 38.14%, 95% CI (29.10, 48.09)			
DOR (for T^+ calculated) = 4.80, 95% CI (1.75, 13.16)				DOR (for T^+ calculated) = 1.61, 95% CI (0.79, 3.28)			
OR (crude; for T^+ reported) = 4.80, 95% CI (NR; p = 0.02)				OR (crude; for T^+ reported) = 1.60, 95% CI (NR; p = 0.12)			
OR (regression-based; reported) = NR List of covariates: NR				OR (regression-based; reported) = NR List of covariates: NR			
Other reported measure = NR				Other reported measure = NR			
Comparison between tests (IGRA vs. TST)							
Ratio of DORs (for T^+ calculated) = 2.98 (95% CI: 1.59, 5.60)							
Ratio of OR (crude; for T^+ reported) = NA							
Ratio of ORs (regression-based; reported) = NA							
Other reported measure = NR							
Association between test results and levels of TB exposure (any risk factor for TB ≥ 1)							
IGRA (QFT-GIT)				**TST≥ 5mm**			

	Exposure level		Total		Exposure level		Total
	Yes	No			Yes	No	
IGRA +	26	6	32	TST +	42	16	58
IGRA -	76	47	123	TST -	60	37	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	102	53	155	Total	102	53	155

Test performance parameters	
IGRA	**TST**
Sensitivity = 26/102 = 25.49%, 95% (18.03, 34.73)	Sensitivity = 42/102 = 41.18%, 95% CI (32.12, 50.88)
Specificity = 47/53 = 88.68%, 95% CI (77.42, 94.71)	Specificity = 37/53 = 69.81%, 95% CI (56.46, 80.48)
PPV = 26/32 = 81.25%, 95% CI (64.69, 91.11)	PPV = 42/58 = 72.41%, 95% CI (59.80, 82.25)
NPV = 47/123 = 38.21%, 95% CI (30.10, 47.03)	NPV = 37/97 = 38.14%, 95% CI (29.10, 48.09)
DOR (for T^+ calculated) = 2.68, 95% CI (1.02, 6.99)	DOR (for T^+ calculated) = 1.61, 95% CI (0.79, 3.28)
OR (crude; for T^+ reported) = 2.68, 95% CI (NR; p = 0.04)	OR (crude; for T^+ reported) = 1.60, 95% CI (NR; p = 0.12)
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = 1.66 (95% CI: 0.90, 3.07)
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (T-SPOT.TB)				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	24	15	39	TST +	41	17	58
IGRA -	79	37	116	TST -	62	35	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	93	52	155	Total	103	52	155

Test performance parameters	
IGRA (T-SPOT.TB)	**TST (>5 mm)**
DOR (for T^+ calculated)$_{TSPOT}$ = 0.74, 95% CI (0.35, 1.59)	DOR $_{TST}$ (for T+ calculated) = 1.36, 95% CI (0.67, 2.74)
OR (crude; for T^+ reported) = 0.75, 95% CI (NR; p = 0.45)	OR (crude; for T+ reported) = 1.36, 95% CI (NR; p = 0.39)
OR (regression-based; reported)$_{TSPOT}$ = 0.51, 95% CI (NR; p = 0.17) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 1.43, 95% CI (NR; p = 0.34) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (QFT-GIT)				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	22	10	32	TST +	41	17	58
IGRA -	81	42	123	TST -	62	35	97
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	103	52	155	Total	103	52	155

Test performance parameters	
IGRA (QFT-GIT)	**TST (>5 mm)**
DOR (for T^+ calculated)$_{QFT}$ = 1.14, 95% CI (0.49, 2.63)	DOR $_{TST}$ (for T+ calculated) = 1.36, 95% CI (0.67, 2.74)
OR (crude; for T^+ reported) = 1.14, 95% CI (NR; p = 0.76)	OR (crude; for T+ reported) = 1.36, 95% CI (NR; p = 0.39)
OR (regression-based; reported)$_{QFT}$ = 1.05, 95% CI (NR; p = 0.90) List of covariates: NR	OR (regression-based; reported) $_{TST}$ = 1.43, 95% CI (NR; p = 0.34) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +≥5mm	TST -	Total
IGRA + (TSPOT)	26	13	39
IGRA -	32	84	116
Indeterminate	0	0	0
Total	58	97	155

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify):

TST + threshold: ≥5mm

Parameters

Kappa = 0.34 (95% CI: 0.17, 0.50)

% concordance = 110/155 = 71.0% (95% CI: 63.38, 77.54)

% discordance = 45/155 = 29.03% (95% CI: 22.46, 36.62)

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +≥5mm	TST -	Total
IGRA + (QFT-GIT)	17	15	32
IGRA -	41	82	123
Indeterminate	0	0	0
Total	58	97	155

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥5mm

Parameters

Kappa = 0.15 (95% CI: 0.01, 0.29)

% concordance = 99/155 = 63.87% (95% CI: 56.06, 71.01)

% discordance = 56/155 = 36.13% (95% CI: 28.99, 43.94)

Other outcomes

Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

These authors demonstrated that IGRAs appeared to be correlated better with TB risk than TST and should be included in LTBI screening of patients who are about to commence anti-TNF therapies. Furthermore, they suggested that in view of the high risk of TB in this patient group, a combination of one IGRA and TST is probably more appropriate for LTBI

Reviewers:
Steroid use was negatively associated with a positive QFT-GIT assay
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Alexander Tsertsvadze

Study details

First author surname year of publication: Anibarro 2012[117]
Country: Spain
Study design: Prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Outbreak investigation
Number of centres: One
Total length of follow up (if applicable): 18 months
Funding (government/private/manufacturer/other - specify)**:** University of Vigo and SUDOE-FEDER (IMMUNONET-SOE1/P1/E014)

Aim of the study

To compare the results of an IGRA with those for the TST in patients with early stage renal disease (ESRD) after a TB outbreak at a dialysis centre

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised (people undergoing haemodialysis treatment)

Participants

Recruitment dates: NR
Total N of recruited patients: 58
Inclusion criteria: All patients who attended the dialysis unit while index case was on duty
Exclusion criteria: Patients who had a previous +ve TST test
Total N of excluded patients: 6
Total N of patients tested with both IGRA and TST: 52
Total N of patients with valid results for both IGRA and TST: 52
Methods of active TB diagnosis (if applicable): Microscopic examination of sputum and sputum culture
Outcomes (study-based) list: Test results, relationship between TST and erythema, concordance between diagnostic tests
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 62 (16.8)
Women (n [%]): 21 [40.4]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 7 [13.5]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): None
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): End stage renal disease (58 [100])
Co-morbidity (n [%]): Diabetes mellitus (8 [15.4])
Type of during-study treatment (n [%]): Immunosuppressive therapy (8[15.3])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (specify): QFT-GIT	52	18	34	0	52
TST: (≥5 mm)	52	11	41	0	52
Test 3 (specify):					

Total N of patients with valid results for both IGRA and TST: 52

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group

Non-exposed	
Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA	QFT-GIT, one ml of whole blood, blood collected immediately before TST, Cellestic Ltd, Carnegie, Australia	0.35 IU/mL	
TST (one and two-step)	Mantoux method, 0.1ml (2 TU) of PPD injected intradermally to the volar surface of the forearm, TST results read 72h after testing, Statens serum Institute, Copenhagen, Denmark	TST ≥ 5mm, a second test was performed five days later if the first TST-1 was <5 mm	Study does not mention how soon after the result will be read for the second TST

Association between test results and incidence of active TB (if applicable)

IGRA				**TST≥5mm (two-step)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	N/A	N/A	11 LTBI treated	TST +	N/A	N/A	11 LTBI treated
IGRA -	0	32	32	TST -	0	32	32
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	0	32	32	Total	0	32	32

Test performance parameters

IGRA	**TST**
Sensitivity = N/A	Sensitivity = N/A
Specificity = N/A	Specificity = N/A
PPV = N/A	PPV = N/A
NPV = 100%, 95% CI (89.28, 100.00)	NPV = 100%, 95% CI (89.28, 100.00)
Cumulative Incidence $_{IGRA+}$ = N/A	Cumulative Incidence $_{TST+}$ = N/A
Cumulative Incidence $_{IGRA-}$ = 0/32 = 0	Cumulative Incidence $_{TST-}$ = 0/32 = 0
Cumulative Incidence Ratio $_{IGRA}$ = N/A	Cumulative Incidence Ratio $_{TST}$ = N/A
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence = NA
Ratio of incidence density rate ratios = NR
Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA				TST			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	3	15	18
IGRA -	0	34	34
Indeterminate	0	0	0
Total	3	49	52

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total (One-step TST)

TST + threshold: ≥ 5mm induration

Parameters

Kappa = 0.21, 95% CI: 0.04, 0.37

% concordance = 37/52 = 71.15% (95% CI: 57.73, 81.67)

% discordance = 15/52 = 28.85% (95% CI: 18.33, 42.27)

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	9	9	18
IGRA -	2	32	34
Indeterminate	0	0	0
Total	11	41	52

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total (Two-step test)

TST + threshold: ≥ 5mm induration

Parameters

Kappa = 0.49, 95% CI: 0.22, 0.74)

% concordance = 41/52 = 78.85% (95% CI: 65.97, 87.76)

% discordance = 11/52 = 21.15% (95% CI: 12.24, 34.03)

Stratification (specify group 2)

	TST +	TST -	Total

IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Other outcomes			
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**		**Health related quality of life mean score (SD) (specify)**
IGRA:	NR		NR
TST:	NR		NR
Test 3 (specify):	NR		NR
Conclusions			
Authors:			
This study demonstrated that QFT-GIT had a better sensitivity than TST in detecting latent TB in haemodialysis patients, after exposure to Mycobacterium tuberculosis. TST administered a second time can be performed to increase the sensitivity			
Reviewers:			
Authors have not presented results stratified by the level of exposure to TB.			
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation			

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Chang 2011[119]
Country: South Korea
Study design: Prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Hospital-based
Number of centres: One
Total length of follow up (if applicable): 18 mo (median)
Funding (government/private/manufacturer/other - specify)**:** IN-SUNG Foundation for Medical Research (CA98051)

Aim of the study

To evaluate the usefulness of IGRA for the diagnosis of LTBI in arthritis patients who received TNF antagonists in South Korea where the incidence of tuberculosis is intermediate (70–90/105 per year) and BCG vaccination is mandatory at birth

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people**:** Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) before starting TNF antagonist

Participants

Recruitment dates: August 2007–July 2009
Total N of recruited patients: 108
Inclusion criteria: Inflammatory arthritis including RA and AS who visited our facility to evaluate LTBI before starting TNF antagonist
Exclusion criteria: Active TB
Total N of excluded patients: 1
Total N of patients tested with both IGRA and TST: 107
Total N of patients with valid results for both IGRA and TST: 100
Methods of active TB diagnosis (if applicable): Medical history (current symptoms, prior history of treatment for tuberculosis, and recent history of contact with a case of active TB) and TST (according to the recommendation of the Korea Food and Drug Administration)
Outcomes (study-based) list: Test results, concordance/discordance, incidence of active TB, prognostic test accuracy indices (sensitivity, specificity, predictive values, false negative/false positive rates)
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 39 (median)
Women (n [%]): 44 [41]
Race/ethnicity (n [%]): Asian
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 63 [59]
History of anti-TB treatment (n [%]): 4 [3.8]
Total incidence of active TB (n [%]): 1 [0.9%]
Chest radiography (yes/no): NR
Clinical examination (yes/no): Yes
Morbidity (n [%]): RA (46 [43]) and AS (61 [57])
Co-morbidity (n [%]): NR
Type of during-study treatment: RA (Glucocorticoid: 31/46, Methotrexate: 39/46), AS (Glucocorticoid: 6/61, Methotrexate: 3/61)

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-IT):	107	36	64	7	100

TST:	107	36	71	0	107
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 100

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NA
Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-IT)	The QuantiFERON-TB Gold In-Tube test (QFT-GIT test; Cellestis Ltd., Carnegie, Australia) performed according to the manufacturer instructions	Positive test result was defined as ≥0.35 IU/mL	Both the TST and QFT-IT were performed on the same day as the screening examination in all patients before initiating TNF antagonists
TST	The TST was performed on the volar side of the forearm using the Mantoux method with 2 tuberculin units (TU) of purified protein derivative RT23 (Statens Serum Institut; Copenhagen, Denmark). This dose is approximately equivalent to the international standard of 5 TU tuberculin PPD-S	Induration size was measured after 48–72h, and we used a 10-mm induration as a positive cut-off value for the TST	

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	37 LTBI treated	TST +	0	16	16
IGRA -	0	64	64	TST -	0	54	54
Indeterminate	0	6	6	Indeterminate	0	0	
Total	0	70	70	Total	0	70	70

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = 70/70 = 100% (95% CI: 94.8, 100)	Specificity = 54/70 = 77.14 (95% CI: 66.05, 85.41)
PPV = NA	PPV = 0/16 = 0
NPV = 64/64 = 100% (95% CI: 94.8, 100)	NPV = 54/54 = 100% (95% CI: 93.4, 100)
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = 0/16 = 0
Cumulative Incidence $_{IGRA-}$ = 0/64 = 0	Cumulative Incidence $_{TST-}$ = 0/54 = 0
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA							
Ratio of incidence density rate ratios = NR							
Other reported measure = NR							
Association between test results and levels of TB exposure (if applicable)							
IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA
Test performance parameters							
IGRA				**TST**			
Sensitivity = NA				Sensitivity = NA			
Specificity = NA				Specificity = NA			
PPV = NA				PPV = NA			
NPV = NA				NPV = NA			
DOR (for T^+ calculated) = NA				DOR (for T^+ calculated) = NA			
OR (crude; for T^+ reported) = NA				OR (crude; for T^+ reported) = NA			
OR (regression-based; reported) = NA List of covariates: NA				OR (regression-based; reported) = NA List of covariates: NA			
Other reported measure = NA				Other reported measure = NA			
Comparison between tests (IGRA vs. TST)							
Ratio of DORs (for T^+ calculated) = NA							
Ratio of OR (crude; for T^+ reported) = NA							
Ratio of ORs (regression-based; reported) = NA							
Other reported measure = NR							
Association between test results and BCG status (if applicable)							
IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR
Test performance parameters							
IGRA				**TST**			
DOR (for T^+ calculated)$_{IGRA}$ = NR				DOR (for T+ calculated)$_{TST}$ = NR			
OR (crude; for T^+ reported) = NR				OR (crude; for T+ reported) = NR			
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR				OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR			
Other reported measure = NR				Other reported measure = NR			
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**							
Total sample							
	TST +		TST -		Total		
IGRA +	19		17		36		
IGRA -	16		48		64		
Indeterminate	1		6		7		
Total	36		71		107		
Description							
Sample definition (e.g., total, if stratified by BCG or condition – specify): total							
TST + threshold: > 10mm							

Parameters			
Kappa = 0.26, 95% CI: 0.07, 0.45			
% concordance = 67/100 = 67.0%, 95% CI: 57.31, 75.44			
% discordance = 33/100 = 33.0%, 95% CI: 24.56, 42.69			
Rheumatoid arthritis (RA)			
	TST +	TST -	Total
IGRA +	8	9	17
IGRA -	1	24	25
Indeterminate	NR	NR	NR
Total	9	33	42
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): RA			
TST + threshold: > 10mm			
Parameters			
Kappa = 0.46, 95% CI: 0.21, 0.72			
% concordance = 32/42 = 76.20%, 95% CI: 61.47, 86.52			
% discordance = 10/42 = 23.80%, 95% CI: 13.48, 38.53			
Ankylosing spondylitis (AS)			
	TST +	TST -	Total
IGRA +	11	8	19
IGRA -	15	24	39
Indeterminate	NR	NR	NR
Total	26	32	58
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Ankylosing spondylitis			
TST + threshold: > 10mm			
Parameters			
Kappa = 0.14, 95% CI: -0.10, 0.39			
% concordance = 35/58 = 60.34%, 95% CI: 47.49, 71.91			
% discordance = 23/58 = 39.66%, 95% CI: 28.09, 52.51			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
IGRA performed better in terms of specificity than TST, but several observations of IGRA were indeterminate; in general, the agreement between IGRA and TST was low; better agreement was observed for rheumatoid arthritis and ankylosing spondylitis
Reviewers:
See above
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Elzi 2011[114]
Country: Switzerland
Study design: Retrospective case only study (no control group)
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community-based cohort
Number of centres: One
Total length of follow up (if applicable): 2 years
Funding (government/private/manufacturer/other - specify)**:** Grants/honoraria received from private manufacturers (Abbott, Bristol-Myers Squibb, Gilead, GlaxoSmithKline, Merck, Roche. M. Hoffmann, Janssen, Pfizer)

Aim of the study

To evaluate the sensitivity of T-SPOT.TB in comparison to TST to identify HIV-infected individuals with latent TB, who therefore qualify for preventive treatment

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised people (HIV)

Participants

Recruitment dates: 1993 to 2005
Total N of recruited patients: 64
Inclusion criteria: NR
Exclusion criteria: NR
Total N of excluded patients: None
Total N of patients tested with both IGRA and TST: 64
Total N of patients with valid results for both IGRA and TST: 44
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Sensitivity, agreement, influence of age, CD count and other covariates on test positivity
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median of 33 (IQR: 31-42) yrs
Women (n [%]): 20/64 [31]
Race/ethnicity (n [%]): White 29/64 [45.3]
Geographic origin (n[%]): NR
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): NR
Clinical examination (yes/no): NR
Morbidity (n [%]): HIV
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (T-SPOT.TB):	64	25	18	21	43
TST: Mantoux	44	22	22	0	44
Test 3 (specify):					

Total N of patients with valid results for both IGRA and TST: 44

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group

Non-exposed	
Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (T-SPOT.TB)	T-SPOT.TB was retrospectively performed using frozen viable lymphocytes of HIV-infected individuals stored within 6 months before culture-confirmed TB occurred T-SPOT.TB was performed by using a commercial kit according to the manufacturer's instructions. Each patient test required 4 wells: 2 for the negative (containing no antigen control) and positive controls and 2for the MTB antigens, Panel A (ESAT-6) and B (CFP-10) Evaluating the number of spots obtained provided a measurement of the frequency of MTB tuberculosis sensitive cells	The test result was considered "positive" if the number of spots per test well was ≥ 6 in either of both Panel A and B. The test result was considered "negative" if both Panel A and B showed < 6 spots. Where the positive control was < 20 spots, or the negative control ≥ 10 spots, the test was scored as "indeterminate"	NR
TST	NR	≥ 5mm for positivity	NR

Association between test results and incidence of active TB (if applicable)

IGRA (T-SPOT.TB)				**TST (≥ 5mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	25	NA		TST +	22	NA	
IGRA -	18	NA		TST -	22	NA	
Indeterminate	21	NA		Indeterminate	0	NA	
Total	64	NA		Total	44	NA	

Test performance parameters

IGRA	**TST (≥ 5mm)**
indeterminate excluded Sensitivity = 25/43 = 58.14% (95% CI: 43.33, 71.62) **indeterminate included** Sensitivity = 25/64 = 39.06% (95% CI: 28.06, 51.31)	Sensitivity = 22/44 = 50.00% (95% CI: 35.83, 64.17)
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR

Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA

Ratio of incidence density rate ratios = NR

Other reported measure = NR

Association between test results and incidence of active TB (if applicable)

TST (≥ 5mm) and IGRA combined (at least one test positive)

	Incidence of active TB		Total
	Yes	No	
TST or IGRA +	29	NA	NA
TST and IGRA -	15	NA	NA
Indeterminate	0	NA	NA
Total	44	NA	NA

Test performance parameters (TST and IGRA combined)

Sensitivity = 29/44 = 65.91% (95% CI: 51.14, 78.12)

Specificity, PPV, NPV, others = NA

Association between test results and levels of TB exposure (if applicable)

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA

Ratio of OR (crude; for T^+ reported) = NA

Ratio of ORs (regression-based; reported) = NA

Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR

IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + (≥ 5mm)	TST -	Total
IGRA +	10	7	17
IGRA -	7	8	15
Indeterminate	5	7	12
Total	22	22	44

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total

TST + threshold: ≥ 5mm

Parameters

Indeterminate excluded
Kappa = 0.12 (95% CI: -0.22, - 0.46)
% concordance = 18/32 = 56.25% (95% CI: 39.33, 71.83)
% discordance = 14/32 = 43.75% (95% CI: 28.17, 60.67)

Indeterminate included
Kappa = 0.14 (95% CI: -0.15, - 0.42)
% concordance = 25/44 = 57.00% (95% CI: 42.22, 70.32)
% discordance = 19/44 = 43.20% (95% CI: 29.68, 57.78)

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR		
Parameters		
Kappa = NR		
% concordance = NR		
% discordance = NR		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
T-SPOT.TB has a similar sensitivity to TST to detect latent TB in HIV infected individuals. There was poor agreement between T-SPOT.TB and TST results. The combination of TST and TSPOT. TB (at least one test positive) resulted in improved sensitivity over TST or IGRA alone		
Reviewers:		
This is a retrospective case only study which does not allow to estimate incidence of active TB between test positive vs. negative groups from baseline (no denominators provided). Likewise, no specificity and predictive values could be estimated; the sample (64 out of 242) may have been highly selected, thus prone to selection bias and limitation in regards to applicability of its results; moreover, for IGRA frozen blood samples were analysed		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details
First author surname year of publication: Kim 2011[116] **Country:** Korea **Study design:** Prospective cohort study **Study setting** (e.g., outbreak investigation, community-based - specify)**:** Tertiary-care hospital **Number of centres:** One **Total length of follow up (if applicable):** median 14 mo (IQR: 8-19) **Funding** (government/private/manufacturer/other - specify)**:** Basic Science Research Program through National Research Foundation (NRF) funded by the Ministry of Education, Science and Technology (MEST) (grant 2008-E00136
Aim of the study
To assess whether an enzyme-linked immunosorbent spot (ELISPOT) assay is capable of predicting active TB development in kidney transplant (KT) recipients with negative TST results and without LTBI risk factors
Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)
Immunocompromised people (kidney transplant [KT] recipients)
Participants
Recruitment dates: June 2008 and December 2009 **Total N of recruited patients:** 324 **Inclusion criteria:** KT patients (age≥16 yrs) with TST – (<10mm) and without TB risk factors (history of close contact with TB case, abnormal CXR, history of untreated or inadequately treated TB, newly infected persons) **Exclusion criteria:** Refusal of informed consent, presence of active TB, presence of skin disease that precluded TST, pediatric renal transplant candidates (<16 years old), TB risk factors, and presence of any contraindication for KT (e.g. malignancy) **Total N of excluded patients:** 28 (n = 12 refusal, pediatric, pancreas transplants, transplantation not done, donor kidney problem; n = 16 LTBI risk factors who received anti-TB preventive therapy) **Total N of patients tested with both IGRA and TST:** 272 (out of 296, 24 with TST + [≥10mm] received anti-TB preventive therapy before KT, leaving 272 KT patients with TST-[<10mm] also tested with IGRA who did not receive anti-TB preventive therapy) **Total N of patients with valid results for both IGRA and TST:** 242 (out of 272 patients, 30 had indeterminate IGRA results) **Methods of active TB diagnosis (if applicable):** Symptoms/signs, sputum AFB smear, and a CT scan **Outcomes (study-based) list:** Development of TB, mortality, KT rejection **Characteristics of participants (total study sample):** 272 patients Mean (range or SD) age (years): Mean age range (40.4-46.0 yrs) Women (n [%]): 126 (46.3) Race/ethnicity (n [%]): NR Geographic origin (n[%]): NR BCG vaccination (n [%]): 215 [79.0] History of anti-TB treatment (n [%]): None Total incidence of active TB (n [%]): 4/272 [1.47] (incidence rate: 0.83 per person-years, 95% CI: 0.23, 2.12) Chest radiography (yes/no): Yes Clinical examination (yes/no): Yes Morbidity (n [%]): Glomerulonephritis 72 [26.5], hypertension 65 [23.9], diabetes mellitus 48 [17.6], unknown 58 [21.3], polycystic kidney 12 [4.4], other 11 [4.0] Co-morbidity (n [%]): NR Type of during-study treatment (n [%]): anti-IL-2 receptor antibodies (238 [87.5]), antithymocyte antibodies (21 [7.7]), rituximab (11 [4.0])

Number of patients tested					
	Total N (tested)	**Total N (test+)**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results available)**
IGRA (T-SPOT.TB):	272	71	171	30	242
TST (Mantoux):	272	0 (≥10mm)	272 (<10mm)	0	272
Test 3 (specify):	Nr	NR	NR	NR	NR

Total N of patients with valid results for both IGRA and TST: 242

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	NA
Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (T-SPOT.TB)	A peripheral venous blood sample was collected from each patient for an ELISPOT assay for the IFN-c - producing T-cell response (i.e. T-SPOT.TB, Oxford Immunotec, Abingdon, UK) All blood samples were collected prior to TST to avoid a possible boosting effect of TST on the ELISPOT assay	NR	The development of TB after KT was observed by attending surgeons, nephrologists and infectious diseases specialists blind to the results of ELISPOT assays, to avoid a verification bias
TST (Mantoux)	The TST was performed by the Mantoux technique, injecting a 2-TU (tuberculin unit) dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm	The positive criterion for TST was 10 mm or greater size of induration 48–72 h after injection, and in accordance with Korea Centers for Diseases Control and Prevention guidelines	NR

Association between test results and incidence of active TB (if applicable)

IGRA				**TST** (≥10mm)			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	4	67	71	TST +	NA	NA	NA

IGRA -	0	171	171	TST -	4	268	272
Indeterminate	0	30	30	Indeterminate	0	0	0
Total	4	268	272	Total	4	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = 4/4 = 100.00% (95% CI: 51.01, 100.00)	Sensitivity = NA
Indeterminate excluded Specificity = 171/238 = 71.84% (95% CI: 65.82, 77.18) **Indeterminate included** Specificity = 201/268 = 75.00% (95% CI: 69.49, 79.81)	Specificity = NA
PPV = 4/71 = 5.63% (95% CI: 2.21, 13.61)	PPV = NA
Indeterminate excluded NPV = 171/171 = 100.00% (95% CI: 97.80, 100.00) **Indeterminate included** NPV = 201/201 = 100.00% (95% CI: 98.12, 100.00)	NPV = 268/272 = 98.53% (95% CI: 96.28, 99.43)
Cumulative Incidence $_{IGRA+}$ = 4/71 = 5.63% (95% CI: 2.21, 13.61)	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = 0/171 = X	Cumulative Incidence $_{TST-}$ = 4/272 = 1.47% (95% CI: 0.43, 3.85)
Cumulative Incidence Ratio $_{IGRA}$ = X	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = 4/122.10 p-yrs = 0.0328 p-yrs = 3.28/100 p-yrs (95% CI: 0.89, 8.39)	Incidence density rate $_{TST+}$ = NA
Indeterminate excluded Incidence density rate $_{IGRA-}$ = 0/307.83 p-yrs = 0.00/100 p-yrs **Indeterminate included** Incidence density rate $_{IGRA-}$ = 0/361.16 p-yrs = 0.00/100 p-yrs	Incidence density rate $_{TST-}$ = 4/483.25 p-yrs = 0.0083 p-yrs = 0.83/100 p-yrs (95% CI: 0.23, 2.12)
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = **Indeterminate excluded** Incidence density rate difference $_{IGRA}$ = 3.3/100 p-yrs (95% CI: 1.3, 5.3) **Indeterminate included** Incidence density rate difference $_{IGRA}$ = 3.3/100 p-yrs (95% CI: 1.4, 5.1)	Other reported measure $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)							
IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NR
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = NR
Other reported measure =

Association between test results and BCG status (if applicable)							
IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR
Parameters
Kappa = NR
% concordance = NR
% discordance = NR

Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Positive ELISPOT results predict subsequent development of TB in KT recipients in whom LTBI cannot be detected by TST or who lack clinical risk factors for LTBI
Reviewers:
The available data did not allow the proper direct comparison between IGAA and TST (no relevant data for TST positives); however, IGRA correctly identified the incidence of 4 TB cases as opposed to TST which was negative in all 4 TB cases
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Peter Auguste
Name of second reviewer: Tara Gurung

Study details

First author surname year of publication: Lee 2009[118]
Country: Taiwan
Study design: Prospective, matched, double cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** NR
Number of centres: One
Total length of follow up (if applicable): 2 yrs follow-up
Funding (government/private/manufacturer/other - specify)**:** National health research institutes, Department of Health, Executive Yuan, republic of China (NHRI-CN-CL-094-PP13) and Kaohsiung Veterans General Hospital, Kaohsuing, Taiwan (VGHKS95-012)

Aim of the study

To compare QFT-G, T-SPOT.TB, and TST in terms of their ability to diagnose LTBI in end stage renal disease(ESRD) patients, and to determine the prevalence of LTBI in ESRD patients compared with healthy controls, the risk factors for QFT-G and TST positivity, and the predictive value of a positive QFT-G, ELISPOT, or TST for active TB disease over a two-year period

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised (ESRD)

Participants

Recruitment dates: September 2005
Total N of recruited patients: 64 patients
Inclusion criteria: Patients with ESRD
Exclusion criteria: NR
Total N of excluded patients: None
Total N of patients tested with both IGRA and TST: 32
Total N of patients with valid results for both IGRA and TST: 32
Methods of active TB diagnosis (if applicable): Asymptomatic cases are diagnosed with a chest x-ray, and symptomatic cases are diagnosed with a sputum TB smear, culture and chest radiography
Outcomes (study-based) list: Primary outcome was LTBI and secondary outcomes was development of active TB, concordance between tests, risk factors for a positive result
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 53.8 (34.4-77.7)
Women (n [%]): 24 [37.5]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): Kaohsiung
BCG vaccination (n [%]): 53 [82.8]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): End stage renal dialysis
Co-morbidity (n [%]): Diabetes mellitus (7 [10.9])
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-G):	32	12	18	2	30
IGRA (ELISPOT):	32	15	17	0	32
TST (≥ 10mm):	32	20	12	0	32
Total N of patients with valid results for both IGRA and TST:					

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	NR
Exposed 1 **(specify):**	NR
Exposed 2 **(specify):**	NR
Exposed 3 **(specify):**	NR
Exposed 4 **(specify):**	NR

Tests			
	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Whole blood was drawn prior to carrying out the TST. The QFT-G was performed according to the respective manufacturer's instructions	A QFT-G analysis software, available for download from the Cellestis Ltd website, was used for quality control assessment and to calculate the test results	NA
TSPOT	Whole blood was drawn prior to carrying out the TST. The T-SPOT.TB was performed according to the respective manufacturer's instructions	NR	NA
TST (two step; ≥ 10mm)	A two-step TST using the Mantoux method with two tuberculin units of tuberculin RT-23 (PPD RT 23 SSI; Statens Serum Institut, Copenhagen, Denmark) was performed according to standard protocol. The reactions were read after 48–72 h. Second TST test was performed 1-3 weeks later for initial negative TST result	≥ 10mm induration for ESRD patients and BCG-unvaccinated individuals, ≥ 15mm induration for BCG-vaccinated, healthy individuals	NA

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-G)				**TST (two-step; ≥10mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	1	11	12	TST +	1	19	20
IGRA -	0	18	18	TST -	1	11	12
Indeterminate	1	1	2 (excluded)	Indeterminate			
Total	2	30	32	Total	2	30	32

Test performance parameters	
IGRA (exclude indeterminate)	**TST**
Sensitivity = 1/1 = 100.00%, 95% CI: 20.65, 100.00	Sensitivity = 1/2 = 50.00% (95% CI: 9.45, 90.55)
Specificity = 18/30 = 60.00%, 95% CI: 44.00, 77.31	Specificity = 11/30 = 36.67%, 95% CI: 21.87, 54.49
PPV = 1/12 = 8.33%, 95% CI: 1.49, 35.39	PPV = 1/20 = 5.00%, 95% CI: 0.89, 23.61
NPV = 18/18 = 100.00%, 95% CI: 82.41, 100.00	NPV = 11/11 = 100.00%, 95% CI:74.12, 100.00
Cumulative Incidence $_{IGRA+}$ = 1/12 = 8.33%, 95% CI (1.49, 35.39)	Cumulative Incidence $_{TST+}$ = 1/20 = 5.00%, 95% CI (0.89, 23.61)
Cumulative Incidence $_{IGRA-}$ = 0/18 = 5.56% (95%	Cumulative Incidence $_{TST-}$ = 0/11 = 9.09% (95%

CI: 5.40, 27.29)	CI: 0.23, 41.3)
Cumulative Incidence Ratio $_{IGRA}$ = 1.55% (95% CI: 0.02, 124.2)	Cumulative Incidence Ratio $_{TST}$ = 0.55% (95% CI: 0.01, 47.06)
Incidence density rate $_{IGRA+}$ = 3.40 per 100 PYS	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence = 2.82% (95% CI: 0.13, 62.64)	
Ratio of incidence density rate ratios = NR	
Other reported measure = NR	
Association between test results and incidence of active TB (if applicable)	

IGRA (TSPOT)				**TST (two-step; ≥10mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	0	15	15	TST +	1	19	20
IGRA -	2	15	17	TST -	1	11	12
Indeterminate	0	0	0	Indeterminate	0	0	0
Total	2	30	32	Total	2	30	32

Test performance parameters	
IGRA	**TST**
Sensitivity = 0/2 = 0.00% (95% CI: 0.00, 65.76)	Sensitivity = 1/2 = 50.00% (95% CI: 9.45, 90.55)
Specificity = 15/30 = 50.00% (95% CI: 33.15, 66.85)	Specificity = 11/30 = 36.67%, 95% CI: 21.87, 54.49
PPV = 0/15 = 0.00% (95% CI: 0.00, 20.39)	PPV = 1/20 = 5.00%, 95% CI: 0.89, 23.61
NPV = 15/17 = 88.24% (95% CI: 65.66, 96.71)	NPV = 11/11 = 100.00%, 95% CI:74.12, 100.00
Cumulative Incidence $_{IGRA+}$ = 0/15 = 6.67% (95% CI: 0.17, 31.9)	Cumulative Incidence $_{TST+}$ = 1/20 = 5.00%, 95% CI (0.89, 23.61)
Cumulative Incidence $_{IGRA-}$ = 2/17 = 11.76% (95% CI: 2.03, 35.59)	Cumulative Incidence $_{TST-}$ = 0/11 = 9.09% (95% CI: 0.23, 41.3)
Cumulative Incidence Ratio $_{IGRA}$ = 0.57% (95% CI: 0.01, 12.1)	Cumulative Incidence Ratio $_{TST}$ = 0.55% (95% CI: 0.01, 47.06)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence = 1.04% (95% CI: 0.06, 17.34)	
Ratio of incidence density rate ratios = NR	
Other reported measure = NR	
Association between test results and levels of TB exposure (if applicable)	

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA

Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA (QFT-G) +	NR	NR	12
IGRA (QFT-G) -	NR	NR	18
Indeterminate	NR	NR	2
Total	20	12	32

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total
TST + threshold: ≥ 10mm induration for ESRD patients and BCG-unvaccinated patients

Parameters

Kappa = 0.25, 95% CI (-0.06,- 0.56)
% concordance = 60.0%
% discordance = NR (40.0%)

Stratification (ESRD on hemodialysis)

	TST +	TST -	Total
IGRA (ELISPOT) +	NR	NR	15
IGRA (ELISPOT)-	NR	NR	17
Indeterminate	NR	NR	0
Total	20	12	32

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): ESRD on hemodialysis
TST + threshold: ≥ 10mm induration for ESRD patients and BCG-unvaccinated patients

Parameters

Kappa = 0.32 95% CI (-0.01, -0.65)
% concordance = 65.6%
% discordance = NR (34.4%)

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
Indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA
TST + threshold: NA

Parameters

Kappa = NA
% concordance = NA

% discordance = NA		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
This pilot study compared test results of TST, QFT-G, and ELISPOT and showed that there was moderate agreement between QFT-G and ELISPOT, but fair agreement between TST and either QFT-G or ELISPOT		
Reviewers:		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Lee 2014[149]
Country: South Korea
Study design: Prospective longitudinal study
Study setting (e.g., outbreak investigation, community-based - specify): tertiary hospital-based
Number of centres: One
Total length of follow up (if applicable): 391 patients followed up for 581.7 person –years; median duration 1.3 years (IQR 0.6-2.3)
Funding (government/private/manufacturer/other - specify): supported by grant from the National Research Foundation of Korea funded by the Ministry of Science, ICT and Future Planning

Aim of the study

To test the hypothesis that hematopoietic stem cell transplant (HCT) recipients who are QFT-TB positive develop active TB more frequently than QFT-TB negative or indeterminate patients; to evaluate whether the QFT-TB assay can predict active TB development in HCT recipients without any clinical risk factors for LTBI

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Hematopoietic stem cell transplant (HCT) recipients

Participants

Recruitment dates: January 2010 and December 2012. Resulting cohort observed until June 2013.
Total N of recruited patients: 409
Inclusion criteria: adult patients admitted for allogeneic HCT
Exclusion criteria: patients with history of close contact with active TB, history of untreated or inadequate treated TB, and the radiograph evidence of old TB. Patients who refused informed consent, presence of active TB, presence of skin disease that precluded the TST (between January 2010 and December 2011), and pediatric HCT candidates (<16 years old)
Total N of excluded patients: 18
Total N of patients tested with both IGRA and TST: 169
Total N of patients with valid results for both IGRA and TST: 159
Methods of active TB diagnosis (if applicable): chest x-ray, a sputum AFB smear and CT scan (pulmonary TB)
Outcomes (study-based) list: development of active TB
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 42.3 [13.8]
Women (n [%]): 183 [46.8%]
Race/ethnicity (n [%]): Korean 409 [100%]
Geographic origin (n[%]): NR
BCG vaccination (n [%]): History of scars (353 [90.7%])
History of anti-TB treatment (n [%]): None
Total incidence of active TB (n [%]): 8/391 [2.04%]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): HCT
Co-morbidity (n [%]): Acute or chronic graft-versus-host disease (151 [38.6%]); diabetes mellitus (32 [8.2%]); liver cirrhosis (4[1.0%]); Solid organ transplant (2[0.5%]); HIV (0)
Type of during-study treatment (n [%]): isoniazid prophylaxis to 5/409 [1.22%] patients with clinical risk factors for LBTI (who were excluded from the analyses)

Number of patients tested

	Total N (tested)	**Total N (test+)**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results available)**

IGRA (QFT-GIT) 1st year enrollment cohort:	391	45	315	31	360
IGRA (QFT-GIT): 2nd year enrollment cohort:	169	26	133	10	159
TST (>5mm): 2nd year enrollment cohort:	169	19	150	0	169
TST (>10mm): 2nd year enrollment cohort:	169	12	157	0	169

Total N of patients with valid results for both IGRA and TST: 159

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NA
Exposed 1 **(specify)**:	NA
Exposed 2 **(specify)**:	NA
Exposed 3 **(specify)**:	NA
Exposed 4 **(specify)**:	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	A peripheral venous blood sample was collected from each patient for the QFT-TB assay (Cellestis, Carnegie, Victoria, Australia), and placed directly into three 1 mL tubes containing, respectively, Mycobacterium tuberculosis early secreted antigenic target of 6 kDa (ESAT)-6, culture filtrate protein (CFP)-10 and TB 7.7, phytohemagglutinin (a mitogen used as a positive control), and (3) saline (Nil used as a negative control). The samples were incubated at 37°C for 16-18 h, then processed and tested for quantitative interferon-g levels (IU/mL). The assay was interpreted according to the manufacturer's instructions. All blood samples were collected prior to the TST to avoid a possible boosting effect of the TST on the QFT-TB assay	NR	
TST≥5mm ≥10mm	The TST was performed by the Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm	The positive criterion for the TST was a 5mm or greater in duration 48-72h after injection	The results of TSTs were measured by the trained nurse

Association between test results and incidence of active TB (if applicable)

IGRA [QFT-GIT]				**TST (≥5mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	3	23	26	TST +	0	19	19

IGRA -	2	131	133	TST -	5	145	150
indeterminate	0	10	10	indeterminate	0	0	0
Total	5	154	159	Total	5	164	169

Test performance parameters	
IGRA (QFT-GIT)	**TST≥5mm**
Sensitivity = 3/5= 60.00% (95% CI: 23.07, 88.24)	Sensitivity = 0/5=0.0% (95% CI: 0.0, 43.45)
Specificity =131/154= 85.06% (95% CI: 78.59, 89.84)	Specificity = 145/164=88.41% (95% CI: 82.61, 92.46)
PPV= 3/26=11.54% (95% CI: 4.00, 28.98)	PPV= 0/19=0.0% (95% CI: 0.0, 16.82)
NPV= 131/133=98.5% (95% CI: 94.68, 99.59)	NPV=145/150=96.67% (95% CI: 92.43, 98.57)
Cumulative Incidence $_{IGRA+}$ = 3/26=11.54% (95% CI: 3.17, 29.80)	Cumulative Incidence $_{TST+}$ = 0/19=2.63% (95% CI: 0.0, 23.22)
Cumulative Incidence $_{IGRA-}$ = 2/133=1.50% (95% CI: 0.07, 5.66)	Cumulative Incidence $_{TST-}$ = 5/150=3.33% (95% CI: 1.22, 7.77)
Cumulative Incidence Ratio $_{IGRA}$ = 7.67 (95% CI: 1.34, 43.67)	Cumulative Incidence Ratio $_{TST}$ = 0.79 (95% CI: 0.04, 13.89)
Incidence density rate $_{IGRA+}$ = 5.43 per 100 p-y (95% CI: 1.12, 15.88)	Incidence density rate $_{TST+}$= 0 per 100 p-y (95% CI: 0.00, 8.41)
Incidence density rate $_{IGRA-}$ = 0.80 per 100 p-y (95% CI: 0.10, 2.88)	Incidence density rate $_{TST-}$ = 1.79 per 100 p-y (95% CI: 0.58, 4.18)
Incidence density rate ratio $_{IGRA}$ = 6.78 per 100 p-y (95% CI: NR)	Incidence density rate ratio $_{TST}$=0.00 per 100 p-y (95% CI: NR)
Other reported measure $_{IGRA}$ = incidence density rate difference: 4.7 per 100 person-years (95% CI: 1.10, 8.30)	Other reported measure $_{TST}$ = incidence density rate difference: -1.79 per 100 person-years (95% CI: NR)
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence ratios = 9.71 (95% CI: 1.71, 55.15)	
Ratio of incidence density rate ratios= NA	
Other reported measure= NR	

Association between test results and incidence of active TB (if applicable)

IGRA [QFT-GIT]				**TST (≥10mm)**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	3	23	26	TST +	0	12	12
IGRA -	2	131	133	TST -	5	152	157
indeterminate	0	10	10	indeterminate	0	0	0
Total	5	154	159	Total	5	164	169

Test performance parameters	
IGRA	**TST**
Sensitivity = 3/5= 60.00% (95% CI: 23.07, 88.24)	Sensitivity = 0/5=0.0% (95% CI: 0.0, 43.45)
Specificity =131/154= 85.06% (95% CI: 78.59, 89.84)	Specificity = 152/164= 92.68% (95% CI: 87.65, 95.77)
PPV= 3/26=11.54% (95% CI: 4.00, 28.98)	PPV= 0/12= 0.0% (95% CI: 0.0, 24.25)
NPV= 131/133=98.5% (95% CI: 94.68, 99.59)	NPV=152/157=96.82% (95% CI: 92.76, 98.63)
Cumulative Incidence $_{IGRA+}$ = 3/26=11.54% (95% CI: 3.17, 29.80)	Cumulative Incidence $_{TST+}$ = 0/12=4.16% (95% CI: 0.0, 33.00)
Cumulative Incidence $_{IGRA-}$ = 2/133=1.50% (95% CI: 0.07, 5.66)	Cumulative Incidence $_{TST-}$ = 5/157=3.18% (95% CI: 1.16, 7.43)
Cumulative Incidence Ratio $_{IGRA}$ = 7.67 (95% CI: 1.34, 43.67)	Cumulative Incidence Ratio $_{TST}$ = 1.31 (95% CI: 0.07, 22.55)
Incidence density rate $_{IGRA+}$ = 5.43 per 100 p-y (95% CI: 1.12, 15.88)	Incidence density rate $_{TST+}$= 0.0% (95% CI: 0.0, 14.93)

Incidence density rate $_{IGRA-}$ = 0.80 per 100 p-y (95% CI: 0.10, 2.88)	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$= NA
Other reported measure $_{IGRA}$ = incidence density rate difference: 4.7 per 100 person-years (95% CI: 1.10, 8.30)	Other reported measure $_{TST}$ == incidence density rate difference: -3.18 per 100 person-years (95% CI: NR)

Comparison between tests (IGRA vs. TST)
Ratio of cumulative incidence ratios = 5.85 (95% CI: 1.05, 32.70)
Ratio of incidence density rate ratios= NA
Other reported measure=NR

Association between test results and levels of TB exposure (if applicable)

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA
NPV= NA	NPV= NA
DOR (for T^+ calculated)= NA	DOR (for T^+ calculated)= NA
OR (crude; for T^+ reported)= NA	OR (crude; for T^+ reported)= NA
OR (regression-based; reported)= NA List of covariates: NA	OR (regression-based; reported)= NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated)= NA
Ratio of OR (crude; for T^+ reported)= NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure= NA

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T+ reported) = NA
OR (regression-based; reported) $_{IGRA}$ = NA List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +≥5mm	TST -	Total

IGRA +	6	20	26
IGRA -	12	121	133
indeterminate	1	9	10
Total	18	141	159
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥5mm			
Parameters			
Kappa = 0.16 (95% CI: 0.01, 0.31)			
% concordance = 127/159 = 79.87% (95% CI: 72.97, 85.37)			
% discordance = 32/159 = 20.13% (95% CI: 14.63, 27.03)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Conclusions			
Authors:			
Positive QFT predicts the incidence of active TB, whereas positive TST does not			
Reviewers:			
QFT performed better than TST at 5 or 10mm in predicting LTBI; sensitivity of QFT was better than that for TST at both thresholds; between test agreement was poor			
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation			

Name of first reviewer: Tara Gurung
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Moon 2013[115]
Country: Korea
Study design: Prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Asan Medical Center
Number of centres: One
Total length of follow up (if applicable): Median 0.8 years (IQR: 0.1–2.6)
Funding (government/private/manufacturer/other - specify)**:** Basic science research program through the National Research Foundation (NRF) funded by the Ministry of Education, Science and Technology (MEST) (grant 2010-0005898

Aim of the study

To compare the QFT-GIT with the TST in HCT candidates for detecting LTBI

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Hematopoietic stem cell transplant (HCT) candidates

Participants

Recruitment dates: Between April 2009 and July 2011
Total N of recruited patients: NR
Inclusion criteria: All adult patients admitted for HCT
Exclusion criteria: NR
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 244
Total N of patients with valid results for both IGRA and TST: 210
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Test results, concordance between the TST and QFT-GIT results, development of tuberculosis
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 47 (35-55)
Women (n [%]): 107 [44]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 201 [82]
History of anti-TB treatment (n [%]): 10 [4]
Total incidence of active TB (n [%]): 2 [0.80]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Acute myelogenous leukemia (72 [30]), acute lymphoblastic leukemia (28 [11]), chronic myelogenous leukemia (4 [2]), aplastic anemia (17 [7]), myelodysplastic syndrome (19 [8]), non-hodgkin's lymphoma (58 [24]), hodgkin's lymphoma (3 [1]), multiple myeloma (38 [16]), plasmacytoma (2 [1]), others (3 [1])
Co-morbidity (n [%]): Diabetes mellitus (25 [10]), hypertension (38 [16]), chronic kidney disease (21 [9]), ESRD with dialysis (1 [0.4]), hepatitis (16 [7]), HIV infection (0 [0.0]), non-hematologic malignancy (9 [4])
Type of during-study treatment (n [%]): Cyclosporine (71 [29]), cyclosporine-MTX (65 [27]), cyclosporine-corticosteroid (8 [3]), corticosteroid therapy (111 [46])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (specify): QFT-	244	40	170	34	210

GIT					
TST: ≥5mm	244	39	205	0	244
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST: 210

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NA
Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-GIT (Cellestis Limited, carnegie, Australia	We used the criteria for positive, negative, and indeterminate outcomes recommended by the manufacturer	Blood samples were collected before performing the TST to avoid a possible boosting effect of the TST on theQFT-GIT test. The lab technicians did not know the results of TST
TST (≥ 5mm)	The TST was carried out using the Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm	≥ 5mm induration 48-72h after injection	NR

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-GIT)				**TST≥5mm**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	1	39	40	TST +	0	39	39
IGRA -	1	169	170	TST -	2	203	205
Indeterminate	0	34	34 (excluded)	Indeterminate	0	0	0
Total	2	208	210	Total	2	242	244

Test performance parameters

IGRA	**TST**
Sensitivity = 1/2 = 50.00%, 95% CI (9.45, 90.55)	Sensitivity = 0/2 = 0.00%, 95% CI (0.00, 65.76)
Specificity = 169/208 = 81.25%, 95% CI (75.4, 85.97)	Specificity = 203/242 = 83.88% (95% CI: 78.73, 87.98)
PPV = 1/40 = 2.50%, 95% CI (0.44, 12.88)	PPV = 0/39 = 0.00% (95% CI: 0.0, 8.96)
NPV = 169/170 = 99.41%, 95% CI (96.74, 99.9)	NPV = 203/205 = 99.02% (95% CI: 96.51, 99.73)
Cumulative Incidence $_{IGRA+}$ = 1/40 = 2.50% (0.44, 12.88)	Cumulative Incidence $_{TST+}$ = 0/39 = 2.56% (95% CI: 0.06, 13.5)
Cumulative Incidence $_{IGRA-}$ = 1/170 = 0.58%, 95% CI (0.00, 3.59)	Cumulative Incidence $_{TST-}$ = 2/205 = 0.97% (95% CI: 0.03, 3.71)
Cumulative Incidence Ratio $_{IGRA}$ = 4.25, 95% CI	Cumulative Incidence Ratio $_{TST}$ = 2.63% (95%

(0.27, 66.49)	CI: 0.04, 51.4)
Incidence density rate $_{IGRA+}$ = 2.80 per 100 person-years, 95% CI (0.07, 15.81)	Incidence density rate $_{TST+}$ = 0 per 100 person-years, 95% CI (0.00, 8.00)
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence = 1.62% (95% CI: 0.16, 16.18)
Ratio of incidence density rate ratios = 1.62% (95% CI: 0.16, 16.18)
Other reported measure (risk difference between QFT $^{+}$ and TST $^{+}$) = 2.80 [95% CI: -2.39, 8.00]; NS

Association between test results and levels of TB exposure (if applicable)

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^{+} calculated) = NA	DOR (for T^{+} calculated) = NA
OR (crude; for T^{+} reported) = NA	OR (crude; for T^{+} reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^{+} calculated) = NA
Ratio of OR (crude; for T^{+} reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample (≥5 mm induration)

	TST +	TST -	Total
IGRA +	9	31	40
IGRA -	24	146	170
Indeterminate	6	28	34 (excluded)
Total	33	177	210

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): total (indeterminate excluded)
TST + threshold: ≥ 5mm induration

Parameters

Kappa = 0.09, 95% CI (-0.04, - 0.22) indeterminate excluded Kappa similar if indeterminate considered as QFT-negative
% concordance = 155/210 = 73.81%, 95% CI (67.47, 79.29)
% discordance = 55/210 = 26.19%, 95% CI (20.71, 32.53)

Stratification (≥10 mm induration**)**

	TST +	TST -	Total
IGRA +	8	32	40

IGRA -	13	157	170
Indeterminate	4	30	34 (excluded)
Total	21	189	210
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total (indeterminate excluded)			
TST + threshold: ≥ 10mm induration			
Parameters			
Kappa = 0.15, 95% CI (0.02, 0.27) indeterminate excluded Kappa similar if indeterminate considered as QFT-negative			
% concordance = 165/210 = = 78.57%, 95% CI (72.53, 83.58)			
% discordance = 45/210 = 21.43%, 95% CI (16.42, 27.47)			
Stratification (Patients with BCG scars)			
	TST + ≥ 5mm	TST -	Total
IGRA +	9	23	32
IGRA -	22	122	144
Indeterminate	0	0	0
Total	31	145	176
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Patients with BCG scars			
TST + threshold: ≥5 mm induration			
Parameters			
Kappa = 0.13, 95% CI (-0.02, 0.27) Kappa similar if threshold ≥10 mm			
% concordance = 131/176 = 74.43%, 95% CI (67.51, 80.31)			
% discordance = 45/176 = 25.57%, 95% CI (19.69, 32.49)			
Stratification (Patients without BCG scars or history of BCG vaccination)			
	TST≥ 5mm +	TST -	Total
IGRA +	0	8	8
IGRA -	2	24	26
Indeterminate	0	0	0
Total	2	32	34
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Patients without BCG scars or history of BCG vaccination			
TST + threshold: ≥ 5mm induration			
Parameters			
Kappa = -0.10, 95% CI (-0.35, 0.14) Kappa similar if threshold ≥10 mm			
% concordance = 70.59%, 95% CI (53.83, 83.17)			
% discordance = 29.41%, 95% CI (16.83, 46.17)			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NA	NA

Conclusions
Authors:
The authors demonstrated that the frequencies of positive outcomes in the two TB screening tests were similar, but the overall agreement between the TST and the QFT-GIT test was poor, regardless of BCG vaccination.

Reviewers:
The overall agreement between the TST and the QFT-GIT test was poor, regardless of BCG vaccination and TST threshold; tests were similar in detecting LTBI through predicting incidence of active TB (risk difference NS)
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; ESRD = end stage renal disease; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Sherkat 2014[155]
Country: Iran
Study design: Prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify): Hospital-based
Number of centres: NR
Total length of follow up (if applicable): 21 months (FU included 9 months prophylactic treatment and 12 months post transplantation)
Funding (government/private/manufacturer/other - specify): Nil

Aim of the study

To compare IGRA (T-SPOT .TB) and TST test in detection of LTBI in kidney transplant candidates and evaluate the agreement between the two tests

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Immunocompromised (kidney transplant candidates – end stage renal disease)

Participants

Recruitment dates: March 2010 to February 2011
Total N of recruited patients: NR
Inclusion criteria: Candidates for receiving a kidney transplant
Exclusion criteria: Active pulmonary and extrapulmonary TB, history of prior TB or isoniazid prophylactic treatment, refusal to continue prophylactic treatment, symptoms of isoniazid-induced hepatitis or drug reaction
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 44
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: between test agreement, incidence of active TB
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 44 (15.5)
Women (n [%]): 15 [66]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): NR
BCG vaccination (n [%]): 12 [27.3]
History of anti-TB treatment (n [%]): None
Total incidence of active TB (n [%]): 1/44 [2.27]
Chest radiography (yes/no): NR
Clinical examination (yes/no): Yes
Morbidity (n [%]): End stage renal disease
Co-morbidity (n [%]): Dialysis (30 [68.2]), hypertension (10 [22.7]), diabetes (10 [22.7]), obstructive uropathy (6 [13.6]), polycystic kidney (6 [13.6]), other renal etiologies (17 [38.6]), others (3 [6.8])
Type of during-study treatment (n [%]): isoniazid prophylaxis (10 [22.7])

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	NR	6	38	NR	44
TST:≥10mm	NR	8	36	NR	44
Test 3 (specify)					

Total N of patients with valid results for both IGRA and TST: 44

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group – NA	
Non-exposed	

Exposed 1 **(specify)**:	NR
Exposed 2 **(specify)**:	NR
Exposed 3 **(specify)**:	NR
Exposed 4 **(specify)**:	NR

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA [TSPOT]	T-SPOT .TB assay (Oxford Immunotec, Oxford, UK) was performed according to the manufacturers' recommendation and defined as positive, negative or indeterminate based on manufacturers' recommended criteria. Briefly, before the TST, 8 ml peripheral venous blood was collected and processed within 4 h. The peripheral blood mononuclear cells) were isolated by standard ficoll-hypaque density-gradient centrifugation. The PBMCs were counted and adjusted to a cell number of 2.5 × 10 PBMCs/1 ml. Four wells of the 96-well Microtitre plates (nil control, positive control, panel A and panel B), precoated with monoclonal antibody to gamma IFN, were seeded with 100 µl of 2.5 × 10 PBMCs/well. Two wells contained different peptide antigens (ESAT-6 [panel A] and CFP-10 [panel B]), the nil control well contained the cell in medium alone, and the positive control well contained the cell that was stimulated with phytohemagglutinin. After the appropriate incubation time (16-20 h) at in a humidified incubator at 37°C and 5% CO, the plates were washed with phosphate-buffered saline (PBS) four times. An appropriate volume of conjugate working solution was prepared (1:200 dilution in PBS) for the secondary incubation (60 min at 2-8°C) after which the wells was washed again (×4), as suggested above. Results are presented as the number of spot-forming cells and the reaction was observed visually		
TST≥10mm	TST was performed using the 5 IU	If induration size was	

	purified protein derivative (PPD) (Pasteur Institute, Tehran, Iran) injection into the volar aspect of the forearm intradermally by trained personnel. A positive test was defined by the size of induration (not the erythema) induced by PPD 48-72 h after the injection	≥10 mm, test was considered positive as recommended by local guidelines (Ministry of Health and Medical Education)	

Association between test results and incidence of active TB (if applicable)

IGRA [TSPOT]				TST≥10mm			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	1	5	6	TST +	1	7	8
IGRA -	0	38	38	TST -	0	36	36
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	1	43	44	Total	1	43	44

Test performance parameters

IGRA	TST
Sensitivity =1/1= 100% (95% CI: 20.65, 100)	Sensitivity = 1/1=100% (95% CI: 20.65, 100)
Specificity = 38/43=88.37% (95% CI: 75.52, 94.93)	Specificity = 36/43=83.72% (95% CI: 70.03, 91.88)
PPV= 1/6=16.67% (95% CI: 3.00, 56.35)	PPV= 1/8=12.5% (95% CI: 2.24, 47.09)
NPV= 38/38=100% (95% CI: 90.82, 100)	NPV= 36/36=100% (95% CI: 90.36, 100)
Cumulative Incidence $_{IGRA+}$ = 1/6=16.67% (95% CI: 3.00, 56.35)	Cumulative Incidence $_{TST+}$ = 1/8=12.5% (95% CI: 0.11, 47.09)
Cumulative Incidence $_{IGRA-}$ = 0/38=1.31 (95% CI: 0.00, 12.86)	Cumulative Incidence $_{TST-}$ = 0/36=1.39 (95% CI: 0.00, 13.49)
Cumulative Incidence Ratio $_{IGRA}$ =12.67 (95% CI: 0.47, 337.8)	Cumulative Incidence Ratio $_{TST}$ =9.00 (95% CI: 0.33, 245.7)
Incidence density rate $_{IGRA+}$ =NR	Incidence density rate $_{TST+}$= NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$= NA
Other reported measure $_{IGRA}$ =NR	Other reported measure $_{TST}$ =NR

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios=1.41 (95% CI: 0.13, 15.20)
Ratio of incidence density rate ratios=NA
Other reported measure= NA

Association between test results and levels of TB exposure (if applicable)

IGRA (specify)				TST (specify)			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV= NA	PPV= NA
NPV= NA	NPV= NA
DOR (for T^+ calculated)= NA	DOR (for T^+ calculated)= NA

OR (crude; for T^+ reported)= NA	OR (crude; for T^+ reported)= NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = NA
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				**TST (≥10mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	2	4	6	TST +	2	6	8
IGRA -	10	28	38	TST -	10	26	36
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR
Total	12	32	44	Total	12	32	44

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$= 1.40 (95% CI: 0.22, 8.85)	DOR (for T+ calculated)$_{TST}$ = 0.86 (95% CI: 0.14, 5.03)
OR (crude; for T^+ reported)= NR (p=0.658)	OR (crude; for T+ reported) = NR (p=1.00)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +≥10mm	TST -	Total
IGRA [TSPOT] +	4	2	6
IGRA [TSPOT] -	4	34	38
indeterminate	NR	NR	NR
Total	8	36	44

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total
TST + threshold: ≥10mm

Parameters

Kappa = 0.49 (95% CI: 0.20, 0.78)
% concordance = 38/44=86.36% (95% CI: 73.29, 93.6)
% discordance = 6/44=13.64% (95% CI: 6.40, 26.71)

Stratification (specify group 1):

	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NA
TST + threshold: NA

Parameters

Kappa = NA
% concordance = NA
% discordance = NA

Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NA	NA	NA
IGRA -	NA	NA	NA
indeterminate	NA	NA	NA
Total	NA	NA	NA
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA			
TST + threshold: NA			
Parameters			
Kappa = NA			
% concordance = NA			
% discordance = NA			
Conclusions			
Authors:			
In kidney transplant candidates both TST and T-SPOT .TB test were comparable for the diagnosis of LTBI with reasonable agreement between the tests. However, further studies are needed to determine the ability of T-SPOT .TB test to detect LTBI and to evaluate the need for prophylaxis in these patients			
Reviewers:			
There was no evidence indicating the superiority of IGRA over TST or vise versa in detecting LTBI; the between test agreement was good; BCG status did not influence TST differentially from TSPOT			
Abbreviations: DOR=diagnostic odds ratio; 95% CI= 95 percent confidence intervals; TB=tuberculosis; BCG=Bacillus Calmette–Guérin; PPV= positive predictive value; NPV=negative predictive value; FPR=false positive rate; FNR=false negative rate; SD=standard deviation			

Recently arrived

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Lucas 2010[145]
Country: Australia
Study design: Retrospective cohort/cross sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community based
Number of centres: NR
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** Oxford Immunotech.

Aim of the study

Comparative study of IGRAs and TST for the diagnosis of LTBI in 524 recently resettled refugee children

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Recently arrived people

Participants

Recruitment dates: January 2007 and March 2008
Total N of recruited patients: 524
Inclusion criteria: Children aged from 5 months to 16 years from refugee families attending the Migrant Health Unit
Exclusion criteria: NR
Total N of excluded patients: Incomplete TSPOT (n = 57) and TST (n = 37)
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 239 (three tests)
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: Association of test positivity with exposure, agreement
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 7.5 (2.8-11.9)
Women (n [%]): 260 [49.6]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): African (411 [78.4]) and Asian (113 [21.56])
BCG vaccination (n [%]): 361 [69.0]
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NR
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): Malaria (486 [92.7]), hepatitis B (356 [68.0]), hepatitis C (492 [94.0]), schistosomiasis (431 [82.2])
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	420 completed tests	38	374	8	412
IGRA (QFT-GIT):	460 completed tests	45	345	70	390
TST:	304 completed tests	54	250	0	304

Total N of patients with valid results for both IGRA and TST: 239

Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group – Household TB contact	
Non-exposed	none
Exposed 1 **(specify):**	definite/suspected
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA (TSPOT)	In keeping with the manufacturer's instructions, 4 ml of blood were drawn for the T-SPOT.TB assay, except for children <2 years when 2-3 ml were drawn depending on ease of venepuncture	Inconclusive assays were defined by an inability to complete the test due to inadequate peripheral blood mononuclear cell (PBMC) yield after PBMC separation, high background, machine failure or red blood cell contamination. Indeterminate assays were defined as a low mitogen-positive control response or a high response to the negative control	NA
IGRA (QFT-GIT)	A 3 ml aliquot of blood was drawn from all study children and the assay was performed according to the manufacturers' protocols	Indeterminate assays were defined as a high IFNg response to the negative control or a low IFNg response to mitogen stimulation in the absence of a positive antigen response	NA
TST≥10mm	TST was performed with purified protein derivative (PPD) by administration of 5 tuberculin units following the Mantoux method. The transverse diameter of skin induration was measured at 48-72 h	NR	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA

Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA

Ratio of incidence density rate ratios = NA

Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (TSPOT)				**TST (≥10 mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	8	Indeterminate	NR	NR	0
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = 2.50 (95% CI: 0.90, 6.50)	OR (crude; for T^+ reported) = 4.00 (95% CI: 1.70, 9.50)
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA

Ratio of OR (crude; for T^+ reported) = 0.63 (95% CI: 0.32, 1.22)

Ratio of ORs (regression-based; reported) = NA

Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10 mm)**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	70	Indeterminate	NR	NR	0
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = 2.40 (95% CI: 1.00, 5.80)	OR (crude; for T^+ reported) = 4.00 (95% CI: 1.70, 9.50)
OR (regression-based; reported) = NR	OR (regression-based; reported) = NR

List of covariates: NA	List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 0.60 (95%CI: 0.32, 1.12)
Ratio of ORs (regression-based; reported) = NA
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA (TSPOT)				**TST (≥10 mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	70	Indeterminate	NR	NR	70
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = 1.80 (95% CI: 0.80, 4.00)	OR (crude; for T+ reported) = 1.70 (95% CI: 0.80, 3.50)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA (QFT-GIT)				**TST (≥10 mm)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	70	Indeterminate	NR	NR	70
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NA	DOR (for T+ calculated)$_{TST}$ = NA
OR (crude; for T^+ reported) = 1.70 (95% CI: 0.80, 3.60)	OR (crude; for T+ reported) = 1.70 (95% CI: 0.80, 3.50)
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NA	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST + ≥10mm	TST -	Total
IGRA (TSPOT) +	NR	NR	NR
IGRA (TSPOT) -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total
TST + threshold: ≥10mm

Parameters

Kappa = 0.45 (95% CI: 0.38, 0.53)
% concordance = NR

% discordance = NR			
Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST + ≥10mm	TST -	Total
IGRA (QFT-GIT) +	NR	NR	NR
IGRA (QFT-GIT) -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.46 (95% CI: 0.39, 0.53)			
% concordance = NR			
% discordance = NR			
Stratification (specify group 1):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2):			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions

Authors:

The two IGRAs showed similar positivity rates across all age groups. Both IGRAs gave an unacceptably high proportion of inconclusive results. Failed tests were the primary cause of inconclusive T-SPOT.TB assays whereas indeterminate results were the primary cause of inconclusive QFT-GIT assays. It is

reasonable to screen using either IGRA with follow-up by the alternative if the test fails. In general, the QFT-GIT is the preferred option for non-African populations but the T-SPOT.TB is recommended when there are epidemiological and/or clinical high risk factors for TB infection. However, both IGRAs have methodological and performance characteristics that limit their usefulness in refugee children, highlighting the need for continued development of screening strategies
Reviewers:
Three tests performed similarly
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Orlando 2010[146]
Country: Italy
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community-based (outpatient ward)
Number of centres: NR
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** The Provincia di Milano, Assessorato alle Politiche Sociali

Aim of the study

To compare the efficiency and efficacy of TST and QFT-IT for the detection of LTBI in recent immigrants from highly endemic countries by intention-to-treat (strategy efficiency) and per-protocol (test efficacy) analyses; this was achieved through the assessment of LTBI prevalence using the one-step TST and QFT-IT, analysis of test results' association, determinants of drop-out and influence of variables related to increased risk of TB exposure on the TST or QFT-IT strategy

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Recently arrived people

Participants

Recruitment dates: July 2005 and July 2007
Total N of recruited patients: NR
Inclusion criteria: NR
Exclusion criteria: Active TB
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 1130
Total N of patients with valid results for both IGRA and TST: 899
Methods of active TB diagnosis (if applicable): Clinical evaluation and chest X-rays were performed by experienced pneumologists
Outcomes (study-based) list: Agreement, association of test positivity with exposure
Characteristics of participants (total study sample)
Mean (range or SD) age (years): Median 35.3 years (IQR: 27.7–44.5)
Women (n [%]): 630 [55.7]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): Latin America (562 [49.73]), Eastern Europe (308 [27.26]), Africa (181 [16.02%]), Asia (79 [6.99])
BCG vaccination (n [%]): 72 [6.37], Unknown (46 [4.07])
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): Yes
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): Treatment for LTBI was offered to 57 of the 79 eligible patients according to standard guidelines

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	1130	337	778	15 (undetermined)	1115
TST (≥10mm):	1129	407 (≥10mm)	492	230 (dropouts)	899

Test 3 (specify):	NA	NA	NA	NA	NA
Total N of patients with valid results for both IGRA and TST: 899					
Levels/groups of exposure to TB in increasing order (if applicable):					
Definition of exposure group - Continent					
Non-exposed	Africa (reference group)				
Exposed 1 **(specify):**	Asia				
Exposed 2 **(specify):**	East Europe				
Exposed 3 **(specify):**	Latin America				
	Definition of exposure group – TB prevalence				
Non-exposed	<50 (reference group)				
Exposed 1 **(specify):**	50-200				
Exposed 2 **(specify):**	>200				
	Definition of exposure group – contact with TB patient				
Non-exposed	No (reference group)				
Exposed 1 **(specify):**	Yes				
Tests					
	Assay used, methodology, timing for test measurement, manufacturer		**Cut-off values/thresholds Definition of test+**		**Other information**
IGRA	QuantiFERON-TB Gold In-Tube (QFT-IT) test (Cellestis Limited, Victoria, Australia): 1 ml of blood was drawn directly into QFT-IT blood collection tubes coated with saline (Nil-control), peptides of ESAT-6, CFP-10 and TB7.7(p4) proteins (MTB specific antigens—TB-antigen) and phytohaemaglutinin (PHA) (Mitogen-control) After overnight incubation at 37◦C, blood collection tubes were centrifuged for 15 min at 2,000–3,000g and stored at -80◦C before testing. The concentration of IFN-c (IU/ml) was determined using an ELISA assay QFT-GIT Analysis Software Version 2.50 (Cellestis Limited, Victoria, Australia) was used to analyse raw data and calculate results		The results were defined positive if the INF-c value after stimulation with TB-antigen minus the value in the Nilcontrol was ≥0.35 UI/ml and ≥25% of Nil; negative if value of TB-antigen minus Nil was<0.35 UI/ml or if that difference was ≥0.35 UI/ml and <25% of Nil, with Mitogen minus Nil ≥0.5 UI/ml; indeterminate for TB antigen minus Nil<0.35 UI/ml or ≥0.35 UI/ml and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time Nil was >0.8 UI/ml		NA
TST	For TST, 0.1 mL (5U) of tuberculin purified protein derivative (Biocine test PPD		A TST ≥ 10 mm of induration was considered positive in persons recently		NA

	Liofilo, Novartis Vaccines and Diagnostics) was injected intradermally into the forearm. Participants were asked to come back for the evaluation of the delayed type hypersensitivity reaction (mean of the induration transverse diameters) 72 h later	arrived from highly endemic areas	

Association between test results and incidence of active TB (if applicable)

IGRA				TST			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA
Other reported measure $_{IGRA}$ = NA	Other reported measure $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				TST (≥10mm)			
	Continent		Total		Continent		Total
	Asia	Africa			Asia	Africa	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	79	181	260	Total	79	181	260

Test performance parameters

IGRA (QFT-GIT)	TST (≥10mm)
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) =
Asia vs. Africa OR (crude; for T^+ reported) = 1.61 (95% CI: 0.90, 2.88)	**Asia vs. Africa** OR (crude; for T^+ reported) = 0.91 (95% CI: 0.50, 1.64)

Asia vs. Africa OR (regression-based; reported) = 1.07 (95% CI: 0.52, 2.23) List of covariates: NR	**Asia vs. Africa** OR (regression-based; reported) = 0.72 (95% CI: 0.34, 1.53) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 1.77 (95% CI: 1.16, 2.70)
Ratio of ORs (regression-based; reported) = 1.49 (95% CI: 0.87, 2.53)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	Continent		Total		Continent		Total
	East Europe	Africa			East Europe	Africa	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	308	181	489	Total	308	181	489

Test performance parameters

IGRA (QFT-GIT)	**TST (≥10mm)**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
East Europe vs. Africa OR (crude; for T^+ reported) = 1.46 (95% CI: 0.96, 2.23)	**East Europe vs. Africa** OR (crude; for T^+ reported) = 0.83 (95% CI: 0.55, 1.25)
East Europe vs. Africa OR (regression-based; reported) = 1.68 (95% CI: 0.91, 3.08) List of covariates: NR	**East Europe vs. Africa** OR (regression-based; reported) = 1.19 (95% CI: 0.66, 2.14) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 1.76 (95% CI: 1.30, 2.37)
Ratio of ORs (regression-based; reported) = 1.41 (95% CI: 0.92, 2.18)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	Continent		Total		Continent		Total
	Latin America	Africa			Latin America	Africa	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	562	181	743	Total	562	181	743

Test performance parameters

IGRA (QFT-GIT)	**TST (≥10mm)**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR

NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
Latin America vs. Africa OR (crude; for T^+ reported) = 1.46 (95% CI: 0.99, 2.16)	**Latin America vs. Africa** OR (crude; for T^+ reported) = 0.86 (95% CI: 0.59, 1.26)
Latin America vs. Africa OR (regression-based; reported) = 0.81 (95% CI: 0.46, 1.42) List of covariates: NR	**Latin America vs. Africa** OR (regression-based; reported) = 0.57 (95% CI: 0.33, 1.00) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 1.70 (95% CI: 1.29, 2.24)
Ratio of ORs (regression-based; reported) = 1.42 (95% CI: 0.95, 2.24)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	TB prevalence		Total		TB prevalence		Total
	50-200	**<50**			**50-200**	**<50**	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA (QFT-GIT)	**TST (≥10mm)**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
50-200 vs. <50 OR (crude; for T^+ reported) = 1.76 (95% CI: 1.10, 2.80)	**50-200 vs. <50** OR (crude; for T^+ reported) = 0.66 (95% CI: 0.44, 1.01)
50-200 vs. <50 OR (regression-based; reported) = 1.34 (95% CI: 0.72, 2.49) List of covariates: NR	**50-200 vs. <50** OR (regression-based; reported) = 0.70 (95% CI: 0.39, 1.25) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)
Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 2.67 (95% CI: 1.94, 3.67)
Ratio of ORs (regression-based; reported) = 1.91 (95% CI: 1.24, 2.95)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	TB prevalence		Total		TB prevalence		Total
	>200	**<50**			**>200**	**<50**	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA (QFT-GIT)	**TST (≥10mm)**

Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
>200 vs. <50 OR (crude; for T^+ reported) = 2.31 (95% CI: 1.48, 3.61)	**>200 vs. <50** OR (crude; for T^+ reported) = 0.99 (95% CI: 0.66, 1.48)
>200 vs. <50 OR (regression-based; reported) = 2.72 (95% CI: 1.70, 5.02) List of covariates: NR	**>200 vs. <50** OR (regression-based; reported) = 1.45 (95% CI: 0.80, 2.62) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 2.33 (95% CI: 1.72, 3.17)
Ratio of ORs (regression-based; reported) = 1.88 (95% CI: 1.25, 2.83)
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)				**TST (≥10mm)**			
	Contact with TB case		Total		Contact with TB case		Total
	Yes	**No**			**Yes**	**No**	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA (QFT-GIT)	**TST (≥10mm)**
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
Contact vs. No contact OR (crude; for T^+ reported) = 2.54 (95% CI: 1.82, 3.54)	**Contact vs. No contact** OR (crude; for T^+ reported) = 1.87 (95% CI: 1.30, 2.69)
Contact vs. No contact OR (regression-based; reported) = 2.11 (95% CI: 1.47, 3.03) List of covariates: NR	**Contact vs. No contact** OR (regression-based; reported) = 1.87 (95% CI: 1.24, 2.80) List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA
Ratio of OR (crude; for T^+ reported) = 1.36 (95% CI: 1.06, 1.75)
Ratio of ORs (regression-based; reported) = 1.13 (95% CI: 0.85, 1.49)
Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR

Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	**TST**
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	887

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): Total

TST + threshold: ≥ 10mm

Parameters

Kappa = 0.38 (95% CI: NR)

% concordance = 625/887 = 70.46% (95% CI: 67.32, 73.43)

% discordance = 262/887 = 29.53% (95% CI: NR)

Stratification (BCG vaccinated)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	56

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG vaccinated

TST + threshold: ≥10mm

Parameters

Kappa = 0.35 (95% CI: NR)

% concordance = 37/56 = 66.07% (95% CI: 52.09, 77.84)

% discordance = 19/56 = 33.92% (95% CI: NR)

Stratification (BCG non-vaccinated)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	789

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): BCG non-vaccinated

TST + threshold: ≥ 10mm

Parameters

Kappa = 0.40 (95% CI: NR)

% concordance = 563/789 = 71.36% (95% CI: 68.04, 74.46)

% discordance = 226/789 = 28.64% (95% CI: NR)

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD)**

		(specify)
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
Continent of origin, class of TB prevalence in the country of origin and contacts with TB patients were found to be significantly associated with the probability of TST and QFT-IT positive result; The drawback of the TST screening strategy in recent immigrants from highly endemic countries is due to low sensitivity/specificity of the test and to high drop-out rate with an overall significant lowering in strategy efficacy/efficiency. Disagreement is due to differences in sensitivity/specificity and in rate of drop-out which is higher for the TST		
Reviewers:		
Kappa was influenced by BCG status which was higher in non-vaccinated people; QFT performed better than TST in relation to contact with TB and TB prevalence; TST was better than QFT in relation to continent		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Saracino 2009[147]
Country: Italy
Study design: Retrospective cohort/cross-sectional study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community-based
Number of centres: NR
Total length of follow up (if applicable): NA
Funding (government/private/manufacturer/other - specify)**:** NR

Aim of the study

To evaluate the agreement between QFT-GIT and TST for latent TB screening in a population of recent immigrants to Italy from high-incidence countries

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Recently arrived people

Participants

Recruitment dates: September 2004 and December 2005
Total N of recruited patients: NR
Inclusion criteria: Recent (less than two months) immigrants to Italy
Exclusion criteria: Active TB, HIV
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: 452
Total N of patients with valid results for both IGRA and TST: 279
Methods of active TB diagnosis (if applicable): NA
Outcomes (study-based) list: Agreement, associations of test positivity and risk factors (born in a country of TB burden, region of origin)
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 27.1 (6.2)
Women (n [%]): 11 [4]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): African (135 [48.4]), Eastern Mediterranean (131 [46.95]), European (7 [2.5]), South-East Asian (6 [2.2])
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): NA
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): NR
Co-morbidity (n [%]): NR
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	452	107	172	173 (169 dropouts and 4 HIV/active TB)	279
TST (≥10mm):	452	72	207	173 (169 dropouts and 4	279

				HIV/active TB)	

Total N of patients with valid results for both IGRA and TST: 279	
Levels/groups of exposure to TB in increasing order (if applicable):	
Definition of exposure group	
Non-exposed	NR
Exposed 1 **(specify):**	30-100
Exposed 2 **(specify):**	101-200
Exposed 3 **(specify):**	201-300
Exposed 4 **(specify):**	>301
Definition of exposure group – Region of origin	
Non-exposed	NR
Exposed 1 **(specify):**	African
Exposed 2 **(specify):**	Eastern Mediterranean
Exposed 3 **(specify):**	European
Exposed 4 **(specify):**	South-East Asian

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	QFT-GIT (Cellestis, Carnegie, Australia) was performed, according to the manufacturer's instructions, by collecting 1mL of whole heparinized blood in two tubes, one containing only heparin as negative control, and the other containing three MT specific antigens: ESAT-6, CFP-10 and TB 7.7 (p4). Tubes were kept at room temperature for a maximum of 16 hours and then incubated at 37°C for 16-24 hours; the tubes were then centrifuged, and the plasma removed and harvested to perform the ELISA. The IFN-γ value for TB-specific antigens was corrected by subtracting the value obtained for the respective negative controls	the test was considered positive if the IFN-γ level was above the cut-off test value (≥0.35 IU/mL)	NA
TST (≥10mm)	TST was administered by injecting 0.1 mL of the standard test dose (5 tuberculin unit, TU) of PPD (BiocineTest-PPD®; Chiron S.r.l., Sovicille, Siena, Italy) according to the Mantoux method	Skin induration was evaluated after 72 hours and considered positive if ≥10 mm. Cut-off points of 5 mm and 15 mm, respectively, were also used for comparison	NA

Association between test results and incidence of active TB (if applicable)

IGRA				**TST**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA

Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
Cumulative Incidence $_{IGRA+}$ = NA	Cumulative Incidence $_{TST+}$ = NA
Cumulative Incidence $_{IGRA-}$ = NA	Cumulative Incidence $_{TST-}$ = NA
Cumulative Incidence Ratio $_{IGRA}$ = NA	Cumulative Incidence Ratio $_{TST}$ = NA
Incidence density rate $_{IGRA+}$ = NA	Incidence density rate $_{TST+}$ = NA
Incidence density rate $_{IGRA-}$ = NA	Incidence density rate $_{TST-}$ = NA
Incidence density rate ratio $_{IGRA}$ = NA	Incidence density rate ratio $_{TST}$ = NA

Comparison between tests (IGRA vs. TST)

Ratio of cumulative incidence ratios = NA
Ratio of incidence density rate ratios = NA
Other reported measure = NA

Association between test results and levels of TB exposure (if applicable)

IGRA						TST					
	Exposure level Region of origin				Total		Exposure level Region of origin				Total
	South-East Asia	Europe	Eastern Mediterranean	Africa			South-East Asia	Europe	Eastern Mediterranean	Africa	
IGRA+	NR	NR	NR	NR	107	TST+	NR	NR	NR	NR	72
IGRA-	NR	NR	NR	NR	172	TST -	NR	NR	NR	NR	207
Indeterminate	NR	NR	NR	NR	173 (excluded)	Indeterminate	NR	NR	NR	NR	173 (excluded)
Total	6	7	131	135	279	Total	6	7	131	135	279

Test performance parameters

IGRA	TST
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T+ reported) = Africa: OR = 1.00, 95% CI: 0.60, 1.70 Eastern Mediterranean: OR = 1.00, 95% CI: 0.60, 1.70 Europe: OR = 1.20, 95% CI: 0.20, 7.30 South-East Asia: OR = 0.30, 95% CI: 0.01,	OR (crude; for T+ reported) = Africa: OR = 1.10, 95% CI: 0.60, 1.90 Eastern Mediterranean: OR = 0.80, 95% CI: 0.50, 1.40 Europe: OR = 4.00, 95% CI: 0.70, 27.80 South-East Asia: OR = 0.60, 9% CI: 0.10, 5.20

2.90	
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = NA	
Ratio of OR (crude; for T^+ reported) = 0.91 (95% CI: 0.61, 1.35) [Africa vs. reference group]	
Ratio of ORs (regression-based; reported) = NA	
Other reported measure = NA	

Association between test results and levels of TB exposure (if applicable)

IGRA (QFT-GIT)						**TST (≥10mm)**					
	Exposure level Born in a country with a TB burden (# cases per 100,000)				Total		Exposure level Born in a country with a TB burden (# cases per 100,000)				Total
	>301	201-300	101-200	30-100			>301	201-300	101-200	30-100	72
IGRA +	NR	NR	NR	NR	107	TST +	NR	NR	NR	NR	207
IGRA -	NR	NR	NR	NR	172	TST -	NR	NR	NR	NR	173 (excluded)
Indeterminate	NR	NR	NR	NR	173 (excluded)	Indeterminate	NR	NR	NR	NR	279
Total	54	197	15	12	279	Total	54	197	15	12	72

Test performance parameters	
IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
30-100: OR (crude; for T+ reported) = 1.20, 95% CI: 0.30, 4.30 101-200: OR (crude; for T+ reported) = 0.80, 95% CI: 0.20, 2.60 201-300: OR (crude; for T+ reported) = 1.00, 95% CI: 0.60, 1.80 >301: OR (crude; for T+ reported) = 1.00, 95% CI: 0.50, 2.00	30-100: OR (crude; for T+ reported) = 3.00, 95% CI: 0.80, 11.8 101-200: OR (crude; for T+ reported) = 1.00, 95% CI: 0.20, 3.70 201-300: OR (crude; for T+ reported) = 0.80, 95% CI: 0.40, 1.40 >301: OR (crude; for T+ reported) = 1.00, 95% CI: 0.50, 2.10
OR (regression-based; reported) = NR List of covariates: NA	OR (regression-based; reported) = NR List of covariates: NA
Other reported measure = NR	Other reported measure = NR
Comparison between tests (IGRA vs. TST)	
Ratio of DORs (for T^+ calculated) = NA	
Ratio of OR (crude; for T^+ reported) = 1.00 (95% CI: 0.60, 1.66) [>301 vs. reference group]	
Ratio of ORs (regression-based; reported) = NA	

Other reported measure = NA							
Association between test results and BCG status (if applicable)							
IGRA (specify)				**TST (specify)**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters	
IGRA	TST
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable) **This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition**			
Total sample			
	TST +	TST -	Total
IGRA +	49	58	107
IGRA -	23	149	172
Indeterminate	NR	NR	173 (excluded)
Total	72	207	279
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): Total			
TST + threshold: ≥10mm			
Parameters			
Kappa = 0.35 (95% CI: 0.23, 0.46)			
% concordance = 198/279 = 70.97% (95% CI: 65.39, 75.98)			
% discordance = 81/279 = 29.03% (95% CI: 24.02, 34.61)			
Stratification (specify group 1)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR		
TST + threshold: NR		
Parameters		
Kappa = NR		
% concordance = NR		
% discordance = NR		
Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR
Conclusions		
Authors:		
The findings indicate that QFT-GIT could be useful for screening recent immigrants with a high rate of unavailable TST results. The overall agreement between QFT-GIT and TST was 70.9%, with a k statistics of 0.35. No single demographic characteristic including sex, age, region of origin and TB burden in the country of origin, was associated with TST and/or QFT-GIT positivity		
Reviewers:		
None of the risk factors was associated with test positivity of either IGRA or TST		
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation		

Name of first reviewer: AlexanderTsertsvadze
Name of second reviewer: Peter Auguste

Study details

First author surname year of publication: Harstad 2010[143]
Country: Norway
Study design: Prospective cohort study
Study setting (e.g., outbreak investigation, community-based - specify)**:** Community - based
Number of centres: NR
Total length of follow up (if applicable): 23-32 months
Funding (government/private/manufacturer/other - specify)**:** Norwegian Health Association; The Regional Health Authorities

Aim of the study

To compare PPV and NPV between QuantiFERON®-TB Gold (QFT-G) and the TST in asylum seekers in Norway

Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)

Recently arrived people

Participants

Recruitment dates: September 2005 to June 2006
Total N of recruited patients: NR
Inclusion criteria: Asylum seekers aged ≥18 years
Exclusion criteria: Active TB
Total N of excluded patients: NR
Total N of patients tested with both IGRA and TST: NR
Total N of patients with valid results for both IGRA and TST: 823
Methods of active TB diagnosis (if applicable): NR
Outcomes (study-based) list: PPV and NPV
Characteristics of participants (total study sample)
Mean (range or SD) age (years): 18–34 yrs (n = 587), 35–49 yrs (n = 201), and ≥ 50 yrs (n = 35)
Women (n [%]): 206 [25.0]
Race/ethnicity (n [%]): NR
Geographic origin (n[%]): Europe (103[12.5]), Africa (347[42.0]), Asia (346[42.0]), other (27[3.3])
BCG vaccination (n [%]): NR
History of anti-TB treatment (n [%]): NR
Total incidence of active TB (n [%]): 9/823 [1.1]
Chest radiography (yes/no): Yes
Clinical examination (yes/no): NR
Morbidity (n [%]): NA
Co-morbidity (n [%]): NA
Type of during-study treatment (n [%]): NR

Number of patients tested

	Total N (tested)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	NR	246	577	NR	823
TST:	NR	426 (≥ 6mm) 128 (≥15mm)	395 (<6mm) 693 (<15mm)	NR	821
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of patients with valid results for both IGRA and TST:

Levels/groups of exposure to TB in increasing order (if applicable):

	Definition of exposure group
Non-exposed	NA

Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	Cut-off values/thresholds Definition of test+	Other information
IGRA	QuantiFERON-TB Gold In-Tube, Cellestis Ltd, Carnegie, VIC, Australia)	NR	NA
TST	TSTs (purified protein derivative RT 23, 2 tuberculin units [TU] from Statens Serum Institute, Copenhagen, Denmark)	≥ 6mm ≥15mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA (QFT-GIT)				**TST ≥ 6mm**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	8	230	238	TST +(≥ 6mm)	8	407	415
IGRA -	1	576	577	TST – (<6mm)	1	394	395
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	9	806	815	Total	9	801	810

Test performance parameters

IGRA	**TST**
Sensitivity = 8/9 = 88.89% (95% CI: 56.5, 98.01)	Sensitivity = 8/9 = 88.89% (95% CI: 56.5, 98.01)
Specificity = 576/806 = 71.46% (95% CI: 68.25, 74.47)	Specificity = 394/801 = 49.19% (95% CI: 45.74, 52.65)
PPV = 8/238 = 3.36% (95% CI: 1.71, 6.49)	PPV = 8/415 = 1.92% (95% CI: 0.98, 3.75)
NPV = 576/577 = 99.83% (95% CI: 99.02, 99.97)	NPV = 394/395 = 99.75% (95% CI: 98.58, 99.96)
Cumulative Incidence $_{IGRA+}$ = 8/238 = 3.36% (95% CI: 1.71, 6.49)	Cumulative Incidence $_{TST+}$ = 8/415 = 1.92% (95% CI: 0.98, 3.75)
Cumulative Incidence $_{IGRA-}$ = 1/577 = 0.17% (95% CI: 0.00, 1.08)	Cumulative Incidence $_{TST-}$ = 1/395 = 0.25% (95% CI: 0.00, 1.57)
Cumulative Incidence Ratio $_{IGRA}$ = 19.39 (95% CI: 2.43, 154.2)	Cumulative Incidence Ratio $_{TST}$ = 7.61 (95% CI: 0.95, 60.59)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR

Comparison between tests (IGRA vs. TST⩾6mm)

Ratio of cumulative incidence ratios = 2.55(95% CI: 0.57, 11.40)
Ratio of incidence density rate ratios = NR
Other reported measure = NR

Association between test results and incidence of active TB (if applicable)

TST (≥ 15mm)

	Incidence of active TB		Total
	Yes	No	
TST + (≥	3	118	121

15mm)			
TST -(< 15mm)	6	686	692
Indeterminate	NR	NR	NR
Total	9	804	813

Test performance parameters (TST≥ 15mm)

Sensitivity = 3/9 = 33.33% (95% CI: 12.06, 64.58)

Specificity = 686/804 = 85.32% (95% CI: 82.71, 87.60)

PPV = 3/121 = 2.48% (95% CI: 0.84, 7.03)

NPV = 686/692 = 99.13% (95% CI: 98.12, 99.6)

Cumulative Incidence $_{IGRA+}$ 3/121 = 2.48% (95% CI: 0.84, 7.03)

Cumulative Incidence $_{IGRA-}$ = 6/692 = 0.86% (95% CI: 0.35, 1.92)

Cumulative Incidence Ratio $_{IGRA}$ = 2.86 (95% CI: 0.725, 11.28)

Incidence density rate $_{IGRA+}$ = NR

Incidence density rate $_{IGRA-}$ = NR

Incidence density rate ratio $_{IGRA}$ = NR

Comparison between tests (IGRA vs. TST⩾15mm)

Ratio of cumulative incidence ratios = 0.38(95% CI: 0.11, 1.34)

Ratio of incidence density rate ratios = NR

Other reported measure = NR

Association between test results and levels of TB exposure (if applicable)

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA	NA	Total	NA	NA	NA

Test performance parameters

IGRA	**TST**
Sensitivity = NA	Sensitivity = NA
Specificity = NA	Specificity = NA
PPV = NA	PPV = NA
NPV = NA	NPV = NA
DOR (for T^+ calculated) = NA	DOR (for T^+ calculated) = NA
OR (crude; for T^+ reported) = NA	OR (crude; for T^+ reported) = NA
OR (regression-based; reported) = NA List of covariates: NA	OR (regression-based; reported) = NA List of covariates: NA
Other reported measure = NA	Other reported measure = NA

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NA

Ratio of OR (crude; for T^+ reported) = NA

Ratio of ORs (regression-based; reported) = NA

Other reported measure = NA

Association between test results and BCG status (if applicable)

IGRA				**TST**			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	**TST**

DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Stratification (specify group 2)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR

Parameters

Kappa = NR

% concordance = NR

% discordance = NR

Other outcomes

Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
Neither PPV nor NPV differed significantly from the corresponding values for TST
Reviewers:
Small sample; differences in follow up between test positives and negatives may have biased the results; some cases may have been prevalent (not incident)
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation

Name of first reviewer: Alexander Tsertsvadze
Name of second reviewer: Peter Auguste

Study details
First author surname year of publication: Kik 2010[144] (companion**:** Kik 2009) **Country:** The Netherlands **Study design:** Prospective cohort study **Study setting** (e.g., outbreak investigation, community-based - specify)**:** Community-based **Number of centres:** Multicenter (n = 15) **Total length of follow up (if applicable):** 24 mo **Funding** (government/private/manufacturer/other - specify)**:** Unrestricted grants from the Netherlands Organization for Health Research and Development (ZonMw; the Hague, the Netherlands)
Aim of the study
To assess the positive/negative predictive values (PPV/NPV), sensitivity, and specificity for TB disease of QFT-GIT, T-SPOT.TB1 and TST in immigrant individuals in the Netherlands who were recently exposed to infectious pulmonary TB patients
Subgroup of interest (i.e., children, recently arrived people, immunocompromised people)
Recently arrived people
Participants
Recruitment dates: April 2005 to July 2007 **Total N of recruited patients:** 433 **Inclusion criteria:** Close contacts (aged ≥16 yrs and born in a TB endemic country) of sputum smear-positive pulmonary TB patients who tested positive on TST (≥5mm) **Exclusion criteria:** Contacts with known conditions associated with an increased risk of progression to disease (including diabetes and HIV infection) and individuals who were given preventive treatment **Total N of excluded patients:** 94 (TST<5mm) **Total N of patients tested with both IGRA and TST:** 339 **Total N of patients with valid results for both IGRA and TST:** 327 **Methods of active TB diagnosis (if applicable):** Contacts diagnosed with TB ≥ 3 months after the diagnosis of the index patient were considered to be incident cases, whereas TB cases diagnosed < 3 months after the diagnosis of the index patient were considered to be co-prevalent and were excluded from the analysis. The diagnosis of TB disease was based on chest radiography, symptoms, smear and/or culture results **Outcomes (study-based) list:** PPV/NPV, sensitivity, and specificity for the incidence of TB disease for QFT-GIT, T-SPOT.TB1 and TST **Characteristics of participants (total study sample)** Mean (range or SD) age (years): n = 53 [15.6%] (range: 16–24), n = 80 [23.6%] (range: 25–34), n = 115 [33.9%] (range: 35–44), and n = 91 [26.8%] (range: ≥45) Women (n [%]): 147 [43.4] Race/ethnicity (n [%]): NR Geographic origin (n[%]): Europe/North America (27 [8.0]), South America (27 [8.0]), Asia (123 [36.3]), Other Africa (98 [28.9]), Sub-Saharan Africa (59 [17.4]), Unknown (5 [1.5]) BCG vaccination (n [%]): 274 [80.8] History of anti-TB treatment (n [%]): None Total incidence of active TB (n [%]): 9/339 [2.65] Chest radiography (yes/no): Yes Clinical examination (yes/no): Yes Morbidity (n [%]): NR Co-morbidity (n [%]): NR Type of during-study treatment (n [%]): None
Number of patients tested

	Total N (tested)	**Total N**	**Total N (test-)**	**Total N (indeterminate)**	**Total N (test results**

		(test+)			available)
IGRA (QFT-GIT)	339	178	149	12	327
IGRA (T-SPOT.TB)	339	181	118	40	299
TST (≥10mm)	339	288	51	0	339
TST (≥15mm)	322	184	138	0	322

Total N of patients with valid results for both IGRA and TST: TST (n = 339), QFT-GIT (n = 327), and T-SPOT.TB (n = 299)

Levels/groups of exposure to TB in increasing order (if applicable):

Definition of exposure group	
Non-exposed	NA
Exposed 1 **(specify):**	NA
Exposed 2 **(specify):**	NA
Exposed 3 **(specify):**	NA
Exposed 4 **(specify):**	NA

Tests

	Assay used, methodology, timing for test measurement, manufacturer	**Cut-off values/thresholds Definition of test+**	**Other information**
IGRA (QFT-GIT)	Performed according to the instructions of the manufacturers and tested in a single laboratory (Leiden University Medical Center, Leiden, the Netherlands)	Two-tube format positive test was defined as ≥ 0.35 IU/mL-[1]	NA
IGRA (T-SPOT.TB)	Performed according to the instructions of the manufacturers and tested in a single laboratory (Leiden University Medical Center, Leiden, the Netherlands)	Interpretation of results was according to the latest criteria defined by the manufacturer	NA
TST	two tuberculin units, purified protein derivative RT23 in Tween-80; Statens Serum Institute, Copenhagen, Denmark) and read after 48–72 h	≥ 10mm ≥ 15mm	NA

Association between test results and incidence of active TB (if applicable)

IGRA(QFT-GIT)				**TST≥10mm**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	5	173	178	TST +	9	279	288
IGRA -	3	146	149	TST -	0	51	51
Indeterminate	1	11	12	Indeterminate	0	0	0
Total	9	330	339	Total	9	330	339

Test performance parameters

IGRA (excluding indeterminate)	**TST**
Sensitivity = 5/8 = 62.50% (95% CI: 30.57, 86.32)	Sensitivity = 9/9 = 100.00% (95% CI: 70.08, 100.00)
Specificity = 146/319 = 45.77% (95% CI: 40.38, 51.25)	Specificity = 51/330 = 15.45% (95% CI: 11.95, 19.75)
PPV = 5/178 = 2.80% (95% CI: 1.20, 6.40)	PPV = 9/288 = 3.12% (95% CI: 1.65, 5.83)
NPV = 146/149 = 98.0% (95% CI: 94.20, 99.31)	NPV = 51/51 = 100.00% (95% CI: 93.00, 100.00)
Cumulative Incidence $_{IGRA+}$ = 5/178 = 2.80%	Cumulative Incidence $_{TST+}$ = 9/288 = 3.12%

(95% CI: 1.20, 6.40)	(95% CI: 1.65, 5.83)
Cumulative Incidence $_{IGRA-}$ = 3/149 = 2.00% (95% CI: 0.42, 6.02)	Cumulative Incidence $_{TST-}$ = 0/51 = 1.96 (95% CI:0.21, 10.4)
Cumulative Incidence Ratio $_{IGRA}$ = 1.39 (95% CI: 0.34, 5.74)	Cumulative Incidence Ratio $_{TST}$ = 1.59 (95% CI: 0.21, 71.2)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Other reported measure $_{IGRA}$ = NR	Other reported measure $_{TST}$ = NR
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence ratios = 0.87 (95% CI: 0.17, 4.56)	
Ratio of incidence density rate ratios = NR	
Other reported measure = NR	

Association between test results and incidence of active TB (if applicable)

IGRA (T-SPOT.TB)				**TST≥15mm**			
	Incidence of active TB		Total		Incidence of active TB		Total
	Yes	No			Yes	No	
IGRA +	6	175	181	TST +	7	177	184
IGRA -	2	116	118	TST -	1	137	138
Indeterminate	1	39	40	Indeterminate	0	0	0
Total	9	330	339	Total	8	314	322

Test performance parameters

IGRA (excluding indeterminate)	**TST**
Sensitivity = 6/8 = 75.00% (95% CI: 40.93, 92.85)	Sensitivity = 7/8 = 87.5% (95% CI: 52.91, 97.76)
Specificity = 116/291 = 39.86% (95% CI: 34.4, 45.58)	Specificity = 137/314 = 43.63% (95% CI: 38.25, 49.16)
PPV = 6/181 = 3.31% (95% CI: 1.52, 7.04)	PPV = 7/184 = 3.80% (95% CI: 1.85, 7.64)
NPV = 98.31% (95% CI: 94.03, 99.53)	NPV = 137/138 = 99.28% (95% CI: 96.01, 99.87)
Cumulative Incidence $_{IGRA+}$ = 6/181 = 3.31% (95% CI: 1.52, 7.04)	Cumulative Incidence $_{TST+}$ = 7/184 = 3.80% (95% CI: 1.85, 7.64)
Cumulative Incidence $_{IGRA-}$ = 2/118 = 1.69% (95% CI: 0.08, 6.35)	Cumulative Incidence $_{TST-}$ = 1/138 = 0.72% (95% CI:0.00, 4.39)
Cumulative Incidence Ratio $_{IGRA}$ = 1.95 (95% CI: 0.40, 9.52)	Cumulative Incidence Ratio $_{TST}$ = 5.25 (95% CI: 0.65, 42.17)
Incidence density rate $_{IGRA+}$ = NR	Incidence density rate $_{TST+}$ = NR
Incidence density rate $_{IGRA-}$ = NR	Incidence density rate $_{TST-}$ = NR
Incidence density rate ratio $_{IGRA}$ = NR	Incidence density rate ratio $_{TST}$ = NR
Comparison between tests (IGRA vs. TST)	
Ratio of cumulative incidence ratios = 0.37(95% CI: 0.10, 1.41)	
Ratio of incidence density rate ratios = NR	
Other reported measure = NR	

Association between test results and levels of TB exposure (if applicable)

IGRA				**TST**			
	Exposure level		Total		Exposure level		Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	TST
Sensitivity = NR	Sensitivity = NR
Specificity = NR	Specificity = NR
PPV = NR	PPV = NR
NPV = NR	NPV = NR
DOR (for T^+ calculated) = NR	DOR (for T^+ calculated) = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T^+ reported) = NR
OR (regression-based; reported) = NR List of covariates: NR	OR (regression-based; reported) = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Comparison between tests (IGRA vs. TST)

Ratio of DORs (for T^+ calculated) = NR
Ratio of OR (crude; for T^+ reported) = NR
Ratio of ORs (regression-based; reported) = NR
Other reported measure = NR

Association between test results and BCG status (if applicable)

IGRA				TST			
	BCG status		Total		BCG status		Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
Total	NR	NR	NR	Total	NR	NR	NR

Test performance parameters

IGRA	TST
DOR (for T^+ calculated)$_{IGRA}$ = NR	DOR (for T+ calculated)$_{TST}$ = NR
OR (crude; for T^+ reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) $_{IGRA}$ = NR List of covariates: NR	OR (regression-based; reported) $_{TST}$ = NR List of covariates: NR
Other reported measure = NR	Other reported measure = NR

Between-test agreement, concordance, and discordance (if applicable)
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition

Total sample

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR

Parameters

Kappa = NR
% concordance = NR
% discordance = NR

Stratification (specify group 1)

	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR

Description

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR

TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify group 2)			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description			
Sample definition (e.g., total, if stratified by BCG or condition – specify): NR			
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			

Other outcomes		
Test and cut-off (if applicable)	**Adverse events n/N (%) (specify)**	**Health related quality of life mean score (SD) (specify)**
IGRA:	NR	NR
TST:	NR	NR
Test 3 (specify):	NR	NR

Conclusions
Authors:
PPVs of QFT-GIT and T-SPOT.TB for subsequent development of TB disease during the first 2 yrs after a contact investigation were comparable to that of the TST, irrespective of the TST cut off (10 or 15 mm)
Reviewers:
The three tests demonstrated similar performance in predicting active TB incidence (PPV and sensitivity); TST (≥15mm) and QFT-GIT demonstrated better specificity compared to TST (≥15mm) and TSPOT.TB
Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence intervals; TB = tuberculosis; BCG = Bacillus Calmette–Guérin; PPV = positive predictive value; NPV = negative predictive value; FPR = false positive rate; FNR = false negative rate; SD = standard deviation