Table S1. Demographics of Included Versus Excluded Participants.

Characteristic	Included Participants (N=10740)	Excluded Participants (N=1394)	p-value
Mean age (SD)	32.2 (17.5)	35.7 (17.1)	<0.001
Foreign-born	8685 (80.9%)	1093 (78.4%)	0.032
Close contact to TB case	991 (9.2%)	110 (7.9%)	0.11
HIV-seropositive	1370 (12.8%)	101 (7.2%)	<0.001

Table S2. Data Used to Calculate Prior Estimates of Sensitivity for the Tuberculin Skin Test and Interferon-γ Release (IGRA) Assays, with Progression to Active Tuberculosis as the Reference Standard.

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up, Yrs	Total Subjects, No.	Positive QFT, No. (%)	Progressed to Active TB, No. (%)	QFT Sensitivity for All Cases of Active TB (%)	Positive TSPOT, No. (%)	Progressed to Active TB, No., (%)	TSPOT Sensitivity for All Cases of Active TB (%)
Zellweger et al. AJRCCM 2015 [1]	TB contacts	Low incidence European countries	2009–2011	≤2.5	5,020 3895 QFT 1,125 TSPOT	1,068/3,895 (27.4)	14/421 (3.3) w/o prev therapy 3/481 (0.6) w/ prev therapy	17/20 (85.0)	299/1125 (26.6)	2/73 (2.7) w/o prev therapy 0/208 (0) w/prev therapy	2/4 (50.0)
Diel et al. AJRCCM 2008 [2]	TB contacts	Germany	2005–2006	2	601	66 (11.0)	6/41 (14.6)	6/6 (100)	N/A	N/A	N/A
Diel et al. AJRCCM 2011 [3] (update)	TB contacts	Germany	2005–2008	4	954	198 (20.8)	19/147 (12.9)	19/19 (100)	N/A	N/A	N/A
Hill et al. PLoS One 2008 [4]	TB contacts	Gambia	2002–2004	2	2348	N/A	N/A	N/A	649/1736 (37.4)	11/649 (1.7)	11/21 (52.4)
Kik et al. Eur Respir J 2010 [5]	TB contacts	The Netherlands	2005–2007	2	339	178/327 (54.4)	5/178 (2.8)	5/8 (62.5)	181/299 (60.5)	6/181 (3.3)	6/8 (75.0)
Lienhardt et al., PLoS One 2010 [6]	TB contacts	Senegal	2004–2006	2	2679	N/A	N/A	N/A	544/952 (57.1)	17/544 (3.1)	17/23 (73.9)
Yoshiyama et al. IJTLD 2010 [7]	TB contacts	Japan	2003–2005	2	3102	419/3,102 (13.5)	20/419 (4.8)	20/39 (51.3)	N/A	N/A	N/A
Higuchi et al. Resp 2007 [8]	TB contacts (students)	Japan	2002	3.5	349	4/88 (4.5)	0/4 (0)	N/A	N/A	N/A	N/A
Bradshaw et al. PLoS One 2011 [9]	TB contacts (health care workers)	Ireland	2007	3	389	37/389 (9.5)	0/37 (0)	N/A	N/A	N/A	N/A
Song et al. Chest 2012	TB contacts (high	Korea	2007	2	1,826	203/270 (75.2), but	11/203 (5.4)	11/11 (100)	N/A	N/A	N/A

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up, Yrs	Total Subjects, No.	Positive QFT, No. (%)	Progressed to Active TB, No. (%)	QFT Sensitivity for All Cases of Active TB (%)	Positive TSPOT, No. (%)	Progressed to Active TB, No., (%)	TSPOT Sensitivity for All Cases of Active TB (%)
[10]	school)					only IGRA tested among 270/1,826 (14.8) with positive TST					
Bakir et al. Ann Intern Med 2008 [11]	Children TB contacts (aged 1–16 yrs)	Turkey	2002–2004	1.3	908	N/A	N/A	N/A	381 (42.0)	11/381 (2.9)	11/15 (73.3)
Kruczak et al. Scand J Infect dis 2014 [12]	Homeless, TB contacts, low risk groups	Krakow, Poland	2007–2009	4-5	785	211/779 (27.1)	8/211 (3.8)	8/12 (66.7)	N/A	N/A	N/A
Pullar et al. BMC ID 2014 [13]	HIV-positive adults	Norway	2009–2010	2	304	77/298 (25.8)	0/77 (0)	N/A	29/117 (24.8)	0/29 (0)	N/A
Santin et al. Diagn Micro Infect Dis 2011 [14]	HIV-positive adults	Spain	2007–2009	~2	135	13/135 (9.6)	0/13 (0)	N/A	N/A	N/A	N/A
Aichelburg et al. CID 2009 [15]	HIV-positive adults	Austria	2006–2007	19 mos.	830	44 (5.3)	3/36 (8.3)	3/3 (100)	N/A	N/A	N/A
Jonnalagadda et al. J Inf Dis 2010 [16]	HIV-positive pregnant women	Kenya	1999–2005	2	333	N/A	N/A	N/A	120/281 (42.7)	6/110 (5.5)	6/9 (66.7)
Lange et al. IJTLD 2012 [17]	Immuno-compromised (only 11% HIV)	Germany	2006–2007	28 mos.	460	38(8.3)	1/38 (2.6)	1/1 (100)	N/A	N/A	N/A
Sester et al. AJRCCM 2014 [18]	Immuno-compromised (50% HIV-positive)	11 European countries	2008–2011	5	1,537	239/1,423 (16.8)	3/215 (1.4)	3/8 (37.5)	266/1378 (19.3)	4/247 (1.6)	4/10 (40.0)
Lee et al. Infect 2009	End-stage renal	Taiwan	2005	2	32	12/30 (40.0)	1/12 (8.3)	1/1 (100)	15/32 (46.9)	0/15 (0)	0/2 (0)

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up, Yrs	Total Subjects, No.	Positive QFT, No. (%)	Progressed to Active TB, No. (%)	QFT Sensitivity for All Cases of Active TB (%)	Positive TSPOT, No. (%)	Progressed to Active TB, No., (%)	TSPOT Sensitivity for All Cases of Active TB (%)
[19]	disease										
Chang et al. Clin Rheum 2011 [20]	Inflammatory arthritis	Korea	2007–2009	1.5	100	36/100 (36.0)	0/36 (0)	N/A	N/A	N/A	N/A
Leung et al. AJRCCM 2010 [21]	Silicosis (males)	Hong Kong	2004–2008	2	308	N/A	N/A	N/A	204/308 (66.2)	15/204 (7.4)	15/17 (88.2)
Kim et al. Am J Transplant 2011 [22]	Kidney transplants	Korea	2008–2009	1.5	312	N/A	N/A	N/A	89/296 (30.1)	4/89 (4.5)	4/4 (100)
Harstad et al. IJTLD 2010 [23]	Asylum seekers	Norway	2005–2006	23–32 mos.	832	246 (29.9)	8/246 (3.3)	8/9 (88.9)	N/A	N/A	N/A
Mahomed et al. PLoS One 2011 [24]	Children aged 12–18 yrs	South Africa	2005–2009	3.8	5,244	2669/5244 (50.9)	39/2669 (0.3)	39/52 (75.0)	N/A	N/A	N/A
Schablon et al. BMC Infect Dis 2011 [25]	Nursing students	Germany	2008–2009	2	194	2/180 (1.1)	0/2 (0)	N/A	N/A	N/A	N/A
Mandalakas et al. AJRCCM 2015 [26]	Children TB contacts (3 mos.–15 years, 22% HIV-positive)	South Africa	2008–2012	3 mos.	1,343	520/1261 (41.2)	85/1343 (6.3)	54/76 (71.1)	302/991 (30.5)	85/1343 (6.3)	45/72 (62.5)

Abbreviations: LTBI = latent tuberculosis infection; N/A = not applicable; IGRA = interferon-γ release assay; QFT = QuantiFERON® Gold In-Tube; TB = tuberculosis; TSPOT = T-SPOT®.TB

Table S3. Data Used to Calculate Prior Estimates of TST Sensitivity for Latent Tuberculosis Infection, with Progression to Active Tuberculosis as the Reference Standard

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up	Subjects, No.	Positive TST, No. (%)	Progressed to Active TB, No. (%)	TST Sensitivity for All Cases of Active TB
Kik et al., Eur Respir J 2010 [5]	Close Contacts (aged ≥16 yrs) HIV-positive excluded	Netherlands (8% born in Europe, 8% S. Am, 36% Asia, 46% Africa)	Apr 2005–Jul 2007	2 yrs	339 (only >5 mm TST were followed)	≥10 mm = 279 ≥15 mm = 177	9	≥10 mm = 9/9 (100%) ≥15 mm = 8/9 (88%)
Diel et al. AJRCCM 2008. Updated in Diel et al., AJRCCM 2011 [2,3]	Close Contacts (age 0–60 yrs)	Germany 59% German-born, 41% not German-born	May 2005–Apr 2008	≥2 yrs	954	≥5 mm = 604 (63%) ≥10 mm = 242 (25%)	19	≥5 mm = 17/19 (89%) ≥10 mm =8/19 (42%)
Sackoff et al., IJTLD 2001 [27]	HIV-positive (median $CD4^+$ 186)	U.S. (New York)	Jan 1995–Dec 1995	6–12 mos.	2,197	≥5 mm = 439	23	≥5 mm = 9/23 (39%)
Zhang et al. Chin Med J 2013[28]	Healthcare workers	Beijing	Unknown	60 mos.	101	≥10 mm = 53	1	≥10 mm = 1/1 (100%)
Torres Costa et al., J Occup Med Toxicol 2011[29]	Healthcare workers	Portugal	Jan 2007–Dec 2010	Mean 19 mos.	2,884	≥10 mm = 2,102	4	≥10 mm = 4/4 (100%)
Bakir et al. Annals 2008 [11]	Pediatric close contacts 1 mo.–16 yrs	Turkey	Oct 2002	Mean 1.3 yrs	908	≥5 mm = 550	15	≥5 mm = 12/15 (80%)
Chang et al. Clin Rheum 2011 [20]	Adults with arthritis	South Korea	Aug 2007–Jul 2009	Median 18 mos.	107	≥10 mm = 36	0	N/A

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up	Subjects, No.	Positive TST, No. (%)	Progressed to Active TB, No. (%)	TST Sensitivity for All Cases of Active TB
Comstock et al. AJE 1974 [30]	Children 1–19 yrs	Puerto Rico	1949–1951	~19 yrs	191,827	≥6mm = 82,269	1,400	≥6 mm = 1400/1400 (100%)
Daley et al. AJRCCM 1998;[31]	Adult intravenous drug users 30.5% HIV+	San Francisco	1990–1994	Median 22 mos.	1109	≥5 mm HIV-positive = 96 ≥10 mm HIV-negative = 336	8 (5 HIV-positive, 3 HIV-negative,)	HIV-positive = 3/5 (60%) HIV-negative = 2/3 (67%)
Del Corral et al. PLOS One 2009 [32]	Close Contacts (4% HIV+)	Columbia	Mar 2005–Dec 2006	2 yrs	502	≥10 mm = 331	37	Unclear how many cases were TST-positive
Giri et al. Occ Med 2014 [33]	Healthcare workers	UK	Apr 2009–Mar 2012	<3 yrs	788	≥6 mm = 191	0	N/A
Gourevitch et al. AIDS 1999 [34]	HIV+ (CD4 range 6-1980)	NYC	1985–1996	<11 yrs	431	≥5 mm = 202	25	16/25 (64%)
Guwatudde et al. AJE 2003 [35]	Contacts (age 0->35y; 10% HIV+)	Uganda	Oct 1995–Feb 1999	2 yrs	1206	≥5 mm = 963 ≥10 mm = 801	25	≥5 mm = 23/25 (92%) ≥10 mm = 20/25 (80%)
Harstad et al. IJTLD 2010 [23]	Adult asylum seekers	Norway	Sept 2005–Jun2006	23–32 mos.	823	≥6 mm = 426 ≥15 mm = 128	9	≥6mm = 8/9 (89%) ≥15 mm = 3/9 (33%)
Higuchi et al. Resp 2007 [8]	School children	Japan	Dec 2002	3.5 yrs.	349	≥30 mm = 95	0	N/A
Higuchi et al. J Inf 2009 [36]	School children	Japan	Jan–Feb 2006	3 yrs.	306	≥5 mm = 200 ≥10 mm = 90	0	N/A
Hill et al. PLOS One 2008 [4]	Close contacts >15y (2% HIV+)	Gambia	Jun 2002–Oct 2004	2 yrs.	2348	≥10 mm = 843	26	14/26 (54%)

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up	Subjects, No.	Positive TST, No. (%)	Progressed to Active TB, No. (%)	TST Sensitivity for All Cases of Active TB
Jeyakumar et al. Med J Malaysia 1999 [37]	Nursing students	Malaysia	Jan 1994–Dec 1996	2 yrs	366	≥15 mm = 102	4	3/4 (75%)
Kim et al. AJT 2011 [22]	Renal transplant	Korea	Jun 2008–Dec 2009	>1 yrs	296	≥10 mm = 24	4	0/4 (0%)
Kruczak et al. Scand J Infect Dis 2014 [12]	Homeless, contacts, and Long term care facility residents	Poland	Jul 2007–Sept 2009	4–5 yrs	701	>10 mm = 338	12	7/12 (58%)
Lee et al. Infection 2009 [19]	End stage renal disease	Taiwan	Sept 2005	2 yrs	32	≥10 mm = 20	2	1/2 (50%)
Lee et al. Infection 2009 [19]	Healthy controls	Taiwan	Sept 2005	2 yrs	32	≥10 mm = 21	0	N/A
Leow et al. Exp Clin Endo Diab 2014 [38]	Diabetics	Singapore	Feb 2007–Feb 2012	>1 yrs	220	≥10 mm = 63	0	N/A
Leung et al. Arch Ped Adol Med 2006 [39]	School children	Hong Kong	1999	4 yrs	656	≥20 mm = 656	10	10/10 (100%)
Leung et al. AJRCCM 2010 [21]	Persons with Silicosis	Hong Kong	Dec 2004–Dec 2008	>1 yrs	308	>10 mm = 203	17	13/17 (76%)
Lienhardt et al. PLOS One 2010 [6]	Contacts (>18y)	Senegal	Mar 2004–Apr 2006	2 yrs	2,458	≥10 mm = 1,591	52	39/52 (75%)
Mahomed et al. PLOS ONE 2011;[24]	Adolescents	South Africa	2005–2009	~2 yrs	5,244	≥10 mm = 2,894	52	40/52 (77%)
Markowitz et al.	HIV+ (median	U.S.	Nov	~4.5 yrs	1,130	≥5 mm = 66	28	8/28 (29%)

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up	Subjects, No.	Positive TST, No. (%)	Progressed to Active TB, No. (%)	TST Sensitivity for All Cases of Active TB
Ann Int Med 1997[40]	CD4+ 410)		1988–Feb 1990					
Pullar et al. BMC Inf Dis 2014 [13]	HIV+ (CD4 ~40-488)	Norway	Jan 2009–Oct 2010	2 yrs	217	≥5 mm = 52	0	N/A
Rakotosamimanana et al. Eur Respir J 2015 [41]	Contacts >1y, all HIV-	Madagascar	Unknown	18 mos.	289	≥14 mm = 123	12	10/12 (83%)
Doherty et al. JCM 2002 [42]	Contacts (<5% HIV+)	Ethiopia	Unknown	2 yrs	24	In vitro PPD stimulation	7	7/7 (100%)
Rueda et al. IJTLD 2014 [43]	Incarcerated men (<1% HIV+)	Colombia	Nov 2012–Dec 2013	1 yrs	829	643 (78%)	4	4/4 (100%)
Santin et al. Diag Micro and Inf Dis 2011 [14]	HIV+ (Median CD4 = 300)	Spain	Mar 2007–Nov 2009	Median 600 days	135	≥5 mm = 9	0	N/A
Selwyn et al. JAMA 1992 [44]	HIV+ intravenous drug users	U.S.	Jun 1988–Dec 1990	31 mos.	120	≥5 mm HIV-positive = 52	5	0/5 (0%)
Sester et al. AJRCCM 2014;[18]	HIV+ (Median CD4 302)	Europe	Jun 2008–May 2011	Median 1.8 yrs	768	≥5 mm = 67	10	4/10 (40%)
Silverman et al. Clin Biochem 2007 [45]	Bladder CA with BCG	Canada	Jun–Jul 2004	2 yrs	22	≥5 mm = 15	0	N/A
Song et al. Chest 2012 [10]	School aged pediatric contacts	Korea	May–Jul 2007	2 yrs	1,826	≥10 mm = 270	21	11/21 (52%)
Thomas et al.	Children	Bangladesh	Apr–Jun	1 yr	302	≥10 mm = 101	0	N/A

Study	Group at High Risk	Country	Yr(s)	Duration of Follow-Up	Subjects, No.	Positive TST, No. (%)	Progressed to Active TB, No. (%)	TST Sensitivity for All Cases of Active TB
Pediatrics 2010 [46]			2009					
Wyndham–Thomas BMC Inf Dis 2015 [47]	HIV+ (Median CD4 517)	Belgium	Dec 2011–Dec 2012	1 yr	46	≥5 mm = 4	0	N/A
Joshi et al. Eur Resp J 2011 [48]	Healthcare workers	India	Jan–Jun 2004	6 yrs	719	TST- and QFT-IT positive = 217	14	6/14 (43%)
Yoshiyama et al. IJTLD 2010 [7]	Contacts	Japan	2003–2005	~579 days	856	≥10 mm = 679	12	10/12 (83%)
Sloot et al. AJRCCM 2014 [49]	Contacts (~7% HIV+)	Netherlands	2002–2011	>10 mos.	4,774	≥10 mm = 681	18	14/18 (78%)
Mandalakas et al. AJRCCM 2015 [26]	Pediatric contacts aged 3m-15y (22% HIV+)	Cape Town, South Africa	2008–2012	3 mos.	1,343 (1,044 HIV-negative, 299 HIV-positive)	≥10 mm if HIV-negative = 436 ≥5 mm if HIV-positive = 93	85	57/85 (67%)

Abbreviations: HIV=human immunodeficiency virus; LTBI = latent tuberculosis infection; N/A = not applicable; QFT-IT = QuantiFERON® Gold In-tube; TB = tuberculosis; TST = tuberculin skin test.

Summary of Test Sensitivity (calculated as the proportion of TST- or IGRA-positive cases among those who progressed to active TB):

QFT-IT
HIV-negative, contacts
Range 51.3%–100%
Weighted average 80/109 (73.4%)

HIV-positive
Range 37.5%–100%
Weighted average 6/11 (54.5%)

Children<5

Only 1 study
54/76 (71.1%)

TSPOT

HIV-negative, contacts
Range 50%–75%
Weighted average 36/56 (64.3%)

HIV-positive
Range 40%–66.7%
Weighted average 10/19 (52.6%)

Children<5
Range 62.5%–73.3%
Weighted average 56/87 (64.4%)

TST

HIV-negative, contacts
Range 54%–100%
Weighted average 143/180 (79%)

HIV-positive
Range 0-64%
Weighted average 40/96 (42%)

Children<5
Range 52%–100%
Weighted average 1,490/1,531 (97%)
Exclude Comstock-90/131

Table S4. Combinations of Test Result for Participants, by Group (by Using Borderline as Negative, Cutoff of ≥8 spots = Positive for TSPOT)

Test Combination (TST/QFT/TSPOT)	FB, HIV-, 5+	FB, HIV-, <5	FB, HIV+, 5+	US, HIV-, 5+	US, HIV+, 5+
– – –	3,802	331	95	592	1,095
– – +	62	0	0	4	4
– + –	186	2	8	22	54
– + +	133	0	0	10	9
+ – –	1,730	116	10	53	41
+ – +	136	0	0	5	0
+ + –	415	7	10	16	9
+ + +	1,467	8	17	73	14
Total	**7,931**	**464**	**140**	**775**	**1,226**

Abbreviations: FB = foreign-born; HIV = human immunodeficiency virus; 5+ = age 5 years and older; <5=under 5 years of age; TST=tuberculin skin test; QFT=QuantiFERON Gold in-tube; TSPOT=TSPOT.TB; +=positive test; -=negative test

Table S5. Estimated Prevalence and Test Characteristics Derived from the Three-Test, Random Effects Model by Using the U.S. TSPOT Cutoff in Specified Groups, Treating Borderline Results (5-, 6-, or 7-spot Difference) as Negative. Parameter Values Are Mean Estimates with 95% Credible Intervals in Parentheses

Parameter	FB, HIV-, 5+	FB, HIV-, <5	FB, HIV+, 5+	US, HIV-, 5+	US, HIV+, 5+
LTBI prevalence	34.0% (27.7–39.3)	3.6% (1.6–6.2)	15.2% (0.1–42.6)	17.3% (12.8–22.4)	3.9% (2.4–5.8)
TST					
Sensitivity	80.6% (72.5–90.5)	69.4% (58.7–80.0)	57.7% (47.9–68.2)	73.4% (62.7–85.4)	54.5% (45.0–64.9)
Specificity	70.0% (68.3–71.5)	73.7% (69.5–77.8)	79.0% (64.7–95.2)	92.2% (89.8–94.4)	96.4% (95.2–97.5)
QFT–IT					
Sensitivity	78.8% (69.5–90.2)	73.4% (57.0–88.1)	57.9% (38.6–74.7)	77.8% (64.4–91.1)	70.0% (55.3–83.9)
Specificity	98.5% (96.1–99.8)	98.8% (97.2–99.8)	82.7% (67.9–98.7)	97.6% (95.7–99.3)	95.7% (94.3–97.0)
TSPOT					
Sensitivity	73.5% (63.8–86.3)	56.7% (39.8–74.6)	47.2% (31.5–68.0)	66.1% (53.0–81.8)	52.5% (38.1–68.2)
Specificity	99.3% (98.0–99.9)	99.6% (98.8–99.9)	91.8% (81.9–99.7)	99.4% (98.5–99.9)	99.6% (99.1–99.9)

Abbreviations: HIV = human immunodeficiency virus; LTBI = latent tuberculosis infection; NPV = negative predictive value; PPV = positive predictive value; QFT-IT = QuantiFERON® Gold In-Tube; TSPOT = T-SPOT®.TB; TST = tuberculin skin test.

Figure S1. Latent tuberculosis prevalence and test characteristics (sensitivity and specificity) by prespecified groups. On the x–axis, the label "CI" stands for the model that assumes conditional independence of the tests, "R" stands for the model that includes a random effect (to model conditional dependence between the tests), and "Prior" shows the literature–based prior distribution (for test sensitivity only). The horizontal lines in the center of the rectangles are the Bayesian posterior means, whereas the top and bottom lines in each box are the boundaries of the first and third quartiles, respectively. The tips of the vertical lines span the 95% credible interval for each parameter. For purposes of this analysis, TSPOT was evaluated by using the international criteria for a positive test (≥6 spots is positive; ≤5 spots is negative).

Abbreviations: CI=conditional independence model; prev = latent tuberculosis prevalence; Prior=scientific literature-based prior distribution (for test sensitivity only); R=random effect model; sensQFT = sensitivity of QuantiFERON® Gold In-Tube; sensTSPOT = sensitivity of T-SPOT®.TB; sensTST = sensitivity of the tuberculin skin test; specQFT = specificity of QuantiFERON Gold In-Tube; specTSPOT = specificity of T-SPOT.TB®; specTST = specificity of the tuberculin skin test.

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