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Comparison of Two Interferon-Gamma Release Assays for Pediatric Tuberculosis Infection

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Abstract

Introduction: Identifying tuberculosis infection (TBI) using interferon-gamma release assays (IGRAs) is a primary component of clinical and public health efforts to prevent pediatric tuberculosis (TB). Pediatric data comparing the 2 IGRAs in the United States are very limited. We compared the performance of the 2 IGRAs among a large pediatric cohort tested for TBI and assessed whether discordance might be due to quantitative results close to test cutoff values.

Methods: Children aged 0–15 years with both T-SPOT.*TB* (T-SPOT) and QuantiFERON-TB Gold In-Tube (QFT-GIT) tests were identified from a US multicenter study enrolling people at elevated risk of TBI or progression to TB disease. Results were compared using McNemar's Chi-square tests with stratification by age category and testing reason. Percent agreement and kappa statistics were also calculated. We characterized quantitative test results among children with discordant QFT-GIT-positive/T-SPOT-negative results.

Results: Among 3793 children, a higher number had positive QFT-GIT than T-SPOT (10.1% vs 7.4%, $P < .001$). This difference was noted for all age categories except <2 years, and for children with close-contact and non-close contact test indications. Among discordant QFT-GIT-positive/T-SPOT-negative children, lowering the positive threshold for T-SPOT to include borderline spot

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Conflicts of interest
None declared.

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counts (5–7) did not eliminate the discordance, nor were QFT-GIT antigen-minus-nil results concentrated in the range just above the standard cutoff of 0.35 IU/mL.

Conclusions: In a large pediatric cohort tested for TBI, QFT-GIT had a higher proportion of positive results than T-SPOT, and discordance was not related to quantitative results close to the established diagnostic cutoffs.

Keywords

T-SPOT.*TB*; children; tuberculosis; pediatric; tuberculosis infection; QuantiFERON-TB Gold In-Tube

INTRODUCTION

Identification and treatment of tuberculosis infection (TBI) are cornerstones of tuberculosis (TB) elimination efforts in the United States and other low-TB-incidence countries.^{1,2} Children represent a priority population within these activities for several reasons, including a higher likelihood of rapid progression to severe disease, particularly among the very young.³ Furthermore, children with TBI who are not treated represent a reservoir of potential future TB cases.

The 2 most common scenarios for TBI screening in children in low-incidence countries are following travel to or relocation from high-TB-incidence countries and in the course of contact investigation of a TB case.⁴ In both situations it is desirable to utilize testing that is sensitive (to avoid missing children with TBI who may progress to active disease) and specific (to avoid unnecessary resource utilization for further evaluation and treatment). Screening for TBI in low-incidence countries, including among younger children <5 years, increasingly relies on the use of interferon-gamma release assays (IGRAs), of which the 2 available in the United States during this study were QuantiFERON-TB Gold In-Tube (QFT-GIT, Qiagen, Maryland, United States) and T-SPOT.*TB* (T-SPOT, Oxford Immunotec, Inc., Massachusetts, United States).⁵ The tuberculin skin test (TST) is limited by poor specificity (particularly in persons vaccinated with Bacille Calmette-Guérin [BCG]), decreasing expertise in placement and interpretation of the test, and a requirement for 2 visits.⁶

Current US guidance expresses no preference for 1 IGRA over the other.⁷ Several studies in adults have examined differences in performance of the 2 assays for the diagnosis of both TB disease and TBI, including in special circumstances such as HIV infection and other immune compromising conditions and older age.^{8,9} Results from these studies are heterogeneous, but most observe equivalence between the assays. Pediatric data comparing the performance of QFT-GIT with T-SPOT are more limited and only a very small number of studies (with very low overall subject numbers) directly compare the 2 IGRAs for diagnosis of TBI in low-TB-incidence settings, with none reporting statistically significant differences between the 2 assays.^{10–12} All studies assessing IGRA test performance in TBI are hampered by the fact that there is no direct test to confirm infection microbiologically.

To inform the optimal use of IGRAs in children at risk for TBI for clinicians and public health programs in the United States, we conducted a study to determine (1) if there were significant differences in test results between the 2 IGRAs performed to identify TBI in children and (2) to assess whether slight changes in cutoff values would impact observed differences. To do this, we analyzed data from children who were tested for TBI with both QFT-GIT and T-SPOT in a prospective study conducted at multiple US-based academic centers and public health facilities.

METHODS

Study Population

The Tuberculosis Epidemiologic Studies Consortium is a partnership of academic and public health TB programs funded by the Centers for Disease Control and Prevention (CDC) to perform observational epidemiologic studies related to the diagnosis, treatment, and prevention of *Mycobacterium tuberculosis* infection.¹³ Participants included in this study were part of a larger study to assess the performance of IGRAs and TST to predict progression to TB disease in persons of all ages who were at high risk of TBI. Detailed comparisons between IGRAs and TST in the pediatric study population were previously reported.⁴ Details of enrollment are described by Ho et al.¹⁴ Briefly, participants were eligible for enrollment if they were (1) close contacts of individuals with microbiologically confirmed pulmonary TB, (2) non-US-born, which includes birth in a country whose population in the United States had a high TB incidence (≥ 100 cases/100 000), or recent arrivals (≤ 5 years) from a country with moderate TB incidence in the United States (10–99 cases/100 000), (3) spent ≥ 30 days in the previous 5 years in countries whose populations in the United States have high TB incidence, (4) member of a local population with $\geq 25\%$ prevalence of TBI, or (5) a person with HIV infection.¹⁵ Participants were enrolled between July 2012 and May 2017.

Participants from the larger study were eligible for inclusion in this study if they were: (1) <15 years old at the time of enrollment and (2) had both IGRA tests performed as part of their initial or subsequent evaluation. Many participants had multiple tests performed at different time points. This occurred either because initial results were missing, indeterminate (QFT-GIT), or invalid (T-SPOT), or because repeat testing was done for contacts following completion of the window period (the 8- to 10-week period after last known exposure to TB case but potentially before IGRA serologic conversion). The most recent test was utilized if the result was interpretable (ie, not indeterminate or invalid) unless the initial test was already positive. This created a dataset where all participants had valid results for both tests and included the most recent result for contacts with repeat tests.

Participants were excluded if they had a diagnosis of TB disease at the time of enrollment or if they were initially deemed a contact to an active case who was subsequently determined to not have TB disease and did not meet any other enrollment criteria. Parental consent was obtained for all child participants, and written assent where required. Sites obtained approval from a local institutional review board (IRB) or deferred to the CDC IRB.

Study Procedures

Participant characteristics, including demographic and TB-related risk factors, were documented at each site with a standardized questionnaire. After enrollment, participants were tested with QFT-GIT, T-SPOT, and TST, although the TST results were not included in this analysis. Tests were performed according to manufacturers' instructions.^{16,17} Final test results and quantitative test characteristics (mitogen, nil, antigen, and antigen-minus-nil for QFT-GIT, and spot count for nil and panel A-minus-nil or panel B-minus-nil for T-SPOT) were recorded. The cutoff for QFT-GIT positivity was ≥ 0.35 IU/mL and for T-SPOT ≥ 8 spots.

Statistical Analysis

Descriptive statistics were used to characterize the study population. The primary comparison was the proportion of positive tests between the 2 IGRAs using McNemar's Chi-square tests with McNemar's Exact tests used for comparisons with small numbers (defined as "b + c" < 25 in the 2×2 table). Percent agreement and kappa statistics were also calculated for the 2 assays. Because the underlying pretest probability of positive results differs between participants evaluated in the context of contact investigation and those with TB infection risk based on exposure in high-incidence settings, we compared positive IGRA proportions for each enrollment category. Subgroup analysis was also done by age group (0–1, 2–4, 5–9, and 10–14 years).

Because we observed a higher proportion of QFT-GIT-positive results compared with T-SPOT, we performed additional analyses to evaluate the possibility that discordance might be due to quantitative values close to the cutoff for positive/negative. The US Food and Drug Administration defines T-SPOT results with counts of 5, 6, or 7 as borderline, and recommends retesting.¹⁷ Some experts have proposed to consider a narrow range above the positive cutoff (0.35–1.0 IU/mL) as a potential borderline result among low-TB-incidence populations that may result in negative results with repeat testing.^{18,19} Among participants with positive QFT-GIT results and negative T-SPOT, we assessed the extent to which defining borderline T-SPOT results as positive would reduce discordance. Similarly, we assessed the quantitative characteristics of the antigen-minus-nil results from QFT-GIT tests from the same subgroup of participants, to characterize the number of results within the proposed borderline range and describe the impact on test comparisons of redefining QFT-GIT results in this range as negative.

RESULTS

Of 3939 subjects in the initial dataset, 10 (0.3%) participants had indeterminate QFT-GIT, 13 (0.3%) had invalid T-SPOTs, 2 (0.1%) had both indeterminate and invalid results, and 121 subjects had at least 1 missing test, resulting in 3793 participants <15 years old who received both QFT-GIT and T-SPOT tests and had valid results (positive or negative) during the study period. The study cohort was comprised of participants of diverse ages and race/ethnicity (Table 1). Most (91.6%) were non-US-born and approximately 11% were close contacts of a TB disease case. A small proportion of subjects (121, 3.2%) had both contact and non-contact reasons for enrollment reported; these cases were considered close contacts

for sub-analyses. Almost half were from Africa and Southeast Asia (data not shown). Approximately two-thirds of participants reported BCG vaccination.

Participants had a higher number of positive QFT-GIT results compared with T-SPOT (10.1% vs 7.4%, $P < .001$; Table 2 and Figure 1A). This observation remained true among both close contacts to an active case (17.6% vs 12.3%, $P < .001$) as well as participants with non-contact test indications (9.3% vs 6.8%, $P < .001$) (Figure 1B). Higher proportions of positive QFT results compared with T-SPOT were observed across all age groups with the exception of children <2 years, in which there were only 3 children with a positive QFT-GIT and 1 with positive T-SPOT (Figure 1C). Among all participants, test agreement was 96.5% with a kappa statistic of 0.78; similar results were noted for contacts (agreement 93.3%, kappa 0.74) and those enrolled with non-contact indications (agreement 96.9, kappa 0.79). There were 118 participants with a positive QFT-GIT and negative T-SPOT and 15 with a positive T-SPOT and negative QFT-GIT. Subjects with either combination of discordant results did not differ from the total sample in terms of age distribution, sex, or race/ethnicity, but the QFT-positive/T-SPOT-negative group had a slightly higher proportion of contacts (21% vs 11%) and slightly lower BCG vaccination (72% vs 65%). Thirteen participants were treated for TB disease within 30 days after initial evaluation. Of these, 9 were QFT-GIT positive and 7 were T-SPOT positive; one of the 2 discordant subjects had a borderline spot count on the T-SPOT.

We then analyzed whether changes in cutoffs for the 2 IGRAs would reduce the observed differences in positive proportions and increase the correlation between the 2 assays (Figure 2). Lowering the T-SPOT-positive threshold by defining spot counts of 5–7 as positive resulted in 48 additional positives but did not eliminate the difference in positive test proportions (10.1% positive QFT-GIT vs 8.7% T-SPOT; $P < .001$, McNemar's test). Of the 118 participants with positive QFT-GIT and negative T-SPOT, 21 (18%) changed to positive on both assays with the ≥ 5 spot criteria. However, an additional 27 participants became T-SPOT positive but QFT-GIT negative (Table 3). Of the 48 additional T-SPOT positives using the lower spot count, 21 (44%) had a positive QFT-GIT. In analysis of quantitative QFT-GIT results among the positive QFT-GIT/negative T-SPOT participants, 52% of antigen-minus-nil results fell between 0.35 and 1.0 IU/mL, and 48% had results > 1 IU/mL; the median was 0.95 IU/mL and interquartile range (IQR) was 0.47–2.81 IU/mL (these values among participants with concordant positive IGRAs was a median of 7.24 and IQR of 4.0–10 IU/mL). Reassigning results in the 0.35–1.0 IU/mL range to negative resulted in 85 fewer QFT-GIT positives, narrowing the difference in positive test proportion (7.6% positive QFT-GIT vs 7.1% T-SPOT; $P = .08$, McNemar's test) but 24 of these added QFT-GIT negatives were from individuals with positive T-SPOTs. Of the 85 subjects with a QFT-GIT antigen-minus-nil of 0.35–1.0 IU/mL, 24 (28%) had a positive T-SPOT.

Among contacts to active cases, lowering the threshold for a positive T-SPOT to ≥ 5 spots increased the number of positives by 24% (12 cases) (Supplementary Table). The overall positive rate increased from 12.3% with the established 8-spot cutoff to 15.2%, but remained lower than the QFT-GIT-positive rate of 17.6% ($P = .05$, exact McNemar's test). Of the 12 new positives with the lower T-SPOT threshold, 7 (58%) were from individuals who were QFT-GIT positive.

DISCUSSION

In this study from a large pediatric population tested for TB infection in the United States, we observed a higher proportion of positive QFT-GIT results than T-SPOT results. This observation was consistent across age groups (except in the <2-year group, where the numbers were too low to be significant), and was noted among both close contacts to active cases as well as among participants screened for non-contact indications. Discordance between the 2 assays was not driven by quantitative results close to the established positive/negative cutoffs for each assay. These findings can help public health and medical providers in selecting an IGRA assay for pediatric TB infection screening among populations at elevated risk of TB infection or progression to TB disease similar to those in this study.

A large body of literature has evaluated the performance of IGRAs compared with TST in pediatric populations, but relatively few studies have compared the 2 IGRA assays to each other. A systematic review of pediatric studies comparing the 2 assays for the diagnosis of TB disease in children found a higher sensitivity of QFT-GIT compared with T-SPOT among patients in high-income countries, but no significant differences in low-income countries when comparison was limited to microbiologically confirmed TB or among immunocompromised patients.¹² Data are very limited for pediatric TB infection screening among otherwise healthy children in low-TB-incidence countries; in a Spanish study of adults and children tested for TB disease or TBI, T-SPOT had higher proportions of positive results overall, but among the 125 pediatric patients screened for TBI there was no difference (36.0% T-SPOT vs 35.2% QFT-GIT).¹⁰

While the IGRAs are commonly considered as a whole, they have notable differences in assay methodology. QFT-GIT assesses cell-mediated immunity through stimulation of CD-4 cells in whole blood with TB antigens ESAT-6, CFP-10, and TB7.7, and measures interferon-gamma using an enzyme-linked immunosorbent assay. T-SPOT measures interferon-gamma release from isolated peripheral blood mononuclear cells after stimulation with ESAT-6 and CFP-10 antigens, using an enzyme-linked immunosorbent spot assay. Despite these differences, there is no clear hypothesis for why one assay would perform better among healthy children with TBI. Both assays result in continuous quantitative output (antigen-minus-nil or spot count) that is converted to a binary result based on values validated to maximize test performance. Therefore, 1 plausible explanation for the differences observed in our population could be that the QFT-GIT-positive/T-SPOT-negative discordant test combinations we observed had quantitative results close to the respective cutoffs. While this is a plausible factor and may explain a proportion of discordant results, our observations do not fully support this hypothesis. Including T-SPOT results with 5, 6, and 7 spots did not completely eliminate the gap in the proportion of positive tests between the 2 assays, and many of these borderline results had negative QFT results—particularly among subjects with non-contact test indications—suggesting that the lower T-SPOT threshold decreased T-SPOT specificity. Among the QFT-GIT-positive/T-SPOT-negative children, approximately half had antigen-minus-nil values for QFT-GIT in the lower range between 0.35 and 1.0 IU/mL cutoff and a significant proportion (25/84) of these had positive T-SPOT tests, suggesting the increased threshold results in decreased sensitivity. Recent (2024) guidance from the American Academy of Pediatrics recommends that for children at

a low epidemiologic risk for TB with low-level positive QFT-GIT (antigen-minus-nil of <1.0 µg/mL) or borderline T-SPOT (spot count of 5–7) should have a second test (either IGRA or TST) performed and considered to have TB infection only if the second test is positive.⁵ This recommendation assumes an equivalence between the T-SPOT results with borderline spot count and QFT-GIT results between 0.35 and 1.0 IU/mL that is not clearly supported by our observations. If the QFT-GIT does indeed have greater sensitivity than T-SPOT, then a recommendation to rely on T-SPOT for low-level QFT-GIT positives may incorrectly discard a true-positive result. Future guidance may need to consider whether a different approach to low-level positive results is warranted depending on which test was performed.

A detrimental impact of time between collection and processing on test sensitivity has been noted for both QFT-GIT and T-SPOT, and an additional potential explanation for our results could be that this impact was greater for the T-SPOT than QFT in our population.^{20–22} T-SPOT samples from all but 1 site (Hawai'i) were sent to the Oxford Immunotec central processing facility in Memphis, TN, United States for testing and all QFT-GIT assays were performed at respective study sites.¹⁴ However, more detailed data on preprocessing time are not available for our study cohort, preventing the assessment of this hypothesis. Improvements to facilitate T-SPOT test automation and extend the allowable time between collection and processing have been recently reported.²³

In the absence of a definitive reference standard for confirmation of TBI, it is not possible to determine whether the observed differences between the 2 assays represent greater sensitivity or lower specificity of QFT-GIT compared with T-SPOT. However, some specific findings in our data tend to support greater QFT-GIT sensitivity. The relative difference in proportion positive between QFT-GIT and T-SPOT in contacts is slightly higher (43%) than in participants with non-contact test indications (35%), which would argue against a consistent level of false positivity among QFT-GIT that would be unaffected by epidemiologic risk. Furthermore, if a significant proportion of QFT-GIT results are false positives, we would have expected more positive results among the youngest participants who have the lowest overall risk of TBI because of their shorter lifetime potential TB exposure. However, there were only 3 positive QFT-GIT results among 221 children <2 years.

Even in the absence of a definitive understanding of whether QFT-GIT is more sensitive or less specific than T-SPOT in children, public health programs and healthcare providers may select tests with the goal of maximizing the identification of potential infection. Children are at high risk of progression to active disease, particularly in the early phase after infection, and young children are at risk of rapid progression to severe disease. TBI treatment is well-tolerated in children and contributes to TB elimination efforts by reducing the pool of potentially infectious future cases. Evidence of the general preference to maximize TBI diagnosis at the cost of some specificity in the United States can be found in the longstanding reliance on TST for this purpose, despite very poor specificity among BCG-vaccinated children. In this context, our data suggest that QFT-GIT might be preferable over T-SPOT. An alternate strategy to maximize sensitivity suggested by our findings would be to consider borderline T-SPOT results as positive among children at higher risk. In our study population, including spot counts of 5–7 resulted in a 24% relative

increase in positives, and the majority of these subjects had a positive QFT-GIT. However, 2 important points must be factored into these considerations. First, though we observed significantly more positive QFT-GIT tests than T-SPOT, instances in which the T-SPOT was positive and QFT-GIT was negative did also occur, so the use of QFT-GIT will not capture every possible positive. Second, if the goal of screening is to prevent active TB, the 2.7% absolute difference in positive results (even if all of these are additional true positives) represents a relatively low number of potential future TB cases. Our observations have limited applicability outside of populations in high-income, low-TB-incidence countries with a low proportion of persons who are immune compromised, malnourished, or have HIV infection, as well as limited applicability for persons being evaluated for diagnosis of TB disease. Nevertheless, this focused population (children considered at risk for TBI or progression to disease) and purpose (screening for infection) represent major components of pediatric TB-related activities in the United States and similar countries. In this study, participants were tested using the QFT-GIT, which has since been replaced by a newer generation, the QuantiFERON-TB Gold Plus designed for enhanced sensitivity due to an additional tube measuring both CD-4 and CD-8 T cell stimulation (while eliminating the TB7.7 antigen).²⁴ In a recent comparison of QFT-GIT and QuantiFERON-TB Gold Plus drawn simultaneously in a US population, Gold Plus was associated with an increase in positive results, consistent with increased sensitivity. However, among 77 children under 15 years old, 100% test concordance between the 2 versions was observed. Whether the reported increase in sensitivity with the newer assay would increase the observed difference in test positivity among children tested for TB infection compared with T-SPOT is unknown.

In conclusion, among a large cohort of children tested for TBI in US TB programs using 2 IGRA assays, the proportion of positive tests was higher for QFT-GIT than T-SPOT. Clinicians and public health programs should recognize these differences and consider potential implications when selecting and interpreting TBI tests for children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The data underlying this article are available in the public domain.²⁵

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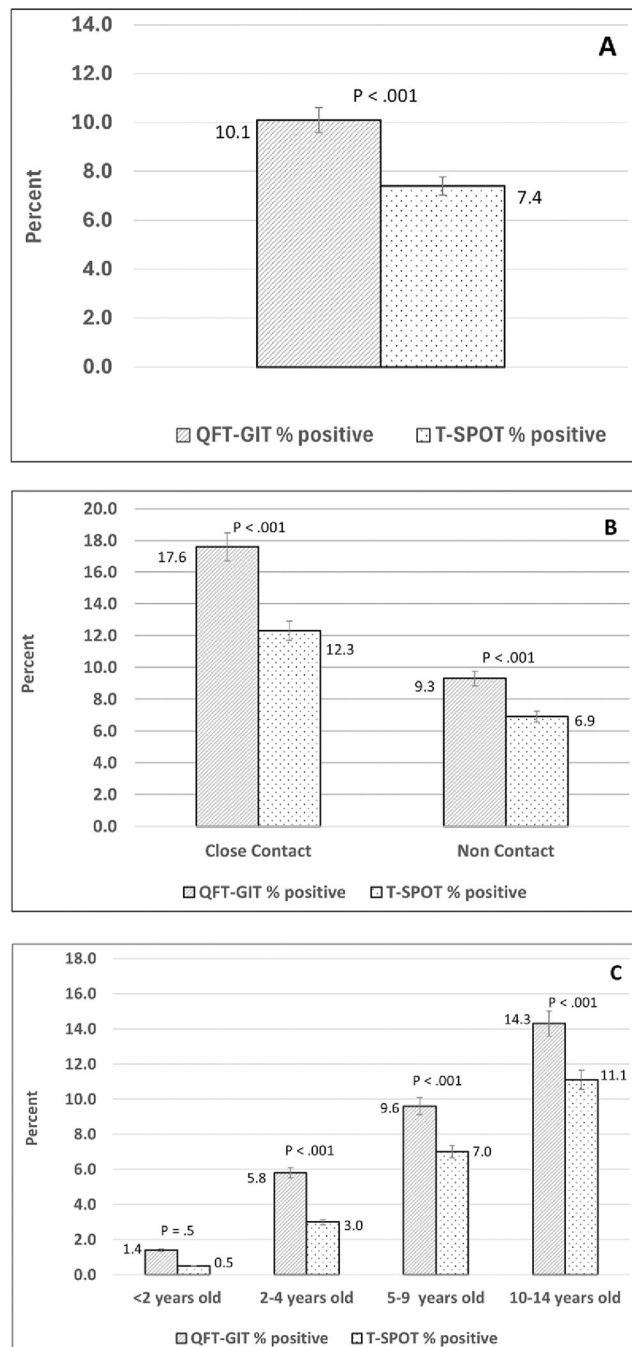


Figure 1.

The Proportion of Positive QuantiFERON-TB Gold In-Tube (QFT-GIT) and T-SPOT. *TB* (T-SPOT) Results Among 3793 Participants Under 15 Years: Overall (A), by Reason for Screening (B; $n = 3773$), and Age Category (C).^{a,b} ^ap-value from McNemar's Chi-square test/exact McNemar's test, ^bError bars for percent

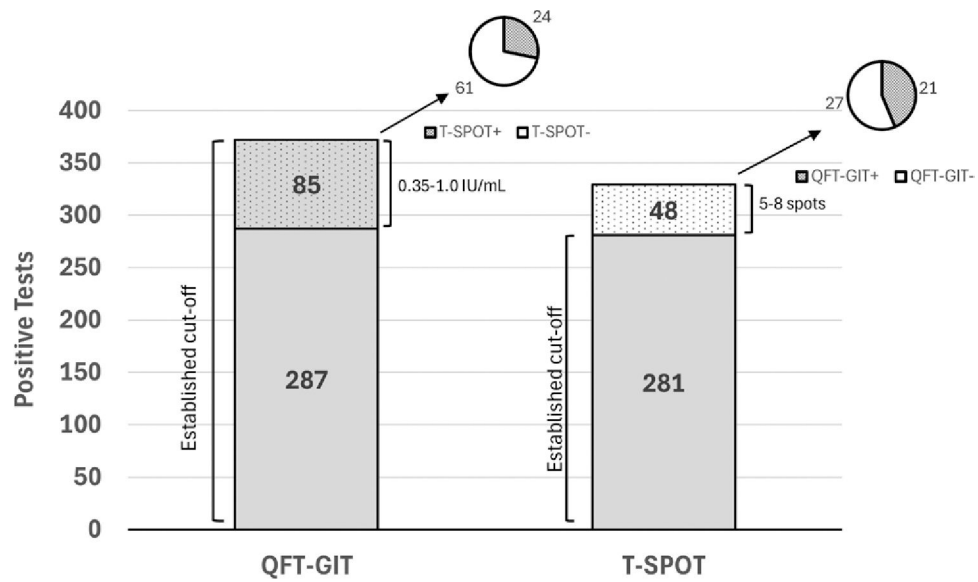


Figure 2. Numbers of Positive QuantiFERON-TB Gold In-Tube (QFT-GIT; $n = 3780$) and T-SPOT.TB (T-SPOT; $n = 3793$) Tests Based on Established Diagnostic and Alternative Cutoffs for Positive Results, With a Demonstration of Opposite Test Results Among Subjects With Quantitative Results in the Range Between Established and Alternative Cutoffs

Table 1.

Demographics and Other Characteristics of 3793 Study Participants Under Age 15 Years With Both T-SPOT, *TB* and QuantiFERON-TB Gold In-Tube Performed and Who Had Positive or Negative Results

Characteristic	N (%)
Gender (% female)	1868 (49.2)
Age category	
<2 years old	221 (5.8)
2–4 years old	712 (18.8)
5–9 years old	1340 (35.3)
10–14 years old	1485 (39.2)
Missing	35 (0.9)
Reason(s) for enrollment	
Close contact to TB ^a case	415 (10.9)
Non-US-born ^b	3473 (91.6)
Spent ≥30 days in a country with high TB-incidence rates ^c	1182 (31.2)
Other ^d	12 (0.3)
Self-reported race/ethnicity ^e	
Hispanic	311 (8.2)
Non-Hispanic	
American Indian or Alaska Native	15 (0.4)
Asian	1278 (33.7)
Black	844 (22.3)
White	207 (5.5)
Native Hawaiian or other Pacific Islander	70 (1.9)
Other	967 (25.5)
Unknown	131 (3.5)
Reported BCG ^f -vaccine receipt	
Yes	2470 (65.6)
No	948 (25.2)
Unknown	375 (9.9)
HIV infected ^g	
Yes	7 (0.2)
No	3739 (98.2)
Unknown	47 (1.2)

^aTuberculosis.

^bBirth in a country whose population in the United States had a high TB incidence (≥100 cases/100 000), or recent arrival (≤5 years) from a country with moderate TB incidence in the United States (10–99 cases/100 000).

^cSpent ≥30 days in the previous 5 years in countries whose populations in the United States have high tuberculosis incidence.

^dMember of a local population with ≥25% prevalence of tuberculosis infection or a person with infection with human immunodeficiency virus.

^e All races are non-Hispanic, subjects may have selected multiple races; “Other” was an available category for selection.

^f Bacille Calmette-Guérin vaccine.

^g Human immunodeficiency virus.

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Table 2.

The Proportion of Positive Interferon-Gamma Release Assay Results Among 3793 Participants Stratified by Tuberculosis Infection Screening Indication and by Age Category

Population	Proportion positive (%)			P value ^{a,b}
	Quantiferon-TB Gold In-Tube	T-SPOT.TB		
Total	384/3793 (10.1)	281/3793 (7.4)		<.001 ^a
Screening indication ^c				
Close contact to an active case	73/415 (17.6)	51/415 (12.3)		<.001 ^b
Non-contact screening indication ^d	311/3358 (9.3)	230/3358 (6.8)		<.001 ^a
Age category (y) ^e				
0–1	3/221 (1.4)	1/221 (0.5)		.5 ^b
2–4	41/712 (5.8)	21/712 (2.9)		<.001 ^b
5–9	128/1340 (9.6)	94/1340 (7.0)		<.001 ^a
10–14	212/1485 (14.3)	165/1485 (11.1)		<.001 ^a

Abbreviation: TB, tuberculosis.

^aMcNemar’s Chi-square test.

^bExact McNemar’s test.

^c*n* = 3773; 20 values missing.

^dEvaluated for TB infection because of birth in a country whose population in the United States had a high TB incidence (≥100 cases/100 000), recent arrivals (≤5 years) from a country with moderate TB incidence in the United States (10–99 cases/100 000), member of a local population with ≥25% prevalence of TBI, spent ≥30 days in the previous 5 years in countries whose populations in the United States have high tuberculosis incidence, or a person with human immunodeficiency virus (HIV) infection, and not also a close contact to an active case.

^e*n* = 3758; 35 values missing.

Table 3.

Interferon-Gamma Release Assay Result Combinations Among Participants Using Different Positive T-SPOT. TB (T-SPOT) and QuantiFERON-TB Gold In-Tube (QFT-GIT) Cutoffs

Test combinations with different T-SPOT cutoffs, n = 3793						
Positive T-SPOT ≥8 spots		Positive T-SPOT ≥5 spots		Change (T-SPOT ≥5 minus T-SPOT ≥8 spots)		
Result pattern	N	%	n	%	N (% change ^d)	
T-SPOT+ total	281	7.4	329	8.7	48 (17%)	
T-SPOT+/QFT-GIT+	266	7.0	287	IB	21 (8%)	
T-SPOT-/QFT-GIT+	118	3.1	97	2.6	-21 (-18%)	
T-SPOT+/QFT-GIT-	15	0.4	42	1.1	27 (180%)	
T-SPOT-/QFT-GIT-	3394	89.5	3367	88.8	-27 (-1%)	
QFT+ total	384	10.1	384	10.1		
Test combinations with different QFT-GIT cutoffs, n = 3780 ^b						
Positive ≥QFT-GIT 0.35 IU/mL		Positive ≥QFT-GIT 1.0 IU/mL ^b		Change (QFT-GIT 1.0 minus QFT-GIT 0.35 IU/mL)		
Result pattern	n	%	n	%	N (% change ^d)	
QFT-GIT+ total	372	9.8	287	IB	-85 (-23%)	
QFT-GIT+/T-SPOT+	255	6.7	231	6.1	-24 (-9%)	
QFT-GIT-/T-SPOT+	15	0.4	39	1.0	24 (160%)	
QFT-GIT+/T-SPOT-	117	3.1	56	1.5	-61 (-52%)	
QFT-GIT-/T-SPOT-	3393	89.8	3454	91.4	61 (2%)	
T-SPOT+ total	270	1.1	270	1.1		

^aPercent change calculated as the number of reclassified positive results with the lower spot count/number of initial results × 100.

^bn = 3780 for these calculations due to missing data.