#### Children

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

#### Study details

First author surname year of publication: Adetifa 2010<sup>105</sup>

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

	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

(TSPO					
T):	57 15			21.5	
TST NR	57   15	8	0	215	
(≥10m m):					
Test 3 NA	NA NA	٨	NA	NA	
(specif	INA INA	Α.	NA .	INA	
y):					
	atients with valid results for both I	GRA a	and TST: 215 for all three tes	ts	
	os of exposure to TB in increasing of				
8 1	Definition of exposure				
Non-	Different house (reference group)	8 F	этор резилия		
exposed	(1118				
Exposed 1	Same house – different room				
(specify):					
Exposed 2	Same house – same room				
(specify):					
Exposed 3	NA				
(specify):	374				
Exposed 4	NA				
(specify): Tests					
Tests	A 4	- C	Cont. off	Other	
	Assay used, methodology, timing test measurement, manufactur	_	Cut-off values/thresholds	Other information	
	test measurement, manuractur	ei	Definition of test+	illioilliation	
IGRA	Carried out according to manufactu	rer's	Where the negative	NA	
(TSPOT)	instructions. The spot unit counting		control had 0-5 spots, a	1111	
,	performed using ELISPOT reader (		positive result was		
	GmbH, Strassburg, Germany)		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		
IGRA	Carried out according to manufactu	rer's	Positive result was	NA	
(QFT-GIT)	instructions. IFN gamma levels		defined as ≥0.35 IU/ml		
	measured using Dynex ELISA read				
	ver. 6.0 (Dynex Technologies, Wes	t			
TCT	Sussex, UK)		>10	NT A	
TST (≥10mm)	Carried out with 2 TU (PPD RT23, Statens Serum Institut, Copenhager		≥10mm threshold for positivity	NA	
(<1011111)	Denmark) immediately after blood	1,	positivity		
	samples' completion. Indurations w	/ere			
	recorded at 48-72 hours				
	between test results and incidence of	of a ativ	vo TD (if annliaghla)		
Association					

	IGR	RA			TS	T	
	Incidence		Total			of active 7	TB Total
	TE						
	Yes	No	1		Yes	No	
IGRA +	NA	NA	NA	TST +	NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indetermi	NA	NA	NA	Indeterminate	NA	NA	NA
nate							
Total	NA	NA	NA	Total	NA	NA	NA
			Test perfor	rmance parame	ters		·
	IGR	RA			TS	T	
Sensitivity	= NA			Sensitivity = N	NΑ		
Specificity	= NA			Specificity = N	NA		
PPV = NA				PPV = NA			
NPV = NA				NPV = NA			
Cumulative	e Incidence IC	$_{SRA^{+}} = NA$		Cumulative In	cidence TST+	= NA	
Cumulative	e Incidence 10	$_{BRA-} = NA$		Cumulative In	cidence TST- =	- NA	
	e Incidence R		- NA	Cumulative In			
Incidence d	lensity rate IG	$_{GRA^{+}} = NA$		Incidence dens	sity rate TST+	NA	
	lensity rate IG			Incidence dens	sity rate TST-	NA	
Incidence d	lensity rate ra	atio <sub>IGRA</sub> =	NA	Incidence dens	sity rate ratio	$_{TST} = NA$	
Other repor	rted measure	$_{IGRA} = NA$		Other reported	measure <sub>TST</sub>	= NA	
		Comp	parison betw	veen tests (IGR.	A vs. TST)		
Ratio of cu	mulative inci	idence rati	os = NA				
Ratio of inc	cidence densi	ity rate rati	ios = NA				
Other repor	rted measure	= NA					
	A • 4•	1 4	1 1 1	11 1 670	D (	·c 1· 1	1.
			test results	and levels of T	`		01e)
	IGRA (QF		Total		TST (≥1		Total
	Sleep pro		Total	_	Sleep prox		Total
	Same	Differ ent			Same	Differe	
		i eni i			house –	nt	
	house –				00m0 m00m	house	
	same	house			same room	house	
IGP A ±	same room	house	22	TST ±			25
IGRA +	same room 14	house 19	33 NR	TST +	15	10	25 NR
IGRA -	same room 14 NR	house 19 NR	NR	TST -	15 NR	10 NR	NR
IGRA - Indetermi	same room 14	house 19		TST - Indeterminat	15	10	
IGRA - Indetermi nate	same room 14 NR NR	house 19 NR NR	NR NR	TST - Indeterminat e	15 NR NR	10 NR NR	NR NR
IGRA - Indetermi	same room 14 NR	house 19 NR	NR NR 215	TST - Indeterminat e Total	15 NR NR NR	10 NR	NR
IGRA - Indetermi nate	same room 14 NR NR NR	house  19  NR  NR  NR	NR NR 215	TST - Indeterminat e	15 NR NR NR	10 NR NR NR	NR NR
IGRA - Indetermi nate Total	same room 14 NR NR NR NR	house  19  NR  NR  NR	NR NR 215	TST - Indeterminat e Total rmance parame	15 NR NR NR NR	10 NR NR NR	NR NR
IGRA - Indetermi nate Total	same room  14  NR  NR  NR  NR  NR	house  19  NR  NR  NR	NR NR 215	TST - Indeterminat e Total rmance parame Sensitivity = N	15 NR NR NR ters	10 NR NR NR	NR NR
IGRA - Indetermi nate Total  Sensitivity Specificity	same room  14  NR  NR  NR  NR  NR	house  19  NR  NR  NR	NR NR 215	TST - Indeterminat e Total rmance parame Sensitivity = N Specificity = N	15 NR NR NR ters	10 NR NR NR	NR NR
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR	same room 14 NR NR NR  NR  NR  IGR  = NR	house  19  NR  NR  NR	NR NR 215	TST - Indeterminat e Total rmance parame Sensitivity = N Specificity = N PPV = NR	15 NR NR NR ters	10 NR NR NR	NR NR
IGRA - Indetermi nate Total  Sensitivity Specificity PPV = NR NPV = NR	same room 14 NR NR NR  NR  IGR = NR	house  19  NR  NR  NR	NR NR 215	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR	15 NR NR NR Eters TS	10 NR NR NR	NR NR
IGRA - Indetermi nate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T	same room  14  NR  NR  NR  IGR  = NR  = NR	house  19 NR NR NR  NR	NR NR 215 Test perfo	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T <sup>+</sup> ca	15 NR NR NR eters TS' R	10 NR NR NR T	NR NR 215
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T	same room 14 NR NR NR  NR  IGR = NR	house  19 NR NR NR  NR	NR NR 215 Test perfo	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T <sup>+</sup> ca Same house sa	15	10 NR NR NR T IR	NR NR 215
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T Same house	same room 14 NR NR NR NR  IGR = NR = NR = NR  **Calculated** **Ge same room**	house  19 NR NR NR NR  NR  NR  NR  NR  NR  NR  N	NR NR 215 Test perfor	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T + ca Same house sa OR (crude; for	15	10 NR NR NR T IR	NR NR 215
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T Same house OR (crude;	same room  14  NR  NR  NR  IGR  = NR  = NR	house  19 NR NR NR NR  NR  NR  NR  NR  NR  NR  N	NR NR 215 Test perfor	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T <sup>+</sup> ca Same house sa	15	10 NR NR NR T IR	NR NR 215
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T Same house OR (crude; 1.20, 9.10)	same room 14 NR NR NR  IGR = NR = NR  T calculated for T report	house  19	NR NR 215 Test performance rent (95% CI:	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T <sup>+</sup> ca Same house sa OR (crude; for 32.10)	15 NR NR NR  Sters  TS' R R  alculated) = N me room vs. T reported)	10     NR     NR     NR  IR  Different = 10.10 (95)	NR NR 215  house 5% CI: 3.20,
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T Same house OR (crude; 1.20, 9.10) Same house	same room 14 NR NR NR NR  IGR = NR = NR = NR  **Calculated** **Ge same room**	house  19	NR NR 215 Test performance rent (95% CI:	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T <sup>+</sup> ca Same house sa OR (crude; for 32.10)  Same house sa	15 NR NR NR eters TS R R alculated) = N me room vs. T + reported)	10     NR     NR     NR     NR  IR     Different = 10.10 (95)	NR NR 215  house 5% CI: 3.20,
IGRA - Indeterminate Total  Sensitivity Specificity PPV = NR NPV = NR DOR (for T Same house OR (crude; 1.20, 9.10) Same house house	same room 14 NR NR NR  IGR = NR = NR  T calculated for T report	house  19  NR  NR  NR  NR  NR  19  NR  NR  NR  NR  10  NR  NR  NR  NR  NR  NR  NR  NR  NR  N	NR NR 215 Test performance erent (95% CI:	TST - Indeterminat e Total  rmance parame  Sensitivity = N Specificity = N PPV = NR NPV = NR DOR (for T <sup>+</sup> ca Same house sa OR (crude; for 32.10)	15 NR NR NR eters TS R R alculated) = N me room vs. T + reported)	10     NR     NR     NR     NR  IR     Different = 10.10 (95)	NR NR 215  house 5% CI: 3.20,

GT 1 40	11.40						.1 .			
CI: 1.40,		.1 .			List of covariates: age, sex, ethnic group					
	variates: age, s		e group		Other man arted measure — NID					
Otner rep	orted measure		• 1		ther reported measure = NR n tests (IGRA vs. TST)					
Datia of I	DODa (for T <sup>+</sup> a			betwee	en tests (IGR	A vs. 151)				
	ORs (for T c			2 (0.29	0.00)					
	OR (crude; for ORs (regression									
			eportea)	= 0.52	(0.29, 0.91)					
Otner rep	orted measure		n tost was	ulta on	d lavals of T	B exposure (i	fannlias	bla)		
	IGRA (TSI		ii test res	uits ai	iu ieveis oi i	TST (≥10r		Die)		
	Sleep pro		Total			Sleep prox		1	Total	
	Same	Differ	Total			Same	Differe	. '	otai	
	house –	ent				house –	nt			
	different	house				different	house			
	room	nouse				room	nouse			
IGRA +	39	18	57	TST -	+	32	10		42	
IGRA -	NR	NR	NR	TST ·		NR	NR		NR	
Indetermi		NR	NR		erminate	NR	NR		NR	
nate	I	INIX	INIX	macu	cillillate	INIX	INIX		INIX	
Total	NR	NR	215	Total		NR	NR		215	
Total	INIX	IVIX			ance param		IVIX		213	
	IGRA		1 cst pt		ance param	TST				
Sensitivit				Sensi	tivity = NR	101				
Specificit				Specificity = NR						
PPV = N	*			PPV = NR						
NPV = N				NPV = NR						
	T calculated	N = NR			(for T <sup>+</sup> calcu	lated) = NR				
	use different r					rent room vs.	Different	t house		
Different		oom vs.		OR (crude; for $T^+$ reported) = 2.40 (95% CI: 1.00, 5.80)						
	e; for T <sup>+</sup> report	(ed) = 2.0	0 (95%	2.10 (2070 01. 1.00, 0.00)						
CI: 0.80,		.cu) 2.0	0 (3570							
	use different r	oom vs.		Same house different room vs. Different house						
Different				OR (regression-based; reported) = 2.90 (95% CI: 1.30,						
	ession-based; r	eported) =	= 2.60	6.70)						
, -	0.90, 7.10)	1 /		List of covariates: age, sex, ethnic group						
List of co	variates: age, s	sex, ethni	c group							
	orted measure			Other	reported me	asure = NR				
		Com	parison	betwee	en tests (IGR	A vs. TST)				
	DORs (for T <sup>+</sup> c									
	OR (crude; for									
	ORs (regression									
	orted measure									
	Association	n between	n test res	ults an	d levels of T	B exposure (i	f applica	ble)		
	IGRA (	TSPOT)				TST (≥	10mm)			
	Sleep prox	imity	Tota	al		Sleep	proximity	у	Total	
	Same	Differen				Same hous	se Diffe	erent		
	house –	t house				- same	ho	use		
	same room					room				
IGRA	14	18	32	2	TST +	15	1	0	25	
+										
IGRA -	NR	NR	NF	}	TST -	NR	N	R	NR	
Indeter	NR	NR	NF	{	Indetermina	a NR	N	R	NR	
					•	•				

minate					te				
Total	NR	NR	215		Total	NR	NR	215	
			Test perf	forma	rmance parameters				
	IC	GRA	•		•	TST			
Sensitivi	ty = NR				Sensitivity = NR				
Specifici	•				Specificity = NR				
PPV = N	•				PPV = NR				
NPV = N					NPV = NR				
	or T <sup>+</sup> calculated	1 = NR				calculated) = N	R		
	ouse same roo	/	want haus	0		same room vs.		1100	
	de; for T <sup>+</sup> repo			•		for T <sup>+</sup> reported) =			
,		rieu) – 5.50	) (93% C1.		32.10)	ioi i reported) -	- 10.10 (93/0	C1. 3.20,	
1.50, 18.50)  Same house same room vs. Different house						same room vs.	Different he	1100	
	ression-based;	reported) =	6.60 (93%	0		ion-based; repor	tea) = 15.00 (	95% CI:	
CI: 1.70,	,	.1 •			4.70, 47.20)		41 .		
	ovariates: age,		group			riates: age, sex,			
Other reported measure = NR Other reported measure = NR									
Comparison between tests (IGRA vs. TST)									
Ratio of	DORs (for T <sup>+</sup>	calculated)	= NA						
Ratio of OR (crude; for $T^+$ reported) = 0.52(0.22, 1.25)									
Ratio of ORs (regression-based; reported) = $0.44(0.18, 1.09)$									
	ported measur				,,				
o unon no			test result	ts and	d levels of TI	B exposure (if a	nnlicable)		
	IGRA (T		i test resur		4 10 (015 01 11	TST (≥10m)			
	Sleep pro		Total			Sleep pro		Total	
	Same house	Differen	- I Otal		ŀ	Same house	Different	10tai	
	– same	t house				– same	house		
ICDA	room	1.0	22	TST	2 .	room	10	25	
IGRA	14	18	32	151	+	15	10	25	
+	NID	NID	NID	TOT		NID	NID	ND	
IGRA	NR	NR	NR	TST	. <b>-</b>	NR	NR	NR	
T 1 4	NID	NID	ND	т 1		NID	ND	ND	
Indeter	NR	NR	NR	Inae	eterminate	NR	NR	NR	
minate	MD	NID	21.5	TD 1	1	NID	NID	215	
Total	NR	NR	215	Tota		NR	NR	215	
			Test perf	forma	nce parame				
	IGF	RA				TST			
Sensitivi					sitivity = NR				
Specifici	•				cificity = NR				
PPV = N				PPV	V = NR				
NPV = N	NR			NPV	V = NR				
DOR (fo	r T <sup>+</sup> calculated	1 = NR		DO	R (for T <sup>+</sup> calc	culated) = NR			
Same ho	use same roo	m vs. Diffe	erent	San	ne house sam	ne room vs. Diff	erent house		
house				OR	(crude; for T	$^{+}$ reported) = 10.	10 (95% CI: 3	3.20,	
OR (crud	de; for T <sup>+</sup> repo	rted) = 5.30	) (95%	32.1	10)	- ,			
CI: 1.50,			*		,				
	ouse same roo	m vs. Diffe	erent	San	ne house sam	ne room vs. Diff	ferent house		
house			- <del>-</del>			pased; reported)		CI: 4.70.	
	ession-based;	reported) =	= 6.60	47.2	. •	, reported)	12.00 (5070	-2,	
	: 1.70, 25.20)	-Sportou)	3.00	1	/	s: age, sex, ethni	c groun		
	ovariates: age,	sex ethnic	groun	2151	. 51 55 (411416)	450, 504, 011111	- Prouh		
	ported measur		2.0up	Oth	er reported m	neasure = NR			
Other re	ported incasul		narisan ha		n tests (IGR				
		Colli	parison be	tweel	i tests (IGKA	1 vs. 131)			

	DORs (for T <sup>+</sup> c						
			= 0.52 (0.22, 1.25				
Ratio of 0	ORs (regression	n-based; repo	rted) = 0.44 (0.13	8, 1.09)			
Other rep	orted measure	= NA					
	Assoc	iation betwe	en test results a	nd BCG statu	s (if applicable)		
	l	GRA			TST		
	BCG st	atus	Total		BCG statu	S	Total
	Yes	No			Yes	No	
IGRA +	NR	NR	NR	TST +	NR	NR	NR
IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeter	NR	NR	NR	Indetermi	NR	NR	NR
minate				nate			
Total	NR	NR	NR	Total	NR	NR	NR
		T	est performance	parameters			
	]	GRA	•	Î	TST		
DOR (for	r T <sup>+</sup> calculated)			DOR (for T-	calculated) <sub>TST</sub> =	NR	
			(95% CI: 0.60,		for T+ reported) =		95% CI:
2.00)	, 1 1 <b>0</b> port	/QII 1110	(22,000,	0.50, 1.70)	- inpolica)		
/	e; for T <sup>+</sup> report	ed) <sub>TSPOT</sub> = 1.1	10 (95% CI:				
0.61, 2.09	_	- ~/10101	(22/0 01.				
	ession-based; re	eported) IGRA	= NR	OR (regress	ion-based; reporte	ed) <sub>тет</sub> =	NR
List of co		T W/ IORA		List of covar		/ 131	
	orted measure	= NR			ed measure = NR		
			ice, and discord			-	
					ion status, and/o	r condi	tion
	nple: QFT-GI		e cut off variety i	Je G vaccinat	ion status, and o	<u> </u>	
1 otal sal		TST (≥10mn	n) +		TST -		Total
IGRA		43			29		72
(QFT-GI	T)	15			2)		12
+	-)						
IGRA		14			129		143
(QFT-GI	T)				1-7		1.0
-	-)						
Indetermi	ina	NR			2		
te					_		
Total							
Descripti	ion						217
		total, if strati	fied by BCG or o	condition – spe	ecify): total – QF	r-GIT	
	reshold: $\geq 10$ mı			ondition spe	211 <i>)</i> , 101111	. 011	
Paramete	_						
		0.39 (0.65)					
	0.52 (95% CI-	U.J., U.UJ.					
Kappa =	0.52 (95%  CI:	% (95% CI. 7	4 15 84 81				
Kappa = % concor	dance = 80.00						
Kappa = % concor % discord	$r_{dance} = 80.009$ $r_{dance} = 20.009$	6 (95% CI: 1:	5.2, 25.85)	ance (if const	cahla)		
Kappa = % concor % discord <b>Between</b> -	rdance = $80.00^{\circ}$ dance = $20.00^{\circ}$ -test agreemen	% (95% CI: 1: nt, concordar	5.2, 25.85) nce, and discord	`		r condi	tion
Kappa = 6% concor % discord Between- This tabl	rdance = 80.000 dance = 20.00% -test agreement le may be strain	6 (95% CI: 13 nt, concordar tified by TST	5.2, 25.85) nce, and discord	`	cable) ion status, and/o	r condi	tion
Kappa = 6% concor % discord Between- This tabl	rdance = $80.00^{\circ}$ dance = $20.00^{\circ}$ -test agreemen	% (95% CI: 13 ht, concordar tified by TST	5.2, 25.85) nce, and discord cut-off value, I	`	ion status, and/o	r condi	
Kappa = % concor % discord Between- This tabl Total san	rdance = 80.000 dance = 20.00% -test agreement le may be strain	% (95% CI: 1: at, concordantified by TST TST (≥10mm	5.2, 25.85) nce, and discord cut-off value, I	`	ion status, and/o	r condi	Total
Kappa = % concor % discord Between- This tabl Total san	rdance = 80.00% dance = 20.00% -test agreement le may be stran	% (95% CI: 13 ht, concordar tified by TST	5.2, 25.85) nce, and discord cut-off value, I	`	ion status, and/o	r condi	
Kappa = % concor % discord Between- This tabl Total san IGRA (TSPOT)	rdance = 80.00% dance = 20.00% -test agreement le may be stran	6 (95% CI: 15 at, concordar tified by TST TST (≥10mm 43	5.2, 25.85) nce, and discord cut-off value, I	`	TST -	r condi	Total 71
Kappa = % concor % discord Between- This tabl Total sar IGRA (TSPOT)	rdance = 80.000 dance = 20.000 -test agreemen le may be strat nple : TSPOT	% (95% CI: 1: at, concordantified by TST TST (≥10mm	5.2, 25.85) nce, and discord cut-off value, I	`	ion status, and/o	r condi	Total
Kappa = 9% concor % discord Between- This tabl Total sar IGRA (TSPOT) IGRA (TSPOT)	rdance = 80.000 dance = 20.009 -test agreemen le may be strain nple : TSPOT	6 (95% CI: 13 at, concordar tified by TST TST (≥10mm 43	5.2, 25.85) nce, and discord cut-off value, I	`	TST - 28	r condi	Total 71 144
Kappa = 9% concor % discord Between- This tabl Total sar IGRA (TSPOT)	rdance = 80.000 dance = 20.009 -test agreemen le may be strain nple : TSPOT	6 (95% CI: 15 at, concordar tified by TST TST (≥10mm 43	5.2, 25.85) nce, and discord cut-off value, I	`	TST -	r condi	Total 71

Total 57 158  Description  Sample definition (e.g., total, if stratified by BCG or condition – specify): Total	215
*	
Sample definition (e.g., total, if stratified by BCG or condition – specify). Total	
	1 -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
Indetermina NR NR	NR
te	
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
Indetermina NR NR	NR
te	111
Total NR NR	NR
Description	1110
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 of life mean
applicable) (specify)	score (SD) (specify)
IGRA: NR	NR
TST: NR	
	NR NB
Test 3 (specify): NR	NR
Conclusions	
Authors:	DCC ''
TST was most responsive of the 3 tests; none of the tests was affected by prior	BCG vaccination
Reviewers:	A. 1 mcm
Similar moderate agreement between TSPOT vs. TST and QFT vs. TST; TSPO	
strongly correlated with sleep proximity than QFT; none of the tests was influe	nced by BCG
vaccination  Abbreviations: DOR = diagnostic odds ratio; 95% CI = 95 percent confidence	
	e; NPV = negative

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

#### **Study details**

First author surname year of publication: Cruz 2011<sup>106</sup>

**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

		1		
Total N	Total N	Total N	Total N	Total N
(tested)	(test+)	(test-)	(indeterminate)	(test results

						available)
IGRA (TSPOT):	185 (30 TB pts not	94	69	)	22	163
(15101).	counted)					
TST (≥15mm):	185	94	69	)	22	163
	(30 TB pts not counted)					
Test 3	NA	NA	N/	A	NA	NA
(specify)						
	nts with valid res					
Levels/groups of	f exposure to TB					
	1	Definition				
Non-exposed	No contact with					
Exposed 1	contact with an i	dentifiable	source c	ase		
(specify):						
Exposed 2	NA					
(specify):						
Exposed 3	NA					
(specify):						
Exposed 4	NA					
(specify):						
Tests	T					Г
	Assay used, me			Cu	t-off values/thresholds	Other
		easuremen facturer	ιτ,		<b>Definition of test+</b>	information
IGRA	The commercial		. Т	Snots	were counted manually	NA
(TSPOT)	SPOT.TB assay	•	5 1-	-	ing a microscope and	INA
(15101)	Immunotec, Oxf		1	-	med by using an	
	Kingdom) was p				nated plate counter by the	
	hours of specime				facturer. Assays with 8 or	
	the laboratory of		111 111		spots were considered	
	investigators (pe		urer		ve, and assays with less	
	instructions. Brid			-	spots were considered	
	used 2 M tuberc				ive. Borderline results	
	antigens, early se	_		_	spots) were excluded	
	target 6-kDa pro	tein (ESAT	Γ <b>-</b> 6)	from	concordance analyses but	
	and culture filtra	te protein 1	10	were	analyzed separately. A	
	(CFP10), to stim		feron-	subgr	oup analysis was	
	production in wa			-	rmed for specimens with	
	enumerated peri	•			spots, because these	
	mononuclear cel			-	mens are sometimes	
	was drawn from		•		dered positive	
	old or older and			intern	ationally.	
	children younger	-				
	Peripheral blood					
	cells were count					
	standardized cell					
	added in the assa	-				
	low T-cell volum					
	cell reactivity was		a by a			
	(phytohemagglu		egative			
	control was used					
	nonspecific cell					

TST (≥15mm)	Trained clinic or health				TSTs were considered positive NA						
131 (21311111)	department			±							
	interpreted	-	-	anu		18					
	Transverse					n or more, 1 children wit					
	measured a			ıd							
	interpreted			ıu	medical problems or exposure to people at high risk, and 5						
	American	_			mm or more for children with						
	criteria	i iioi acic 50	ocicty		suspected disease or who were						
	Critcria				-	compromise					
						en with iden					
					source ca						
Association between test results and incidence							9)				
	IGRA				(2)		ST				
	Incidence	of T	Γotal				nce of	Total			
	active TI					activ					
	Yes No	)				Yes	No				
IGRA +	NA NA		NA		TST +	NA	NA	NA			
IGRA -	NA NA		NA		TST -	NA	NA	NA			
Indeterminate	NA NA		NA	Ir	ndetermina		NA	NA			
Total	NA NA		NA		Total	NA	NA	NA			
	<u> </u>	Test	perform	nance	paramete	rs					
	IGRA		•		•		ST				
Sensitivity = NA				S	ensitivity =	NA					
Specificity = NA				Specificity = NA							
PPV = NA					PPV = NA						
NPV = NA				N	PV = NA						
Cumulative Incid	lence <sub>IGRA+</sub> =	NA		С	umulative	Incidence TS	$S_{T+} = NA$				
Cumulative Incid						Incidence TS					
Cumulative Incid					Cumulative Incidence Ratio <sub>TST</sub> = NA						
Incidence density					Incidence density rate <sub>TST+</sub> = NA						
Incidence density				Incidence density rate <sub>TST</sub> = NA							
Incidence density				Incidence density rate ratio <sub>TST</sub> = NA							
Other reported m				Other reported measure $_{TST} = NA$							
•		Compariso	n betwe								
Ratio of cumulati					`	,					
Ratio of incidence	e density rat	e ratios = N	ĪΑ								
Other reported m	easure = $NA$	1									
Asso	ociation bet	ween test r	esults a	nd lev	vels of TB	exposure (i	f applica	ble)			
IC	GRA (TSPO	T)				TST≥1	5mm				
	Exposu		Total			Exposu	1	Total			
	High/Yes	Low/No				High/Yes	Low/N				
IGRA +	NR	NR	NR	TST		NR	NR	NR			
IGRA -	NR	NR	NR	TST		NR	NR	NR			
Indeterminate	NR	NR	NR		terminate	NR	NR	NR			
Total	NR	NR	NR	Tota	1	NR	NR	NR			
		Test	perfori	nance	paramete						
IGRA						TS	T				
							Sensitivity = NR				
Sensitivity = NR			ž					Specificity = NR			
Specificity = $NR$				Spec	ificity = N	R					
Specificity = NR PPV = NR				Spec PPV	eificity = N = NR	R					
Specificity = NR PPV = NR NPV = NR				Spec PPV NPV	ificity = N = NR ' = NR						
Specificity = NR PPV = NR	culated) = NI			Spec PPV NPV DOR	$\begin{aligned} & \text{eificity} &= N \\ & = NR \\ & \text{Y} &= NR \\ & \text{R} & \text{(for T}^+ \text{ ca} \end{aligned}$	R $ culated  = 1$ $T^{+}reported$					

OR (regression-based; reported) = 4.41 [95%					OR (regression-based; reported) = 0.48 [95% CI:					
CI: 1.78, 10.94				0.26, 0.91]						
List of covariate		N.T.D.		List of covariates: NR Other reported measure = NR						
Other reported:	measure =									
D i CDOD	(C TE <sup>±</sup> 1			een tes	ts (IGRA vs. TS	5T)				
Ratio of DORs										
Ratio of OR (cr				0 (0.50/	GL 7.00 16.0					
Ratio of ORs (r			ted) = 9.19	9 (95%	C1: 5.23, 16.3)					
Other reported				7.	I D C C · · · · · · ·	c 11	***			
			n test resi	ults an	d BCG status (i	t applica TS	,			
		IGRA BCG status Total		1			Total			
-	Yes	No	101a	1	-	BCG : Yes	No	Total		
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		Total					
10181	NR				parameters	NR	NR	NR		
	IC	RA	st periori	папсе	parameters	TS	Т			
DOR (for T <sup>+</sup> ca					DOR (for T+ ca					
OR (crude; for					OR (crude; for					
		<u></u>			2.29, 9.95]	•				
OR (regression-	-based; rep	orted) <sub>IGRA</sub> =	= 0.69 [95%	%	OR (regression-based; reported) $_{TST} = 4.32$					
CI: 0.37, 1.31]					[95% CI: 1.02,					
List of covariate	es: NR				18.35]					
0.1		N.T.D.			List of covariat		N.T.			
Other reported			7 74		Other reported		= NR			
					nce (if applicab CG vaccination		and/or co	ndition		
Total sample		TST +			TST -					
		TST +			TST -			Total		
		TST +			TST - NR			Total NR		
Total sample										
IGRA + IGRA - Indeterminate		NR NR NR			NR NR NR			NR NR NR		
IGRA + IGRA - Indeterminate Total		NR NR			NR NR			NR NR		
IGRA + IGRA - Indeterminate Total Description		NR NR NR NR			NR NR NR NR			NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition		NR NR NR NR	ied by BC	G or co	NR NR NR	y): total		NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold		NR NR NR NR	ied by BC	G or co	NR NR NR NR	y): total		NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters		NR NR NR NR	ied by BC	G or co	NR NR NR NR	y): total		NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR	d: ≥15mm	NR NR NR NR	ied by BC	G or co	NR NR NR NR	y): total		NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance	d: ≥15mm = NR	NR NR NR NR	ied by BC	G or co	NR NR NR NR	y): total		NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + thresholor Parameters Kappa = NR % concordance % discordance	d: ≥15mm = NR = NR	NR NR NR NR tal, if stratif	ied by BC	G or co	NR NR NR NR	y): total		NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance	d: ≥15mm = NR = NR	NR NR NR NR NR tal, if stratif	ied by BC	G or co	NR NR NR NR Ondition – specify	y): total		NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance % discordance Stratification (	d: ≥15mm = NR = NR	NR NR NR NR tal, if stratif	ied by BC	G or co	NR NR NR NR ondition – specify	y): total		NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance % discordance Stratification (  IGRA +	d: ≥15mm = NR = NR	NR NR NR NR tal, if stratif	ied by BC	G or co	NR NR NR NR ondition – specify	y): total		NR NR NR Total NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + thresholo Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA -	d: ≥15mm = NR = NR	NR NR NR NR tal, if stratif  TST + NR NR	ied by BC	G or co	NR NR NR NR ondition – specify	y): total		NR NR NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate	d: ≥15mm = NR = NR	NR NR NR NR NR tal, if stratif  TST + NR NR NR NR	ied by BC	G or co	NR NR NR NR Ondition – specify  TST - NR NR NR NR	y): total		NR NR NR NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total	d: ≥15mm = NR = NR	NR NR NR NR tal, if stratif  TST + NR NR	ied by BC	G or co	NR NR NR NR ondition – specify	y): total		NR NR NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + threshold Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description	d: ≥15mm  = NR = NR specify gro	NR NR NR NR tal, if stratif  TST + NR NR NR NR NR NR			NR NR NR NR Ondition – specify  TST - NR NR NR NR NR NR			NR NR NR NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + thresholo Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description Sample definition	e: ≥15mm  = NR = NR  specify group  on (e.g., total)	NR NR NR NR tal, if stratif  TST + NR NR NR NR NR NR			NR NR NR NR Ondition – specify  TST - NR NR NR NR			NR NR NR NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + thresholo Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description Sample definition Sample definition	e: ≥15mm  = NR = NR  specify group  on (e.g., total)	NR NR NR NR tal, if stratif  TST + NR NR NR NR NR NR			NR NR NR NR Ondition – specify  TST - NR NR NR NR NR NR			NR NR NR NR NR NR NR		
IGRA + IGRA - Indeterminate Total Description Sample definition TST + thresholo Parameters Kappa = NR % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description Sample definition	e: ≥15mm  = NR = NR  specify group  on (e.g., total)	NR NR NR NR tal, if stratif  TST + NR NR NR NR NR NR			NR NR NR NR Ondition – specify  TST - NR NR NR NR NR NR			NR NR NR NR NR NR 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				

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

TST + threshold: NR

# **Parameters**

Kappa = NR

% concordance = NR

% discordance = NR

7 0 40-0 7 0 - 10-1									
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<sup>107</sup>

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%]

·	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 mn	1):		270	71	183	1	16 254				
Test 3 (specif	fy)	-	NA	NA	NA NA				NA		
Total N of pa	ıtien	ts with	valid resu	lts for bot	th IGRA and TS	ST: 254					
Levels/group	s of	exposui			ng order (if app						
Definition of exposure group –											
			index case		Adult index				index case		
			B diagnos		smear gra	de			the day		
Non-exposed Smear-positive TB					Negative		Minority	y of da	y (< 6 h)		
Exposed 1		Smear-	negative, c	ulture-	Scanty		Majority	of day	y (> 7 h)		
(specify):		positive	_		•						
Exposed 2 (specify):		Clinica	1 TB		1+		NA				
Exposed 3		NA			2+		NA				
(specify):											
Exposed 4		NA			3+		NA				
(specify):											
Tests											
			sed, methe	O. ,	iming for test acturer		Cut-off es/thresh		Other information		
IGRA (QFT-GIT) TST≥5 mm	min fro per ins con con by bet inc into and we EL the pro Sen injurted.	n after T m the rig formed a tructions atrol and aducted a the same ween bloubation erquartil d centrific re stored ISA test Mantou atein der cum Insti-	ST placements of the placement of the pl	tent. Blood FT-GIT te to the man ided nil con in tubes. A laboratory echnician. ion and in in (median 10). Follow rvested plant to 28 de using Tube (D) RT-23 shagen, De sly into the	sufacturer's introl, mitogen issays were at the study site Average intervalitation of a 5, range 2–60, wing stimulation asma specimens days prior to erculin purified (2 units, Statens en mark) was a left forearm and	An in mm v a posid during	Results were calculated and interpreted by the assay software as positive, negative or indeterminate  An induration of \$\geq 5\$ mm was considered a positive test during the study				
Association b	oetw			id inciden	ce of active TB	(if applic					
		IGRA		TD + 1	-	1 .	TST	1	TD 4 1		
			ence of ve TB No	Total			dence of ive TB No		Total		
IGRA +		NA	NA	NA	TST +	NA	NA	İ	NA		
IGRA -		NA	NA	NA	TST -	NA	NA		NA		
Indetermina	te	NA	NA	NA	Indeterminate		NA		NA		
Total		NA	NA	NA	Total	NA	NA		NA		
1000					rmance parame						
		IGRA		THE PETITO			TST				
Sensitivity =	NΔ	IJI			Sensitivity = 1	NA	151				
Specificity =					Specificity = 1						
specificity –	INA				Specificity – 1	11/1					

PPV = NA			PPV = NA						
NPV = NA		NPV = NA							
					idence	- N/A			
Cumulative Incidence <sub>IGRA</sub> . = NA				Cumulative Incidence <sub>TST+</sub> = NA Cumulative Incidence <sub>TST-</sub> = NA					
Cumulative Incidence Ratio <sub>IGRA</sub> = NA				Cumulative Inc					
Incidence density rate <sub>IGRA+</sub> = NA				Incidence densi					
Incidence density				Incidence densi	_				
Incidence density				Incidence densi	•				
Other reported m				Other reported					
Other reported in			n hetwa	een tests (IGRA		1 1/1 1			
Ratio of cumulat				ten tests (IGRA	<b>V3.</b> 101)				
Ratio of incidence									
Other reported m			17.1						
_			results a	and levels of TB	exposure (i	f applicabl	(e)		
	RA (QFT-G				TST (≥				
10	Exposur		Total		Exposur		Total		
	High/Yes	Low/No	10141		High/Yes	Low/No	10141		
IGRA +	46	32	78	TST +	42	29	71		
IGRA -	108	81	189	TST -	99	81	180		
Indeterminate	0	0	0	Indeterminate	0	0	0		
Total	154	113	267	Total	141	110	251		
10001	10.			nance paramete		110			
	IGRA		P		TST				
<b>Exposure to ind</b>	ex case duri	ing the day	v (see	Exposure to index case during the day (see 2 x 2					
2 x 2 above)		0		<b>above)</b> Sensitivity = $42/141 = 29.79\%$ (95% CI:					
Sensitivity = 46/	154 = 29.879	% (95% CI	: 23.2,	22.86, 37.79)					
37.52)		`		,					
<b>Exposure to ind</b>	ex case duri	ing the day	y (see	Exposure to index case during the day (see 2 x 2					
2 x 2 above)				<b>above)</b> Specificity = 81/110 = 73.64% (95% CI:					
Specificity = 81/	113 = 71.689	% (95% CI	:	64.71, 80.97)					
62.77, 79.17)									
<b>Exposure to ind</b>	ex case duri	ing the day	y (see	Exposure to index case during the day (see 2 x 2					
2 x 2 above)	0.0=0/.0=0/	GY 45 00		<b>above)</b> PPV = 42/71 = 59.15% (95% CI: 47.54,					
PPV = 46/78 = 5	8.97% (95%	CI: 47.89,		69.83)					
69.22)							( 2 2		
Exposure to ind	ex case duri	ing the day	y (see	Exposure to in					
2 x 2 above)	42.960/ (05)	0/ CI. 2/ 0	1	above) NPV =	45.00% (95)	% CI: 37.9	1, 52.30)		
NPV = 81/189 = 49.99)	42.80% (93	% C1: 30.0	1,						
DOR (for T <sup>+</sup> calc	vulated) = no	t aalaulata	A	DOP (for T <sup>+</sup> as	laulatad) = :	not coloulat	ead.		
OR (crude; for T			u	DOR (for $T^+$ calculated) = not calculated					
Adult index case				OR (crude; for T <sup>+</sup> reported) =					
Smear-positive T			ın)	Adult index case type of TB diagnosis Smear-positive TB: 1.00 (reference group)					
Smear-negative,	,	_	1	Smear-negative, culture-positive TB: 0.17 (95% CI:					
(95% CI: 0.05, 0	-			0.05, 0.60)					
Clinical TB: 0.81		.45, 1.50)		Clinical TB: 0.4	46 (95% CI:	0.24, 0.89)	)		
Adult index case	smear grade	;		Adult index cas	se smear gra	de			
Negative: 1.00 (r		-		Negative: 1.00					
Scanty: 0.3 (95%	_	* /		Scanty: NR		1 /			
1+: 1.50 (95% C				1+: 2.81 (95%	CI: 1.20, 6.7	<b>'</b> 0)			
2+: 1.50 (95% C				2+: 2.90 (95%	,	/			
3+: 3.20 (95% C				,					
				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) =	OR (regression-based; reported) =
Adult index case type of TB diagnosis	Adult index case type of TB diagnosis
Smear-positive TB: 1.00 (reference group)	Smear-positive TB: 1.00 (reference group)
Smear-negative, culture-positive TB: 0.84	Smear-negative, culture-positive TB: 2.70 (95% CI:
(95% CI: 0.09, 7.80)	0.56, 13.0)
Clinical TB: 3.90 (95% CI: 0.67, 23.5)	Clinical TB: NR
Adult index case smear grade	Adult index case smear grade
Negative: 1.00 (reference group)	Negative: 1.00 (reference group)
Scanty: NR	Scanty: NR
1+: 5.50 (95% CI: 0.89, 34.70)	1+: 7.90 (95% CI: 1.50, 41.00)
2+: 8.70 (95% CI: 1.20, 62.00)	2+: 15.70 (95% CI: 2.60, 92.0)
3+: 11.40 (95% CI: 1.80, 72.00)	3+: 11.70 (95% CI: 2.20, 62.00)
Exposure to index case during the day	Exposure to index case during the day
Minority of day (< 6 h) – 1.00 reference group	Minority of day (< 6 h) – 1.00 reference group
Majority of day (> 7 h): 1.30 (95% CI: 0.69,	Majority of day (> 7 h): 1.10 (95% CI: 0.58, 2.10)
2.30)	List of covariates: 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) = 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	Total		i 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	257 5		Total	243	4	247			
		Tes	t perfor	mance narameter	<u> </u>					

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

	e = NR	<u> </u>	Other reported measure = NR			
- C		discordance (if applicable)	tua and/an aanditian			
Total sample	atinea by 181 cut-oii	value, BCG vaccination star	tus, and/or condition			
Total sample	TCT + (>5mm)	TST -	Total			
ICD A (OET CIT) +	TST + (≥5mm)		75			
IGRA (QFT-GIT) +	56	19				
IGRA -	12	149	161			
Indeterminate	3	15	18			
Total	71	183	254			
Description						
		CG or condition – specify): to	otal			
$TST + threshold: \ge 5m$	m					
Parameters						
Kappa = $0.68 (95\% C)$	I: 0.56, 0.81) indetermin	ate excluded				
% concordance = 205/	236 = 86.86% (95% CI)	81.96, 90.59); indeterminate	e excluded			
		0.41, 18.04) indeterminate exc				
Stratification (≥10mr						
	TST +(≥10mm)	TST -	Total			
IGRA +	48	27	75			
IGRA -	7	154	161			
Indeterminate	2	16	18			
Total	57	197	254			
Description	31	197	234			
	total if atmotified by D	CC on condition and if it is	2421			
		CG or condition – specify): to	otai			
TST + threshold: ≥10r	<u>nm</u>					
Parameters Oct (0.50/ G)	T 0.51 0.50					
Kappa = $0.64 (95\% C)$	· /					
		80 54 89 5)				
% concordance = 202/						
% discordance = 34/23	36 = 14.41% (95% CI: 1					
	36 = 14.41% (95% CI: 1 y group 2):	0.5, 19.46)				
% discordance = 34/23 Stratification (specify	36 = 14.41% (95% CI: 1		Total			
% discordance = 34/23	36 = 14.41% (95% CI: 1 y group 2):	0.5, 19.46)	Total NR			
% discordance = 34/23 Stratification (specify	36 = 14.41% (95% CI: 1 y <b>group 2):</b> TST +	0.5, 19.46)				
% discordance = 34/23 <b>Stratification (specify</b> IGRA +	36 = 14.41% (95% CI: 1 y group 2): TST + NR	0.5, 19.46)  TST -  NR	NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA -	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR	0.5, 19.46)  TST -  NR  NR	NR NR			
% discordance = 34/23 Stratification (specify  IGRA +  IGRA -  Indeterminate  Total	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR	0.5, 19.46)  TST -  NR  NR  NR	NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total  Description	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR	0.5, 19.46)  TST -  NR  NR  NR  NR  NR	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR	0.5, 19.46)  TST -  NR  NR  NR	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate  Total  Description  Sample definition (e.g  TST + threshold: NR	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR	0.5, 19.46)  TST -  NR  NR  NR  NR  NR	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate  Total Description Sample definition (e.g TST + threshold: NR Parameters	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR	0.5, 19.46)  TST -  NR  NR  NR  NR  NR	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR	0.5, 19.46)  TST -  NR  NR  NR  NR  NR	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR	0.5, 19.46)  TST -  NR  NR  NR  NR  NR	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR NR	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N	NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR NR NR	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N	NR NR NR NR NR			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if	36 = 14.41% (95% CI: 1 y group 2):  TST +  NR  NR  NR  NR  NR  Oth  Adverse eve	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N	NR NR NR NR NR Health related quality			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR	36 = 14.41% (95% CI: 1 y group 2): TST + NR NR NR NR NR NR	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N	NR NR NR NR NR Health related quality of life mean score (SD)			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate  Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)	36 = 14.41% (95% CI: 1 y group 2):  TST +  NR  NR  NR  NR  NR  Oth  Adverse eve	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N	NR NR NR NR NR VR VR VR VR VS			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate  Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)  IGRA:	36 = 14.41% (95% CI: 1 y group 2):  TST +  NR  NR  NR  NR  NR  Oth  Adverse eve	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N  ner outcomes  nts n/N (%)	NR N			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total  Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)  IGRA: TST:	36 = 14.41% (95% CI: 1 y group 2):  TST +  NR  NR  NR  NR  NR  Oth  Adverse eve	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N  her outcomes  nts n/N (%)	NR N			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate  Total Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)  IGRA:	36 = 14.41% (95% CI: 1 y group 2):  TST +  NR  NR  NR  NR  NR  Otl  Adverse eve (specify)	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N  mer outcomes  nts n/N (%)  NR  NR  NR	NR N			
% discordance = 34/23 Stratification (specify  IGRA + IGRA - Indeterminate Total  Description Sample definition (e.g TST + threshold: NR Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)  IGRA: TST:	36 = 14.41% (95% CI: 1 y group 2):  TST +  NR  NR  NR  NR  NR  Otl  Adverse eve (specify)	O.5, 19.46)  TST -  NR  NR  NR  NR  CG or condition – specify): N  her outcomes  nts n/N (%)	NR N			

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  $\geq 2$  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<sup>148</sup>

**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):

	Dofin	ition of an		***	mi assa da Cimir	i.a.a. (a.	- h -1	<u> </u>
Non avnogad	Delin	NR	posure group	– vai	rious delimi	nons (se	ee below	)
Non-exposed	o oifu).		to gavenoo					
Exposed 1 (spe			to source					
	Exposed 2 (specify): Hours/day exposure Exposed 3 (specify): Cohabitants, n							
Exposed 4 (spe	ecity):	Rooms, n						
Tests	A	141				4 . CC		0.41
			odology, tim	ıng				Other information
	10	manufa	surement,	values/thresholds Definition of test+			Information	
IGRA	OventiEI		d In-Tube assa		QFT-GIT			
(QFT-GIT)			EN Inc., Valer		considered			
(Qr 1-Gii)	CA, USA		En inc., valei	icia,	if the inter	-		
	CA, USF	1)			response t	-	•	
	Fach par	ticinant ha	d 73 ml of blo	od	minus the		_	
		nich was p		ou	control wa	_		
		-	nufacturer's		and also >			
	instruction		inaractarer 5		negative c			
					negative i		criteria	
					were not i			
					indetermin	nate if e	ither	
					the negati	ve cont	rol had	
					a result of	>8 IU/	ml or	
					the positive control had			
					a result of			
TST(≥5mm)	TST (5 to	ıberculin u	nits purified	An induration of ≥5 mm				
	protein d	erivative [	PPD]; Tuberso	1,	was considered positive,			
	Sanofi Pa	asteur Lt, 7	Toronto, ON,	as every subject was a				
			med using the		close cont			
			An intradermal		culture-pr	oven ca		
		of 0.1 ml						
			volar surface					
			ansverse diamo	eter				
		tion was re						
	L		ministration					
Association be			nd incidence	of ac	tive TB (if			
	IGF			TST (>5mm)				·
	<b>I</b>	ence of	Total				ence of	Total
		ve TB					e TB	
¥65 :	Yes	No	37.		mam .	Yes	No	N
IGRA +	NA	NA	NA		TST +	NA	NA	NA
IGRA -	NA	NA	NA		TST -	NA	NA	NA
indeterminate		NA	NA	ınde	eterminate	NA	NA	NA
Total	NA	NA	NA S		Total	NA	NA	NA
	¥.~-		Test perform	ance	parameter	S	TDCTD.	
G	IGF	KA		C	.,,	A	TST	
Sensitivity = N					$\frac{\text{sitivity} = N}{N}$			
Specificity = N	NΑ			_	$\frac{\text{cificity} = N}{N}$	A		
PPV= NA					r = NA			
NPV= NA	• 1	NT A			V = NA	' 1	3.7	<u> </u>
Cumulative Inc					nulative Inc			
Cumulative In			N.T. A		nulative Inc			
Cumulative In			NA		nulative Inc			
Incidence dens	ity rate IGE	A+ = NA		Incidence density rate <sub>TST+</sub> = NA				

Incidence densit				Incidence dens					
Incidence density rate ratio <sub>IGRA</sub> = NA				Incidence dens					
Other reported measure <sub>IGRA</sub> = NA				Other reported measure $_{TST} = NA$					
				een tests (IGRA v	s. TST)				
Ratio of cumula	tive incidenc	e ratios = N	NΑ						
Ratio of inciden	ce density ra	te ratios = 1	NA						
Other reported n	neasure = NA	4							
Aga	osistian hat	xxxoon tost	mognilta a	and lavals of TD o	vnosumo (id	f annliaghla)			
Ass	IGRA-GIT		results a	nd levels of TB e					
	Exposus		Total	TST≥5mm  Exposure level Tota					
	High/Yes	Low/No	Total	-		Total			
IGRA +	NA	NA	NA	TST +	High/Ye NA	NA	NA		
IGRA -	NA NA	NA NA	<del>                                     </del>	TST -	NA NA		NA NA		
indeterminate	ł		NA			NA			
	NA	NA	NA	indeterminate	NA NA	NA	NA		
Total	NA	NA Togé	NA	Total	NA	NA	NA		
	IGRA	Test	periori	nance parameter	TS	r			
Sensitivity = NR				Congitivity - ND		I			
				Sensitivity = NR					
Specificity = NR $PPV = NR$				Specificity = NR PPV = NR					
NPV = NR				NPV = NR					
	1-4-4) — NI	D			1-41\ <b>\</b>	ID.			
DOR (for T <sup>+</sup> cal				DOR (for T <sup>+</sup> calc					
OR (crude; for T				OR (crude; for T <sup>+</sup> reported) = NR					
OR (regression-			1 45)	OR (regression-based; reported) =					
Exposure to sour				Exposure to source: NR (p=NR; NS)					
Hours/day expos	,			Hours/day exposure: NR (p=NR; NS) # of cohabitants: NR (p=NR; NS)					
# of conaoriants: # of rooms: 1.12	*		13)	# of conabitants. NK (p=NK, NS)  # of rooms: NR (p=NR; NS)					
# 01 1001118. 1.12	. (93 /0 CI U.)	77, 1.01)		# 01 100IIIS. INK (p=INK, INS)					
List of covariate	es age sex l	istory of		List of covariates: age, sex, history of					
BCG vaccination				BCG vaccination, intensity of exposure, exposure					
exposure time of				time of the contacts to a source case, exposure to a					
exposure to a dr				drug-susceptible case, and exposure to a drug-					
exposure to a dr				resistant case					
Other reported n				Other reported measure = NR					
•		Compariso	n betwe	een tests (IGRA v	s. TST)				
Ratio of DORs (	for T calcul	ated) = NA							
Ratio of OR (cru									
Ratio of ORs (re	gression-bas	sed; reporte	d) = NA						
Other reported n	neasure = NA	4							
	Associatio	n between	test res	ults and BCG sta	tus (if app	licable)			
	IGRA				T	ST			
	BCG s	tatus	Total			CG 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		
Total	NA	NA	NA	Total	NA	NA	NA		
		Test	perfori	nance parameter					
	IGRA					ST			
DOR (for T <sup>+</sup> cal				DOR (for T+ calculated) <sub>TST</sub> = NA					
OR (crude; for T	reported) =	- NA		OR (crude; fo	or T+ repor	ted) = NA			

OR (regression-based; reported) <sub>IGRA</sub> = NA	OR (regression-based; reported) <sub>TST</sub> = NA			
List of covariates: NA	List of covariates: NA			
Other reported measure = NA	Other reported measure = NA			
Between-test agreement, concordance, and dis	cordance (if applicable)			
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition				
Total sample				

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

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)

Structure (Specify Struct 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)

Structured (Specify Structure)								
	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<sup>108</sup>

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 (indetermina te)	Total N (test results available)
IGRA (QFT-GIT):	Unclear	2669	2562	13	5244
<b>TST</b> (≥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 (speci	fy):	Current or prior TB household contact							
Exposed 2 (speci		BCG sca	-						
Exposed 3 (speci			orted as being	given					
Exposed 4 (speci		NA		<u> </u>					
Tests	<i>v /</i>								
Assay used, methodology, timi test measurement, manufact							Other informatio n		
IGRA	-	QuantiFERON- TB Gold In-Tube				sult was			
		GIT, Cellestis, Carnegie, Victoria Australia)				ive if th			NA
TST			n either forearn	a naina		$was \ge 0$ sult was			
131	2 tubero Institut, Induration	ulin units o Copenhage on at the TS	of RT23 (Staten en, Denmark). ST site was read	s Serum d 48-96	1	ive if in			NA
			uler or a caliper	; by					
		ersonnel							
Association betw			d incidence of	active TI	3 (if ap	plicab			
	IGI		T .				TST		
	Incidence of active TB		Total			Incidence of active TB		_	Total
TOP 1	Yes	No	37.1	mam		Yes	No		
IGRA +	NA	NA	NA	TST		NA	NA		NA
IGRA -	NA	NA	NA	TST		NA	NA		NA
Indeterminate	NA	NA	NA	Indeterr e		NA	NA		NA
Total	NA	NA	NA	Tota		NA	NA		NA
			est performan	ce param	eters				
	IGI	RA					TST		
Sensitivity = $NA$				Sensitiv					
Specificity = NA				Specific		NA			
PPV = NA				PPV = 1					
NPV = NA		27.4		NPV = 1		• •		37.4	
Cumulative Incid	lence <sub>IGRA</sub>	$_{+} = NA$		Cumula	tive In	cidence	TST+ =	NA	
Cumulative Incid			Λ	Cumula					NT <b>A</b>
Cumulative Incid			A	Cumula					NA
Incidence density rate $_{IGRA+} = NA$ Incidence density rate $_{IGRA-} = NA$			Incidend						
Incidence density				Incidence density rate $_{TST-} = NA$ Incidence density rate ratio $_{TST} = NA$				Γ Δ	
Other reported m			1	Other re		_			Λ
onici reported ili	casure [G]		rison between t				TST -	11/1	
Ratio of cumulati	ive incide			coto (IGI	VJ.	131)			
Ratio of cumulati									
Other reported m			1111						
			and levels of T	_	ure (cı	ırrent	or pric	or TB	household
Ţ	GRA (O	FT-GIT)	Conte			TS	T≥ 5m	m	
		are level	Total				sure le		Total
ļ	Yes	No	2			Yes		lo	
IGRA +	888	1781	2669	TST +		950	_	044	2894
IGRA -	444	2118	2562	TST -		382	_	68	2350
Indeterminate	0	13	13	Indeterr	ninat	0	_	0	0

			(excluded)	e			
Total	1332	3912	5244	Total	1332	3912	5244
10441	1332			ce parameters	1332	3712	3211
	IGI		po		Т	ST	
Sensitivity = 888			% CI (64.09,	Sensitivity = 9			, 95% CI
69.15)				(68.83, 73.69)			,
Specificity = 2118/3899 = 54.32%, 95% CI (52.75,				Specificity = 1	968/391	2 = 50.31	%, 95% CI
55.88)		ŕ	` `	(48.74, 51.87)			
PPV = 888/2669	PPV = 888/2669 = 33.27%, 95% CI (31.51, 35.08)			PPV = 950/289	94 = 32.8	33%, 95%	CI (31.14,
				34.56)			
NPV = 2118/256	52 = 82.67	7%, 95% C	I (81.16,	NPV = 1968/2	350 = 83	.74%, 959	% CI (82.2,
84.09)			•	85.18)			•
DOR (for T <sup>+</sup> calc	culated) =	2.38, 95%	CI (2.09,	DOR (for T <sup>+</sup> ca	alculated	(1) = 2.52, 9	95% CI (2.20,
2.71)				2.88)			
OR (crude; for $T^+$ reported) = 2.40, 95% CI (2.11, OR (crude; for $T^+$ reported) = 2.52, 95% CI							
2.74)				(2.20, 2.88)			
OR (regression-based; reported) = $1.90$ , $95\%$ CI OR (regression-based; reported) = $2.00$ ( $1.70$ ,						= 2.00 (1.70,	
(1.70, 2.20)				2.30)			
List of covariates				List of covaria			
Other reported m	neasure =			Other reported		e = 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)						
]		FT-GIT)			1	≥ 5mm)	I
		CG status	Total			status	Total
	Ye		+		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		3554	Total	2064	1490	3554
			est performan	ce parameters			
	IGI					ST	
DOR (for T <sup>+</sup> calc	culated) <sub>IG</sub>	RA = NA	=0/ OY /0 0 5	DOR (for T+ c			
OR (crude; for T	reported	1) = 0.99, 9	5% CI (0.86,	OR (crude; for	1+ repo	rted) = 1.	16, 95% CI
1.12)	1	4 - 1\	– NID	(1.0, 1.33)	. 1 1	1	_ NID
OR (regression-b		orted) <sub>IGRA</sub>	= NK	OR (regression		reported)	$_{\text{LSL}} = NK$
List of covariates		ND		List of covaria		ND	
Other reported m			and dis-	Other reported		: - NK	
Between-test ag						e and/or	condition
This table may		ieu by 181	cut-on value	, beg vaccinati	on statu	s, and/or	condition
<b>Total sample</b> ≥ 5		то	T +	TST -			Total
ICD A ±		TST +			•		Total NR
IGRA +		NR NR		NR NR			NR NR
-							
Total	IndeterminateNRNRNRTotalNRNRNR						
<b>Description</b>		ľ	VIX	NR			NR
Sample definition	n (e.g. to	tal if atrati	fied by BCC a	r condition and	oify): tot	a1	
TST + threshold:		ıaı, 11 SHALL	ned by BCG 0	condition – spec	.11y <i>j</i> . toti	a1	
	. <u> </u>						
Parameters							

Kappa = 0.70, 95% CI: 0	0.68, 0.71		
% concordance = 84.8%	(95% CI NR)		
% discordance = NR			
<b>Total sample (≥ 10mm)</b>			
		-~-	

Total sample (2 Tomin)								
	TST +	TST -	Total					
IGRA +	NR	NR	NR					
IGRA -	NR	NR	NR					
Indeterminate	NR	NR	NR					
Total	NR	NR	NR					

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)

10tal sample (2 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):

 $\overline{TST}$  + threshold:  $\geq 15$ mm

#### **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 Adverse events n/N (%) Health related quality applicable) of life mean score (SD) (specify) (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<sup>150</sup>

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):  $94.8 \pm 51.9$  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<sup>+</sup>/QFT<sup>-</sup> results); isoniazid (n=8 children with TST<sup>+</sup>/QFT<sup>+</sup> results but no symptoms – assumed with LTBI); isoniazid, rifampicin and pyrazinamide (n=4 children with TST<sup>+</sup>/QFT<sup>+</sup> results with symptoms –with TB)

	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
		alid results for both			
Levels/groups of	or exposure	to TB in increasing	of exposure grou		
Non-exposed		NA	or exposure grou	<u>p</u>	
Exposed 1 (spec	oify).	NA			
Exposed 1 (spec		NA			
Exposed 2 (spec		NA			
Exposed 4 (spec		NA			
Tests		1471			
1 0000	Assav II	sed, methodology,	Cut-off value	s/thresholds	Other information
		ning for test	Definition		
		easurement,			
	I .	anufacturer			
IGRA (QFT-	Peripheral	blood samples	A positive resu	lt was defined	
GIT)	_	n in the laboratory,	if the difference		
	where the	y were processed by	levels between		
		ysicians and	and negative co		
		l according to	greater than or		
		irer's instructions.	0.35 IU/mL and		
		child, total 3 mL	than 25% of the		
		od was taken, then	Also for determ		
	blood was collected		nil control mus	t  be < 8.0	
	in three special tubes: gray-		IU/mL		
	(negative control, "nil"), red- (test tube), and purple-				
		ive control;			
		oated) tubes. Test			
	_	ecially designed			
		collection which is			
		th M. tuberculosis-			
	specific an	ntigens (ESAT-6,			
		nd a portion of TB			
	7.7). Once	e blood was			
	I .	it is essential to			
		dequate shaking for			
		o dissolve. They			
		bated at 37°C for 16			
		rs and centrifugation			
		for 15 minutes, then			
		as separated. The FIFN-γ was			
	I .	by using the QFT			
	ELISA	by using the QFT			
TST(≥15mm)		en underwent a TST	When interpret	ing a TST	-
- ~ 1 (=10 mm)	-	of purified protein	result, the wide	•	
		, according to	induration, not		
		al Mantoux method	was measured i	•	
			after 72 hours b		
			physician or nu	•	
			was considered		
			an induration w		
			regardless of B		
			vaccination sca	r numbers	

Association between	en test resu	lts and ii	icidence of	f active TB (if ap	plicable)				
	IGRA-GI			TST (≥15mm)					
	Inciden		Total		Incidence of		1	Total	
	active	TB			activ	e TB			
	Yes	No			Yes	No	1		
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								
	IGRA-GI	Γ			TST	≥15mm	l		
Sensitivity = NA	Sensitivity = NA				NΑ				
Specificity = 69/69	= 100% (95	5% CI: N	R)	Specificity = (	0/69 = 0.0	)% (95%	6 CI: NI	R)	
PPV= NA				PPV = 0/69 = 0	.0% (95%	6 CI: NI	R)		
NPV = 69/69 = 1009	% (95% CI:	NR)		NPV = NA					
Cumulative Inciden	$ce_{IGRA+} = N$	NΑ		Cumulative In CI: NR)	cidence 1	$r_{ST+} = 0/$	69 = 0.0	)% (95%	
Cumulative Inciden	ce = 0	$\frac{1}{160} = 0.09$	0/2 (05%	Cumulative In	cidence -	= N	۸		
CI: NR)	CC IGRA- U	0.0	70 (2270	Cumulative in	cidence 1	ST- 142	1		
Cumulative Inciden	ce Ratio rer	A = NA		Cumulative In	cidence I	Ratio rea	= NA		
Incidence density ra				Incidence dens					
Incidence density ra				Incidence dens					
Incidence density ra				Incidence dens					
Other reported mean									
other reported mea			n hetweei		Other reported measure <sub>TST</sub> = NR  tests (IGRA vs. TST)				
Ratio of cumulative				reses (research	101)				
Ratio of incidence of									
Other reported mea		141105 1	11						
		een test	results and	d levels of TB ex	posure (i	f applic	able)		
11000	IGRA					ST	<i></i>		
		ire level	Total			sure lev	ve1	Total	
	High/Yes				High/Y		w/No	10001	
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	
	·			nce parameters					
	IGRA		1		Т	ST			
Sensitivity = NA				Sensitivity = NA					
Specificity = NA				Specificity = NA					
PPV= NA				PPV= NA					
NPV= NA				NPV= NA					
DOR (for T <sup>+</sup> calcula	ated) = NA			$\frac{1}{1}$ DOR (for T <sup>+</sup> calculated) = NA					
OR (crude; for T <sup>+</sup> re		JA		OR (crude; for T <sup>+</sup> reported) = NA					
OR (regression-base				OR (regression-based; reported) = NA					
List of covariates: N		,		List of covariates: NA					
				Other reported i		= NA			
	Comparison between tests (IGRA vs. TST)								
Ratio of DORs (for				(					
Ratio of OR (crude; for $T^+$ reported) = NA									
Ratio of ORs (regre									
Other reported mean		, p							
•		between	test result	ts and BCG statu	ıs (if ann	licable)			
Association between test results and BCG status (if applicable)									

IGRA			TST					
		BCG status Total			3 status	Total		
	Yes	No			Yes	No	1	
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	
10111	1171			e parameters	1171	11/11	1171	
	IGRA	тезе р	CI IOI Munes	parameters	TS	T		
DOR (for T <sup>+</sup> calcula		Ā		DOR (for T+ ca				
OR (crude; for T <sup>+</sup> re				OR (crude; for				
OR (regression-base				OR (regression			= N A	
List of covariates: N		IGRA 1111		List of covariat		ported) 151	1111	
Other reported mea				Other reported		= NA		
Between-test agree		ordance a	nd discords			1121		
This table may be						nd/or cond	ition	
Total sample		101 000	011 (0100) 2			114701 00114	101011	
1 otal sample		TST +		TST -			Total	
IGRA +		NA		NA			NA	
IGRA -		NA		NA			NA	
indeterminate		NA		NA			NA	
Total		NA		NA NA			NA	
Description		11/11		1171			1121	
Sample definition (	e g total if	stratified b	y BCG or co	ondition – specify	z)· ΝΔ			
TST + threshold: N		stratifica t	by BCG of C	ondition – specify	y). INA			
Parameters	A							
Kappa = NA % concordance = N	T A							
% discordance = N								
		`						
Stratification (spec	eny group 1	TST +		TST -			Total	
IGRA +		NA		NA			NA	
IGRA -		NA NA		NA NA			NA NA	
indeterminate		NA NA		NA NA			NA	
Total		NA		NA			NA	
Description	4 4 1 °C	4 4°C° 11	DCC	1:4: :C	)			
Sample definition (		stratified b	y BCG or co	ondition – specify	/): NA			
TST + threshold: N	A							
Parameters								
Kappa = NA	r .							
$\frac{\% \text{ concordance} = N}{}$								
% discordance = NA								
Stratification (spec	cify group 2		1				m . 1	
		TST +		TST -			Total	
IGRA +		NA		NA			NA	
IGRA -		NA		NA			NA	
indeterminate		NA		NA			NA	
Total NA NA NA					NA			
Description								
0 1 1 0 4 6		1 1	TY DCC an a	andition anosifi	7). NIA			
Sample definition (		stratified b	by BCG of co	onamon – specity	y). INA			
TST + threshold: N		stratified b	BCG or co	ondition – specify	y). INA			
		stratified b	by BCG or co	ondition – specify	y). 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<sup>109</sup>

**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  $\geq 10$ mm

**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):  $29 \pm 16$  months

Women (n [%]): 57 [40.1] Race/ethnicity (n [%]): NR Geographic origin (n[%]): NR BCG vaccination (n [%]): 142

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):							
		T .		exposure group			
Non-exposed						-	sure time or < 40
				ned period of infe			
Exposed 1 (s)	pecify):						egate exposure to
			t with active TI	$3 \ge 40$ hours in clo	sed roc	oms	
Exposed 2 (s)		NA					
Exposed 3 (s)		NA					
Exposed 4 (s)	pecify):	NA					
Tests				T			
			thodology,	Cut-off		Othe	r information
			easurement,	values/thresh			
		nanufacti		Definition of t		71.1	
IGRA	QFT-GIT	*		$\geq 0.35 \text{ IU/mL}$ as			imples for QFT-
(QFT-GIT)	Chadstone	, Australia	a)	recommended b	y the		e drawn under
				manufacturer.			ized condition in
						-	ital at the same
							ST. The test was ed indeterminate
							lue of the
							control well was
						-	0.5 IU/mL,
							il negative control
		was more than 8 IU/L					
TST≥ 10	Two tuber	culin units	s of			NA	
mm	standardiz	ed purified	d protein				
			Tuberculin				
	PPD RT 2	3, Statens	Serum				
	Institute, C	Copenhage	en, Denmark)				
	injected in	to the vol	ar aspect of				
	the forearr						
			neasured by a				
			orker 68 to				
	72 hours la						
Association I			and incidence	of active TB (if a			
	IGI			TST			
		lence of	Total			ence of	Total
		ive TB				ve TB	
ICDA	Yes	No	NT A	TOT	Yes	No	NT A
IGRA +	NA NA	NA NA	NA NA	TST +	NA	NA NA	NA NA
IGRA -	NA NA	NA NA	NA NA	TST -	NA	NA NA	NA NA
Indetermina		NA NA	NA NA	Indeterminate	NA	NA NA	NA NA
Total	NA	NA	NA Test newfermer	Total	NA	NA	NA
	ICI		rest performa	ance parameters		тст	
Consitivity	IGF	AA		Congitivity - NI		TST	
Sensitivity =				Sensitivity = NA Specificity = NA			
Specificity = NA				$\begin{array}{c} Specificity - NA \\ PPV = NA \end{array}$	1		
PPV = NA				t			
NPV = NA	noidonas	_ NT A		NPV = NA	idanaa	NT A	
Cumulative In				Cumulative Inci			
Cumulative In			NI A	Cumulative Inci			- NI A
Cumulative In			INA	Cumulative Inci			- I <b>N</b> A
Incidence density rate $_{IGRA^{+}} = NA$			Incidence density rate $_{TST+} = NA$				

Y 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				Incidence density rate — NA				
	Incidence density rate <sub>IGRA-</sub> = NA Incidence density rate ratio <sub>IGRA</sub> = NA				Incidence density rate <sub>TST</sub> . = NA			
			Α	Incidence density rate ratio <sub>TST</sub> = NA				
Other reported me	easure IG			Other reported measure <sub>TST</sub> = NA en tests (IGRA vs. TST)				
D-4: C1-4:-				en tests (IGRA v	<b>S. 151</b> )			
Ratio of cumulativ								
Ratio of incidence			s = NA					
Other reported me								
			est results ar	d levels of TB ex			(1)	
IGI	RA (QF				TST≥ 1			
		ire level	Total		Exposu		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	Indeterminate	0	0	0	
			(excluded)					
Total	87	54	141	Total	87	55	142	
			Test perforn	nance parameter				
	IGR A	4			TS'	Γ		
Sensitivity = 17/8 29.08)	7 = 19.5	4%, 95%	(12.57,	Sensitivity = 23	/87 = 26.44	%, 95% (18	3.31, 36.56)	
Specificity = 53/54 = 98.15%, 95% (90.23, 99.67)			Specificity = 54	$\sqrt{55} = 98.18$	3%, 95% (90	).39, 99.68)		
PPV = 17/18 = 94	144% 9	5% (74.24	1 99 01)	PPV = 23/24 = 9	95 83% 95	% CI (79.76	5 99 26)	
NPV = 53/123 = 4				PPV = 23/24 = 95.83%, 95% CI (79.76, 99.26) NPV = 54/118 = 45.76%, 95% CI (37.05, 54.74)				
$\frac{\text{NI V} = 33/123 = 3}{\text{DOR (for T}^{+} \text{ calculation}}$				DOR (for T <sup>+</sup> calculated) = $19.41, 95\%$ CI (2.53,				
(1.66, 99.80)	uraicu) –	12.07, 9.	70 C1	148.40)				
OR (crude; for T <sup>+</sup>	rapartas	1) = 1.66	059/ CI	OR (crude; for $T^+$ reported) = 1.75, 95% CI (0.92,				
(0.92, 3.35) error	reported	1) – 1.00,	93/0 CI	3.35) error				
OR (regression-ba	and man	ortad) — N	J <b>D</b>	OR (regression-based; reported) = NR				
List of covariates:		ortea) – r	NK	List of covariate		nied) – NK		
Other reported me		ND		Other reported measure = NR				
Other reported inc	zasure –		wisan hatrya			VIX.		
D. C. CDOD (C	Tr <sup>+</sup> 1			en tests (IGRA v	<b>S. 151</b> )			
Ratio of DORs (fo				1: 0.15, 2.89)				
Ratio of OR (crud								
Ratio of ORs (reg			orted) = NA					
Other reported me								
			een test resu	lts and BCG sta				
	IGRA (					10 mm)		
	-	G status	Total			status	Total	
	Yes	No			Yes	No		
IGRA +	NR	NR	_	TST +	NR	NR	NR	
IGRA -	NR	NR	NR	TST -	NR	NR	NR	
Indeterminate	NR	NR	NR	Indeterminat		NR	NR	
Total	NR	NR	NR	Total	NR	NR	NR	
		,	Test perforn	nance parameter	'S			
		OT/QFT			TST (>	>5 mm)		
DOR (for T <sup>+</sup> calcu			NR	DOR TST (for	T+ calcula	ted) = NR		
OR (crude; for T <sup>+</sup>	reported	l) = NR		OR (crude; f	or T+ repor	ted) = NR		
OR (regression-based; reported) $_{OFT} = NR$			OR (regression-based; reported) $_{TST} = NR$					
OR (regression-ba				List of covar		, , , , ,		
` •	List of covariates: NR							
Other reported me	easure =	NR		Other reported measure = NR				
Between-test agr			ance, and dis					
Detricen test agreement, concordance, and assertance (if appreciate)								

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		

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  $\leq$  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

#### Study details

First author surname year of publication: Perez-Porcuna 2014<sup>151</sup>

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

rumber of patients tester	1 tumber of putients 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						
<b>TST</b> : ≥ 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 co	ontinuous covariate						
		um tuberculosis contact (MTC	c) score: 0-15					
Non-exposed	NA							
Exposed (specify):	infectivity of the index c	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	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,	result  ≥ 10mm positivity threshold  according to the protocols of the WHO	Experienced laboratory technicians who were unaware of the data of the study subjects					

						1			
		Copenha		$\geq$ 5-9 mm weak re					
			a) and read 72	$\geq$ 10mm strong re	action				
		hours the			**`				
Association bety			d incidence of	active TB (if appli					
	IGF				TST				
	Incide		Total		Inciden		Γotal		
	active				active				
	Yes	No			Yes	No			
IGRA +	NA	NA	NA	TST +	NA		NA		
IGRA -	NA	NA	NA	TST -	NA		NA		
indeterminate	NA	NA	NA	indeterminate	NA	NA	NA		
Total	NA	NA	NA	Total	NA	NA	NA		
		T	est performan	ce parameters					
	IGF	RA			TST				
Sensitivity = NA	•			Sensitivity = NA	1				
Specificity = NA				Specificity = NA	Λ				
PPV = NA				PPV = NA					
NPV = NA				NPV = NA					
Cumulative Incid	lence <sub>IGRA+</sub>	. = NA		Cumulative Inci	dence TST+	= NA			
Cumulative Incid				Cumulative Inci					
Cumulative Incid			Ā	Cumulative Inci					
Incidence density				Incidence densit					
Incidence density				Incidence densit					
Incidence density			A		Incidence density rate ratio <sub>TST</sub> = NA				
Other reported m				Other reported n					
	TOIC		rison between	tests (IGRA vs. TS		1			
Ratio of cumulat	ive incider			(					
Ratio of incidence									
Other reported m									
			est results and	levels of TB exposi	ıre (if anı	nlicable)			
	IGRA (QF		est results and		ΓST (≥10)				
		e level (#	of Total			e level (# of	Total		
	-	of exposu				of exposure	Total		
		ndex case				ndex case)			
		s Low/				s Low/No			
IGRA +	NR	NF		TST +	NR	NR	NR		
IGRA -	NR	NR	+	TST -	NR	NR	NR		
indeterminate	NR	NR		indeterminate	NR	NR	NR		
Total	NR	NR		Total	NR	NR	NR		
Total	IVIX			ce parameters	IVIX	INIX	IVIX		
	ICD		est per for man		тст				
Canaitivity - NA	IGR	A		Consitivity - NA	TST				
Sensitivity = NA				Sensitivity = NA					
Specificity = NA	<u> </u>			Specificity = NA					
PPV = NA				PPV = NA					
NPV = NA	1 . 4\ =	T 4		NPV = NA	4 , 45 .	N.T. A			
DOR (for T <sup>+</sup> calc			0.004	DOR (for T <sup>+</sup> calc			201		
OR (crude; for T				OR (crude; for T					
OR is associated		ınıt ıncrea	ise in # of	OR is associated	with one i	ınıt ıncrease	ın # of		
exposure months		. 4\	D ( 0.55=)	exposure months		. 45	(O.F.C.) ==		
OR (regression-b				OR (regression-b		orted) = 1.15	(95% CI		
OR is associated		ınıt increa	ise in # of	1.04, 1.27; $p = 0$ .		•, •	. ,, ,		
							in # at		
exposure months List of covariates				OR is associated exposure months	with one i	ınıt increase	111 # 01		

				List of covariate				
Other reported n				Other reported m		R		
			n between 1	tests (IGRA vs. TS	ST)			
Ratio of DORs (								
Ratio of OR (cru								
Ratio of ORs (re			l) = NA					
Other reported n								
Ass	ociation bety	ween test r	esults and l	levels of TB expos				
]	IGRA (QFT-	-GIT)			TST (≥10m	m)		
	Exposure le	evel (MTC	Total		Exposu	re level	Total	
	SCOI	re)			(MTC	score)		
	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	
			1	ce parameters		,		
	IGRA	1000			TST			
Sensitivity = NA				Sensitivity = NA				
Specificity = $NA$				Specificity = NA				
PPV= NA	· ·			PPV= NA	•			
NPV= NA				NPV= NA				
DOR (for T <sup>+</sup> cale	outleted) = N/	\		<u> </u>	aulatad) = N	ΓΛ		
OR (crude; for T			021)	DOR (for $T^+$ calculated) = NA OR (crude; for $T^+$ reported) = NR (p<0.001)				
OR (crude, for f				OR (crude, for f				
	with one uni	t merease i	II WITC	MTC score	with one un	iit iiiciease	111 #	
OR (regression-l	agadi rananta	(d) = 1 16 (	050/ CI	OR (regression-l	202041 2020	tod) = 1.20	(050/ CI	
		ea) – 1.16 (	93% CI			ieu) – 1.29	(93% CI	
1.01, 1.33; $p = 0$ OR is associated		t inaranga i	n MTC	1.08, 1.54; $p = 0$		it inaraasa	in MTC	
	with one uni	t ilicrease i	II WITC	OR is associated with one unit increase in MTC score				
score List of covariate	a. ND			List of covariates: NR				
						D		
Other reported n			b -4 4	Other reported m		K		
D. C. CDOD (			n between i	tests (IGRA vs. TS	51)			
Ratio of DORs (			<u> </u>					
Ratio of OR (cru				50/ CI 0.00 1.01)				
		ed; reported	(9) = 0.90	5% CI: 0.80, 1.01)				
Other reported n		• .		1000		`		
			test results	and BCG status (		-		
	IGRA (G		1		TST (10m)		m . 1	
	BCG st		Total			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	indeterminate	NR	NR	NR	
Total	107	9	116	Total	107	9	116	
		Test	performan	ce parameters				
	IGRA				TST			
DOR (for T <sup>+</sup> cale	culated) <sub>IGRA</sub> =	3.89	(95% CI:	DOR (for T+ cal	culated) <sub>TST</sub> =	= 1.85	(95%	
0.46, 32.33)				CI: 0.36, 9.36)				
OR (crude; for T	reported) =	NR		OR (crude; for T	+ reported)	= NR		
OR (regression-l			R	OR (regression-b			?	
List of covariate		,		List of covariates		,		
Other reported n		-		Other reported m		R		

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

	9 - 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):** 

	8 - 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

# 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

#### Study details

First author surname year of publication: Rutherford 2012a<sup>110</sup> and Rutherford 2012b<sup>111</sup> (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					
<b>TST</b> (≥10mm):	304	145	157	2	302					
Test 3 (specify):	NA	NA	NA	NA	NA					
Total N of patients with valid res	Total N of patients with valid results for both IGRA and TST: 288									

Levels/groups	of exposure	e to TB i	n increasi	ng order (if app	licable):				
gg				oup – Character		case smear	r positivity	r	
Non-exposed	-		Scanty an	d 1+					
Exposed 1 (spe	cify):		2+	<del></del>					
Exposed 2 (spe			3+						
Province (CP)		Defi	nition of e	xposure group -	Relationshi	p to child			
Non-exposed		Other	1 8 1		•				
Exposed 1 (spe	cify):		Aunt/uncl	e					
Exposed 2 (spe			Parent						
•		Definition	on of expo	osure group – Sl	eeping proxi	mity to ch	ild		
Non-exposed			Different						
Exposed 1 (specify): Same room									
Exposed 2 (spe	cify):		Same bed						
	De	efinition (	of exposu	re group – Time	spent with o	child (# hrs	s/day)		
Non-exposed			< 2						
Exposed 1 (spe			2 - 8						
Exposed 2 (spe	ecify):		> 8						
Tests									
	Assay	y used, n	used, methodology, timing for test measurement, manufacturer				Cut-o values/th lds Defin of tes	resho iition	Other informati on
IGRA (QFT- GIT)	ml was immutogen ar placed in a centrifuged was condu	mediately and antiger an incuba d and stor cted and	ml of venous blood was collected into a syringe; 1 tely transferred to each of the QFT-GIT tubes (nil, gen). The tubes were vigorously hand-shaken and abator within 3 h. Incubated samples were stored at 4°C for up to 1 month. The QFT-GIT assay nd interpreted according to the manufacturer's g specific software					1,11	
TST (≥10mm)	TST was p using two Biofarma®	erformed tuberculi , Bandu	by the stunction to the stunction of the	udy nurse followi purified protein o sia). Induration v rmed by the stud	lerivative (PF vas measured	D; RT23	An induration of ≥10 mm was considered positive		NA
Association be				nce of active TB		e)	positive		
		IGRA				-)	TST		
			ence of re TB	Total			of active B		Total
		Yes	No			Yes	No		
IGRA		NA	NA	NA	TST +	NA	NA		NA
IGRA		NA	NA	NA	TST -	NA	NA		NA
Indetermi	inate	NA	NA	NA	Indetermi nate	NA	NA		NA
Total		NA	NA	NA	Total	NA	NA		NA
			Tes	st performance j	parameters				
		IGRA					TST		
Sensitivity = N	A				Sensitivity	= NA			
Specificity = N	A				Specificity	= NA			
PPV = NA					PPV = NA				
NPV = NA					NPV = NA				
Cumulative Inc	idence IGRA+	= NA			Cumulative		$_{TST+} = NA$		
	Cumulative Incidence $_{IGRA^-} = NA$				Cumulative Incidence <sub>TST</sub> = NA				
Cumulative Inc			NΑ		Cumulative Incidence Ratio $_{TST} = NA$				
Incidence densi					Incidence d				

Incidence density					Incidence density rate $_{TST-} = NA$				
Incidence density rate ratio <sub>IGRA</sub> = NA					Incidence density rate ratio $_{TST} = NA$				
Other reported m	neasure	$_{\rm IGRA} = 1$			Other reported measure $_{TST} = NA$				
				ison between tes	sts (IGRA vs.	TST)			
Ratio of cumulat									
Ratio of incidence			ratios = NA						
Other reported m									
				st results and lev	els of TB exp				
			FT-GIT)				(≥10mm		1 .
			re level	Total			osure lev		Total
	cha		stics of TB				istics of T		
			se			Sme	ar positiv	ity	
	3+		ositivity			3+	2+	Canat	}
	3+	2+	Scanty/1+			3+	2+	Scant W/1+	
IGRA +	75	36	40	152	TST +	78	34	y/1+ 33	145
IGRA -	45	34	59	138	TST -	48	38	71	157
Indeterminate	NR	NR	NR	14 (excluded)	Indetermin	NR	NR	NR	2.
macterminate	IVIX	111	IVIX	14 (cxcluded)	ate	INIX	IVIX	IVIX	(excluded)
Total	120	70	99	290	Total	126	72	104	302
Total	120	70		est performance		120	12	101	302
		IGI		est periorimanee	parameters		TST		
Trend in ORs ac	ross the			e(p = 0.001)	Trend in OR	s across the		of expos	sure (p =
		8		<i>d</i> ,,,,	0.000)		8		d'
Scanty/1+: OR (	crude;	reported	d = 1.00  (refe)	rence group)	,				
2+: OR (crude; r					Scanty/1+: C	R (crude; 1	reported)	= 1.00 (r	eference
3+: OR (crude; r					group)		•		
	-				2+: OR (crude; reported) = 1.80 (95% CI: 0.89, 3.63)				
3+ vs. scanty/1+	-				3+: OR (crude; reported) = 3.35 (95% CI: 1.81, 6.21)				
Sensitivity = 75/									
Specificity = 59/					3+ vs. scanty/1+				
PPV = 75/115 =					Sensitivity =				
NPV = 59/104 =					Specificity =	71/104 = 6	58.27% (9	95% CI: :	58.81,
DOR (for T <sup>+</sup> calc					76.43)				
OR (crude; for T					PPV = 78/111 = 70.27% (95% CI: 61.21, 77.98) NPV = 71/119 = 59.66% (95% CI: 50.68, 68.04)				
OR (regression-b									
List of covariates			elationship to c	child, marital	DOR (for T <sup>+</sup> calculated) = 3.50 (95% CI: 2.02, 6.04) OR (crude; for T <sup>+</sup> reported) = 3.35 (95% CI: 1.81,				
status of househo						or I report	tea) = 3.3	5 (95% (	71: 1.81,
Other reported m	icasure	- NK			6.21) OR (regression	on based: "	enorted) -	- 2 02 (0	50/ CI:
					1.59, 5.39)	on-vaseu, r	eported)	- 4.93 (9	5 /0 CI.
					List of covar	iates: TR c	ase's rela	tionship	to child
					Other reporte			попашр	to child
			Compar	ison between tes			1111		
3+ vs. scanty/1+			Compai		(201411)	-~-,			
Ratio of DORs (		calculat	ed) = 0.70 (95)	% CI: 0.47, 1.04	)				
3+ vs. scanty/1+			, (**						
Ratio of OR (cru		T <sup>+</sup> repo	orted) = $0.73$ (	95% CI: 0.45, 1.1	7)				
3+ vs. scanty/1+		•		-					
Ratio of ORs (re		n-basec	d; reported) =	0.78(95% CI: 0.4	7, 1.28)				
Other reported m									
	As	sociatio	n between te	st results and lev	els of TB exp	osure (if a	pplicable	)	
	I		(FT-GIT)	_			T (≥10mi		
		Expos	ure level	Total		Exp	osure lev	el	Total

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

#### Test performance parameters

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)

**IGRA** 

#### 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<sup>+</sup> calculated) = 5.36 (95% CI: 2.52, 11.41) OR (crude; for T<sup>+</sup> 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 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) = 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<sup>+</sup> calculated) = 5.86 (95% CI: 2.61, 13.14)

OR (crude; for T<sup>+</sup> 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)									
	IG	RA (QF	T-GIT)	TST (≥10mm)					
	E	xposure	level	Total		Exposure level		Total	
	Sleeping proximity to					Sleepin	g proxim	ity to child	
	child								
	Same	Same	Different			Same	Same	Different	
	bed	room	room			bed	room	room	
IGRA +	93	15	43	152	TST +	85	13	47	145
IGRA -	64	12	62	138	TST -	80	15	62	157

Indeterminat	NR	NR	NR	14 (excluded)	Indeterminate	NR	NR	NR	2
e									(exclud
									ed)
Total	157	27	105	290	Total	165	28	109	302
				Test performanc	e parameters				
		IGRA	=				TST		
Trend in ORs a	are $(p = 0.006)$	Trend in ORs at 0.186)	Trend in ORs across the gradient of exposure (p = 0.186)						
Different room	: OR (cru	ide; repo	rted) = 1.0	0 (reference					
group)					Different room:	OR (crue	de; repor	ted) = 1.00	
Same room: O	R (crude;	reported	1) = 1.87 (9)	95% CI: 0.70,	(reference group	o)			
5.02)					Same room: OR	(crude;	reported)	$= 1.21 (95^\circ)$	% CI:
Same bed: OR	(crude; r	eported)	=2.01(95)	% CI: 1.12,	0.41, 3.53)				
3.61)					Same bed: OR (crude; reported) = 1.35 (95% CI: 0.79,				
					2.32)				
Same bed vs.									
Sensitivity = 9					Same bed vs. different room				
Specificity = 6					Sensitivity = 85/165 = 51.52% (95% CI: 43.94, 59.02) Specificity = 62/109 = 56.88% (95% CI: 47.51, 65.79)				
PPV = 93/136									
NPV = 62/126					PPV = 85/132 = 64.39% (95% CI: 55.92, 72.05)				
DOR (for T <sup>+</sup> ca			NPV = 62/142 = 43.66% (95% CI: 35.78, 51.88)						
OR (crude; for			DOR (for T <sup>+</sup> calculated) = 1.40 (95% CI: 0.86, 2.28) OR (crude; for T <sup>+</sup> reported) = 1.35 (95% CI: 0.79,						
OR (regression	= 1.45 (95	% CI: 0./0,	` '	ı reporte	ea) = 1.35	(95% CI: (	J./9,		
2.99)	, <b>,</b>	1	1. !	94 6 .1.94	2.32)				
		s relation	isnip to ch	ild, age of child,	OR (regression-based; reported) = NR List of covariates: NA				
smear positivit	-	ND					NID		
Other reported	measure	= NK			Other reported 1	neasure =	= NK		

# 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

o ther reperteu									
Association between test results and levels of TB exposure (if applicable)									
IGRA (QFT-GIT) TST (≥10mm)									
	E	xposure le	vel	Total		E	Exposure level		
	Time spent with child					Time	spent wi	th child	
		h/day					h/day		
	>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
Indeterminat	NR	NR	NR	14 (excluded)	Indeterminate	NR	NR	NR	2
e									(excluded
									)
Total	150	92	47	290	Total	158	96	48	302
			7	Test performanc	e parameters				

1 est per for mane	1 est per for mance par ameters						
IGRA	TST						
Trend in ORs across the gradient of exposure $(p = 0.948)$	Trend in ORs across the gradient of exposure (p =						
<2 h: OR (crude; reported) = 1.00 (reference group)	0.494)						
2-8 h: OR (crude; reported) = 0.78 (95% CI: 0.33, 1.80)	<pre>&lt;2 h: OR (crude; reported) = 1.00 (reference group)</pre>						
>8 h: OR (crude; reported) = 0.83 (95% CI: 0.38, 1.79)	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<sup>+</sup> calculated) = 0.80 (95% CI: 0.41, 1.55) OR (crude; for T<sup>+</sup> reported) = 0.83 (95% CI: 0.38, 1.79) OR (regression-based; reported) = NR List of covariates: NA

>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<sup>+</sup> calculated) = 0.64 (95% CI: 0.33, 1.24) OR (crude; for T<sup>+</sup> reported) = 0.64 (95% CI: 0.31, 1.36)

>8 h: OR (crude; reported) = 0.64 (95% CI: 0.31,

OR (regression-based; reported) = NR List of covariates: NA

Other reported measure = NR

# Comparison between tests (IGRA vs. TST)

1.36)

#### >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

Other reported measure = NR

Association between test results and BCG status (if applicable)							
IGRA (QFT-GIT)				TST (≥10mm)			
	BCG :	BCG status			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 <sup>+</sup> calculated) <sub>IGRA</sub> = 0.49 (95% CI: 0.26, 0.94)	DOR (for T+ calculated) <sub>TST</sub> = $0.68$ (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) <sub>IGRA</sub> = 0.60 (95% CI: 0.26,	OR (regression-based; reported) $_{TST} = NR$						
1.38)	List of covariates: NA						
List of covariates: TB case's relationship to child, marital							

status of household head

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)		
$\frac{\%}{2}$ concordance = $\frac{235}{292} = \frac{80}{1000}$ .			
% discordance = $57/292 = 19.52$			
Stratification (specify group 1		TOT	T 1
ICDA	TST +	TST -	Total
IGRA +	NR	NR NB	NR
IGRA -	NR	NR NR	NR
Indeterminate	NR	NR NR	NR
Total	NR	NR	NR
Description	10.11. 200	10 \ 275	
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		1 2/	
151   UII CSHOIU, INIX			
Parameters			
Parameters			
Parameters Kappa = NR % concordance = NR			
Parameters Kappa = NR % concordance = NR % discordance = NR	):		
Parameters Kappa = NR % concordance = NR		TST -	Total
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2	TST +		Total NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2	TST + NR	NR	NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2  IGRA + IGRA -	TST + NR NR	NR NR	NR NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2  IGRA + IGRA - Indeterminate	TST + NR NR NR	NR NR NR	NR NR NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2  IGRA + IGRA - Indeterminate Total	TST + NR NR	NR NR	NR NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2  IGRA + IGRA - Indeterminate Total Description	TST + NR NR NR NR NR	NR NR NR NR	NR NR NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2  IGRA + IGRA - Indeterminate Total Description Sample definition (e.g., total, if	TST + NR NR NR NR NR	NR NR NR NR	NR NR NR
Parameters Kappa = NR % concordance = NR % discordance = NR Stratification (specify group 2  IGRA + IGRA - Indeterminate Total Description	TST + NR NR NR NR NR	NR NR NR NR	NR NR 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

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

#### **Study details**

First author surname year of publication: Talbot 2012<sup>112</sup>

**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):

HAMMITIAN	IT AVNACIIPA AF	niin
Dennique	of exposure gr	VUV

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

		Ι,	nonulati	on], or occupa	utional evno	cure)				_
Exposed 2 (s	necify):		NA	onj, or occupa	ttionar expos	surc)				
Exposed 2 (s			NA							
Exposed 3 (s			NA							
Tests	pecify).		IVA							
Tests	Acca	v need	method	lology timing	for test	1	Cut-	off		Other
	Assa		l, methodology, timing for test surement, manufacturer				Cut-off values/thresholds Definition of test+			information
IGRA (T- SPOT.TB)	spot. instruct monon Ficol Counted into a rati-int study p the present ESAT-(positive The PE reveale enzyme interfer substraresults algorith company in the present substraction	TB accordions for uclear collensity and properties of the collensity and properties of the collensity articipal articipal articipal articipal dissipation articipal dissipation articipal articipal dissipation articipal articip	sted for LTBI by using T- cording to the manufacturer's for use. Peripheral blood cells (PBMCs) were harvested by gradient centrifugation, washed, plated at 2.5 × 105 cells per well rane-bottomed plate coated with n-γ antibody. PBMCs from each sant were incubated overnight in of the provided TB antigens CFP-10, along with controls orgen control and a nil control). producing interferon-γ were pots by incubation with an ugated secondary antibody for and a color-producing enzyme of the package insert where, the nil control, 8 spots and above d 4 spots and below is negative				NA			
TST>				ed by trained		АТ	ST was	conside	red	
15mm				d the Mantoux	method	positive if there was				
	guideli	nes		g to published		for s risk expe	nduration students factors to osure	with no for TB		NA
Association	between	test re	sults an	d incidence o	f active TB	(if a	pplicabl	e)		
		IGRA						ST		
		1	ence of re TB No	Total			Incider active Yes			Total
IGRA	+	NA	NA	NA	TST +		NA	NA		NA
IGRA		NA	NA	NA	TST -		NA	NA		NA
Indetermi	nate	NA	NA	NA	Indetermin	nate	NA	NA		NA
Total		NA	NA	NA	Total	_	NA	NA		NA
				est performa	nce parame	eters				
		IGRA					Т	ST		
Sensitivity =	NA				Sensitivity	v = NA				
Specificity =					Specificity					
PPV = NA					PPV = NA					
NPV = NA					NPV = NA					
Cumulative 1	ncidence	2 IGR 4 + =	= NA		Cumulativ		idence To	$S_{T+} = NA$	Α	
Cumulative l					Cumulativ					
Cumulative l				A	Cumulativ					A
Incidence density rate $_{IGRA^{+}} = NA$			Incidence density rate $_{TST^+} = NA$							

Incidence density rate		Τ Δ		Incidence den	city rate	= N Δ		
Incidence density rate <sub>IGRA</sub> = NA Incidence density rate <sub>TST</sub> = NA Incidence density rate ratio <sub>IGRA</sub> = NA Incidence density rate ratio <sub>TST</sub> = NA								
		Other reported						
Other reported measu			on hotavo	en tests (IGRA v		$\Gamma - NA$		
Ratio of cumulative i				en tests (IGRA v	8. 151)			
Ratio of incidence de		ratios –	INA					
Other reported measu		-414		.lf.TD	(TD			
	etween te Г-SPOТ.		s and lev	els of TB exposu	re (TB expo TST≥15		group)	
IGRA (			T-4-1				T-4-1	
	Exposu		Total		Exposure		Total	
	Non-	Low			Non-low	Low		
ICDA (T	low	0	NID	TCT	ND	2	ND	
IGRA (T-	NR	0	NR	TST +	NR	2	NR	
SPOT.TB) +	) ID	104	NID	mar.	NID	100	) ID	
IGRA (T-	NR	124	NR	TST -	NR	122	NR	
SPOT.TB) -	NID	NID	0	T 1	) ID	) ID		
Indeterminate	NR	NR	0	Indeterminate	NR	NR	0	
Total	NR	124	NR	Total	NR	124	NR	
		Test	t perforn	nance parameter				
	GRA				TST			
Sensitivity = NA				Sensitivity = NA				
Specificity = 124/124	l = 100.00	)% (95%	CI: 97,	Specificity = 12	2/124 = 98.3	39% (95%	CI: 94.31,	
100.00)				99.56)				
PPV = NA				PPV = NA				
NPV = NA				NPV = NA				
DOR (for T <sup>+</sup> calculat				DOR (for T <sup>+</sup> cal				
OR (crude; for T <sup>+</sup> rep				$OR (crude; for T^+ reported) = NA$				
OR (regression-based		l) = NA		OR (regression-based; reported) = NA				
List of covariates: NA	4			List of covariates: NA				
Other reported measu	ire = NR			Other reported measure = NR				
	Co	mparis	on betwe	en tests (IGRA v	s. TST)			
Ratio of DORs (for T	+ calculat	ed) = NA	Α					
Ratio of OR (crude; f	or T <sup>+</sup> repo	orted) = 1	NΑ					
Ratio of ORs (regress	sion-based	l; reporte	ed) = NA					
Other reported measu	ire = NA							
		between	test resu	ilts and BCG sta	tus (if appli	cable)		
IGF	RA (TSPC	T)			TST (>1	15 mm)		
	BCG s		Total			status	Total	
	Yes	No	1		Yes	No		
IGRA +	NR	NR	NR	TST +	NR	NR	NR	
IGRA -	NR	NR	NR	TST -	NR	NR	NR	
Indeterminate	NR	NR	NR	Indetermina		NR	NR	
Total	NR	NR	NR	Total	NR	NR	NR	
,				nance parameter				
	IGRA	2 031	purn		TS	T		
DOR (for T <sup>+</sup> calculate		$_{\rm ET} = NR$		DOR <sub>TST</sub> (for				
OR (crude; for T <sup>+</sup> rep				OR (crude;				
OR (regression-based			P	OR (regress			r = NR	
OR (regression-based				List of cova		ported) TS	- 1117	
List of covariates: NI		TSPOT —	1117	List of cova	rianos, INN			
Other reported measu				Other report	ed mangure :	= ND		
Between-test agreen		ondone	and di-			_ 1 <b>N</b> IC		
This table may be st						and/an a	andition	
i ms table may be st	raumeu D	y 151 C	ut-on va	iue, DCG vaccin	ation status	, and/or co	JIIUIHOII	

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

#### Study details

First author surname year of publication: Tieu 2014<sup>154</sup>

**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)

Total incidence of active TB (n [%]): NA

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

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

<b>TST:</b> ≥15mm		136	48	88	0	136			
TSPOT		136	36	100	0	136			
	xwith w				Ŭ	130			
	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									
Exposed 1 (specify)									
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)	):		t score (≥13	/					
3. Definition				/	ex case				
Non-exposed	01 011 01			in household					
Exposed 1 (specify)	):			ousehold with					
Exposed 2 (specify)				ousehold wit					
						with TB index ca	ase		
Non-exposed		0-7 hours			<u>r</u> <u>y</u>				
Exposed 1 (specify)	):	≥8 hours							
		_	– Duration	of contact w	ith TB index c	ase in last 12 mo	nths		
Non-exposed		≤7 months							
Exposed 1 (specify	):	>7 months							
6. Definition		sure group	– Index TE	case history					
Non-exposed	Ì		id fast smea						
Exposed 1 (specify)	):		id fast smea						
Tests	•	•		-					
Assay used, methodology, Cut-off Other information									
	Assa	y used, me	thodology,	C	ut-off	Other inform	nation		
		timing fo	r test	values/	thresholds	Other inform	nation		
	measu	timing fo irement, m	r test anufacture	values/ r Definiti	thresholds on of test+	Other inforn	nation		
IGRA (QFT-	measu The ch	timing four timing four trement, mad	r test anufacture whole blood	r Definition Results w	thresholds ion of test+ vere reported	Other inform	nation		
IGRA (QFT- GIT)	measu The ch	timing fourement, maildren had eripheral blo	r test anufacture whole blood bod	r Definition  Results was positive	thresholds ion of test+ vere reported e, negative,	Other inform	nation		
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, –	The chand permonant for the release	timing for a rement, manildren had beripheral blomuclear cells interferonce assay (QF	r test canufacture whole blood cod s collection gamma NGIT)	r Definition  Results was positive or indeter according manufact guideline	thresholds ion of test+ vere reported e, negative, rminate g to the urers'	Study investiga site coordinator clinicians were	ntors, rs, and blinded		
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GIT)  TST≥10mm	The chand per monor for the release.  The bloom the to the accord manufusing period control.	timing for a rement, manildren had be ripheral blomuclear cells a continuation of the same day	whole blood od so collection gamma (NGIT)  es were sent of collection for testing estructions d negative  sit, the T (0.1 ml ernational	r Definition  Results was positive or indeter according manufact guideline  Positive of values for were defit the manustandard.  The size of induration determined	thresholds ton of test+ vere reported e, negative, minate g to the urers' s cutoff r the tests ned using facturers' guidelines  of TST n was ed	Study investiga site coordinator clinicians were to the results of IGRAs until the had completed enrollment and	ators, rs, and blinded f the e study		
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GIT)  TST≥10mm	The chand per monor for the release.  The bloom the to the accord manufusing period control.  At the children solution units of protein on the result is health.	timing for a rement, manildren had be ripheral blomuclear cells a continue assay (QF dood sample same day of laboratory filing to the facturers' in positive and laboratory from the facturers of tuberculing the derivative forearm for the reading by care person	whole blood od so collection regamma (NGIT)  es were sent of collection for testing estructions d negative  sit, the err (0.1 ml ernational in purified estimated) implanted by trained	r Definition or indeternation of an indeternation defined as a spositive or indeternation of an indeternation of an indeternation of an indeternation of a spositive of an indeternation o	thresholds ton of test+ vere reported e, negative, minate g to the turers' s tutoff or the tests ned using facturers' guidelines  of TST on was ed ring the on width (or e diameter) trated lesion; tivity was	Study investiga site coordinator clinicians were to the results of IGRAs until the had completed enrollment and	ators, rs, and blinded f the e study		

	national	guidelines						
T-SPOT.TB		dren had wh	ole blood	Results were repo	orted			
1 51 01.11		pheral blood		as positive, negative,				
		clear cells c		or indeterminate	, ,			
		nterferon-ga						
		assay (TSPO		Positive cutoff va	Positive cutoff values			
			,	were defined usir	ıg			
	The bloo	od samples v	vere sent	the manufacturers	_			
	on the sa	ame day of o	collection	standard guidelin	es			
	to the la	boratory for	testing					
	accordin							
		cturers' instr						
		sitive and n	egative					
	controls	7. 7.	4.7	11 TD (12 V				
Association bety			cidence of	active TB (if appli		,		
	IGRA		m . 1		TST			
	Incidenc		Total		Incider		Т	otal
	active				active			
ICD A	Yes	No NA	NT A	TOT	Yes	No	*	Τ Α
IGRA + IGRA -	NA NA	NA NA	NA NA	TST +	NA NA	NA NA		JA
indeterminate	NA NA	NA NA	NA NA	TST - indeterminate	NA NA	NA NA		IA IA
Total	<del>                                     </del>	NA NA	NA NA	Total	NA NA	NA NA		IA IA
Total	NA			ce parameters	NA	NA	I.	NA.
	IGRA		jei iui iliali		TST	,		
Sensitivity = NA				Sensitivity = NA				
Specificity = NA				Specificity = NA				
$\frac{\text{Specificity} - \text{NA}}{\text{PPV} = \text{NA}}$	<u> </u>			PPV = NA				
NPV = NA				NPV = NA				
Cumulative Incid	lence roper =	: N Δ		Cumulative Incidence $_{TST+} = NA$				
Cumulative Incid				Cumulative Incidence TST+ = NA  Cumulative Incidence TST- = NA				
Cumulative Incid					Cumulative Incidence Ratio <sub>TST</sub> = NA			
Incidence density				Incidence densi			12.1	
Incidence density				Incidence densi	•			
Incidence density				Incidence densi			A	
Other reported m				Other reported i				
			between t	ests (IGRA vs. TS		31		
Ratio of cumulat	ive incidence	e ratios = NA	4	`				
Ratio of incidence	e density rat	e ratios = N	A					
Other reported m	neasure = NA	١						
Ass	ociation bet	ween test re	sults and l	evels of TB exposi				
]	IGRA (QFT			,	<b>ΓST (≥10</b>			
	Exposu	1	Total			sure level		Total
	High/Yes	Low/No			High/Ye	s 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
			performan	ce parameters				
G 1.1 1. 3.2.1	IGRA			G	TST			
Sensitivity = NA				Sensitivity = NA				
Specificity = NA				Specificity = NA				
PPV= NA				PPV= NA				

NPV= NA	NPV= NA
$\overline{DOR \text{ (for T}^+ \text{ calculated)} = NA}$	$DOR (for T^{+} calculated) = NA$
OR (crude; for T <sup>+</sup> reported) =	OR (crude; for T <sup>+</sup> reported) =
TB contact score (range 6-19)	TB contact score (range 6-19)
Score 8-10 (reference/non-exposed): 1.0	Score 8-10 (reference/non-exposed): 1.0
Score 11-12: 2.00 (95% CI: 0.38, 10.61)	Score 11-12: 3.97 (95% CI: 1.19, 13.28)
Score 13-14: 3.64 (95% CI: 0.75,17.77)	Score 13-14: 4.40 (95% CI: 1.38, 14.08)
Score 15-16: 7.50 (95% CI: 1.35, 41.71)	Score 15-16: 7.33 (95% CI: 1.67,32.21)
56016 15 10. 7.50 (7570 61. 1.55, 11.71)	56016 13 10. 7.33 (3370 61. 1.07,32.21)
TB contact score (range 6-19)	TB contact score (range 6-19)
Score 8-12 (reference/non-exposed): 1.0	Score 8-12 (reference/non-exposed): 1.0
Score $\geq$ 13: 4.04 (95% CI: 1.81, 8.99)	Score ≥13: 2.59 (95% CI: 1.28, 5.23)
(2000)	(**************************************
Relationship to TB index case	Relationship to TB index case
Relative other contact (reference/non-exposed): 1.0	Relative other contact (reference/non-exposed):
Second caregiver: 3.95 (95% CI: 1.50, 10.43)	1.0
Primary caregiver: 3.25 (95% CI: 1.36, 7.77)	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	Duration of average contact per day with TB
0-7 hours (reference/non-exposed): 1.0	index case
≥8 hours: 1.75 (95% CI: 0.78, 4.00)	0-7 hours (reference/non-exposed): 1.0
	≥8 hours: 2.27 (95% CI: 1.08, 4.76)
<b>Duration of contact with TB index case in last 12</b>	
months	Duration of contact with TB index case in
≤7 months (reference/non-exposed): 1.0	last 12 months
>7 months: 1.96 (95% CI: 0.99, 3.84)	≤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-	Index TB case history
exposed): 1.0	Sputum acid fast smear negative
Sputum acid fast smear positive: 0.97 (95% CI:	(reference/non-exposed): 1.0
0.27, 3.33)	Sputum acid fast smear positive: 2.38 (95% CI:
OD (	0.49, 11.11)
OR (regression-based; reported) = TB contact score (range 6-19)	OR (regression-based; reported) = TB contact score (range 6-19)
Score 8-10 (reference/non-exposed): 1.0	Score 8-10 (reference/non-exposed): 1.0
Score 11-12: NR	Score 11-12: NR
Score 13-14: NR	Score 13-14: NR
Score 15-14: NR	Score 15-14. NR
SCOIC 13-10, INK	SCOIC 13-10. INK
TB contact score (range 6-19)	TB contact score (range 6-19)
Score 8-12 (reference/non-exposed): 1.0	Score 8-12 (reference/non-exposed): 1.0
Score ≥13: 1.98 (95% CI: 0.64, 6.11)	Score ≥13: 2.21 (95% CI: 0.99, 4.98)
	2007 _10. 2.21 (2070 01. 0.22), 1.20)
Relationship to TB index case	Relationship to TB index case
Relative other contact (reference/non-exposed): 1.0	Relative other contact (reference/non-exposed):
Second caregiver: 3.95 (95% CI: 1.25, 12.52)	1.0
Primary caregiver: 4.07 (95% CI: 1.38, 11.99)	Second caregiver: NR
	Primary caregiver: NR
Duration of average contact per day with TB	
index case	Duration of average contact per day with TB
0-7 hours (reference/non-exposed): 1.0	index case
≥8 hours: NR	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

Other reported measure = 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

# Comparison between tests (IGRA vs. TST)

#### Ratio of DORs (for T<sup>+</sup> calculated)=NA

Ratio of OR (crude; for T<sup>+</sup> 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 (spo	ecify)	T	ST (speci	fy)							
	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 parametersIGRATSTDOR (for $T^+$ calculated) $_{IGRA} = NR$ DOR (for $T^+$ calculated) $_{TST} = NR$ OR (crude; for $T^+$ reported) = NROR (crude; for $T^+$ reported) = NROR (regression-based; reported) $_{IGRA} = NR$ OR (regression-based; reported) $_{TST} = NR$ List of covariates: NRList of covariates: NROther reported measure = NROther 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)

	31=40.46% (95% CI: 32.44, 49.02	<i></i>	
This table may be str	ent, concordance, and discordan atified by TST cut-off value, BC		l/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 cor	ndition – specify): total	
$TST + threshold: \ge 15n$	nm		
Parameters			
Kappa = $0.53 (95\% CI)$	0.38, 0.69)		
% concordance = [29+	75]/131=79.39% (95% CI 71.67,	85.43)	
% discordance = 27/13	31=20.61% (95% CI 14.57, 28.33)		
	ent, concordance, and discordan	` <b>*</b> * * *	
-	atified by TST cut-off value, BC	G vaccination status, and	l/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			
	, total, if stratified by BCG or cor	ndition – specify): total	
$TST + threshold: \ge 10n$	nm		
Parameters			
Kappa = $0.23$ (95% CI			
	41]/131=55.73% (95% CI 47.18,		
% discordance = 58/13	31=44.27% (95% CI 36.05, 52.82)		
Between-test agreeme	ent, concordance, and discordan	ce (if applicable)	
This table may be str	atified by TST cut-off value, BC	G vaccination status, and	l/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 cor	ndition – specify): total	
TST + threshold: ≥15n	nm		
Parameters			
Kappa = 0.51 (95% CI			
% concordance = [27+	76]/131 = 78.63% (95% CI 70.84	, 84.78)	
	31 = 21.37% (95% CI 15.22, 29.10		
Stratification (specify			
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
		- 1-2	1 111

NR

NR

NR

NR

NR

NR

indeterminate

Description

Total

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

#### **Parameters**

Kappa = NR

% concordance = NR

% discordance = NR

**Stratification (specify group 2):** 

Stratification (speerly 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**

 $\overline{\text{Kappa}} = \text{NR}$ 

% 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

#### **Study details**

First author surname year of publication: Tsolia 2010<sup>113</sup>

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

Number of patients tested							
	Total N	Total N	Total	Total N	Total N		
	(tested)	(test+)	N	(indetermina	(test results available)		
			(test-)	te)			
IGRA (QFT-	99 (patients in	32	63	4	95		
GIT):	contact with						
	adult TB)						
<b>TST</b> (≥ 5mm):	99 (patients in	55	44	0	99		
	contact with						
	adult TB)						
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 ex	posure	e to TB	in increasing	orde	r (if applica	ole):		
			f exposure grou			an adı	ılt TB	
Non-exposed			old occasional c					
Exposed 1	Non-l	nouseho	old regular cont	act				
(specify):								
Exposed 2	House	ehold c	ontact					
(specify):								
Exposed 3	NA							
(specify):								
Exposed 4	NA							
(specify):								
Tests								
	1	•	ed, methodolog		Cut-o		Other info	rmation
	timii		test measureme	ent,	values/thro			
		mai	nufacturer		s Definiti			
					test+			
IGRA (QFT-GIT)			Cellestis Limited		> 10 IU/mI	_	Indeterminate	
	Carne	egie, V	ictoria, Australi	a)			the QFT-GIT	
							excluded from	the
TST ≥ 5mm or	D11::C	iad nua	tein derivative		> 10mm fo	r BCC	analysis NA	
181 ≥ 5mm or ≥10mm	1	-	(Statens Serum	1	immunized	DOG	1 <b>N</b> / <b>1</b>	
210IIIII			enhagen,	1	children			
	1		ciniagen,		$\geq 5$ mm for	non-		
	Denmark) ≥ 5mm for non- BCG immunized							
					children	mzea		
Association betwee	n test 1	results	and incidence	of ac		pplicab	ole)	
	IGRA				`		ΓST	
	Incid	ence	Total	Incidence of active To				
	of ac	ctive					TB	
	T.	В						
	Yes	No				Yes	No	
IGRA +	NA	NA	NA		TST +	NA	NA	NA
IGRA -	NA	NA	NA		TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Ind	eterminate	NA	NA	NA
Total	NA	NA	NA		Total	NA	NA	NA
			Test perform	ance	parameters			
	IGRA						ΓST	
Sensitivity = NA					sitivity = NA			
Specificity = NA					cificity = NA	1		
PPV = NA					V = NA			
NPV = NA		<b>.</b> - :			V = NA	•		
Cumulative Incidend					nulative Inci			
Cumulative Incidence			<b>N</b> T 4		nulative Inci			
Cumulative Incidend			= NA				$\frac{\text{atio }_{TST} = NA}{NA}$	
Incidence density ra					dence densit			
Incidence density ra			NT A		dence densit			
Incidence density ra							$tio_{TST} = NA$	
Other reported meas	ure <sub>IGR</sub>				er reported n		$_{\text{TST}} = \text{NA}$	
D 41 C 1 4			parison betwee	n tes	ts (IGRA vs	. TST)		
Ratio of cumulative								
Ratio of incidence d			los = NA					
Other reported meas	ure = N	NA						

Associa	ation between	test results an	nd levels of	TB expo	sure (Type of co	ntact with TB	case)	
		FT-GIT)		TST≥5mm				
		ire level	Total		Exposur		Total	
	Non-	Non-			Non-	Non-		
	household	household			household	household		
	regular	occasional			regular	occasional		
IGRA +	9	1	10	TST +	18	7	25	
IGRA -	18	10	28	TST -	10	4	14	
Indetermi	1	0	1	Indete	0	0	0	
nate				rminat				
				e				
Total	28	11	39	Total	28	11	39	
			performan	ce paran				
		RA			TS			
Sensitivity 52.18)	= 9/27 = 33.3	3% (95% CI: 1	8.64,	Sensitiv 79.29)	vity = 18/28 = 64.	.29% (95% CI:	45.83,	
Specificity 98.38)	= 10/11 = 90.	91% (95% CI:	62.26,	Specific 64.62)	$ext{ity} = 4/11 = 36.3$	36% (95% CI: 1	15.17,	
	0 = 90.00% (9)	5% CI: 59.58, 9	98 21)		18/25 = 72.00% (	95% CI: 52 42	85 72)	
		95% CI: 20.71		t	4/14 = 28.57% (9)			
		= 5.00 (95% C)			or T <sup>+</sup> calculated)			
45.39)		2.00 (5270 23	., 0.00,	4.39)	01 1 (41)	1.00 (5070 0	., .,	
	for T <sup>+</sup> reporte	d = NR			de; for T <sup>+</sup> reporte	ed) = NR		
	sion-based; re				ression-based; re			
	ariates: NA	r - · · · · /		List of covariates: NA				
	rted measure =	= NR		Other reported measure = NR				
1			n between	tests (IGRA vs. TST)				
Ratio of Do	ORs (for T <sup>+</sup> ca	lculated) = 4.83						
Ratio of Ol	R (crude; for T	$r^+$ reported) = N	ΙA					
Ratio of Ol	Rs (regression	-based; reported	d) = NA					
Other repor	rted measure =	= NA						
Associa	ation between	test results ar	nd levels of	TB expo	sure (Type of co	ntact with TB	case)	
	IGRA (Q	FT-GIT)			TST≥	5mm		
	Exposi	ire level	Total		Exposur	e level	Total	
	Household	Non-			Household	Non-		
		household				household		
		occasional				occasional		
IGRA +	22	1	23	TST +	30	7	37	
IGRA -	35	10	45	TST -	30	4	34	
Indetermi	3	0	3	Indete	0	0	0	
nate				rminat				
Total	60	11	71	e Total	60	11	71	
			performan					
	IG	RA			TS	ST		
Sensitivity 51.57)	=22/57=38.	6% (95% CI: 2	7.06,	Sensitiv 62.27)	vity = 30/60 = 50.5	.00% (95% CI:	37.73,	
	= 10/11 = 90.	91% (95% CI:	62.26,	Specificity = 4/11 = 36.36% (95% CI: 15.17,				
	23 = 95.65%	95% CI: 79.01,	99 23)	64.62)	30/37 = 81.08% (	05% CI: 65 70	90 52)	
-		95% CI: 79.01,			$\frac{30/37 - 81.08\%}{4/34 = 11.76\%}$			
		= 6.28 (95% Cl			or $T^+$ calculated)			
`	carculated)	- 0.20 (93/0 C)	1. 0.75,	`	or reacculated)	- 0.37 (93/0 C	1. 0.13,	
52.56)					2.15)			

OD ( 1 C 7	p† (1)	NID		OP ( 1 C	Tr <sup>+</sup> ( 1)	NID			
OR (crude; for T			D	OR (crude; for					
, 1			OR (regression	, I	ed) = NR				
			List of covaria						
Other reported n				Other reported					
				tests (IGRA vs.	TST)				
Ratio of DORs (				3.07, 39.60)					
Ratio of OR (cru									
Ratio of ORs (re			orted) = NA						
Other reported n									
	Associatio	n betwe	en test results	and BCG statu					
	IGRA (Q	FT-GIT			TST≥5	mm			
	BCG sta	atus	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	Indeterm	in NR	NR	NR		
ı				ate					
Total	NR	NR	NR	Total	NR	NR	NR		
		Т	est performan	ce parameters			•		
	IGI		•		TST				
DOR (for T <sup>+</sup> cal	culated) <sub>OFT</sub> =	= NR		DOR TST	(for T+ calcula	ted) = NR			
OR (crude; for T					le; for T+ repo				
OR (regression-			0.19, 95% CI		OR (regression-based; reported) <sub>TST</sub> =				
(0.06, 0.60)	, - · <sub>P</sub> - ·		,,,,,,,,,,	\	20.34, 95% CI (5.60, 73.89)				
List of covariate	s: NR				List of covariates: NR				
Other reported n		R			Other reported measure = NR				
Between-test ag			nce and disco			- 112			
This table may						d/or condi	tion		
Total sample		- ~ J - ~ J	011 (011)	, 200 , 400	2011 2000 000 001	., 01 001141			
1 otal sample		TST	+	TS	T -		Total		
IGRA +		29	· ·		3		32		
IGRA -		24			39		63		
Indeterminate		2			2		4		
Total		55			44				
<b>Description</b>					+		99		
Sample definition	n (a.g. total	if atrati	fied by PCC o	r condition and	noify): Total				
		, 11 Strati	ned by BCG o	condition – spe	ciry). Total				
TST + threshold	<u>∠</u> 3 IIIIII								
Parameters 0.45 0	50/ CI (0.27	0 (2)							
Kappa = $0.45, 9$			50/ CT (61.01.7	70. (7)					
% concordance									
% discordance =			% CI (20.33, 3	8.19)					
Stratification (I	BCG vaccin				<b>T</b>	T .	T 1		
YCD 1		TST		TS			<u>Fotal</u>		
IGRA +		NR		N			NR		
IGRA -		NR		N			NR		
Indeterminate		NR					NR		
Total		NR		N	R		43		
Description									
Sample definition	on (e.g., total	, if strati	fied by BCG o	r condition – spe	ecify): BCG va	ccinated			
TST + threshold	: ≥10 mm								
Parameters									
Kappa = $0.13$ (p	= 0.06)								
% concordance		5.50% (9	5% CI NR)						

% discordance = NR			
Stratification (non-Bo	CG 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 BC	CG or condition – specify): BCG vaccina	ited
TST + threshold: ≥5 m	m		
Parameters			
$V_{\text{anno}} = 0.01 (n = 0.0)$			

Kappa = 0.91 (p = 0.06)

% concordance = 50/52 = 96.20% (95% CI NR)

% discordance = NR

**Stratification (Household contact)** 

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

**Study details** 

First author surname year of publication: Diel 2011<sup>102</sup>

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 natients tested

Number of patients tested								
	Total N	Total	Total N	Total N	Total N			
	(tested)	N	(test-)	(indeterminate)	(test results			
					available)			
		(test+)						

ICD A (OFT	CIT	126	22		22	NIE		106		
IGRA (QFT-		126	23		33		NR 106			
TST (>5mm)							106 106			
Total N of pa	,		ts for both							
chemoprophy			ts for both	IONA	and 191.	104 (2 p	aticitis iv	cciving		
	Levels/groups of exposure to TB in increasing order (if applicable):									
			Definition of							
Non-exposed										
Exposed 1 (s)		NR								
Exposed 2 (s)		NR								
Exposed 3 (s)	pecify):	NR								
Exposed 4 (s)	pecify):	NR								
Tests	T				1					
			ology, timin	_	Cut			ther information		
	test mea	isurement,	manufactu	rer	values/th					
IGRA	Danfannad		o 41a o		Definition		+			
IGRA (QFT-GIT)	Performed manufactur				IFN-g of O					
(QF1-GI1)			ie, Australia	)	10/1111 01 §	51 Calci		essors of the TST		
	(Cenestis I	ou, cumos.	10, 1 tustrum	,				e blinded to QFT		
	The maxin	nal level of	IFN-g accur	ately				lts and vice versa.		
	detected by		C	•				ration was read by ned and well-		
	QFT ELIS	A is 10 IU/1	ml, and thus							
	_	iter than thi	s are reporte	d as				perienced public alth nurses. If there		
	10 IU/ml						Was	a borderline result		
TST			Mantoux met					(e.g., 5 mm exactly), a		
			10-GT (Chir	on	n scored as positive at > 5mm or >			second reading was		
		Iarburg, Ge ent to 5 unit	•		10mm			performed by a		
		al purified p			1011111			different nurse to		
			D-S] standar	d).				fy this result. If		
		_	nl (2 tuberci	, ,				e was		
	units) of pi	irified prote	ein derivativ	e				greement, a third e read the TST		
	`	ens Serum						the consensus		
	1 0		k), which is					lt used		
		to Tubercul	lin-10-GT				1034	11 4504		
	(Chiron Be		11 11	6 49	ED (16	** *				
Association l			a incidence	of acti	ve IB (if a			<u> </u>		
	IGR	lence of	Total				(>5mm	) Total		
		ve TB	Total				e TB	Total		
	Yes	No				Yes	No			
IGRA +	6	15	21		TST +	6	34	40		
IGRA -	0	83	83		TST -	0	64	64		
Indetermina	te 0	0	0		eterminate	0	0	0		
Total	6	98	104		Total	6	98	104		
		T	est perform	ance p	arameters					
	IGR						ГSТ			
Sensitivity =		`						CI: 60.97, 100)		
Specificity = 90.5)				73.9	Specificity = 64/98 = 65.31% (95% CI: 55.47, 73.99)					
PPV = 6/21 =				PPV = 6/40 = 15.00% (95% CI: 7.06, 29.07)						
NPV = 83/83	= 100% (95	% CI: 95.5	8, 100)	NPV	J = 64/64 =	100% (	95% CI:	94.34, 100)		

G 1 1: I :1		6/21 20	570/	G 1 .: T	• 1	6/40	15.000/ (050/				
Cumulative Incide	.57%	Cumulative Incidence $_{TST+} = 6/40 = 15.00\% (95\%)$									
(95% CI: 13.81, 49.96)				CI: 7.06, 29.07)							
Cumulative Incidence $_{IGRA}$ = 0/83 = 1.20% (95%)				Cumulative Incidence $_{TST-} = 0/64 = 1.55\%$ (95%)							
CI: 0.03, 6.53)				CI: 0.04, 8.4)							
Cumulative Incidence Ratio <sub>IGRA</sub> = 23.7% (95%				Cumulative Incidence Ratio $_{TST} = 9.6\%$ (95% CI:							
CI: 2.57, 110.3)		1.08, 448.2)									
Incidence density		Incidence density rate $_{TST^+} = NR$									
Incidence density		Incidence density rate <sub>TST-</sub> = NR									
Incidence density		Incidence density rate ratio $_{TST} = NR$									
Other reported me	easure <sub>IGRA</sub> =	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										
	Incidence	e of	Total	TST (>10mm) Incidence of Total							
	active		1 Otal		active TB		10001				
	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				
Total	6	98	104	Total	6	98	104				
Total	0					96	104				
	ICDA	1 681	perioriii	nce parameters							
0 :::: (/6	IGRA	0/ CT (0.0	7 100	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.	49.96)	PPV = 4/40 = 10% (95% CI: 3.96, 23.05)									
NPV = 83/83 = 10	100)	NPV = 62/64 = 96.88% (95% CI: 89.3, 99.14)									
Cumulative Incide		Cumulative Incidence $_{TST+} = 4/40 = 10.00\%$ (95%)									
(95% CI: 13.81, 4		CI: 3.958, 23.05)									
Cumulative Incide		0/83 = 1.2	0% (95%	Cumulative Incidence $_{TST}$ = 2/64 = 3.12% (95%)							
CI: 0.03, 6.53)	idiai										
Cumulative Incide	ence Ratio	$G_{RA} = 23.7$	% (95%	CI: 0.22, 11.33 Cumulative Incidence Ratio <sub>TST</sub> = 3.20% (95% CI:							
CI: 2.57, 110.3)	1	J/	( / 0	0.61, 16.67)							
Incidence density	rate IGRA+ =	NR		Incidence density rate $_{TST+} = NR$							
Incidence density				Incidence density rate $_{TST^{-}} = NR$							
Incidence density				Incidence den							
	-		n hetwee	n tests (IGRA v		151 111					
Ratio of cumulativ				1							
Ratio of cumulati				C1. 2.00, 20.07)							
Other reported me			1117								
			roculta en	d levels of TB e	vnoshro (	f annliaahl	<i>y</i>				
ASSO	IGRA	ween test	csuits all	u ieveis of 1 B e	xposure (1 TS						
	Total				Total						
	Exposu	1	Total			ire level	Total				
ICDA	High/Yes	Low/No	NT A	TOT	High/Yes		NT A				
IGRA +	NA	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					
$\overline{DOR}$ (for $T^+$ calculated) = NA					$DOR  ext{ (for T}^+  ext{ calculated)} = NA$					
OR (crude; for T <sup>+</sup> reported) = NA					OR (crude; for $T^+$ reported) = NA					
OR (regression-based; reported) = NA					OR (regression-based; reported) = NA					
List of covariates				List of covariates: NA						
Other reported m	easure = NA	1		Ot	Other reported measure = NA					
	(	Compariso	n betwee	en t	ests (IGRA vs. 7	ΓST)				
Ratio of DORs (f	or T <sup>+</sup> calcula	ated) = NA								
Ratio of OR (crud	de; for T <sup>+</sup> rep	ported) = N	A							
Ratio of ORs (reg	gression-base	ed; reported	d = NA							
Other reported m	easure = NA	1								
	Association	n between	test resu	lts :	and BCG status	(if appli	cable)			
IGRA TST										
	BCG s	status	Total				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	perform	and	e parameters					
	IGRA			TST						
DOR (for T <sup>+</sup> calc	ulated) <sub>IGRA</sub> =	= NA		DOR (for T+ calculated) <sub>TST</sub> = NA						
OR (crude; for T				OR (crude; for T+ reported) = NA						
OR (regression-based; reported) <sub>IGRA</sub> = NA				OR (regression-based; reported) $_{TST} = NA$						
List of covariates: NA				List of covariates: NA						
Other reported m					Other reported		= NA			
Between-test agr							11/	1*4*		
This table may b	e stratined	by 181 ct	it-oii vai	ue,	BCG vaccinatio	on status,	, and/or c	onaition		
Total sample	T	TOT		Г	TOT			T. 4 1		
ICD A		TST +			TST -		Total			
IGRA + IGRA -		NR			NR NR		NR NR			
Indeterminate		NR NB			NR NR			NR		
Total		NR NR			NR NR			NR		
<b>Description</b>		INIX			INIX			INIX		
Sample definition	(e.g. total	if stratified	l by RCC	i or	condition space	ify):				
TST + threshold:		11 Stratified	1 by BCC	J 01	condition – spec	11y).				
Parameters Parameters	111									
Kappa = NR										
% concordance =	NR									
% discordance =										
Stratification (sp		1)								
Structure (5)	cerry group	TST +		Г	TST -			Total		
IGRA +		NR			NR			NR		
IGRA -		NR			NR			NR		
Indeterminate		NR			NR			NR		
Total		NR			NR			NR		
Description		1111			1,11					
Sample definition	(e.g., total	if stratified	1 by BCC	ior	condition – spec	ify): NR				
Zampie delimition	. (0.5., 10141,	50.0011100	- 0, DCC	. 01	tonamon spec	j, i (IC				

TST + threshold: NR
Parameters
Kappa = NR
% concordance = NR
% discordance = NR
Stratification (specify group 2)

Stratification (specify group 2)							
	TST +	TST -	Total				
IGRA +	NR	NR	NR				
IGRA -	NR	NR	NR				
Indeterminate	NR	NR	NR				
Total	NR	NR	NR				

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

TST + threshold: NR

## **Parameters**

Kappa = NR

% concordance = NR

% discordance = NR

	п	n	Δ	r	$\mathbf{a}$	m	т	n	n	m	es
v	w	ш	•		v	u	w	v	v		

\$ 122 T \$ 122						
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

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

## Study details

First author surname year of publication: Mahomed 2011a<sup>103</sup>

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

	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	NI	₹	NR
1 2 7	Total N of patients with valid results for both							
Levels/groups of o								
g					posure group			
Non-exposed		NA			<u> </u>			
Exposed 1 (specify	/):	NA						
Exposed 2 (specify		NA						
Exposed 3 (specify		NA						
Exposed 4 (specify		NA						
Tests	7-							
1 0000		Ass	ay used,		Cut-o	ff	Oth	er information
			ology, tim	ing	values/thro			
		for test n			<b>Definition</b>			
			ufacturer					
IGRA		QFT-GIT,	In-tube		≥ 0.35 IU/m	L		
		method, (0					NT A	
		Limited, C					NA	
		Victoria, A	Australia)					
TST		Mantoux 1	nethod or	1	≥ 5mm		People	with a recent
		either fore		g 2				old contact, TB
		tuberculin						symptoms, a
		RT23, ind					-	e TST ≥10 mm
		read 48-96						ion or a positive
		with a ruler or caliper by			r		_	ere referred for
		trained personnel,					two sputum smears. If	
		(Statens Serum Institut,					results of either or both	
		Denmark)					were sputum positive for	
							acid fast bacilli, the sputum were cultured,	
							-	hest x-ray and
							HIV tes	•
							underta	
Association between	on tost	roculte one	d inciden	co of	active TR (if	annlicah	L	KCII.
		Tesuits and	u meruem	01	active ID (II		r≥5mm	
10.		dence of	Total				ence of	Total
	_	ive TB	Total	1		acti		1 Otal
	Yes	No	1			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
Total	52	5192	5244		Total	52	5192	5244
2 3 441		-			ce parameters		01/2	2211
	IGR		or perior		- parameter		TST	
Sensitivity = 39/52			I (61.79.		Sensitivity =			95% CI (63.87,
84.77)			- (~,,		86.28)	. 5, 52		
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	1.46%,	95% CI (1.0	07, 1.99)				%, 95%	CI (1.02, 1.88)
NPV = 2562/2575								5% CI (99.11,
99.7)		,	` '		99.71)		, -	,
Cumulative Incide 95% CI (1.07, 1.99		_+ = 39/2669	9 = 1.46%	,	Cumulative Incidence $_{TST+} = 40/2894 = 1.38\%$ , 95% CI (1.02, 1.87)			
		= 13/2575	5 = 0.50%				<sub>тет</sub> = 12	$\sqrt{2350} = 0.51\%$
Camaran ve merue	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 <sub>IGRA</sub> = 2.89, 95% CI	Cumulative Incidence Ratio $_{TST} = 2.71$ (95% CI:
(1.55, 5.40)	1.42, 5.14)
Incidence density rate $_{IGRA+} = 0.64$ per 100 person	Incidence density rate $_{TST^+} = 0.60$ per 100 person
years, 95% CI (0.45, 0.87)	years, 95% CI (0.43, 0.82)
Incidence density rate $_{IGRA-}$ = 0.22 per 100 person	Incidence density rate $_{TST-}$ = 0.22 per 100 person
years, 95% CI (0.12, 0.38)	years, 95% CI (0.11, 0.39)
Incidence density rate ratio <sub>IGRA</sub> = 2.92, 95% CI	Incidence density rate ratio $_{TST} = 2.73, 95\%$ CI
(1.58, 5.67)	(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)								
		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 <sup>+</sup> reported) = NA	$OR (crude; for T^+ reported) = NA$			
OR (regression-based; reported) = NA	OR (regression-based; reported) = NA			
List of covariates: 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

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

TST + threshold: NR

#### **Parameters**

 $\overline{\text{Kappa}} = \text{NR}$ 

% concordance = NR

% discordance = NR

Stratification (specify group 2)

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

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

## Study details

First author surname year of publication: Noorbakhsh 2011<sup>104</sup>

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

 $\textbf{Funding} \ (\textbf{government/private/manufacturer/other-specify}) \textbf{:} \ Research \ Centre \ of \ Paediatric \ Infectious$ 

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

TST (≥ 10mm):   NR									
Test 3 (specify)	IGRA (QFT-G):		NR	18			NR	_	59
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								L	NA
Definition of exposure group	*								
Non-exposed   Nor	Levels/groups of	exposur					le):		
Exposed 2 (specify): NR   NR   NR   Exposed 2 (specify): NR				inition of	exposur	e group			
Exposed 2 (specify): NR   Stay used, specify   NR   Stay used, methodology, timing for test measurement, manufacturer   Not reported   No									
Exposed 3 (specify): NR    Exposed 4 (specify): NR									
Tests   Assay used, methodology, timing for test measurement, manufacturer									
Tests    Assay used, methodology, timing for test measurement, manufacturer   Section									
Assay used, methodology, timing for test measurement, manufacturer   September   Septe		y):	NR						
For test measurement, manufacturer   values/thresbolds   Information	Tests			7.7		ı	C . CC		
Total   Acceptable   Total									
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    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 crythema) was read after 48–72 hours    A reactive TST was an induration diameter of the raised, blanched weal (not the crythema) was read after 48–72 hours    Association between test results and incidence of active TB (if applicable)		1							information
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 antigenfree 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    TST (≥ 10mm)	ICDA (OFT C)	Г 4			1			test+	NTA
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$ \begin{array}{ c c c c } \hline 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 \muL plasma was removed from each well and the concentration of IFN-\gamma was determined using the assay kits  \hline \textbf{TST} \ ( \ge 10 \text{mm}) \hline \ For the TST \ a test dose (0.1 \ mL) of 5 \\ tuberculin units of purified protein derivative solution (Pasteur Institut, 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  \hline \  \  \   \   \   \   \   \   \   \$									
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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  Association between test results and incidence of active TB (if applicable)  IGRA (QFT-G) TST $\geq 10$ mm  Incidence of active TB  Yes No Indeterminate NR NR NR			`			≥ 10mm	l		
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Association between test results and incidence of active TB (if applicable)   IGRA (QFT-G)									
Association between test results and incidence of active TB (if applicable)           IGRA (QFT-G)         TST ≥ 10mm           Incidence of active TB         Total active TB         Incidence of active TB         Total active TB           Yes         No         Yes         No           IGRA +         10         8         18         TST +         3         5         8           IGRA -         0         41         41         TST -         7         43         50           Indeterminate         NR         NR         Indeterminate         0         1         1           Total         10         49         59         Total         10         49         59           Test performacers           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, 95.47)         Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)				,					
IGRA (QFT-G)       TST≥ 10mm         Incidence of active TB       Total active TB       Incidence of active TB       Total active TB         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         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, 95.47)       Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)	Aggoriation					TD (:f	anlia-1-1		
$ \begin{array}{ c c c c c }\hline & Incidence \ of \\ active \ TB \\ \hline Yes & No \\ \hline \\ IGRA + & 10 & 8 & 18 & TST + & 3 & 5 & 8 \\ \hline IGRA - & 0 & 41 & 41 & TST - & 7 & 43 & 50 \\ \hline Indeterminate & NR & NR & NR & Indeterminate & 0 & 1 & 1 \\ \hline Total & 10 & 49 & 59 & Total & 10 & 49 & 59 \\ \hline \hline \\ \hline \hline \\ Sensitivity = 10/10 = 100.00\%, 95\% \ CI \ (72.25, \\ 100.00) & Specificity = 41/49 = 83.67\%, 95\% \ CI \ (70.96, \\ 91.49) & Specificity = 43/48 = 89.58\%, 95\% \ (77.83, 95.47) \\ \hline \\ $				ncidence (	or active	1D (II 8)			
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				10141					1 Otal
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           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, 95.47)         Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)			1						
IGRA -         0         41         41         TST -         7         43         50           Indeterminate         NR         NR         NR         Indeterminate         0         1         1           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, 95.47)         Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)	IGRA+	<del> </del>	+ +	18	Т9	+ T2			8
Indeterminate         NR         NR         NR         Indeterminate         0         1         1           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)			1					-	
			+						1
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)								-	59
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)	1 3 641	10						.,	
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100.00) 60.32) Specificity = 41/49 = 83.67%, 95% CI (70.96, 91.49) Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)	Sensitivity = 10/1			(72.25.	Sensit	tivity = 3/			5% CI (10.78.
Specificity = 41/49 = 83.67%, 95% CI (70.96, 91.49) Specificity = 43/48 = 89.58%, 95% (77.83, 95.47)									
91.49) 95.47)					95% (77.83,				
, ,			,	- 1				, -	- 7
PPV = 10/18 = 55.56%, 95% CI (33.72, 75.44)   PPV = 3/8 = 37.50%, 95% CI (13.68, 69.43)	PPV = 10/18 = 55	.56%, 95	% CI (33.72.	, 75.44)	PPV =	= 3/8 = 37	7.50%, 9	5% 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 $_{IGRA+} = 10/18 = 55.56\%$ ,	Cumulative Incidence $_{TST+} = 3/8 = 37.5\%$ , 95%
95% CI (33.72, 75.44)	CI (13.49, 69.62)
Cumulative Incidence $_{IGRA-} = 0/41 = 2.41\%$ (95%)	Cumulative Incidence $_{TST}$ = 7/50 = 14.00%, 95%
CI: 0.06, 12.9)	CI (6.63, 26.50)
Cumulative Incidence Ratio <sub>IGRA</sub> = 22.78% (95%	Cumulative Incidence Ratio <sub>TST</sub> = 2.68% (95%
CI: 2.75, 101.1)	CI: 0.86, 8.27)
Incidence density rate $IGRA+ = NR$	Incidence density rate $_{TST+} = NR$
Incidence density rate <sub>IGRA</sub> . = 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 =  $\overline{NR}$ 

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

IGRA					TS	Γ	
	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 <sup>+</sup> calculated) = NA	DOR (for $T^+$ calculated) = NA
OR (crude; for T <sup>+</sup> reported) = NA	$OR (crude; for T^{+}reported) = NA$
OR (regression-based; reported) = NA	OR (regression-based; reported) = NA
List of covariates: 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			

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

### Study details

First author surname year of publication: Song 2014<sup>152</sup>

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)

	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
<b>TST</b> ≥10mm	2982	663	2319	0	2982
TST≥15mm	2982	231	2751	0	2982

T42 (:							
Test 3 (specify)	• 41	11 14 6 1 41	ICDA LECE 2.066				
		valid results for both	,				
Levels/groups of exposure to TB in increasing order (if applicable): NA							
Definition of exposure group –							
Non-exposed NA							
Exposed 1 (specify):							
Exposed 2 (specify):		NA					
Exposed 3 (specify):		NA					
Exposed 4 (specify):		NA					
Tests			C , ee				
		Assay used,	Cut-off	Other information			
	me	ethodology, timing for	values/thresholds				
		test measurement,	Definition of test+				
ICDA IOET	$\Omega$ I	manufacturer	A Otiernon1				
IGRA –[QFT-	_	T Gold In-Tube	A QuantiFERON value of 0.35 international				
GIT]	`	ellestis Inc, Valencia,	units or more was				
		A) tests were performed cording to the	deemed positive				
		cording to the inufacturer's	according to				
		structions. Briefly,	manufacturer's				
		nole blood was	instructions				
		llected by venipuncture	mstructions				
		om each subject at the					
		te of injection of PPD					
		d incubated for 16–24					
		urs in 3 separate					
		nditions: 1) a mixture		To eliminate the			
of		,		possibility of false-			
	3 TB antigens from RD1			positive IGRA results			
		d RD11 (ESAT-6,		due to PPD reagents,			
	CF	P-10, and		blood samples were			
		37.7); 2) a mitogen as a		collected before PPD			
	po	sitive control; and 3) a		injection			
	mo	ock stimulation as a					
	ne	gative control (nil).					
		llowing the					
		mulations, 150 mL of					
		e supernatant was					
		rvested from each tube.					
		en, 50 mL of each					
		pernatant was used to					
		termine its interferon					
gamma (IFN-c)							
	l	ncentration by the ISA					
TST≥10mm	_	radermal injection (0.1	The maximal transverse				
13121011111		) of 2 tuberculin units	size of induration was				
	l	purified protein	read 48–72 hours later				
	l	rivative (RT 23;	with a ruler or a caliper				
	l	atens Serum Institute,	by a research nurse				
		penhagen, Denmark)					
		o the anterior surface	≥10mm				
		the forearm with a	≥15mm				
		sposable syringe and a					
	410	posacio syringe una a	1	l .			

	27-9	gauge nee	edle by using						
			technique						
Association betw				of active TB (if	applical	ble)			
	RA (QF			· ·		`≥10m	m		
		ence of	Total		Incide	Incidence of Total			
	activ	ve TB			activ	e TB			
	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 perform	ance parameter	S				
	IGR/		•	,		TST			
Sensitivity = 11/2 67.04)	3=47.83	% (95% (	CI: 29.24,	Sensitivity =13/	/23=56.5	52% (9	5% CI: 3	66.81, 74.37)	
Specificity = 263' 88.45, 90.65)	7/2943=8	39.6% (95	5% CI:	Specificity = 23 79.49)	09/2959	9=78.03	3% (95%	CI: 76.51,	
PPV= 11/317=3.4	7% (95%	6 CI: 1.9	4, 6.10)	PPV= 13/663=1	.96% (9	95% CI	: 1.14, 3	.32)	
NPV= 2637/2649				NPV= 2309/23					
99.74)		(				, , , (	, , , , , , , , , , , , , , , , , , , ,	, ,	
Cumulative Incide	ence IGRA	$_{+} = 11/31$	7=3.47%	Cumulative Inc	idence T	$s_{T+} = 1$	3/663=1.	96% (95%	
(95% CI: 1.87, 6.				CI: 1.11, 3.36)	1	51.			
Cumulative Incide		= 12/26	49=0.45%	Cumulative Inc	idence T	$s_{T_{-}} = 10$	)/2319=0	).43% (95%	
(95% CI: 0.24, 0.				CI: 0.22, 0.80)		51-		( )	
Cumulative Incide		$io_{IGRA} = 7$	'.66 (95%	Cumulative Incidence Ratio <sub>TST</sub> =4.55 (95% CI:					
CI: 3.41, 17.21)		10101		2.00, 10.32)					
Incidence density	rate <sub>IGRA</sub>	+ = NR		Incidence density rate <sub>TST+</sub> = NR					
Incidence density				Incidence density rate <sub>TST</sub> = NR					
Incidence density			VR.	Incidence density rate ratio <sub>TST</sub> = NR					
Other reported me				Other reported measure $_{TST}$ = OR=4.62 (95% CI:					
CI: 3.46, 18.06)				2.02, 10.58)					
		Compa	arison betwee	en tests (IGRA vs. TST)					
Ratio of cumulati	ve incide	nce ratio	s=1.68 (95% (	CI: 0.94, 3.03)					
Ratio of incidence	density	rate ratio	s=NA						
Other reported me	easure= (	OR = 1.7	1 (95% CI: 0.9	94, 3.11)					
Association betw	een test	results a	nd incidence	of active TB (if	applical	ble)			
I	GRA (Q	FT-GIT	)		T	ST≥15	mm		
	Incide	ence of	Total			Incide	nce of	Total	
	activ	re TB				activ	е ТВ		
	Yes	No				Yes	No		
IGRA +	11	306	317	TST +	-	13	218	231	
IGRA -	12	2637	2649	TST -		10	2741	2751	
indeterminate	NR	NR	16	indetermi	nate	0	0	0	
Total	23	2943	2966	Total		23	2959	2982	
			Test perform	ance parameter	S				
	IG	RA				TST			
Sensitivity = 11/2	3=47.839	% (95% (	CI: 29.24, 67.0	94) Sensitivity 74.37)	=13/23=	=56.52	% (95%	CI: 36.81,	
Specificity = 2637 90.65)	7/2943=8	39.6% (95	5% CI: 88.45,	Specificity 91.64, 93.5		/2959=	92.63%	(95% CI:	
PPV= 11/317=3.4	7% (95%	6 CI· 1 0	4 6 10)	PPV= 13/2		0% (05	% CI- 3	31 9 38)	
141 v - 203 // 2049	NPV= 2637/2649=99.55% (95% CI: 99.21, 99.74)					NPV= 2741/2751=99.64% (95% CI: 99.33, 99.80)			

G 1 41 T 11	ICDA	11/217	2.470/		• 1	12/221 5	(20/		
Cumulative Incid		F = 11/317=	Cumulative Incidence $_{TST+} = 13/231=5.62\%$						
(95% CI: 1.87, 6.		10/0640	0.450/	(95% CI: 3.23, 9.47) Cumulative Incidence <sub>TST</sub> . = 10/2741=0.36%					
Cumulative Incid		= 12/2649=	=0.45%			10/2/41=0	.36%		
(95% CI: 0.24, 0.		CD A 7 (	(050/ CI	(95% CI: 0.18, 0.67)					
Cumulative Incid	ence Ratio I	GRA = /.66	Cumulative Incidence Ratio $_{TST} = 15.48 (95\%)$						
3.41, 17.21)	4 ICD A	NID		CI: 6.86, 34.92)		NID.			
Incidence density				Incidence densit	•				
Incidence density				Incidence densi					
Incidence density			2 (0 #0 ( GY	Incidence densi			. (0.50/		
Other reported me	easure IGRA	A = OR = 7.90	) (95% CI:	Other reported i		OR=16.35	(95%		
3.46, 18.06)		~ .	•	CI: 7.08, 37.71)					
7 1 2 1 1				ests (IGRA vs. TS	<b>T</b> )				
Ratio of cumulati				0.28, 0.89)					
Ratio of incidence									
Other reported me									
Asso			esults and lo	evels of TB exposu					
	IGRA (spe			'	TST (specify				
_	Exposu		Total		Exposur		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	performanc	e parameters					
	IGRA			TST					
Sensitivity = NA				Sensitivity = NA					
Specificity = NA				Specificity = NA					
PPV = NA				PPV = NA					
NPV = NA				NPV = NA					
DOR (for T <sup>+</sup> calc	ulated) = NA	4		DOR (for T <sup>+</sup> calc	culated) = NA	1			
OR (crude; for T				OR (crude; for T					
OR (regression-ba				OR (regression-based; reported) = NA					
List of covariates		,		List of covariates: NA					
Other reported me	easure = NA	1		Other reported measure = NA					
•			n between to	ests (IGRA vs. TS	T)				
Ratio of DORs (fe									
Ratio of OR (cruc			A						
Ratio of ORs (reg									
Other reported me									
•	Association	ı between t	est results a	and BCG status (i	f applicable)				
	IGRA (spe			1	TST (specify				
	BCG s		Total			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		
				e parameters	- 1				
	IGRA	1050	or man	- Datamore 15	TST				
DOR (for T <sup>+</sup> calc		= NA		DOR (for T+ cale		NA			
OR (crude; for T									
	- Portou)		OR (crude; for T+ reported) = NA						
	ased: report	$P(A)_{ACDA} = N$	OR (regression-based; reported) TST = NA						
OR (regression-ba		$ed)_{IGRA} = N$	A	List of covariates	· •	$(a)_{TST} = NA$	Λ		

Other reported measu	re = NA		
<u> </u>	nent, concordance, and discor	Other reported measure = NA	1
		BCG vaccination status, and	or condition
Total sample	ratified by 131 cut-off value,	, Ded vaccination status, and	or condition
1 otal sample	TST ≥10mm	TST -	Total
IGRA +	231	86	317
IGRA -	430	2,219	2,649
		ŕ	
indeterminate	2	14	16
Total	663	2,319	2982
<b>Description</b>	1 1 1 1 1 1 1 1 1 1 1 DCC	11.11	
	g., total, if stratified by BCG or	condition – specify): total	
TST + threshold: ≥10	)mm		
Parameters	ST 0.040 0.404)		
Kappa = 0.38 (95% 0)	, ,		
	[1+2,219]/2,966 = 82.6% (95%)		
	0+86]/2,966 = 17.4% (95% CI:		
	nent, concordance, and discor		
	tratified 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
indatamainat -	0	16	16
maeterminate	V	10	
	231	2,751	2,982
Total  Description			
Total <b>Description</b>		2,751	
Total <b>Description</b>	g., total, if stratified by BCG or	2,751	
Total <b>Description</b> Sample definition (e.	g., total, if stratified by BCG or	2,751	
Total <b>Description</b> Sample definition (e. TST + threshold: ≥15	g., total, if stratified by BCG or 5mm	2,751	
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% (	g., total, if stratified by BCG or 5mm	2,751 condition – specify): total	
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16]	g., total, if stratified by BCG or 5mm CI: 0.50, 0.61)	2,751 condition – specify): total CI: 91.51, 93.41)	
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16]	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI:	2,751 condition – specify): total CI: 91.51, 93.41)	
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% 0 % concordance = [16] % discordance = [68]	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI:	2,751 condition – specify): total CI: 91.51, 93.41)	
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16%	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% CI: fy group 1):	2,751 condition – specify): total CI: 91.51, 93.41) 6.59, 8.48)	2,982
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68-Stratification (speci	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST - NA	2,982  Total  NA
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% 0 % concordance = [16] % discordance = [68]	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -	2,982 Total
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA	2,751  condition – specify): total  CI: 91.51, 93.41)  6.59, 8.48)  TST -  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% etc.) 64-154]/2,966 = 7.48% (95% CI: 64 group 1):  TST +  NA  NA  NA	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA	Total NA NA
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 · Stratification (speci)  IGRA + IGRA - indeterminate  Total  Description	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) (3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [168	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) (3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥15  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) (3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥13  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 * Stratification (specification (specification)	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci  IGRA +  IGRA -  indeterminate  Total  Description  Sample definition (e. TST + threshold: NA Parameters  Kappa = NA  % concordance = NA	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) (3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci  IGRA +  IGRA -  indeterminate  Total  Description  Sample definition (e. TST + threshold: NA Parameters  Kappa = NA  % concordance = NA % discordance = NA % discordance = NA	231 g., total, if stratified by BCG or 5mm CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  ONA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA	Total NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci  IGRA +  IGRA -  indeterminate  Total  Description  Sample definition (e. TST + threshold: NA Parameters  Kappa = NA  % concordance = NA  % discordance = NA	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  Sq., total, if stratified by BCG or 6.4  fy group 2):	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA  Condition – specify): NA	Total NA NA NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥13  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 * Stratification (specion	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  Sq., total, if stratified by BCG or 5mm  TST +  TST +  TST +  NA  NA  NA  NA  NA  NA  NA  NA  TST +  TST +  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  TCONDITION NA  TST -  TST -  TST -  NA  NA  NA  NA  NA  NA  TCONDITION NA  TST -  T	Total NA NA NA NA Total
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci  IGRA + IGRA - indeterminate  Total  Description  Sample definition (e. TST + threshold: NA Parameters  Kappa = NA % concordance = NA % discordance = NA % discordance = NA Stratification (speci	g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) (3+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  Sq., total, if stratified by BCG or 1.5	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  TCONDITION  TST -  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	Total NA NA NA NA NA NA NA NA NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci  IGRA + IGRA - indeterminate  Total  Description  Sample definition (e. TST + threshold: NA Parameters  Kappa = NA % concordance = NA % discordance = NA Stratification (speci	g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	Total NA
Total  Description  Sample definition (e. TST + threshold: ≥13  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (speci  IGRA + IGRA - indeterminate  Total  Description  Sample definition (e. TST + threshold: NA  Parameters  Kappa = NA  % concordance = NA  % discordance = NA  Stratification (speci	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  SI, total, if stratified by BCG or 5m 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  TST -  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	Total NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 Stratification (specion of the second of the se	g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	Total NA
Total  Description  Sample definition (e. TST + threshold: ≥1:  Parameters  Kappa = 0.55 (95% € % concordance = [16 % discordance = [68 * Stratification (specification (s	231 g., total, if stratified by BCG or 5mm  CI: 0.50, 0.61) 63+2581]/2,966 = 92.52% (95% +154]/2,966 = 7.48% (95% CI: fy group 1):  TST +  NA  NA  NA  NA  SI, total, if stratified by BCG or 5m 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2,751  condition – specify): total  CI: 91.51, 93.41) 6.59, 8.48)  TST -  NA  NA  NA  NA  TST -  NA  NA  NA  NA  NA  NA  NA  NA  NA  N	Total NA

Parameters	
Kappa = NA	
% concordance = NA	

## **Conclusions**

## **Authors:**

% discordance = NA

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

# **Immunocompromised**

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

Study details

First author surname year of publication: Ahmadinejad 2013<sup>120</sup>

**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])

	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 patien	ts with	valid resu	lts for both IC	GRA and TST:	164					
					rder (if applica						
					xposure group						
Non-exp				y of exposure							
Exposed	l 1 (specif										
Exposed	ed 2 (specify): NA										
Exposed	osed 3 (specify): NA										
Exposed	l 4 (specif	y):	NA								
Tests											
				y, timing for nufacturer	Cut-off values/thresholds Definition of test+			Other information			
IGRA (QFT- GIT)	QuantiFI (QFT-Gi		B Gold In	-Tube test	NR						
TST	and 1 mI designate tubes. Af they were after acquain, and were kep of interference (ELISA)  0.1 mL fi solution inches (with an a	was ad ed as the fter vigore sent to uisition  s were reat 37°C. ged at 20 the result at >70°c ron-gam linked in the from 5 tu was injected at 20 changle of a sent to the 5 changle of	eshaken ar Then the soon of the laboral through the soon of the laboral through the soon of the laboral through through the laboral through throug	h of the 3 tubes en, and antigering of the tubes attory up to 6 h and incubated samples were RCF rate for 15 ma samples measurement		st e test wa	≥10	For prevention of potential boosting effect of TST on QFT, blood sampling and purified protein derivative (PPD) injection were done simultaneously for all patients			
Associa		oon tost	raculte ar	d incidence o	f active TB (if a	annlica	hla)				
11550014	CLOIL DOCT	IGR.			(II (II (		TST				
		Incid	ence of ve TB	Total		Incide	ence of TB	f Total			
IGR	A+	NA	NA	NA	TST +	NA	NA	NA			
	RA -	NA	NA	NA NA	TST -	NA	NA				
	minate	NA NA	NA NA	NA NA	Indeterminate	NA	NA NA				
			+	+							
10	tal	NA	NA	NA Seet newforms	Total	NA	NA	NA			
		ICD		est performa	nce parameters		тст				
Camait:	ityr — NT A	IGR.	1		Canaitivit		TST				
	ity = NA				Sensitivity = $N$						
	ity = NA				Specificity = N	A					
PPV = NPV					$\frac{PPV = NA}{NDV - NA}$						
	$NPV = NA$ $NPV = NA$ Cumulative Incidence $_{IGRA^{+}} = NA$ Cumulative Incidence $_{TST^{+}} = NA$										
					Cumulative Inc						
Cumulative Incidence $_{IGRA-} = NA$ Cumulative Incidence $_{TST-} = NA$											

Cumulative Incide	ence Ratio IC	$g_{RA} = NA$		Cumulative Incidence Ratio <sub>TST</sub> = NA					
Incidence density	rate <sub>IGRA+</sub> =	NA		Incidence density rate $_{TST+} = NA$					
Incidence density	rate <sub>IGRA-</sub> = ]	NA		Incidence density rate TST- = NA					
Incidence density				Incidence density rate ratio $_{TST} = NA$					
Other reported me				Other reported measure <sub>TST</sub> = NA					
•			n betwe	en tests (IGRA vs. TST)					
Ratio of cumulativ				(					
Ratio of incidence									
Other reported me			17.1						
			ecults a	nd levels of TR e	vnosure (if a	nnlicable)			
	RA (QFT-G		courts ar	nd levels of TB exposure (if applicable)  TST (≥10mm)					
101	Exposur		Total		Exposure		Total		
	_	Low/No	Total		High/Yes	Low/No	Total		
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		
1 Utai	J					139	104		
	IGRA	Test	periorii	nance parameter	TST				
Sensitivity = $0/5$ =				Sensitivity = $0/5$					
Indeterminate ex				Specificity = 13		50/ <sub>2</sub> (0.50/ <sub>2</sub> C	T. 77 12		
		0/ (050/ C)	Γ.	88.59)	3/139 – 83.0.	370 (9370 C	1. / /.12,		
Specificity = 121/71.44, 84.32)	134 – 78.37	% (93% C	l:	88.39)					
Indeterminate in	aludad								
		0/ (0 <b>5</b> 0/ C)	r.						
Specificity = 126/	139 – 79.23	% (93% C	l:						
72.29, 84.82)	20/			DDV - 0/26 - 0	000/				
PPV = 0/33 = 0.00				PPV = 0/26 = 0.		50/ CI 01/	0.00.44)		
Indeterminate ex		'0/ CT 01 0	٠	NPV = 133/138	= 96.38% (9	5% CI: 91.	8, 98.44)		
NPV = 121/126 = 0.000	96.03% (93	% CI: 91.0	15,						
98.29) Indeterminate in	aludad								
		30/ CI, O1 2	0						
NPV = 126/131 = 98.36)	90.18% (93	% CI: 91.3	00,						
DOR (for T <sup>+</sup> calcu	$\frac{1}{10000000000000000000000000000000000$	10		DOR (for T <sup>+</sup> coloulated) = 0.00					
				DOR (for $T^+$ calculated) = 0.00					
OR (crude; for T				OR (crude; for $T^+$ reported) = NR					
OR (regression-ba		(a) = NR		OR (regression-based; reported) = NR					
List of covariates:				List of covariates:					
Other reported me			. h . t	Other reported measure = NR					
D-4:- CDOD (C			n betwe	en tests (IGRA v	s. 181)				
Ratio of DORs (fo			D						
Ratio of OR (crud									
Ratio of ORs (regi			) = NR						
Other reported me				1, 1500	/ / / 6				
			est resu	lts and BCG sta	` 11				
IG	GRA (QFT-				TST (≥1				
	BCG s		Total			status	Total		
I CD 4	Yes	No		mcm :	Yes	No	2.5		
IGRA +	28	5	33	TST +	23	3	26		
IGRA -	118	8	126	TST -	128	10	138		
Indeterminate	5	0	5	Indeterminat	+	0	0		
Total	151	13	164	Total	151	13	164		
Test performance parameters									
10111	IGRA		perforn	nance parameter	s TST				

DOR (for T <sup>+</sup> calculated	$O_{IGRA} = 0.38 (95\% \text{ CI: } 0.11)$	DOR (for T+ calculated) $_{TST}$ =	0.60 (95% CI:	
1.24)		0.15, 2.34)		
OR (crude; for T <sup>+</sup> repor		OR (crude; for T+ reported) =	= NR	
OR (regression-based; 1	reported) $_{IGRA} = NR$	OR (regression-based; reported) $_{TST} = NR$		
List of covariates: NR		List of covariates: NR		
Other reported measure		Other reported measure = NR	2	
	nt, concordance, and disc			
<b>*</b>	tified by TST cut-off valu	e, BCG vaccination status, and	d/or condition	
Total sample				
	TST +	TST -	Total	
IGRA +	13	20	33	
IGRA -	12	114	126	
Indeterminate	1	4	5	
Total	26	138	164	
Description				
		or condition – specify): total		
TST + threshold: ≥10m	m			
Parameters				
Indeterminate exclude	ed			
Kappa = $0.32$ (95% CI:	0.17, 0.48)			
Indeterminate include	d			
Kappa = $0.32$ (95% CI:	0.17, 0.47)			
Indeterminate exclude				
	59 = 79.87% (95% CI: 72.	97, 85.37)		
Indeterminate include				
	64 = 79.88% (95% CI: 73.	09, 85.3)		
	% (95% CI: 14.63, 27.03)			
<b>Stratification (specify</b>				
	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				
<b>Stratification (specify</b>	group 2)			
	TST +	TST -	Total	
IGRA +	NR	NR	NR	
IGRA -	NR	NR	NR	
Indeterminate	NR	NR	NR	
Total	NR	NR	NR	
Description				
•	total, if stratified by BCG	or condition – specify): NR		
TST + threshold: NR	,			
Parameters Parameters				
Kappa = NR				
% concordance = NR				
% discordance = NR				
, o albeolaunee 1410				

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

### **Study details**

First author surname year of publication: Al Jahdali 2013<sup>121</sup>

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

Transpor or patternes test					
	Total N	Total	Total N	Total N	Total N
	(tested)	N	(test-)	(indeterminate)	(test results
				,	available)
		(test+)			,
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-exp	osed			ikelihood of						
Exposed	1 (specif	y):	High likel	lihood of LT	BI (contact with T	B case,	abnorma	l chest X-ray,		
			DM, imm	unosuppressa	ant in the last 12 N	M, failed	l kidney t	ransplant or		
			BMI≤20)							
Exposed	2 (specif	<b>y</b> ):	NA							
Exposed	3 (specif	<b>y</b> ):	NA							
Exposed	4 (specif	<b>y</b> ):	NA							
Tests										
	Assay	used, m	ethodolog	gy, timing	Cut-off value			Other		
	1		neasurem	ent,	Definition	n of test	t+	information		
			ufacturer							
IGRA				ling to the	A value of 0.35			ļ		
			nstruction		for the relationsh		•			
				ed in each	TB antigen tube]		•			
				containing	negative control					
	_		ontrol), 1 v		considered to be					
			emaggluti		If the IFN- γ leve			IGRA blood		
	_		and 1 with		IU/ml in the TB	_		was collected		
	_	•	6, CFP-10		the mitogen cont		-	before the		
			bes were i		$(\geq 0.5 \text{ IU/ml})$ , the		ıs	administration		
	_		20 h at 37		recorded as nega	itive		of		
		_		tubes were				the TST		
			the plasm							
				nd frozen at						
			ment of II							
			equently p	erformed						
	in batch		4.1 .4.1			240		37.		
TST				study was	An induration of	NA				
			erculin Pui		in transverse dia					
			re (Mantor nanufactur		as the threshold t					
	Sanofi I		iaiiuiaciui	ed by	test results as po					
	Sanon	astcui			Patients with an					
	Limited	Toronto	o, Ontario,	Canada	less than 10mm upon initial					
		*	perienced		testing were cons					
		-	-	TSTs. Five	negative and wer					
		-	0.1 ml) of		second TST with					
		,	derivative		to elicit a potenti					
	_	-	ed via intra	` '	response. The re-					
			olar surfa		from the 2-step t					
			not have t		in all further ana	_				
	arteriov	enous ve	ssel. The r	esponses	was considered t					
			72 h by tl	-	either the 1st or 2					
			ring the n		a response of 10	mm or r	nore			
		y schedul	_							
	HD visi	t								
Associat	ion betw			d incidence	of active TB (if a					
		IGR/					TST			
			ence of	Total			ence of	Total		
		activ	ye TB			activ	re TB			
		Yes	No			Yes	No			
IGR	A +	NA	NA	NA	TST +	NA	NA	NA		

IGRA -	NA	NA	NA	TST -	NA	NA	NA	
indeterminate	NA	NA	NA	indeterminate		NA	NA	
Total	NA	NA	NA	Total	NA	NA	NA	
				ance parameter				
	IGRA		•	TST				
Sensitivity = NA				Sensitivity = NA				
Specificity = NA				Specificity = NA				
PPV = NA				PPV = NA				
NPV = NA				NPV = NA				
Cumulative Incide	ence <sub>IGRA+</sub> =	NA		Cumulative Ir	ncidence TS	$S_{T+} = NA$		
Cumulative Incide				Cumulative Ir				
Cumulative Incide	ence Ratio IC	$g_{RA} = NA$		Cumulative Ir			A	
Incidence density				Incidence den				
Incidence density				Incidence den				
Incidence density				Incidence den			1	
Other reported me				Other reported		$_{\text{TST}} = \text{NA}$		
				n tests (IGRA v	s. TST)			
Ratio of cumulativ								
Ratio of incidence			ÍA .					
Other reported me			*.			10 10 11	`	
			esults an	d levels of TB e			e)	
IGI	RA (QFT-G		T . 1	-		10mm)	T . 1	
	Exposu		Total			ure level	Total	
ICDA	High/Yes		65	TOTAL	High/Yes	_	26	
IGRA +	51	14	65	TST +	19	7	26	
IGRA -	103	32 ND	135	TST -	135	39	174	
indeterminate Total	NR 154	NR 46	NR 200	indeterminate Total	NR 154	NR 46	NR 200	
Total	134			ance parameter		40	200	
	IGRA	1681	per for in	ance parameter		ST		
Sensitivity = 51/1		6 (95% CI:	26.00	Sensitivity = 19			CI: 8.04	
41.00)	51 55.127	0 (2270 C1.	20.00,	18.47)	7131 12	.5 170 (5570	C1. 0.0 1,	
Specificity = 32/4	6 = 69.57%	(95% CI: 5	55.19.	Specificity = 39	9/46 = 84.7	78% (95% C	I: 71.78.	
80.92)		(,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,	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 = 2				NPV = 39/174 = 22.41% (95% CI: 16.85, 29.17)				
31.54)								
DOR (for T+ calc	ulated) = 1.	13 (95% CI	[: 0.55,	DOR (for T <sup>+</sup> ca	lculated) =	= 0.78 (95%	CI: 0.31,	
2.31)				2.00)				
OR (crude; for T <sup>+</sup>				OR (crude; for				
OR (regression-ba		ed) = NR		OR (regression		ported) = NR	2	
List of covariates:				List of covariat				
Other reported me			• .	Other reported		NR		
D. C. CDOD CO				n tests (IGRA v	s. TST)			
Ratio of DORs (fo			_	1: 0./9, 2.64)				
Ratio of OR (crud								
Ratio of ORs (reg			ı) – NK					
Other reported me			ost moore	ts and DCC sta	tus (if ar-	dicable		
	Association IGRA	between t	est resul	ts and BCG sta		rst		
	BCG s	etatue	Total			G status	Total	
	Yes	No	Total		Yes	No	] I Otal	
IGRA +	NR	NR	NR	TST +	NR	NR	NR	
10101	1111	1 117	1117	101	1111	1117	1 117	

IGRA -	NID	ND	NID	TST -	ND	ND	NID			
	NR	NR	NR		NR	NR	NR			
indeterminate	NR	NR	NR	indeterminate	NR	NR	NR			
Total	NR	NR	NR	Total	NR	NR	NR			
	ICD	Test	performa	nce parameters	OD.	200				
	IGRA					ST				
DOR (for T calcu				DOR (for T+ c						
	OR (crude; for $T^+$ reported) = NR  OR (crude; for $T^+$ reported) = NR									
	OR (regression-based; reported) $_{IGRA} = NR$ OR (regression-based; reported) $_{TST} = NR$									
List of covariates: NR  List of covariates: NR										
Other reported measure = NR  Other reported measure = NR  Between-test agreement, concordance, and discordance (if applicable)										
9				`						
•	e stratified	by TST cu	it-off valu	e, BCG vaccination	on status	, and/or c	ondition			
Total sample										
		TST +		TST -			Total			
IGRA +		21		44			65			
IGRA -		5		130			135			
indeterminate		NR		NR			NR			
Total		26		174			200			
Description										
		if stratified	l by BCG	or condition – spec	cify): tota	1				
TST + threshold:	≥10mm									
Parameters										
Kappa = $0.34 (95)$										
% concordance =	151/200 = 7	5.50% (95	% CI: 69.	10, 80.94)						
% discordance = 4	49/200 = 24.	5% (95%	CI: 19.06,	30.90)						
Stratification (sp	ecify group	1)								
		TST +		TST -	-		Total			
IGRA +		NR		NR			NR			
IGRA -		NR		NR	NR		NR			
indeterminate		NR		NR		NR				
Total		NR		NR			NR			
Description										
Sample definition	(e.g., total,	if stratified	l by BCG	or condition – spec	cify): NR					
TST + threshold:	NR		•	•	•					
Parameters										
Kappa = NR										
% concordance =	NR									
% discordance = 1	NR									
Stratification (sp	ecify group	2)								
` 1		TST +		TST -			Total			
IGRA +		NR		NR			NR			
IGRA -		NR		NR			NR			
indeterminate		NR	+	NR			NR			
Total		NR		NR			NR			
Description				1110			1,11			
	(e.g. total	if stratified	1 by BCG	or condition – spec	cify)· NR					
TST + threshold:		saaaaa	, U, DCO	or condition spec	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,					
Parameters	. 111									
Kappa = NR										
% concordance =	NP									
% discordance = 1										
70 discordance = 1	NIV.		Othor	nutaomas.						
Tost and out off	Test and cut-off (if Adverse events n/N (%) Health related quality									
1 CSt and Cut-off	(11	Auve	ise events	э п/14 ( /0)		meann re	iaicu quaiity			

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

### Study details

First author surname year of publication: Ates 2009<sup>122</sup>

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	Total N (test-)	Total N (indeterminate)	Total N (test results available)
		(test+)			
IGRA (QFT-GIT):	275	115	131	29	246
<b>TST</b> (≥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-exp	nosed		No Tuber	culosis exposu	re				
	1 1 (specify			osis exposure	10				
	1 2 (specify		NA	isis exposure					
	1 2 (specify 1 3 (specify		NA						
	1 4 (specify	,	NA						
Tests	14 (specify	(); <u> </u>	INA						
1 6515	A ssay v	used met	hadalagr	timing for	Cut-off valu	os/thro	holds	Other	
				, timing for ufacturer	Definitio			information	
IGRA				rmed in two	According to			Information	
IGNA	-		-	ected first into	analysis softw	-			
	each of th				were recorded				
				trol tube, a	negative and i				
				d a mitogen	The whole blo				
				ted at 37°C as	just before he				
	soon as po				Just before he	modiary	515	Observers were	
	incubation							blinded to the	
		-		vas removed				results of the	
				ELISA was				TST	
	performed								
				ufacturer's					
	specificat	ions and	the ELISA	A readout was					
	analyzed	using the	QTF-GIT	analysis					
	software								
TST	TST were	administ	ered and	its results	A skilled nurs	NA			
				o American	the transverse				
				(1). Briefly, a	indurations w				
	trained nu	-		•	ruler, and an o	-			
	tuberculin				physician veri				
				on of 0.1 ml	results. A pos				
	(5 tubercu			ea protein	result was defined as an induration diameter of 10				
	derivative			ulaamia) imta	mm or larger				
	the volar			Bulgaria) into	mm or larger				
Associa					active TB (if ap	nliaahl	(a)		
Associa	tion betwe			i incluence of	active 1B (II ap				
		IGRA		Total			rst ence of	Total	
				1 otai			ence of e TB	Total	
			e TB						
ICI	RA+	Yes NA	No NA	NA	TST +	Yes NA	No NA	NA	
	RA -	NA NA	NA NA	NA NA	TST -	NA	NA	NA NA	
	rminate	NA NA	NA NA	NA NA	Indeterminate	NA	NA	NA NA	
	otal	NA	NA	NA NA	Total	NA	NA	NA NA	
1,	- Cui	11/1		L	ce parameters	11/1	11/1	11/1	
		IGRA		or per for man	co parameters	7	ΓST		
Sensitiv	vity = NA	IGINA			Sensitivity = N				
					Specificity = $N$				
PPV = 1					$\frac{\text{Specificity}}{\text{PPV} = \text{NA}}$				
NPV = NA					NPV = NA				
Cumulative Incidence $_{IGRA+} = NA$					Cumulative Inc	idence -	$_{\Gamma ST+}=N$	A	
Cumulative Incidence <sub>IGRA+</sub> = NA  Cumulative Incidence <sub>IGRA-</sub> = NA					Cumulative Inc				
	Cumulative Incidence <sub>IGRA</sub> . = NA  Cumulative Incidence Ratio <sub>IGRA</sub> = NA						Ratio <sub>TST</sub>		
	Incidence density rate $_{IGRA}$ = NA								
	ce density i				Incidence density rate $_{TST+} = NA$ Incidence density rate $_{TST-} = NA$				
moracii	co delibity i	ute IGRA-	T 41 7		including delisity rate TST. – IVA				

Incidence density rate ratio   Incidence   NA								
Comparison between tests (IGRA vs. TST)	Incidence density	rate ratio <sub>IGR</sub>	A = NA		Incidence der	sity rate rat	$io_{TST} = NA$	A
Ratio of cumulative incidence ratios = NA Ratio of incidence density rate ratios = NA  Association between test results and levels of TB exposure (if applicable)    TST≥10m	Other reported me	asure <sub>IGRA</sub> =	NA		Other reporte	d measure T	ST = NA	
Ratio of incidence density rate ratios = NA					n tests (IGRA v	s. TST)		
Other reported measure = NA	Ratio of cumulativ	e incidence	ratios = NA	A				
Association between test results and levels of TB exposure (if applicable)   IGRA (QFT-GIT)	Ratio of incidence	density rate	ratios = N	A				
Total   Exposure level   High/Yes   Low/No   Total   Exposure level   High/Yes   Low/No   High/Yes   Low	Other reported me	asure = NA						
Exposure level   High/Yes   Low/No   GRA +   10   105   115   TST +   5   87   92     IGRA -   7   124   131   TST -   12   155   167     Indeterminate   NR   NR   29   Indeterminate   NR   NR   16     Total				esults an	d levels of TB e			2)
High/Yes   Low/No   IIS   TST +   5   87   92	IGI			_				
IGRA +		_	1	Total				Total
IGRA -								
Indeterminate								
Total								167
Test performance parameters   IGRA		NR	NR			NR	NR	
TGRA	Total							275
Sensitivity = 10/17 = 58.82% (95% CI: 36.01, 78.39)   Sensitivity = 5/17 = 29.41% (95% CI: 13.28, 78.39)   Salian   Sensitivity = 15/17 = 29.41% (95% CI: 13.28, 78.39)   Specificity = 124/229 = 54.15% (95% CI: 36.04)   Specificity = 125/243 = 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, NPV = 155/167 = 92.81% (95% CI: 87.86, 97.39)   S.84)   NPV = 155/167 = 92.81% (95% CI: 0.25, 2.17)     OR (for T* calculated) = 1.68 (95% CI: 0.62, 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)   1.45)     List of covariates: NR Other reported measure = NR			Test <sub>I</sub>	performa	ance parameter			
S3.13    Specificity = 124/229 = 54.15% (95% CI:   Specificity = 155/243 = 64.05% (95% CI: 57.83, 47.68, 60.48)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 0.25, 2.15)   Specificity = 155/243 = 64.05% (95% CI: 57.83, 20)   Specificity = 155/243 = 64.05% (95% CI: 69.83, 20)   Specificity = 155/243 = 64.05% (95% CI: 234, 12.10)   Specificity = 155/243 = 64.05% (95% CI: 0.25, 2.45% (10.95% CI: 0.45, 2.45% (10.95								
Specificity = 124/229 = 54.15% (95% CI:   Specificity = 155/243 = 64.05% (95% CI: 57.83, 69.83)	•	7 = 58.82%	(95% CI: 3	6.01,	•	17 = 29.41%	% (95% CI:	: 13.28,
47.68, 60.48   69.83   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)   95.84   95% CI: 2.34, 12.10     DOR (for T* calculated) = 1.68 (95% CI: 0.62, 4.58)   90.00 (for T* calculated) = 0.74 (95% CI: 0.25, 2.17)     OR (crude; for T* reported) = NR								
NPV = 124/131 = 94.66% (95% CI: 89.38, 97.39)		$229 = 54.15^{\circ}$	% (95% CI	:	1	55/243 = 64	.05% (95%	CI: 57.83,
NPV = 124/131 = 94.66% (95% CI: 89.38, 97.39)	PPV = 10/115 = 8.	.69% (95% (	CI: 4.792,	15.27)	PPV = 5/92 = 5	5.43% (95%	CI: 2.34, 1	2.10)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	NPV = 124/131 =	94.66% (95	% CI: 89.3	8,				
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	97.39)				95.84)			
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	DOR (for T <sup>+</sup> calcu	lated) = 1.63	8 (95% CI:	0.62,	DOR (for T <sup>+</sup> ca	lculated) =	0.74 (95%	CI: 0.25,
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	4.58)				2.17)			
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	OR (crude; for T <sup>+</sup> 1	reported) = 1	NR		OR (crude; for	T <sup>+</sup> reported)	=NR	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	OR (regression-ba	sed; reported	d) = 1.30 (0)	0.43,	OR (regression	-based; repo	orted) = 0.4	9 (0.17,
$ \begin{array}{ c c c c } \hline \textbf{Other reported measure} = NR & \textbf{Other reported measure} = NR \\ \hline \textbf{Comparison between tests (IGRA vs. TST)} \\ \hline \textbf{Ratio of DORs (for $T^+$ calculated)} = 2.27 (95\% \text{ CI: } 1.07, 4.81) \\ \hline \textbf{Ratio of OR (crude; for $T^+$ reported)} = NR \\ \hline \textbf{Ratio of ORs (regression-based; reported)} = 2.65 (95\% \text{ CI: } 1.21, 5.82) \\ \hline \textbf{Other reported measure} = NR \\ \hline \textbf{Association between test results and BCG status (if applicable)} \\ \hline \textbf{IGRA} & \textbf{TST} \\ \hline \textbf{BCG status} & \textbf{Total} & \textbf{BCG status} & \textbf{Total} \\ \hline \textbf{Yes} & \textbf{No} & \textbf{STST} \\ \hline \textbf{IGRA} + & 57 & 58 & 115 & \textbf{TST} + & 45 & 47 & 92 \\ \hline \textbf{IGRA} - & 61 & 70 & 131 & \textbf{TST} - & 88 & 79 & 167 \\ \hline \textbf{Indeterminate} & \textbf{NR} & \textbf{NR} & 29 & \textbf{Indeterminate} & \textbf{NR} & \textbf{NR} & 16 \\ \hline \textbf{Total} & & 275 & \textbf{Total} & 275 \\ \hline \textbf{Total} & & 275 & \textbf{Total} & 275 \\ \hline \textbf{DOR (for $T^+$ calculated)}_{IGRA} = 1.13 (95\% \text{ CI: } 0.68, \ 0.51, 1.43) \\ \hline \textbf{OR (crude; for $T^+$ reported)} = \textbf{NR} & \textbf{OR (regression-based; reported)}_{IGRA} = 1.14 (95\% \\ \hline \textbf{CI: } 0.68, 1.92) & \textbf{CI: } 0.50, 1.51) \\ \hline \textbf{List of covariates: NR} & \textbf{Other reported measure} = \textbf{NR} \\ \hline \end{tabular}$	3.91)				1.45)			
$ \begin{array}{ c c c c } \hline \textbf{Comparison between tests (IGRA vs. TST)} \\ \hline \textbf{Ratio of DORs (for $T^+$ calculated) = 2.27 (95\% CI: 1.07, 4.81)} \\ \hline \textbf{Ratio of OR (crude; for $T^+$ reported) = NR} \\ \hline \textbf{Ratio of ORs (regression-based; reported) = 2.65 (95\% CI: 1.21, 5.82)} \\ \hline \textbf{Other reported measure = NR} \\ \hline \hline \textbf{Association between test results and BCG status (if applicable)} \\ \hline \textbf{IGRA} & \textbf{TST} \\ \hline \textbf{BCG status} & \textbf{Total} & \textbf{BCG status} \\ \hline \textbf{Yes} & \textbf{No} & \textbf{TST} \\ \hline \textbf{1GRA} & \textbf{TST} + \textbf{45} & \textbf{47} & \textbf{92} \\ \hline \textbf{IGRA} & \textbf{57} & \textbf{58} & \textbf{115} & \textbf{TST} + \textbf{45} & \textbf{47} & \textbf{92} \\ \hline \textbf{IGRA} & \textbf{61} & \textbf{70} & \textbf{131} & \textbf{TST} - \textbf{88} & \textbf{79} & \textbf{167} \\ \hline \textbf{Indeterminate} & \textbf{NR} & \textbf{NR} & \textbf{29} & \textbf{Indeterminate} & \textbf{NR} & \textbf{NR} & \textbf{16} \\ \hline \textbf{Total} & \textbf{275} & \textbf{Total} & \textbf{275} \\ \hline \textbf{Test performance parameters} \\ \hline \textbf{IGRA} & \textbf{IGRA} & \textbf{1.13 (95\% CI: 0.68, 0.51, 1.43)} \\ \hline \textbf{OOR (for $T^+$ calculated)}_{IGRA} = \textbf{1.13 (95\% CI: 0.68, 0.51, 1.43)} \\ \hline \textbf{OR (regression-based; reported)} & \textbf{NR} & \textbf{OR (regression-based; reported)}_{IGRA} = \textbf{1.14 (95\% CI: 0.50, 1.51)} \\ \hline \textbf{List of covariates: NR} & \textbf{Other reported measure = NR} \\ \hline \end{tabular}$								
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Other reported me						NR .	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $					,	s. TST)		
$ \begin{array}{ c c c c } \hline \text{Ratio of ORs (regression-based; reported)} = 2.65 \ (95\% \ \text{CI: } 1.21, 5.82) \\ \hline \textbf{Other reported measure} = NR \\ \hline \hline \textbf{Association between test results and BCG status (if applicable)} \\ \hline \textbf{IGRA} & \textbf{TST} \\ \hline \textbf{BCG status} & \textbf{Total} & \textbf{BCG status} & \textbf{Total} \\ \hline \textbf{Yes} & \textbf{No} & \textbf{Yes} & \textbf{No} \\ \hline \textbf{IGRA} + & 57 & 58 & 115 & \textbf{TST} + & 45 & 47 & 92 \\ \hline \textbf{IGRA} - & 61 & 70 & 131 & \textbf{TST} - & 88 & 79 & 167 \\ \hline \textbf{Indeterminate} & \textbf{NR} & \textbf{NR} & 29 & \textbf{Indeterminate} & \textbf{NR} & \textbf{NR} & 16 \\ \hline \textbf{Total} & & \textbf{275} & \textbf{Total} & & \textbf{275} \\ \hline \textbf{Total} & & \textbf{STST} \\ \hline \textbf{DOR (for $T^+$ calculated)}_{IGRA} = 1.13 \ (95\% \ \text{CI: } 0.68, \\ 1.86) & & 0.51, 1.43) \\ \hline \textbf{OR (crude; for $T^+$ reported)} = \textbf{NR} & \textbf{OR (crude; for $T^+$ reported)} = \textbf{NR} \\ \hline \textbf{OR (regression-based; reported)}_{IGRA} = 1.14 \ (95\% \\ \textbf{CI: } 0.68, 1.92) & \textbf{CI: } 0.50, 1.51) \\ \textbf{List of covariates: NR} & \textbf{Other reported measure} = \textbf{NR} \\ \hline \end{array}$					: 1.07, 4.81)			
$ \begin{array}{ c c c c } \hline \textbf{Other reported measure} = NR \\ \hline & \textbf{Association between test results and BCG status (if applicable)} \\ \hline \textbf{IGRA} & \textbf{TST} \\ \hline & BCG \text{ status} & Total & BCG \text{ status} & Total \\ \hline & Yes & No & Yes & No & Yes & No \\ \hline \hline \textbf{IGRA} + & 57 & 58 & 115 & TST + & 45 & 47 & 92 \\ \hline \textbf{IGRA} - & 61 & 70 & 131 & TST - & 88 & 79 & 167 \\ \hline \textbf{Indeterminate} & NR & NR & 29 & Indeterminate & NR & NR & 16 \\ \hline \textbf{Total} & & 275 & Total & & 275 \\ \hline \hline \textbf{Total} & & 275 & Total & & 275 \\ \hline \textbf{TOTAL} & & & & & & & & & & & & & & & & & & &$								
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			d; reported	) = 2.65 (	(95% CI: 1.21, 5	.82)		
$ \begin{tabular}{ c c c c c c c } \hline IGRA & Total & BCG status & Total & Yes & No & Yes & $								
	I	Association	between t	est resul	ts and BCG sta	tus (if appli	cable)	
				Total				Total
							<del></del>	
					_		+	<b>†</b>
Total275Total275Test performance parametersIGRATSTDOR (for T+ calculated) $_{IGRA} = 1.13$ (95% CI: 0.68, 0.51, 1.43)OR (crude; for T+ reported) = NROR (crude; for T+ reported) = NROR (regression-based; reported) $_{IGRA} = 1.14$ (95% CI: 0.50, 1.51)OR (regression-based; reported) $_{TST} = 0.87$ (95% CI: 0.50, 1.51)List of covariates: NRList of covariates: NROther reported measure = NROther reported measure = NR							+	
		NR	NR		_	e NR	NR	
$ \begin{array}{ c c c } \hline \textbf{IGRA} & \textbf{TST} \\ \hline DOR (for T^+ calculated)_{IGRA} = 1.13 \ (95\% \ CI: \ 0.68, \\ 1.86) & 0.51, \ 1.43) \\ \hline OR (crude; for T^+ reported) = NR & OR (crude; for T+ reported) = NR \\ \hline OR (regression-based; reported)_{IGRA} = 1.14 \ (95\% \\ \hline CI: \ 0.68, \ 1.92) & CI: \ 0.50, \ 1.51) \\ \hline List of covariates: NR & List of covariates: NR \\ \hline Other reported measure = NR & Other reported measure = NR \\ \hline \end{array} $	Total							275
$\begin{array}{lll} DOR \ (for \ T^+ \ calculated)_{IGRA} = 1.13 \ (95\% \ CI: \ 0.68, \\ 1.86) & 0.51, \ 1.43) \\ OR \ (crude; \ for \ T^+ \ reported) = NR & OR \ (crude; \ for \ T^+ \ reported) = NR \\ OR \ (regression-based; \ reported)_{IGRA} = 1.14 \ (95\% \\ CI: \ 0.68, \ 1.92) & CI: \ 0.50, \ 1.51) \\ List \ of \ covariates: \ NR & List \ of \ covariates: \ NR \\ Other \ reported \ measure = NR & Other \ reported \ measure = NR \\ \end{array}$			Test	performa	ance parameter			
$ \begin{array}{ll} 1.86) & 0.51, 1.43) \\ \hline OR (crude; for T^+ reported) = NR & OR (crude; for T+ reported) = NR \\ \hline OR (regression-based; reported)_{IGRA} = 1.14 (95\% \\ CI: 0.68, 1.92) & CI: 0.50, 1.51) \\ List of covariates: NR & List of covariates: NR \\ \hline Other reported measure = NR & Other reported measure = NR \\ \hline \end{array} $								
$ \begin{array}{lll} \text{OR (crude; for T}^+\text{reported}) = \text{NR} & \text{OR (crude; for T}^+\text{ reported}) = \text{NR} \\ \text{OR (regression-based; reported)}_{\text{IGRA}} = 1.14 \ (95\% \\ \text{CI: } 0.68, 1.92) & \text{CI: } 0.50, 1.51) \\ \text{List of covariates: NR} & \text{List of covariates: NR} \\ \text{Other reported measure} = \text{NR} & \text{Other reported measure} = \text{NR} \\ \end{array} $	,	lated) <sub>IGRA</sub> =	1.13 (95%	CI: 0.68		calculated)	TST = 0.85 (	(95% CI:
OR (regression-based; reported) $_{IGRA} = 1.14$ (95% CI: 0.68, 1.92) OR (regression-based; reported) $_{TST} = 0.87$ (95% CI: 0.50, 1.51) List of covariates: NR List of covariates: NR Other reported measure = NR		reported) = 1	NR			or T+ report	ed) = NR	
CI: 0.68, 1.92) List of covariates: NR  Other reported measure = NR  CI: 0.50, 1.51) List of covariates: NR  Other reported measure = NR				14 (95%				= 0.87 (95%
Other reported measure = NR Other reported measure = NR	, ,	•		·	, -		,	`
	List of covariates:	NR						
Between-test agreement, concordance, and discordance (if applicable)							= NR	
	Between-test agree	eement, con	cordance,	and disc	ordance (if app	licable)		

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						

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

	other dutcomes	
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

### **Study details**

First author surname year of publication: Casas 2011a<sup>123</sup>

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- $\alpha$  therapy)

## **Participants**

Recruitment dates: NR

**Total N of recruited patients: 323** 

 $\textbf{Inclusion criteria:} \ Patients \ with \ immune-mediated \ inflammatory \ diseases \ (IMID) \ before \ anti-TNF-\alpha$ 

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])

Training of patterness test	• • •				
	Total N	Total	Total N	Total N	Total N

			(tested)	N	(test-)	(indetern	erminate) (test results available)			
				(test+)						
IGRA (QF		<b>)</b> :	214	45	157	12		214		
TST (≥5 m			214	52	162	0		214		
Test 3 (spe	• /		NA	NA	NA	NA		NA		
					IGRA and TS					
Levels/gro	ups of				order (if appli					
Definition of exposure group - risk factors for TB infection										
Non-expose			No risk fact							
Exposed 1	(specif	y):			fection (birth or				_	
					TB contact, pr					
F 10				n care woi	ker, abnormal o	cnest X-ray	, and his	story	of past 1B)	
Exposed 2			NA							
Exposed 3			NA							
Exposed 4	(specif	y):	NA							
Tests			41 1 1	4	C + 66	1 //1			0.0	
	Assa	•	methodolog	•		values/thr			Other	
			measuremenufacturer	ent,	Den	nition of to	est+		information	
IGRA	Onont		Inuracturer  I®-TB Gold	in_Tube	According to	<u> </u>			NA	
(QFT-			ere collected		manufacture		regulte		IVA	
GIT)			as performed							
GII)			T-6, CFP-10		indeterminat					
	_	_	hemagglutir		IFN-γ produ					
	_		sma samples		with indeter					
			lyzed in the		retested					
			Laboratory	(Clinical						
	Micro	biology	Department)	in						
	accord	lance wi	th the manuf	facturer's						
	instru	ctions								
TST			ormed accord						NA	
			od using 2 U		experienced		_			
			-23 (Statens			standard protocol (in the left forearm and transverse diameter				
	Institu	ite, Cope	enhagen, Der	ımark)						
					measuremen					
					≥5 mm at 48 as positive	5−/∠ 11 was	conside	ieu		
Association	n hetw	een tost	results and	incidance	of active TB (	if annlicat	ale)			
11550Clatio	H DCIN	IGR		meruence	or active 1D (		TST			
			ence of	Total			nce of		Total	
			ve TB	- 0 101		activ				
	ļ	Yes	No			Yes	No			
IGRA -	+	NA	NA	NA	TST +	NA	NA		NA	
IGRA		NA	NA	NA	TST -	NA	NA		NA	
indetermi	nate	NA	NA	NA	indeterminat		NA			
Total	-	NA NA NA Total NA NA NA					NA			
			Tes	t perforn	nance paramet	ers				
		IGR					TST			
Sensitivity	= NA				Sensitivity =	- NA				
Specificity					Specificity =					
DDII 31:					PPV = NA					
PPV = NA		$ \begin{array}{ccc}                                   $								

Cumulative Incid	anca =	NΙΛ		Cumulative In	ncidanca	- NI A		
Cumulative Incidence <sub>IGRA</sub> . = NA				Cumulative In			Α.	
Cumulative Incidence Ratio <sub>IGRA</sub> = NA				Cumulative In			A	
Incidence density				Incidence der				
Incidence density				Incidence der				
Incidence density				Incidence der			Λ	
Other reported m			_	Other reporte		ST = NA		
				en tests (IGRA	vs. TST)			
Ratio of cumulati								
Ratio of incidenc			<u>IA</u>					
Other reported m								
Association between test results and levels of TB exposure (if applicable)								
IG	RA (QFT-G	IT)			TST (≥	5mm)		
	Exposui	e level	Total		Exposur	e 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		nance paramete	rs			
	IGRA		1	•	TS'	T		
Sensitivity = NR				Sensitivity = N				
Specificity = NR				Specificity = N				
PPV = NR				PPV = NR				
NPV = NR				NPV = NR				
DOR (for T <sup>+</sup> calc	ulated) = NE	)		$DOR (for T^+ calculated) = NR$				
OR (crude; for T			CI	OR (crude; for $T^{+}$ reported) = 2.80 (95% CI: 1.40,				
1.20, 5.10)	reported) –	2.30 (93/0	CI.	5.50)				
OR (regression-b	acadı mamanta	$\frac{1}{(4)} = 2.00 ($	050/	/	hagadi yang	mtad) = 2.0	0 (050/ CI.	
, -	aseu, reporte	(a) - 2.90	95/0	OR (regression-based; reported) = 2.90 (95% CI:				
CI: 1.30, 6.30) List of covariates	· ogo gondo	r DCC		1.40, 6.00) List of covariates: age, gender, BCG vaccination,				
vaccination, and			otmont	and immunosuppressive treatment				
Other reported m			atment	Other reported measure = NR				
Other reported in			n hotzyc	en tests (IGRA vs. TST)				
D. C. CDOD (6				en tests (IGRA)	vs. 151)			
Ratio of DORs (f				CI 0.54 1.40)				
Ratio of OR (crue					1.72)			
Ratio of ORs (reg			1) = 1.00	(95% CI: 0.58,	1.73)			
Other reported m								
			test resu	lts and BCG sta				
IC	RA (QFT-0				TST (≥			
	BCG s		Total			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 NR	12	indeterminate		0	0	
Total	NR	214	Total	NR	NR	214		
Test performance parameters								
		TS	ST					
$\frac{\mathbf{IGRA}}{\mathbf{DOR} \text{ (for T}^{+} \text{ calculated)}_{\mathbf{IGRA}} = \mathbf{NR}}$				DOR (for T+	calculated) <sub>T</sub>	$r_{ST} = NR$		
OR (crude; for $T^+$ reported) = 1.20 (95% CI:						(95% CI: 0.90,		
0.50, 3.20)				OR (crude; for T+ reported) = 1.70 (95% CI: 0.90, 3.40)				
OR (regression-based; reported) <sub>IGRA</sub> = NR				OR (regression-based; reported) <sub>TST</sub> = 1.50 (95%				
List of covariates		, 15101		CI: 0.70, 3.40)				
210 01 00 variation 1111						i		

			gender, risk factors for TB,						
0.1	N.D.	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 out off yelloo PCC versions in status, and/or condition									
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition									
Total sample	TICT -	TOTAL CONTRACTOR OF THE CONTRA	T . 1						
TOP 1	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: ≥5mn	n								
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)									
<b>Stratification (specify</b>	<u> </u>								
	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 BC	G or condition – specify): N	TR .						
TST + threshold: NR	•								
Parameters									
Kappa = NR									
% concordance = NR									
% discordance = NR									
<b>Stratification (specify</b>	group 2)								
\ 1	TST +	TST -	Total						
IGRA +	NR	NR	NR						
IGRA -	NR	NR	NR						
indeterminate	NR	NR	NR						
Total	NR	NR	NR						
Description	1112 1111								
	total, if stratified by BC	G or condition – specify): N	TR						
TST + threshold: NR	, iii.a., ii bilaniica oʻj Be	pointing	·= -						
Parameters Parameters									
Kappa = NR									
% concordance = NR									
% discordance = NR									
70 discordance – IVIX	Otho	r outcomes							
Test and cut-off (if	Adverse ever		Health related quality						
applicable)	(specify)	11.5 11/14 ( /0)	of life mean score						
аррисане) (specify)			(SD) (specify)						
IGRA:		NR	NR						
TST:		NR NR	NR NR						
Test 3 (specify):		NR NR	NR NR						
Conclusions									
Authors:									
AHIDORS:									

### **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)

## Study details

First author surname year of publication: Casas 2011b<sup>124</sup>

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

- values of Proceedings							
	Total N	Total	Total N	Total N	Total N		

		(tested)	N (test+		(test-)		(indeterr	ninate)	`	st results vailable)
			)						av	anabic
	(FT-GIT):	95	42	51			2		95	
TST (2 st ≥5mm):	tep;	95	44	51			0	0 95		
Test 3 (s)	pecify):	NA	NA	NA			NA		NA	
	• •	vith valid re	sults for	both	IGRA a	ınd T	'ST: 95			
		osure to TB								
		Definition	n of expo	sure	group -	risk	factors for '	ТВ		
Non-expo	osed	No risk fac	tors for T	ГВ						
Exposed	1						vith TB, abn			
(specify)	•						th a high TB			ism, drug
			evious sta	ay in	prison, a	nd in	volvement w	vith health	care)	
Exposed		NA								
(specify)										
Exposed (specify):		NA								
Exposed		NA								
(specify)	•									
Tests						,				
		ed, methodo		_		C	ut-off value		lds	Other
	mea	asurement,	manufac	turer	•		Definition	of test+		informat
TCD 4	TI OFT I	T	C 1	•		D	1,	1		ion
IGRA		T test was pe					ults were sc		1	NA
(QFT-		with the ma			J of		itive [interfe		I	
GIT)		s. Briefly, 3 d					35 IU/mL (tl erculosis—sp		ton	
		o antigens (t					e minus the		3011	
		perculosis–si				I	ative [interfe	/	1 <	
		hytohemagg					IU/mL (the		,1	
		blood sampl					erculosis-sp		gen	
		t the Mycoba					e minus the i			
	The blood	samples for	QFT-IT t	esting	g were	inde	eterminate [i	nterferon-	С	
	collected in	nmediately b	pefore the	e TST	was	leve	el < 0.5 (the	mitogen tu	ıbe	
	performed					I	us the nil tu		0	
						I	mL (the nil t	/ -		
						I	ording to the	-		
							rferon-c. Pla		les	
							n indetermin	ate results		
TST (2	The TCT	as performe	d in the 1	oft for	ranrm		e retested induration	> 5 mm c+	18	NA
151 (2 step; ≥		to the Manto					2 hours was			11/71
5 mm)	_						itive result in			
			stein derivative RT-23 (2 U/0.1 s Serum Institute, Copenhagen,			-	the nationa			
			In all cases, the TST was			I	delines	- F-32		
	-		ed and evaluated by experienced							
		result for th	•	-						
		ne test was a		_	•					
		later (the 2-s		, and	that					
		considered d				L				
Associati		test results	and inci	denc	e of activ	ve TB				
		GRA						<u>rst</u>	1	m . 1
	Ir	cidence	Total				Incid	ence of		Total

	of a	ictive		active TB				
		ГВ						
	Yes	No			Yes	No		
IGRA +	NA	NA	NA	TST +	NA	NA	NA	
IGRA -	NA	NA	NA	TST -	NA	NA	NA	
Indetermina		NA	NA	Indeterminate	NA	NA	NA	
Total	NA	NA	NA	Total	NA	NA	NA	
10141	1111	1111		nance parameter		1111	1111	
	IGI	RA	Test periori	iunce pur umeter		TST		
Sensitivity =				Sensitivity = NA		101		
Specificity =				Specificity = NA				
$\frac{\text{SPECIFICITY}}{\text{PPV} = \text{NA}}$	1171			$\frac{\text{SPCCITICITY}  \text{FM}}{\text{PPV} = \text{NA}}$				
NPV = NA				NPV = NA				
Cumulative 1	Incidence	$_{\rm ND} = N$	Δ	Cumulative Inci	dence =	$_{\text{orb.}} = NA$		
Cumulative l				Cumulative Inci				
Cumulative l				Cumulative Inci			Τ Λ	
Incidence de				Incidence densit			VA.	
Incidence de				Incidence densit				
Incidence de				Incidence densit			Δ	
Other reporte				Other reported r			Α	
Other reports	cu measure			en tests (IGRA v				
Ratio of cum	vulativa ina			eli tests (IGNA v	5. 151	)		
Ratio of cuin								
		_	atios – NA					
Other reported measure = NA  Association between test results and levels of TB exposure (if applicable)							abla)	
-	IGRA (C	ure level				$step; \ge 5 \text{ m}$		
	High/Yes					posure level Yes Low/	<del></del>	
IGRA +	27	15	42	TST +	30	14 Low/	44	
IGRA -	33	20	53	TST -	30	21	51	
Indetermin	NR	NR	2	Indetermina	0	0	0	
	INK	INK	-		U	0	U	
ate Total	60	35	(excluded 95	) te Total	60	35	95	
Total	1 00	33		nance parameter		33	93	
	10	RA	Test periorii	Tance parameter	S	TST		
Sansitivity -			5% CI: 33.09,	Songitivity =	20/60 -		50/ CI: 27 72	
57.51)	27/00 - 43	0.00% (9	3% C1. 33.09,	Sensitivity = 30/60 = 50.00% (95% CI: 37.73, 62.27)				
	20/35 = 5	7 1/10/2 (0	5% CI: 40.86,	Specificity =	21/35 =	60 00% (04	5% CI: 43 57	
72.02)	20/33 — 3	7.17/0 ()	370 C1. <del>4</del> 0.60,	74.45)	21/33 -	00.0070 ().	770 C1. <del>4</del> 3.57,	
	r = 64.29%	(95% CI	[: 49.17, 77.01)		= 68 18	% (95% CI	53 44 80 00)	
			I: 25.94, 51.19)	PPV = 30/44 = 68.18% (95% CI: 53.44, 80.00) NPV = 21/51 = 41.18% (95% CI: 28.75, 54.83)				
			(95% CI: 0.47,				95% CI: 0.64,	
2.52)	carculated	, 1.01	(5570 C1. 0.47,	3.49)	carcarat	cu) 1.50 (	) 5 / 0 C1. 0.0 · 1,	
	OR (crude; for $T^+$ reported) = 1.66 (95% CI:					orted = 1.2	5 (95% CI:	
0.66, 3.33)				` '	OR (crude; for $T^+$ reported) = 1.25 (95% CI:			
OR (regression-based; reported) = 1.50 (95% CI:					0.50, 2.50)  OR (regression based: reported) = 1.80 (05% CI:			
0.50, 4.10)				OR (regression-based; reported) = 1.80 (95% CI: 0.60, 5.10)				
List of covariates: age, sex, albumin, BCG				ates: ag	e. sex. albui	nin, BCG status,		
status, Model for End-Stage Liver Disease								
(MELD) sco			Model for End-Stage Liver Disease (MELD) score					
Other reports		= NR		Other reported	d measi	ıre = NR		
			nparison betwe	en tests (IGRA v				
Ratio of DO	Rs (for T <sup>+</sup> c							
Ratio of DORs (for $T^+$ calculated) = 0.67 (95% CI: 0.37, 1.24)								

Ratio of OR (cr									
			ed) = 0.83 (9)	5% CI: 0.39, 1.79	))				
Other reported measure = NR									
			test results	and BCG status					
IGRA					TST				
	BCG	status	Total		BC	G 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	Indeterminat	0	0	0		
TD + 1	20	65	(excluded	_	20	65	0.5		
Total	30	65 TF	95	Total	30	65	95		
	· · ·		performan	ce parameters		T.O.T.			
	IGR			7 7 7 7		TST	0.5 (0.50)		
DOR (for T <sup>+</sup> ca 1.54)	ilculated) <sub>IGR</sub>	$\Lambda = 0.63 (95)$	% CI: 0.26,	DOR (for T+ of 0.35, 2.00)	calcula	$(ted)_{TST} = 0$	.83 (95% CI:		
OR (crude; for	T <sup>+</sup> reported)	= 0.62 (95%)	6 CI: 0.26,	OR (crude; fo	r T+ re	ported) = (	0.83 (95% CI:		
1.42)				0.35, 2.00)		·			
OR (regression	_	$rted)_{IGRA} =$	NR	OR (regressio			$)_{TST} = NR$		
List of covariat				List of covaria					
Other reported				Other reported		ıre = NR			
				rdance (if applic					
This table may	y be stratifie	ed by TST o	ut-off value	, BCG vaccination	on stat	us, 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 definiti	on (e.g., tota	ıl, if stratific	ed by BCG o	r condition – spec	ify): to	tal			
TST + threshol	d: ≥ 5 mm	-		•	-				
Parameters									
Kappa = $0.57$ (	95% CI: 0.3	7, 0.77)							
% concordance			(95% CI: 6	9.71, 85.94)					
% discordance				4.93, 49.58)					
Stratification (			(, , , , , , , , , ,						
		TST +		TST -			Total		
IGRA +		NR		NR			NR		
IGRA -		NR		NR			NR		
Indeterminate		NR		NR			NR		
Total		NR		NR			NR		
Description		1117		TVIX			1117		
	on (e.g. tota	1 if stratific	ed by RCG o	r condition – spec	ify). N	R			
TST + threshol		u, 11 stratiff	a by BCO (	i condition – spec	11y J. 1V	11			
Parameters Parameters	W 1111								
Kappa = NR									
% concordance	v = NP								
% discordance									
Stratification (		un 2)							
Stratification (	specify gro	TST +		TST -			Total		
ICD A									
IGRA +		NR		NR NB			NR		
IGRA -	1	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, 0.280)

# **Study details**

First author surname year of publication: Chkhartishvili 2013<sup>125</sup>

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

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			

			1	1					
TST (≥5 mi						236			
				IGRA and TS					
Levels/group	Levels/groups of exposure to TB in increasing order (if applicable):								
>T 1	Definition of exposure group - Household Member treated for TB  Non-exposed No household member treated for TB								
Non-exposed					3				
Exposed 1 (s)			nember t	reated for TB					
Exposed 2 (s)		NA							
Exposed 3 (s)		NA NA							
Exposed 4 (s)	pecity):	NA							
Tests	A			4 - CC 1 /4]-		C	Other		
		ay used, ogy, timing fo			resholds Definition test+	11 01	information		
		asurement,	)1		iesi+		Illiormation		
		ufacturer							
IGRA	Each partic		the (	)FT-GIT result	was considered po	sitive			
(QFT-	-	tely 12 ml of	if the	-	was considered po	Sitivo			
GIT)		n, which was			esponse to TB antig	gens	Blood was		
		according to		_	control was $\geq 0.35$	J	drawn for		
	the manufa			_	% of the negative		the IGRAs		
	instruction	S			these criteria were	not	prior to the		
			met;	and indetermin	ate if either the		placement		
			_		d a result of > 8 IU/		of the TST		
					ol had a result of <	0.5			
			IU/n						
IGRA	Each partic	•			peripheral blood				
(TSPOT)		tely 12 ml of			PBMCs) were isola				
		n, which was			a nil control, a pos				
	the manufa	according to			hytohemagglutinin				
	instruction				s (CFP-10 and ESA its were counted us		Blood was		
	msuuction	3			er System (Autoimi		drawn for		
					any). The test result		the IGRAs		
			_		if the response to e		prior to the		
					minus the nil contr		placement		
			was	≥ 6 spot formin	g cells, or twice the	e nil	of the TST		
			cont	rol. The result v	was considered				
					control spot count				
					ells or if the readin				
			_		was < 20 spot form	ning			
TECTE	mi mom	C	cells		5 6: 1 ::				
TST		vas performed			5 mm of induration	was			
	using the N	Aantoux n intradermal		idered positive					
	injection o purified pr								
	derivative								
	administer								
	volar surfa								
		he transverse							
		f induration							
	was record								
	millimeter	s 48–72 hours	S						
	after admir								
Association l	between tes	t results and	incidenc	e of active TB	(if applicable)				

			,	ΓST				
	IGRA Incidence of Total				Incide		Total	
	active		Total		active		Total	
	Yes	No			Yes	No		
IGRA +	NA	NA	NA	TST +	NA	NA	NA	
IGRA -	NA NA	NA NA	NA NA	TST -		NA NA	NA NA	
					NA NA			
Indeterminate	NA NA	NA	NA	Indeterminate	NA	NA	NA	
Total	NA	NA	NA	Total	NA	NA	NA	
	ICD		est periori	mance parameter		POT		
G MAN AND AND AND AND AND AND AND AND AND A	IGRA			0 111 11 2		ΓST		
Sensitivity = NA				Sensitivity = N				
Specificity = NA				Specificity = N	\A			
PPV = NA				PPV = NA				
NPV = NA				NPV = NA				
Cumulative Incid				Cumulative In				
Cumulative Incid				Cumulative In				
Cumulative Incid			A	Cumulative In			A	
Incidence density	rate <sub>IGRA</sub> -	= NA		Incidence dens	ity rate T	ST+=NA		
Incidence density	rate <sub>IGRA-</sub>	= NA		Incidence dens	ity rate T	ST- = NA		
Incidence density	rate ratio	$_{IGRA} = NA$	A	Incidence dens	ity rate ra	atio $_{TST} = NA$	1	
Other reported m	easure <sub>IGR</sub>	A = NA		Other reported	measure	$_{TST} = NA$		
		Compar	ison betwe	een tests (IGRA v	vs. TST)			
Ratio of cumulat	ive incide	nce ratios	= NA					
Ratio of incidence	e density	rate ratios	= NA					
Other reported m								
•			st results a	and levels of TB	exposure	(if applicab	ole)	
	RA (QFT					≥ 5 mm	,	
		sure level	Total			ure level	Total	
		s Low/N				s Low/No	1	
IGRA +	NR	NR	70	TST +	NR	NR	41	
IGRA -	NR	NR	167	TST -	NR	NR	195	
Indeterminate	NR	NR		Indeterminate	NR	NR	4	
Total	13	227	240	Total	13	227	240	
10141	13			nance parameter		22,	2.0	
	IGRA		est periori	панее рагантете		ST		
Sensitivity = NR				Sensitivity = NE		51		
Specificity = NR				Sensitivity = NR Specificity = NR				
PPV = NR	•			PPV = NR				
NPV = NR				NPV = NR				
DOR (for T <sup>+</sup> calc	nulated) –	NID		DOR (for T <sup>+</sup> cal	culated) -	- NID		
OR (crude; for T			50/ CI.	OR (crude; for 7			50/ CL 0.20	
, ,	reported	) – 0.43 (9	370 CI.	5.62)	reporte	u) – 1.48 (9.	0% CI. 0.39,	
0.09, 1.97)	acadı rana	wtod) – M	D	/	hagadı va	acetad) = NE	<u> </u>	
				OR (regression- List of covariate		ported) – Nr		
						- NID		
Other reported measure = NR  Comparison between tests (IGRA vs. TST)								
Datia af DOD (	C Tr <sup>+</sup> 1			een tests (IGRA )	<b>(S. 151)</b>			
Ratio of DORs (f				/ CI 0.10 0.00\				
Ratio of OR (cru								
Ratio of ORs (reg			ortea) = NA	-				
Other reported m						(10 ×	• `	
			st results a	nd levels of TB e	_		le)	
IC	GRA (TSI		1			≥ 5 mm	T = :	
	Expos	sure level	Total		Expos	ure 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		
Total	13			nance paramete		221	240		
	IGRA	1030	periori	панее рагантете	TS				
Sensitivity = NR	10101			Sensitivity = NI					
Specificity = NR				Specificity = N					
PPV = NR				PPV = NR					
NPV = NR				NPV = NR					
DOR (for T <sup>+</sup> calcu	ılated) = N	R		DOR (for T <sup>+</sup> ca	lculated) = 1	NR			
OR (crude; for T <sup>+</sup>			v CI.	OR (crude; for			% CI: 0.39		
0.44, 5.00)	reported)	1.10 (557)	0 01.	5.62)	r reported)	1.10 (55	, 0 01. 0.5),		
OR (regression-ba	sed: report	ed) = NR		OR (regression-	-based: reno	rted) = NR			
List of covariates:		<i>(u)</i>		List of covariate		1104) 1111			
Other reported me		₹		Other reported		NR			
			n betwe	en tests (IGRA		-			
Ratio of DORs (fo									
Ratio of OR (crud				6 CI: 0.40, 2.51)					
Ratio of ORs (regi									
Other reported me									
			test resi	ults and BCG st	atus (if app	licable)			
	RA (QFT-					≥ 5 mm			
	BCG st		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	Indeterminat	e NR	NR	4		
Total	173	67	240	Total	173	67	240		
		Test	perforr	nance paramete	rs				
	IGRA			TST					
DOR (for T <sup>+</sup> calcu	ılated) <sub>IGRA</sub> =	= NR		DOR (for T+ calculated) <sub>TST</sub> = NR					
OR (crude; for T <sup>+</sup>	reported) =	1.41 (95%	ωCI:	OR (crude; for T+ reported) = 2.55 (95% CI:					
0.38, 5.29)				0.32, 20.18)					
OR (regression-ba		$ed)_{IGRA} = 1$	NR	OR (regressi	on-based; re	eported) <sub>TST</sub>	= NR		
List of covariates:					List of covariates: NA				
Other reported me				Other reporte					
			test resi	ults and BCG st					
IC	GRA (TSP					≥ 5 mm			
<u> </u>	BCG s		Total			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	Indeterminat		NR	4		
Total	173	67	240	Total	173	67	240		
	*~=	Test	perforr	nance paramete		CIT			
DOD (6 77+ 1	IGRA	NID		DOD (2 =		ST			
DOR (for T <sup>+</sup> calcu			/ CT	DOR (for T+			(050/ CI		
OR (crude; for T <sup>+</sup> )	reported) =	1./8 (95%	o CI:	OR (crude; f	or 1+ repor	tea) = 2.55	(95% CI:		
0.38, 8.28)				0.32, 20.18)					
	1 .	1\ 3	ID		1 1	OR (regression-based; reported) <sub>TST</sub> = NR List of covariates: NA			
OR (regression-ba List of covariates:		$ed)_{IGRA} = 1$	NR	OR (regressi		eported) TST	=NR		

041	ND	O41					
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	atilied by 151 cut-on va	nue, DCG vaccination status, and	u/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	11	173	230				
	total if stratified by BC	G or condition – specify): QFT-GI	T (total)				
$TST + threshold: \ge 5$	-	o er condition specify). Q11 of	(total)				
Parameters							
	I: 0.17, 0.42) calculated –	indeterminate excluded					
	I: 0.16, 0.42) reported						
		8.27, 79.44) calculated– indetermi	nate excluded				
	\	56, 31.73) calculated– indetermina					
	ent, concordance, and di						
9		llue, BCG vaccination status, and	d/or condition				
Total sample							
	$TST + (\geq 5 \text{ mm})$	TST -	Total				
IGRA (TSPOT) +	20	36	56				
IGRA (TSPOT) -	18	143	161				
Indeterminate	3	16	19				
Total	41	195	236				
Description							
		G or condition – specify): TSPOT	(total)				
TST + threshold: =>5	mm						
Parameters							
	I: 0.14, 0.40) calculated –	indeterminate excluded					
	I: 0.07, 0.29) reported						
		8.96, 80.4) calculated-indetermin					
% discordance = $54/2$	17 = 24.88% (95% CI: 19	.6, 31.04) calculated—indeterminate	te excluded				
Stratification (specif	y group 1)						
	TST +	TST -	Total				
IGRA +	NR	NR	NR				
IGRA -	NR	NR	NR				
Indeterminate	NR	NR	NR				
Total	NR	NR	NR				
Description							
1 \	g., total, if stratified by BC	G or condition – specify): NR					
TST + threshold: NR							
Parameters							
Kappa = NR							
% concordance = NR							
% discordance = NR	<u> </u>						
Stratification (specif							
	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	

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:**

% concordance = NR % discordance = NR

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

**Study details** 

First author surname year of publication: Chung 2010a<sup>126</sup>

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
<b>TST</b> ≥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

D 11/	10	. 1 -	D1 1 1	. 1			. 1 6	* . *.*		
Exposed 1 (s)	pecify)		_		latent TB infection consisted of patients with a with TB patients, old TB lesions on CXR, or a					
			•		vith 1B patients,	old IB	lesions or	CXR, or a		
Evnoged 2 (gr	nooifu)		NA	TB infection						
Exposed 2 (s) Exposed 3 (s)			NA NA							
Exposed 3 (s)			NA NA							
Tests	pecity	)•   1	NA.							
1 0515	Ass	eav used	method	lology, timing	Cut-off va	lues/th	resholds	Other		
	Ass	-	st measu			tion of t		information		
			ianufacti	· ·	Benni		.cst ·	inioi mation		
IGRA	Who			acted just	Results of ea	ch test v	vere			
(QFT-GIT)				two IFN-c	classified as					
( )		-		performed	or indetermin		_	NIA		
	l .	_		facturer's	described	, 1		NA		
	l .	_		Ltd., Carnegie,						
	Victo	oria, Aus	stralia)							
IGRA	The	TSPOT ·	was also <sub>l</sub>	performed	Results of ea	ch test v	vere			
(TSPOT)	accon	rding to	the manu	facturer's	classified as 1	ositive	negative	NA		
	l .		Oxford In	nmunotec,	or indetermin	ate, as p	previously	IVA		
		rd, UK)				described				
TST	l .			e IGRAs, 2-TU						
	of purified protein derivative RT23				mm size of th					
		m Institu		two measures	nents		NA			
	-		Denmarl	*						
intradermally injoined side of the forear the patient's vasc										
	_			e patients'						
				neasured the						
				nduration after						
		indepen								
Association 1				d incidence of	active TB (if ap	pplicabl	e)			
		IGR/					ΓST			
			nce of	Total			ence of	Total		
		activ	e TB				e TB			
		Yes	No	1		Yes	No			
IGRA +		NA	NA	NA	TST +	NA	NA	NA		
IGRA -		NA	NA	NA	TST -	NA	NA	NA		
Indetermina	ate	NA	NA	NA	Indeterminate	NA	NA	NA		
Total		NA	NA	NA	Total	NA	NA	NA		
			T	est performan	ce parameters					
		IGR/	\			7	ΓST			
Sensitivity =	NA				Sensitivity = $N$	A				
Specificity =	NA				Specificity = N	A				
PPV = NA					PPV = NA					
NPV = NA					NPV = NA					
Cumulative I					Cumulative Inc					
Cumulative I					Cumulative Inc					
Cumulative I				A	Cumulative Inc			NA		
Incidence der					Incidence densi	_				
Incidence der					Incidence densi					
Incidence der				Α	Incidence densi	_				
Other reporte	d mea	sure <sub>IGRA</sub>	$\Lambda = NA$		Other reported	measure	$e_{TST} = NA$			

	С	omparisor	betwee	en tests (IGRA v	s. TST)		
Ratio of cumulativ				•	/		
Ratio of incidence							
Other reported me							
Assoc	ciation betw	een test re	esults ar	nd levels of TB ex	xposure (if	applicable)	
	RA (QFT-G				TST≥10		
	Exposur		Total		Exposu		Total
	High/Yes	Low/No			High/Yes		
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
	1			146 patients; 21			
Test perior	IGRA	inicici's (b	ascu on	140 patients, 21	TST		iuucu)
Sensitivity = 0/17		05% CI: 30	06	Sensitivity = 2/1			2 28 34 34)
Sensitivity = 9/17 = 52.94% (95% CI: 30.96, 73.84)							
Specificity = 82/129 = 63.57% (95% CI: 54.98, 71.37)				Specificity = 99, 83.20)	/129 = 76.74	ŀ% (95% C	I: 68.75,
PPV = 9/56 = 16.07% (95% CI: 8.69, 27.81)				PPV = 2/32 = 6.	25% (95% (	CI: 1.73, 20	0.15)
NPV = 82/90 = 91	.11% (95%	CI: 83.43,	95.43)	NPV = 99/114 =	86.84% (95	5% CI: 79.4	42, 91.86)
DOR (for T <sup>+</sup> calcusts 5.43)	alated) = 1.96	6 (95% CI:	0.71,	DOR (for T <sup>+</sup> cal 2.03)	culated) = 0	.44 (95% C	CI: 0.09,
$\overline{OR}$ (crude; for $T^+$ reported) = NA (reported)			OR (crude; for 7	reported) =	= NA (repo	orted only for	
only for total sample of 167 patients that			total sample of 1			•	
included 21 previous TB patients)			previous TB pat		111010101010		
OR (regression-ba				OR (regression-		ted) = (rep	orted only
(reported only for		*	ients	for total sample			•
that included 21 pr		-	101100	previous TB pat	-	1100 011000 1110	10000 = 1
List of covariates:		,		List of covariate			
Other reported me				Other reported r		R	
other reported me		omnarisor	hetwe	en tests (IGRA v			
Ratio of DORs (fo					3. 101)		
Ratio of OR (crud				71. 1.72, 11.51)			
Ratio of ORs (regi							
Other reported me		a, reported	) 11/1				
_		roon tost ro	enlte or	nd levels of TB ex	vnosuro (if	annlicable	
	RA (TSPO)		suits ai		TST≥10		
10	Exposur		Total		Exposu		Total
	High/Yes	Low/No	Totai		High/Yes	Low/No	Total
IGRA +	8	75	83	TST +	2	30	32
IGRA -	9	54	63	TST -	15	99	114
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR
-	17	129	146	Total	17	129	146
Total	L				l	·	
1 est perfor	IGRA	inieters (D	aseu on	146 patients; 21	TST		iuueu)
Sensitivity = 8/17		95% CI: 26	.16,	Sensitivity = 2/1			3.28, 34.34)
69.04)	20 41 0 60	(0.50/ 57	22.72	G 'G''	/100 505	10/ (050/ ~	
Specificity = 54/12 50.49)	29 = 41.86%	6 (95% CI:	33.70,	Specificity = 99, 83.20)	/129 = 76.74	₽% (95% C	1: 68.75,
PPV = 8/83 = 9.64	1% (95% CI:	4.96, 17.8	(88)	PPV = 2/32 = 6.	25% (95% (	CI: 1.73, 20	0.15)
NPV = 54/63 = 85				NPV = 99/114 =			
DOR (for T <sup>+</sup> calculated)	alated) = 0.64	4 (95% CI:	0.23,	DOR (for T <sup>+</sup> cal 2.03)	culated) = 0	.44 (95% C	CI: 0.09,
1./0)				4.03)			

OR (crude; for T <sup>+</sup>	reported) =	NA (repor	ted	OR	Corude: for T <sup>+</sup> re	enorted) =	NA (repo	rted only for	
only for total sam	. ,	\ <b>1</b>		OR (crude; for T <sup>+</sup> reported) = NA (reported only for total sample of 167 patients that included 21					
included 21 previo					previous TB patients) OR (regression-based; reported) = (reported only				
OR (regression-ba									
` 1	(reported only for total sample of 167 patients				total sample of		nts that inc	luded 21	
that included 21 previous TB patients)					vious TB patient	/			
List of covariates:					st of covariates: N				
Other reported me					her reported mea		R		
					ests (IGRA vs. T	ST)			
Ratio of DORs (fo				I: 0.	.56, 3.76)				
Ratio of OR (crud									
Ratio of ORs (reg			$1 = \mathbf{N}\mathbf{A}$						
Other reported me									
			test resul	lts a	nd BCG status	<u> </u>			
-	IGRA (QF		1			TST ≥		<u> </u>	
	BCG :		Total				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	perform	anc	e parameters				
	IGRA					TS	T		
DOR (for T <sup>+</sup> calcu	ılated) <sub>IGRA</sub> =	- NR			DOR (for T+ calculated) <sub>TST</sub> = NR				
OR (crude; for T <sup>+</sup>	reported) =	NA (repor	ted only	for	OR (crude; for	T+ repor	ted) = NA	(reported	
129 low risk patie	nts that also	included 2	21 previo	us	only for 129 lo	w risk pa	tients that a	also included	
TB patients)					21 previous TB	patients)	)		
OR (regression-ba	sed; reporte	$(d)_{IGRA} = N$	ΙA		OR (regression	-based; re	eported) TST	r = NA	
(reported only for	129 low ris	k patients t	hat also		(reported only	for 129 lc	w risk pati	ients that	
included 21 previo	ous TB patie	ents)			also included 2	1 previou	s TB patie	nts)	
List of covariates:	NA				List of covariat	es: NA			
Other reported me	easure = NR				Other reported	measure	= NR		
	Association	between	test resul	lts a	and BCG status	(if applic	cable)		
]	IGRA (TSP	(TO				TS	T		
	BCG s	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	perform	anc	e parameters				
	IGRA					TS	T		
DOR (for T <sup>+</sup> calcu	ılated) <sub>IGRA</sub> =	- NR			DOR (for T+ ca	alculated)	$T_{TST} = NR$		
OR (crude; for T <sup>+</sup>			ted only	for	OR (crude; for	T+ repor	ted) = NA	(reported	
129 low risk patie	nts that also	included 2	21 previo	us	only for 129 lo	w risk pat	tients that a	also included	
TB patients)					21 previous TB	-			
OR (regression-ba	sed; reporte	$(d)_{IGRA} = N$	ΙA		OR (regression	-based; re	eported) TST	r = NA	
(reported only for					(reported only				
included 21 previo		-			also included 2		-		
List of covariates:		,			List of covariat	-	1	,	
Other reported me					Other reported		= NR		
Between-test agr			, and disc	corc	•				
This table may b							and/or co	ndition	
		J		,					

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

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)** 

Structure (Specify	8- v-p -/		
	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)** 

Structure (specify	5· · · · · · · · · · · · · · · · · · ·		
	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 (%)	Health related quality of life								
	(specify)	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

# **Study details**

First author surname year of publication: Costantino 2013<sup>127</sup>

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
<b>TST</b> (≥ <b>5</b> mm):	563	196	318	49	514

					1	т			
Test 3 (spe			NA	NA	NA	NA			NA
						and TST: 56			
Levels/gro	oups of	exposi	ure to TB	in increa	sing order	(if applicable	e):		
	Defi	nition	of exposu	re group	- conventi	onal risk fact	ors (CR	F) of LTB	SI
Non-expos	sed	1	No CRF o	f LTBI					
Exposed 1	(specif	<b>y</b> ): (	CRF of L7	BI: histo	ry of active	TB treated be	fore 197	0 or not tr	eated for at
		1	least 6 mo	nths inclu	ding 2 mon	ths with a con	nbinatior	of rifamp	oicine and
		1	pyrazinam	ide, close	contact wit	th a patient wi	th active	TB, and o	ehest
		1	radiograph	suggesti	ve of previo	ous TB infection	on		
Exposed 2	(specif	<b>y</b> ): 1	NA						
Exposed 3	(specif	<b>y</b> ): 1	NA						
Exposed 4	(specif	<b>y</b> ): 1	NA						
Tests									
	Assa	ay used	d, method	ology,	Cut-off va	alues/thresho	lds Defir	nition of	Other
			est measu			test+			information
	`		ufacturer						
IGRA	T-SPC	OT.TB	assays we	ere	Assays we	ere considered	indetern	ninate if	To avoid any
(TSPOT			ccording to			ve control (cel			potential
)	_		r's instruc			lone) spot cou			boosting
					than 10 sp	ots (referred to	o hereaft	er as a	effect of TST
					high nil co	ontrol) or if the	e positivo	e	on IGRA
					control (co	ell suspension	stimulat	ed with	results, all T-
						agglutinin) sp			SPOT.TB
						20 spots (low			assays were
					control). For determinate tests, T- performed				
						assays were in		d	before
						to the manufa			initiating
						dations by sul			TST
						of the negative			
						t spot count be			
						fic antigen ES			
						fic antigen CF		test	
						dered positive			
						was equal to,	_	r than,	
						herwise, the to	est was		
		~=-			considered		2.5		
TST ≥ 5	I		s perform	ed with		tion diameter		or more	NA
mm		rculin		1 0	was consid	dered a positiv	e test		
	1	-	ng to 0.1 n						
			ein deriva						
	`	-	Sanofi Pasi						
		,	according						
	II .		thod. Tub						
			intraderm	•					
	II .		and 72 h						
	I		skin indur	ılıon					
Aggasist'	1	ecordec		and in all	longs of - 1	ivo TD (if -	nligativ		
Associatio	on betw			and incid	ence of act	ive TB (if ap			
	П		IGRA	т	oto1		1	rst lange of	Total
			lence of	1	otal			lence of	Total
			ive TB					ve TB	-
ICD 4	_	Yes	No	```	.T <b>A</b>	TOT	Yes	No	NT A
IGRA		NA	NA		NA	TST +	NA NA	NA NA	NA NA
IGRA	-	NA	NA	1	NΑ	TST -	NA	NA	NA

Indeterminate	NA	NA	NA	Indetermin	NA	NA	NA			
Total	NA	NA	NA	ate Total	NA	NA	NA			
Total	11/1			nance parameters	1471	11/1	11/2			
	IG		periorin		7	ΓST				
Sensitivity = NA	10.			Sensitivity						
Specificity = NA				Specificity						
PPV = NA				PPV = NA						
NPV = NA				NPV = NA						
Cumulative Incid	ence IGRA-	= NA			$\begin{array}{c} \text{NI V - NA} \\ \text{Cumulative Incidence} \\ \text{TST+} = \text{NA} \end{array}$					
Cumulative Incid				Cumulative						
Cumulative Incid						e Ratio <sub>TST</sub> =	NA			
Incidence density				Incidence d						
Incidence density				Incidence d						
Incidence density						e ratio <sub>TST</sub> =	NA			
Other reported m						$_{\text{ITE}} = NA$				
	TOK		on betwee	en tests (IGRA vs.		- 101 - 111				
Ratio of cumulati	ve incide				,					
Ratio of incidenc										
Other reported m										
			results an	d levels of TB exp	osure (if	applicable)				
	GRA (TS)			1	TST ≥ 5					
		sure level	Total		Expo	sure level	Total			
	High/Ye				High/Ye		o			
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	perform	ance parameters			·			
	IGRA				TST	Γ				
Indeterminate in	ıcluded			Indeterminate included						
Sensitivity = $23/6$	54 = 35.94	% (95% CI:	25.29,	Sensitivity = 31/64 = 48.44% (95% CI: 36.63,						
48.18)				60.42)						
Indeterminate ex				Indeterminate excluded						
Sensitivity = 23/4	18 = 47.92	2% (95% CI:	34.47,	Sensitivity = 31/49 = 63.27% (95% CI: 49.27,						
61.67)				75.34)						
Indeterminate in				Indeterminate in						
Specificity = 400	/499 = 80	.16% (95% C	CI:	Specificity = 334/499 = 66.93% (95% CI: 62.69,						
76.44, 83.42)	.1 .1 .1			70.92)						
Indeterminate ex		910/ (050/ 6	٦٢.	Indeterminate ex Specificity = 300		520/ (O50/ <b>(</b>	71. 60.06			
Specificity = 328	/42/ = /6	.81% (95% C	JI:	68.73)	/465 = 64.	32% (93% C	1: 60.06,			
72.58, 80.57 PPV = 23/122 = 1	19 950/ (0	59/ CI: 12 0	26.70)	PPV = 31/196 = 1	15 920/	(11.27	21.58)			
		5/0 C1. 14.9	, 20.70)	Indeterminate in		(11.37,	41.30)			
	Indeterminate included NPV = 400/441 = 90.70% (95% CI: 87.63,			NPV = 334/367 =		95% CI- 87	64 93 53)			
NPV = 400/441 = 90.70% (95% CI: 87.63, 93.07)			Indeterminate ex		2270 01. 07.	, , , , , , , , ,				
/	Indeterminate excluded			NPV = 300/318 =		95% CI: 91	23, 96.39)			
NPV = 328/353 =		(95% CI: 89.	75,		, v (		- , - <del> /</del> /			
			,							
95.16)				i						
95.16) Indeterminate in	ıcluded			Indeterminate in	ıcluded	DOR (for $T^+$ calculated) = 1.90 (95% CI: 1.12,				
		2.26 (95% C	I: 1.30,			1.90 (95% C	I: 1.12,			
Indeterminate in	ulated) =	2.26 (95% C	I: 1.30,		ulated) = 1	1.90 (95% C	I: 1.12,			

DOR (for T+ ca	alculated) =	3.05 (95%	CI: 1.65,	DOR (for T+ calculate	ted) = 3.13 (	95% CI:	1.70,
5.60)	•	·		5.77)			•
$OR (crude; for T^+ reported) = NR$				OR (crude; for T <sup>+</sup> rep	orted) = NR	•	
OR (regression-	-based; repo	orted) = 2.70	) (95%	OR (regression-based	l; reported)	= 1.95 (95	5% CI:
CI: 1.49, 4.89)				1.13, 3.36)			
List of covariat	es: NR			List of covariates: NI	}		
Other reported	measure = 1	VR.		Other reported measu	ire = NR		
				en tests (IGRA vs. TS	Γ)		
Ratio of DORs				CI: 0.63, 1.51)			
Ratio of OR (cr							
			ed) = 1.38	(95% CI: 0.92, 2.09)			
Other reported							
			ı test resu	lts and BCG status (if		)	
	IGRA (TS		1	TS	$ST \ge 5 \text{ mm}$		_
		status	Total		-	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
			t perforn	nance parameters			
	IGRA				TST		
DOR (for T <sup>+</sup> ca				DOR (for T+ calculat			
OR (crude; for				OR (crude; for T+ rep			
OR (regression-		orted) <sub>IGRA</sub> =	0.39	OR (regression-based; reported) $_{TST} = NR$ (p =			
(95% CI: 0.24,	/			0.11, NS)			
List of covariat				List of covariates: NI			
Other reported				Other reported measu			
				scordance (if applicable		, 10	<b>,.</b>
	be stratin	ed by TST	cut-off va	lue, BCG vaccination	status, and	or condi	tion
Total sample		TICT IS	<u>.                                      </u>	TOTAL			otal
ICD A (ECDOE)		$TST + \geq 5$	mm		TST -		
IGRA (TSPOT)		59		51			110
IGRA (TSPOT) Indeterminate	) -	114		220		-	334
		172		271			111
Total	1	173		271		1 '	444

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

 $TST + threshold: \ge 5 \text{ mm}$ 

# **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

 $TST + threshold: \geq 5 mm$ 

# **Parameters**

Kappa = 0.15 (95% CI: NA)							
% concordance = NA	A						
% discordance = NA	<b>L</b>						
Stratification (BCG	not vaccinated)						
	TST +	TST -	Total				
IGRA (TSPOT) +	NR	NR	NR				
IGRA (TSPOT) -	IGRA (TSPOT) - NR NR NR						
Indeterminate	NR	NR	NR				
Total	NR	NR	NR				

Sample definition (e.g., total, if stratified by BCG or condition - specify): BCG not vaccinated

 $\overline{\text{TST}} + \text{threshold} \ge 5 \text{ mm}$ 

# **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

### Study details

First author surname year of publication: Hadaya 2013<sup>128</sup>

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 (indeterminat e)	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 go or adenopathy, suggestive fibrotic scars) and/or close contact with TE Exposed 2 (specify): NA  Exposed 3 (specify): NA  Exposed 4 (specify): NA  Tests  Assay used, methodology, timing for test measurement, manufacturer values/thresholds Definition of test+  IGRA Blood samplings for determination of (QFT- M. tuberculosis-specific QGIT manufacturer's determination of (Cellestis) were processed, and scored recommendations tuberculosis	B patient		
Exposed 2 (specify): NA  Exposed 3 (specify): NA  Exposed 4 (specify): NA  Tests  Assay used, methodology, timing for test measurement, manufacturer values/thresholds Definition of test+  IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT manufacturer's determination de			
Exposed 3 (specify): NA  Exposed 4 (specify): NA  Tests  Assay used, methodology, timing for test measurement, manufacturer  IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT  Blood samplings for determination of determination of determination determinati	ormation		
Exposed 4 (specify): NA  Tests  Assay used, methodology, timing for test measurement, manufacturer values/thresholds Definition of test+  IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT manufacturer's determination	ormation		
Tests  Assay used, methodology, timing for test measurement, manufacturer  IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT  Cut-off values/thresholds Definition of test+  According to the manufacturer's determination determin	ormation		
Assay used, methodology, timing for test measurement, manufacturer values/thresholds Definition of test+  IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT manufacturer's determination	ormation		
test measurement, manufacturer values/thresholds Definition of test+  IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT manufacturer's determination	ormation		
IGRA Blood samplings for determination of QFT- M. tuberculosis-specific QGIT Blood samp manufacturer's determination			
IGRA Blood samplings for determination of QFT- According to the manufacturer's determination determination of M. tuberculosis-specific QGIT manufacturer's			
(QFT- M. tuberculosis-specific QGIT manufacturer's determination	lings for		
	_		
according to the manufacturer's QGIT (Celle	-		
recommendations. Peripheral venous interferon-	cotio) and		
blood samples were processed by our F-secreting	T cells (T-		
laboratory within 3 hr SPOT.TB (0			
Immunotec			
performed			
simultaneou	ısly		
IGRA Blood samplings for determination of According to the NA			
(TSPOT) M. tuberculosis-specific interferon-F- manufacturer's			
secreting T cells (T-SPOT.TB (Oxford   recommendations			
Immunotec) were processed, and			
scored according to the manufacturer's			
recommendations. Peripheral venous			
blood samples were processed by our			
laboratory within 3 hr			
TST≥5m   A TST was performed intradermally,   Results of TST were   NA	NA		
m according to the Mantoux technique, considered positive if			
using two units of purified protein the transverse			
derivative (RT-23; Statens Serum diameter, measured 48 Institute, Copenhagen, Denmark), to 72 hr after injection,			
which is the biological equivalent of $\frac{1072 \text{ in after injection}}{\text{was } \geq 5 \text{ mm}}$			
five units of US purified protein			
derivative			
Association between test results and incidence of active TB (if applicable)			
IGRA TST			
Incidence of Total Incidence of	Total		
active TB active TB	10001		
Yes No Yes No			
IGRA + NA NA NA TST + NA NA	NA		
	NA		
IGRA - NA NA NA TST - NA NA	NA		
IGRA -NANANATST -NANAIndeterminaNANANAIndeterminNANA			
Indetermina NA NA NA Indetermin NA NA	NA		
Indetermina NA NA NA Indetermin NA NA te	NA		
Indetermina teNANANAIndetermin ateNANATotalNANANATotalNANA	NA		
Indetermina te     NA     NA     NA     Indetermin ate     NA     NA       Total     NA     NA     NA     Total     NA     NA       Test performance parameters	NA		
Indetermina te         NA         NA         NA ate         NA ate         NA nA	NA		
	NA		

				1			
Incidence der				Incidence density rate $_{TST+} = NA$			
Incidence der	isity rate <sub>IGRA</sub>	$_{-}$ = NA		Incidence density rate $_{TST-} = NA$			
Incidence der	sity rate ratio	$o_{IGRA} = NA$		Incidence density rate ratio $_{TST} = NA$			
Other reporte	d measure IGF	$_{RA} = Na$		Other reported measure $_{TST} = NA$			
		Compari	son between	tests (IGRA vs. TST)			
Ratio of cum	ulative incide	nce ratios =	NA				
Ratio of incid	lence density	rate ratios =	NA				
Other reporte	d measure =	NA					
	Association	between test	t results and	levels of TB e	xposure (if a	applicable)	
	IGRA (Q	FT-GIT)			TST≥	5mm	
	Exposu	re level	Total		Exposu	re level	Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	14	28	42	TST +	3	6	9
	(calculated)	(calculated)	(calculated)		(calculated)	(calculated)	(calculated)
IGRA -	28	113	141	TST -	39	135	174
т 1	(calculated)	(calculated)	(calculated)	T 1 .	(calculated)	(calculated)	(calculated)
Indetermina	NR	NR	3 (excluded)	Indetermin	NR	NR	0
te	40	1.41	102	ate	40	1.41	102
Total	42	141	183	Total	42	141	183
			st performan	ce parameter			
	IGI				TS		
Sensitivity =	33.30% (95%	6 CI: 19.60, 4	19.50)	Sensitivity =	7.10% (95%	6 CI: 1.50, 19	9.50)
reported							
Specificity =	80.10% (95%	6 CI: 72.90, 8	86.20)	Specificity =	95.50% (95	% CI: 90.80,	98.20)
reported							
PPV = 33.339				PPV = 33.33% (95% CI: 12.06, 64.58) calculated			
NPV = 81.10				NPV = 78.40% (95% CI: 71.70, 84.20)			
DOR (for T <sup>+</sup> 4.32)	calculated) =	2.01 (95% C	CI: 0.94,	DOR (for T <sup>+</sup> calculated) = 1. 73 (95% CI: 0.41, 7.24)			
OR (crude; fo	or T <sup>+</sup> reported	= NR		$OR (crude; for T^{+}reported) = NR$			
OR (regression	on-based; rep	orted) = NR		OR (regression-based; reported) = NR			
List of covari	ates: NA			List of covariates: NA			
Other reporte	d measure =	NR		Other reported measure = NR			
				ests (IGRA vs. TST)			
Ratio of DOR				.51, 2.66)			
Ratio of OR (	crude; for T	reported) = 1	NA				
Ratio of ORs	(regression-b	pased; report	ed) = NA				
Other reporte	d measure =	NA					
	Association	between test	t results and	levels of TB e	xposure (if a	applicable)	
	IGRA (1	TSPOT)			TST≥	5mm	
	Exposu	re level	Total		Exposu	re level	Total
	High/Yes	Low/No			High/Yes	Low/No	
IGRA +	14	20	34	TST +	3	6	9
	(calculated)	(calculated)	(calculated)		(calculated)	(calculated)	(calculated)
IGRA -	28	121	149	TST -	39	135	174
T 1 :	(calculated)	(calculated)	(calculated)	T 1	(calculated)	(calculate)	(calculated)
Indetermina	NR	NR	2 (excluded)	Indetermin	NR	NR	0
te	42	1.41	102	ate	40	1.41	102
Total	42	141	183	Total	42	141	183
			st performan	ce parameter			
a	IGI		40.50	a	TS		2.50)
Sensitivity =				Sensitivity =			
Specificity =					95.50% (95		
PPV = 41.18% (95% CI: 26.37, 57.78) calculated				PPV = 33.33% (95% CI: 12.06, 64.58) calculated			

	1/ (O50/ CI.	75 00 97 60	<i>))</i>	1  NPV = 78 40%	6 (71.70, 8	4 20)				
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,				DOR (for $T^+$ calculated) = 1.73 (95% CI: 0.41,					
6.71)				7.24)						
OR (crude; fo				$OR (crude; for T^+ reported) = NR$						
OR (regressio		orted) = NR	2	OR (regression		ported) = N	R			
List of covaria				List of covaria	tes: NA					
Other reported measure = $NR$			Other reported	measure =	= NR					
		Compar	ison between	tests (IGRA vs.	TST)					
Ratio of DOR	s (for T cal	culated) = 1	.75 (95% CI:	0.76, 4.04)						
Ratio of OR (	crude; for T <sup>⁴</sup>	reported) =	NA							
Ratio of ORs	(regression-l	based; repor	rted) = NA							
Other reported	d measure =	NA								
	Associa	ation betwe	en test result	s and BCG statu	s (if appli	cable)				
	IGI	RA			TS	T				
	BCG	status	Total		BCC	3 status	Total			
	Yes	No	1		Yes	No	7			
IGRA +	NR	NR	NR	TST +	NR	NR	NR			
IGRA -	NR	NR	NR	TST -	NR	NR	NR			
Indetermina	NR	NR	NR	Indeterminat	NR	NR	NR			
te	.=-			e						
Total	NR	NR	NR	Total	NR	NR	NR			
- 111		<del> </del>	1	nce parameters						
	IGI				TS	T				
DOD (C. T+										
DOR (for $T^+$ calculated) <sub>IGRA</sub> = NR OR (crude; for $T^+$ reported) = NR				DOR (for T+ c	alculated) <sub>T</sub>	$_{\text{CT}} = \text{NR}$	OR (crude; for T+ reported) = NR			
				DOR (for T+ c						
OR (crude; fo	r T <sup>+</sup> reported	l) = NR	= NIR	OR (crude; for	T+ reporte	ed) = NR	NR			
OR (crude; fo OR (regressio	or T <sup>+</sup> reported on-based; rep	l) = NR	= NR	OR (crude; for OR (regression	T+ reportents.	ed) = NR	NR			
OR (crude; fo OR (regressio List of covaria	or T <sup>+</sup> reported on-based; rep ates: NR	l) = NR orted) <sub>IGRA</sub> =	= NR	OR (crude; for OR (regression List of covaria	T+ reported	ed) = NR ported) <sub>TST</sub> =	NR			
OR (crude; fo OR (regressio List of covaria Other reported	or T <sup>+</sup> reported on-based; rep ates: NR d measure =	l) = NR orted) <sub>IGRA</sub> = NR		OR (crude; for OR (regression List of covaria Other reported	T+ reported a-based; reported: NR measure =	ed) = NR ported) <sub>TST</sub> =	NR			
OR (crude; fo OR (regressio List of covaria Other reported Between-test	or T <sup>+</sup> reported on-based; rep ates: NR d measure = agreement,	l) = NR orted) <sub>IGRA</sub> = NR concordan	ce, and disco	OR (crude; for OR (regression List of covaria Other reported rdance (if applic	T+ reported reported; reported; reported; NR measure = able)	ed) = NR ported) <sub>TST</sub> =				
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OR (crude; fo OR (regressio List of covaria Other reported Between-test	or T <sup>+</sup> reported on-based; rep ates: NR d measure = agreement, ay be stratif	) = NR orted) <sub>IGRA</sub> = NR concordan ied by TST	ce, and discor	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported tes: NR measure = able) on status,	ed) = NR ported) <sub>TST</sub> =	dition			
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OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample	or T <sup>+</sup> reported on-based; rep ates: NR d measure = agreement, ay be stratif	) = NR orted) <sub>IGRA</sub> = NR concordan ied by TST	ce, and discorted cut-off value	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported tes: NR measure = able) on status,	ed) = NR ported) <sub>TST</sub> =	dition			
OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample	or T <sup>+</sup> reported on-based; rep ates: NR d measure = agreement, ay be stratif	l) = NR orted) <sub>IGRA</sub> =  NR concordan ied by TST  NR	ce, and discording to the control of	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported tes: NR measure = able) on status,  ST - NR	ed) = NR ported) <sub>TST</sub> =	Total 47			
OR (crude; for OR (regression List of covarian Other reported Between-test This table material sample IGRA (QFT-Covarian Control of the Covarian Co	or T <sup>+</sup> reported on-based; rep ates: NR d measure = agreement, ay be stratif	) = NR orted) <sub>IGRA</sub> =  NR concordan ied by TST	ce, and discording to the control of	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported tes: NR measure = able) on status,	ed) = NR ported) <sub>TST</sub> =	dition Total			
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OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample IGRA (QFT-C) + IGRA (QFT-C) - indeterminate	or T <sup>+</sup> reported on-based; rep ates: NR d measure = agreement, ay be stratif GIT)	nted) = NR orted) IGRA =  NR concordan ied by TST  NR  NR	ce, and discording the cut-off value	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST = NR and/or cond	Total 47 153 (excluded)			
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OR (crude; for OR (regression List of covariate Other reported Between-test This table material Total sample IGRA (QFT-C) - indeterminate Total Description Sample definition of the OR A (DFT-C) indeterminate Total Description Sample definition of the OR A (DFT-C) indeterminate Total Description Sample definition of the OR (Crude; for	or T <sup>+</sup> reported on-based; repates: NR d measure = agreement, ay be stratif	nr NR concordan ied by TST  TST NR NR NR	ce, and discording to the control of	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST =  NR  and/or cond	Total 47 153 (excluded)			
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OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample IGRA (QFT-C) + IGRA (QFT-C) - indeterminate Total Description Sample defini TST + threshol Parameters Kappa = 0.11	or T <sup>+</sup> reported on-based; repates: NR d measure = agreement, ay be stratiff of the stratification of	nr NR concordan ied by TST  TST NR NR NR	ce, and discording to the control of	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST =  NR  and/or cond	Total 47 153 (excluded)			
OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample IGRA (QFT-C) + IGRA (QFT-C) - indeterminate Total Description Sample defini TST + threshot Parameters Kappa = 0.11 % concordance % discordance	or T <sup>+</sup> reported on-based; repates: NR d measure = agreement, ay be stratif distriction (e.g., to old: ≥5mm (P = 0.010) to e = NR e = NR	n) = NR orted) IGRA =  NR concordan ied by TST  NR  NR  NR  NR  1 NR  1 NR  1 NR  1 NR  1 NR  1 NR  2 NR  4 NR  5 NR  1	ce, and discording to the cut-off value of value of the cut-off value of the cut-off value of va	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST =  NR  and/or cond	Total 47 153 (excluded)			
OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample IGRA (QFT-C) + IGRA (QFT-C) - indeterminate Total Description Sample definit TST + threshot Parameters Kappa = 0.11 % concordance % discordance	or T <sup>+</sup> reported on-based; repates: NR d measure = agreement, ay be stratification (e.g., to old: ≥5mm  (P = 0.010) the = NR agreement, agreem	n) = NR orted) IGRA =  NR concordan ied by TST  NR  NR  NR  concordan ied by TST  NR  NR  Oncordan ied by TST	ce, and discorder to the control of	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST =  NR and/or cond  (n = 200)	Total 47 153 (excluded) 200			
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OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample  IGRA (QFT-C) + IGRA (QFT-C) - indeterminate Total Description Sample definit TST + thresho Parameters Kappa = 0.11 % concordance % discordance Between-test This table ma Total sample	or T <sup>+</sup> reported on-based; repates: NR d measure = agreement, ay be stratiff of the stratification of the strat	n) = NR orted) IGRA =  NR concordan ied by TST  NR  NR  NR  concordan ied by TST  NR  TST  NR  NR  NR  NR  NR  NR  NR  NR  NR  N	ce, and discording the second cut-off value ce, and discording cut-off value ce, and discording cut-off value ce.	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST =  NR and/or cond  (n = 200)	Total 47 153 (excluded) 200  lition  Total 41			
OR (crude; fo OR (regressio List of covaria Other reported Between-test This table ma Total sample IGRA (QFT-C) + IGRA (QFT-C) - indeterminate Total Description Sample defini TST + threshot Parameters Kappa = 0.11 % concordance % discordance Between-test This table ma Total sample	or T <sup>+</sup> reported on-based; repates: NR d measure = agreement, ay be stratification (e.g., to old: ≥5mm  (P = 0.010) to e = NR agreement, ay be stratification (e.g., to old: ≥7mm)  (T) + T) -	D) = NR orted) IGRA =  NR concordan ied by TST  NR  NR  NR  orted) IGRA =  TST  NR  TST  NR  TST  NR  TST  TST  T	ce, and discording to the control of	OR (crude; for OR (regression List of covaria Other reported rdance (if applic, BCG vaccinati	T+ reported a-based; reported	ed) = NR ported) TST =  NR and/or cond  (n = 200)	Total 47 153 (excluded) 200  lition  Total			

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)**

Stratification (spe	chy 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)**

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

	other dutedness							
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)

### Study details

First author surname year of publication: Hsia 2012<sup>129</sup>

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	Tota	Total N	Total N (indeterminate)	Total N
	(tested)	l N	(test-)		(test
					results
		(test			availab
		+)			le)

ICRA (	QFT-GIT	). [2	2282	160	2081	41				2241
TST (≥5	_		2282	215	2067	0				2282
	specify):		NA	NA	NA	NA				NA
			lid results							11/1
			to TB in i							
	, <u>r</u>		efinition of					on		
Non-exp	osed		North Ame							
Exposed	1 (specify	y): \	Western Eu	rope						
Exposed	2 (specify	y): A	Asia							
	3 (specify		Eastern Eur	ope						
Exposed	4 (specify	y): I	Latin Amer	rica						
Tests										
	Assa		ethodolog					lues/thresh		Other
			ement, ma					ion of test	+	inform ation
IGRA			was the IC				ding to			NA
(QFT-			ndard veni				acture			
GIT)	-		gle visit to					lts were		
			the M tube					duplicate		
	_	-	G-GIT test and the control of the co					same sam	pie.	
			this IGRA					nitially e on the IG	R A	
	_		y. In additi		_			cond samp		
			the manua					d tested, an		
			already pre	-	_			were used		
		_	le-handling			detern	determine study eligibility			
	performe	d at inves	stigational	sites, and	a central					
			ned the enz							
			say-based	_	-					
			n patient ac		the					
TECTE			erpretation		1	TT1 TT	TI TOT 1 1			
TST			ormed accousing 5 tub				The TST was deemed			
			erivative (P				positive for latent TB			
	-		(Statens S				infection according to the local country guidelines for			
			worker re				defining an			
			Γ at 48–72		-		immunosuppressed			
	placemer							e absence	of	
						local g	guidelii	nes, accord	ling to	
						-	esence	of indurati	on 5	
						mm		* `		
Associa	tion betwe		esults and	incidence	e of active	TB (if ap	plicab			
			ence of	Т-	otal		T <sub>m</sub> a.	dence of	7	otal
			ence of e TB	10	ııdı		1	tive TB		otai
		Yes	No				Ye	No	-	
		103	110				S	110		
IGR	2A +	NA	NA	N	A	TST +	NA	NA		NA
IGF	RA -	NA	NA		Ā	TST -	NA	NA		NA
Indeter	rminate	NA	NA	N	A	Indeter	NA	NA		NA
						minate				
Тс	otal	NA	NA		A	Total	NA	NA		NA
				st perforr	nance par	ameters				
		IG	RA					TST		

Sensitivity = NA					Sensitivity = NA			
Specificity = NA					icity = NA			
PPV = NA				PPV =	PPV = NA			
NPV = NA				NPV =	NPV = NA			
Cumulative I	Cumulative Incidence $_{IGRA^{+}} = NA$				lative Inciden	$ce_{TST+} = N$	A	
Cumulative Incidence <sub>IGRA</sub> . = NA				Cumu	lative Inciden	$ce_{TST} = N$	A	
Cumulative Incidence Ratio <sub>IGRA</sub> = NA					lative Inciden			
	nsity rate $_{IGRA^{+}} = NA$			Incide	nce density ra	ate $_{TST+} = N$	A	
	nsity rate $_{IGRA}$ = NA				nce density ra			
	nsity rate ratio <sub>IGRA</sub> =	NA			nce density ra			
Other reported measure IGRA = NA					reported mea			
Comparison between tests (						561-6 151 1	12.2	
Ratio of cum		•	Ween test	o (IOILI)	3. 151)			
Ratio of cumulative incidence ratios = NA  Ratio of incidence density rate ratios = NA								
Other reported measure = NA								
_	Association between	n tost wasult	a and lava	la of TD o	vnosuvo (if o	nnliaahla		
			s and leve	18 01 1 D 6		<u>ppncable)</u> ≥5 mm		
IGRA (QFT-GIT)							T-4-1	
	Exposure level Total				Exposur		Total	
TCD 4	High/Yes	Low/No	1.60	mam .	High/Yes	Low/No	21.5	
IGRA +	NR	NR	160	TST +	NR	NR	215	
IGRA -	NR	NR	2081	TST -	NR	NR	2067	
Indetermina	NR	NR	41	Indeter	NR	NR	0	
te				minate				
Total	Vary by geographic	c region	2282	Total	Total Vary by geographic 2282			
				region				
		Test perfo	ormance p	arameter				
	IGRA			TST				
Sensitivity =	NR			Sensitivity = NR				
Specificity =	NR			Specificity = NR				
PPV = NR				PPV = NR				
NPV = NR				NPV = NR				
DOR (for T <sup>+</sup>	calculated) = NR			DOR (fo	r T <sup>+</sup> calculate	d = NR		
OR (crude; fo	or $T^+$ reported) = NR			OR (crud	le; for T <sup>+</sup> repo	orted) = NR	_	
	on-based; reported) =			OR (regression-based; reported) =				
	ope vs. North Americ		% CI:		Europe vs. N			
1.99, 5.83)	1			(95% CI: 1.30, 3.38)				
	a vs. North America	: 3.43 (95%	CI: 1.64,	Latin America vs. North America: 1.56 (95%				
7.19)			,	CI: 0.80, 3.05)				
/	pe vs. North America	a: 3.58 (95%	CI:	Eastern Europe vs. North America: 0.95				
1.93, 6.63)	•	`		(95% CI: 0.53, 1.70)				
	h America: 8.48 (95)	% CI: 4.78,	15.03)	Asia vs. North America: 7.47 (95% CI: 4.61,				
		Ź	,	12.08)				
List of covari	ates: baseline metho	trexate use.	baseline	/				
steroid use, d	isease type, age, and	prior BCG		List of covariates: : baseline methotrexate				
vaccination	, , , , , , , , , , , , , , , , , , ,	•		use, base	line steroid u	se, disease	type, age,	
				use, baseline steroid use, disease type, age, and prior BCG vaccination				
Other reporte	ed measure = NR			Other reported measure = NR				
1		parison bet	ween tests					
Ratio of DOF	Rs (for T <sup>+</sup> calculated)				,			
	(crude; for T <sup>+</sup> reporte							
	(regression-based; r	•						
	ope vs. North Americ		% CI: 1 13	3, 2,34)				
	a vs. North America							
Latin / milette	a . s. moran ramenca	. 2.20 (73)	, 0 01. 1.32	, 5.00)				

Eastern Europe					, 5.81)				
Asia vs. North			0.77, 1.66	5)					
Other reported	measure = NR								
	Association	n between tes	st results	and	BCG status (i	f appli	cable)		
	IGRA (QF	T-GIT)				TST	≥5 mm		
	BCG	status	Tota	ıl		BCC	status	Total	
	Yes	No	1			Yes	No		
IGRA +	71	72	143		TST +	119	62	181	
IGRA -	NR	NR	1853		TST -	NR	NR	1848	
Indeterminate	9	24	33		Indeterminat e	NR	NR	0	
Total	781	1248	2029		Total	781	1248	2029	
		Test pe	erformar	nce pa	arameters				
	IGR.			Î		Т	ST		
DOR (for T <sup>+</sup> ca	lculated) <sub>IGRA</sub> =	= NR			DOR (for T+ o	calculat	$ed)_{TST} = N$	JR	
OR (crude; for					OR (crude; for				
OR (regression-			) (95% C	:I·	OR (regression				
0.66, 1.51)					(95% CI: 1.71		, reported	7131 2	
List of covariate					T :	. 1	1	1	
steroid use, dise	ease type, age,	and geograpi	nic regioi	n	List of covaria			,	
					baseline steroi		iisease tyj	be, age, and	
O41 ND					geographic region				
Other reported measure = NR  Other reported measure = NR  Between-test agreement, concordance, and discordance (if applicable)									
This table may					`		and/or c	ondition	
Total sample									
•		TST +			TST -			Total	
IGRA +			59		101			160	
IGRA -		NR			NR			2081	
Indeterminate		NR			NR			41	
Total		215			2067			2282	
Description		-	I		200,				
Sample definition	on (e.g., total.	if stratified b	v BCG o	r con	dition – specify	v): total			
TST + threshold			<i>)</i>			,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
Parameters	<u></u>								
Kappa = $0.22 (9)$	95% CI: 0.15	0.27)							
% concordance		0.27)							
% discordance									
Stratification (		1). RCG-va	ccinated	1					
Stratification (	speerly group	TST +	cemateu		TST -			Total	
IGRA +		28			43			71	
IGRA -		91			619			710	
Indeterminate		0 (excluded)			9 (excluded)	`	0.4	(excluded)	
Total		119			662	,	7 (	781	
<b>Description</b>		117			002			/ 01	
	on (a.g. total	if stratified 1	v BCC ~	r oor	dition amosif	v). DCC	1 vanningt	ad	
Sample definition		11 Suannea b	у все о	or COII	umon – specify	y). DCC	vaccinat	cu	
TST + threshold	ı. ∠3 IIIM								
Parameters	)50/ CL 0 12	0.27)1 1	to d						
Kappa = $0.20 (9)$				4 07	20) - 1 1 1 1				
% concordance		,							
% discordance		,			96) calculated				
Stratification (	specify group		n-vaccin	ated				T . 1	
		TST +			TST -			Total	

IGRA +	24	48	72
IGRA -	38	1138	1176
Indeterminate	6 (excluded)	18 (excluded)	24 (excluded)
Total	62	1186	1248

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

# **Study details**

First author surname year of publication: Kim 2010<sup>130</sup>

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

Number of patients tested

	Total N (tested)	Tota I N (test +)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (TSPOT):	209	65	119	25	184
<b>TST</b> (≥5mm):	209	47	162	0	209
<b>TST</b> (≥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 (spe		(i) close contact with a person with pulmonary tuberculosis within the last						
Process (SP)		year, (ii) abnormal chest radiography, (iii) a history of untreated or						
		inadequately treated TB, or (iv) newly acquired infection (recent						
		conversion	on of the tuber	culin sl	kin test	to posit	tive status)	)
Exposed 2 (spe	ecify):	NA						
Exposed 3 (spe	ecify):	NA						
Exposed 4 (spe	cify):	NA						
Tests								
		sed, methodology, timing for				Cut		Other
	test mea	suremen	t, manufactu	rer			resholds	information
TCD 4		1	11 1 1				of test+	
IGRA			blood sample	was			criteria for	
(TSPOT)			patient for the		-		ative, and	samples were
	ELISPOT a					e outcomes ommended		
		oducing T-cell response (i.e., T-OT.TB, Oxford Immunotec,				e manuf		avoid the
		Abingdon, UK). Peripheral blood			by till	. manul		possible
	mononuclear cells (PBMC) were							boosting
	separated from peripheral venous			olood				effect of TST
	within 4 h from sampling, and 2.5							on the
	PBMC were plated per well in we			ls				ELISPOT
	*	coated with anti-human IFN-g						assay
	antibody							
			tured at 37°C					
			counted with a					
		-	e (ELiSpot04	· HK,				
	Strassberg,	_	tika GmbH,					
TST (≥5mm			que, injecting	 я	The positive criterion for			or NA
or ≥10mm)			d protein deriv		TST was ≥10 mm size of			
,	RT23 (State			induration 48-72 h after				
			rk) intraderma					
	into the fore				_			
Association be			d incidence of	f active	TB (if	applic	able)	
	IGRA		T				TST	
	Incide		Total				lence of	Total
	active						ve TB	
YGD .	Yes	No	27.1	man		Yes	No	27.1
IGRA +	NA NA	NA	NA	<del>                                     </del>	T +	NA	NA	NA
IGRA -	NA NA	NA	NA NA	1	T -	NA NA	NA NA	NA NA
Indeterminate	e NA	NA	NA		ermin	NA	NA	NA
Total	NA	NA	NA		te tal	NA	NA	NA
Total	11//1		est performai				INA	INA
	IGRA		- Por Ioi iliai	Par	AIII CC		TST	
Sensitivity = N				Sensit	tivity =	NA	IDI	
Specificity = N				1	ficity =			
PPV = NA				PPV =				
NPV = NA				NPV				
Cumulative Inc	idence <sub>IGRA+</sub>	= NA		<del>                                     </del>		Inciden	$ce_{TST+} = N$	ΙA
Cumulative Inc				Cumulative Incidence TST- = NA				
Cumulative Inc			Α	1			ce Ratio TS	
Incidence density rate <sub>IGRA+</sub> = NA				Incidence density rate <sub>TST+</sub> = NA				

	ensity rate <sub>IGRA</sub>			Incidence density				
	ensity rate ratio			Incidence density rate ratio $_{TST} = NA$				
Other report	ed measure IGF	RA = NA		Other reported measure $_{TST} = NA$				
		Compariso	on between t	ests (IGRA vs. 7	TST)			
Ratio of cum	nulative incide	nce ratios = N	NΑ					
Ratio of inci	dence density	rate ratios = 1	NA					
Other report	ed measure =	NA						
	Association b	etween test i	results and l	evels of TB expo	sure (if applica	ble)		
	IGRA (1	TSPOT)			TST (≥5mm)			
	Exposu	re level	Total		Exposure 1	evel	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	
Indetermin	3	22	25	Indeterminate	0	0	0	
ate	(excluded)	(excluded)	(excluded)					
Total	22	187	209	Total	22	187	209	
		Test	performanc	e parameters				
	IGI		•		TST			
Sensitivity = 10/19 = 52.63% (95% CI: 31.71, 72.67)				Sensitivity = 8/ 57.05)	/22 = 36.36% (9	5% CI: 1	9.73,	
Specificity = 110/165 = 66.67% (95% CI: 59.17,				/	48/187 = 79.14%	/ <sub>-</sub> (050/ <sub>-</sub> (	٦٢٠	
73.41)				72.76, 84.35)	+6/16/ - /9.14/	0 (93/0 (	<b>∠1.</b>	
	5 = 15.38% (9:	5% CI · 8 57	26.06)	PPV = 8/47 = 17.02% (95% CI: 8.88, 30.14)				
	$\frac{3-13.3876(9.3)}{119=92.44\%}$			NPV = 148/162 = 91.36% (95% CI:				
95.97)	117 — 72,4470	(9370 C	1. 60.23,	86.02, 94.78)				
	calculated) =	2 22 (95% C	I· 0.85	DOR (for $T^+$ calculated) = 2.17 (95% CI: 0.85,				
5.78)	calculated) –	2.22 (9370 C	1. 0.65,	5.54)				
	for T <sup>+</sup> reported	) = 2.35 (95%)	CI: 0.90	OR (crude; for $T^+$ reported) = 2.17 (95% CI:				
6.12)	or reported	) 2.33 (337)	0.70,	0.85, 5.54)				
	ion-based; rep	orted) = 2.38	(95% CI:	OR (regression-based; reported) = 2.11 (95%				
0.87, 6.52)		2.50	(>070 01.	CI: 0.82, 5.46)	ouseu, reperiou	.,	(>0)	
List of covar	riates: age			List of covariat	es: age			
	ed measure =	NR		Other reported				
			n between t	ests (IGRA vs. 7				
Ratio of DO	Rs (for T <sup>+</sup> calc				,			
	(crude; for T <sup>+</sup>		_					
				% CI: 0.56, 2.28	)			
	ed measure =			,	/			
•			results and l	evels of TB expo	sure (if applica	ble)		
	IGRA (1			,	TST (≥10mm)			
	Exposu		Total		Exposure 1		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	
Indetermin	3	22(exclud	25(exclud	Indeterminate	0	0	0	
ate	(excluded)	ed)	ed)					
Total	22	187	209	Total	22	187	209	
				ce parameters				
	IGI				TST			
Sensitivity =	= 10/19 = 52.63		31.71,	Sensitivity = 4/	$\sqrt{22} = 18.18\% (9)$	5% CI: 7	.31,	
72.67)		(	,	38.52)		,	,	
//				, ,				

Specificit	$x_{V} = 110/165 =$	= 66.67% (95%	CI: 50 17	Specificity = 1	70/187	= 90 91% (95%	ζ.CI:	
73.41)	y - 110/103 -	- 00.0770 (9370	C1. 39.17,	Specificity = 170/187 = 90.91% (95% CI: 85.92, 94.25)				
PPV = 10	0/65 = 15.38%	(95% CI: 8.57	, 26.06)	PPV = 4/21 = 19.05% (95% CI: 7.66, 40.00)				
NPV = 1	10/119 = 92.44	4% (95%	CI: 86.25,	NPV = 170/188 = 90.43% (95% CI: 85.37,				
95.97)				93.86)				
DOR (for	T calculated	) = 2.22 (95%)	CI: 0.85,	DOR (for T <sup>+</sup> c	alculated	d) = 2.22 (95%)	CI: 0.67,	
5.78)				7.32)				
OR (crud 6.12)	e; for T <sup>+</sup> repor	ted) = 2.35 (95)	OR (crude; for 0.67, 7.32)	r T <sup>+</sup> repo	rted) = 2.22 (9)	5% CI:		
	ession-based:	reported) = $2.3$	8 (05%	OR (regression	n_hased:	reported = 2	12 (05%	
CI:0.87, 6		reported) – 2.3	0 (93/0	CI: 0.60, 7.49)		reported) – 2.	12 (9370	
	variates: age			List of covaria				
	orted measure	e = NR	Other reported		e = NR			
1			son between t	ests (IGRA vs.				
Ratio of I	OORs (for T <sup>+</sup>	calculated) = 1			,			
		$T^{+}$ reported) =						
Ratio of 0	ORs (regression	n-based; repor	ted) = 1.12 (95)	% CI: 0.49, 2.50	5)			
	orted measure							
	Asso	ciation betwee	n test results	and BCG status	s (if app	licable)		
	IGRA	(TSPOT)			TST	(≥5mm)		
	BCG	status	Total		В	CG status	Total	
	Yes	No			Yes	No		
IGRA +	48	17	65	TST +	38	9	47	
IGRA -	97	22	119	TST -	125	37	162	
Indeter	18	7	25	Indeterminat	0	0	0	
minate	(excluded)	(excluded)	(excluded)	e				
Total	163	46	209	Total	163	46	209	
	1	Te GRA	st performano	ce parameters	7	ΓST		
DOR (for		$O_{IGRA} = 0.64 (9)$	5% CI: 0.31	DOR (for T+ o			(95%	
1.32)		JIGRA 0.01 ()	270 21. 0.21,	CI: 0.55, 2.82)		a)151 1.20	(3570	
	e; for T <sup>+</sup> repor	ted) = 0.69 (95	% CI: 0.36,	OR (crude; for		orted) = $1.25$ (9	95% CI:	
1.34)	, 1	, (	,	0.55, 2.82)	1	,		
OR (regre	ession-based;	reported) <sub>IGRA</sub> =	- NR	OR (regression	n-based;	reported) TST =	NR	
List of co	variates: NA	- /		List of covaria	ites: NA	- /		
Other rep	orted measure	e = NR		Other reported	l measur	e = NR		
	Asso	ciation betwee	n test results :	and BCG status (if applicable)				
		(TSPOT)				(≥10mm)		
		status	Total		В	CG status	Total	
	Yes	No			Yes	No		
IGRA +	48	17	65	TST +	16	5	21	
IGRA -	97	22	119	TST -	147	41	188	
Indeter	18	7	25	Indeterminat	0	0	0	
minate	(excluded)	(excluded)	(excluded)	e	1.65	1.6		
Total	163	46	209	Total	163	46	209	
	,		st performano	e parameters	7	POT		
DOD (for		$\frac{(GRA)}{(GRA)} = 0.64 (9)$	50/ CI. 0.21	DOR (for T+ c		TST = 0.80 (0	50/ CI.	
1.32)	1 carculated	) <sub>IGRA</sub> – 0.04 (9	3% CI: 0.31,	0.30, 2.58	carcurate	$a)_{TST} = 0.89 (9)$	3% CI:	
,	e: for T <sup>+</sup> repor	ted) = 0.69 (95	% CI: 0.36	OR (crude; for	r T+ ren	orted) = 0.89 (0.00)	)5% CI·	
1.34)	c, 101 1 1cp01	0.09 (93	70 01. 0.30,	0.31, 2.58)	i i icpo	0.09	/J/U C1.	
	ession-based:	reported) <sub>IGRA</sub> =	NR		n-based·	reported) TOT =	NR	
		-Portou) IGRA	- 124	OR (regression-based; reported) <sub>TST</sub> = NR				
List of co	List of covariates: NA				List of covariates: NA			

Other reported measu	re = NR	Other reported measu	ure = NR
Between-test agreem	ent, concordance, and dis	scordance (if applicable)	
·	ratified by TST cut-off va	lue, BCG vaccination sta	tus, 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	g., total, if stratified by BCC	G or condition – specify): to	otal
TST + threshold: ≥10	mm		
Parameters			
Kappa = $0.23 (95\% C)$	I: 0.12, 0.34)		
	/184 = 71.2% (95% CI: 64.	27, 77.25)	
% discordance = 53/1	,	I: 22.75, 35.73)	
Stratification (BCG	,		
,	TST + (≥10mm)	TST -	Total
IGRA (TSPOT) +	10	38	48
IGRA (TSPOT) -	5	92	97
Indeterminate	NR	NR	NR
Total	15	130	145
Description			
	g., total, if stratified by BCC	G or condition – specify): I	BCG vaccinated
TST + threshold: ≥10		1 2/	
Parameters			
Kappa = 0.19 (95% C)	I: 0.06, 0.31)		
	$\sqrt{145} = 70.34\%$ (95% CI: 62)	2.46, 77.18)	
	45 = 29.66% (95% CI: 22.8		
Stratification (specif	`	- , ,	
( <b>P</b> • • • • • • • • • • • • • • • • • • •	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
Indeterminate	NR	NR	NR
Total	NR	NR	NR
Description	1110	1110	1111
	g., total, if stratified by BCC	G or condition – specify): N	JR
TST + threshold: NR	,,, total, if stratified by Dec	3 of condition—specify).	· · ·
Parameters			
Parameters Kappa = NR			
Parameters Kappa = NR % concordance = NR			
Parameters Kappa = NR % concordance = NR	Othar	outcomes	
Parameters Kappa = NR % concordance = NR % discordance = NR		· outcomes	Health related quality of
Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if	Adverse event		
Parameters Kappa = NR % concordance = NR % discordance = NR			life mean score (SD)
Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)	Adverse event	s n/N (%)	life mean score (SD) (specify)
Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)  IGRA:	Adverse event	s n/N (%) NR	life mean score (SD) (specify)  NR
Parameters Kappa = NR % concordance = NR % discordance = NR Test and cut-off (if applicable)	Adverse event	s n/N (%)	(specify)

# **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

### Study details

First author surname year of publication: Kim 2013b<sup>131</sup>

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

	Tot al N (test ed)	Total N (test+)	Total N (test-)	Total N (indeterminate)	Total N (test results available)
IGRA (QFT-GIT):	126	53	67	6	120
<b>TST</b> (≥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 L	ΓΒΙ group							
Exposed 1 (spec	eify):	(1) patients with a history of LTBI or active TB; (2) patients with abnormal								
P		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 (spec	eify):	NA								
Exposed 3 (spec		NA								
Exposed 4 (spec	\ 1 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \									
Tests										
	Assay	used, 1	methodolo	gy, timing fo	r test		Cut-off	i	Other	
	n	neasui	rement, ma	anufacturer		val	ues/thres	holds	information	
						Def	finition of	test+		
IGRA (QFT-	QuantiFE	RON-	TB Gold I	n-Tube test		A p	ositive QI	FT-	NA	
GIT)				amples were			result wa			
			-	for QFT-GIT		defi	ined as IF	N-c		
				test according		-	onse of T			
				s (Cellestis L		1	gen minus			
				lia). Blood sa			he Nil tub			
				ood collection			35 IU/mL	and		
				ng heparin alo	one (Nil		% of the			
	, .		ontrol), on			_	ative cont	rol		
				gen tube, pos		valı	ıe			
		and one with TB-specific antigens								
		5, CFP-10, and TB 7.7). The three								
		re incubated for 20 h at 37°C. The								
		ation of IFN-c was measured by the ymelinked immunosorbent assay.								
					ay.					
			are provide	calculating t	ha					
	results	uici w	as used for	calculating t	iic					
TST (≥5mm		was ne	erformed h	y injecting a	2-TII	The	transvers	e	NA	
or ≥10mm)				s Serum Insti			uration sit		1171	
or Eromm)				tradermally in			asured by			
			/	ordance with		trained nurse in				
	Mantoux				-	mm after 48–72 h				
							uration $\geq 1$			
						1	defined a			
							itive TST			
Association bet	ween test	result	s and incid	dence of activ	ve TB (if					
	IGRA						TST			
	Incide	ence	Total		Incide	nce o	f active		Total	
	of ac	tive				TB				
	TI	3	]							
	Yes	N			Yes	-	No			
		0								
IGRA +	NA	N	NA	TST +	NA		NA		NA	
		A		_			_			
IGRA -	NA	N	NA	TST -	NA		NA		NA	
		A								
Indeterminate	NA	N	NA	Indetermi	NA		NA		NA	
/TD : 1	374	A	37.4	nate	3.7.4		3 T A		» T.A	
Total	NA	N	NA	Total	NA		NA		NA	
		A	]							

Test performance parameters									
	IGRA			•	TST				
Sensitivity =	NA		S	Sensitivity = NA					
Specificity =	NA		S	Specificity = $NA$					
PPV = NA			F	PPV = NA					
NPV = NA			1	NPV = NA					
Cumulative I	ncidence IGRA+	= NA	(	Cumulative Incidence $_{TST+} = NA$					
Cumulative I	ncidence <sub>IGRA-</sub> =	= NA	(	Cumulative Incidence	$_{TST-} = NA$				
Cumulative I	ncidence Ratio	$_{\rm IGRA} = 1$	NA (	Cumulative Incidence	Ratio $_{TST} = NA$				
Incidence der	nsity rate IGRA+	= NA	I	ncidence density rate	$_{TST+} = NA$				
Incidence der	nsity rate IGRA-	= NA	I	ncidence density rate	$_{TST-} = NA$				
Incidence der	nsity rate ratio I	$G_{GRA} = N$		ncidence density rate					
Other reporte	d measure <sub>IGRA</sub>			Other reported measur					
				ween tests (IGRA vs	. TST)				
	ulative inciden								
	lence density ra		os = NA						
	d measure = $N$								
			test results	s and levels of TB ex		able)			
	IGRA (QFT-				TST (≥10mm)		T .		
	Exposure le		Total		Exposure le		Total		
	High/Yes	Low			High/Yes	Low/			
		/No				No			
IGRA +	11	42	53	TST +	13	10	23		
IGRA -	4	63	67	TST -	2	94	96		
Indetermina	1	5	6	Indeterminate	1	6	7		
te			(excluded	d			(exclud		
T-4-1	1.6	110	126	Total	16	110	ed)		
Total	16	110	-		10	110	126		
	IGRA		Test perio	ormance parameters	тет				
Consitivity -	$\frac{13}{11/15} = 73.33\%$	/ (059/	CI: 49.05	, Sensitivity = 13/1	TST 5 - 86 679/ (059/	CI: 62.1	2 06 26)		
89.1)	11/15 – 75.55	70 (9370	C1. 40.03,	, Selisitivity – 13/1	3 - 80.07/0 (93/0	C1. 02.1	2, 90.20)		
	63/105 = 60.00	)% (959	% CI:	Specificity = 94/104 = 90.38% (95% CI: 83.2,					
50.44, 68.86)		(,,,,	·	94.69)					
	= 20.75% (95%	6 CI: 1	2.00,	PPV = 13/23 = 56.52% (95% CI: 36.81, 74.37)					
33.46)	,			11 ( 15/25 50.5270 (7570 01. 50.01, 14.51)					
	= 94.03% (95%	% CI: 8	5.63,	NPV = 94/96 = 97	7.92% (95% CI: 9	2.72, 99.	43)		
97.65)	`				<u> </u>				
`	calculated) = 4	.12 (95	% CI: 1.23	3, DOR (for $T^+$ calculated) = 61.1 (95% CI: 12.03,					
13.82)				310.4)					
· ·	or T <sup>+</sup> reported)	= 4.13	(95% CI:	OR (crude; for T <sup>+</sup>	reported) = $0.6\overline{1}$ (	(95% CI:	0.13,		
1.23, 13.82)				2.91) -error					
, ,	on-based; repor	ted) = 4	1.62 (95%	OR (regression-ba	(sed; reported) = (	0.40 (95%)	% CI:		
CI: 1.15, 18.6	*			0.07. 2.20) -error					
List of covariates: NR List of covariates: NR									
Other reporte	d measure = $N$			Other reported me					
D // 0505	) (C FC <sup>+</sup> 1			ween tests (IGRA vs	. TST)				
				% CI: 0.02, 0.19)					
	Ratio of OR (crude; for $T^+$ reported) = NA								
	Ratio of ORs (regression-based; reported) = NA								
Other reporte	Other reported measure = NA  Association between test results and BCG status (if applicable)								
			een test r	esuits and BCG stati					
	IGRA (QFT-	GII)			<b>TST</b> (≥10mm)				

	DCC	status	Total	1	DC(	G status	Total					
}	Yes	No	Total		Yes	No	- Total					
IGRA +	50	3	53	TST +	22	1	23					
IGRA -	60	7	67	TST -	86	10	96					
Indetermi	5	1	6	Indetermina	7	0	7					
nate	3	1	(excluded)	te	/		(excluded)					
Total	115	11	126	Total	115	11	126					
Test performance parameters												
	I	GRA	Test perior			ST						
DOR (for T			94 (95% CI:	DOR (for T <sup>+</sup> c			(95% CI:					
0.47, 7.91)		VW/IGRA 11	, (,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	0.32, 21.06)	, and an and an ) 12	,, _,,,	(50,001.					
	for T <sup>+</sup> ren	orted) = 1.9	94 (95% CI:		r T <sup>+</sup> reported	d = 2.56 (95%)	CI: 0.31.					
0.48, 7.91)		,	(	21.06)	.1	.,	,					
	sion-based	d; reported)	$I_{GRA} = 2.32$		n-based; rer	ported) $_{TST} = 3.3$	32 (95% CI:					
(95% CI: 0.50, 10.66) 0.38, 28.97)												
List of covariates: NR  List of covariates: NR												
Other repor	rted measi	ire = NR		Other reported	d measure =	NR						
Between-te	est agreen	nent, conco	rdance, and d	liscordance (if a	pplicable)							
This table	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 samp	ole											
		TST	+	TST -		Т	otal					
		(≥10m	m)									
IGRA (QF		17										
IGRA (QF		6										
Indetermina	ate	0										
Total		23		96			119					
Description												
	Sample definition (e.g., total, if stratified by BCG or condition – specify): total											
TST + three		)mm										
Parameter		T. 0.10.0.4	1)									
		CI: 0.10, 0.4		( 2 4 72 (1)								
			0% (95% CI: 5									
			% (95% CI: 26	5.39, 43.66)								
Stratincati	on (speci	fy group 2)		TOT			-4-1					
ICD A			T +	TST -			otal					
IGRA +			IR	NR NR			NR NR					
IGRA -	242		IR	NR NR			NR NB					
Indetermina	ate		IR ID	NR ND			NR ND					
Total	n	N	IR .	NR			NR					
Description Sample def		a total in	trotified 1 De	7C on san 1:4: -	amanif-)	NID						
		<u> </u>	stratified by Bo	CG or condition	– specity):	NK						
TST + three												
Parameter												
Kappa = N												
% concorda												
% discorda	nce = NR		041	or outcomes								
Tost and a	nt off (:f	T .		er outcomes	I 1	Hoolth volated	quality of					
Test and cut-off (if applicable)  Adverse events n/N (%)  (specify)  Health related quality life mean score (SD)												
applicable	,	1	specify)			ne mean score	(SD)					
IGRA:				NR		specify) NR	•					
TST:				NR		NR						
	cify).											
rest 3 (spe	ciiyj.			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

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

#### **Study details**

First author surname year of publication: Kim 2013c<sup>132</sup>

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  $\pm$ 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):  $44.7 \pm 11.5$ 

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-	106	21	81	4	102
GIT					
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

**Definition of exposure group** 

Non-exposed NR

Exposed 1 (specify): History of treated tuberculosis										
Exposed 1 (sp Exposed 2 (sp		_		1 chest radiogr						
Exposed 2 (sp Exposed 3 (sp		_	П	i chest radiogi	арп					
Exposed 5 (sp			A							
Tests	echy).	111	A							
1 6818	A ccov 1	icod	motho	dology, timing	Cut-off va	luos/thr	ncholde	Other		
	•			uology, tillini urement,		tion of te		information		
	10		anufact		Denini	non or tt	311	miormation		
IGRA	QuantiF			d In-Tube	A positive QF	T-GIT w	as defined	i NA		
	(QFT-G				as $\geq 0.35 \text{ IU/r}$					
	` -		-	nufacturer's	the presence of					
	instructi	ons	(Cellest	ic Ltd,	antigen minus	antigen minus that of the Nil				
	Carnegi	e, Vi	ictoria, A	Australia)	tude					
TST≥10		-		on the volar	The TST was			e NA		
mm				by injection of	if the size of t					
				ose of perified		to 72 ho	urs after			
	-			T-23 according	g the injection.					
	to the M				6 41 ED 416	** * * *	1.5			
Association b				and incidence	of active TB (if a					
		GRA		Total		Incide	TST	Tot-1		
	Incidence Total of active							Total		
	TB					active TB				
	Ye		No			Yes	No			
IGRA +	N/	-	NA	NA	TST +	NA	NA	NA		
IGRA -	NA NA	_	NA	NA	TST -	NA	NA	NA		
Indeterminat			NA	NA	Indeterminate	NA	NA	NA		
Total	NA NA	_	NA	NA	Total	NA	NA	NA		
					ance parameters					
	I	GRA	\		1		CST			
Sensitivity = N	NA				Sensitivity = N	A				
Specificity = 1	NA				Specificity = N	A				
PPV = NA					PPV = NA					
NPV = NA					NPV = NA					
Cumulative In					Cumulative Incidence <sub>TST+</sub> = NA					
Cumulative In					Cumulative Incidence $_{TST-} = NA$					
Cumulative In				NA		Cumulative Incidence Ratio <sub>TST</sub> = NA				
Incidence dens	_					Incidence density rate $_{TST^+} = NA$				
Incidence dens					Incidence densi					
Incidence dens				NA		Incidence density rate ratio $_{TST} = NA$				
Other reported	d measur	e <sub>IGR</sub>			Other reported		$_{\text{TST}} = \text{NA}$			
D. C.	1	• 1			en tests (IGRA vs	s. TST)				
Ratio of cumu										
Ratio of incide				DS = INA						
Other reported				ts and larvals -	f TD ownsows C	Jistor: -	f twooted	tuboroulosis)		
				ts and levels 0	of TB exposure (1		10 mm	tuber culosis)		
	IGRA (	_	sure	Total	ı		ure level	Total		
		expo lev		Total		Expos	ure level	1 Otal		
	v	es	No	1	-	Yes	No	-		
IGRA +		2	17	19	TST +	NR	NR	12		
IGRA -		)	74	74	TST -	NR	NR	81		
Indeterminate		R	NR	4	Indeterminate	NR	NR	0		
macterimiate	1	11	1417	т	macterinilate	1 41/	1117	U		

			(excluded)						
Total	2	91	93	Total	NR	NR	93		
Total					nce parameters				
	IGRA		rest periorii	TST					
Sensitivity = 2/2 =		5% CI (	34.24.100)	Sensitivity = NR					
Specificity = $74/9$				Specificity = NR					
88.00)	1 - 61.32	/0, 93/0	C1 (72.10,	Specificity – M	IX.				
PPV = 2/19 = 10.5	CI (2.9	3 31 30)	PPV = NR						
NPV = 74/74 = 10				NPV = NR					
DOR (for T <sup>+</sup> calcu			00, 100)	DOR (for T <sup>+</sup> cal	lculated) = N	VR			
OR (crude; for T <sup>+</sup> 1				OR (crude; for					
OR (regression-ba			21 95%	OR (regression-			R (NS)		
CI (NR)	sea, repo	rica)		List of covariate		1100) 111	(115)		
List of covariates:	NR								
Other reported me		JR		Other reported i	measure = N	IR			
			arison betwee	en tests (IGRA v					
Ratio of DORs (fo	r T <sup>+</sup> calc			· ·	/				
Ratio of OR (crude									
Ratio of ORs (regr									
Other reported me			,						
Association between test results and levels of TB exposure (Abnormal chest radiograph)									
IGR	RA (QFT	-GIT)			TST TST≥	10 mm			
	Expo	sure	Total		Exposure	e level	Total		
	lev				-				
	Yes	No			Yes	No			
IGRA +	3	16	19	TST +	NR	NR	12		
IGRA -	1	73	74	TST -	NR	NR	81		
Indeterminate	0	0	4	Indeterminate	NR	NR	0		
			(excluded)						
Total	4	89	93	Total	NR	NR	93		
			Test perform	ance parameter					
	IGRA				TST	Γ			
Sensitivity = $3/4$ =	75.00%,	95% C	(30.06,	Sensitivity = NR					
95.44)									
Specificity = 73/89	$\theta = 82.02$	%, 95%	CI (72.77,	Specificity = N	R				
88.62)	100/ 050	OT (5.5	2 27 57	DDV VD					
PPV = 3/19 = 15.7				PPV = NR					
NPV = 73/74 = 98				NPV = NR	1 1 ( 1) 3	ID			
DOR (for T <sup>+</sup> calcu	lated) =	13.69, 9:	5% CI (1.33,	DOR (for T <sup>+</sup> cal	iculated) = f	NK			
140.30) OR (crude; for T <sup>+</sup> 1	ran artad)	- ND		OR (crude; for	T <sup>+</sup> ran artad)	- NID			
OR (regression-ba			7 05 059/	OR (regression-			D (NC)		
CI (1.22, 636.62)	sea, repo	rteu) – 2	27.93, 93%	List of covariate		rtea) – N.	K (NS)		
List of covariates:	NP			List of Covarian	58. IVIX				
Other reported me		I <b>P</b>		Other reported 1	measure = N	T <b>P</b>			
Other reported me	asurc – r		rison hetwe	en tests (IGRA v					
Ratio of DORs (fo	r T <sup>+</sup> calc			ch tests (IORA v	3. 131)				
Ratio of OR (crude									
Ratio of ORs (regr	•								
Other reported me			1110						
			een test resu	lts and BCG sta	tus (if annli	cable)			
	A (TSPC				TST (≥				
131	BCG		Total			status	Total		
L			1	1					

	Yes	No			Yes	No				
ICD A	+		ND	TOT						
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)									
					TST (>					
DOR (for T <sup>+</sup> calcu			NR	DOR TST (for T-						
OR (crude; for T <sup>+</sup>				OR (crude; for						
OR (regression-ba				OR (regression-		ported) TS	$S_{\rm T} = NR$			
OR (regression-ba		orted) <sub>TSP</sub>	$_{\rm OT} = NR$	List of covariate	es: NR					
List of covariates:										
Other reported me				Other reported		= NR				
				cordance (if applic						
	e stratifi	ed by T	ST cut-off val	ue, BCG vaccination	on status	, and/or	condition			
Total sample										
		TS	T +	TST -			Total			
IGRA +			6	13			19			
IGRA -			6	68			74			
Indeterminate			0	0			0			
Total			12	81			93			
Description										
Sample definition	(e.g., tot	al, if stra	tified by BCG	or condition - spec	eify): Tota	al less Ind	leterminate			
results										
TST + threshold:	≥10 mm									
Parameters										
Kappa = $0.27, 95^{\circ}$	% CI (0.0	7, 0.46)								
% concordance =	74/93 = 7	79.57%,	95% CI (70.28	3, 86.51)						
% discordance =	19/93 = 2	0.43%,	95% CI (13.49)	, 29.72)						
Stratification (sp				,						
` •			T +	TST -	TST -					
IGRA +		1	VR.	NR			NR			
IGRA -		N	VR.	NR			NR			
Indeterminate		N	VR.	NR			NR			
Total		n n	VR.	NR			NR			
Description										
	(e.g., tot	al. if stra	tified by BCG	or condition – spec	cify): NR					
TST + threshold:	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \		· · · · · · · · · · · · · · · · · · ·	1						
Parameters										
Kappa = NR										
% concordance =	NR									
% discordance = 1										
Stratification (sp		un 2)								
or armeation (sp	gru		T +	TST -			Total			
IGRA +			VR	NR			NR			
IGRA -			IR	NR						
Indeterminate			IR	NR			NR NR			
Total				NR NR			NR			
Description Sample definition	(a.g. +a+	ol if atm	atified by DCC	or condition area	oify). NID					
		ai, ii Stra	unica by BCG	or condition – spec	.11y). NK					
TST + threshold:	NK									
Parameters NP										
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

### Study details

First author surname year of publication: Kleinert 2012<sup>133</sup>

**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

Transfer of patients tested										
	Total N (tested)	Total N	Total N (test-)	Total N (indeterminate)	Total N (test results available)					
		(test+)								
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					nd risk factors (CRF) were present				
Exposed 1 (spe	cify):				ctor (CRF) defined as the presence of at least one of				
1 (1	• /		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 (spe	cify):	NA							
Exposed 3 (spe		NA							
Exposed 4 (spe	cify):	NA	NA						
Tests									
	Assay used, methodology,				Cut-off		Ot	her	information
	timing for test				values/threshold				
		easuremen			<b>Definition of test</b>	;+			
		anufacture							
IGRA (QFT-	_	on TB Gol		NI	R		-		ts received one
<b>G</b> )		red in acco	rdance						RA, either
	with cont						TSPO		
	guideline	s 101 uppressed p	antionts:						ending on what able in the
		uppressed pere mainly							ding laboratory
	the two p		oused on				Corres	pon	anig idooratory
		ESAT-6 and	d CFP-						
	10								
IGRA	TSPOT.T	B (TSPOT	)	Th	ne cut-off for TSP	All patients received one			
(TSPOT)	administe	red in acco	rdance	po	sitivity was ≥6 sp	ots	type of IGRA, either		
	with contemporary						TSPOT.TB or		
	guideline						QFT, depending on what		
		uppressed p							ible in the
		ere mainly	based on				corres	pone	ding laboratory
	the two p		1 CED						
	_	ESAT-6 and	d CFP-						
TST	10 NR			TST with a diameter of			All patients received a		
	IVIX			>5 mm skin induration			TST		
				was considered positive			151		
Association be	tween test	results and	d incidenc		of active TB (if applicable)				
	IGR						TST		
		dence of	Total			Inci	dence o	of	Total
		ive TB					tive TB		
	Yes	No				Yes	s No	)	
IGRA +	NA	NA	NA		TST +	NA	. NA	1	NA
IGRA -	NA	NA	NA		TST -	NA		-	NA
Indeterminate		NA	NA		Indeterminate	NA		-	NA
Total	NA	NA	NA		Total	NA	NA	1	NA
			est perfor	mar	nce parameters				
a	IGR	A			a		TST		
Sensitivity = N					Sensitivity = NA				
Specificity = NA					Specificity = NA	1			
PPV = NA					PPV = NA				
NPV = NA	• 1	<b>3.</b> T.4			NPV = NA	1		NT 4	
Cumulative Inc					Cumulative Inci				
Cumulative Incidence <sub>IGRA-</sub> = NA  Cumulative Incidence Ratio <sub>IGRA</sub> = NA					Cumulative Incidence <sub>TST</sub> . = NA Cumulative Incidence Ratio <sub>TST</sub> = NA				
			Α						- NA
Incidence densi	iy rate <sub>IGRA</sub>	+ - INA			Incidence density rate $_{TST+} = NA$				

Incidence density	rate $_{IGRA-} = 1$	NA	Incidence dens				
Incidence density	rate ratio <sub>IGR</sub>	A = NA	Incidence dens	ity rate ratio	$_{TST} = NA$		
Other reported me	Other reported		= NA				
	between	tests (IGRA vs.	TST)				
Ratio of cumulativ	e incidence	ratios = NA	A				
Ratio of incidence	density rate	ratios = N	A				
Other reported me	asure = NA						
Assoc	ciation betw	een test re	sults and	levels of TB exp	oosure (if a	pplicable)	
I		TST (≥5	mm)				
	Exposui	e level	Total		Exposu	e 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	performai	nce parameters			
I	GRA(QFT-	<b>G</b> )			TST (>5	mm)	
Sensitivity = 9/54 28.74)	= 16.67% (9	95% CI: 9.0	)2,	Sensitivity = 48 48.21)	8/122 = 39.3	4% (95% (	CI: 31.13,
Specificity = 590/95.17)	631 = 93.5%	6 (95% CI:	91.3,	Specificity = 12 CI: 89.52, 92.4		91.12%	(95%
PPV = 9/50 = 18.0	00% (95% C	I: 9.77, 30.	.8)	PPV = 48/173 =		5% CI: 21.	.61, 34.85)
NPV = 590/635 =		NPV = 1282/1356 = 94.54% (95% CI: 93.2, 95.63)					
DOR (for T <sup>+</sup> calcu	1.31.	DOR (for T <sup>+</sup> ca	lculated) =	6.65 (95%	CI: 4.42.		
6.29)		- (		9.99)			
OR (crude; for T <sup>+</sup>	reported) = 1		OR (crude; for	T <sup>+</sup> reported)	= NR		
OR (regression-ba			95% CI:	OR (regression-based; reported) = 6.20 (95% CI: 4.08, 9.44)			
List of covariates:	NR			List of covariates: NR			
Other reported me				Other reported measure = NR			
T T		Compariso	n betweer	n tests (QFT vs. TST)			
Ratio of DORs (fo					101)		
Ratio of OR (crud			_	0.20, 0.00)			
Ratio of ORs (regi				95% CI: 0.26, 0.6	58)		
Other reported me		а, теропеч	) 01.2 (>	7576 C1. 0.20, 0.08)			
•		een test re	sults and	levels of TB exp	osure (if a	nnlicable)	
	GRA (TSPC		buits una	CVCIS OF TECK	TST (≥5		
-	Exposu		Total		Exposu		Total
	High/Yes	Low/No			High/Yes	Low/No	1
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
				nce parameters		1.07	
I	GRA (TSPC		. J. LUI III di	parameters	TST (>5	mm)	
Sensitivity = 24/68 47.16)		5.00,	TST (≥5 mm)  Sensitivity = 48/122 = 39.34% (95% CI: 31.13, 48.21)				
Specificity = 730/ 95.53)	776 = 94.07	% (95% CI	: 92.18,	Specificity = 1282/1407 = 91.12% (95% CI: 89.52, 92.49)			
PPV = 24/70 = 34	29% (95%)	CI: 24 25 4	45 96)	89.52, 92.49) PPV = 48/173 = 27.75% (95% CI: 21.61, 34.85)			
NPV = 730/774 =		(95% CI		NPV = 1282/1356 = 94.54% (95% CI: 21.61, 34.85)			
95.74)	)T.J4/U	(2270 CI	. , , , ,	NPV = 1282/1356 = 94.54% (95% C1: 93.2, 95.63)			
<u>'</u>		73.03)					

DOR (for T <sup>+</sup> calcu	alated) = 8	8.65 (95% CI:	DOR (for T+ calculated) = 6.65 (95% CI: 4.42,					
15.46)	9.99)							
$OR (crude; for T^{+}reported) = NR$					OR (crude; for $T$ + reported) = $NR$			
OR (regression-ba	ised; repo	rted) = 8.74 (9)	95% CI:	OR (regression-b			0 (95% CI:	
4.83, 15.82)				4.08, 9.44) List o	f covariate	es: NR		
List of covariates:								
Other reported me	asure = N		7 (	Other reported m		<u>NR</u>		
D. C. CDOD (C	Tr <sup>+</sup> 1			tests (IGRA vs. T	ST)			
Ratio of DORs (fo				0.91, 1.87)				
Ratio of OR (crud				250/ CT 0 05 2 0 0				
			(1) = 1.41 (1)	95% CI: 0.97, 2.04)				
Other reported me			4 14	I DCC 4 4	(°C 1°	111		
-			est result	s and BCG status				
IG		OT/QFT)	TD 1		TST (≥5		T . 1	
		G status	Total			status	Total	
TCD 4	Yes	No	120	TOTAL :	Yes	No	150	
IGRA +	14	106	120	TST +	50	123	173	
IGRA -	190	1219	1409	TST -	154	1202	1356	
Indeterminate	204	1225	1.500	Indeterminate	204	1225	1.500	
Total	204	1325	1529	Total	204	1325	1529	
YOU	D A (FIGD		pertorma	nce parameters	TECHE (			
		OT/QFT)	10 #0 / CV	DOD (2 F	TST (≥5		(0.50/	
DOR (for T <sup>+</sup> calcu	ılated) <sub>TSP</sub>	$_{\text{OT/QFT}} = 0.84$ (	95% CI:	DOR TST (for T	+ calculat	(ed) = 3.17	(95%	
0.47, 1.51)	. 1			CI: 2.19, 4.58)	<b></b>	1) 3.70		
OR (crude; for T <sup>+</sup>			2 (0.50/ 0)	OR (crude; for			2 0 7	
OR (regression-based; reported) <sub>QFT</sub> = 0.43 (95% CI: OR (regression-based; reported) <sub>TST</sub> = 2.95								
0.17, 1.10)	1		07 (050/	(95% CI: 2.00,				
OR (regression-ba	isea; repo	$rtea)_{TSPOT} = 1$	.07 (95%	List of covarian	tes: NK			
CI: 0.47, 2.43) List of covariates:	ND							
Other reported me		JD		Other reported	*********	– NID		
			and disa	ordance (if applica		- IVIX		
						and/ar aan	dition	
This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition  Total sample								
Total Sample		TST + (≥ <b>5</b>	mm)	TST -		T	Total	
IGRA (QFT/TSPC	)T) +	66	11111)	54	•		120	
IGRA (QFT/TSPC		107						
Indeterminate	)1) <del>-</del>	NR		1302 NR			1409 NR	
Total	+	173		1356			1529	
<b>Description</b>		1/3		1330			1041	
Sample definition (e.g., total, if stratified by BCG or condition – specify): total								
TST + threshold: >5 mm								
Parameters								
	% CI: 0.3	4 0 44)						
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 = 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 = 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 = 1					11 _ 00	+561165, 1	)	
Stratification (BC				-, -=/				
The state of the s	- J . WCOII	TST +	+ T	TST -			Total	
ICD A (OFT/TCD)	2.50	101		151			_ 0 0001	

IGRA (QFT/TSPOT) +

IGRA (QFT/TSPOT) -

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

#### **Study details**

First author surname year of publication: Laffitte 2009<sup>134</sup>

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
<b>TST (≥5mm):</b>	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

T 1 /	c	4 (10.10)		1 (0)	
Levels/gran	ing of evnocin	re to IK in	incressing	order (11	f applicable):

Definition of	of exposure	group -	probable	LTBI
---------------	-------------	---------	----------	------

Non-exposed No probable LTBI

Exposed 1 (specify):		activ tube	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		NA	NA								
(specify):											
Exposed 3		NA									
(specify):											
Exposed 4		NA									
(specify):											
Tests	1					66 1 (1)		0.141		0.0	
		Assay used, Cut methodology, timing for test measurement, manufacturer			Cut	Cut-off values/thresholds Definition of test+ informati					
IGRA (TSPO)	Γ)	NR			NR					NA	
TST (≥ 5mm o		NR				TST was consid	ered posi	tive if th	ne	NA	
≥10mm)						ration diameter					
Association be	twee	n test 1	results an	d incid	lence	of active TB (if	applicab	ole)			
		IGRA						TST			
		idence tive T		Total			Incidence of active TB			Total	
	Ye		No					Yes No			
ICD A				NIA		TCT	NA			NIA	
IGRA + IGRA -	NA NA		NA NA	NA NA		TST +	NA NA	NA NA		NA NA	
Indeterminate	N/		NA NA	NA		Indeterminate	NA NA	NA		NA NA	
Total	N/		NA NA	NA		Total	NA	NA		NA NA	
Total	117	1 1			forms	nance parameters					
		IGRA		est per	101 1116	TST					
Sensitivity = N	A	1010	_			Sensitivity = N		101			
Specificity = N						Specificity = NA					
PPV = NA						PPV = NA					
NPV = NA						NPV = NA					
Cumulative Inc	idenc	e <sub>IGR A</sub>	= NA			Cumulative Incidence $_{TST+} = NA$					
Cumulative Inc						Cumulative Incidence <sub>TST</sub> . = NA					
Cumulative Inc				A		Cumulative Incidence Ratio <sub>TST</sub> = NA					
Incidence densi						Incidence density rate $_{TST^+} = NA$					
Incidence densi						Incidence den					
Incidence densi	ty rat	e ratio	$_{IGRA} = NA$	1		Incidence dens	sity rate r	atio <sub>TST</sub>	= NA		
Other reported measure $_{IGRA} = NA$					Other reported measure <sub>TST</sub> = NA						
			Compai	ison b	etwee	n tests (IGRA v	s. TST)				
Ratio of cumulative incidence ratios = NA											
Ratio of incidence density rate ratios = NA											
Other reported measure = NA											
				st resu	lts an	d levels of TB e	_		icabl	e)	
IG		TSPO		T # :		Т	TST (≥		1		
		xposur 1/Yes	e level Low/No	Tota	I		Expo High/Ye	sure leves Lov	el v/No	Total	
IGRA +	8		2	10	TS	T +	11	9		20	
IGRA -	14		26	40	_	T -	11	19		30	
Indeterminate	NR		NR	NR	Inc	leterminate	NR	NR		NR	

Total	Total 22 28 50 Total 22 28 50							
	Test performance parameters							
	IGRA					TST		
19.73, 57.05)	Sensitivity = 8/22 = 36.36% (95% CI: 19.73, 57.05)					= 50.00% (9)	5% CI: 30.	72, 69.28)
Specificity = 2 77.35, 98.02)	6/28 = 92.86	5% (95% C	I:	1	Specificity = 19/28 =	= 67.86% (9	5% CI: 49.	34, 82.07)
PPV = 8/10 = 8 94.33)	PPV = 8/10 = 80.00% (95% CI: 49.02, PPV = 11/20 = 55.00% (95% CI: 34.21, 74.18)						.18)	
NPV = 26/40 = 77.87)	·			]	NPV = 19/30 = 63.3	3% (95% C	I: 45.51, 78	3.13)
DOR (for T <sup>+</sup> ca 1.38, 39.87)	,	`		]	DOR (for T <sup>+</sup> calcula	ted) = 2.11 (	(95% CI: 0	.67, 6.68)
OR (crude; for CI: 1.38, 39.90	))				OR (crude; for T <sup>+</sup> rep	·		[: 0.93, 9.70)
OR (regression		orted) = NR	2		OR (regression-base		=NR	
List of covarian				+	List of covariates: N			
Other reported	measure = N				Other reported meas			
					ween tests (IGRA v	vs. TST)		
					% CI: 1.25, 9.96)			
					95% CI: 0.87, 7.05)			
Ratio of ORs (			ted) =	= <u>N</u>	NA			
	Other reported measure = NA							
Association between test results and levels of TB exposure (if applicable)								
IGRA (TSPOT) TST (≥10mm)								
	Exposur	re level	Tota	ıl		Exposui	re 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
		Te	st per	rfo	ormance parameter	rs		
	IGRA					TST		
Sensitivity = 8, 19.73, 57.05)	/22 = 36.36%	% (95% CI:		1	Sensitivity = 12/22 =	= 54.55% (9)	5% CI: 34.	66, 73.08)
Specificity = 2 77.35, 98.02)	6/28 = 92.86	5% (95% C	I:	,	Specificity = 22/28 =	= 78.57% (9	5% CI: 60.	46, 89.79)
PPV = 8/10 = 8 94.33)	`			]	PPV = 12/18 = 66.67	7% (95% CI	: 43.75, 83	.72)
77.87)	NPV = 26/40 = 65.00% (95% CI: 49.51, NPV = 22/32 = 68.75% (95% CI: 51.43, 82.05)							
1.38, 39.87)	DOR (for $T^+$ calculated) = 7.43 (95% CI: DOR (for $T^+$ calculated) = 4.40 (95% CI: 1.28, 15.09)							
OR (crude; for $T^+$ reported) = 7.43 (95% OR (crude; for $T^+$ reported) = 2.08 (95% CI: 0.64, 6.73) CI: 1.38, 39.90)								
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 <sup>+</sup> calc				% CI: 0.58, 4.89)			
					05% CI: 1.25, 10.18)			
Ratio of ORs (								
			,	1				
Other reported measure = NA								

	Assoc	iation het	ween test	t results and BCG status	s (if ann	licable)		
IG	RA (TS)		ween test	TST (≥5mm)				
BCG status Total			BCG status			Total		
	Yes	No	1 Otal		Yes	No	Total	
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	
Total	43	] 3		rformance parameters	43	3	30	
	IGRA		Test per		TST			
DOR (for T <sup>+</sup> ca			0.(050/	DOR (for T+ calculated		02 (050/ C	1. 0. 20. 29. 20)	
CI: 0.01, 10.07		IGRA – 1.0	0 (93%	DOR (101 1+ calculated	$1)_{TST} - 2.5$	92 (93% C	1. 0.30, 28.29)	
OR (crude; for		ad = ND		OR (crude; for T+ repo	rtod) = N	T <b>D</b>		
OR (regression			- ND	OR (regression-based;				
List of covariat		eported) IG	$_{\rm RA}$ – $NK$	List of covariates: NA	reported)	TST - INK		
		_ NID			NID			
Other reported				Other reported measure		P1.1.X		
IC			ween test	results and BCG status				
16	RA (TS)		Total	13	ST (≥10n		Total	
	Yes	status	Total		Yes	status No	Total	
ICD A		No	1.0	TOT		<b>-</b>	10	
IGRA +	9	1	10	TST +	17	1	18	
IGRA -	36	4	40	TST -	28	4	32 ND	
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR	
Total 45 5 50				Total	45	5	50	
Test performance parameters								
$\frac{\text{IGRA}}{\text{DOR (for T}^{+} \text{ calculated})_{\text{IGRA}} = 1.00 (95\%)}$				DOD (C. T. 1. 1. 1.	TST	42 (050/ 6)	1 0 25 22 57)	
		$_{\rm IGRA} = 1.0$	0 (95%	DOR (for T+ calculated	$1)_{TST} = 2.4$	43 (95% C	1: 0.25, 23.57)	
CI: 0.01, 10.07		1) ND		OD ( 1 C T)	( 1) N	ID.		
OR (crude; for			NID	OR (crude; for T+ repo				
OR (regression		eported) <sub>IG</sub>	$_{RA} = NR$	OR (regression-based;	reported)	$_{\text{TST}} = NR$		
List of covariat		NID		List of covariates: NA	MD			
Other reported			1	Other reported measure				
				d discordance (if applie		dl/		
	be strat	inea by 1	S1 cut-0	off value, BCG vaccinati	ion statu	s, and/or c	condition	
Total sample		TST (≥5n	2.522	TST -			Total	
IGRA (TSPOT		131 ( <u>≥</u> 311	IIII) T	2			10101	
IGRA (TSPOT		12		28			40	
Indeterminate	<i>,</i> -	NR		NR			NR	
Total		20		30			50	
		20		] 30			30	
Description  Sample definition (a.g. total if attentified by DCC or condition, angelify), total								
Sample definition (e.g., total, if stratified by BCG or condition – specify): total								
TST + threshold: ≥5mm  Parameters								
Kappa = 0.36 (	050/ CI-	0.12.0.61	0.00101104	ad .				
1.1			j carcurate	cu				
Kappa = 0.33 (CI NR) reported % concordance = 36/50 = 72.00% (95% CI: 58.33, 82.53)								
			_					
% discordance			(93% CI:	1/.4/, 41.0/)				
Stratification (	specify g		1	TOT		T	To4-1	
ICDA		TST		TST -			Total	
IGRA +		NR		NR			NR NB	
IGRA -		NR		NR			NR	
Indeterminate		NR		NR			NR	

T 1	ND	ND	ND			
Total	NR	NR	NR			
Description	1 '0	PGG 11:1	2.370			
		BCG or condition – specify	): NR			
TST + threshold: NR						
Parameters						
Kappa = NR						
% concordance = NF						
% discordance = NR						
Stratification (speci						
	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)	(specify)		of life mean score (SD)			
,	(1 )/	(specify)				
IGRA:	NR NR					
TST:		NR NR				
Test 3 (specify):		NR	NR			
	<u> </u>	Conclusions	·			
Authors						

#### 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

Name of first reviewer: Peter Auguste

Name of second reviewer: Alexander Tsertsvadze

### Study details

First author surname year of publication: Maritsi 2011<sup>135</sup>

**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-TNF $\alpha$  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	Total N (test-)	Total N (indeterminate)	Total N (test results
	, ,	(40041)	` '		available)
		(test+)			
IGRA (QFT-	23	1	20	2	23
GIT):					
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-ris								
Exposed 1		High-risk group (TB risk evaluation was performed using the questionnai						ınaire	
(specify):		formulated by the United States Pediatric Tuberculosis Collaborative							
		Group, which was published in 2004 [3])							
Exposed 2	NA								
(specify):									
Exposed 3	NA								
(specify):									
Exposed 4	NA								
(specify):									
Tests	<del>.</del>				00	0.17			
		used, meth		Cut-of		Other	' into	rmation	
		timing for t		values/thre					
ICDA (OFT CIT		ement, mai				A41		4 - 1 414	
IGRA (QFT-GIT)		eron-TB gol Cellestis Co		Not reported				ested that QTB are	
		a. The meth				esuns reported		-	
		ing of the te		+		regative		isitive,	
	been rep	_	st have no			ndetern			
TST	Not repo			Not reported		Not repo		<u>•</u>	
Association between			oidoneo of			voi repe	nica		
Association betwe	IGRA	ints and int	Juence of		TS	Г			
	Inciden	ce of	Total		Inciden			Total	
	active		Total	active TB				Total	
	Yes	No		Yes No					
IGRA +	NA 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	
				ce parameters					
	IGRA		<u> </u>		TS	Γ			
Sensitivity = NA				Sensitivity = N		_			
Specificity = NA				Specificity = N					
PPV = NA				PPV = NA					
NPV = NA				NPV = NA					
	Cumulative Incidence $_{IGRA^{+}} = NA$ Cumulative Incidence $_{TST^{+}} = NA$								
Cumulative Incide				Cumulative In					
Cumulative Incide				Cumulative In			= NA		
Incidence density i				Incidence dens					
Incidence density i				Incidence dens					
Incidence density i				Incidence dens			NA		
Other reported mea	asure <sub>IGRA</sub> =	NA		Other reported					
			between t	tests (IGRA vs.					
Ratio of cumulativ	e incidence	ratios = NA	Λ						
Ratio of incidence	density rate	ratios = NA	Α						
Other reported mea	asure = NR								
Association between test results and levels of TB exposure (high-risk group)									
	IGRA (GIT				TST (N				
	Exposu	ire level	Total		Exposu	re level	1	Total	
	High/Yes	Low/No			High/Yes	Low/			
	Trigii/ Tes								
IGRA +	1	0	1	TST +	0	0		0	
IGRA + IGRA - Indeterminate	<u> </u>		1 20 2	TST + TST - Indeterminate	0 3 NR	0 11 NR		0 14	

							(exclude)	
Total	3	20	23	Total	3	11	14	
		Test pe	erforma	nce parameters				
IGRA (ex	clude indete				exclude ind	eterminate	e)	
Sensitivity = $1/3$ =		,	9.23)	Sensitivity = $0/3 = 0.0\%$ , 95% CI (0.0, 56.15)				
Specificity = 18/18				Specificity = 11.				
	100.00)					,	( , , ,	
PPV = 1/1 = 100.0	0%, 95% CI	(20.65, 10	0.00)	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 <sup>+</sup> calcul				DOR (for T <sup>+</sup> cal				
OR (crude; for T <sup>+</sup> r				OR (crude; for 7				
OR (regression-bas				OR (regression-				
List of covariates:				List of covariate				
Other reported mea	sure = NR			Other reported r	neasure = N	A		
· · · · · · · · · · · · · · · · · · ·		mparison	between	tests (IGRA vs.				
Ratio of DORs (for				( 2	,,			
Ratio of OR (crude								
Ratio of ORs (regre								
Other reported measure = NR								
Association between test results and BCG status (if applicable)								
IGRA (TSPOT/QFT) TST (NR mm)								
	BCG s	status	Total		BCC	3 status	Total	
	Yes	No			Yes	No	1	
IGRA +	NR	NR	NR	TST +	NR	NR	NR	
IGRA -	NR	NR	NR	TST -	NR	NR	NR	
Indeterminate	NR	NR	NR	Indeterminat	te NR	NR	NR	
Total	NR	NR	NR	Total	NR	NR	NR	
		Test p	erforma	nce parameters				
IGI	RA (TSPOT	/QFT)			TST (NI	R mm)		
DOR (for T <sup>+</sup> calcul	ated) <sub>TSPOT/QE</sub>	$r_{\rm T} = NR$		DOR TST (for	T+ calcula	ted) = NR		
OR (crude; for T <sup>+</sup> r	eported) = N	IR		OR (crude; f				
OR (regression-bas		/ 🔍		OR (regressi		eported) TST	=NR	
OR (regression-bas		$)_{TSPOT} = NI$	2	List of covar	riates: NR			
List of covariates:								
Other reported mea				Other reporte		= NR		
Between-test agre				`				
This table may be	stratified b	y TST cut-	off valu	e, BCG vaccinati	ion status, a	ind/or con	dition	
Total sample		TPC/TP +		The co			TD 4 1	
ICDA		TST +		TS'			Total	
IGRA +		NR		N			NR	
IGRA -		NR		N			NR NR	
Indeterminate						NR		
Total		NK	NR NR NR				NK	
Description Sample definition (	(a.g. tata1 :4	etrotified 1	w DCC	or condition see	oify). ND			
TST + threshold: N		suaumeu (	у все (	or condition – spe	CITY). INK			
Parameters	(1/							
Kappa = NR								
% concordance = N	J <b>P</b>							
% discordance = N								
Stratification (spe		)						
Stratification (spe	city group i	TST +		TS	T -		Total	
IGRA +		NR		N			NR	
10101		111/		111.	11		1.117	

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)** 

Stratification (specify g	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:**

#### Study details

First author surname year of publication: Mutsvangwa 2010<sup>136</sup>

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

T 1 / C	4 (10)	T .		1	( · · ·	1. 11.
Levels/groups of	evnosure to	K in	increasing	order	lit ann	dicable)

Definition of	exposure gro	up — house	hold	l cont	tact	i
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Non-exposed Contact of index control (no	) TB)	
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Exposed 1		Contoo	t of indo	y TD agga						
(specify):		Contact of index TB case								
Exposed 2		NA								
(specify):										
Exposed 3		NA								
(specify):		1 1/2 1								
Exposed 4		NA								
(specify):		11/1								
(speerly).		Definit	ion of ex	xposure group	12 — (	near status	of inde	Y CASES		
Non-exposed				, culture negati		iicai status	or mac	A cases		
Exposed 1				, culture negati, culture positiv						
(specify):		Silicai	negative	, culture positi	vC					
Exposed 2		Smear	nositive	culture positiv	re.					
(specify):		Silicui	positi • <b>c</b> ,	carrare positiv	•					
Tests										
	As	sav use	d. meth	odology, timir	ıg	Cut-off v	values/t	hreshol	ds	Other
				surement,		Defir	nition o	f test+		information
			manufa					-		
IGRA	Bloo			or ELISpot		ELISpot pl	ates we	re sent to	)	Persons
(TSPOT)	1			er the TST was	s	Oxford for				performing
				says were carri		counting (A		-		and reading
	out	it as described elsewhere.				Germany)				the assays
	Dup	uplicate wells contained no								were blind
	anti	ntigen (negative control),								to all
	phy	hytohaemagglutinin (positive								personal
	cont	trol) (IC	CN Biom	edical, Aurora	,					identifiers
	Ohi	o, USA	) at 5 mg	g/ml or 13 pairs	s					and TST
	of d	uplicat	e wells e	ach containing						results
			eptide p							
				verlapping 15-						
				ing the length of	of					
				genic target-6						
				protein-10, on						
				is based. The						
	1			of each peptide	2					
	_	10 mg								
TST (two				otocol was used	1	If the first i				NA
stage;				e baseline for		mm, then a				
≥10mm)				ent TST		placed after		-		
				ommended by		were expre				
	1			units of RT-23		of the two i				
				in derivative) i		sizes ≥10 n	nm were	e conside	ered	
				Serum Institut,		positive				
				ark) were						
				lly into the read at 48-72h						
				ssment followe						
			and asse ded techi		u					
Association be					f act	tive TR (if s	nnlical	ole)		
Association De	C TT CC	IGRA		na incluence o	ı ac	(II (II (		TST		
			ence of	Total				nce of		Total
			re TB	Total				e TB		101111
	}	Yes	No				Yes	No		
IGRA +		NA	NA	NA		TST +	NA	NA		NA
IONA		T 41 7	T 47 T	1 1/1 1		101	1 1/1	1 1/1		1 1/1 1

IGRA -	NA	NA	NA	TST -	NA	NA	NA	
Indeterminate	NA NA	NA NA	NA	Indeterminate		NA NA	NA NA	
Total	NA NA	NA NA	NA NA	Total	NA NA	NA NA	NA NA	
Total	NA			ance parameter		IVA	INA	
	IGRA	1 65	periorii			TST		
Sensitivity = NA	IONA			Sensitivity = 1		151		
Specificity = NA				Specificity = 1				
PPV = NA				PPV = NA	NA			
NPV = NA				NPV = NA				
Cumulative Inciden		- NI A		Cumulative In	cidence -	– NA		
Cumulative Inciden				Cumulative In				
Cumulative Inciden				Cumulative In			JA	
Incidence density ra				Incidence den			1/1	
Incidence density ra				Incidence den				
Incidence density ra				Incidence den			A	
Other reported mea				Other reported			7.1	
Other reported med			n hetwe	en tests (IGRA v		181 1421		
Ratio of cumulative				in tests (IGIAI)	, s. 151)			
Ratio of incidence of								
Other reported mea								
			results ar	nd levels of TB e	exposure	(if applicat	ole)	
	RA (TSPO					nm; two sto		
		ıre level	Total			sure level	Total	
	Index	Index			Index	Index	1	
	case	control			case	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	perform	ance parameter	:s		<u> </u>	
	IGRA				]	ΓST		
Sensitivity = 19/55	= 34.55%	(95% CI:	23.36,	Sensitivity = 27/55 = 49.09% (95% CI: 36.38,				
47.75)				61.92)				
Specificity = 15/18	= 83.33%	(95% CI:	60.78,	Specificity = 12/18 = 66.67% (95% CI: 43.75,				
94.16)				83.72)				
PPV = 19/22 = 86.3				PPV = 27/33 = 81.82% (95% CI: 65.61, 91.39)				
NPV = 15/51 = 29.4				NPV = 12/40 =				
DOR (for T <sup>+</sup> calculated)	ated) = 2.6	64 (95% C	I: 0.67,	DOR (for T <sup>+</sup> ca	lculated)	= 1.93 (95%	% CI: 0.63,	
10.27)				5.87)				
OR (crude; for T <sup>+</sup> re				$OR (crude; for T^+ reported) = NR$				
OR (regression-bas		ed) = NR		OR (regression		eported) = N	IR	
List of covariates: N				List of covariat		) ID		
Other reported mea			7 4	Other reported		= NK		
D ', CDOD (C				en tests (IGRA v	/s. 151)			
Ratio of DORs (for				1: 0.56, 3.36)				
Ratio of OR (crude:								
Ratio of ORs (regre			u) – NA					
Other reported mea			nogriles a	d lovels of TD	vncarra	(if applicate	ala)	
			results ar	d levels of TB e		<u> </u>		
IGH	RA (TSPC		Total	13		nm; two-sto	Total	
		ire level	1 Otal		Expos High	sure level	1 Otal	
IGRA +	High NR	Low NR	NR	TST +	NR	Low NR	NR	
IONA T	1NIX	INIX	INIX	191 -	1NIX	INIC	INIX	

IGRA -	NR	NR	NR	TST -	NR	NR	NR	
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR	
Total	NR	NR	NR	Total	NR	NR	NR	
Total	INK			nance paramete		INK	INK	
	IGRA	16	st periorn		TS	T		
Sensitivity = NA	IGNA			Sensitivity = N		71		
Specificity = NA				Specificity = N				
PPV = NA				PPV = NA	A			
NPV = NA				NPV = NA				
DOR (for T <sup>+</sup> calcul	ated) – N	Λ		DOR (for T <sup>+</sup> ca	loulated) =	- N/A		
OR (crude; for T <sup>+</sup>				OR (crude; fo				
Smear culture =			un)	Smear culture			roun)	
Smear culture +=				Smear - culture				
Smear + culture + =	4 80 (95%	6 CI: 1.04	5, 12.05)	Smear + culture				
OR (regression-ba			5, 21.71)	OR (regression				
Smear culture =			aun)	Smear culture				
Smear - culture +=				Smear - culture				
Smear + culture + =				Smear + culture				
List of covariates:	\	- ,	, ,	List of covarian			,	
Other reported mea	sure = NF			Other reported	measure =	NR		
			son betwe	en tests (IGRA v				
Ratio of DORs (for					/			
Ratio of OR (crude				6 CI: 0.48, 3.91) [	Smear + cu	ılture + vs	s. Smear –	
culture –]	, ,	,		, , , ,				
Ratio of ORs (regre	ession-bas	ed; repor	ted) = 1.56	(95% CI: 0.51, 4	1.76) [Smea	ar + cultur	re + vs. Smear –	
culture –]		, 1	,		/ <b>L</b>			
Other reported measure = NA								
Other reported mea	isure = N <i>A</i>	A						
			n test resu	ılts and BCG sta	tus (if app	olicable)		
A		n betwee	n test resu	ilts and BCG sta	tus (if app			
A	Associatio	n betwee fy)	n test resu	alts and BCG sta	TST (s		Total	
A	Association RA (speci	n betwee fy)		alts and BCG sta	TST (s	pecify)	Total	
A	RA (speci BCG	n betwee fy) status		alts and BCG sta	TST (s	pecify) status	Total	
IG	RA (speci BCG Yes	n betwee fy) status No	Total		TST (s BCC Yes	pecify) S status No		
IGRA +	Association RA (speci BCG Yes NR	n betwee fy) status No NR	Total NR	TST +	TST (s BCC Yes NR	pecify) 3 status No NR	NR	
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IGRA + IGRA - Indeterminate Total	RA (speci BCG Yes NR NR NR NR NR	n betwee ify) status No NR NR NR NR Te	Total  NR NR NR NR NR	TST + TST - Indeterminate Total	TST (s	pecify) S status No NR NR NR NR NR	NR NR NR	
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IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r	RA (special special sp	n betwee ify) status No NR NR NR NR NR NR NR Te	NR NR NR NR NR St perforn	TST + TST - Indeterminate Total nance parameter DOR (for T+ can or continuous)	TST (s  BCC  Yes  NR  NR  NR  NR  TS  TS  alculated) <sub>TS</sub>	Pecify	NR NR NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas	RA (speciation) RA (speciation) RA (speciation) RA (speciation) RA (speciation) RE NR NR NR NR NR NR NR NR NR Seported) = ged; reported	n betwee ify) status No NR NR NR NR NR NR NR Te	NR NR NR NR NR St perforn	TST + TST - Indeterminate Total Tance parameter DOR (for T+ construction of the constr	TST (s  BCC  Yes  NR  NR  NR  NR  TS  Alculated) TS  T+ reporte  -based; rep	Pecify	NR NR NR NR	
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IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas) List of covariates: Other reported mea	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) IGRA =	Total  NR  NR  NR  NR  NR  St perforn	TST + TST - Indeterminate Total Tance parameter  DOR (for T+ construction of the covariate	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte  based; rep  res: NR  measure =	No	NR NR NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates: ) Other reported mea Between-test agre	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) <sub>IGRA</sub> =	Total  NR  NR  NR  NR  NR  St perforn  NR	TST + TST - Indeterminate Total TOTA	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte -based; rep tes: NR  measure = plicable)	No	NR NR NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates:) Other reported mea Between-test agre This table may be	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) <sub>IGRA</sub> =	Total  NR  NR  NR  NR  NR  St perforn  NR	TST + TST - Indeterminate Total TOTA	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte -based; rep tes: NR  measure = plicable)	No	NR NR NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates: ) Other reported mea Between-test agre	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) <sub>IGRA</sub> = R ncordan by TST	NR NR NR NR St perforn  NR ce, and discut-off va	TST + TST - Indeterminate Total Tance parameter  DOR (for T+ construction of the covariant	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) TS  T+ reporte -based; rep tes: NR  measure = plicable) tation statu	No	NR NR NR NR NR NR  NR	
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IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates: ) Other reported mea Between-test agre This table may be Total sample  IGRA +	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) IGRA =  R TST NR	Total  NR  NR  NR  NR  St perforn  NR  ce, and discut-off va	TST + TST - Indeterminate Total  nance parameter  DOR (for T+ can or	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte  based; rep  res: NR  measure =  plicable)  ration statu  T -  R	No	NR NR NR NR NR Total NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates:) Other reported mea Between-test agre This table may be Total sample  IGRA + IGRA -	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) IGRA = R TST NR NR	Total  NR NR NR NR St perforn  NR  NR  Lee, and discut-off va	TST + TST - Indeterminate Total Tota	TST (s  BCC  Yes  NR  NR  NR  NR  NR  S  alculated) <sub>TS</sub> T+ reporte -based; rep res: NR  measure = plicable) ation statu  T -  R  R	No	NR NR NR NR NR  NR  Total NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates:) Other reported mea Between-test agre This table may be Total sample  IGRA + IGRA - Indeterminate	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR ed) IGRA = R ncordan NR NR NR TST NR NR	Total  NR NR NR NR st perform  NR ce, and discut-off va	TST + TST - Indeterminate Total Total Total DOR (for T+ construction of the covariant of th	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte -based; repres: NR measure = plicable) ation statu  T -  R  R	No	NR NR NR NR NR  NR  Total NR NR NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates: Other reported mea Between-test agre This table may be Total sample  IGRA + IGRA - Indeterminate Total	RA (special property of the special property of the sp	n betwee ify) status No NR NR NR NR Te = NR = NR ed) IGRA = R TST NR NR	Total  NR NR NR NR st perform  NR ce, and discut-off va	TST + TST - Indeterminate Total Tota	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte -based; repres: NR measure = plicable) ation statu  T -  R  R	No	NR NR NR NR NR  NR  Total NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates: I Other reported mea Between-test agree This table may be Total sample  IGRA + IGRA - Indeterminate Total Description	RA (special RA (sp	n betwee ify) status No NR NR NR Te = NR = NR ed) IGRA =  Cordance TST NR	Total  NR NR NR NR St perform  NR  NR  Left of the state	TST + TST - Indeterminate Total Tance parameter  DOR (for T+ c: OR (crude; for OR (regression List of covariat Other reported scordance (if applue, BCG vaccin  TS N N N N	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte  -based; rep  res: NR  measure =  plicable)  ation statu  T -  R  R  R	pecify) G status No NR NR NR NR NR NR NR NR NR ST GT GT = NR d) = NR orted) TST NR  Is, and/or	NR NR NR NR NR  NR  Total NR NR NR NR	
IGRA + IGRA - Indeterminate Total  DOR (for T <sup>+</sup> calcul OR (crude; for T <sup>+</sup> r OR (regression-bas List of covariates: Other reported mea Between-test agre This table may be Total sample  IGRA + IGRA - Indeterminate Total	RA (special RA (sp	n betwee ify) status No NR NR NR Te = NR = NR ed) IGRA =  Cordance TST NR	Total  NR NR NR NR St perform  NR  NR  Left of the state	TST + TST - Indeterminate Total Tance parameter  DOR (for T+ c: OR (crude; for OR (regression List of covariat Other reported scordance (if applue, BCG vaccin  TS N N N N	TST (s  BCC  Yes  NR  NR  NR  NR  NR  TS  alculated) <sub>TS</sub> T+ reporte  -based; rep  res: NR  measure =  plicable)  ation statu  T -  R  R  R	pecify) G status No NR NR NR NR NR NR NR NR NR ST GT GT = NR d) = NR orted) TST NR  Is, and/or	NR NR NR NR NR  NR  Total NR NR NR 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

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

#### Study details

First author surname year of publication: Papay 2011<sup>137</sup>

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  $36.6 \pm 11.3$ 

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 (spe Tests	cify):	NA							
Tests	metho test	measi	used, , timing urement		Cut-off values/thresholds Definition of test+				Other information
IGRA	QFT-G Carneg	IT, Ce	llestis,		≥0.35	IU/mL			NA
TST	Tuberc protein RT23, Institut Denma method	ulin pu deriva Staten e, Cope rk), Ma	rified tive (PP Serum enhagen antoux	,	consid indura withou test res	ople with IM, TS ered positive if the tion was ≥ 5mm. It IM but have IE sult was >10 mm	he size of For peo BD a posi	ple	NA
Association be			lts and	incide	ence of	active TB (if ap			
	10		ence of ve TB No	Т	otal		Incider active Yes	nce of	Total
IGRA +	-	NA	NA	N	ĪΑ	TST +	NA	NA	NA
IGRA -		NA	NA		NA	TST -	NA	NA	NA
Indetermin		NA	NA		ĪΑ	Indeterminate	NA	NA	NA
Total		NA	NA	N	ĪΑ	Total	NA	NA	NA
			Tes	t perf	orman	ce parameters			
	I	GRA				TST			
Sensitivity = $N$	A					Sensitivity = N.	A		
Specificity = $N$	A					Specificity = N	A		
PPV = NA						PPV = NA			
NPV = NA						NPV = NA			
Cumulative Inc						Cumulative Incidence $_{TST+} = NA$			
Cumulative Inc						Cumulative Incidence <sub>TST-</sub> = NA			
Cumulative Inc						Cumulative Incidence Ratio <sub>TST</sub> = NA			
Incidence densi						Incidence density rate <sub>TST+</sub> = NA			
Incidence densi						Incidence density rate ratio = NA			
Incidence densi						Incidence density rate ratio <sub>TST</sub> = NA			
Other reported	measure			_		Other reported measure <sub>TST</sub> = NA			
Datio of 1	otiva i :				tween t	ests (IGRA vs.	181)		
Ratio of cumula Ratio of incider									
Other reported		-	ranos =	INA					
			sulte one	lave	ls of TI	R avnosuro (Dro	sence of	risk foot	tors for LTRN
Association	IGRA (			1 10 7 6	15 01 11	B exposure (Presence of risk factors for LTBI TST (≥5 mm)			
		osure le		Т	otal			ire level	Total
	Yes		No				Yes	No	<del></del>
IGRA +	9		6		15	TST +	15	11	26
IGRA -	56	1	21		77	TST -	54	128	
Indeterminate	4		12		16 luded)	Indeterminate	0	0	0
Total	69	1	39		.08	Total	69	139	208
			Tes	t perf	orman	ce parameters			
	(excludi		etermina	ite)		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,	Specificity = 128/139 = 92.09% (95% CI: 86.38,
97.82)	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,	DOR (for $T^+$ calculated) = 3.23 (95% CI: 1.39,
9.54)	7.49)
OR (crude; for $T^{+}$ reported) = 3.20 (95% CI: 1.10,	OR (crude; for $T^+$ reported) = 3.20 (95% CI:
10.10)	1.40, 7.50)
OR (regression-based; reported) = 3.50 (95% CI:	OR (regression-based; reported) = 3.70 (95%
1.20, 11.30)	CI: 1.50, 9.60)
List of covariates: 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) = 1.00 (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 Tota		Total		Exposure	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	Indeterminate	0	0	0
			(excluded)				
Total	29	179	208	Total	29	179	208

**Test performance parameters** 

1 est per for mance par ameters							
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,	Specificity = 164/179 = 91.62%, 95% CI (86.64,						
96.21)	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,	DOR (for $T^+$ calculated) = 6.68, 95% CI (2.67,						
7.87)	16.73)						
$OR (crude; for T^+ reported) = NR$	$OR (crude; for T^+ reported) = NR$						
OR (regression-based; reported) = NR	OR (regression-based; reported) = NR						
List of covariates: 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 =  $\overline{NR}$ 

Association between test results and levels of TB exposure (history of contact with active TB)

IGRA (QFT-GIT)				TST(≥5 mm)			
	Exposu	re level	Total		Exposure	e 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
YCD	· • • • • • • • • • • • • • • • • • • •				nce parameters			
		ng indete				xcluding in		
Sensitivity = 2/ 50.98)	Sensitivity = 2/10 = 20.00%, 95% CI (5.668, 50.98)					1 = 36.36%	6, 95% CI	(15.17,
Specificity = 10 95.78)	69/182 =	92.86%,	95% CI	(88.16,	Specificity = 17: 92.51)	5/197 = 88.	83%, 95%	6 CI (83.67,
PPV = 2/15 = 1					PPV = 4/26 = 15			
NPV = 169/17' 97.69)	/ = 95.48	8%, 95%	CI (91.3 <sup>2</sup>	ι,	NPV = 175/182	= 96.15%,	95% CI (	92.27, 98.12)
DOR (for T <sup>+</sup> ca	alculated	)=3.25, 9	95% CI (	0.62,	DOR (for T <sup>+</sup> cal	culated) = 4	1.54, 95%	CI (1.23,
16.91)	T <sup>+</sup> **** ***	+ a d\ — NID			16.78)	2 <sup>+</sup> man ant a d)	– NID	
OR (crude; for OR (regression					OR (crude; for TOR (regression-			R
List of covariat		reported)	- MIX		List of covariate		rica) – M	IX.
Other reported		e = NR			Other reported n		JR	
1			parison	between	tests (IGRA vs.			
Ratio of DORs					0.24, 2.10)	,		
Ratio of OR (cr								
Ratio of ORs (1			reported)	= NA				
Other reported								
Association				levels of	TB exposure (Cl			e of LTBI)
		(QFT-GI				TST(≥5		
		sure level		Total		Exposur		Total
	Yes	No				Yes	No	
IGRA +	1	14		15	TST +	5	21	26
IGRA -	10	167		177	TST -	6	176	182
Indeterminate	0	16	(ex	16 (cluded)	Indeterminate	0	0	0
Total	11	197		208	Total	11	197	208
			Test p	erforma	nce parameters			
		ing indete				TST		
Sensitivity = 1/	/11 = 9.0	9%, 95%	CI (1.62	, 37.74)	Sensitivity = 5 71.99)	/11 = 45.45	%, 95% (	CI (21.27,
Specificity = 1 (95.34)	67/181 =	92.27%,	95% CI	(87.44,	Specificity = 176/197 = 89.34%, 95% CI (84.25, 92.92)			
PPV = 1/15 = 6	5.66%, 9	5% CI (1.	18, 29.8	2)	PPV = 5/26 = 19.23%, 95% CI (8.50, 37.88)			
NPV = 167/17	7 = 94.35	5%, 95%	CI (89.91	, 96.9)	NPV = 176/182 = 96.7%, 95% CI (93, 98.48)			
DOR (for T <sup>+</sup> ca 10.01)	alculated	) = 1.19, 9	95% CI (	0.14,	DOR (for T <sup>+</sup> calculated) = 6.98, 95% CI (1.96, 24.87)			
OR (crude; for	T <sup>+</sup> repor	ted) = 1.2	0, 95% (	CI: 0.10,	OR (crude; for $T^+$ reported) = 6.30, 95% CI:			
6.90					1.70, 22.90			
OR (regression-based; reported) = 1.10, 95% CI: 0.10, 7.70				OR (regression-based; reported) = 4.90, 95% CI: 1.10, 19.9				
List of covariat	tes: NR				List of covaria	tes: NR		
Other reported		e = NR			Other reported		NR	
Comparison between tests (IGRA vs. TST)								
Ratio of DORs	_							
Ratio of OR (ca								
			reported)	=0.22 (9)	95% CI: 0.06, 0.8	5)		
Other reported	measure	e = NR						

Assoc	iation	between	n test 1	results and	levels of TB expo	sure (IM t	reatmen	ıt)	
IGRA (QFT-GIT) TST(≥5 mm)									
	Exposure level			Total		Exposure leve		Total	
	Yes	No				Yes	No		
IGRA +	7	8		15	TST +	18	8	26	
IGRA - 1	130	47		177	TST -	131	51	182	
	12	4		16	Indeterminate	0	0	0	
				(excluded)					
Total 1	149	59		208	Total	149	59	208	
·			Tes	t performa	nce parameters				
IGRA (ex	IGRA (excluding indeterminate) TST								
DOR (for $T^+$ calculated) = 0.31 (95% CI: 0.10,					DOR (for T <sup>+</sup> ca	DOR (for $T^+$ calculated) = 0.87 (95% CI: 0.35,			
0.92)	,	`		,	2.14)	,		,	
OR (crude; for T <sup>+</sup>	report	ted) = 0.3	80 (95%	6 CI: 0.10,	OR (crude; for	T <sup>+</sup> reported	() = 0.90	(95% CI:	
0.90)		,	`	ĺ	0.40, 2.30)				
OR (regression-ba	sed; r	eported)	= 0.30	(95% CI:		OR (regression-based; reported) = 0.90 (95%			
0.10, 0.90)	, -	· · · · /			CI: 0.40, 2.60)				
List of covariates:	NR					List of covariates: NR			
Other reported me		=			Other reported				
			etween	test resul	ts and BCG status		ble)		
		(specify				TST (spe			
		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	
			L		ince parameters				
	10	GRA	100	· p • · · · · · ·		TST	,		
$\overline{DOR}$ (for $T^+$ calculated) <sub>IGRA</sub> = NR				DOR (for T+ ca	DOR (for T+ calculated) <sub>TST</sub> = NR				
OR (crude; for T <sup>+</sup>						OR (crude; for T+ reported) = NR			
				NR		OR (regression-based; reported) $_{TST} = NR$			
` •	OR (regression-based; reported) <sub>IGRA</sub> = NR List of covariates: NR				List of covariates: NR				
Other reported me		= NR				Other reported measure = NR			
•			rdanc	e. and disc	ordance (if application		1111		
					ie, BCG vaccination		and/or c	ondition	
Total sample		<u>_</u>			,	,			
			TST	+	TST -			Total	
IGRA +		157			20		177		
IGRA -			9		6			15	
Indeterminate		0		0	0		0		
Total			166			26		192	
Description									
	(e.g.	total, if s	tratifie	ed by BCG	or condition – spec	ify): total			
TST + threshold:	· ·			, 200	эт эт эт	.,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
Parameters Parameters									
	% CI (	0.07.03	4)						
Kappa = 0.21, 95% CI (0.07, 0.34) % concordance = 163/192 = 84.90%, 95% CI (79.15, 89.27)									
% concordance = 163/192 = 84.90%, 95% CI (79.13, 89.27) % discordance = 29/192 = 15.10%, 95% CI (10.73, 20.85)									
% discordance = 29/192 = 13.10%, 95% CI (10.73, 20.83)  Stratification (specify group 1)									
Stratification (spi	city	51 oup 1)	TST	+	ТОТ	`_		Total	
IGRA +		NR		+	TST - NR		NR		
IGRA -			NR		NR			NR NR	
IUIVA =		1	1111		INI			TAIK	

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				
<b>Stratification (specify</b>	group 2)			
	TST +	TST -	Total	
IGRA +	NR	NR	NR	
IGRA -	NR	NR	NR	
Indeterminate	NR	NR	NR	
111001011111111010		NR	NR	

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

TST + threshold: NR

#### **Parameters**

Kappa = NR

% concordance = NR

% discordance = NR

041	. 4
Orner	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

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

#### **Study details**

First author surname year of publication: Ramos 2013<sup>138</sup>

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

Number of patients tested								
	Total N	Total	Total N	Total N	Total N			
	(tested)	N	(test-)	(indeterminate)	(test results			

		(test+				available)		
		)						
IGRA (QFT-	153	15	137		1	152		
GIT):								
TST (≥5mm):	153	43	110		0	153		
Test 3 (specify):	NA	NA	NA		NA	NA		
Total N of paties	nts with valid result	ts for bot	th IGI	RA and	<b>TST:</b> 152			
Levels/groups of	f exposure to TB in	increasiı	ng ord	der (if a	pplicable):			
					n a TB endemic area			
Non-exposed	Not born in a TE	3 endemi	c area					
Exposed 1	Born in a TB end	demic are	ea					
(specify):								
				story of	contact with TB patien	ts		
Non-exposed	No contact with		nts					
Exposed 1	Contact with TB	patients						
(specify):								
Tests			Т	<i>C</i> :		0.0		
	Assay used, met				off values/thresholds Definition of test+	Other information		
	timing for test me manufactu		:III,	J	Deminion of test+	information		
IGRA (QFT-	For QFG, three alice		l ml	Accordi	ing to the instructions th	e QFG and		
GIT)	of undiluted heparis	-		According to the instructions, the result was considered to be TST were				
GII)		blood were collected in three			if the IFN-c level after	performed		
	tubes: one containing TB			-	tion with TB antigens	simultaneousl		
		antigens (ESAT-6, CFP-10,			egative control was	y in a blinded		
	and TB7.7), a positive control				U/ml. The test was	fashion		
	tube containing			conside	;			
	phytohemagglutinin, and a			level wa	as <0.35 IU/ml after			
		negative control tube. Blood			tion of the negative			
		samples were incubated for						
		16–20 h at 37°C. Plasma			The test result was considered to			
	*	samples were then harvested				)		
		for IFN-c quantification by a			terminate if (1) the			
	ELISA	single-step sandwich-type			e control was ≥8.0 IU/ml			
	LLISA			<0.5 IU	ne positive control was			
	The test was perfor	med		30.5 TO/IIII				
	according to the			Moreov	er, the test result was			
	manufacturer's inst	ructions		considered to be				
	(Cellestis, Carnegie				diate if IFN-c level was			
				≥0.10 IU	U/ml but <0.35 IU/ml			
TST( ≥5mm)	Study participants				s deemed positive if the	QFG and		
	injected with 0.1 m			indurati		TST were		
	tuberculin (2 tuberc		S	diamete	er was more than 5 mm	performed		
	, ·	of PPD) (Tuberculina PPD; Evans 2UT, UCB Pharma, S.A.				simultaneousl		
						y in a blinded fashion		
	Madrid, Spain) in accordance with the American Thoracic					148111011		
	Society guidelines.		´					
	transverse skin indu							
	diameter was meas							
	48–72h later							
L						I		

Association b	etween test r	esults and	incidence of	f active TB (if	applicable	e)			
IGRA						ST			
Incidence of Total				Inciden	ce of	active TB	Total		
	ac	tive TB							
		s No			Yes		No		
IGRA +	- NA	NA NA	NA	TST +	NA		NA	NA	
IGRA -	NA	NA NA	NA	TST -	NA		NA	NA	
Indetermin	ate NA	NA NA	NA	Indetermina te	NA		NA	NA	
Total	NA	NA	NA	Total	NA		NA	NA	
		Tes	st performai	nce parameter	'S				
	IGRA	1			T	CST			
Sensitivity = N				Sensitivity =					
Specificity = N	NΑ			Specificity =	NA				
PPV = NA				PPV = NA					
NPV = NA				NPV = NA					
Cumulative In	cidence IGRA+	= NA		Cumulative I					
Cumulative In				Cumulative I	ncidence T	$_{\rm ST-}=$	NA		
Cumulative In				Cumulative I					
Incidence dens	sity rate <sub>IGRA+</sub>	= NA		Incidence der	nsity rate T	$ST+=\frac{1}{2}$	NA		
Incidence dens				Incidence der					
Incidence dens				Incidence density rate ratio <sub>TST</sub> = NA					
Other reported	l measure <sub>IGRA</sub>			Other reporte		TST =	NA		
		Comparis	son between	tests (IGRA v	s. TST)				
Ratio of cumu									
Ratio of incide	ence density r	ate ratios =	NA						
Other reported	l measure = $N$	IR							
A	ssociation be	tween test	results and	levels of TB e	xposure (i	if app	olicable)		
		FT-GIT)					5mm)		
		ire level	Tota	ı1	E	xposu	ire level	Total	
	Born in	Not born	in		Born		Not born		
	TB	TB			TE		in TB		
	endemic	endemi	2		ender	mic	endemic		
	area	area			are		area		
IGRA +	4	11	15	TST +	4		39	43	
IGRA -	4	133	137	TST -	4		106	110	
Indeterminat	NR	NR	1	Indeter	mi 0		0	0	
e	(excluded)	(excluded	<del></del>					1.5-	
Total	8	144	152	Total	8		145	153	
			st performai	nce parameter	'S	- TENCIF			
~ · · · · ·		RA	1 50 50 10)	a	TST				
Sensitivity = 4	·/8 = 50.00%	(95% C1: 2	1.52, 78.48)	78.48)	Sensitivity = 4/8 = 50.00% (95% CI: 21.52, 78.48)				
Specificity = 133/144 = 92.36% (95% CI: 86.84, 95.6				/   1	/				
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 =	NPV = 106/110 = 96.36% (95% CI: 91.02,				
DOR (for $T^+$ calculated) = 12.09 (95% CI: 2.65, 55.07)					98.58) 7) DOP (for T <sup>+</sup> coloulated) = 2.72 (95% CI;				
	aicuiaicu) — I	12.07 (33/0	01. 2.03, 33	/	' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' '				
OR (crude; for	· T <sup>+</sup> reported)	= NR			0.65, 11.40)  OP (arrido: for T <sup>+</sup> reported) = NP				
OR (crude, for OR (regression			30 (95% CI:		OR (crude; for T <sup>+</sup> reported) = NR OR (regression-based; reported) = 3.10				
4.60, 18.5) err		110u) – 29.3	00 (90 /0 CI.	, -	•		reported) – S	,.10	
7.00, 10.3) CII	UΙ			(3370 C	(95% CI: 0.70, 13.70)				

				ariates: age,				
		List of covariates: age, sex						
measure = N			rted measure	e = NR				
				TST)				
		`	53, 12.89)					
regression-ba	ised; report	ed) = NA						
measure = N	A							
ssociation be	etween test	results and lev	vels of TB expo	sure (if app	olicable)			
IGRA (Q	FT-GIT)			TST (≥	5mm)			
Exposi	ire level	Total		Exposure level Tot				
Contact	No conta	ct		Contact	No	1		
with TB	with TB			with TB	contact with TB			
3	12	15	TST +	4	39	43		
4	133	137	TST -		107	110		
NR	NR	1	Indetermi	0	0	0		
(excluded)	(excluded	) (excluded)	nate					
	`	152		7	146	153		
		t performance		·	_			
IG		- P	Purcus and a second a second and a second an	TS	T			
		5.82, 74.95)	Sensitivity			I: 25.05,		
			84.18)					
33/145 = 91.	72% (95%	CI: 86.09, 95.2						
20.000/ (050/	CI. 7.04	15 10)						
20.00% (93%) 7 – 07.00% (	050/ CL 03	13.19)						
			99.07)	99.07)				
alculated) = 8	3.31 (95% (	CI: 1.66, 41.56)	,	DOR (for T <sup>+</sup> calculated) = 3.66 (95% CI: 0.78, 17.08)				
n-based; repo	rted) = 8.00	(95% CI: 1.40		OR (regression-based; reported) = 3.20				
tes age sex			,					
	T <b>D</b>			C /				
illeasure – N		on hotswoon to			5 — IVIX			
(for T <sup>+</sup> color				131)				
			J, 7.00j					
			4 CI: 0.76 9.26	)				
		cuj – 2.30 (93%	0 (1. 0./0, 8.20)	J				
		tost marilta a	nd RCC status	(if applied	ala)			
		i test results al	iu DCG status	` <b>*</b> * * * * * * * * * * * * * * * * * *				
		Tatal				Tat-1		
		1 otal				Total		
		1.5	TOT			12		
						43		
						110		
		-	Indeterminate	0	0	0		
excluded) (	excluded	(excluded)						
9 1	23	152	Total	29	124	153		
- 1				27	121	1 2 2 2		
ICP		e per for manee	parameters	TST				
		% CI: 1.50	DOR (for T+			% CI·		
uicuiaicu)IGR/	T.57 (95	70 01. 1.50,	1.10, 5.89)	Jaiouraiou) <sub>T</sub>	2.5+ (95	70 01.		
	rude; for T <sup>+</sup> r regression-ba measure = N sociation be IGRA (Q Expost Contact with TB  3 4 NR (excluded) 7  IG /7 = 42.86%  33/145 = 91. 20.00% (95% 7 = 97.08% ( alculated) = 8  T <sup>+</sup> reported) 1-based; reported; reported; for T <sup>+</sup> r regression-ba measure = N Associati IGRA (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes  1 (R Excluded) (0 1) 1 (QI BCG sta Yes	(for T <sup>+</sup> calculated) = 4.2     rude; for T <sup>+</sup> reported) = 1     regression-based; report     measure = NA     sociation between test     IGRA (QFT-GIT)     Exposure level     Contact   No contact with TB     3	(for T <sup>+</sup> calculated) = 4.44 (95% CI: 1.5     rude; for T <sup>+</sup> reported) = NA     regression-based; reported	Contract   Contract	rude; for T* reported) = NA regression-based; reported) = NA measure = NA ssociation between test results and levels of TB exposure (if app IGRA (QFT-GIT)  Exposure level Contact with TB  3	(for T <sup>+</sup> calculated) = 4.44 (95% CI: 1.53, 12.89) rude; for T <sup>+</sup> reported) = NA regression-based; reported) = NA measure = NA sociation between test results and levels of TB exposure (if applicable)  IGRA (QFT-GIT)  Exposure level Contact   No contact with TB   with TB    3		

OR (crude; for T <sup>+</sup> reported) = NR	OR (crude; for T+ reported) = NR
OR (regression-based; reported) <sub>IGRA</sub> = 5.10 (95%	OR (regression-based; reported) $_{TST} = 2.40$
CI: 1.50, 17.50)	(95% CI: 1.01, 5.80)
List of covariates: Age, sex	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**

 $\overline{\text{Kappa}} = 0.35 \text{ (95\% CI: 0.22, 0.48)}$ 

% 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<sup>139</sup>

**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
<b>TST</b> (≥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					

forearm with 0.1 mL (5TU) second TST one week later	Exposed 1 (spe	cify):	person h worked	aving TB, indi	patient with TB ca ividuals who had homs as patients with the contact)	ousehol	d contac	t with or who had
No chest radiograph changes consistent with old TB				Definition o	f exposure group-	3		
Exposed 1 (specify):   Chest radiograph changes consistent with old TB   Tests	Non-exposed		No ches				TB	
Assay used, methodology, timing for test measurement, manufacturer   CIGRA (QFT-G)		cify):						
Assay used, methodology, timing for test measurement, manufacturer		<u> </u>	01100014	arograph than	500 001101000110 ((1111	010 12		
Timing for test measurement, manufacturer	1000	Assa	v used m	ethodology	Cut-off		Ot	her information
In the TB antigen tube minus the negative control tube was considered to be a positive test result		11354	timing for measure	or test ment,	values/thresh			ner miormution
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		IGRA (QFT-G), not reported  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		orted	in the TB antigen minus the negative control tube was considered to be	tube ve		
$ \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	TST≥ 10mm			≥ 10mm induration was considered to be a		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		
$ \begin{array}{ c c c c } \hline & Incidence \\ of active \\ \hline TB \\ \hline \hline Yes & No \\ \hline \hline Yes & No \\ \hline \hline Yes & No \\ \hline \hline \end{tabular}                                    $	Association be	tween t	est result	and incidend	ce of active TB (if	applica	ble)	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $								
$ \begin{array}{ c c c c c c } \hline Yes & No \\ \hline IGRA + & NA & NA & NA & TST + & NA & NA & NA \\ \hline IGRA - & NA & NA & NA & TST - & NA & NA & NA \\ \hline Indeterminate & NA & NA & NA & Indeterminate & NA & NA & NA \\ \hline Total & NA & NA & NA & Total & NA & NA & NA \\ \hline \hline Total & NA & NA & NA & Total & NA & NA & NA \\ \hline \hline \hline & & & & & & & & & & & & & & & &$			f active	Total				Total
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Υe		†		Yes	No	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	IGRA+			NA	TST +	-	+	NA
$ \begin{array}{ c c c c c } \hline \mbox{Indeterminate} & NA & NA & NA & NA & NA & NA \\ \hline \mbox{Total} & NA & NA & NA & Total & NA & NA & NA \\ \hline \mbox{Total} & NA & NA & NA & Total & NA & NA & NA \\ \hline \mbox{Test performance parameters} \\ \hline \mbox{Sensitivity} = NA & Sensitivity = NA \\ \hline \mbox{Specificity} = NA & Specificity = NA \\ \hline \mbox{Specificity} = NA & Specificity = NA \\ \hline \mbox{PPV} = NA & PPV = NA \\ \hline \mbox{NPV} = NA & NPV = NA \\ \hline \mbox{Cumulative Incidence }_{IGRA^+} = NA & Cumulative Incidence }_{IGRA^-} = NA & Cumulative Incidence }_{IGRA^-} = NA & Cumulative Incidence Ratio }_{IGRA} = NA & Cumulative Incidence Ratio }_{IGRA} = NA & Incidence density rate }_{IGRA^-} = NA & Incidence density rate }_{IGRA^-} = NA & Incidence density rate }_{IGRA^-} = NA & Incidence density rate ratio }_{IGRA} = NA & Incidence density rate rati$								
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IGRATSTSensitivity = NASensitivity = NASpecificity = NASpecificity = NAPPV = NAPPV = NANPV = NANPV = NACumulative Incidence $_{IGRA+}$ = NACumulative Incidence $_{TST+}$ = NACumulative Incidence Ratio $_{IGRA}$ = NACumulative Incidence Ratio $_{TST-}$ = NAIncidence density rate $_{IGRA+}$ = NAIncidence density rate $_{TST+}$ = NAIncidence density rate $_{IGRA-}$ = NAIncidence density rate $_{TST-}$ = NAIncidence density rate ratio $_{IGRA}$ = NAIncidence density rate ratio $_{TST-}$ = NAOther reported measure $_{IGRA}$ = NAOther reported measure $_{TST-}$ = NAComparison between tests (IGRA vs. TST)Ratio of cumulative incidence ratios = NA	Total	1112	ı INA				11/1	INA
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Cumulative Incidence $_{IGRA+} = NA$ Cumulative Incidence $_{TST+} = NA$ Cumulative Incidence $_{IGRA-} = NA$ Cumulative Incidence Ratio $_{TST-} = NA$ Cumulative Incidence Ratio $_{IGRA} = NA$ Cumulative Incidence Ratio $_{TST-} = NA$ Incidence density rate $_{IGRA+} = NA$ Incidence density rate $_{TST-} = NA$ Incidence density rate 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								
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 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		• •	<u> </u>					
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 ratio $_{TST-}$ = 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								
Incidence density rate $_{IGRA+} = NA$ Incidence density rate $_{TST+} = NA$ Incidence density rate $_{TST-} = NA$ Incidence density rate $_{TST-} = NA$ Incidence density rate ratio $_{TST-} = NA$ Incidence density rate ratio $_{TST-} = NA$ Other reported measure $_{TST-} = NA$ Other reported measure $_{TST-} = NA$ Comparison between tests (IGRA vs. TST)  Ratio of cumulative incidence ratios = $NA$								
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 = $NA$	Cumulative Incidence Ratio <sub>IGRA</sub> = NA			+			= 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 = $NA$	Incidence density rate <sub>IGRA+</sub> = NA							
Other reported measure $_{IGRA} = NA$ Other reported measure $_{TST} = NA$ Comparison between tests (IGRA vs. TST)  Ratio of cumulative incidence ratios = $NA$	Incidence densi	ty rate I	$_{GRA-} = NA$		Incidence density	rate TS	T = NA	
Other reported measure $_{IGRA} = NA$ Other reported measure $_{TST} = NA$ Comparison between tests (IGRA vs. TST)  Ratio of cumulative incidence ratios = $NA$								
Comparison between tests (IGRA vs. TST)  Ratio of cumulative incidence ratios = NA	-							
Ratio of cumulative incidence ratios = NA								
Ratio of incidence density rate ratios = NA	Ratio of cumula	Ratio of cumulative incidence ratios = NA						
	Ratio of incider	nce dens	ity rate ra	tios = NA				

Other reported measure = NR								
			esults and	l levels of TB expo	osure (Prev	ious TB d	lisease)	
	(QFT-G				TST≥ 1		, , , , , , , , , , , , , , , , , , , ,	
	Expo		Total		Exposur	e level	Total	
	lev	el			•			
	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	
		7	Test perfo	rmance paramete	ers			
	IGRA				TST	Γ		
Sensitivity = 6/8 = 92.85)	75%, 959	% CI (40	).93,	Sensitivity = 3/8	= 37.5%, 95	5% CI (13.	68, 69.43)	
Specificity = 55/92 (49.57, 69.22)	= 59.780	%, 95%	CI	Specificity = 61/9	92 = 66.3%,	95% CI (	56.17, 75.14)	
$ \begin{array}{c} \text{PPV} = 6/43 = 13.93 \\ 27.26 \end{array} $	5%, 95%	CI (6.55	56,	PPV = 3/34 = 8.8	24%, 95%	CI (3.047,	22.96)	
NPV = 55/57 = 96.	49%, 959	% CI (88	3.08,	NPV = 61/66 = 9	2.42%, 95%	6 CI (83.40	5, 96.72)	
99.03) DOR (for T <sup>+</sup> calcul	ated) = 4	.46, 95%	% CI	DOR (for T <sup>+</sup> calc	ulated) = 1.	18, 95% C	CI (0.26, 5.26)	
(0.85, 23.31)	. 10	3.70		0 D ( 1 0 m <sup>+</sup>	+ 10	3.TD (3.TG)		
OR (crude; for T <sup>+</sup> re			0.5.0.701	OR (crude; for T				
OR (regression-bas	ed; repor	ted) = 2	.06, 95%	OR (regression-based; reported) = NR (NS)				
CI (0.30, 12.80)	A I D			List of covariates: NR				
List of covariates:		D		0.1 . 1	NII	`		
Other reported mea	sure = N		l4	Other reported me		(		
Ratio of DORs (for	T <sup>+</sup> colou			veen tests (IGRA	vs. 151)			
Ratio of DORs (for Ratio of OR (crude				0 C1. 1.21, 11.63)				
Ratio of OR (crude				Λ				
Other reported mea			orca) - iv	A				
			ılte and la	vels of TB exposu	ıra (Pravio	us contact	with TR)	
	A (QFT-0		iits and ic	Exposu	TST (≥1		with 1D)	
IGNA	Expo		Total		Exposur		Total	
	lev		Total		Exposui	C ICVCI	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	
- 5 001			L	rmance paramete			100	
	IGRA		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	TST				
Sensitivity = 10/13		6, 95% (	CI (49.74,	Sensitivity = 6/1			(23.21, 70.86)	
91.82)								
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. 98.19)	74%, 95%	% CI (85	5.63,	NPV = 59/66 =	NPV = 59/66 = 89.39%, 95% CI (79.69, 94.77)			
DOR (for T <sup>+</sup> calcul	ated) = 5	.45, 95%	6 CI	DOR (for T <sup>+</sup> cal	culated) = 1	.81, 95%	CI (0.55, 5.87)	
(1.40, 21.27)								

OR (crude; for $T^+$ reported) = NR				OR (crude; for $T^+$ reported) = NR (NS)				
OR (regression-based; reported) = 5.08, 95%				OR (regression-		ted) = NR	R (NS)	
CI (1.20, 21.20)				List of covariates: NR				
List of covariates:						_		
Other reported mea	sure = N			Other reported i		R		
D 11 0D 0D 10	m <sup>+</sup> 1			een tests (IGRA	vs. TST)			
Ratio of DORs (for				CI: 1.20, 7.56)				
Ratio of OR (crude								
Ratio of ORs (regression-based; reported) = NA								
Other reported mea								
			ilts and lev	els of TB exposu			n changes)	
IGRA	A (QFT-				TST≥1		<b></b>	
	Expo		Total		Exposure	e level	Total	
	lev				**			
7.00	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	
		7	Test perfor	mance paramete		_		
~	IGRA			~	TS		(10.10.10.70)	
Sensitivity = 11/16	= 68.759	%, 95%	CI (44.40,	Sensitivity = 4/	16 = 25.00%	6, 95% CI	(10.18, 49.50)	
85.84)	61.00	2/ 050/	CT (51.00	G 'C' '	4/0.4 64.20	0/ 050/ 6	N (52 (2 52 52)	
Specificity = 52/84	$= 61.90^{\circ}$	%, 95%	CI (51.22,	Specificity = 54/84 = 64.29%, 95% CI (53.62, 73.70)				
71.55)	500/ O50	/ CI (14	02	PPV = 4/34 = 11.76%, 95% CI (4.67, 26.62)				
PPV = 11/43 = 25.3	.93,	PPV = 4/34 = 1	FFV - 4/34 - 11.70/0, 93/0 CI (4.07, 20.02)					
$\frac{40.24)}{\text{NPV} = 52/57 = 91.}$	220/ 050	)/ CI (01	1.05	NDV - 54/66 -	01 020/ 05	0/ CI (70	05 00 20)	
96.19	2370, 93	% CI (8.	1.03,	NPV = 34/00 =	NPV = 54/66 = 81.82%, 95% CI (70.85, 89.28)			
DOR (for T <sup>+</sup> calcul	(atad) - 3	57 050	/- CI	DOR (for T <sup>+</sup> ca	loulated) = (	0.60 0.50/-	CI (0.18, 2.02)	
(1.14, 11.24)	aica = 3	1.51, 957	0 C1	DOR (101 1 Ca	ilculated) – (	7.00, 75/0	C1 (0.16, 2.02)	
OR (crude; for T <sup>+</sup> r	enorted)	= NR		OR (crude; for	T <sup>+</sup> reported)	= NR (NS	3)	
OR (regression-bas			06 95%	OR (regression				
CI (2.10, 11.90)	cu, repor	ica) 3	.00, 7570	List of covariat		1104) 111	(115)	
List of covariates:	NR			List of covariat	05. 1110			
Other reported mea		R		Other reported	measure = N	IR		
	100110		rison betw	een tests (IGRA				
Ratio of DORs (for	T calcu			,				
Ratio of OR (crude				,				
Ratio of ORs (regre				A				
Other reported mea			, - 12					
			een test res	sults and BCG st	tatus (if ann	licable)		
	A (QFT-				TST ≥1			
	BCG		Total			status	Total	
	Yes	No	1	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 <sup>+</sup> calcul		= 1.89 (	95% CI:	DOR <sub>TST</sub> (for T+ calculated) = 4.28 (95% CI: 1.35,				
0.75, 4.73)	/ \/ 1	(		13.64)	/	ζ-	,	
· · ·								

OR (crude; for $T^+$ reported) = NR (NS)	OR (crude; for T+ reported) = NR (SS)
OR (regression-based; reported) $_{QFT} = NR$	OR (regression-based; reported) $_{TST} = 4.10$ (1.30,
(NS)	13.90)
List of covariates: 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	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

 $TST + threshold: \ge 10mm$ 

#### **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

 $TST + threshold: \ge 10mm$ 

#### **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

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

#### **Study details**

First author surname year of publication: Shen 2012<sup>140</sup>

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  $n = 40 (42.9 \pm 18.6)$ ; No TB exposure group ( $n = 39 \times 17.6$ ) 37.8  $\pm 17.6$ 

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):	70	26	44	0	70
ELISPOT					
<b>TST</b> (≥5 mm):	70	34	36	0	70
Test 3 (specify):	NA	NA	NA	NA	NA

Total N of p	atients	with v	alid resu	ılts for both	IGR	A and TST:			
							ble):		
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 $(n = 39)$									
	xposed 1 (specify): History of exposure to tuberculosis (suspected having TB, but no								
1	1 0/		•	ns of TB, n =		<b>\</b>	1	υ	,
Exposed 2 (s	pecify)	:	NA	/					
Exposed 3 (specify): NA									
Exposed 4 (s			NA						
Tests	<u>peerry</u>	<u>·                                     </u>	1111						
1000	Ass	av iise	d. metho	dology, timir	10	Cut-off val	ues/thr	esholds	Other
	1155	-		urement,	-8	Definiti			information
			manufac			2011110	.011 01 04		111101111111111111
IGRA	IFN-ν			y (Beijing		Not stated			NA
(TSPOT)				nology Inc.,		1 (or stated			1111
(15151)				d according to	)				
	1			commendatio					
TST≥5				y intradermal		TST was co	nsidere	d	NA
mm				nethod) of 0.1		positive wh		<b>.</b>	1111
				ording to curre	ent	transverse d		of	
	\	,		he induration		induration v			
						induidation v	5 1.		
		measured with a ruler by a ned physician 72 hours after the							
injection									
Association between test results and incidence of active TB (if applicable)									
110000111111	2001100	IGRA			1	001/0 12 (110		TST	
			ence of	Total	1			nce of	Total
			ve TB	10141			activ		10141
		Yes	No				Yes	No	
IGRA +		NA	NA	NA	1	TST +	NA	NA	NA
IGRA -		NA	NA	NA		TST -	NA	NA	NA
Indetermin		NA	NA	NA	In	determinate	NA	NA	NA
Total		NA	NA	NA		Total	NA	NA	NA
Total		1 17 1		Test perform	ance			1171	1171
		IGRA		rest periorii		parameters		TST	
Sensitivity =	NΔ	IJKA			Sa	$n_{\text{citivity}} = N_{\text{c}}$		101	
Specificity =					Sensitivity = NA Specificity = NA				
$\frac{\text{Specificity} - \text{PPV} = \text{NA}}{\text{PPV} = \text{NA}}$	11/1				PPV = NA				
$\frac{PPV - NA}{NPV = NA}$					NPV = NA				
	noidon	20	— NT A		Cumulative Incidence <sub>TST+</sub> = NA				
Cumulative I									
Cumulative I				AT A	Cumulative Incidence TST. = NA				
	Cumulative Incidence Ratio <sub>IGRA</sub> = NA					Cumulative Incidence Ratio <sub>TST</sub> = NA			
Incidence density rate <sub>IGRA+</sub> = NA					Incidence density rate <sub>TST+</sub> = NA				
Incidence density rate <sub>IGRA</sub> = NA				Incidence density rate <sub>TST</sub> = NA					
·						Incidence density rate ratio <sub>TST</sub> = 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)									
ASSO	IGRA (TSPOT)  TST≥5mm								
ASSO		A (TSI	POT) sure leve			1		'≥5mm ure level	Total

	Vac	No			Vac	No	
ICDA	Yes	No	26	TOT	Yes	No	2.4
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
	ICDA	<u> 1e</u>	st periori	nance parameters		T	
Citiit 22/21	IGRA	050/ CI	(52.41	Citiit 10/	TS		I (42.92
Sensitivity = 22/31 83.9)				Sensitivity = 19/3 76.27)			
Specificity = 35/39 95.94)	= 89.74%	6 (95% C	I: 76.42,	Specificity = 24/3	39 = 61.54	ŀ% (95% C	II: 45.9, 75.11)
PPV = 22/26 = 84.6 93.85)	62% (95%	CI: 66.4	7,	PPV = 19/34 = 5	5.88% (95	% CI: 39.4	15, 71.12)
NPV = 35/44 = 79.	55% (95%	6 CI: 65.5	5, 88.85)	NPV = 24/36 = 6	6.67% (95	5% CI: 50.	33, 79.79)
DOR (for T <sup>+</sup> calcul 5.87, 77.93)				DOR (for T <sup>+</sup> calc			
OR (crude; for T <sup>+</sup> re	enorted) =	: NR		OR (crude; for T	reported)	= NR	
OR (regression-bas				OR (regression-b			•
List of covariates: 1		$ca_j - mc$		List of covariates			•
Other reported mea		· · · · · · · · · · · · · · · · · · ·		Other reported m		JP.	
Other reported filea			son hetwe	een tests (IGRA v		VIC	
Ratio of DORs (for					. 151)		
				21. 3.71, 17.20)			
Ratio of OR (crude; for T <sup>+</sup> 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)							
IGRA	BCG s		Total			status	Total
	Yes	No	Total		Yes	No	10181
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
Total	NK			nance parameters		INK	INK
ICD	A (TSDO)		st periori	hance parameters		\5 mm)	
DOR (for T <sup>+</sup> calcul	A (TSPO)		<u> </u>	DOR <sub>TST</sub> (for '		>5 mm)	
OR (for 1 calcul				OR (crude; fo			
OR (regression-bas			NID	OR (regressio			
OR (regression-bas				List of covaria		eported) TS	T - NK
List of covariates: 1		cu) <sub>TSPOT</sub> -	- 111	List of covaria	iics. IVIX		
		)		Other reported	1 maggura	- ND	
Other reported mea			oo end d:			- 11L	
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		NR
IGRA -		NR		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							

#### 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)

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 NR NR Test 3 (specify):

#### **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)

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

#### Study details

First author surname year of publication: Souza 2014<sup>153</sup>

**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

				<u> </u>				
Test 3 (specify)								
				GRA and TST: 29				
				ng order (if appl				
	<u>Definition</u>		ure group –	History of contact	with ind	lex case		
Non-exposed		No						
Exposed 1 (specify		Yes						
Exposed 2 (specify		NR						
Exposed 3 (specify		NR						
Exposed 4 (specify	y):	NR						
_								
Tests	T .							
		used, met timing for	thodology,	Cut-off values/ Definition of		lds	Other information	
		measurem		Denintion (	or test-		IIIIOI IIIatioii	
		manufact						
ICDA (OFT	_			Positive result wa		ana d		
IGRA (QFT- GIT)	_	HT was pering to the	riorinea	if the difference b		ered		
GII)		acturer's in	etruction	interferon respons				
	Illallula	acturer 8 m	istruction	antigens and nega				
				was >0.35 UI/mL				
				interferon respons				
				antigens was ≥25°				
				to the negative co				
				response				
				1				
				QFT-GIT was con				
				to be indeterminat				
				interferon respons				
				negative control v				
				or <0.5UI/mL cor	o the			
				positive control	1			
TST≥5mm		•	submitted	Injection and read				
		using 0.11		induration 72 to 9				
		T 23 (2 un	its of	injection were per	by a			
	tubercu	ılın)		trained HCW				
				Positive result wa				
				induration was ≥5				
Association bety	veen tes	t results •	and incide	nce of active TB (		icable)		
11350CIUCIOII DECV	IGR		ana meraer			ST		
		lence of	Total			ence of	Total	
		ve TB	1000			e TB	10001	
	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	
		Tes	t performa	nce parameters				
	IGR	A			T	ST		
Sensitivity = NA				Sensitivity = NA				
Specificity = NA				Specificity = NA				
PPV= NA		PPV= NA						
NPV= NA				NPV= NA				
	-	-						

Cumulative Incider	$lce_{IGR\Delta+} = N$	JA		Cumulative Incidence <sub>TST+</sub> = NA				
Cumulative Incider				Cumulative Incidence TST = NA				
Cumulative Incider				Cumulative Incidence Ratio $_{TST} = NA$				
Incidence density ra				Incidence density rate <sub>TST+</sub> = NA				
Incidence density ra				Incidence density rate $_{TST-} = NA$				
Incidence density ra				Incidence density rate ratio <sub>TST</sub> = NA				
Other reported mea				Other reported				
1,100			etween	tests (IGRA vs				
Ratio of cumulative		_			, , , , , , , , , , , , , , , , , , , ,			
Ratio of incidence								
Other reported mea								
•		n test resu	ılts and	levels of TB ex	posure (if	applicable	e)	
	A (QFT-C				TST (≥5ı		,	
	Exposu		Total		Exposu		Total	
	High/Yes	Low/No			High/Yes	Low/No	1	
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 pe	rforma	nce parameters				
	IGRA				TST			
Sensitivity = 0/35=	0.00% (95%	CI: 0.0, 9.	89)	Sensitivity = 1/3	35=2.86% (9	95% CI: 0.5	50, 14.53)	
Specificity = 245/2				Specificity =251/259=96.91% (95% CI: 94.02,				
97.03)	(0 #0 / OX 0	0.00.01)		98.43)	10//0#0//0			
PPV= 0/13=0.00%			\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	PPV=1/9= 11.1				
NPV= 245/280=87				NPV=251/285=				
DOR (for T <sup>+</sup> calcul 4.24)	ated)= 0.50	(95% CI: 0	.06,	DOR (for T <sup>+</sup> cal 7.61)	culated)= 0	.93 (95% C	1: 0.11,	
OR (crude; for T <sup>+</sup> re	enorted)= 0	49 (95% CI	I· 0 06	OR (crude; for 7	Γ <sup>+</sup> reported)=	= 0.92 (95%	6 CI: 0.11	
3.82)	oported) o.	15 (5570 61	. 0.00,	7.61)	r reported)	0.52 (557	0 01. 0.11,	
OR (regression-bas	ed; reported	)= NR		OR (regression-based; reported)= 1.21 (95% CI:				
	, 1	•		0.13, 11.16)				
List of covariates: 1	NR			List of covariates: NR				
Other reported mea				Other reported measure =NR				
	Con	iparison b	etween	tests (IGRA vs	. TST)			
Ratio of DORs (for								
Ratio of OR (crude	; for T <sup>+</sup> repo	rted) = 0.53	3 (95% C	T: 0.12, 2.42)				
Ratio of ORs (regre		; reported)	= NA					
Other reported mea								
Ass	ociation be	etween tes	t results	and BCG state	us (if appli	icable)		
IG	RA (specif	fy)			TST (spe			
	BCG s	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 NA	NA	indeterminate	NA	NA	NA	
Total	NA	Total	NA	NA	NA			
		Test pe	rforma	nce parameters				
	IGRA			TST				
DOR (for T <sup>+</sup> calcul	ated) <sub>IGRA</sub> = 1	NA		DOR (for T+ cal	lculated) <sub>TST</sub>	=NA		
OR (crude; for T <sup>+</sup> re				OR (crude; for 7				
OR (regression-bas	ed; reported	$)_{IGRA} = NA$		OR (regression-	based; repor	$rted)_{TST} = N$	VA	
		151 1.12						

List of covariates: NA		List of covariates: NA				
Other reported measure	= NA	Other reported measure = NA				
		discordance (if applicable)				
<u> </u>		f value, BCG vaccination status	. and/or			
condition	······································		,			
Total sample						
20002 500020	TST +(≥5mm)	TST -	Total			
IGRA +	6	8	14			
IGRA -	4	281	285			
indeterminate	0	1	1			
Total	10	289	299			
Description						
	otal, if stratified by BCG	or condition – specify): total				
TST + threshold: >5mm	oun, it summing by Dec	specify), veim				
Parameters						
Kappa = 0.48 (95% CI: 0)	37 () 59)					
	9 = 96.00% (95% CI: 93	12 97 69)				
	= 4.01% (95% CI: 2.31,					
Stratification (specify						
struction (specify	TST +	TST -	Total			
IGRA +	NA	NA	NA			
IGRA -	NA	NA	NA			
indeterminate	NA	NA	NA			
Total	NA	NA	NA			
Description	1111	1111	1111			
	otal_if stratified by BCC	G or condition – specify): NA				
TST + threshold: NA	otal, il stratifica by BCC	s or condition—specify). 1471				
Parameters Parameters						
Kappa = NA						
% concordance = NA						
% discordance = NA						
Stratification (specify	group 2):					
struction (specify	TST +	TST -	Total			
IGRA +	NA	NA	NA			
IGRA -	NA	NA	NA			
indeterminate	NA	NA	NA			
Total	NA	NA	NA			
<b>Description</b>	1111	1111	1171			
<u>*</u>	otal if stratified by RCC	G or condition – specify): NA				
TST + threshold: NA	oui, ii suuilled by DCC	of condition—specify). 1471				
Parameters						
Kanna = NA						
Kappa = NA % concordance = NA						
% concordance = NA % discordance = NA						

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)

Name of first reviewer: Peter Auguste

Name of second reviewer: Alexander Tsertsvadze

#### Study details

First author surname year of publication: Takeda 2011<sup>141</sup>

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

Number of patients to	esteu				
	Total N	Total	Total N	Total N	Total N
	(tested)	N	(test-)	(indeterminate)	(test results
					available)
		(test+)			
IGRA (QFT-2G):	71	2	46	23	71
<b>TST</b> ( ≥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/grou	ups of ext	osure	e to TB in	increasing	g or	der (if applicab	ole):			
	1 1				_	xposure group	- ) -			
Non-expose	ed	Wit	thout risk							
Exposed 1 (		Wit	th risk fac	tors for LT	BI (	I (history of household TB contact; chest X ray				
						B showing nodules, fibrotic scars, calcified				
		gra	nulomas,	basal thicke	enin	g; history of ac	tive T	B)		
Exposed 2 (	(specify):	NA						-		
Exposed 3 (	(specify):	NA								
Exposed 4 (	(specify):	NA	-							
Tests										
	Assa	y used	d, method	lology,		Cut-off		Other in	formation	
	timing		est measu		1	alues/threshold				
			ufacturei		+	efinition of test				
IGRA	~		B Gold (C	- / /	$\geq$	0.35 IU/mL			t if the IFN-γ	
(QFT-	Cellestis	, Carr	iegie, Aus	stralia					tigen stimulated	
GIT)									35 IU/mL and in	
									ells was ≥0.5	
								J/mL. Resul		
									leterminate if	
								•	I in the antigen	
								imulated wel		
								the antigen-	ne IFN-γ level	
									ow half of the	
									gative control	
								as > 0.7  IU/r		
TST≥10	0.1 mL c	of tube	erculin pu	rified	>1	0 mm, accordin		A		
mm			tive (PPD)			the usual	8 1			
	-			ulin units	cri	iterion of the TS	Т			
			ppon BCC		in	Japan				
	Manufac	turing	g, Tokyo,	Japan)						
	into the	venral	surface o	of the						
			induration							
			ours later							
Association				d incidenc	e of	f active TB (if a	pplica	ıble)		
		IGR/		T				TST	T	
			ence of	Total				idence of	Total	
			re TB					ctive TB		
¥ ~~ ·		es	No			<b></b>	Yes	No	<b></b>	
IGRA -		NA_	NA	NA		TST +	NA	NA	NA	
IGRA -		NA.	NA	NA		TST -	NA	NA	NA NA	
Indetermin	-	VA	NA	NA NA	_	Indeterminate	NA	NA NA	NA NA	
Total	1 1	NA_	NA	NA		Total	NA	NA	NA	
		ICD		est periori	man	ice parameters		тст		
Consitivity		IGR/	1			Consitivity - N	Λ	TST		
Sensitivity Specificity					-	$\frac{\text{Sensitivity} = N}{\text{Specificity} = N}$				
PPV = NA	- INA				-	Specificity - N $PPV = NA$	Λ			
PPV = NA NPV = NA					-	PPV = NA NPV = NA				
	Incidence		— Nī A				idono	- NTA		
Cumulative					$\dashv$	Cumulative Inc				
Cumulative				٨		Cumulative Incidence <sub>TST</sub> . = NA  Cumulative Incidence Ratio <sub>TST</sub> = NA				
Cumulative				Α	-				INA	
Incidence density rate $_{IGRA+} = NA$					Incidence density rate $_{TST+} = NA$					

Incidence density	rate IGPA =	NA		Incidence den	sity rate <sub>TST-</sub> =	NA			
Incidence density				Incidence density rate ratio <sub>TST</sub> = NA					
Other reported me				Other reported measure $_{TST} = NA$					
other reported in			n betwee	en tests (IGRA v		1111			
Ratio of cumulati				on cests (16121)	3. 151)				
Ratio of incidence									
Other reported me			121						
			cults an	d levels of TB ex	vnosure (risk	for LTRD			
11000	IGRA	con test it	suits uii		TST	ioi Libij			
	Exposu	e level	Total		Exposure	e level	Total		
	High/Yes	Low/No	1000	}	High/Yes	Low/No	10001		
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		
10001		·		ance parameter					
	IGRA				TST				
Including indeter		test negati	ve	Sensitivity = 1/		5% CI (1.2	27, 31.47)		
Sensitivity = $2/26$				Selisitivity	7.11.70, 5	270 01 (1.2	.,, 31,)		
24.14)	7.7070 (5.	370 C1. 2.1	٠,						
Excluding indete	erminate								
Sensitivity = $2/18$		95% CI: 3.	10.						
32.80)	`		,						
Including indeter	rminate-as 1	test negati	ve	Specificity = 27	7/29 = 93.10%	, 95% CI (	78.04,		
Specificity = 45/4				98.09)		,			
100.00)				·					
<b>Excluding indete</b>	erminate								
Specificity = 30/3	60 = 100.00%	% (95% CI:	88.65,						
100.00)									
PPV = 2/2 = 100.				PPV = 1/3 = 33.33%, 95% CI (6.15, 79.23)					
Including indeter	rminate-as 1	test negati	ve	NPV = 27/40 = 67.50%, 95%  CI  (52.02, 79.92)					
NPV = 45/69 = 63	,	CI: 53.45,	75.38)						
Excluding indete									
NPV = 30/46 = 63									
DOR (for T <sup>+</sup> calc	ulated) = 3.7	5 (95% CI	: 0.31,	DOR (for $T^+$ calculated) = 1.04, 95% CI (0.08,					
44.6)				12.53)					
OR (crude; for T <sup>+</sup>				$OR (crude; for T^+ reported) = NR$					
OR (regression-ba		d) = NR		OR (regression	/ 1	ed) = NR			
List of covariates				List of covariates: NR					
Other reported me			•	Other reported					
<b>D</b>				en tests (IGRA v	s. TST)				
Ratio of DORs (fo				1: 0.59, 21.99)					
Ratio of OR (crud									
Ratio of ORs (reg			1) = NA						
Other reported me									
			test resu	lts and BCG sta		,			
IG	RA (TSPOT				TST (>5				
	BCG s		Total			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	Indetermina		NA	NA		
Total	NA	NA	NA	Total	NA	NA	NA		

	Test perform	nance parameters				
IGRA (T	SPOT/QFT)	TST (>5				
DOR (for T <sup>+</sup> calculated)	$_{TSPOT/QFT} = NA$	DOR TST (for T+ calculate	ed) = NA			
OR (crude; for T <sup>+</sup> report	ed) = NA	OR (crude; for T+ reporte	ed) = NA			
OR (regression-based; r		OR (regression-based; rep	OR (regression-based; reported) $_{TST} = NA$			
OR (regression-based; r	$eported)_{TSPOT} = NA$	List of covariates: NA				
List of covariates: NA						
Other reported measure	=NR	Other reported measure =	NR			
		cordance (if applicable)				
This table may be stra	tified by TST cut-off val	lue, 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						
	total, if stratified by BCC	G or condition – specify): NR				
TST + threshold: NR	,	1 2/				
Parameters						
Kappa = NR						
% concordance = NR						
% discordance = NR						
Stratification (specify s	proun 1)					
Stratification (specify §	TST +	TST -	Total			
IGRA +	NR	NR	NR			
IGRA -	NR	NR NR	NR			
Indeterminate	NR NR	NR NR	NR			
Total	NR NR	NR NR	NR			
	NK	INK	NK NK			
Description	4-4-1 :C-44:C-41 DCC	7 4:4: : <del>C</del>				
	total, if stratified by BCC	G or condition – specify): NA				
TST + threshold: NA						
Parameters						
Kappa = NA						
% concordance = NA						
% discordance = NA						
Stratification (specify §		T ====				
	TST +	TST -	Total			
IGRA +	NR	NR	NR			
IGRA -	NR	NR	NR			
Indeterminate	NR	NR	NR			
Total	NR	NR	NR			
Description						
	total, if stratified by BCC	G or condition – specify): NR				
TST + threshold: NR						
Parameters						
Kappa = NR						
% concordance = NR						
% discordance = NR						
		outcomes				
Test and cut-off (if applicable)	st and cut-off (if Adverse events n/N (%) Health related					

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

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

#### **Study details**

First author surname year of publication: Vassilopolous 2011<sup>142</sup>

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):  $52 \pm 16$ 

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

<b>TST</b> (≥ 5mm):			157	4	58	97		2			155
Total N of pati	ients w	vith va	alid resu	lts for	both IC	GRA and TS	<b>T:</b> 1	55			
Levels/groups											
				Definit	tion of e	xposure gro	up				
Non-exposed		No	history	of prev	ious TB	contact					
Exposed 1 (spe	cify):	His	story of p	reviou	ıs TB co	ntact					
	•	•	•	Definit	tion of e	xposure gro	up				
Non-exposed		Che	est x-ray	witho	ut signs	suggestive of	old	TB			
Exposed 2 (spe	cify):	Ch	est x-ray	sugge	stive of	old TB					
				Definit	tion of e	xposure gro	up				
Non-exposed		No	risk fact	tor for	TB (≥ 1)	)					
Exposed 3 (spe	cify):	An	y risk fa	ctor for	r TB (≥	1) including:	age	>50 yea	ırs, ches	t X-ray	suggestive
		of o	old/heale	d TB,	contact	with a person	wit	h TB, aı	nd birth	or resi	dence in a
		cou	ıntry wit	h a hig	h TB pr	evalence (nor	1-Gr	eek nati	onality)	)	
Tests											
			y used,			Cut-off		O	ther inf	format	ion
			logy, tin			thresholds/					
			easuren			nition of					
			facturei	•		test+			1 0		
IGRA (QFT-		-GIT v			NR						IGRAs was
GIT)	-		accordin	g to					just prio		
	the manufacturer's instructions					application in order to					
	mstrt	structions						potential interference with the IGRA results			
IGRA	The	he T-SPOT.TB assay							draw fo	r hoth	IGRAs was
(TSPOT)			ned as	say	NR				just pri		
(15101)			describe	d					in orde		
	picvi	ousty	describe	u							th the IGRA
							results				in the restar
TST≥ 5mm	Mant	oux m	ethod of	f 0.1	A TST	`was	NA				
			of purific		considered						
			ivative (		positive when the						
	RT 2	3; Stat	tens Seri	ım	diamet	neter of					
	Instit	ute, C	openhag	en,	transve	transverse					
	Denn	nark)			indura	tion was ≥					
					5mm						
Association be				nd inci	dence o	f active TB (	if ap				
		IGRA							ΓST		
			ence of	Te	otal			Incide			Total
	L		re TB				ļ	activ			
ICD 4		Yes	No		T A	mam :		Yes	No		NT A
IGRA +		NA	NA		NA TA	TST +		NA	NA		NA
IGRA -		NA	NA		NA TA	TST -	,	NA	NA		NA
Indeterminat		NA	NA		NA TA	Indetermina	ate	NA	NA		NA
Total		NA	NA		NA weeks	Total	0.7	NA	NA		NA
		ICDA		est pe	eriorma	nce paramet	ers		гот		
Congitivit	IGRA						_ NT		ΓST		
Sensitivity = N						Sensitivity :					
Specificity = NA						Specificity = NA					
PPV = NA $NDV - NA$						PPV = NA					
	NPV = NA Cumulative Incidence $IGRA+ = NA$						NPV = NA				
						Cumulative Incidence <sub>TST+</sub> = NA					
Cumulative Incidence <sub>IGRA-</sub> = NA						Cumulative Incidence <sub>TST</sub> . = NA					

G 1 . T . 1	D .:	27.4			'1 D	37		
Cumulative Inciden				Cumulative Incidence Ratio <sub>TST</sub> = NA				
Incidence density ra				Incidence density rate <sub>TST+</sub> = NA				
Incidence density ra				Incidence density rate TST. = NA				
Incidence density ra				Incidence density rate ratio $_{TST} = NA$				
Other reported meas				Other reported measure $_{TST} = NA$				
				en tests (IGRA v	s. TST)			
Ratio of cumulative								
Ratio of incidence d		ratios =	NA					
Other reported meas	sure = NR							
Associa	ation betw	een test	results an	d levels of TB ex	xposure (T)	B exposure	e)	
IGRA	(T-SPOT	.TB)			TST≥ 5	5mm		
	Exposure level Total				Exposur	e 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	
		Tes	t perform	ance parameter	S			
	IGRA			•	TS	Γ		
Sensitivity = 5/20 =	25.00%, 9	95% CI (1	11.19,	Sensitivity = 10	$\sqrt{20} = 50.00$	0%, 95% C	I (29.93,	
46.87)				70.07)				
Specificity = 101/13	35 = 74.81	%, 95% (	CI	Specificity = 87	7/135 = 64.4	14%, 95% (	CI (56.07,	
(66.88, 81.38)				72.02)				
PPV = 5/39 = 12.82	%, 95% C	I (5.60, 2	6.71)	PPV = 10/58 =	17.24%, 95	% CI (9.64	, 28.91)	
NPV = 101/116 = 8	7.07%, 95	% CI (79	.76,	NPV = 87/97 =	89.69%, 95	5% CI (82.0	05, 94.3)	
92.00)	. 1) 0.0	0.050/.0	Y (0.22	DOD (2 FF	1 1 . 1	4.04.0#0/	GY (0. <b>5</b> 0	
DOR (for T <sup>+</sup> calcula	(ted) = 0.9	9, 95% C	1 (0.33,	DOR (for T <sup>+</sup> ca	lculated) =	1.81, 95%	CI (0.70,	
2.92)	. 1	0.00.050	/ CT	4.66)	TP <sup>+</sup> . 1\	1.01.05	A/ CL AID	
OR (crude; for $T^+$ re (NR; p = 0.99)	ported) =	0.99, 95%	6 CI	OR (crude; for ' = 0.22)	I reported)	) = 1.81, 95	% CI (NR; p	
OR (regression-base	ed: reporte	d = 0.89	. 95% CI	/				
(NR; p = 0.86)	· · · · · · · · · · · · · · · · · · ·	.,	,	(NR; p = 0.30)				
List of covariates: N	IR.			List of covariates: NR				
Other reported meas				Other reported		NR		
		omparis	on betwee	en tests (IGRA v		·		
Ratio of DORs (for					,,			
Ratio of OR (crude;								
Ratio of ORs (regre								
Other reported meas			<i>(</i> ) 1 (11					
Ĭ.			results an	d levels of TB ex	nosure (T	R exposure	2)	
	A (QFT-G		results un		TST≥ 5			
TGIC	Exposu		Total		Exposur		Total	
	Yes	No	1 Otal		Yes	No	10111	
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	
1 Utal	20					133	133	
	ICDA	1 es	t periorm	ance parameter		Г		
Giti it 2/20	<b>IGRA</b>	)50/ CT (	7.22	G	TS		1 (20.02	
Sensitivity = $3/20 = 36.04$ )	15.00%, 9	95% CI (5	5.23,	Sensitivity = 10/20 = 50.00%, 95% CI (29.93, 70.07)			1 (29.93,	
Specificity = 106/135 = 78.52%, 95% CI				Specificity = 87/135 = 64.44%, 95% CI (56.07,				
(70.85, 84.61)		.,		72.02)				
(70.85, 84.61)								

Comparison between tests (ICPA vs. TST)						
Other reported measure = NR	Other reported measure = NR					
List of covariates: NR	List of covariates: NR					
(NR; p = 0.41)	(NR; p = 0.30)					
OR (regression-based; reported) = 0.55, 95% CI	OR (regression-based; reported) = 1.73, 95% CI					
(NR; p = 0.5)	= 0.22)					
OR (crude; for $T^+$ reported) = 0.64, 95% CI	OR (crude; for $T^+$ reported) = 1.81, 95% CI (NR; p					
2.35)	4.66)					
DOR (for $T^+$ calculated) = 0.64, 95% CI (0.17,	DOR (for $T^+$ calculated) = 1.81, 95% CI (0.70,					
91.19)						
NPV = 106/123 = 86.18%, 95% CI (78.98,	NPV = 87/97 = 89.69%, 95% CI (82.05, 94.3)					
PPV = 3/32 = 9.37%, 95% CI (3.24, 24.22)	PPV = 10/58 = 17.24%, 95% CI (9.64, 28.91)					

#### 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**

rest per for mance par ameters					
IGRA	TST				
Sensitivity = 4/14 = 28.57%, 95% CI (11.72,	Sensitivity = 9/14 = 64.29%, 95% CI (38.76,				
54.65)	83.66)				
Specificity = 106/141 = 75.18%, 95% CI	Specificity = 92/141 = 65.25%, 95% CI (57.08,				
(67.44, 81.58)	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,	NPV = 92/97 = 94.85%, 95% CI (88.5, 97.78)				
95.25)					
DOR (for $T^+$ calculated) = 2.21, 95% CI (0.35,	DOR (for $T^+$ calculated) = 3.38, 95% CI (1.07,				
4.10)	10.64)				
OR (crude; for $T^+$ reported) = 2.21, 95% CI	OR (crude; for $T^+$ reported) = 3.38, 95% CI (NR; p				
(NR; p = 0.76)	= 0.04)				
OR (regression-based; reported) = 0.48, 95% CI	OR (regression-based; reported) = 3.50, 95% CI				
(NR; p = 0.31)	(NR; p = 0.05)				
List of covariates: 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) = 0.65 (95% CI: 0.28, 1.54)

Ratio of OR (crude; for T<sup>+</sup> reported) = NA

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

Other reported measure =  $\overline{NR}$ 

# 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	
		Tes	t perform	ance parameter				
	IGRA				TS			
Sensitivity = 58.33%	% (95% CI	: 38.83, 7	75.53)	Sensitivity = 9/ 83.66)	14 = 64.29%	%, 95% CI	(38.76,	
Specificity = 80.14% (95% CI: 72.8, 85.89)			Specificity = 92 72.61)	2/141 = 65.2	25%, 95%	CI (57.08,		
PPV = 33.33% (95%	6 CI: 21.0	1, 48.45)		PPV = 9/58 = 1	5.52%, 95%	6 CI (8.38.	26.93)	
NPV = 91.87% (95%)				NPV = 92/97 =				
DOR (for T <sup>+</sup> calcula 14.05)				DOR (for T <sup>+</sup> ca 10.64)				
OR (crude; for $T^+$ re (NR; $p = 0.44$ )	ported) =	1.61, 95%	% CI	OR (crude; for = 0.04)	T <sup>+</sup> reported)	= 3.38, 95	5% CI (NR; p	
OR (regression-base	ed: reporte	d) = 1.29	. 95% CI	OR (regression	-based: repo	orted = 3.5	50. 95% CI	
(NR; $p = 0.72$ )	, 1 op 0110	u) 1>	, , , , , , , , ,	(NR; p = 0.05)	ouses, rep	,1000)	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
List of covariates: N	IR			List of covariat	es: NR			
Other reported measurements				Other reported		NR.		
T		omparis	on betwee	en tests (IGRA v				
Ratio of DORs (for								
Ratio of OR (crude;				, ,				
Ratio of ORs (regres								
Other reported meas								
		st results	and leve	ls of TB exposur	e (any risk	factor for	· TB ≥ 1)	
	(T-SPOT			TST≥ 5mm				
	Exposur		Total		Exposur	e 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	
		Tes	t perform	ance parameter	S			
	IGRA				TS	Γ		
Sensitivity = 34/102 42.94)	2 = 33.33%	o, 95% Cl	[ (24.94,	Sensitivity = 42/102 = 41.18%, 95% CI (32.12, 50.88)				
Specificity = 48/53 = 95.9)	= 90.57%,	95% (79	0.75,	Specificity = 37 80.48)	7/53 = 69.81	%, 95% C	CI (56.46,	
PPV = 34/39 = 87.1	8%, 95%	CI (73.29	, 94.4)	PPV = 42/58 = 72.41%, 95% CI (59.80, 82.25)				
NPV = 48/116 = 41				NPV = 37/97 = 38.14%, 95% CI (29.10, 48.09)				
50.48)	,	`	*					
DOR (for T <sup>+</sup> calcula	ted) = 4.8	0, 95% C	I (1.75,	DOR (for $T^+$ calculated) = 1.61, 95% CI (0.79,				
13.16)				3.28)				
OR (crude; for T <sup>+</sup> re	ported) = 0	4.80, 95%	% CI	OR (crude; for $T^+$ reported) = 1.60, 95% CI (NR; p				
(NR; p = 0.02)	<u> </u>			= 0.12)				
OR (regression-based; reported) = NR			OR (regression-based; reported) = NR					
	List of covariates: NR			List of covariat				
Other reported meas				Other reported		VR		
	-			en tests (IGRA v	s. TST)			
Ratio of DORs (for				I: 1.59, 5.60)				
Ratio of OR (crude;								
Ratio of ORs (regres		d; reporte	ed) = NA					
Other reported meas								
			and level	s of TB exposur			$TB \ge 1$	
IGRA	A (QFT-G	IT)			TST≥ 5	5mm		

	Exposu	e level	Total		Exposur	e level	Total	
	Yes	No	Total		Yes	No	Total	
IGRA +	26	6	32	TST +	42	16	58	
IGRA -	76	47	123	TST -	60	37	97	
Indeterminate	0	0	<del>                                     </del>	Indeterminate	0	0	0	
	-		0					
Total	102	53	155	Total	102	53	155	
	ICDA	Tes	t performa	ance parameters	TD CF			
G ::: :: 26/100	IGRA	0.50/_(1	0.02	G ::: :: 42	TS7		CI (22.12	
Sensitivity = $26/102$	z = 25.49%	o, 95% (1	8.03,	Sensitivity = $42/$	102 = 41.1	8%, 95%	CI (32.12,	
34.73)	00.600/	0.50/ .CIT	(55.40	50.88)	(50, 60, 0.1	0/ 050/ 6	T (FC AC	
Specificity = 47/53	= 88.68%,	95% CI	(77.42,	Specificity = 37	53 = 69.81	%, 95% C	1 (56.46,	
94.71)	50/ 050/	OY (64.66	01.11)	80.48)	2 410/ 05	0/ OT (50 )	20. 02.05)	
PPV = 26/32 = 81.2				PPV = 42/58 = 7				
NPV = 47/123 = 38	.21%, 95%	6 CI (30.	10,	NPV = 37/97 = 3	38.14%, 95	% CI (29.	10, 48.09)	
47.03)	4) = -	0 0 = 0 / 0	~~ / / / / / / / / / / / / / / / / / /		4 4			
DOR (for T <sup>+</sup> calcula	ated) = 2.6	8, 95% C	CI (1.02,	DOR (for T <sup>+</sup> cal	culated) =	1.61, 95%	CI (0.79,	
6.99)				3.28)				
OR (crude; for T <sup>+</sup> re	ported) =	2.68, 95%	% CI	OR (crude; for T	reported)	= 1.60, 93	5% CI (NR; p	
(NR; p = 0.04)				= 0.12)		4		
OR (regression-base		d) = NR		OR (regression-		rted) = NI	₹	
List of covariates: N				List of covariate				
Other reported meas			_	Other reported n		NR .		
				n tests (IGRA vs	. TST)			
Ratio of DORs (for				[: 0.90, 3.07)				
Ratio of OR (crude;								
Ratio of ORs (regre		d; report	ed) = NA					
Other reported meas								
A	ssociation	betweer	ı test resul	ts and BCG stat	us (if appli	icable)		
IGR.	A (T-SPO					ST		
	BCG s	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	
		Tes	t performa	ance parameters				
IGR.	A (T-SPO	T.TB)			TST (>	>5 mm)		
DOR (for T <sup>+</sup> calcula	ited) <sub>TSPOT</sub>	= 0.74, 9	5% CI	DOR TST (for	T+ calcula	ted) = 1.3	6, 95% CI	
(0.35, 1.59)	,	,		(0.67, 2.74)				
OR (crude; for T <sup>+</sup> re	ported) =	0.75, 95%	% CI (NR; 1	p OR (crude; for T+ reported) = 1.36, 95% CI				
= 0.45)	- /			(NR; p = 0.39)	9)			
OR (regression-base	ed; reporte	$d)_{TSPOT} =$	0.51, 95%			eported) TS	$s_{\rm T} = 1.43, 95\%$	
CI (NR; $p = 0.17$ )								
				CI (IVIX, $p - V$	List of covariates: NR			
List of covariates: N	<b>I</b> R							
					ates: NR	= NR		
List of covariates: N Other reported meas	sure = NR	betweer	ı test resul	List of covar	ates: NR d measure			
List of covariates: N Other reported meas	sure = NR		ı test resul	List of covar	ates: NR d measure us (if appli			
List of covariates: N Other reported meas	sure = NR ssociation	GIT)	test resul	List of covar	ates: NR d measure us (if appli	icable)	Total	
List of covariates: N Other reported meas	sure = NR ssociation RA (QFT- BCG s	GIT) status		List of covar	ates: NR d measure us (if appli TS	ST status	Total	
List of covariates: N Other reported meas A IGF	sure = NR ssociation RA (QFT-	GIT)		List of covar	ates: NR d measure us (if appli T3 BCG Yes	icable) ST		
List of covariates: N Other reported meas	sure = NR ssociation RA (QFT- BCG s Yes	GIT) status No	Total	Other reporte ts and BCG stat	ates: NR d measure us (if appli T) BCG	status No	Total  58 97	
List of covariates: N Other reported meas  IGF  IGRA + IGRA -	sure = NR ssociation RA (QFT- BCG s Yes 22	status No 10 42	Total 32	List of covar Other reporte ts and BCG stat TST + TST -	ates: NR d measure us (if appli  BCG Yes 41 62	status No 17 35	58 97	
List of covariates: N Other reported meas  IGF  IGRA +	sure = NR ssociation RA (QFT- BCG s Yes 22 81	status No 10	Total 32 123	List of covar Other reporte ts and BCG stat	ates: NR d measure us (if appli  BCG Yes 41 62	status No 17	58	

Test performance parameters					
IGRA (QFT-GIT)	TST (>5 mm)				
DOR (for $T^+$ calculated) <sub>QFT</sub> = 1.14, 95% CI (0.49,	$DOR_{TST}$ (for T+ calculated) = 1.36, 95% CI				
2.63)	(0.67, 2.74)				
OR (crude; for $T^+$ reported) = 1.14, 95% CI (NR; p	OR (crude; for T+ reported) = 1.36, 95% CI				
= 0.76)	(NR; p = 0.39)				
OR (regression-based; reported) <sub>QFT</sub> = 1.05, 95% CI	OR (regression-based; reported) $_{TST} = 1.43, 95\%$				
(NR; p = 0.90)	CI (NR; p = 0.34)				
List of covariates: 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 + (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

	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

Name of first reviewer: Peter Auguste

Name of second reviewer: Alexander Tsertsvadze

#### **Study details**

First author surname year of publication: Anibarro 2012<sup>117</sup>

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

Number of patients	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
<b>TST:</b> (≥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   NA		1							
Exposed 2   NA   (specify):	Non-exposed								
Exposed 2 (specify):   Exposed 3 (specify):   NA (specify):   Tests	_	NA							
Exposed 3   NA   (specify):									
Exposed 3 (specify):	_	NA							
Exposed 4 (specify):   Tests	_	NA							
Assay used, methodology, timing for test   Cut-off values/thresholds   Definition of test +   Manufacturer									
Assay used, methodology, timing for test measurement, manufacturer		NA							
Assay used, methodology, timing for test measurement, manufacturer									
timing for test measurement, manufacturer  IGRA	Tests								
Measurement, manufactures   Definition of test+		Ass						Other information	
IGRA									
GRA				,	Definition	of test-	-		
$ \begin{array}{ c c c c } \hline & blood, blood collected \\ immediately before TST, \\ Cellestic Ltd, Carnegie, \\ Australia \\ \hline \hline {TST (one and two-step)} & Mantoux method, 0, lml (2) \\ TU) of PPD injected \\ intradermally to the volar \\ surface of the forearm, TST \\ results read 72h after testing, \\ Statens serum Institute, \\ Copenhagen, Denmark \\ \hline \hline {Association between test results and incidence of active TB (if applicable)} \\ \hline \hline {IGRA} & TST \geq 5mm, a second \\ days later if the first \\ TST-1 was <5 mm \\ \hline \hline {TST-1 was} <5 mm \\ \hline$									
immediately before TST, Cellestic Ltd, Carnegie, Australia     TST (one and two-step)	IGRA				0.35 IU/mL				
Australia   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-1 was <5 mm   ST-1 wa									
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				Carnegie,					
$ \begin{array}{ c c c c } \textbf{step}) & TU) \text{ of PPD injected} \\ & \text{intradermally to the volar} \\ & \text{surface of the forearm, TST} \\ & \text{results read 72h after testing,} \\ & \text{Statens serum Institute,} \\ & \text{Copenhagen, Denmark} \\ \hline                                  $									
$ \begin{array}{ c c c c } \hline & intradermally to the volar surface of the forearm, TST results read 72h after testing, Statens serum Institute, Copenhagen, Denmark \\ \hline & IGRA & TST-5mm (two-step) \\ \hline & IGRA & TST-5mm (two-step) \\ \hline & Incidence of active TB & Incidence of active TB & Yes No \\ \hline & IGRA & INTAING & Incidence of active TB & Yes No \\ \hline & IGRA & INTAING & Incidence of active TB & Yes No \\ \hline & IGRA & N/A & N/A & 11 LTBI & TST + N/A & N/A & 11 LTBI treated \\ \hline & IGRA & O & 32 & 32 & TST - O & 32 & 32 \\ \hline & Indeterminate & 0 & 0 & 0 & Indeterminate & 0 & 0 & 0 \\ \hline & Total & 0 & 32 & 32 & Total & 0 & 32 & 32 \\ \hline & Test performance parameters & TST & Sensitivity = N/A & Specificity = N/A & Specificity = N/A & Specificity = N/A & PPV = N/A \\ \hline & NPV = 100\%, 95\% CI (89.28, 100.00) & NPV = 100\%, 95\% CI (89.28, 100.00) \\ \hline & Cumulative Incidence _{IGRA} = N/A & Cumulative Incidence _{IGRA} = N/A & Cumulative Incidence Ratio _{IGRA} = N/A & Cumulative Incidence Ratio _{IGRA} = N/A & Incidence density rate _{IGRA} = N/R & Incidence density rate _{IGRA} = N/R & Incidence density rate ratio 0 & I$	,			,				•	
surface of the forearm, TST results read 72h after testing, Statens serum Institute, Copenhagen, Denmark  Association between test results and incidence of active TB (if applicable)    IGRA   TST≥5mm (two-step)	step)								
results read 72h after testing, Statens serum Institute, Copenhagen, Denmark  Association between test results and incidence of active TB (if applicable)  IGRA  Incidence of active TB  Yes No  IGRA+  N/A N/A N/A 11 LTBI ITST+ N/A N/A N/A 11 LTBI treated  IGRA-  IGRA			•						
						mm			
Copenhagen, Denmark				-			1	second TST	
Association between test results and incidence of active TB (if applicable)IGRATotal active TBIncidence of active TBTotal active TBYesNoIncidence of active TBTotal active TBYesNoYesNoIGRA +N/AN/A11 LTBI treatedIGRA -03232TST -03232Indeterminate000Indeterminate000Total03232Total03232Test performance parametersIGRATSTSensitivity = N/ASpecificity = N/ASpecificity = N/ASpecificity = N/APPV = N/APPV = N/ANPV = 100%, 95% CI (89.28, 100.00)NPV = 100%, 95% CI (89.28, 100.00)Cumulative Incidence $_{IGRA}$ = N/ACumulative Incidence $_{TST}$ = N/ACumulative Incidence Ratio $_{IGRA}$ = N/ACumulative Incidence Ratio $_{TST}$ = N/AIncidence density rate $_{IGRA}$ = NRIncidence density rate $_{TST}$ = NRIncidence density rate $_{IGRA}$ = NRIncidence density rate $_{TST}$ = NRIncidence density rate $_{IGRA}$ = NRIncidence density rate ratio $_{TST}$ = NRRatio of cumulative incidence = NARatio of incidence density rate ratios = NROther reported measure = NR									
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$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Association between			ia inclaence of				4)	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $				T-4-1	1				
$ \begin{array}{ c c c c c } \hline \textbf{Yes} & \textbf{No} \\ \hline \textbf{IGRA} + & \textbf{N/A} & \textbf{N/A} & \textbf{N/A} & \textbf{11} \ \textbf{LTBI} \\ \hline \textbf{ITATBI} & \textbf{TST} + & \textbf{N/A} & \textbf{N/A} & \textbf{11} \ \textbf{LTBI} \ \textbf{ITATBI} \\ \hline \textbf{IGRA} - & \textbf{0} & \textbf{32} & \textbf{32} & \textbf{TST} - & \textbf{0} & \textbf{32} & \textbf{32} \\ \hline \textbf{Indeterminate} & \textbf{0} & \textbf{0} & \textbf{0} & \textbf{Indeterminate} & \textbf{0} & \textbf{0} & \textbf{0} \\ \hline \textbf{Total} & \textbf{0} & \textbf{32} & \textbf{32} & \textbf{Total} & \textbf{0} & \textbf{32} & \textbf{32} \\ \hline \hline \textbf{Total} & \textbf{0} & \textbf{32} & \textbf{32} & \textbf{Total} & \textbf{0} & \textbf{32} & \textbf{32} \\ \hline \textbf{TST} \\ \hline \textbf{Sensitivity} = \textbf{N/A} & \textbf{Sensitivity} = \textbf{N/A} \\ \hline \textbf{Specificity} = \textbf{N/A} & \textbf{Specificity} = \textbf{N/A} \\ \hline \textbf{Specificity} = \textbf{N/A} & \textbf{Specificity} = \textbf{N/A} \\ \hline \textbf{PPV} = \textbf{N/A} & \textbf{PPV} = \textbf{N/A} \\ \hline \textbf{NPV} = \textbf{100\%}, 95\% \ \textbf{CI} (89.28, 100.00) & \textbf{NPV} = \textbf{100\%}, 95\% \ \textbf{CI} (89.28, 100.00) \\ \hline \textbf{Cumulative Incidence} \ \textbf{I}_{\textbf{IGRA}} = \textbf{N/A} & \textbf{Cumulative Incidence} \ \textbf{TST} = \textbf{N/A} \\ \hline \textbf{Cumulative Incidence Ratio} \ \textbf{I}_{\textbf{GRA}} = \textbf{N/A} & \textbf{Cumulative Incidence} \ \textbf{Ratio} \ \textbf{G}_{\textbf{RA}} = \textbf{N/A} \\ \hline \textbf{Incidence density rate} \ \textbf{I}_{\textbf{GRA}} = \textbf{N/A} & \textbf{Cumulative Incidence} \ \textbf{Ratio} \ \textbf{TST} = \textbf{N/A} \\ \hline \textbf{Incidence density rate} \ \textbf{I}_{\textbf{GRA}} = \textbf{NR} & \textbf{Incidence density rate} \ \textbf{TST} = \textbf{NR} \\ \hline \textbf{Incidence density rate} \ \textbf{Tato} \ \textbf{Incidence} \ \textbf{density rate} \ \textbf{ratio} \ \textbf{TST} = \textbf{NR} \\ \hline \textbf{Incidence density rate ratio} \ \textbf{Incidence} \ \textbf{density rate} \ \textbf{ratio} \ \textbf{TST} = \textbf{NR} \\ \hline \textbf{Ratio of cumulative incidence} = \textbf{NA} \\ \hline \textbf{Ratio of incidence density rate ratios} = \textbf{NR} \\ \hline \textbf{Other reported measure} = \textbf{NR} \\ \hline \textbf{Other reported measure} = \textbf{NR} \\ \hline \end{tabular} $				Total				lotai	
$ \begin{array}{ c c c c c } \hline IGRA + & N/A & N/A & 11 \ LTBI \\ \hline IGRA - & 0 & 32 & 32 & TST - & 0 & 32 & 32 \\ \hline Indeterminate & 0 & 0 & 0 & Indeterminate & 0 & 0 & 0 \\ \hline Total & 0 & 32 & 32 & Total & 0 & 32 & 32 \\ \hline \hline \textbf{Test performance parameters} \\ \hline \hline \textbf{IGRA} & & \textbf{TST} \\ \hline \textbf{Sensitivity} = N/A & Sensitivity = N/A \\ \hline \textbf{Specificity} = N/A & Specificity = N/A \\ \hline \textbf{Specificity} = N/A & Specificity = N/A \\ \hline \textbf{PPV} = N/A & PPV = N/A \\ \hline \textbf{NPV} = 100\%, 95\% \ CI \ (89.28, 100.00) & NPV = 100\%, 95\% \ CI \ (89.28, 100.00) \\ \hline \textbf{Cumulative Incidence}_{IGRA^+} = N/A & Cumulative Incidence \ \textbf{TST} = N/A \\ \hline \textbf{Cumulative Incidence Ratio}_{IGRA} = N/A & Cumulative Incidence Ratio \ \textbf{TST} = N/A \\ \hline \textbf{Incidence density rate}_{IGRA^+} = NR & Incidence density rate \ \textbf{TST} = NR \\ \hline \textbf{Incidence density rate ratio}_{IGRA} = NR & Incidence density rate \ \textbf{TST} = NR \\ \hline \textbf{Incidence density rate ratio}_{IGRA} = NR & Incidence density rate ratio \ \textbf{TST} = NR \\ \hline \textbf{Ratio of cumulative incidence} = NA \\ \hline \textbf{Ratio of incidence density rate ratios} = NR \\ \hline \textbf{Other reported measure} = NR \\ \hline \end{tabular}$			1	-					
$ \begin{array}{ c c c c c } \hline IGRA - & 0 & 32 & 32 & TST - & 0 & 32 & 32 \\ \hline Indeterminate & 0 & 0 & 0 & Indeterminate & 0 & 0 & 0 \\ \hline Total & 0 & 32 & 32 & Total & 0 & 32 & 32 \\ \hline \hline \hline \textbf{Test performance parameters} \\ \hline \hline \textbf{IGRA} & \textbf{TST} \\ \hline \textbf{Sensitivity} = N/A & Sensitivity = N/A \\ \hline \textbf{Specificity} = N/A & Specificity = N/A \\ \hline \textbf{PPV} = N/A & PPV = N/A \\ \hline \textbf{NPV} = 100\%, 95\% \text{ CI (89.28, 100.00)} & NPV = 100\%, 95\% \text{ CI (89.28, 100.00)} \\ \hline \textbf{Cumulative Incidence }_{IGRA^+} = N/A & Cumulative Incidence _{TST^+} = N/A \\ \hline \textbf{Cumulative Incidence Ratio }_{IGRA} = N/A & Cumulative Incidence Ratio _{TST} = N/A \\ \hline \textbf{Incidence density rate }_{IGRA^+} = NR & Incidence density rate _{TST^+} = NR \\ \hline \textbf{Incidence density rate ratio }_{IGRA} = NR & Incidence density rate ratio _{TST} = NR \\ \hline \textbf{Incidence density rate ratio }_{IGRA} = NR & Incidence density rate ratio _{TST} = NR \\ \hline \textbf{Ratio of cumulative incidence} = NA \\ \hline \textbf{Ratio of incidence density rate ratios} = NR \\ \hline \textbf{Other reported measure} = NR \\ \hline \hline \end{tabular}$	ICDA			11 I TDI	TOT			11 I TDI 44-1	
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$ \begin{array}{c c} \textbf{IGRA} & \textbf{TST} \\ \hline \textbf{Sensitivity} = \text{N/A} & \textbf{Sensitivity} = \text{N/A} \\ \hline \textbf{Specificity} = \text{N/A} & \textbf{Specificity} = \text{N/A} \\ \hline \textbf{PPV} = \text{N/A} & \textbf{Specificity} = \text{N/A} \\ \hline \textbf{PPV} = \text{N/A} & \textbf{PPV} = \text{N/A} \\ \hline \textbf{NPV} = 100\%, 95\% \text{ CI (89.28, 100.00)} & \textbf{NPV} = 100\%, 95\% \text{ CI (89.28, 100.00)} \\ \hline \textbf{Cumulative Incidence}_{IGRA^+} = \textbf{N/A} & \textbf{Cumulative Incidence}_{IGRA^+} = \textbf{N/A} \\ \hline \textbf{Cumulative Incidence}_{IGRA^-} = 0/32 = 0 & \textbf{Cumulative Incidence}_{IGRA^-} = 0/32 = 0 \\ \hline \textbf{Cumulative Incidence}_{IGRA^+} = \textbf{N/A} & \textbf{Cumulative Incidence}_{IGRA^-} = \textbf{N/A} \\ \hline \textbf{Incidence}_{IGRA^+} = \textbf{NR} & \textbf{Incidence}_{IGRA^+} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Incidence}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Comparison between tests}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Ratio}_{IGRA^-} = \textbf{NR} & \textbf{Incidence}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Other}_{IGRA^-} = \textbf{NR} \\ \hline \textbf{Other}_{$									
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Comparison between tests (IGRA vs. TST)  Ratio of cumulative incidence = NA  Ratio of incidence density rate ratios = NR  Other reported measure = NR				D					
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DOR (for T <sup>+</sup> calcula OR (crude; for T <sup>+</sup> re OR (regression-base List of covariates: N Other reported meas Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regres Other reported meas Between-test agree This table may be s Total sample	eported) = 1 ed; reported NA sure = NR  C T <sup>+</sup> calculat ; for T <sup>+</sup> reported ession-base sure = NR  ement, con	NA d) = NA  omparison ted) = NA orted) = NA d; reported)  cordance,	A ) = NA	NPV = NA DOR (for T <sup>+</sup> ca OR (crude; for OR (regression List of covariat Other reported en tests (IGRA v	T <sup>+</sup> reported) -based; reportes: NA measure = N	= NA orted) = NA	
Between-test agree This table may be s Total sample	eported) = 1 ed; reported NA sure = NR  C T <sup>+</sup> calculat ; for T <sup>+</sup> reported ession-base sure = NR  ement, con	NA d) = NA  omparison ted) = NA orted) = NA d; reported)  cordance,	A ) = NA	DOR (for T <sup>+</sup> ca OR (crude; for OR (regression List of covariat Other reported en tests (IGRA v	T <sup>+</sup> reported) -based; reportes: NA measure = N	= NA orted) = NA	
OR (crude; for T <sup>+</sup> re OR (regression-base List of covariates: N Other reported meas Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regres Other reported meas Between-test agree This table may be s Total sample	eported) = 1 ed; reported NA sure = NR  C T <sup>+</sup> calculat ; for T <sup>+</sup> reported ession-base sure = NR  ement, con	NA d) = NA  omparison ted) = NA orted) = NA d; reported)  cordance,	A ) = NA	OR (crude; for OR (regression List of covariat Other reported en tests (IGRA v	T <sup>+</sup> reported) -based; reportes: NA measure = N	= NA orted) = NA	
OR (crude; for T <sup>+</sup> re OR (regression-base List of covariates: N Other reported meas Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regres Other reported meas Between-test agree This table may be s Total sample	eported) = 1 ed; reported NA sure = NR  C T <sup>+</sup> calculat ; for T <sup>+</sup> reported ession-base sure = NR  ement, con	NA d) = NA  omparison ted) = NA orted) = NA d; reported)  cordance,	A ) = NA	OR (regression List of covariat Other reported en tests (IGRA v	-based; reportes: NA measure = N	orted) = NA	
OR (regression-base List of covariates: N Other reported meas Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regression) Other reported meas Between-test agree This table may be s Total sample	ed; reported NA sure = NR C T <sup>+</sup> calculat ; for T <sup>+</sup> repossion-base sure = NR ement, con	omparison ted) = NA orted) = NA d; reported) cordance,	A ) = NA	OR (regression List of covariat Other reported en tests (IGRA v	-based; reportes: NA measure = N	orted) = NA	
List of covariates: N Other reported meas Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regree) Other reported meas Between-test agree This table may be s Total sample	NA sure = NR C T calculate for T repersion-bases sure = NR ement, con	omparison ted) = NA orted) = NA d; reported) cordance,	A ) = NA	List of covariat Other reported en tests (IGRA v	tes: NA measure = N	·	
Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regres Other reported meas Between-test agree This table may be s Total sample	T <sup>+</sup> calcular s for T <sup>+</sup> repossion-base sure = NR ement, con	ted) = NA orted) = NA d; reported) cordance,	A ) = NA	en tests (IGRA v		NR	
Ratio of DORs (for Ratio of OR (crude; Ratio of ORs (regres Other reported meas Between-test agree This table may be s Total sample	T <sup>+</sup> calcular s for T <sup>+</sup> repossion-base sure = NR ement, con	ted) = NA orted) = NA d; reported) cordance,	A ) = NA	en tests (IGRA v			
Ratio of OR (crude; Ratio of ORs (regree Other reported meas Between-test agree This table may be s Total sample	T <sup>+</sup> calculates for T <sup>+</sup> reposition-based sure = NR <b>ement, con</b>	ted) = NA orted) = NA d; reported) cordance,	A ) = NA				
Ratio of OR (crude; Ratio of ORs (regree Other reported meas Between-test agree This table may be s Total sample	s for T <sup>+</sup> reposition-base sure = NR ement, con	orted) = NA d; reported) cordance,	) = NA				
Ratio of ORs (regree Other reported meas Between-test agree This table may be s	ession-base sure = NR ement, con	d; reported)	) = NA				
Other reported meas Between-test agree This table may be s Total sample	sure = NR ement, con	cordance,	•				
Between-test agree This table may be s Total sample	ement, con		and dia				
This table may be s Total sample			allu uls	cordance (if app	olicable)		
Total sample		by TST cut				, and/or co	ndition
•							
IGRA +		TST +		TS	ST -		Total
IOIUI		3			15		18
IGRA -		0			34		34
Indeterminate		0			0		0
Total		3			19		52
Description	,						
Sample definition (e	e.g., total, i	f stratified	by BCC	G or condition – s	pecify): tota	ıl (One-step	TST)
$TST + threshold: \geq 3$					• /		,
Parameters							
Kappa = $0.21, 95\%$	CI: 0.04, 0	0.37					
% concordance = 37			CI: 57.7	3, 81.67)			
% discordance = 15							
Stratification (spec							
\ 1		TST +		TS	ST -		Total
IGRA +		9		+	9		18
IGRA -		2		3	32		34
Indeterminate		0			0		0
Total		11			<del>1</del> 1		52
Description							
Sample definition (e	e.g., total. i	f stratified	by BCC	3 or condition – s	pecify): tota	1 (Two-sten	test)
$TST + threshold: \geq 3$					1 377 - 2000	,	- /
Parameters							
Kappa = $0.49, 95\%$	CI: 0.22. 0	0.74)					
1000000000000000000000000000000000000			T: 65 9	7. 87.76)			
% discordance = 11							
Stratification (spec			J1. 12.2.	., 5 1.05)			
Stratification (spec	group	TST +		ТС	ST -		Total

TST

Exposure level

High/Yes Low/No

Total

IGRA

Exposure level

High/Yes Low/No

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
	Canalysians	

### **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.

#### Study details

First author surname year of publication: Chang 2011<sup>119</sup>

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 pati	ients with	valid resul	lts for both I	GRA	A and TST: 1	00		
Levels/groups	of exposui	e to TB in	increasing	orde	r (if applicab	le):		
		I	<b>Definition of</b>	expo	sure group			
Non-exposed		NA						
Exposed 1 (spe	cify):	NA						
Exposed 2 (spe	cify):	NA						
Exposed 3 (spe	cify):	NA						
Exposed 4 (spe	cify):	NA						
Tests	• •							
	Assay u	sed, metho	dology, timi	ing	Cut-off val	ues/thres	holds	Other
		test meas			Definit	ion of tes	t+	information
		manufac	turer					
IGRA (QFT-	The Quar	tiFERON-	TB Gold In-		Positive test	result wa	ıs	
IT)	Tube test	(QFT-GIT	test;		defined as ≥	0.35 IU/r	nL	
	Cellestis	Ltd., Carne	egie, Australi	a)				Both the TST
	performe	d according	g to the					and QFT-IT
		urer instru						were performed
TST			med on the		Induration s			on the same day
			earm using th		measured at	ter 48–72	h, and	as the screening
	Mantoux	method wi	th 2 tubercul	in	we used a 1	0-mm		examination in
	units (TU	) of purifie	ed protein		induration a			all patients
			atens Serum		off value for	r the TST		before initiating
	Institut; C	Copenhagei	n, Denmark).					TNF
		is approxi						antagonists
		t to the int						
	standard o	of 5 TU tul	perculin PPD	-S				
Association be			d incidence	of ac	ctive TB (if a			
	IGR					TS	nce of	
		ence of	Total			Total		
	acti	ve TB				activ	е ТВ	
	Yes	No				Yes	No	
IGRA +	NA	NA	37 LTBI		TST +	0	16	16
			treated					
IGRA -	0	64	64		TST -	0	54	54
Indeterminate	0	6	6	Iı	ndeterminate	0	0	
Total	0	70	70		Total	0	70	70
		T	est perform	ance	parameters			
	IGR	A				TS	ST	
Sensitivity = $N$				_	nsitivity = NA			
Specificity = 70	$0/70 = 100^\circ$	% (95% CI	: 94.8, 100)	Sp	ecificity = 54	/70 = 77.	14 (95%	6 CI: 66.05,
					.41)			
PPV = NA				PF	V = 0/16 = 0			
NPV = 64/64 =	100% (95)	% CI: 94.8	, 100)	NI	PV = 54/54 =	100% (95	5% CI: 9	93.4, 100)
Cumulative Inc	idence IGRA	$A_{+} = NA$		Cı	mulative Inci	idence <sub>TST</sub>	$r_{+} = 0/16$	$\delta = 0$
Cumulative Inc			0		ımulative Inci			
Cumulative Inc					mulative Inc			
Incidence densi					cidence densi			
Incidence densi					cidence densi			
Incidence densi	_		?		cidence densi			NR
Other reported					her reported 1			
Julia reported			ison hetwee		ts (IGRA vs.		31 111	
		Compai	15011 Detwee	11 103	of MICH	101)		

Ratio of cumulati	Ratio of cumulative incidence ratios = NA											
Ratio of incidence	e density rate	e ratios = N	IR									
Other reported me	easure = NR											
Asso	ciation bety	veen test r	esults ar	nd leve	els of TB exp	osure (if a	pplicable)					
	IGRA				TST							
	Exposui	e level	Total			Exposui	e 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	1	NA	NA	NA				
		Test	perform	nance	parameters							
	IGRA					TST						
Sensitivity = NA					itivity = NA							
Specificity = NA					exificity = NA							
PPV = NA				PPV	= NA							
NPV = NA				NPV	r = NA							
DOR (for T <sup>+</sup> calc	ulated) = NA	Λ		DOR	R (for T calc	ulated) = N.	A					
OR (crude; for T <sup>+</sup>	reported) =	NA			crude; for T							
OR (regression-ba	ased; reporte	ed) = NA		OR (	regression-b	ased; report	ed) = NA					
List of covariates	: NA			List	of covariates	: NA						
Other reported me	easure = NA	-		Othe	r reported m	easure = NA	A					
	C	Compariso	n betwee	en test	ts (IGRA vs.	TST)						
Ratio of DORs (fe	or T <sup>+</sup> calcula	ted) = NA										
Ratio of OR (crud	le; for T <sup>+</sup> rep	orted) = N	A									
Ratio of ORs (reg	ression-base	ed; reported	l) = NA									
Other reported me	easure = NR											
	Association	between 1	test resu	lts an	d BCG statu	s (if applic	able)					
	IGRA					TS						
	BCG s	tatus	Tota	al			3 status	Total				
	Yes	No				Yes	No					
IGRA +	NR	NR	NR	1	TST +	NR	NR	NR				
IGRA -	NR	NR	NR	1	TST -	NR	NR	NR				
Indeterminate	NR	NR	NR	2	Indetermina	te NR	NR	NR				
Total	NR	NR	NR	2	Total	NR	NR	NR				
		Test	perform	nance	parameters							
	IGRA					TS						
DOR (for T <sup>+</sup> calc					DOR (for T-							
OR (crude; for T <sup>+</sup>					OR (crude; for T+ reported) = NR							
OR (regression-ba		$(ed)_{IGRA} = N$	R		OR (regress		reported) T	$_{ST} = NR$				
List of covariates				List of covariates: NR								
Other reported me					Other report		=NR					
Between-test agr												
This table may b	e stratified	by TST cu	t-off val	lue, Bo	CG vaccinat	ion status,	and/or co	ndition				
Total sample				T								
		TST +			TST			Total				
IGRA +		19			17			36				
IGRA -		16			48			64				
Indeterminate		1			6			7				
Total		36			71			107				
Description												
Sample definition		if stratified	by BCC	ਤੇ or co	ndition – spe	ecify): 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 =  $23/\overline{58} = 39.66\%$ , 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

### **Study details**

First author surname year of publication: Elzi 2011<sup>114</sup>

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

Number of patient	Total N (tested)	Total N	Total N (test-)	Total N (indeterminate)	Total N (test results
		(test+)			available)
IGRA (T-	64	25	18	21	43
SPOT.TB):					
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-expose	d									
Exposed 1	u	NA								
(specify):		INA								
Exposed 2		NA								
(specify):		1471								
Exposed 3		NA								
(specify):		1471								
Exposed 4		NΔ	NA							
(specify):		INA								
Tests										
1 0303	Ass	av used	methodo	logy, timing for tes	t Cut-off	values/t	hresholds	Other		
	1133			manufacturer		Cut-off values/thresholds Definition of test+				
IGRA (T- SPOT.TB)	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 2 for 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  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 ≥ 10 spots, the test was scored as "indeterminate"							NR		
TST	01 11	112 14001	NI		≥ 5mm fo	or positiv	itv	NR		
	betw	een test r		nd incidence of acti						
		GRA (T-					(≥ 5mm)			
			nce of	Total		Total				
		activ	е ТВ			act	ive TB			
		Yes	No			Yes	No			
IGRA +		25	NA		TST +	22	NA			
IGRA -		18	NA		TST -	22	NA			
Indetermin	ate	21	NA		Indetermi nate	0	NA			
Total		64	NA		Total	44	NA			
			Т	est performance p	arameters					
		IG	RA			TST	(≥ 5mm)			
indetermina	ate ex	cluded			Sensitivity	= 22/44 =	= 50.00% (9:	5% CI:		
Sensitivity = 25/43 = 58.14% (95% CI: 43.33, 71.62) <b>indeterminate included</b>				35.83, 64.17)						
Sensitivity =	= 25/64	4 = 39.06	% (95% (	CI: 28.06, 51.31)						
Specificity =	- NA				Specificity	= NA				
PPV = NA					PPV = NA					
NPV = NA					NPV = NA					
Cumulative	Incide	ence <sub>IGRA+</sub>	= NA			Incidence	$e_{TST+} = NA$			
Cumulative					Cumulative					
Cumulative				VA.			e Ratio <sub>TST</sub> =	= NA		
Incidence de							$te_{TST+} = NR$			
		10101				<i>J</i>	101.			

Incidence dens	sity rate <sub>IGRA-</sub> =	NR		Incid	lence den	sity rate	$_{\rm r} = NR$	
Incidence dens		Incidence density rate <sub>TST</sub> . = NR Incidence density rate ratio <sub>TST</sub> = NA						
						l measure		1
Other reported	l measure <sub>IGRA</sub> =	omparison b	etween				rst = INIX	
Ratio of cumu	lative incidence			tests (101t	21 750 18	- )		
Ratio of incide	ence density rate	e ratios = NR						
Other reported	l measure = NR							
Association b	etween test res	ults and incid	lence of	f active TB	(if applie	cable)		
	TST (≥ 5m	m) and IGR	4 comb	ined (at lea	ast one te	st positive	e)	
		Incidence of	of active	e TB			Total	
	Y			No				
TST or	2	9		NA	Λ		NA	
IGRA +								
TST and	1	5		NA	Α		NA	
IGRA -				37.1			37.1	
Indetermin	(	)		NA	Λ		NA	
ate	4	4		%T A			NT A	
Total	4	4		NA	1		NA	
	Togt man	oumenac na	am at a	g (TCT and	LICDA	ombined)		
Sansitivity - 2		ormance par			I IGKA C	omomea)		
	$\frac{29/44 = 65.91\%}{29}$ PV, NPV, others		4, /8.1.	۷)				
	ssociation bety		lts and	levels of T	Revnes	re (if ann	licable)	
A	IGRA	veen test resu	its anu	levels of 1.	D exposu	TST	ilcable)	
		ure level	Tota		Exposure level			Total
	High/Yes		1014		П	igh/Yes	Low/N	Totai
	Iligii/ i es	LOW/NO	1		11	igii/ i es	0	
IGRA +	NA	NA	NA	TST +		NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA		NA	NA
Indeterminate	NA	NA	NA	Indetermi	ina	NA	NA	NA
Total	NA	NA	NA	te Total		NA	NA	NA
Total	1171			ice parame	eters	1171	1 17 1	1 1/1
	IGRA	1 est per	ioi iiiai	Parame		TST		
Sensitivity = N				Sensitivity	v = NA	131		
Specificity = N				Sensitivity = NA Specificity = NA				
PPV = NA				PPV = NA				
NPV = NA				NPV = NA				
	alculated) = NA	Λ		$DOR (for T^+ calculated) = NA$				
	$T^{+}$ reported) =			OR (crude; for T <sup>+</sup> reported) = NA				
OR (regression	n-based; reporte	ed) = NA				ed; reporte		
List of covaria	ites: NA			List of covariates: NA				
Other reported	l measure = NR			Other reported measure = NR				
		omparison b	etween	tests (IGR	A vs. TS	Γ)		
	s (for T <sup>+</sup> calcula							
	crude; for T <sup>+</sup> rep							
	regression-base		NA					
Other reported	l measure = $NA$							
		between test	results	and BCG	status (if			
		RA					ST	
	BCG s		To	otal			G status	Tot
ICD	Yes	No	*	ID.	TOT.	Yes	No	al
IGRA +	NR	NR	N	VR.	TST +	NR	NR	NR

IGRA -	NR	NR	NR	TST -	NR	NR	NR
Indeterminat	NR			Indeterm	NR	NR	NR
e	1110	1110	1110	inate	1111	1110	1111
Total	NR	NR NR		Total	NR	NR	NR
			erformance p				
	IC	GRA			TST		
DOR (for T <sup>+</sup> ca		DOR (for T	Γ+ calculate	$d)_{TST} = NR$			
OR (crude; for					for T+ repo		
OR (regression			₹		sion-based;		
List of covariat		i i joka		NR	,	· r · · · · · / ·	.51
					ariates: NR		
Other reported	measure = NF	{		Other repo	rted measur	e = NR	
			and discordar	ce (if applicable)			
				CG vaccination st		r conditio	n
Total sample	/		,				
		TST + (≥ 5m	nm)	TST -		То	tal
IGRA +		10		7			7
IGRA -		7		8			5
Indeterminate		5		7			2
Total		22		22		4	
Description							•
	ion (e.g. total	if stratified l	by BCG or cor	ndition – specify):	total		
TST + threshol		11 5010011100	0, 200 01 00	idition specify).			
101 1111101							
Parameters							
Parameters Indeterminate	excluded						
Indeterminate		2 0.46)					
Indeterminate Kappa = 0.12 (	95% CI: -0.22		CI: 39.33, 71.8	3)			
Indeterminate Kappa = 0.12 ( % concordance	95% CI: -0.22 e = 18/32 = 56	.25% (95% C		·			
Indeterminate Kappa = 0.12 (	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43.	.25% (95% C		·			
Indeterminate Kappa = 0.12 ( % concordance % discordance	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included	.25% (95% C 75% (95% C		·			
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15	.25% (95% C) 75% (95% C) 4, - 0.42)	I: 28.17, 60.67	7)			
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 (	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57	.25% (95% C 75% (95% C , - 0.42) .00% (95% C	I: 28.17, 60.67 CI: 42.22, 70.3	2)			
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e <b>included</b> 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43.	.25% (95% C 75% (95% C , - 0.42) .00% (95% C 20% (95% C	I: 28.17, 60.67 CI: 42.22, 70.3	2)			
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Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e <b>included</b> 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43.	.25% (95% C 75% (95% C , - 0.42) .00% (95% C 20% (95% C	I: 28.17, 60.67 CI: 42.22, 70.3	2)	-	To N	
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e <b>included</b> 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43.	.25% (95% C 75% (95% C , - 0.42) .00% (95% C 20% (95% C p 1) TST +	I: 28.17, 60.67 CI: 42.22, 70.3	2) 3) TST -			R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification (  IGRA + IGRA -	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e <b>included</b> 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43.	.25% (95% C 75% (95% C , - 0.42) .00% (95% C 20% (95% C p 1) TST + NR	I: 28.17, 60.67 CI: 42.22, 70.3	2) 2) 3) TST - NR	-	N	R R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification ( IGRA +	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e <b>included</b> 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43.	.25% (95% C 75% (95% C 7, - 0.42) .00% (95% C 20% (95% C p 1) TST + NR	I: 28.17, 60.67 CI: 42.22, 70.3	2) 2) 3) TST - NR NR	-	N N N	R R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification ( IGRA + IGRA - Indeterminate Total	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e <b>included</b> 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43.	.25% (95% C 75% (95% C 75% (95% C .00% (95% C 20% (95% C p 1) TST + NR NR	I: 28.17, 60.67 CI: 42.22, 70.3	2) 2) 3) TST - NR NR NR		N N N	R R R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification ( IGRA + IGRA - Indeterminate Total Description	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43. (specify group	.25% (95% C 75% (95% C 75% (95% C ., - 0.42) .00% (95% C 20% (95% C p 1) TST + NR NR NR	I: 28.17, 60.67 EI: 42.22, 70.3 I: 29.68, 57.78	2) 3) TST - NR NR NR NR		N N N	R R R
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Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification ( IGRA + IGRA - Indeterminate Total Description	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43. (specify group	.25% (95% C 75% (95% C 75% (95% C ., - 0.42) .00% (95% C 20% (95% C p 1) TST + NR NR NR	I: 28.17, 60.67 EI: 42.22, 70.3 I: 29.68, 57.78	2) 3) TST - NR NR NR NR		N N N	R R R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification ( IGRA + IGRA - Indeterminate Total Description Sample definiti TST + threshol Parameters	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43. (specify group	.25% (95% C 75% (95% C 75% (95% C ., - 0.42) .00% (95% C 20% (95% C p 1) TST + NR NR NR	I: 28.17, 60.67 EI: 42.22, 70.3 I: 29.68, 57.78	2) 3) TST - NR NR NR NR		N N N	R R R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description Sample definiti TST + threshol Parameters Kappa = NR	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43. (specify group	.25% (95% C 75% (95% C 75% (95% C ., - 0.42) .00% (95% C 20% (95% C p 1) TST + NR NR NR	I: 28.17, 60.67  EI: 42.22, 70.3  I: 29.68, 57.78	2) 3) TST - NR NR NR NR		N N N	R R R
Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description Sample definiti TST + threshol Parameters Kappa = NR % concordance	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43. (specify group ion (e.g., total, d: NR	.25% (95% C 75% (95% C 75% (95% C ., - 0.42) .00% (95% C 20% (95% C p 1) TST + NR NR NR	I: 28.17, 60.67  EI: 42.22, 70.3  I: 29.68, 57.78	2) 3) TST - NR NR NR NR		N N N	R R R
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Indeterminate Kappa = 0.12 ( % concordance % discordance Indeterminate Kappa = 0.14 ( % concordance % discordance Stratification (  IGRA + IGRA - Indeterminate Total Description Sample definiti TST + threshol Parameters Kappa = NR % concordance % discordance % discordance Stratification ( IGRA +	95% CI: -0.22 e = 18/32 = 56 = 14/32 = 43. e included 95% CI: -0.15 e = 25/44 = 57 = 19/44 = 43. (specify group ion (e.g., total, d: NR	.25% (95% C) .75%	I: 28.17, 60.67 EI: 42.22, 70.3 I: 29.68, 57.78 by BCG or co	TST - NR NR NR NR NR TST- NR	NR	N N N N N N N N N N N N N N N N N N N	R R R R
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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

## Study details

First author surname year of publication: Kim 2011<sup>116</sup>

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 pa	tients	tested	l					
, , , , , , , , , , , , , , , , , , ,		T	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			272	0	272	0		272
(Mantoux):				(≥10mm)	(<10mm)			
Test 3 (specify			Nr	NR	NR	NR		NR
					A and TST: 24			
Levels/groups	of ex	posure			er (if applicable	e):		
Non aynogad		NA	De	efinition of exp	osure group			
Non-exposed Exposed 1		NA NA						
(specify):	1	NA.						
Exposed 2	N	NA						
(specify):								
Exposed 3	1	NA						
(specify):								
Exposed 4	1	NA						
(specify): Tests								
1 6818	Ass	av iise	d. methodo	ology, timing	Cut-off values	s/thresholds	T	Other
	1155	-	est measur		Definition		inf	ormation
			manufactu					
TST (Mantoux)	was an E prod SPO Abir All t prior boos ELIS	collect LISPC lucing DT.TB, ngdon, blood s r to TS sting et SPOT	ted from ea OT assay for T-cell responsive Oxford Im UK) samples we of to avoid ffect of TST assay	re collected a possible Γ on the	The positive cr		of TE was of attend surge nephi infect diseas specia to the ELIS to avo	ons, rologists and tious ses alists blind e results of POT assays,
(Mantoux)	Mantoux technique, injecting a 2- TU (tuberculin unit) dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm				greater size of it 48–72 h after in and in accordan Korea Centers Diseases Contr Prevention guid	induration njection, nce with for ol and		
Association be	etweer			incidence of a	ctive TB (if app	olicable)		
		IGR		- ·		<b>TST</b> (≥10m	im)	<b>T</b> . 1
		acti	lence of ve TB	Total		Incidence of active TB		Total
ICD A		Yes	No 67	71	TOT	Yes No		NI A
IGRA +		4	67	71	TST +	NA NA	1	NA

IGRA -	0	171		171	TST -	4	268	3 2	272	
Indeterminate	0	30		30	Indeterminate	0	0		0	
Total	4	268		272	Total	4	NA	1	NA	
		Te	st p	erforma	nce parameters					
	IGRA				П	ΓST				
Sensitivity = $4/4$ =	100.00%	6 (95% CI:	51.0	01,	Sensitivity = 1	NA				
100.00)										
Indeterminate ex	cluded				Specificity = 1	NA				
Specificity = 171/238 = 71.84% (95% CI: 65.82,										
77.18)		`								
Indeterminate in	cluded									
Specificity = 201/2	268 = 75.	00% (95%	CI:	69.49,						
79.81)										
PPV = 4/71 = 5.63	3% (95%	CI: 2.21, 1	3.61	1)	PPV = NA					
Indeterminate ex	cluded				NPV = 268/27	72 = 98.5	3% (	(95% CI: 9	6.28,	
NPV = 171/171 =	100.00%	(95% CI:	97.8	0,	99.43)					
100.00)										
Indeterminate in										
NPV = 201/201 =	100.00%	(95% CI:	98.1	2,						
100.00)										
Cumulative Incide	nce <sub>IGRA+</sub>	= 4/71 = 5	5.63%	% (95%	Cumulative Ir	cidence -	TST+ =	= NA		
CI: 2.21, 13.61)										
Cumulative Incide	nce <sub>IGRA</sub> -	= 0/171 =	X		Cumulative Ir	Cumulative Incidence $_{TST}$ = 4/272 = 1.47%				
					(95% CI: 0.43	3, 3.85)				
Cumulative Incide	nce Ratio	$_{IGRA} = X$			Cumulative Incidence Ratio $_{TST} = NA$					
Incidence density	rate <sub>IGRA+</sub>	=4/122.10	0 p-y	yrs =	Incidence density rate $_{TST+} = NA$					
0.0328  p-yrs = 3.2		rs (95% C	I: 0.	.89, 8.39)						
Indeterminate ex					Incidence density rate $_{TST}$ = 4/483.25 p-yrs =					
Incidence density	rate <sub>IGRA-</sub>	= 0/307.83	3 р-у	$r_{\rm rs} =$	0.0083  p-yrs = 0.83/100  p-yrs (95%  CI:  0.23,					
0.00/100 p-yrs					2.12)					
Indeterminate in			_							
Incidence density	rate <sub>IGRA-</sub>	= 0/361.16	р-у	$r_{\rm rs} =$						
0.00/100 p-yrs		27.4			x 11 1	•		27.4		
Incidence density					Incidence den					
Other reported me		_ =			Other reported	d measur	e <sub>TST</sub>	= NR		
Indeterminate ex			2.0	1/100						
Incidence density		rence <sub>IGRA</sub>	- 3.3	5/100 p-						
yrs (95% CI: 1.3, 5	/									
Indeterminate in		onaa -	_ 2 2	2/100						
Incidence density		CHCC IGRA	- 3.3	5/100 p-						
yrs (95% CI: 1.4, :	J.1 <i>j</i>	Compari	con	hotwoon	tests (IGRA vs.	TCT				
Ratio of cumulativ	o incida-				iesis (IGRA VS.	151)				
Ratio of cumulative Ratio of incidence										
			- INP	1						
Other reported me			t was	sulta and	lovals of TD	2051140	fon-	aliaabla)		
ASSOC	IGRA		t res	suits and	levels of TB exp		i app ST	oncable)		
	1			Total				a laval	Total	
		osure level		10181		_		e level	10181	
ICDA	High/Y			NID	TOT	High/Y	es	Low/No	) ID	
IGRA +	NR	NR		NR	TST +	NR NB		NR NB	NR	
IGRA -	NR	NR		NR	TST -	NR	-	NR NR	NR	
Indeterminate	NR	NR		NR	Indeterminate	NR		NR	NR	

NR

NR

Total

NR

Total

NR

NR

NR

		Test p	erforman	ce parameters				
IGRA				TST				
Sensitivity = NR				Sensitivity = NR				
Specificity = NR				Specificity = NR				
PPV = NR				PPV = NR				
NPV = NR				NPV = NR				
DOR (for T <sup>+</sup> calcul	ated) = NR			DOR (for T <sup>+</sup> calcu	lated) = N	R		
OR (crude; for T <sup>+</sup> re		NR		OR (crude; for T <sup>+</sup> 1				
OR (regression-bas		1) = NR		OR (regression-ba	sed; report	ted) = NR		
List of covariates: 1				List of covariates:				
Other reported mea				Other reported me		R		
			between	tests (IGRA vs. TS	ST)			
Ratio of DORs (for								
Ratio of OR (crude								
Ratio of ORs (regre		d; reported)	=NR					
Other reported mea								
A		between te	est results	and BCG status (		ble)		
	IGRA				TST			
	BCG s		Total			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 p	erforman	ce parameters				
DOD (2 mt 1 1	IGRA	3.7D		DOD (2. T) 1	TST	2.75		
DOR (for T <sup>+</sup> calcul				DOR (for T+ calculated) <sub>TST</sub> = NR OR (crude; for T+ reported) = NR				
OR (crude; for T <sup>+</sup> re	* '		`				NID	
OR (regression-bas List of covariates: 1		$_{\rm I)_{\rm IGRA}} = NF$	(	OR (regression-l		ortea) <sub>TST</sub> =	NK	
Other reported mea				Other reported n		NID		
Between-test agree		cordance (	and disco			IVIX		
This table may be						nd/or cond	lition	
Total sample	stratifica k	y 181 cut	OII value	, Ded vaccination	status, a	na/or conc	111111	
1 otal sample		TST +		TST -		Т	otal	
IGRA +		NR		NR NR				
IGRA -		NR		NR			NR	
Indeterminate		NR		NR NR				
Total		NR		NR NR				
Description								
Sample definition (	e.g., total, i	f stratified	by BCG o	r condition – specif	y): NR			
TST + threshold: N	R							
Parameters								
Kappa = NR								
% concordance = $N$								
% discordance = N								
Stratification (specify group 1)								
TST +				TST - Total				
IGRA +		NR		NR NR				
IGRA -		NR		NR			NR	
Indeterminate		NR		NR			NR NB	
Total		NR		NR			NR	
Description								

TST + threshold: NR

### **Parameters**

Kappa = NR

% concordance = NR

% discordance = NR

**Stratification (specify group 2)** 

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

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

#### **Study details**

First author surname year of publication: Lee 2009<sup>118</sup>

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
<b>TST</b> (≥ 10mm):	32	20	12	0	32
Total N of patients with v	alid results fo	or both IC	GRA and TST:	_	

Levels/groups of e	exposure	to TB in i	ncreasing ord	ler (if	applicable	e):		
		De	efinition of ex	posure	group			
Non-exposed	NR							
Exposed 1 (specify	·):	NR						
Exposed 2 (specify	·):	NR						
Exposed 3 (specify		NR						
Exposed 4 (specify	·):	NR						
Tests					1			
			thodology, tin	ning		Cut-off		Other
			easurement,			thresho		information
TOD L (OTT	***** 1		facturer			ion of to		
IGRA (QFT-			drawn prior to		A QFT-C	•		NA
GIT)		_	ST. The QFT	-G	software,			
			cording to the		download			
	instruc	tive manufa	acturer s		Cellestis			
	mstruc	HOHS			was used control a	-	•	
					to calcula			
					results	iic iiic ic	,sı	
TSPOT	Whole	blood was	drawn prior to	)	NR			NA
		g out the T		-	1,11			- 12 2
		T.TB was						
		ing to the r						
		acturer's in						
TST (two step; ≥	A two-	step TST u	sing the Mant	oux	≥ 10mm	induratio	on for	NA
10mm)	method	d with two	tuberculin unit	ts of	ESRD pa	tients ar	nd	
	tubercu	ılin RT-23	(PPD RT 23 S	SSI;	BCG-unv	ed		
			stitut, Copenha		individua			
			rformed accor					
			col. The reaction		BCG-vac			
			3–72 h. Second		healthy in	ndividua	.ls	
			formed 1-3 we					
		r initial ne						
			incidence of	active TB (if applicable)				0 \
10	GRA (Q		T-4-1		181	(two-st		
		ence of	Total				nce of	Total
		ve TB					e TB	+
IGRA +	Yes 1	No 11	12	т	ST +	Yes 1	No 19	20
IGRA + IGRA -	0	18	18	_	ST -	1	11	12
Indeterminate	1	10	2	_	erminate	1	11	12
muciciminate	1	1	(excluded)	indet	Cillillate			
Total	2	30	32	7	Γotal	2	30	32
10.01			st performance				20	32
IGRA (e)	xclude ir			para	alliotol 5	T	ST	
IGRA (exclude indeterminate) Sensitivity = 1/1 = 100.00%, 95% CI: 20.65,			Sensi	tivitv = 1/			% CI: 9.45,	
100.00				90.55	•		- / 5 ( ) 5	,
Specificity = 18/30	= 60.00	%, 95% CI	: 44.00.		/	$\frac{1}{30} = 36$	5.67%.	95% CI: 21.87,
77.31		, ,	7	54.49	•			,
PPV = 1/12 = 8.33	%, 95%	CI: 1.49, 3	5.39			.00%, 9:	5% CI:	0.89, 23.61
NPV = 18/18 = 100								CI:74.12, 100.00
Cumulative Incider				1				20 = 5.00%, 95%
CI (1.49, 35.39)			•		.89, 23.61			,
Cumulative Incider	ice IGRA-	= 0/18 = 5	.56% (95%	Cumulative Incidence $_{TST}$ = 0/11 = 9.09% (95%)				
	10101		( , •			1		( , 0

CI: 5.40, 27.29) CI: 0.23, 41.3)								
	<del></del>	Cumulative Incidence Ratio $_{TST} = 0.55\%$ (95%)						
Cumulative Incidence Ratio $_{IGRA}$ = 1.55% (95% CI: 0.02, 124.2)					CI: 0.01, 47.06)			
Incidence density r	ate ICBA+ = 1	3.40 per 10	00 PYS	Incidence den		$_{\text{T}_{\perp}} = \text{NR}$		
Incidence density r			0110	Incidence den	_			
Incidence density r				Incidence den			NR	
Other reported mea				Other reported				
Cinci reported med			n hetween	tests (IGRA vs.		151 111	<u> </u>	
Ratio of cumulativ					101)			
Ratio of incidence				,				
Other reported mea								
Association between		ılts and in	cidence of	active TB (if a	oplicable)			
	GRA (TSP				ST (two-st	ep; ≥10r	nm)	
	Incidend		Total		Incider			Total
	active				active			
	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	performan	ce parameters	'			
	IGRA				TS	T		
Sensitivity = 0/2 =	0.00% (95%	6 CI: 0.00,	, 65.76)	Sensitivity = 1 90.55)	1/2 = 50.00	)% (95%	CI: 9	0.45,
Specificity = 15/30	0 = 50.00%	(95% CI: 3	3.15,	Specificity = 11/30 = 36.67%, 95% CI: 21.87,				
66.85)	0/ (050/ CI	0.00.20.2	10)	54.49				
PPV = 0/15 = 0.00				PPV = 1/20 = 5.00%, 95% CI: 0.89, 23.61				
NPV = 15/17 = 88				NPV = 11/11 = 100.00%, 95% CI:74.12, 100.00				
Cumulative Incider CI: 0.17, 31.9)	$nce_{IGRA+} = 0$	0/15 = 6.6	/% (95%	Cumulative Incidence $_{TST+} = 1/20 = 5.00\%, 95\%$ CI (0.89, 23.61)				
Cumulative Incide	$nce_{ICRA} = 2$	$\frac{1}{2}/17 = 11.7$	6% (95%	Cumulative Incidence $_{TST}$ = 0/11 = 9.09% (95%)				
CI: 2.03, 35.59)	HOU IGRA- 2	2/1/ 11./	070 (2270	CI: 0.23, 41.3)				
Cumulative Incide	nce Ratio is	$_{\rm RA} = 0.57\%$	6 (95% CI:	Cumulative Ir		atio TST =	= 0.55	% (95%
0.01, 12.1)	100 110010 10	KA OIO / /	0 (>0 /0 01.	CI: 0.01, 47.0		131	0.00	70 (2070
Incidence density r	ate $_{IGRA+} = 1$	NR		Incidence den		$T_{T+} = NR$		
Incidence density r				Incidence den				
Incidence density r				Incidence den			NR	
Other reported mea	asure <sub>IGRA</sub> =	NR		Other reported				
			between	tests (IGRA vs.	TST)			
Ratio of cumulativ								
Ratio of incidence	density rate	ratios = N	R					
Other reported mea	asure = NR							
Assoc	iation betw	een test re	esults and	levels of TB exp	osure (if a	applicab	ole)	
	IGRA				TS'	Γ		
	Exposure level Total				Expos	ure level		Total
	High/Yes Low/No			High/Yes	_			
IGRA +			TST +	NA	NA		NA	
IGRA -				TST -	NA	NA	_	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	Α	NA
Total	NA	NA	NA	Total	NA	NA	\ <u> </u>	NA
		Test	performan	ce 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	OR (regression-based; reported) = NA
List of covariates: 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:**

## **Study details**

First author surname year of publication: Lee 2014<sup>149</sup>

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)

N	um	ber	of	pat	tient	ts 1	tesi	ted	
---	----	-----	----	-----	-------	------	------	-----	--

Number of patients tested					
	Total N	Total	Total N	Total N	Total N
	(tested)	N	(test-)	(indeterminate)	(test results
					available)
		(test+)			

IGRA (QFT-GIT)   391    45    315    31    360			1			- I			T = co
IGRA (QFT-GIT):   169   26   133   10   159   159   159   169   150   169   169   150   169   169   150   169   169   169   157   169				45	315	3	1		360
2				26	122	1/	1		150
TST (> Samp.):  2 <sup>nd</sup> year enrollment cohort:  TST (> 169   19   150   169				26	133	10	J		159
2nd year enrollment cohort:		ient conort		19	150	0			160
169	\ /	ient cohort		17	150	0			107
Total N of patients with valid results for both IGRA and TST: 159		icht conort		12	157	0			169
Total N of patients with valid results for both IGRA and TST: 159		ent cohort		12	157				109
Non-exposed   NA				for both IG	RA an	d TST: 15	59		1
Non-exposed 1 (specify): NA    Exposed 2 (specify): NA     Exposed 3 (specify): NA     Exposed 4 (specify): NA     Exposed 4 (specify): NA     Exposed 4 (specify): NA     Exposed 4 (specify): NA     Exposed 5 (specify): NA     Exposed 6 (specify): NA     Exposed 6 (specify): NA     Exposed 6 (specify): NA     Exposed 6 (specify): NA     Exposed 7 (specify): NA     Exposed 8 (specify): NA     Exposed 9 (specify): Na									
Exposed 2 (specify): NA  Exposed 3 (specify): NA  Exposed 4 (specify): NA  Tests    A Saxy used, methodology, timing for test measurement, manufacturer collected from each patient for the QFT-TB assay (Cellestis, Carnegic, 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  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   TGRA [QFT-GIT]   TST (≥5mm)   TGRA [QFT-GIT]   Total active TB   Yes   No   Total   Total active TB   Yes   No   Total   Tota		•							
Exposed 3 (specify): NA  Exposed 4 (specify): NA  Tests    Assay used, methodology, timing for test measurement, manufacturer'   Values/thresholds Definition of test   NR    IGRA (QFT- GIT)	Non-exposed		NA						
Exposed 3 (specify): NA   Natronal	Exposed 1 (spec	ify):	NA						
Tests	Exposed 2 (spec	ify):	NA						
Assay used, methodology, timing for test measurement, manufacturer   Values/thresholds Definition of test+			NA						
Assay used, methodology, timing for test measurement, manufacturer   Value/thresholds Definition of test   NR	Exposed 4 (spec	ify):	NA						
TGRA (QFT-GT)	Tests								
IGRA (QFT-GIT)									er information
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  TST≥5mm ≥10mm   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    Association between test results and incidence of active TB (if applicable)   TST (≥5mm)      Incidence of active TB   Yes   No   Total		test mea	asuremen	t, manufactu	ırer				
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  TST≥5mm ≥10mm Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  Association between test results and incidence of active TB (if applicable)  TGRA [QFT-GIT] Total active TB Yes No							on of test	<u>t</u> +	
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  TST≥5mm	, -					NR			
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	GIT)								
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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  TST≥5mm ≥10mm		/	and nlagg	d dimantly int					
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  Test sams ≥10mm  The TST was performed by the dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  Association between test results and incidence of active TB (if applicable)  Total  active TB Yes No  Title SAMT  Total					.0				
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  TST≥5mm				-					
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  TST≥5mm ≥10mm					nic				
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  TST≥5mm ≥10mm									
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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  TST≥5mm									
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  TST≥5mm ≥10mm									
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  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  TST ≥5mm   Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  TST was a 5mm or greater in duration 48-72h after injection  Association between test results and incidence of active TB (if applicable)  TST (≥5mm)  Total   Incidence of active TB   Yes   No   Yes   No   Total		-		` /					
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  The TST was performed by the ≥10mm  Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  Association between test results and incidence of active TB  Incidence of active TB Yes No  The positive criterion for the TST was a 5mm or greater in duration 48-72h after injection  TST (≥5mm)  Total active TB Yes No					or 16-				
(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  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  Association between test results and incidence of active TB (if applicable)  IGRA [QFT-GIT]  Total  Incidence of active TB  Yes No  Yes No		18 h, then	processed	and tested for	or				
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  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  Association between test results and incidence of active TB (if applicable)  TST (≥5mm)  Association between test results and incidence of active TB (if applicable)  Incidence of active TB Yes No Yes No		quantitativ	e interfero	n-g levels					
instructions. All blood samples were collected prior to the TST to avoid a possible boosting effect of the TST on the QFT-TB assay  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  Association between test results and incidence of active TB (if applicable)  TST was a 5mm or greater in duration 48-72h after injection  Association between test results and incidence of active TB (if applicable)  Incidence of active TB Yes No Yes No		(IU/mL). 7	The assay	was interpret	ed				
Collected prior to the TST to avoid a possible boosting effect of the TST on the QFT-TB assay		_							
TST≥5mm ≥10mm  Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  TST (≥5mm)  Association between test results and incidence of active TB (if applicable)  IGRA [QFT-GIT]  Incidence of active TB Yes No  The results of TSTs were measured by the TST was a 5mm or greater in duration 48-72h after injection  TST (≥5mm)  TST (≥5mm)  Incidence of active TB Yes No									
TST≥5mm  ≥10mm  Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  TST was a 5mm or greater in duration 48-72h after injection  Association between test results and incidence of active TB (if applicable)  IGRA [QFT-GIT]  Incidence of active TB Active TB Yes No  The results of TSTs were measured by the trained nurse  TST was a 5mm or greater in duration 48-72h after injection  TST (≥5mm)  Incidence of Total active TB Yes No		_							
TST≥5mm ≥10mm  Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  Association between test results and incidence of active TB (if applicable)  IGRA [QFT-GIT]  Incidence of active TB Active TB Yes No  The results of TSTs were measured by the TST was a 5mm or greater in duration 48-72h after injection  48-72h after injection  TST (≥5mm)  Incidence of Total active TB Yes No		_	_	ect of the TS	ol on				
Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm   Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm   48-72h after injection      Association between test results and incidence of active TB (if applicable)	TCT> 5			d lav- 41		The	41	Trl.	magyalta of TOT
dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm   48-72h after injection      Association between test results and incidence of active TB (if applicable)			-	•	TH				
RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm $48-72h$ after injection  Association between test results and incidence of active TB (if applicable)  IGRA [QFT-GIT] TST ( $\geq 5mm$ )  Incidence of active TB  active TB  Yes No Yes No								•	
								Tallica Hulst	
				nally	_		••		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			, muuuulii						
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Association bety			incidence of	f active			)	
Incidence of active TB Yes No Incidence of active TB Yes No Yes No						T			
active TB         active TB           Yes         No             Yes         No				Total			1		Total
ICDA +		Yes	No				Yes	No	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	IGRA +	3	23	26	Т	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	
						ce parameters		
	RA (QFT					≥5mm		
Sensitivity = $3/5 = 6$				Sensitivity = $0/3$				
Specificity =131/15 89.84)	54= 85.06	5% (95% C	CI: 78.59,	Specificity = 14 92.46)	5/164=8	88.41% (	95% CI: 82.61,	
PPV= 3/26=11.54%	6 (95% C	I: 4.00, 28	3.98)	PPV= 0/19=0.0	% (95%	CI: 0.0,	16.82)	
NPV= 131/133=98				NPV=145/150=				
Cumulative Incider	ice <sub>IGRA+</sub> =	= 3/26=11	.54% (95%	Cumulative Inc		_		
CI: 3.17, 29.80)			`	CI: 0.0, 23.22)			`	
Cumulative Incider	ice <sub>IGRA-</sub> =	2/133=1.	50% (95%	Cumulative Inc	idence <sub>T</sub>	$s_{\rm ST-} = 5/1$	50=3.33% (95%	
CI: 0.07, 5.66)				CI: 1.22, 7.77)				
Cumulative Incider	nce Ratio	$_{\rm IGRA} = 7.6$	7 (95% CI:	Cumulative Inc	idence F	Ratio <sub>TST</sub>	= 0.79 (95%	
1.34, 43.67)				CI: 0.04, 13.89)	ı		•	
Incidence density r	ate <sub>IGRA+</sub> =	= 5.43 per	100 p-y	Incidence densi	ty rate T	$_{ST+}=0$ pe	er 100 p-y (95%	
(95% CI: 1.12, 15.8	38)			CI: 0.00, 8.41)				
Incidence density r	ate <sub>IGRA-</sub> =	0.80 per	100 р-у	Incidence densi	ty rate T	ST = 1.79	9 per 100 p-y	
(95% CI: 0.10, 2.88	3)			(95% CI: 0.58,	4.18)			
Incidence density r	ate ratio <sub>I</sub>	$_{\rm GRA}=6.78$	per 100 p-y	Incidence densi	ty rate ra	atio <sub>TST</sub> =	0.00 per 100 p-y	
(95% CI: NR)				(95% CI: NR)				
Other reported mea	sure <sub>IGRA</sub>	= incidenc	e density	Other reported i				
rate difference: 4.7	per 100 p	erson-yea	rs (95% CI:		-1.79 pe	er 100 pe	rson-years (95%	
1.10, 8.30)				CI: NR)				
				tests (IGRA vs. 7	rst)			
Ratio of cumulative				[: 1.71, 55.15)				
Ratio of incidence			NA					
Other reported mea								
Association betwe			incidence of	active TB (if app				
IG	RA [QFT			TST (≥10mm)				
		ence of	Total			ence of	Total	
		re TB				e TB		
	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	
	ICD		st performan	ce parameters	700	COR		
G ::: :: 2/5	IGRA		2.07.00.24)	TST				
Sensitivity = $3/5 = 6$				Sensitivity = 0/5=0.0% (95% CI: 0.0, 43.45)				
Specificity =131/15	54= 85.06	% (95% C	71: 78.59,	Specificity = 152/164= 92.68% (95% CI: 87.65,				
89.84)	/ (050/ 0	1. 4.00. 20	00)	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=152/157=96.82% (95% CI: 92.76, 98.63)					
NPV= 131/133=98.5% (95% CI: 94.68, 99.59)					_			
Cumulative Incidence <sub>IGRA+</sub> = 3/26=11.54% (95% CI: 3.17, 29.80)			Cumulative Incidence <sub>TST+</sub> = 0/12=4.16% (95% CI: 0.0, 33.00)					
Cumulative Incidence $_{IGRA-} = 2/133=1.50\%$ (95%				idence <sub>T</sub>	$_{ST-} = 5/1$	57=3.18% (95%		
CI: 0.07, 5.66)			CI: 1.16, 7.43)					
Cumulative Incider 1.34, 43.67)	ice Ratio	$_{\rm IGRA} = 7.6$	7 (95% CI:	Cumulative Inci	idence F	Ratio <sub>TST</sub>	= 1.31 (95% CI:	
Incidence density re (95% CI: 1.12, 15.8		= 5.43 per	100 p-y	Incidence densir	ty rate T	ST+=0.0	% (95% CI: 0.0,	
(70/0 01, 1,12, 13.0		111701						

Incidence density ra	ate $_{IGRA_{-}}=0$ .	80 per 100	p-v	Incidence den	sity rate TST.	= NR		
(95% CI: 0.10, 2.88)								
Incidence density ra				Incidence den				
Other reported mea				Other reported			•	
rate difference: 4.7	per 100 pers	son-years (9	95% CI:	rate difference	e: -3.18 per 1	00 person-y	rears (95%	
1.10, 8.30)				CI: NR)				
	Co	mparison l	between	tests (IGRA vs.	TST)			
Ratio of cumulative	e incidence r	atios = 5.85	5 (95% (	CI: 1.05, 32.70)				
Ratio of incidence	density rate	ratios= NA						
Other reported mea	sure=NR							
		en test res	ults and	levels of TB ex	posure (if ar	oplicable)		
	IGRA				TST	,		
	Exposu	re level	Total		Exposur	e level	Total	
	High/Yes	Low/No	10001		High/Yes	Low/No	10001	
IGRA +	NA	NA	NA	TST +	NA	NA	NA	
IGRA -	NA	NA	NA	TST -	NA	NA	NA	
indeterminate	NA NA	NA NA	NA	indeterminate	NA	NA	NA	
Total	NA NA	NA NA	NA	Total			NA NA	
Total	NA				NA	NA	NA	
	ICDA	1 est pe	eriorma	nce parameters	TECTE			
G 1.1.1. 37.1	IGRA			G	TST			
Sensitivity = NA				Sensitivity = N				
Specificity = NA				Specificity = N	<u>A</u>			
PPV= NA				PPV= NA				
NPV= NA				NPV= NA				
DOR (for T <sup>+</sup> calcul	ated)= NA			DOR (for T <sup>+</sup> calculated)= NA				
OR (crude; for T <sup>+</sup> re	eported)= N.	A		OR (crude; for T <sup>+</sup> reported)= NA				
OR (regression-bas	ed; reported	)= NA		OR (regression-based; reported)= NA				
List of covariates:	NA			List of covariates: NA				
Other reported mea	sure = NA			Other reported measure = NA				
	Co	mparison	between	tests (IGRA vs.	TST)			
Ratio of DORs (for					,			
Ratio of OR (crude								
Ratio of ORs (regre			= NA					
Other reported mea		, reported)	- 112					
*		netween tes	t result	s and BCG statu	ıs (if annlice	able)		
	IGRA	octween tes	ot i couit	s and DCG state	TS'			
	BCG s	tatue	Total			status	Total	
	Yes	No	1 Otal		Yes	No	Total	
ICD A	-	-	NT A	TOT		+	NT A	
IGRA +	NA NA	NA NA	NA NA	TST +	NA NA	NA NA	NA NA	
IGRA -	NA NA	NA NA	NA	TST -	NA to NA	NA NA	NA	
indeterminate	NA	NA	NA	indetermina		NA	NA	
Total	NA	NA	NA	Total	NA	NA	NA	
		Test pe	erforma	nce parameters				
	IGRA				TS'			
DOR (for T <sup>+</sup> calcul				$DOR (for T+ calculated)_{TST} = NA$				
$OR (crude; for T^{+}reported) = NA$				OR (crude; for T+ reported) = NA				
OR (regression-bas	ed; reported	$)_{IGRA} = NA$		OR (regress	ion-based; re	eported) TST =	= NA	
List of covariates:	NA			List of cova	riates: NA			
Other reported mea	sure = NA			Other report	ed measure	$= \overline{NA}$		
Between-test agreement, concordance, and discordance (if applicable)								
This table may be				`		and/or cond	lition	
Total sample		,		,	,			
		TST +≥5m	m	TS	ST -		Total	
		_ ~		1.	-		- 0 0001	

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)** 

\ <b>1</b>	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

#### **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<sup>115</sup>

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

Exclusion criteria. NK

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

Number of patients teste	u				
	Total N (tested)	Total N	Total N (test-)	Total N (indeterminate)	Total N (test results available)
		(test+)			
IGRA (specify): QFT-	244	40	170	34	210

TST: ≥5mm	CYM		I				1	
Test 3 (specify):   NA	GIT		211	20	20.5			244
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		• `						
NA	<u> </u>	v /					-	NA
Non-exposed								
Non-exposed   NA	Levels/group	s of exposul				ie):		
Exposed 2 (specify): NA	Non exposed			Jennition of	exposure group			
Exposed 2 (specify): NA		ecify).						
Exposed 3 (specify): NA								
Assay used, methodology, timing for test measurement, manufacturer   Cellestis Limited, carnegie, Australia   Ceromination of test+   Cerominate during the Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm   Sassociation between test results and incidence of active TB   Total active TB   Yes   No   IGRA +								
Assay used, methodology, timing for test measurement, manufacturer   CGRA (QFT-GIT)   Carnegic, Australia   We used the criteria for 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								
timing for test measurement, manufacturer  IGRA (QFT-GIT)  QFT-GIT (Cellestis Limited, carnegie, Australia  Definition of test+  We used the criteria for positive, negative, and indeterminate outcomes recommended by the manufacturer  TST (≥  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  Association between test results and incidence of active TB (if applicable)  IGRA (QFT-GIT)  Incidence of active TB  Yes No  IGRA + 1 39 40 TST + 0 39 39 39  IGRA - 1 169 170 TST - 2 203 205  Indeterminate 0 34 34 Indeterminate 0 0 0 0  Total 2 208 210 Total 2 242 244  Test performance parameters  IGRA  Test performance parameters  IGRA  Sensitivity = 1/2 = 50.00%, 95% CI (9.45, 90.55)  Specificity = 169/208 = 81.25%, 95% CI (75.4, 87.98)  NPV = 169/170 = 99.41%, 95% CI (96.74, 99.9)  NPV = 203/205 = 99.02% (95% CI: 0.0, 8.96)  NPV = 203/205 = 99.02% (95% CI: 0.0, 8.96)  NPV = 203/205 = 99.02% (95% CI: 0.06, 13.5)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.44, 12.88)  Cumulative Incidence IGRA+ = 1/40 = 2.50% (0.4	Tests	, , , , , , , , , , , , , , , , , , ,	1					
Total		Assay ı	ısed, meth	odology,	Cut-off		Oth	er information
GRA (QFT-GIT)   Cellestis Limited, carnegie, Australia   We used the criteria for positive, negative, and indeterminate outcomes recommended by the manufacturer   ST on theQFT-GIT test. The lab technicians did not know the results of TST					values/thresh	olds		
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		n	nanufactui	rer	Definition of	test+		
Indeterminate outcomes recommended by the manufacturer	IGRA			Limited,	We used the crite	eria for		
Tecommended by the manufacturer	(QFT-GIT)	carnegie, A	Australia					
manufacturer   boosting effect of the TST on theQFT-GIT test. The lab technicians did not know the results of TST								
TST on theQFT-GIT test. The lab technicians did not know the results of TST  TST(≥ 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  Association between test results and incidence of active TB (if applicable)    IGRA (QFT-GIT)						the the		
TST (≥   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   Statistical Total   Statistical Total Total Total Total   Statistical Total Total Total Total Total   Statistical Total					manufacturer			•
Carrell   Car								_
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  Association between test results and incidence of active TB (if applicable)  IGRA (QFT-GIT)  Separation of TST  TST≥5mm  Incidence of active TB  Yes No  IGRA + 1 39 40 TST + 0 39 39  IGRA - 1 169 170 TST - 2 203 205  Indeterminate 0 34 34 Indeterminate 0 0 0  Total 2 208 210 Total 2 242 244  Test performance parameters  IGRA  Sensitivity = 1/2 = 50.00%, 95% CI (9.45, 90.55)  Specificity = 169/208 = 81.25%, 95% CI (75.4, 85.97)  PPV = 1/40 = 2.50%, 95% CI (0.44, 12.88)  NR  of TST  NR  NR  NR  NR  NR  NR  NR  NR  NR  N								
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  Association between test results and incidence of active TB (if applicable)    IGRA (QFT-GIT)								
the Mantoux technique, injecting a 2-TU dose of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) intradermally into the forearm  Association between test results and incidence of active TB (if applicable)    IGRA (QFT-GIT)   TST≥5mm	TST (≥	The TST v	vas carried	out using	≥ 5mm induratio	n 48-		
derivative RT23 (Statens Serum   Institut, Copenhagen, Denmark)   intradermally into the forearm	5mm)			_	72h after injectio	n		
Institut, Copenhagen, Denmark   intradermally into the forearm		a 2-TU dos	se of purifi	ed protein	_			
Intradermally into the forearm			,					
Association between test results and incidence of active TB (if applicable)   IGRA (QFT-GIT)								
$ \begin{array}{ c c c c } \hline \textbf{IGRA (QFT-GIT)} & \textbf{TST} \geq 5mm \\ \hline & & & & & & & & & & & & & & & & & &$							<u> </u>	
Incidence of active TB   Yes   No   Yes   Yes   No   Yes   Yes   No   Yes   No   Yes	Association b			d incidence (	of active TB (if ap			
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $				Total				Total
				Total				Total
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			1	-				
IGRA -         1         169         170         TST -         2         203         205           Indeterminate         0         34         34         Indeterminate         0         0         0           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, 87.98)         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, Cumulative Incidence TST+ = 0/39 = 2.56% (95% CI: 0.06, 13.5)	IGRA +		+	40	TST +			39
$ \begin{array}{ c c c c c c } \hline \text{Indeterminate} & 0 & 34 & 34 & \text{Indeterminate} & 0 & 0 & 0 \\ \hline \hline \text{Total} & 2 & 208 & 210 & \text{Total} & 2 & 242 & 244 \\ \hline \hline \hline \hline \textbf{Test performance parameters} \\ \hline \hline \textbf{Sensitivity} = 1/2 = 50.00\%, 95\% \text{ CI } (9.45, 90.55) & \text{Sensitivity} = 0/2 = 0.00\%, 95\% \text{ CI } (0.00, 65.76) \\ \hline \textbf{Specificity} = 169/208 = 81.25\%, 95\% \text{ CI } (75.4, & \text{Specificity} = 203/242 = 83.88\% (95\% \text{ CI: } 78.73, 85.97) & 87.98) \\ \hline \textbf{PPV} = 1/40 = 2.50\%, 95\% \text{ CI } (0.44, 12.88) & \textbf{PPV} = 0/39 = 0.00\% (95\% \text{ CI: } 0.0, 8.96) \\ \hline \textbf{NPV} = 169/170 = 99.41\%, 95\% \text{ CI } (96.74, 99.9) & \textbf{NPV} = 203/205 = 99.02\% (95\% \text{ CI: } 96.51, 99.73) \\ \hline \textbf{Cumulative Incidence}_{\text{IGRA+}} = 1/40 = 2.50\% (0.44, & \text{Cumulative Incidence}_{\text{TST+}} = 0/39 = 2.56\% (95\% \text{ CI: } 0.06, 13.5) \\ \hline \textbf{CI: } 0.06, 13.5) & \textbf{CI: } 0.06, 13.5 \\ \hline \end{array}$				ł	_			
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		te 0	+	ļ				_
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, 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, Cumulative Incidence $_{TST^+} = 0/39 = 2.56\%$ (95% CI: 0.06, 13.5)				(excluded)				
IGRATSTSensitivity = $1/2 = 50.00\%$ , 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, Cumulative Incidence $_{TST+} = 0/39 = 2.56\%$ (95% CI: 0.06, 13.5)	Total	2	208		Total	2	242	244
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, 87.98) 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 $160$ CI: 0.06, 13.5) CI: 0.06, 13.5)				est performa	ance parameters			
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 $160$ CI: 0.06, 13.5)  CI: 0.06, 13.5)								
85.97) 87.98) 87.98) $ PPV = 1/40 = 2.50\%, 95\% \text{ CI } (0.44, 12.88) \\ NPV = 169/170 = 99.41\%, 95\% \text{ CI } (96.74, 99.9) \\ NPV = 203/205 = 99.02\% (95\% \text{ CI: } 96.51, 99.73) \\ Cumulative Incidence _{IGRA^{+}} = 1/40 = 2.50\% (0.44, 2.50\% $							_	
$ \begin{array}{lll} \text{NPV} = 169/170 = 99.41\%, 95\% \text{ CI } (96.74, 99.9) & \text{NPV} = 203/205 = 99.02\%  (95\% \text{ CI: } 96.51, \\ 99.73) \\ \text{Cumulative Incidence}_{\text{IGRA+}} = 1/40 = 2.50\%  (0.44, \\ 12.88) & \text{CI: } 0.06, 13.5) \\ \end{array} $	Specificity = 1 85.97)	169/208 = 8	1.25%, 95%	% CI (75.4,	1 .	)3/242 =	83.88%	(95% CI: 78.73,
Cumulative Incidence $_{IGRA^{+}} = 1/40 = 2.50\%$ (0.44, Cumulative Incidence $_{TST^{+}} = 0/39 = 2.56\%$ (95% CI: 0.06, 13.5)					PPV = 0/39 = 0	.00% (9	5% CI: (	0.0, 8.96)
Cumulative Incidence $_{IGRA+} = 1/40 = 2.50\%$ (0.44, Cumulative Incidence $_{TST+} = 0/39 = 2.56\%$ (95% 12.88)	$NPV = 169/\overline{17}$	$70 = 99.41 $ $\frac{1}{6}$	o, 95% CI (	96.74, 99.9)		5 = 99.02	2% (95%	6 CI: 96.51,
12.88) CI: 0.06, 13.5)	Cumulative In	icidence IGRA	A+ = 1/40 =	2.50% (0.44,		idence <sub>T</sub>	$ST^{+} = 0/3$	9 = 2.56% (95%)
Cumulativa Incidence $= 1/170 = 0.589$ / Cumulativa Incidence $= 2/205 = 0.079$ / (059/	12.88)				CI: 0.06, 13.5)			,
Cumulative Incidence $_{IGRA-} = 1/170 = 0.58\%$ , CI (0.00, 3.59) Cumulative Incidence $_{TST-} = 2/205 = 0.97\%$ (95% CI: 0.03, 3.71)			$A_{-} = \overline{1/170} =$	= 0.58%,		idence T	$\overline{\text{ST-}} = 2/2$	$05 = 0.\overline{97\%} (95\%)$
Cumulative Incidence Ratio <sub>IGRA</sub> = 4.25, 95% CI Cumulative Incidence Ratio <sub>TST</sub> = 2.63% (95%			io <sub>IGRA</sub> = 4	.25, 95% CI	<u> </u>	idence F	Ratio <sub>TST</sub>	= 2.63% (95%

(0.27, 66, 40)				CI. 0.04 51 4	1		
(0.27, 66.49)	-4-	2 00 10	00	CI: 0.04, 51.4		_ 0 1	00
Incidence density raperson-years, 95%			)0	Incidence den years, 95% C			oo person-
Incidence density ra				Incidence den			
Incidence density ra				Incidence den			)
incluence density is			n hotwoo	en tests (IGRA v		IO TST - INI	<u> </u>
Ratio of cumulative					s. 151)		
Ratio of incidence of					9)		
Other reported mea						0/ <sub>2</sub> CI <sub>2</sub> 2 3	0 8 001· NS
				d levels of TB e			
ASSUCI	IGRA	veen test r	esuits an	lu leveis of 1 b e.	TST		5)
		a 1arva1	Total				Total
-	Exposur	Low/No	Total		Exposus	Low/No	Total
	High/Yes		NT A	TST +	High/Yes		NT A
IGRA +	NA	NA	NA		NA	NA	NA
IGRA -	NA	NA	NA	TST -	NA	NA	NA
Indeterminate	NA	NA	NA	Indeterminate	NA	NA	NA
Total	NA	NA Tr. 4	NA	Total	NA	NA	NA
		Test	perform	ance parameter			
~	IGRA			~	TST	ľ	
Sensitivity = NA				Sensitivity = N			
Specificity = NA				Specificity = N	A		
PPV = NA				PPV = NA			
NPV = NA				NPV = NA			
DOR (for T <sup>+</sup> calculated)				DOR (for T <sup>+</sup> ca			
OR (crude; for T <sup>+</sup> re				OR (crude; for			
OR (regression-base		d) = NA		OR (regression		orted) = NA	A
List of covariates: N				List of covariat			
Other reported mea				Other reported		VΑ	
			n betwee	n tests (IGRA v	s. TST)		
Ratio of DORs (for							
Ratio of OR (crude:							
Ratio of ORs (regre	ession-base	d; reported	I) = NA				
Other reported mea	sure = NA						
Between-test agree				`			
This table may be		•	t-off val	ue, BCG vaccina	ation status	, and/or c	<u>ondition</u>
Total sample (≥5 n	nm indura					1	
		TST +			ST -		Total
IGRA +		9		ł	<u> </u>		40
IGRA -		24			46		170
Indeterminate		6			28	34	4 (excluded)
Total		33		1	77		210
Description							
Sample definition (excluded)	e.g., total,	if stratified	by BCG	or condition – s <sub>l</sub>	pecify): total	l (indetern	ninate
$TST + threshold: \geq$	5mm indu	ration					
Parameters	ZIIIII IIIGU						
Kappa = $0.09, 95\%$	CI (-0.04	- 0.22) ind	etermina	te excluded			

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)

Struction (1 actents	o with Deed scars,		
	$TST + \ge 5mm$	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)

Stratification (Latient	s without DCG scars of i	istory of DCO 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)

Study details

First author surname year of publication: Sherkat 2014<sup>155</sup>

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
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Tests			
	Assay used, methodology, timing	Cut-off	Other
	for test measurement,	values/thresholds	information
	manufacturer	Definition of test+	
IGRA	T-SPOT .TB assay (Oxford		
[TSPOT]	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 $2.5 \times 10 \text{ PBMCs/1 ml.}$		
	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)					≥10 mm, test was				
(Pasteur Institute, Tehran, Iran)					considered positive as				
injection into the volar aspect of the				he					
1	forearm intradermally by trained				guidelines (Ministry of				
	ersonnel. A	-			Health and Medical				
	efined by th				Education)				
,	ot the eryth		•	D					
	8-72 h after								
Association betw			icidence (	of ac	tive TB (if ap				
10	GRA [TSPO		Tr. 4 1		TST≥10mm				
	Inciden		Total		Incidence of active TB			I otai	
	active								
ICDA	Yes	No			TOTAL I	Yes	No		
IGRA +	1	5	6		TST +	1	7	8	
IGRA -	0	38	38		TST -	0	36	36	
indeterminate	NR	NR	NR	ın	determinate	NR	NR	NR	
Total	1	43	44		Total	1	43	44	
	ICDA	Test	pertorma	ance	parameters	/IDC/ID			
C '4' '4 1/1	IGRA	CI 20 65	100)	C	1/1	TST	/ CI 20 65	100)	
Sensitivity =1/1=					$\frac{\text{sitivity} = 1/1 = 1}{\text{sitivity}} = \frac{1}{1 + 1}$	,			
Specificity = 38/4 94.93)	3=88.3 /%	95% CI: 7:	5.52,	91.8	ecificity = 36/4 88)	3=83.72%	(95% C1: /	0.03,	
PPV= 1/6=16.67%	6 (95% CI:	3.00, 56.35	)	PPV	V= 1/8=12.5%	(95% CI: 2	2.24, 47.09)		
NPV= 38/38=100	% (95% CI	90.82, 100	))	NP	V= 36/36=100	% (95% C	[: 90.36, 10	0)	
Cumulative Incidence <sub>IGRA+</sub> = 1/6=16.67% (95%					Cumulative Incidence $_{TST+} = 1/8 = 12.5\%$ (95% CI:				
CI: 3.00, 56.35)		0/20 1 21	(0.50/		0.11, 47.09)				
Cumulative Incide	ence <sub>IGRA-</sub> =	0/38=1.31	(95%		Cumulative Incidence <sub>TST-</sub> = 0/36=1.39 (95% CI:				
CI: 0.00, 12.86)	naa Datia	-12.67	(050/		0.00, 13.49)				
Cumulative Incidence Ratio $_{IGRA}$ =12.67 (95% CI: 0.47, 337.8) Cumulative Incidence Ratio $_{TST}$ =9.00 (95% CI: 0.47, 337.8)						73% CI.			
Incidence density	rate =	NIP			idence density	rate = `	NIP.		
Incidence density					idence density				
Incidence density					idence density				
Other reported inc	Other reported measure <sub>IGRA</sub> =NR Other reported measure <sub>TST</sub> =NR  Comparison between tests (IGRA vs. TST)								
Ratio of cumulativ						101)			
Ratio of incidence					15, 10.20)				
Other reported me									
			esults and	d lev	els of TB exp	osure (if a	pplicable)		
IGRA (specify)				TST (specify)					
		ure level	Total				ire level	Total	
	High/Yes	•	_		Ī	High/Yes	Low/No	1	
IGRA +	NA	NA	NA	TS	ST +	NA	NA	NA	
IGRA -	NA	NA	NA	_	ST -	NA	NA	NA	
indeterminate	NA	NA	NA	in	determinate	NA	NA	NA	
Total	NA	NA	NA	To	otal	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 <sup>+</sup> calculated)= NA				D	DOR (for T <sup>+</sup> calculated)= NA				

OR (regression-based; reported) = NA List of covariates: NA Other reported measure = NA  Comparison between tests (IGRA vs. TST)  Ratio of DORs (for T <sup>+</sup> calculated) = NA Ratio of OR (regression-based; reported) = NA Ratio of ORs (regression-based; reported) = NA Other reported measure = NA  Ratio of ORs (regression-based; reported) = NA Other reported measure = NA  Association between test results and BCG status (if applicable)  IGRA (TSPOT)    BCG status   Total     Yes   No     IGRA +   2   4   6   TST +   2   6   8     IGRA -   10   28   38   TST -   10   26   36     Iderarminate   NR   NR   NR   indeterminate   NR   NR   NR     Total   12   32   44   Total   12   32   44     Total   12   32   44   Total   12   32   32   44     Total   12   32   44   Total   12   32   44     Total   12   32   44   Total   12   32   44     Total   15   30   50   60     OR (regression-based; reported) = NR (p=0.658)   OR (regression-based; reported) = NR (p=1.00)     OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)     OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)     OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)     OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)     OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)     OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regression-based; reported)   NR (p=1.00)   OR (regressi	OR (crude: for T <sup>+</sup> r	OR (crude; for T <sup>+</sup> reported)= NA  OR (crude; for T <sup>+</sup> reported)= NA								
List of covariates: NA					OR (regression-ba	sed: renor	ted) = NA			
Other reported measure = NA			<i>a)</i> 1171				1171			
Comparison between tests (IGRA vs. TST)										
Ratio of DORs (for T' calculated) = NA										
Ratio of OR (crude; for T' reported) = NA	Ratio of DORs (for			i between	iteses (IORA vs. 12	,1,				
Ratio of ORs (regression-based; reported) = NA				Λ						
Other reported measure = NA	`									
Association between test results and BCG status (if applicable)   IGRA (TSPOT)			u, reported	1) – NA						
TST (≥10mm)   BCG status			hotavoon t	ost mosult	s and DCC status (i	f annliae	hla)			
BCG status										
IGRA +	10			Total				Total		
IGRA +				Total				1 Otal		
IGRA -   10   28   38   TST -   10   26   36   indeterminate   NR   NR   NR   NR   indeterminate   NR   NR   NR   NR   Total   12   32   44   Total	ICD A			6	TCT			0		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $										
Total   12   32   44   Total   12   32   44     Test performance parameters										
Test performance parameters           IGRA         TST           DOR (for T <sup>+</sup> calculated) <sub>IGRA</sub> = 1.40 (95% CI: 0.22, 8.85)         DOR (for T <sup>+</sup> calculated) <sub>IGRA</sub> = 0.86 (95% CI: 0.14, 5.03)           OR (crude; for T <sup>+</sup> reported) = NR (p=0.658)         OR (crude; for T+ reported) = NR (p=1.00)           OR (regression-based; reported) $I_{IGRA}$ = NR         OR (regression-based; reported) $I_{ISR}$ = NR           List of covariates: NA         Other reported measure = NR           Determine the may be stratified by TST cut-off value, BCG vaccination status, and/or condition         Total           Total sample         TST + ≥10mm         TST -         Total           IGRA [TSPOT] + 4         2         6         6           IGRA [TSPOT] - 4         34         38         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         Total           IGRA - NA								<del></del>		
TST	1 ota1	12				12	32	44		
$ \begin{array}{ c c c c } \hline DOR (for T^+ calculated)_{IGRA} = 1.40 (95\% CI: 0.22, \\ 8.85) & 5.03 \\ \hline DOR (crude; for T^+ reported) = NR (p=0.658) & OR (crude; for T+ reported) = NR (p=1.00) \\ \hline OR (crude; for T^+ reported) = NR (p=0.658) & OR (crude; for T+ reported) = NR (p=1.00) \\ \hline OR (regression-based; reported)  _{IGRA} = NR & OR (regression-based; reported)  _{TST} = NR \\ \hline List of covariates: NA & List of covariates: NA \\ \hline Other reported measure = NR & Other reported measure = NR \\ \hline \textbf{Between-test agreement, concordance, and discordance (if applicable)} \\ \hline \textbf{This table may be stratified by TST cut-off value, BCG vaccination status, and/or condition} \\ \hline \textbf{Total sample} & TST + \ge 10 \text{mm} & TST - & Total \\ \hline \textbf{IGRA} [TSPOT] + & 4 & 2 & 6 \\ \hline \textbf{IGRA} [TSPOT] - & 4 & 34 & 38 \\ \hline \textbf{Indeterminate} & NR & NR & NR \\ \hline \textbf{Total} & 8 & 36 & 44 \\ \hline \textbf{Description} \\ \hline \textbf{Sample definition (e.g., total, if stratified by BCG or condition - specify): Total} \\ \hline \textbf{TST + threshold: } \ge 10 \text{mm} \\ \hline \textbf{Parameters} \\ \hline \textbf{Kappa} = 0.49 (95\% CI: 0.20, 0.78) \\ \% \ \text{concordance} = 38/44 = 86.36\% (95\% CI: 73.29, 93.6) \\ \% \ \text{discordance} = 6/44 = 13.64\% (95\% CI: 6.40, 26.71) \\ \hline \textbf{Stratification (specify group 1):} \\ \hline \textbf{TST} + & TST - & Total \\ \hline \textbf{IGRA} + & NA & NA & NA & NA \\ \hline \textbf{IGRA} - & NA$		ICDA	Test	periorma	nce parameters	TOT				
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	DOD (C T+ 1 1		1 40 (050/	CI 0.22	DOD (C. T.) 1		0.06.605	)/ CI 0 14		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		latea) <sub>IGRA</sub> =	1.40 (95%	CI: 0.22,		natea) <sub>TST</sub>	= 0.86 (95)	% C1: 0.14,		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		4 1) 3	ID ( 0.64	•0)	/	4 1)	NID (	1.00)		
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										
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			$a)_{IGRA} = N$	K						
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							D			
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 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 NA  IGRA - NA NA NA  IGRA - NA NA NA  Total NA NA NA  TST + threshold: NA  Parameters  Kappa = NA % concordance = NA	1		1	1 1.			K			
Total sampleIGRA [TSPOT] +426IGRA [TSPOT] -43438indeterminateNRNRNRTotal83644DescriptionSample definition (e.g., total, if stratified by BCG or condition – specify): TotalTST + threshold: ≥10mmTST + threshold: ≥10mmParametersKappa = 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 -TotalIGRA +NANANAIGRA -NANANAIGRA -NANANAIGRA -NANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotal <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>1/</td> <td>3:4:</td>							1/	3:4:		
TST +≥10mm   TST -   Total     IGRA [TSPOT] +   4   2   6     IGRA [TSPOT] -   4   34   38     indeterminate   NR   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   NA     IGRA -   NA   NA   NA   NA     IGRA -   NA   NA   NA   NA     Total   NA   NA   NA   NA     TST + threshold: NA   NA   NA     TST + threshold: NA     Parameters     Kappa = NA     % concordance = NA	•	stratinea	<u> </u>	t-oii vaiu	e, BCG vaccination	status, a	na/or con	aition		
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 NA         IGRA - NA NA NA NA         indeterminate       NA NA NA NA         Total       NA NA NA NA NA         Total       NA N	1 otai sampie		TCT 1>10		TOT		<u> </u>	T-4-1		
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         NA       NA       NA       NA         Total       NA       NA <td>ICD A [TCDOT]  </td> <td></td> <td></td> <td>IIIIII</td> <td></td> <td></td> <td></td> <td></td>	ICD A [TCDOT]			IIIIII						
indeterminate NR 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 NA  IGRA - NA NA NA NA  IGRA - NA NA NA NA  Total NA NA NA NA  Parameters  Kappa = NA % concordance = NA					<u>-</u>					
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 NA NA         IGRA - NA NA NA NA         Indeterminate NA NA NA NA NA         Total NA NA NA NA         Pascription         Sample definition (e.g., total, if stratified by BCG or condition – specify): NA         TST + threshold: NA         Parameters         Kappa = NA         % concordance = NA										
DescriptionSample definition (e.g., total, if stratified by BCG or condition – specify): TotalTST + threshold: ≥10mmParametersKappa = 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):IGRA +NANANAIGRA -NANANAindeterminateNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANATotalNANANAParametersNANANA% concordance = NA										
Sample definition (e.g., total, if stratified by BCG or condition – specify): Total			8		36			44		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		( , , 1	· C · · · · C · 1	1 DCC	1' '.	· \ T + 1				
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         Parameters       NA       NA       NA         Kappa = NA       % concordance = NA			ii stratified	by BCG (	or condition – specii	y): Totai				
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		10mm								
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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										
TST + TST - Total     IGRA + NA NA NA NA     IGRA - NA NA NA NA     indeterminate NA NA NA NA NA     Total NA				0.40, 26.	(1)					
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	Stratification (spe	cny group	,	1	TOTAL			T-4-1		
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	ICD A									
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										
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										
Description Sample definition (e.g., total, if stratified by BCG or condition – specify): NA TST + threshold: NA Parameters Kappa = NA % concordance = NA										
Sample definition (e.g., total, if stratified by BCG or condition – specify): NA TST + threshold: NA Parameters  Kappa = NA % concordance = NA							NA			
TST + threshold: NA  Parameters  Kappa = NA % concordance = NA	*									
Parameters  Kappa = NA % concordance = NA										
Kappa = NA % concordance = NA										
% concordance = NA										
		T.1								
% 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<sup>145</sup>

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

1 (difficer of patients	testea				
	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         definite/suspected           (specify):         Exposed 2           (specify):         NA           (specify):         Exposed 3           (specify):         NA           (specify):         Tests	
Exposed 1         definite/suspected           (specify):         Exposed 2           (specify):         NA           Exposed 3         NA           (specify):         Exposed 4           (specify):         NA           Tests         Tests	
(specify):         Exposed 2         NA           (specify):         Exposed 3         NA           (specify):         Exposed 4         NA           (specify):         Tests	
(specify):         Exposed 3         NA           (specify):         Exposed 4         NA           (specify):         Tests	
Exposed 3	
(specify):  Exposed 4 NA (specify):  Tests	
Exposed 4 NA (specify): Tests	
(specify): Tests	
Tests	
Assay used, methodology, timing Cut-off values/thresholds	
00/ 0	Other
,	formation
manufacturer	27.4
IGRA In keeping with the manufacturer's Inconclusive assays were defined	NA
(TSPOT) instructions, 4 ml of blood were by an inability to complete the test	
drawn for the T-SPOT.TB assay, due to inadequate peripheral blood	
except for children <2 years when 2-3 mononuclear cell (PBMC) yield after PBMC separation, high	
ml were drawn depending on ease of venepuncture 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	
IGRA A 3 ml aliquot of blood was drawn Indeterminate assays were defined	NA
(QFT-GIT) from all study children and the assay as a high IFNg response to the	
was performed according to the negative control or a low IFNg	
manufacturers' protocols response to mitogen stimulation in	
the absence of a positive antigen	
response	
<b>TST≥10mm</b> TST was performed with purified NR	NA
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	
Association between test results and incidence of active TB (if applicable)	
IGRA TST	
	Total
Incidence of active TB Incidence of active TB	
Incidence of Total Incidence of	
Incidence of active TB Incidence of active TB	NA
Incidence of active TB  Yes No Yes No  Incidence of active TB  Yes No	NA NA
Incidence of active TB	
Incidence of active TB	NA
Incidence of active TB	NA NA
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	NA NA
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	NA NA

L Champelatirea Incidence				Cumulative Incidence <sub>TST</sub> . = NA				
Cumulative Incidence		- NT A						
Cumulative Incidence		= INA		Cumulative Incidence Ratio <sub>TST</sub> = NA				
Incidence density rate				Incidence density rate <sub>TST+</sub> = NA				
Incidence density rate		>T.A		Incidence density rate <sub>TST</sub> = NA				
Incidence density rate				Incidence density rate ratio $_{TST} = NA$				
Other reported measu				Other reported		= NA		
5 1 0 1 1			etween	tests (IGRA vs. 7	TST)			
Ratio of cumulative i								
Ratio of incidence de		los = NA						
Other reported measu					(4.0	** ** *		
			its and	levels of TB exposure (if applicable)  TST (≥10 mm)				
IGI	RA (TSPOT		T . 1			- T		
	Exposu		Total		Exposur		Total	
	High/Yes	Low/No			High/Yes			
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 per	forman	ce parameters				
	IGRA				TST			
Sensitivity = NR				Sensitivity = NI				
Specificity = NR				Specificity = N	R			
PPV = NR				PPV = NR NPV = NR				
	NPV = NR							
DOR (for T <sup>+</sup> calculate				DOR (for T <sup>+</sup> ca				
OR (crude; for T <sup>+</sup> rep	orted) = 2.50	) (95% CI: 0	).90,	OR (crude; for $T^+$ reported) = 4.00 (95% CI: 1.70,				
6.50)				9.50)				
OR (regression-based		· NR		OR (regression-based; reported) = NR				
List of covariates: NA				List of covariates: NA				
Other reported measu				Other reported measure = NR				
			etween	tests (IGRA vs. 7	ΓST)			
Ratio of DORs (for T								
Ratio of OR (crude; f				0.32, 1.22)				
Ratio of ORs (regress		eported) = N	ΙA					
Other reported measu								
Association between test results and					4.2			
Associ	ation betwe			levels of TB expo		,		
Associ	ation betwee A (QFT-GI	Γ)	lts and	levels of TB expo	TST (≥10	mm)	m . 1	
Associ	ation betwee A (QFT-GI Exposu	Γ) re level		levels of TB exp	TST (≥10 Exposur	mm) e level	Total	
Associ IGR	ation betwee A (QFT-GI) Exposu High/Yes	re level Low/No	Its and		TST (≥10 Exposur High/Yes	mm) re level Low/No		
Associ IGR IGRA +	ation betwee A (QFT-GI Exposu High/Yes NR	re level Low/No NR	Total	TST +	TST (≥10 Exposur High/Yes NR	mm) re level Low/No NR	NR	
Associ IGR IGRA + IGRA -	ation betwee A (QFT-GI' Exposu High/Yes NR NR	re level Low/No NR NR	Total  NR NR	TST + TST -	TST (≥10 Exposur High/Yes NR NR	mm) re level Low/No NR NR	NR NR	
IGRA + IGRA - Indeterminate	Ation betwee A (QFT-GI' Exposu High/Yes NR NR NR	re level Low/No NR NR NR	Total  NR NR 70	TST + TST - Indeterminate	TST (≥10 Exposur High/Yes NR NR NR	mm) re level Low/No NR NR NR	NR NR 0	
Associ IGR IGRA + IGRA -	ation betwee A (QFT-GI' Exposu High/Yes NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate Total	TST (≥10 Exposur High/Yes NR NR	mm) re level Low/No NR NR	NR NR	
IGRA + IGRA - Indeterminate	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate	TST (≥10  Exposur High/Yes NR NR NR NR	mm) re level Low/No NR NR NR NR	NR NR 0	
IGRA + IGRA - Indeterminate Total	Ation betwee A (QFT-GI' Exposu High/Yes NR NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters	TST (≥10  Exposur High/Yes NR NR NR NR NR	mm) re level Low/No NR NR NR NR	NR NR 0	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters Sensitivity = NI	TST (≥10  Exposur High/Yes NR NR NR NR NR	mm) re level Low/No NR NR NR NR	NR NR 0	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR Specificity = NR	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters  Sensitivity = NI Specificity = NI	TST (≥10  Exposur High/Yes NR NR NR NR NR	mm) re level Low/No NR NR NR NR	NR NR 0	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR Specificity = NR PPV = NR	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters Sensitivity = NI Specificity = NI PPV = NR	TST (≥10  Exposur High/Yes NR NR NR NR NR	mm) re level Low/No NR NR NR NR	NR NR 0	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR Specificity = NR PPV = NR NPV = NR	Ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR	re level Low/No NR NR NR NR NR	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters  Sensitivity = NI Specificity = NI PPV = NR NPV = NR	TST (≥10  Exposur High/Yes NR NR NR NR R R R	mm) re level Low/No NR NR NR NR	NR NR 0	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR Specificity = NR PPV = NR NPV = NR DOR (for T <sup>+</sup> calculate	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR IGRA	re level Low/No NR NR NR NR Test per	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters  Sensitivity = NI Specificity = NI PPV = NR NPV = NR DOR (for T <sup>+</sup> ca	TST (≥10  Exposur High/Yes NR NR NR NR R R  Contact of the second of th	mm) re level Low/No NR NR NR NR	NR NR 0 NR	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR Specificity = NR PPV = NR NPV = NR DOR (for T <sup>+</sup> calculate OR (crude; for T <sup>+</sup> rep	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR IGRA	re level Low/No NR NR NR NR Test per	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters  Sensitivity = NI Specificity = NI PPV = NR NPV = NR DOR (for T <sup>+</sup> ca OR (crude; for	TST (≥10  Exposur High/Yes NR NR NR NR R R  Contact of the second of th	mm) re level Low/No NR NR NR NR	NR NR 0 NR	
IGRA + IGRA - Indeterminate Total  Sensitivity = NR Specificity = NR PPV = NR NPV = NR DOR (for T <sup>+</sup> calculate	ation betwee A (QFT-GI' Exposu High/Yes NR NR NR NR IGRA  ed) = NA orted) = 2.40	re level Low/No NR NR NR NR Test per	Total  NR NR 70 NR	TST + TST - Indeterminate Total ce parameters  Sensitivity = NI Specificity = NI PPV = NR NPV = NR DOR (for T <sup>+</sup> ca	TST (≥10  Exposur High/Yes NR NR NR NR R  TST R R  Culated) = N  Γ⁺reported)	mm) re level Low/No NR NR NR NR NR	NR NR 0 NR	

T' C ' A				T:	3.7.4			
List of covariates: NA				List of covariates:		ID		
Other reported measu			• .	Other reported me		NR .		
			on between	tests (IGRA vs. TS	T)			
Ratio of DORs (for T								
Ratio of OR (crude; for				0.32, 1.12)				
Ratio of ORs (regress		eported)	) = NA					
Other reported measu	re = NA							
A	ssociation b	etween	test result	s and BCG status (i	f applica	ble)		
IGR	RA (TSPOT	')			<b>ΓST</b> (≥10	mm)		
	BCG st	atus	Total		BCC	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	performa	nce parameters			•	
	IGRA			T .	TST	1		
DOR (for T <sup>+</sup> calculate		1		DOR (for T+ calcu				
OR (crude; for T <sup>+</sup> repo			CI: 0.80	OR (crude; for T+			5% CI: 0.80	
4.00)	110	3 (3370)	c1. 0.00,	3.50)	reperieu	, 1.,0 ().	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
	· reported)	$_{\rm NDA} = NI$	?	OR (regression-ba	sed: reno	$rted)_{xex} = 1$	VR	
OR (regression-based; reported) <sub>IGRA</sub> = NR List of covariates: NA				List of covariates:		181	. 110	
Other reported measure = NR				Other reported me		IR		
-		otwoon	tost result	s and BCG status (i				
	A (QFT-GI		test result	1	rappnea ΓST (≥10			
IGRA	BCG st		Total	-		status	Total	
	Yes	No	Total		Yes		Total	
IGRA +	NR	NR	NR	TST +	NR	No NR	NR	
IGRA -	NR	NR	NR	TST -	NR	NR	NR	
Indeterminate	NR		70				<u> </u>	
		NR		Indeterminate Total	NR NB	NR	70	
Total	NR	NR	NR		NR	NR	NR	
	TCD 4	Test	periorma	nce parameters	TELOTE	,		
DOD (C. 15 <sup>†</sup> 1 1 1 )	IGRA			DOD (C. T. 1	TST			
DOR (for T <sup>+</sup> calculate				DOR (for T+ calcu				
OR (crude; for T <sup>+</sup> repo	orted) = $1.70$	0 (95% (	CI: 0.80,	OR (crude; for T+ 3.50)	reported	) = 1.70 (95	5% CI: 0.80,	
OR (regression-based	; reported) I	$_{GRA} = NI$	R	OR (regression-ba	sed; repo	$rted)_{TST} = 1$	NR	
List of covariates: NA	1			List of covariates:	ist of covariates: NA			
Other reported measu	re = NR			Other reported me	asure = N	IR		
Between-test agreem	ent, concor	dance,	and discor	dance (if applicable	e)			
This table may be st					*	d/or condi	tion	
Total sample			,					
•	TS	T + ≥10	mm	TST	-		Total	
IGRA (TSPOT) +		NR		NR			NR	
IGRA (TSPOT) -		NR		NR			NR	
Indeterminate		NR		NR			NR	
Total		NR		NR			NR	
Description				1110				
Sample definition (e.g	total if e	ratified	hy BCG or	condition – specify)	· Total			
TST + threshold: ≥10:		aumou	<i>5, 200 01</i>	condition specify)	. 10111			
Parameters								
Kappa = 0.45 (95% C	1.038 053	3)						
**		"						
% concordance = NR								

% discordance = NR			
Between-test agreemen	t, concordance, and discordan	ce (if applicable)	
This table may be strat	tified by TST cut-off value, BC	G 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 con	dition – specify): total	
TST + threshold: ≥10mr	n		
Parameters			
Kappa = $0.46 (95\% CI)$	0.39, 0.53)		
% concordance = NR			
% discordance = NR			
Stratification (specify s	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 con	ndition – specify): NR	
TST + threshold: NR			
Parameters			
Kappa = NR			
% concordance = NR			
% discordance = NR			
Stratification (specify s	group 2):		
	TST +	TST -	Total
IGRA +	NR	NR	NR
IGRA -	NR	NR	NR
	NR	NR	NR
Indeterminate			
Indeterminate Total	NR	NR	NR

### **Parameters**

Kappa = NR

% concordance = NR

% discordance = NR

Othor	outcomes
Uner	onicomes

Test and cut-off (if applicable)	Adverse events n/N (%)	Health related quality of life
	(specify)	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

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

#### **Study details**

First author surname year of publication: Orlando 2010<sup>146</sup>

**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-	1130	337	778	15	1115
GIT):				(undetermined)	
<b>TST</b> (≥10mm):	1129	407 (≥10mm)	492	230 (dropouts)	899

timing for test measurement, manufacturer    Countifer   Countife	
Levels/groups of exposure to TB in increasing order (if applicable):   Definition of exposure group - Continent	
Definition of exposure group - Continent	
Exposed 1 (specify):  Exposed 2 (specify):  Exposed 3 (specify):  Definition of exposure group − TB prevalence  Non-exposed Exposed 1 (specify):  Exposed 2 (specify):  Exposed 1 (specify):  Exposed 2 (specify):  Definition of exposure group − contact with TB patient  Non-exposed No (reference group)  Exposed 1 (specify):  Definition of exposure group − contact with TB patient  Non-exposed No (reference group)  Exposed 1 (specify):  Tests  Assay used, methodology, timing for test measurement, manufacturer  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  South TB prevalence  Cut-off values/thresholds Definition of test+  information in the Nil- positive if the INF-c value after stimulation with TB- antigen minus the value in the Nil-control 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 <0.5 UI/ml or every time	
(specify):   Exposed 2   East Europe   (specify):     Exposed 3   (Specify):	
Exposed 2   (specify):	
Exposed 2   (specify):	
Exposed 3 (specify):	
Specify   Definition of exposure group - TB prevalence	
Definition of exposure group - TB prevalence	
Non-exposed   <50 (reference group)	
Exposed 1 (specify):  Exposed 2 (specify):  Definition of exposure group – contact with TB patient  Non-exposed  No (reference group)  Exposed 1 (specify):  Tests  Assay used, methodology, timing for test measurement, manufacturer  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  Definition of exposure group – contact with TB patient  Definition of test+  Definition of test+  Definition of test+  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<0.5 UI/ml and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	
Exposed 2   >200	
Exposed 2 (specify):   Definition of exposure group - contact with TB patient	
Specify :   Definition of exposure group — contact with TB patient	
Definition of exposure group – contact with TB patient	
Non-exposed   No (reference group)	
Exposed 1 (specify):  Tests  Assay used, methodology, timing for test measurement, manufacturer  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 (Nilcontrol), 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  Cut-off values/thresholds Definition of test+ information inform	
Cut-off values/thresholds   Definition of test+   Definition of	
Assay used, methodology, timing for test measurement, manufacturer  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  Cut-off values/thresholds Definition of test+  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 and <25% of Nil, with Mitogen minus Nil<0.35 UI/ml and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	
Assay used, methodology, timing for test measurement, manufacturer    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 (Nilcontrol), 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   Cut-off values/thresholds   Definition of test+   Information of test+   Definition of test-	
timing for test measurement, manufacturer    QuantiFERON-TB Gold InTube (QFT-IT) test (Cellestis Limited, Victoria, Australia): 1 ml of blood was drawn directly into QFT-IT blood collection tubes coated with saline (Nilcontrol), peptides of ESAT-6, CFP-10 and TB7.7(p4) proteins (MTB specific antigens—TBantigen) 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   Definition of test+   information information of test+   information of the Nilcontrol was ≥0.35   UI/ml and ≥25% of Nil; indeterminate for TB antigen minus Nil ≥0.5 UI/ml or ≥0.35 UI/ml and <25% of Nil, with Mitogen minus Nil	
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  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, or every time	ther
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  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 and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	mation
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  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 or ≥0.35 UI/ml and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	
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  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	NA
ml of blood was drawn directly into QFT-IT blood collection tubes coated with saline (Nilcontrol), 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  matigen 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	
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  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 and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	
tubes coated with saline (Nilcontrol), 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  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	
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  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	
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  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	
(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  UI/ml or if that difference was ≥0.35 UI/ml and <25% of Nil, with Mitogen minus nil ≥0.5 UI/ml or indeterminate for TB antigen minus Nil <0.35 UI/ml and <25% of Nil, with Mitogen minus Nil <0.5 UI/ml, or every time	
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  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	
(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  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	
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  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	
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 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	
37°C, blood collection tubes were centrifuged for 15 min at 2,000−3,000g and stored at - 80°C before testing. The 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	
were centrifuged for 15 min at 2,000–3,000g and stored at - 80°C before testing. The ≥0.35 UI/ml and <25% of Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	
2,000–3,000g and stored at - Nil, with Mitogen minus Nil<0.5 UI/ml, or every time	
80°C before testing. The Nil<0.5 UI/ml, or every time	
concentration of IFN-c (IU/ml) Nil was >0.8 UI/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	
	NΑ
	12 1
derivative (Biocine test PPD positive in persons recently	
tuberculin purified protein induration was considered	NΑ

	Liofilo	, Novartis	Vaccines	and arrived fi	rom high	lv ende	mic	
		stics) was		areas				
		rmally into						
		oants were						
		or the evalu						
		type hype						
		n (mean of		•				
		rse diamet						
Association between					applical	ole)		
	IGRA					ΓST		
		ence of	Total		Incid			Total
	activ	e TB			of ac			
					T	В		
	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
		Tes	t perforn	nance parameter				
~	IGRA			~		<b>TST</b>		
Sensitivity = NA				Sensitivity = N.				
Specificity = NA				Specificity = N	A			
PPV = NA				PPV = NA				
NPV = NA				NPV = NA				
Cumulative Inciden	ce <sub>IGRA+</sub> =	= NA		Cumulative Inc				
Cumulative Inciden	ce <sub>IGRA-</sub> =	- NA		Cumulative Incidence $_{TST-} = NA$				
Cumulative Inciden	ce Ratio	IGRA = NA		Cumulative Incidence Ratio $_{TST} = NA$				
Incidence density ra				Incidence density rate $_{TST^+} = NA$				
Incidence density ra	te <sub>IGRA-</sub> =	NA NA		Incidence density rate $_{TST-} = NA$				
Incidence density ra				Incidence densi	ty rate ra	itio <sub>TST</sub> :	= NA	
Other reported meas				Other reported measure $_{TST} = NA$				
				en tests (IGRA v	s. TST)			
Ratio of cumulative								
Ratio of incidence d			NA					
Other reported meas								
			results a	nd levels of TB e	_			
IGRA	(QFT-		- I			≥10mn	1)	1
		ntinent	Total	-		tinent		Total
ICD 4	Asia	Africa		TOTAL:	Asia	Afri		) ID
IGRA +	NR	NR	NR	TST +	NR	NI		NR
IGRA -	NR	NR	NR	TST -	NR	NI		NR
Indeterminate	NR	NR	NR	Indeterminate	NR	NI		NR
Total	79	181	260	Total	79	18	1	260
ICD	(OFT.		t perforn	nance parameter		×10	•)	
	(QFT-0	J11)		Congitivity - NI	,	≥10mn	1)	
Sensitivity = NR				Sensitivity = NE				
Specificity = NR				Specificity = NF				
PPV = NR				PPV = NR				
NPV = NR	4-4\ 33	D		NPV = NR	1 / 1			
DOR (for T <sup>+</sup> calcula	itea) = N	K		DOR (for T <sup>+</sup> cal	culated)	=		
Asia vs. Africa		- 1 (1 (0.50	/ CI	Asia vs. Africa	p+	. 4)	01 (050)	CI. 0.50
OR (crude; for T <sup>+</sup> re	ported) =	= 1.61 (95%	∕₀ CI:	OR (crude; for 7	reporte	ea) = 0.9	91 (95%	o CI: 0.50,
0.90, 2.88)				1.64)				

Asia vs. Africa  OR (regression-based; reported) = $1.07 (95\%)$ CI: $0.52, 2.23$ ) List of covariates: NR  Other reported measure = NR  Comparison between tests (IGRA vs. TST)  Ratio of DORs (for T <sup>+</sup> calculated) = NA  Ratio of OR (crude; for T <sup>+</sup> reported) = $1.77 (95\%)$ CI: $1.16, 2.70$ )  Ratio of ORs (regression-based; reported) = $1.49 (95\%)$ CI: $0.87, 2.53$ )	5% CI:				
CI: $0.52$ , $2.23$ ) List of covariates: NR  Other reported measure = NR  Comparison between tests (IGRA vs. TST)  Ratio of DORs (for T <sup>+</sup> calculated) = NA  Ratio of OR (crude; for T <sup>+</sup> reported) = 1.77 (95% CI: 1.16, 2.70)  Ratio of ORs (regression-based; reported) = 1.49 (95% CI: 0.87, 2.53)	5% CI:				
List of covariates: 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 = 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)					
Comparison between tests (IGRA vs. TST)  Ratio of DORs (for T <sup>+</sup> calculated) = NA  Ratio of OR (crude; for T <sup>+</sup> reported) = 1.77 (95% CI: 1.16, 2.70)  Ratio of ORs (regression-based; reported) = 1.49 (95% CI: 0.87, 2.53)					
Ratio of DORs (for T <sup>+</sup> calculated) = NA Ratio of OR (crude; for T <sup>+</sup> 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 = NR				
Ratio of OR (crude; for T <sup>+</sup> reported) = 1.77 (95% CI: 1.16, 2.70) Ratio of ORs (regression-based; reported) = 1.49 (95% CI: 0.87, 2.53)					
Ratio of ORs (regression-based; reported) = 1.49 (95% CI: 0.87, 2.53)					
0.1					
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 Africa East Africa					
Europe Europe					
IGRA + NR NR NR TST + NR NR	NR				
IGRA - NR NR NR TST - NR NR	NR				
Indeterminate         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 $NPV = NR$	NPV = NR				
DOR (for $T^+$ calculated) = NR DOR (for $T^+$ calculated) = NR	DOR (for $T^+$ calculated) = NR				
East Europe vs. Africa East Europe vs. Africa					
OR (crude; for $T^+$ reported) = 1.46 (95% CI: OR (crude; for $T^+$ reported) = 0.83 (95% CI)	OR (crude; for $T^+$ reported) = 0.83 (95% CI: 0.55,				
0.96, 2.23) 1.25)	,				
East Europe vs. Africa East Europe vs. Africa	*				
OR (regression-based; reported) = 1.68 (95% OR (regression-based; reported) = 1.19 (95%)	5% CI:				
CI: 0.91, 3.08) 0.66, 2.14)					
List of covariates: 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 <sup>+</sup> 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)	m · 1				
	Total				
Latin Africa Latin Africa					
America America	NID				
IGRA + NR NR NR TST + NR NR	NR				
IGRA - NR NR TST - NR NR	NR				
Indeterminate 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 <sup>+</sup> calcula	ted) = NR				lculated) =	NR		
Latin America vs. A				DOR (for T <sup>+</sup> calculated) = NR <b>Latin America vs. Africa</b>				
OR (crude; for T <sup>+</sup> re		46 (050/	CI				059/ CI: 0.50	
0.99, 2.16)	porteu) – 1.	40 (93/0	CI.	OR (crude; for T <sup>+</sup> reported) = 0.86 (95% CI: 0.59, 1.26)				
Latin America vs. A	A frice			Latin America vs. Africa				
		) = 0.91 (	050/				57 (050/ CI.	
OR (regression-base CI: 0.46, 1.42)	a, reported	) – 0.81 (	9370	OR (regression 0.33, 1.00)	-based, repo	311eu) – C	7.37 (93% CI.	
List of covariates: N	TD			List of covariat	agi ND			
						NID		
Other reported meas		n h otrvo	Other reported		NK			
Patie of DOPa (for '			n betwe	en tests (IGRA	vs. 151)			
Ratio of DORs (for			70 (050)	( CL 1 20 2 24)				
Ratio of OR (crude;					2.24)			
Ratio of ORs (regres		; reported	1) = 1.42	2 (95% CI: 0.95, 1	2.24)			
Other reported meas			•					
			esults a	nd levels of TB	_ `		ble)	
IGRA	(QFT-GI		- ·		TST (≥			
	TB prev		Total		TB prev		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-GI	Γ)			TST (≥	10mm)		
Sensitivity = NR				Sensitivity = NR				
Specificity = NR				Specificity = NR				
PPV = NR				PPV = NR				
NPV = NR				NPV = NR				
DOR (for T <sup>+</sup> calcula	ted) = NR			$DOR (for T^+ calculated) = NR$				
50-200 vs. <50	/			50-200 vs. <50				
OR (crude; for T <sup>+</sup> re	ported = 1	76 (95%	CI:	OR (crude; for	T <sup>+</sup> reported	= 0.66 (	95% CI: 0.44.	
1.10, 2.80)	r	(, , ,		1.01)	P	, (	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
50-200 vs. <50				50-200 vs. <50				
OR (regression-base	d: reported	= 1.34 (	95%	OR (regression	-based: reno	orted) = 0	0.70 (95% CI:	
CI: 0.72, 2.49)	,	,	/ 0	0.39, 1.25)	ж, т •р ч	,	(5-2,0-02)	
List of covariates: N	R			List of covariat	es: NR			
Other reported meas				Other reported		NR		
F 2212 2 224		mpariso	n betwe	en tests (IGRA				
Ratio of DORs (for				(_021				
Ratio of OR (crude;			67 (95%	6 CI: 1 94 3 67)				
Ratio of OR (crude,					2.95)			
Other reported meas		, reported	·/ 1.71	. (70/0 01, 1,24,	,.,			
1		en test r	esults a	nd levels of TB	evnosure (i	f annlice	hle)	
	(QFT-GI		courts a	la levels of 1D	TST (≥		iore)	
IGKA	TB prev	,	Total		TB prev		Total	
	>200	< <b>50</b>	Total		>200	< <b>50</b>	Total	
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	
				nance paramete				
IGRA	(QFT-GI			F	TST (≥	10mm)		
TOTAL	(10 119)	- /			151 (2.	- 311111)		

Schsitivity 1410				G if it ND					
Specificity = NR				Specificity = NR					
PPV = NR				PPV = NR					
NPV = NR				NPV = NR					
DOR (for T <sup>+</sup> calcula	ted) = NR			DOR (for T <sup>+</sup> ca	lculated) =	NR			
>200 vs. <50				>200 vs. <50	<b>.</b>				
OR (crude; for T <sup>+</sup> re	ported) = 2.	31 (95%	CI:	OR (crude; for	T <sup>+</sup> reported)	0 = 0.99	95% CI: 0.66,		
1.48, 3.61)				1.48)					
>200 vs. <50				>200 vs. <50					
OR (regression-base	ed; reported)	= 2.72 (	95%	OR (regression-	-based; repo	orted) = 1	.45 (95% CI:		
CI: 1.70, 5.02)				0.80, 2.62)					
List of covariates: N				List of covariate					
Other reported meas			•	Other reported		NR .			
			n betwe	en tests (IGRA v	vs. TST)				
Ratio of DORs (for									
Ratio of OR (crude;									
Ratio of ORs (regres		; reported	(1) = 1.88	3 (95% CI: 1.25, 2	2.83)				
Other reported meas									
			esults a	nd levels of TB			ble)		
IGRA	(QFT-GI		1		TST (≥1				
	Contact v	vith TB	Total		Contact w	vith TB	Total		
	cas		ļ		cas				
	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		
			perforn	nance parameter					
	(QFT-GIT	Γ)			TST (≥1	l0mm)			
Sensitivity = NR				Sensitivity = N					
Specificity = NR				Specificity = N	R				
PPV = NR				PPV = NR					
NPV = NR				NPV = NR					
DOR (for T <sup>+</sup> calcula				DOR (for T <sup>+</sup> ca		NR			
Contact vs. No con				Contact vs. No contact OR (crude; for T <sup>+</sup> reported) = 1.87 (95% CI: 1.30,					
OR (crude; for T <sup>+</sup> re	ported) = 2.	54 (95%	CI:		T' reported)	= 1.87 (9)	95% CI: 1.30,		
1.82, 3.54)				2.69)					
Contact vs. No con		2 1 1 /	0.50/	Contact vs. No		. 1\ 1	05 (050/ GI		
OR (regression-base	ed; reported	) = 2.11 (	95%	OR (regression-	-based; repo	orted) = 1	.87 (95% CI:		
CI: 1.47, 3.03)	(D)			1.24, 2.80)	ND				
List of covariates: N				List of covariate		ID			
Other reported meas			n h a4	Other reported		NK			
Datia of DOD- (C. )			n betwe	en tests (IGRA	vs. 151)				
Ratio of DORs (for			26 (0.50)	CT. 1.0C. 1.75					
Ratio of OR (crude;					1 40)				
Ratio of ORs (regres		; reported	1) = 1.13	(95% CI: 0.85,	1.49)				
	Other reported measure = NA								
As	Association between test results and BCG status (if applicable)								
	IGRA	4-4	Tr 4 1			ST	T-4 1		
	BCG st		Total			status	Total		
ICDA	Yes	No	NIP	TOT	Yes	No	MD		
IGRA +	NR	NR	NR	TST +	NR	NR	NR		
IGRA -	NR	NR	NR	TST -	NR	NR	NR		

Sensitivity = NR

Sensitivity = NR

Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR		
Total	NR	NR	NR	Total	NR	NR	NR		
				ance parameters	- 1				
	IGRA	1000	perrorm		Т	ST			
DOR (for T <sup>+</sup> calculat		VR		DOR (for T+ cal					
OR (crude; for T <sup>+</sup> rep					OR (crude; for T+ reported) = NR				
OR (regression-based			JR	OR (regression-					
List of covariates: NI		) IGIOT		List of covariate		· P / 1	51		
Other reported measu				Other reported r		= NR			
Between-test agreen		ordance	, and disc	cordance (if applic	cable)				
This table may be st			•	`		ıs, and/o	r 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	l by BCG	or condition – spe	cify): To	otal			
$TST + threshold: \ge 10$				1					
Parameters									
Kappa = 0.38 (95%)	ZI: NR)								
% concordance = 625		.46% (95	% CI: 67	.32, 73.43)					
% discordance = 262									
Stratification (BCG			, 0 01, 1 (1	-)					
TST + TST -							Total		
IGRA +		NR		NR			NR		
IGRA -		NR		NR			NR		
Indeterminate		NR		NR			NR		
Total		NR		NR			56		
Description		1110		1112					
Sample definition (e.	g total if	stratified	1 by BCG	or condition – spe	cify): Bo	CG vacci	nated		
$TST + threshold: \ge 10$		Struttifice	i oj bec	or condition spe	city). B	ed vacer	nated		
Parameters									
Kappa = $0.35 (95\%)$	'I· NR)								
% concordance = $37/$		7% (95%	CI: 52 09	9 77 84)					
% discordance = 19/5	$\frac{50}{66} = 33.92$	% (95%)	CI: NR)	, , , , , , , , , , , , , , , , , , , ,					
Stratification (BCG			O1. 111()						
Structure (DCC)	IIII vacci	TST +		TST -			Total		
IGRA +	+	NR		NR			NR		
IGRA -	+	NR		NR			NR		
Indeterminate	+	NR		NR NR			NR NR		
Total	+	NR		NR NR			789		
<b>Description</b>		1117		INIX			109		
Sample definition (e.	g total if	ctrotific	l by BCC	or condition and	cify). D	CG non r	vaccinated		
TST + threshold: $\geq 10$		Suamie	1 UY DCC	or condition – spe	спу <i>)</i> . В	CO HOH-V	acciliated		
Parameters Parameters	J111111								
	T. NID								
Kappa = $0.40 (95\%)$		260/ (05	0/ CI. 60	04 74 46)					
$\frac{\%}{\%}$ concordance = $563$									
% discordance = 226	1/89 = 28.	04% (95		·					
TT	30 27	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \		outcomes	1	TT 1/1	. 1. 4. 3		
Test and cut-off (if a	ipplicable	-		nts n/N (%)			related quality		
		(spe	ciiy)			oi iiie m	nean 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

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

#### Study details

First author surname year of publication: Saracino 2009<sup>147</sup>

**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

Number of patients te	Total N (tested)	Total N	Total N (test-)	Total N (indetermi	Total N (test results
		(test+)		nate)	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

		1			1	HIV/active		
						нгу/асцуе ГВ)		
Total N of n	vationts w	ith valid	l results for	hoth ICR	A and TST: 2			
					r (if applicab			
Levels/grou	ps of exp	osure to			sure group	16).		
Non-exposed	d	NR	Denniti	on or expo	sure group			
Exposed 1 (s		30-100	)					
Exposed 1 (s								
Exposed 2 (s								
Exposed 3 (s								
Exposed 4 (s	specify).	>301	on of ovnosu	ro group	Region of o	rigin		
Non-exposed		NR	on or exposu	re group -	Region of o	ı ığın		
Exposed 1 (s		Afr	ican					
Exposed 1 (s			tern Mediterr	nnann				
Exposed 2 (s		_	opean	ancan				
Exposed 3 (s			th-East Asia	n				
Tests	specify):	Sou	uii-East Asiai	П				
1 0515	Accovi	sed ma	thodology, t	iming for	Cut	-off		Other
			nent, manuf		values/th		in	formation
	test ii	icasui cii	iiciit, iiiaiiui	acturer	Definition		111	ioimation
IGRA	OFT-GI	T (Celles	stis, Carnegie	<u> </u>	the test was			
(QFT-	_	`	erformed, acc	*	positive if the			
GIT)			's instruction	_	level was ab			
311)			f whole hepa		cut-off test			
			es, one conta		(≥0.35 IU/m			
			egative contr	_	(	)		
			ing three MT					
			6, CFP-10 an					
			kept at room					
			maximum o				NA	
			cubated at 3'					
			tubes were th					
			the plasma re					
	,		perform the					
			for TB-speci					
		•	rected by sub					
	_		d for the resp	_				
	negative	controls						
TST			stered by inje	ecting 0.1	Skin indura	tion was	NA	
(≥10mm)			rd test dose (		evaluated at			
			(U) of PPD		hours and co			
			D®; Chiron S		positive if ≥			
			Italy) accord	ing to the	Cut-off poir			
	x method	mm and 15	*					
respectively, were also								
used for comparison								
Association	between		lts and incid	dence of ac	tive TB (if a)			
		IGRA		T		TST	·	
		Inciden	ce of active	Total		Incidence		Total
			TB			of active		
						TB		T
		Yes	No			Yes	No	
IGRA		NA	NA	NA	TST +	NA	NA	NA
IGRA		NA	NA	NA	TST -	NA	NA	NA

In	determi	nate	NA	NA	N	A	Indetermin	n NA	N.	4	NA			
	- TD - 1		NT A	27.4			ate	27.4			27.4			
	Total		NA	NA Test	N		Total	NA	N.	A	NA			
			IGRA	Test	perioriii	апсе р	ce parameters TST							
Sensi	tivity =	NA	IONA				Sensitivity = NA							
	ficity =						Specificity = NA							
	= NA	- 11 -					$\frac{\text{PPV} = \text{NA}}{\text{PPV}}$							
	= NA						NPV = NA							
Cumu	ılative I	ncidence	$t_{IGRA^+} = N$	ĪΑ			Cumulativ	e Incidenc	e <sub>TST+</sub> =	NA				
			$e_{IGRA-} = N$					e Incidenc						
Cumu	ılative I	ncidence	Ratio IGR	A = NA			Cumulativ	e Incidenc	e Ratio	TST = 1	NA			
			$_{IGRA^{+}} = N$					density rate						
			$_{IGRA-} = N$					density rate						
Incide	ence der	nsity rate	ratio <sub>IGRA</sub>		• .			density rate	e ratio TS	ST = N	IA			
D. C	<u> </u>	1				n tests	(IGRA vs	s. TST)						
			ncidence r											
				ratios – r	NA									
Other				en test r	eculte an	d level	ls of TR ev	posure (if	annlica	hle)				
	1:		GRA	en test i	csuits an		IS OI ID CA	TS'		DIC)				
			ure level		Total		Exp	osure level		Т	otal			
			of origin					on of origin						
	Sout	Euro	Easter	Afric	1		Sout	Europe	Easter	A				
	h-	pe	n	a			h-	1	n	fri				
	East		Medite				East		Medit	ca				
	Asia		rranea				Asia		errane					
			n						an	ļ				
IG	NR	NR	NR	NR	107	TST	NR	NR	NR	N	72			
RA						+				R				
+ IG	NR	NR	NR	NR	172	TST	- NR	NR	NR	N	207			
RA	IVIX	INIX	IVIX	INIX	1/2	151	-   1111	INIX	INIX	R	207			
-										1				
Ind	NR	NR	NR	NR	173	Inde	NR	NR	NR	N	173			
eter					(exclu	ermi				R	(exclude			
min					ded)	ate					d)			
ate														
Tot	6	7	131	135	279	Tota	1 6	7	131	13	279			
al				700 4	C					5				
		1	CD A	Test	periorma	ance p	arameters		T					
Congi	tivity =		GRA			Song	itivity – N	TS'	1					
						Sensitivity = NA Specificity = NA								
Specificity = NA PPV = NA							= NA	Λ						
						•	$\overline{I} = NA$							
$\frac{NV - NA}{DOR \text{ (for T}^+ \text{ calculated)} = NA}$								lculated) =	· NA					
OR (crude; for T+ reported) =						•		T+ reporte						
,	Africa: OR = 1.00, 95% CI: 0.60, 1.70							.10, 95% (		1.90				
			n: OR = 1		6 CI:			rranean: O			6 CI: 0.50,			
0.60,						1.40								
1 *			5% CI: 0.				•	1.00, 95% (						
South	n-East A	sia: OR	= 0.30, 95	% CI: 0	.01,	Sout	h-East Asia	a: OR = 0.6	50, 9% (	ZI: 0.1	10, 5.20			

• • •						T					
2.90											
			; reported) =	= NR		OR (regression-based; reported) = NR					
List c	of covari	ates: NA	1			List of covariates: NA					
Other	r reporte	d measu	re = NR			Other reported measure = NR					
	Comparison between tests (IGRA vs. TST)										
			+ calculated								
Ratio	of OR (	crude; fo	or T <sup>+</sup> reporte	ed) = 0	.91 (95%	CI: 0.61, 1.35) [.	Africa	vs. refer	ence g	roup]	
Ratio	Ratio of ORs (regression-based; reported) = NA										
Other	Other reported measure = NA										
	A	ssociati	on between	test r	esults and	d levels of TB ex	posur	e (if app	olicable	e)	
			(QFT-GIT					Γ (≥10m		,	
			ure level	•	Total	Е	xposur	e level			Total
	Born		ıntry with a	TB		Born in a co			B burd	en	
			ırden			(# cases per 10					
	(# case	s per 10	0,000)			1	, ,				
	>301	201-	101-200	30-			>30	201-	101	30-	72
		300		100			1	300	_	100	
									200		
IG	NR	NR	NR	NR	107	TST +	NR	NR	NR	NR	207
RA											
+											
IG	NR	NR	NR	NR	172	TST -	NR	NR	NR	NR	173
RA											(excl
_											uded
											)
Ind	NR	NR	NR	NR	173	Indeterminate	NR	NR	NR	NR	279
eter	1,12	1,12	1,120	1,12	(exclu					1,11	
min					ded)						
ate					(304)						
Tot	54	197	15	12	279	Total	54	197	15	12	72
al								,			, –
				l	Test 1	performance pa	ramete	ers	1		l
		I	GRA			TST					
Sensi	tivity =					Sensitivity = NA					
	ificity =					Specificity = NA					
-	= NA	- 11-1				PPV = NA					
	= NA					PPV = NA NPV = NA					
		calculate	ed) = NA			$NPV = NA$ $DOR  ext{ (for T}^+  ext{ calculated)} = NA$					
	`		or T+ repor	ted) = 1	1.20	`				x = 3.00	05%
	CI: 0.30		or 1 - repor	ica)	1.20,	30-100: OR (crude; for T+ reported) = 3.00, 95% CI: 0.80, 11.8					
		,	for T+ repor	rted) =	0.80	101-200: OR (d	ernder i	or T+ r	enorted	) = 1.0	0
	CI: 0.20		ioi i icpoi	-	0.00,	95% CI: 0.20, 3			porteu	, 1.0	٠,
			for T+ repor	rted) =	1.00	201-300: OR (d		or T+ r	enorted	0 = 0.8	0
	CI: 0.60		ioi i icpoi	-	1.00,	95% CI: 0.40,			porteu	, 0.0	,
			T+ reported	(1) = 1.0	0. 95%	>301: OR (crud		T+ reno	rted) =	1.00	95%
	.50, 2.00		1 Toponio	0, 20/0	CI: 0.50, 2.10	, 101	- 1 <b>0</b> p0	,	1.00,		
			: reported) =	= NR		OR (regression	-based	reporte	d = N	R	
						List of covariat			, IN		
Other	теропе	u measu		narica	n hetween	Other reported n tests (IGRA v					
Ratio	of DOP	e (for T				ii tests (IGNA V	. 131	)			
	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]										
			ion-based; i			C1. 0.00, 1.00)	/ 201 \	s. 101010	once gi	oupj	
Natio	OI OKS	(regress	ion-based, I	еропе	$\mu_{j} - NA$						

Other reported	measure	= NA						
	Associ	iation between t	est results an	d BC	G stat	us (if applica	ıble)	
IGRA (specify	)				]	ST (specify)	)	
		BCG status	Total			BCG status		Total
	Yes	No				Yes	No	
IGRA +	NR	NR	NR	TS	T +	NR	NR	NR
IGRA -	NR	NR	NR	TS	T -	NR	NR	NR
Indeterminate	NR	NR	NR	Inc	deter	NR	NR	NR
				minate				
Total	NR		NR	To		NR	NR	NR
			performance	paran	neters			
		IGRA					TST	
DOR (for T <sup>+</sup> ca						(for T+ calc		
OR (crude; for					OR (	crude; for T-	⊦ reporte	ed) = NR
		reported) $_{IGRA} = N$	VR.		OR (	regression-b	ased; rep	$ported)_{TST} =$
List of covariat	es: NR				NR			
					List	of covariates	: NR	
Other reported						r reported m	easure =	NR
Between-test a	greemei	nt, concordance	, and discorda	ance (i	if app	licable)		
	be stra	tified by TST cu	it-off value, B	CG v	accina	tion status,	and/or o	condition
Total sample								
		TST -	<del> </del>		T	ST -		Total
IGRA +		49				58		107
IGRA -		23			1	49	172	
Indeterminate		NR			]	NR	173 (excluded)	
Total		72			2	207		279
Description								
Sample definiti	on (e.g.,	total, if stratified	d by BCG or c	onditio	on – sp	ecify): Total		
TST + threshol	d: ≥10m	m						
Parameters								
Kappa = $0.35$ (9)	95% CI:	0.23, 0.46)						
% concordance	= 198/2	79 = 70.97% (95)	% CI: 65.39,	75.98)				
% discordance	= 81/279	9 = 29.03% (95%)	CI: 24.02, 34	.61)				
Stratification (	specify	group 1)						
		TST -	+		Т	ST -		Total
IGRA +		NR			]	NR		NR
IGRA -		NR			]	NR		NR
Indeterminate		NR			]	NR		NR
Total		NR			]	NR		NR
Description								
Sample definiti	on (e.g.,	total, if stratified	d by BCG or c	onditio	on – sp	ecify): NR		
TST + threshol	d: NR							
Parameters								
Kappa = NR								
% concordance	= NR							
% discordance	= NR							
Stratification (	specify	group 2)						
		TST -	F		T	ST -		Total
IGRA +		NR			NR		NR	
IGRA -		NR				NR		NR
Indeterminate		NR				NR	1	NR
Total		NR				NR	1	NR
Description		1,11						

Sample definition (e.g., total, if stratified by BCG or condition – specify): NR
TST + threshold: NR
Parameters
Kappa = NR
% concordance = NR
% discordance = NR

01	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

Name of first reviewer: AlexanderTsertsvadze Name of second reviewer: Peter Auguste

**Study details** 

First author surname year of publication: Harstad 2010<sup>143</sup>

**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  $\ge 50$  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

Number of patients tested											
	Total N	Total N	Total N	Total N	Total N						
	(tested)	(test+)	(test-)	(indeterminate)	(test results						
					available)						
IGRA (QFT-GIT):	NR	246	577	NR	823						
TST:	NR	426 (≥	395	NR	821						
		6mm)	(<6mm)								
		128	693								
		(≥15mm)	(<15mm)								
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

Б 117	· C )	NT A						_	
Exposed 1 (speci		NA							
Exposed 2 (speci		NA							
Exposed 3 (speci		NA							
Exposed 4 (speci	ity):	NA							
Tests	A		411.1		C 4 . 66		041		
		ay used, me			Cut-off Othe values/thresholds			er information	
	UIIIIIII	g for test mo manufact		ent,	Definition of				
IGRA	Ouantil	FERON-TB	urer		NR	test+	NA		
IGKA	_		etic I td		INIX		INA		
	Gold In-Tube, Cellestis Ltd, Carnegie, VIC, Australia)								
TST		ourified prote		ative	≥ 6mm		NA		
101		2 tuberculin			≥15mm		1111		
		atens Serum	_	_					
		agen, Denm							
Association bety				ice of	active TB (if a)	pplicab	le)		
		FT-GIT)					<b>≥</b> 6mm		
		idence of	Tota	1		Incide	nce of	Total	
	ac	tive TB				activ	e TB		
	Yes					Yes	No		
IGRA +	8	230	238		TST +(≥	8	407	415	
					6mm)				
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	
			est perfo	rman	ce parameters				
	IG						ΓST		
Sensitivity = 8/9								% CI: 56.5, 98.01)	
Specificity = 576 74.47)	5/806 = 7	/1.46% (95%	6 CI: 68.2		Specificity = 394/801 = 49.19% (95% CI: 45.74, 52.65)				
PPV = 8/238 = 3					PPV = 8/415 = 1.92% (95% CI: 0.98, 3.75)				
NPV = 576/577 = 99.97)	= 99.83%	% (95% CI: 9	99.02,		NPV = 394/395 = 99.75% (95% CI: 98.58, 99.96)				
Cumulative Incid	lence <sub>IGR</sub>	A+ = 8/238 =	=		Cumulative Incidence $_{TST^{+}} = 8/415 = 1.92\%$ (95%)				
3.36% (95% CI:					CI: 0.98, 3.75)				
Cumulative Incid 0.17% (95% CI:					Cumulative Incidence $_{TST-} = 1/395 = 0.25\%$ (95% CI: 0.00, 1.57)				
Cumulative Incid		-		_	Cumulative Inc	idence I	Ratio rer	=	
19.39 (95% CI: 2					7.61 (95% CI: (				
Incidence density					Incidence densi			₹	
Incidence density					Incidence densi				
Incidence density				-	Incidence densi	•			
Other reported m	neasure 10	$g_{RA} = NR$			Other reported	measure	$T_{ST} = NF$	}	
					s (IGRA vs. TS	T≥6mr	n)		
Ratio of cumulat				5% CI:	0.57, 11.40)				
Ratio of incidence			= NR						
Other reported m									
Association bety	ween tes	t results an				pplicab	le)		
	T				15mm)	ı		T . 1	
			lence of a	active				Total	
TCT + />		Yes			No			121	
TST + (≥		3			118			121	

15mm)								
TST -(< 15mm)		6		686	686			
Indeterminate	1	NR.		NR		NR		
Total		9		804		813		
	Te	st perform	ance pa	rameters (TST≥	15mm)			
Sensitivity = $3/9$ =	33.33% (95	5% CI: 12.0	06, 64.58	5)				
Specificity = 686/8	804 = 85.32	% (95% C	I: 82.71,	87.60)				
PPV = 3/121 = 2.4	18% (95% C	I: 0.84, 7.0	3)					
NPV = 686/692 =	99.13% (95	% CI: 98.1	2, 99.6)					
Cumulative Incide	nce IGRA+ 3/	121 = 2.489	% (95%	CI: 0.84, 7.03)				
Cumulative Incide	ence $_{IGRA-} = \epsilon$	6/692 = 0.8	6% (95%	6 CI: 0.35, 1.92)				
Cumulative Incide			95% CI:	0.725, 11.28)				
Incidence density	rate $_{IGRA+} = 1$	NR						
Incidence density	rate <sub>IGRA</sub> = 1	NR						
Incidence density	rate ratio <sub>IGR</sub>	A = NR						
	Comp	arison bet	ween tes	sts (IGRA vs. TS	5T≥15mm)			
Ratio of cumulativ	e incidence	ratios = 0.3	38(95% (	CI: 0.11, 1.34)				
Ratio of incidence	density rate	ratios = N	R					
Other reported me	asure = NR							
Assoc	ciation betw	een test re	sults an	d levels of TB ex	posure (if	applicable)		
	IGRA				TST	Γ		
	Exposu	re level	Total		Exposur	e 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 p	erform	ance parameters	}			
	IGRA				TST	Γ		
Sensitivity = NA				Sensitivity = $NA$				
Specificity = NA				Specificity = NA				
PPV = NA				PPV = NA				
NPV = NA				NPV = NA				
DOR (for T <sup>+</sup> calcu				DOR (for T <sup>+</sup> cal				
OR (crude; for T <sup>+</sup>				OR (crude; for 7				
OR (regression-ba		d) = NA		OR (regression-		rted) = NA		
List of covariates:	NA			List of covariate	es: NA			
Other reported me				Other reported r		JA .		
			betwee	n tests (IGRA vs	s. TST)			
Ratio of DORs (fo								
Ratio of OR (crud								
Ratio of ORs (regi		d; reported	) = NA					
Other reported me								
		between to	est resul	ts and BCG stat	` 11	,		
	IGRA	-				ST		
	BCG s		Total			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	Indeterminat		NR	NR	
Total	NR	NR	NR	Total	NR	NR	NR	
Total								
10111	IGRA	Test p	erform	ance parameters		ST		

DOR (for $T^+$ calculated) <sub>IGRA</sub> = NR			DOR (for T+ calculated) <sub>TST</sub> = NR				
$OR (crude; for T^{+}reported) = NR$			OR (crude; for T+ reported) = NR				
OR (regression-based; reported) <sub>IGRA</sub> = NR				OR (regression-based; reported) $_{TST} = NR$			
List of covariates: NR			List of covariates: NR	191			
Other reported measure	= NR		Other reported measure	e = NR			
Between-test agreemen		dance, and disc	<u> </u>				
			ue, BCG vaccination statu	s, and/or condition			
Total sample				,			
	П	TST +	TST -	Total			
IGRA +		NR	NR	NR			
IGRA -		NR	NR	NR			
Indeterminate		NR	NR	NR			
Total		NR	NR	NR			
Description							
Sample definition (e.g., t	total, if str	atified by BCG	or condition – specify): NF	}			
TST + threshold: NR		•	• •				
Parameters							
Kappa = NR							
% concordance = NR							
% discordance = NR							
Stratification (specify g	(roup 1)						
	7	TST +	TST -	Total			
IGRA +		NR	NR	NR			
IGRA -		NR	NR	NR			
Indeterminate		NR	NR	NR			
Total		NR	NR	NR			
Description							
Sample definition (e.g., t	total, if str	atified by BCG	or condition - specify): NF	}			
TST + threshold: NR							
Parameters							
Kappa = NR							
% concordance = NR							
% discordance = NR							
Stratification (specify g	(roup 2)						
	Т	TST +	TST -	Total			
IGRA +		NR	NR	NR			
IGRA -		NR	NR	NR			
Indeterminate		NR	NR	NR			
Total		NR	NR	NR			
Description							
1	total, if str	atified by BCG	or condition – specify): NF	₹			
TST + threshold: NR							
Parameters							
Kappa = NR							
% concordance = NR							
% discordance = NR							
			outcomes				
Test and cut-off (if applicable)		Adverse events n/N (%)		Health related quality			
		(specify)		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)

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

#### **Study details**

First author surname year of publication: Kik 2010<sup>144</sup> (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

 $\textbf{Funding} \ (\textbf{government/private/manufacturer/other-specify}) \textbf{:} \ Unrestricted \ grants \ from \ the \ Netherlands$ 

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  $\geq$  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: 245)

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

1 turnoti di patiento testea							
	Total N	Total	Total N	Total N	Total N		
	(tested)	N	(test-)	(indeterminate)	(test results		

			(test+)				available)
IGRA (QFT-GI	<u>L)</u>	339	178	149	12		327
IGRA (T-SPOT.		339	181	118	40		299
TST (≥10mm)	, )	339	288	51	0		339
TST (≥15mm)		322	184	138	0		322
Total N of patier	nts with v				ST(n =	339). OF	
327), and T-SPO					51 (II	,, QI	1 011 (II
Levels/groups of			ncreasing of	der (if applicab	le):		
20,010,810,800	· · · · · · · · · · · · · · · · · · ·			xposure group	10)1		
Non-exposed		NA					
Exposed 1 (speci	fv):	NA					
Exposed 2 (speci		NA					
Exposed 3 (speci		NA					
Exposed 4 (speci	• /	NA					
Tests	19)•	11/11					
1 0505	Acca	y used, met	hodology	Cut-off value	uas/thras	holds	Other
		•	easurement,		on of tes		information
	tilling	manufact		Denniti	on or tes		linioimation
IGRA (QFT-	Perform	ed accordin		Two-tube for	mat nosit	ive test	NA
GIT)			nanufacturers		Two-tube format positive test was defined as $\geq 0.35$		
GII)				IU/mL-1			
		ed in a single laboratory University Medical  IU/mL-¹					
	,	•	Netherlands)				
IGRA (T-		ed accordin		Interpretation	of result	s was	NA
SPOT.TB)			nanufacturers				1171
51 01.11)				defined by the manufacturer			
		ed in a single laboratory University Medical  defined			c manara	cturer	
	,	•	Netherlands)				
TST		erculin units		> 10mm			NA
		derivative R		≥ 15mm			
		80; Statens					
		nstitute, Co	penhagen.				
			after 48–72				
	h	,					
Association betw		results and	incidence o	f active TB (if a	pplicable	e)	
	GRA(QF						
		lence of	Total		Incide	nce of	Total
	acti	ve TB			activ	e TB	
	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
				nce parameters			
IGRA (excluding indeterminate)				TST			
Sensitivity = $5/8 = 62.50\%$ (95% CI: 30.57,				Sensitivity = 9/9 = 100.00% (95% CI: 70.08,			
86.32)				100.00)			
Specificity = 146/319 = 45.77% (95% CI: 40.38,				Specificity = 51/330 = 15.45% (95% CI: 11.95,			
51.25)			,	19.75)			
	80% (959	% CI: 1.20	6.40)		3.12% (	95% CI·	1.65, 5.83)
PPV = 5/178 = 2.80% (95% CI: 1.20, 6.40)				PPV = 9/288 = 3.12% (95% CI: 1.65, 5.83)			

NPV = 51/51 = 100.00%

Cumulative Incidence  $_{TST+} = 9/288 = 3.12\%$ 

100.00)

(95% CI: 93.00,

NPV = 146/149 = 98.0% (95% CI: 94.20, 99.31)

Cumulative Incidence  $_{IGRA^+} = 5/178 = 2.80\%$ 

(95% CI: 1.20, 6.4	0)			(95% CI: 1.65, 5.83)					
	Cumulative Incidence $_{TST}$ = 0/51 = 1.96 (95%)								
Cumulative Incidence $_{IGRA-} = 3/149 = 2.00\%$ (95% CI: 0.42, 6.02)				CI:0.21, 10.4)					
Cumulative Incide		$R_{A} = 1.39$ (9)	95% CI:	Cumulative In		$io_{TST} = 1.5$	9 (95% CI:		
0.34, 5.74)	10.	101		0.21, 71.2)		151	(		
Incidence density	rate $_{IGRA+} = 1$	NR		Incidence dens	sity rate TST+	= NR			
Incidence density				Incidence dens	-				
Incidence density				Incidence dens					
Other reported me				Other reported	_				
•			between	n tests (IGRA vs		*			
Ratio of cumulativ					,				
Ratio of incidence	density rate	ratios = NI	2						
Other reported me	asure = NR								
Association between	een test resu	ılts and inc	cidence o	of active TB (if a	pplicable)				
IGF	RA (T-SPO)	Г.ТВ)			TST≥15	5mm			
	Incidenc	e of	Total		Incidenc	e of	Total		
	active 7	ГВ			active	ГВ			
	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		
Total	9	330	339	Total	8	314	322		
				nce parameters	<u> </u>				
-	cluding ind				TST				
Sensitivity = $6/8$ =	75.00% (95	5% CI: 40.9	3,	Sensitivity = 7/8 = 87.5% (95% CI: 52.91, 97.76)					
92.85)									
Specificity = 116/2	291 = 39.869	% (95% CI:	34.4,	Specificity = 1	137/314 = 43	3.63% (95%	% CI: 38.25,		
45.58)				49.16)	49.16)   PPV = 7/184 = 3.80% (95% CI: 1.85, 7.64)				
PPV = 6/181 = 3.3			4)						
NPV = 98.31% (9)	5% CI: 94.0	3, 99.53)		NPV = 137/13	88 = 99.28%	(95% CI: 9	96.01,		
G 1 1 7 11		C/101 2.2	10/	99.87)		7/104	2.000/		
Cumulative Incide		5/181 = 3.3	1%	Cumulative In		= 1//184 =	3.80%		
(95% CI: 1.52, 7.0		0/110 — 1 60	70/	(95% CI: 1.85		_ 1/120 _ /	0.720/ (0.50/		
Cumulative Incide (95% CI: 0.08, 6.3		2/116 – 1.05	970	Cumulative In CI:0.00, 4.39)		- 1/136 - (	0.7270 (9370		
Cumulative Incide		- 1 05 (0	)5% CI:	Cumulative In		io – 5.2	5 (05% CI:		
0.40, 9.52)	nce Kano IG	RA - 1.93 (5	75 /0 C1.	0.65, 42.17)	cidence Kai	10 <sub>TST</sub> – 3.2	3 (9370 C1.		
Incidence density	rate con = 1	VR			Incidence density rate $_{TST+} = NR$				
Incidence density				Incidence density rate <sub>TST+</sub> = NR					
Incidence density				Incidence density rate ratio <sub>TST</sub> = NR					
incraonee density			between	tests (IGRA vs. TST)					
Ratio of cumulativ					~-)				
Ratio of incidence									
Other reported me		-30100 111	·-						
		een test re	sults and	d levels of TB ex	posure (if a	pplicable)			
12230	IGRA				TST				
Exposure level Total				Exposu		Total			
High/Yes Low/No				High/Yes	Low/No	1			
IGRA +	NR	NR	NR	TST +	NR	NR	NR		
IGRA -	NR	NR	NR	TST -	NR	NR	NR		
Indeterminate	NR	NR	NR	Indeterminate	NR	NR	NR		
		1		Total	NR	NR	NR		
Total NR NR NR				10001	1111	- 1	1117		

IGRA				TST			
Sensitivity = NR				Sensitivity = $NR$			
Specificity = NR				Specificity = $NR$			
PPV = NR				PPV = NR			
NPV = NR				NPV = NR			
DOR (for T <sup>+</sup> calcu				DOR (for T <sup>+</sup> calcul	ated) = N	IR	
OR (crude; for T <sup>+</sup>				OR (crude; for T <sup>+</sup> re			
OR (regression-ba		d) = NR		OR (regression-bas		ted) = NR	
List of covariates:				List of covariates: 1			
Other reported me				Other reported mea		R	
			n between	n tests (IGRA vs. T	ST)		
Ratio of DORs (fo							
Ratio of OR (crud							
Ratio of ORs (regi		d; reported	) = NR				
Other reported me							
		between t	est resul	ts and BCG status (			
	IGRA				TS		T
	BCG s		Total			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
	ICDA	Test	performa	ance parameters	TO	Т	
DOD (C. T <sup>+</sup> 1	IGRA	NID		$\frac{TST}{DOR (for T+ calculated)_{TST} = NR}$			
DOR (for T <sup>+</sup> calcu				`			
OR (crude; for T <sup>+</sup> ) OR (regression-ba			D	OR (crude; for one of or o			- ND
List of covariates:		u) <sub>IGRA</sub> – IN	K	List of covariate		portea) <sub>TST</sub>	- NK
Other reported me				Other reported 1		- ND	
		cordance	and disc	cordance (if applica		1110	
				ie, BCG vaccination		and/or co	ndition
Total sample		oj 101 <b>v</b> a		, 200 ;		wii w , 01	
		TST +		TST -			Total
IGRA +		NR		NR			NR
IGRA -		NR			NR		
Indeterminate		NR		NR	NR		
Total		NR		NR NR			NR
Description							
Sample definition	(e.g., total, i	f stratified	by BCG	or condition - speci	fy): NR		
TST + threshold: 1	NR						
Parameters							
Kappa = NR							
% concordance = 1							
% discordance = N							
Stratification (spe	ecify group						
		TST +		TST -			Total
IGRA +		NR			NR		NR
IGRA -		NR		NR			NR
Indeterminate		NR		NR			NR
Total		NR		NR NR			
Description	,		1		0 > 3 = =		
Sample definition	(e.g., total, i	t stratified	by BCG	or condition – speci	ty): NR		

TST + threshold: NR	
Parameters	
Kappa = NR	

% concordance = NR

% discordance = NR

Stratification (specify group 2)

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

O VIII O WOODING							
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