Evaluation of QuantiFERON®-TB Gold-Plus in Healthcare Workers in a Low-Incidence Setting

Hee-Won Moon,[1,3] Rajiv L. Gaur[1], Sara Shu-Hwa Tien[4], Mary Spangler[4], Madhukar Pai[5] and Niaz Banaei[1,2,6]

[1]Pathology and [2]Medicine, Division of Infectious Diseases & Geographic Medicine, Stanford University School of Medicine, Stanford, CA, [3]Department of Laboratory Medicine, Konkuk University School of Medicine, Seoul, Korea, [4]Occupational Health Clinic, Stanford Health Care, [5]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Canada, [6]Clinical Microbiology Laboratory, Stanford Health Care, CA, USA

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Correspondence

Niaz Banaei, MD

Rm. 1602, 3375 Hillview Ave, Palo Alto, CA 94304

Phone: 650-736-8052 Fax 650-725-5671

E-mail: nbanaei@stanford.edu

ABSTRACT

Background: Although launched in 2015, little is known about the accuracy of QuantiFERON-TB Gold-Plus (QFT-Plus) for diagnosis of latent *M. tuberculosis* infection (LTBI). Unlike its predecessor, QFT-Plus utilizes two antigen tubes to elicit an immune response from CD4+ and CD8+ T lymphocytes. We conducted a cross-sectional study in low-risk healthcare workers (HCWs) at a single U.S. center to compare QFT-Plus to QuantiFERON-TB Gold in-tube (QFT).

Method: 989 HCWs were tested with both QFT and QFT-Plus. Risk factors for LTBI were obtained from a questionnaire. QFT-Plus was considered positive if either antigen tube 1 (TB1) or TB2 tested positive, per the manufacturer's recommendations, or if both TB1 and TB2 tested positive, using a conservative definition. Results were compared using Cohen's Kappa and linear regression, respectively.

Results: Agreement of QFT with QFT-Plus was high at 95.6% (95% CI, 94.3-96.9, Kappa, 0.57). Majority of discordant results between QFT and QFT-Plus TB1 (84.8%) and QFT and QFT-Plus TB2 (88.6%) fell within the range of 0.2-0.7 IU/mL. Positivity rate in 626 HCWs with no identifiable risk factors and no self-reported history of positive LTBI tests was 2.1% (CI, 1.0-3.2) and 3.0% (CI, 1.7-4.3) with QFT and QFT-Plus, respectively. A conservative definition of QFT-Plus positive yielded a positivity rate of 1.0% (CI, 0.2-1.7, $P = 0.0002$ vs. QFT-Plus and 0.07 vs. QFT). On follow-up testing, of 11 HCWs with discordant QFT-Plus results, 90.9% (10/11) had a negative QFT result.

Conclusions: The QFT-Plus assay showed high degree of agreement with QFT in U.S. HCWs. A conservative interpretation of QFT-Plus identified nearly all non-reproducible positive results in low-risk HCWs. Larger studies are needed to validate the latter finding and to more clearly define conditions under which a conservative interpretation can be used to minimize non-reproducible positive results in low-risk populations.

Key words: QFT, QFT-Plus, Healthcare worker, low-incidence, Tuberculosis

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72 **INTRODUCTION**

73 Periodic screening for latent *Mycobacterium tuberculosis* infection (LTBI) is a mandated
74 component of occupation and student health programs in many high-income countries (1). It
75 is intended to identify recently infected individuals and treat them with preventive therapy to
76 avoid development of active disease (2).

77 In the past decade, many health care institutions in the U.S. have switched from tuberculin
78 skin test (TST) to interferon-γ (IFN-γ) release assay (IGRA), in particular the QuantiFERON-
79 TB Gold in-tube assay (QFT, Cellestis/Qiagen, Carnegie, Australia), for annual screening of
80 health care workers (HCWs) (1, 3). Advantages of IGRA over the TST include improved
81 specificity in individuals with bacillus Calmette–Guérin (BCG) vaccination and certain non-
82 tuberculous mycobacterial infections. Moreover, IGRA eliminates the need for a second
83 nurse visit, thus offering operational and economic advantages over TST (2). However,
84 studies conducted in HCWs and students in low-incidence settings have shown high
85 conversion rates with IGRA which exceed the historical or contemporary TST rates (4-
86 6). Also, high rates of reversions and issues with poor reproducibility have also been
87 documented (4, 7). Since positive results can precipitate unnecessary follow up and

preventive treatment in low-risk HCWs, the accuracy of IGRA has important implications for patient safety and overutilization of resources (8).

In 2015, the next generation of QFT, QuantiFERON-TB Gold-Plus (QFT-Plus) (Qiagen), was launched in Europe and is undergoing clinical trials in the U.S. QFT-Plus employs two TB antigen tubes (TB1 and TB2) for diagnosis of *M. tuberculosis* (MTB) infection. Per the manufacturer's recommendations, QFT-Plus is interpreted positive when either antigen tube results positive. Both antigen tubes include peptides from MTB complex-specific antigens ESAT-6 and CFP-10. While peptides in TB1 and QFT antigen tube are designed to elicit an IFN-γ response from CD4+ helper T lymphocytes, TB2 contains an additional set of peptides to also elicit a response from CD8+ cytotoxic T lymphocytes. CD8+ T lymphocytes are an important component of host immunity to MTB and produce IFN-γ in vitro after stimulation with MTB antigens (9-11). Moreover, ESAT-6- and CFP-10-responsive CD8+ T lymphocytes are more frequently detected in subjects with active TB than during latent infection (12-14). They are also detected at a higher frequency after recent infection compared with remote infection (14, 15). Therefore, detection of antigen-responsive CD4+ and CD8+ lymphocytes in QFT-Plus is designed for higher sensitivity in active TB cases and after recent exposure. This was recently suggested in a cohort of 119 patients with active TB (84.9% sensitivity with QFT-Plus TB2 vs. 80.7% with TB1) (16). However, follow-up studies directly comparing QFT to QFT-Plus in active TB patients did not show a difference in sensitivity (15, 17, 18). Furthermore, the sensitivity and specificity of QFT-Plus for LTBI in low-risk individuals such as low-risk North American HCWs remains to be

determined. Given the simultaneous availability of two antigen tube results, discordant TB1 and TB2 results might indicate false positive results.

In a cross-sectional study, we prospectively compared the performance of QFT-Plus to QFT in low-risk HCWs undergoing TB screening at an academic institution in the U.S. We also tested the hypothesis that a more conservative definition of QFT-Plus positivity based on double-positive antigen tube results would reduce positivity rate in low-risk HCWs.

METHODS

Ethics

] Per Stanford University Institutional Review Board (IRB), this study was exempt from written informed consent because it constituted a quality improvement project for pre-market validation of QFT-Plus.

Study Design

A cross-sectional study was conducted in HCWs at Stanford Health Care to compare the performance of QFT-Plus to QFT and to test the hypothesis that a more conservative interpretation of QFT-Plus results would reduce positivity rate in low-risk HCWs. HCWs with no risk factors and discordant QFT-Plus results were evaluated for LTBI and active tuberculosis (TB) on their follow-up visits.

Subjects

130 Between August 7th and November 19th, 2015, HCWs presenting to the Stanford Health
131 Care Occupational Health Clinic for annual and new employee LTBI screening were
132 randomly enrolled in this study. The occupational health program performs QFT on all
133 HCWs with a negative or undocumented history of LTBI. Risk factors for TB exposure are
134 routinely collected using a questionnaire. HCWs are also evaluated for active TB. LTBI
135 risk factors assessed in a questionnaire include history of close contact with a TB patient,
136 country of birth outside U.S., long-term stay outside the U.S., travel to endemic countries,
137 and employment or volunteer work at high-risk facilities (correctional facility or homeless
138 shelter). Previous history of TST and IGRA positivity and BCG vaccination were also
139 assessed. Positivity rates of QFT and QFT-Plus was assessed in HCWs with no identifiable
140 risk factors and no self-reported history of positive TST or IGRA and also in HCWs with a
141 documented history of negative QFT result in previous year. No-risk HCWs with discordant
142 QFT-Plus results (n = 13) were assessed for active TB and retested with QFT and QFT-Plus
143 on their follow-up visits.
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145 **QFT and QFT-Plus testing**
146 Blood was drawn, in a single venipuncture, for QFT and QFT-Plus in the following tube
147 order: purge, Nil, QFT-Plus TB1, QFT-Plus TB2, QFT TB Antigen, and Mitogen. Both
148 assays were performed according to the manufacturer's instructions outlined in the package
149 insert. Briefly, blood was drawn into vacutainer tubes up to 1 mL mark and mixed gently.
150 The samples were incubated immediately at 37°C for 16–24 hours and then transported to the
151 clinical microbiology laboratory for ELISA. The plasma was separated by centrifugation and

stored at ambient temperature for same-day ELISA or stored at 4°C for ELISA within 72 hours. ELISA was performed within 24 hours on an automated robotic ELISA system (DSX; Dynex Technologies, Chantilly, VA). Plasma samples derived from each subject were tested on the same ELISA plate. For QFT, the results are considered positive when TB Antigen minus Nil IFN-γ concentration was ≥ 0.35 IU/mL and ≥25% of Nil value. For QFT-Plus, two different interpretative criteria were applied. First, per the manufacturer's instructions, the QFT-Plus assay was interpreted as positive when either TB antigen tube (TB1 or TB2) minus Nil IFN-γ concentration was ≥ 0.35 IU/mL and ≥25% of Nil value. Second, using a conservative interpretative criteria (QFT-Plus-C), QFT-Plus was interpreted as positive when both TB antigen tubes (TB1 and TB2) minus Nil IFN-γ concentration were ≥ 0.35 IU/mL and ≥25% of Nil value. TB1 and TB2 results were also analyzed separately using the QFT interpretive criteria.

Statistical Analysis

Concordance between binary results was measured using Cohen's Kappa (19, 20). Linear regression was used to evaluate quantitative relations between continuous variables. The confidence intervals (CIs) for proportions were calculated from the binomial distribution. The McNemar's test was used to compare proportions. Sample size was calculated as previously described (21). All reported *P* values were two-tailed and calculated with statistical significance set at *P* less than 0.05. Statistical analysis was performed using MedCalc Statistical Software (version 12.3.0, MedCalc Software, Mariakerke, Belgium) and IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, NY, USA).

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176 **RESULTS**

177 **Results with QFT and QFT-Plus**

178 In total, 989 HCWs were tested with QFT and QFT-Plus. Demographic data and LTBI risk
179 factors for all HCWs are summarized in Table 1. Two (0.2%) HCWs had indeterminate
180 results with both QFT and QFT-Plus and were therefore excluded from further analysis.
181 Figure 1 summarizes the QFT and QFT-Plus results for the remaining 987 HCWs.
182 Positivity rate with QFT, QFT-Plus, QFT-Plus TB1, and QFT-Plus TB2 was 4.3 % (95% CI,
183 3.0-5.6), 6.4% (CI, 4.9-7.9), 4.2% (CI, 3.0-5.5), and 5.2% (CI, 3.8-6.6), respectively (Table
184 2). Among 31 subjects that tested positive by both QFT and QFT-Plus, 61.3% had one or
185 more risk factors for LTBI. Among 913 subjects that tested negative by both assays, 20.9%
186 had one or more risk factors for LTBI (Supplementary table 1). Among 82 subjects with past
187 history of positive QFT or TST, positivity rate was 20.7% (CI, 11.9-29.5) with QFT and 26.8%
188 (CI, 17.2-36.4) with QFT-Plus. Among 68 subjects with history of BCG vaccination,
189 positivity rate was 17.6% (CI, 8.6-26.7) with QFT and 22.1% (CI, 12.2-32.0) with QFT-Plus.

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191 **Qualitative and quantitative comparisons between QFT and QFT-Plus**

192 Binary agreement between QFT and QFT-Plus, QFT-Plus TB1, and QFT-Plus TB2 was >95%
193 overall (Table 2 and 3). Agreement in HCWs with one or more risk factors was 90.1% (CI,
194 86.3-94.0), 93.1% (CI, 89.8-96.4), and 93.5% (CI, 90.3-96.7), respectively (Kappa, 0.60, 0.61,
195 and 0.69, respectively). Among 42 (4.3%) HCWs with a positive QFT result, 11 (26.2%)

were negative with QFT-Plus (Table 2 and Figure 1). Among 945 (95.7%) HCWs with a negative QFT result, 32 (3.4%) were positive with QFT-Plus (Table 2 and Figure 1). As shown in Figure 2, 84.8% (28/33) and 88.6% (31/35) of HCWs with discordant results between QFT and QFT-Plus TB1 and QFT-Plus TB2, respectively, had a response within the range of 0.2-0.7 IU/mL for one or both assays. Similarly, among 34 HCWs with discrepant results between QFT-Plus TB1 and QFT-Plus TB2, 30 (88.2%) were within the same range. In 626 HCWs with no risk factors for LTBI, 76.9% (10/13) and 81.3% (13/16) of discrepancies between QFT and QFT-Plus TB1 and QFT-Plus TB2, respectively, were within the range of 0.2-0.7 IU/mL (Supplementary figure 1).

Quantitative IFN-γ results obtained with QFT showed high degree of correlation with QFT-Plus TB1 and QFT-Plus TB2 (Pearson's correlation coefficient (R) = 0.74 and 0.75, respectively) (Supplementary figure 2). QFT-Plus TB1 and QFT-Plus TB2 also showed very high correlation with each other (R = 0.90). The median TB response in HCWs with positive results was not significantly different between QFT and QFT-Plus TB1 (2.29 vs. 1.77, n=25, P = 0.21), QFT and QFT-Plus TB2 (1.58 vs. 1.40, n=29, P = 1.0), and QFT-Plus TB1 and TB2 (1.77 vs. 1.89, n=29, P = 0.29).

Positivity rates with QFT and QFT-Plus in no-risk HCWs

Among 626 HCWs with no identifiable risk factors and no self-reported history of positive TST or IGRA, the positivity rate with QFT and QFT-Plus was 2.1% (CI, 1.0-3.2) and 3.0% (CI, 1.7-4.3), respectively, (Table 4). A more conservative interpretation of QFT-Plus positivity (QFT-Plus-C), based on a double-positive TB1 and TB2 result, yielded a positivity

rate of 1.0% (CI, 0.2-1.7) which is significantly lower compared with QFT-Plus ($P < 0.001$) and showed a reduced trend compared with QFT ($P = 0.07$) (Table 4). Among 310 HCWs with a documented history of negative QFT result and no risk factors for LTBI, the positivity rate was 2.6% (CI, 0.8-4.4), 2.6% (CI, 0.8-4.4), and 0.6% (CI, 0-1.5), with QFT, QFT-Plus, QFT-Plus-C, respectively. In this group, the positivity rate with QFT-Plus-C was significantly lower compared with QFT-Plus ($P = 0.03$) and QFT ($P = 0.03$).

Follow-up data was available for 11 of the 13 HCWs with discordant QFT-Plus results (Table 5). Zero HCWs developed active tuberculosis during the follow-up period. Ten HCWs had a negative QFT and 6 of 7 HCWs had a negative QFT-Plus (TB1 or TB2), respectively, 9 to 13 months from enrollment. One HCW (study ID No. 6937) who was positive with QFT and QFT-Plus TB2 on enrollment was subsequently positive with QFT after short-term retesting and with QFT and QFT-Plus (TB1 and TB2) 13 months later. Although this HCW did not have any known risk factors for LTBI, he was diagnosed with LTBI and was treated accordingly.

DISCUSSION

The objective of this study was to compare the performance of QFT-Plus to QFT in low-risk HCWs at a U.S. institution and to test the hypothesis that a more conservative interpretation of QFT-Plus results will reduce positivity rate in HCWs with no known risk factors for LTBI. Overall we found a high degree of agreement (>95%) between QFT-Plus and QFT. We also observed high degree of correlation between quantitative QFT-Plus (TB1 and TB2) and QFT

240 results. For the small number of patients with discordant results, the discordance was mostly
241 due to quantitative results bordering the assay cutoff (0.2-0.7 IU/mL) (22-25). The latter
242 finding is consistent with patterns of discordant results reported in prior IGRA reproducibility
243 studies and suggests that sources of variability previously described for QFT may also be
244 acting on QFT-Plus (25).
245
246 Importantly, in this study we found that 2.1% and 3.0% of 626 HCWs with no identifiable
247 risk factors for LTBI had positive QFT and QFT-Plus results, respectively. The higher
248 positivity rate with QFT-Plus was more frequently due to positive results with TB2 than TB1
249 (2.4% vs. 1.6%). Although IGRAs are more specific than TST in BCG-vaccinated
250 populations (2), IGRAs have proven less specific in low-risk North American HCWs and
251 college students (2). False positive results are likely attributed to one of many sources of
252 variability that cause IGRA results to cross the assay cutoff (25). Because of increasing
253 awareness and recommendations (4, 26), practitioners commonly confirm positive IGRA
254 results in low-risk patients with a short-term follow-up test, which results in added health
255 care costs and overutilization of resources. The QFT-Plus assay, which employs two antigen
256 tubes, was developed for increasing assay sensitivity for active TB by eliciting an IFN-γ
257 response from both CD4+ and CD8+ T lymphocytes. The manufacturer interprets QFT-Plus
258 results as positive when either TB1 or TB2 response reaches the assay cutoff. We showed
259 that a more conservative definition of QFT-Plus positivity, based on double-positive antigen
260 tube results (TB1 and TB2), significantly reduces the positivity rate to 0.6% in risk-free
261 HCWs with a prior negative QFT, which is closer to historical TST conversion rates and

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somewhat better aligned with the TB epidemiology in the US (4, 7). If we apply the conservative definition to a cohort of 106 low-risk controls from a recent study (16), the positivity rate would drop from 2.8% to 0%. In our study, follow-up investigation of 11 no-risk HCWs with discordant QFT-Plus TB1 and TB2 results showed that in all but one, follow-up testing with QFT and QFT-Plus (TB1 or TB2) remained negative. This finding suggests the conservative interpretation may be a useful strategy for increasing QFT-Plus specificity in low-risk settings. However, larger studies are needed to validate the conservative definition and to better define conditions (i.e., quantitative cutoffs) under which a conservative interpretation can be used to accurately identify non-reproducible positive results in low-risk populations.

Reproducibility studies have identified different causes of IGRA variability (25). The sources of variability can be broadly classified as pre-analytical, analytical, post-analytical, manufacturing and immunological (25). The use of standardized IGRA testing protocols may minimize variable results after serial testing (25). In this study, QFT and the QFT-Plus assays were simultaneously performed using the same pre-analytical test processes. In this setting, apart from differences in antigen makeup in TB2, analytical variability would have had to arise from ELISA. Metcalfe and colleagues estimated that variability of QFT derived from ELISA is ±0.6 IU/mL for all individuals and ±0.24 IU/mL for subjects with initial response in the borderline range of 0.25 to 0.8 IU/mL (23). This is consistent with our study in which most discordant results (84.8% for QFT vs. QFT-Plus TB1 and 88.6% for QFT vs. QFT-Plus TB2) lie in a range of 0.2 to 0.7 IU/mL. The fact that we saw a similar finding in HCWs

with no risk factors for LTBI argues for a borderline zone which accounts for variability due to random sources.

This study had several strengths and weaknesses. The strengths of our study include availability of LTBI risk factors for participants. This allowed us to identify low-risk HCW and calculate positivity rate in this population. In addition, we had prior QFT results for a subset of patients with no risk factors which allowed us to also assess positivity rate in this group. Further, the number of study participants was large and sufficient for comparison of two assays in low-risk HCWs. Lastly, with standardization of pre-analytical processes (25) and simultaneous testing design, we minimized the pre-analytical sources of variability. The fact that all testing was performed under routine clinical practice should render our findings applicable to other health care institutions in non-endemic settings. The limitation of this study includes low number of latently infected HCWs which limited our ability to assess agreement between assays in HCWs with LTBI. It also limited our ability to assess the performance of QFT-Plus in recently exposed versus remotely infected HCWs (14). However, this distribution reflects the low incidence setting we are operating in and therefore our interest to improve assay specificity. Future observational studies in high incidence settings with long term follow ups are needed to assess the sensitivity of QFT-Plus for LTBI after recent exposure.

In conclusion, the QFT-Plus assay showed high agreement with the QFT assay in low-risk HCW. A conservative interpretation of QFT-Plus identified nearly all positive results in

Journal of Clinical Microbiology

HCW with no known risk factors for LTBI. Larger studies are needed to validate our findings and to better characterize the conservative interpretation in low-risk populations.

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403

404 **FIGURE LEGENDS**

405

406 **Figure 1. Schematic overview of QFT and QFT-Plus results.**

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408 **Figure 2. Quantitative results in healthcare workers with discordant QFT and QFT-**
409 **Plus results.** Plots show quantitative results for QFT versus QFT-Plus TB1 (A) and QFT
410 versus QFT-Plus TB2 (B) in healthcare workers with discordant results. The dashed reference
411 lines at 0.35 IU/mL are the assay cutoffs and the shaded areas mark the borderline range of
412 0.2–0.7 IU/mL.

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Table 1. Demographic data and LTBI risk factors

Category	n=989
Age in yrs, mean ± SD	38.0 ± 11.5
Male gender (%)	301 (30.4%)
Prior positive QFT or TST, No. (%)	82 (8.3%)
BCG vaccination, No. (%)	68 (6.9%)
LTBI risk factor	
0 risk factors, No. (%)	653 (66.0%)
1 risk factor, No. (%)	107 (10.8%)
≥2 risk factors, No. (%)	124 (12.6%)
Unknown, No. (%)	105 (10.6%)

QFT, QuantiFERON-TB Gold; TST, tuberculin skin test; BCG, bacillus Calmette–Guérin; LTBI, latent tuberculosis infection

LRBI risk factors per the questionnaire

Table 2. Qualitative comparison between QFT and QFT-Plus

QFT	QFT-Plus		QFT-Plus TB1		QFT-Plus TB2		QFT-Plus-C	
	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
Positive	31 (3.1%)	11 (1.1%)	25 (2.5%)	17 (1.7%)	29 (2.9%)	13 (1.3%)	23 (2.3%)	19 (1.9%)
Negative	32 (3.2%)	913 (92.5%)	16 (1.6%)	929 (94.1%)	22 (2.2%)	923 (93.5%)	6 (0.6%)	939 (95.1%)
Total	63 (6.4%)	924 (93.6%)	41 (4.2%)	946 (95.8%)	51 (5.2%)	936 (94.8%)	29 (2.9%)	958 (97.1%)

QFT, QuantiFERON-TB Gold; QFT-Plus, QuantiFERON-TB Gold-plus; QFT-Plus-C, QuantiFERON-TB Gold-Plus using a conservative interpretation (TB1 and TB2).

Table 3. Qualitative agreement between QFT and QFT-Plus

Comparison	Agreement (%, 95% CI)	Kappa (95% CI)
QFT vs QFT-Plus	944/987 (95.6, 94.3-96.9)	0.57 (0.44-0.70)
QFT vs QFT-Plus TB1	954/987 (96.7, 95.6-97.8)	0.59 (0.45-0.72)
QFT vs QFT-Plus TB2	952/987 (96.5, 95.4-97.7)	0.61 (0.48-0.73)
QFT vs QFT-Plus-C	962/987 (97.4, 96.4-98.4)	0.64 (0.50-0.78)
QFT-Plus TB1 vs QFT-Plus TB2	953/987 (96.6, 95.5-97.7)	0.61 (0.49-0.74)

QFT, QuantiFERON-TB Gold; QFT-Plus, QuantiFERON-TB Gold-Plus; QFT-Plus-C, QuantiFERON-TB Gold-Plus using a conservative interpretation (TB1 and TB2); CI, confidence interval.

Journal of Clinical Microbiology
JCM
Journal of Clinical Microbiology

Table 4. Positivity rates with QFT and QFT-Plus in 626 healthcare workers with no LTBI risk factors and no prior positive tests

Assay	No. of positives	Positivity rate (95% CI)	P^*
QFT	13	2.1% (1.0-3.2)	-
QFT-Plus	19	3.0% (1.7-4.3)	0.24
QFT-Plus TB1	10	1.6% (0.6-2.6)	0.58
QFT-Plus TB2	15	2.4% (1.2-3.6)	0.80
QFT-Plus-C†	6	1.0% (0.2-1.7)	0.07

QFT, QuantiFERON-TB Gold; QFT-Plus, QuantiFERON-TB Gold-Plus; QFT-Plus-C, QuantiFERON-TB Gold-Plus using a conservative interpretation (TB1 and TB2), *Compared with QFT using McNemar's test, $^\dagger P = 0.0002$ compared with that of QFT-Plus

Journal of Clinical Microbiology

Table 5. Follow-up results for 13 no-risk healthcare workers with discordant QFT-Plus results.

			Enrollment Result				Follow-up Result						
			QFT		QFT-Plus		QFT		QFT-Plus		Since last screen		
Study No.	Age (yr)	Sex (M/F)	Initial screen	Short-term retest	TB1	TB2	Annual screen	Short-term retest	TB1	TB2	Interval (mo)	TB exposure	Active TB
6937	53	M	0.4	0.44	0.27	0.77	1.01	ND	0.91	1.12	13	No	No
823	30	M	0.47	0.16	0.34	0.36	0.16	ND	ND	ND	12	No	No
907	28	F	1.47	0.02	0.5	0.05	0.03	ND	ND	ND	13	No	No
1716	38	F	0.06	ND	0.45	0.25	0.16	ND	0.21	0.25	12	No	No
3958	28	F	0.07	ND	1.85	0.14	0	ND	0.03	0.01	13	No	No
6258	28	F	0.02	ND	5.11	0.02	0	ND	ND	ND	10	No	No
3720	26	F	0	ND	0	1.26	0	ND	0.13	0.15	13	No	No
4749	58	F	0	ND	0	0.67	0	ND	0.00	0.34	12	No	No
885	34	F	0.06	ND	0.23	0.62	0.03	ND	0.01	0.17	9	No	No
6156	23	F	0	ND	0.04	0.60	ND	ND	ND	ND	NA	NA	NA
2262	51	M	0.01	ND	0.06	0.48	0.01	ND	0.01	0.03	11	No	No
1588	55	M	0.28	ND	0.23	0.36	0.6	0.15	ND	ND	12	No	No
4698	43	F	0	ND	0.01	0.35	ND	ND	ND	ND	NA	NA	NA

TB Ag minus Nil (IU/mL) are shown and positive results are shaded.

ID no., identification number; yr, year; M, male; F, female, mo, month; TB, tuberculosis; ND, not done; NA, not available

Journal of Clinical Microbiology

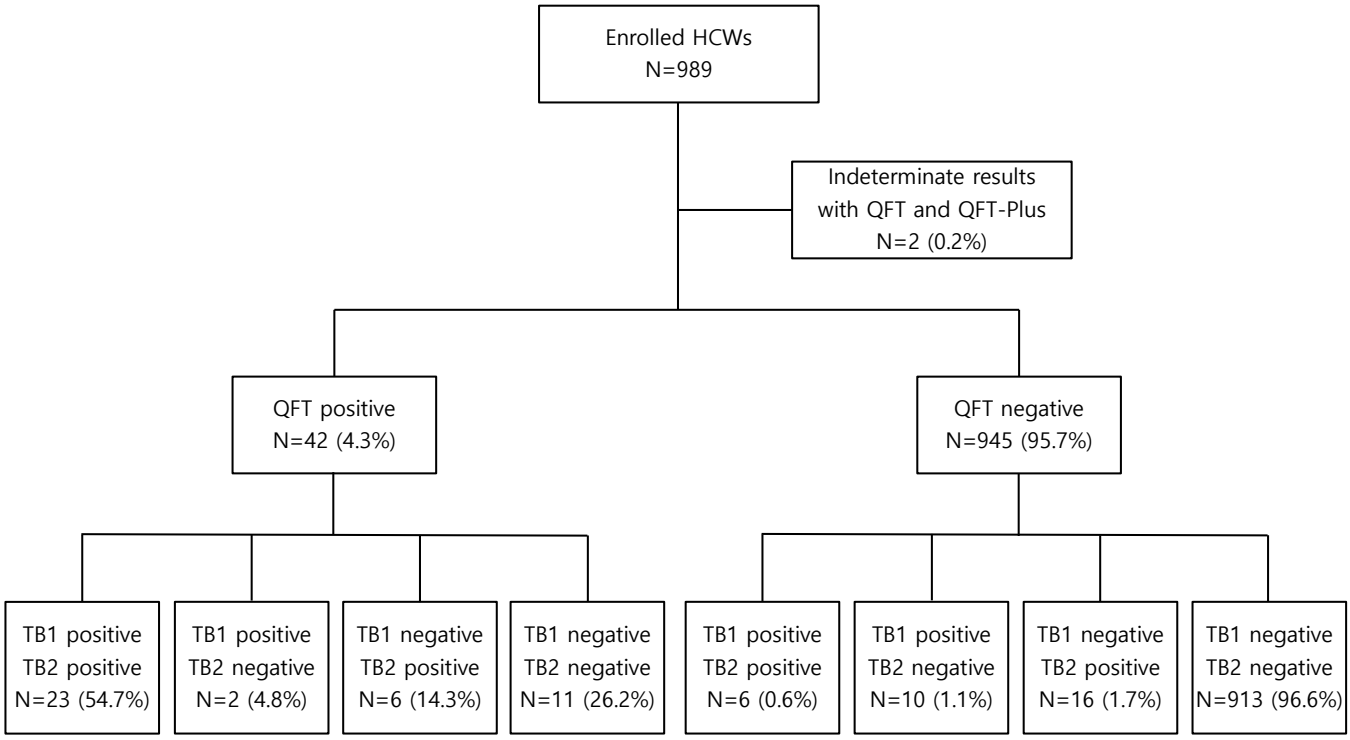

Figure 1. Schematic overview of QFT and QFT-Plus results.

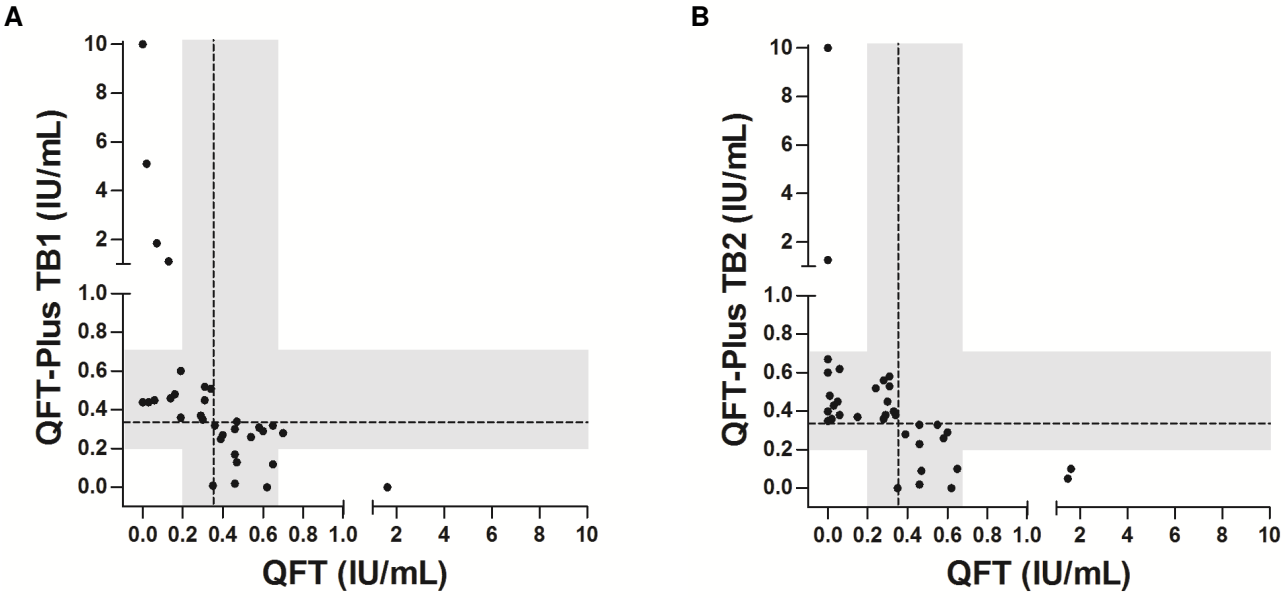

Figure 2. Quantitative results in healthcare workers with discordant QFT and QFT-Plus results. Plots show quantitative results for QFT versus QFT-Plus TB1 (A) and QFT versus QFT-Plus TB2 (B) in healthcare workers with discordant results. The dashed reference lines at 0.35 IU/mL are the assay cutoffs and the shaded areas mark the borderline range of 0.2–0.7 IU/mL.