Original Article

Tuberculin Skin Test and QuantiFERON®-TB Gold In-Tube Test for Diagnosing Latent Tuberculosis Infection among Thai Healthcare Workers

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SUMMARY: A cross-sectional study was conducted on the performance of the tuberculin skin test (TST) and QuantiFERON®-TB Gold In-Tube test (QFT-IT) for detecting latent tuberculosis infection among Thai healthcare workers (HCWs). Each HCW underwent both the TST and QFT-IT during the annual health screening. Among the 260 HCWs enrolled, the median age was 30 years (range 19–60 years), 92% were women, 64% were nurses and nurse assistants, 78% were Bacillus Calmette Guérin vaccinated, and 37% had previously taken the TST. Correlation between TST reaction size and the interferon- γ level was weak ($r = 0.29$; $P < 0.001$). Of the HCWs, 38% and 20% had a reactive TST and a positive QFT-IT, respectively. Using QFT-IT positivity as a standard for latent tuberculosis diagnosis, the cut-off for TST reactivity with the best performance was ≥ 13 mm with a sensitivity, specificity, false positivity, and false negativity of 71%, 70%, 30%, and 29%, respectively (area under the curve 0.73; $P < 0.001$). The independent factor associated with a false reactive TST was a previous TST (adjusted odds ratio 1.83; $P = 0.04$). Our findings suggest that the QFT-IT may be the preferred test among HCWs with previous TST. In settings where the QFT-IT is not available, appropriate cut-offs for TST reactivity should be evaluated for use among HCWs.

INTRODUCTION

Tuberculosis (TB) is an important communicable disease and contributes to significant morbidity and mortality worldwide. Healthcare workers (HCWs) are among the population at-risk for acquiring TB, given the higher chance of TB exposure through their work (1). A TB screening program for HCWs has been recommended by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). The use of an interferon gamma release assay (IGRA) is preferred for testing persons who have received the Bacillus Calmette Guérin (BCG) vaccine. Moreover, an IGRA or a tuberculin skin test (TST) may be used without preference for periodic screening of persons who might have occupational exposure to *Mycobacteria tuberculosis* with special considerations regarding conversions and reversions (2,3). Previous TB screening programs along with isoniazid (INH) prophylaxis in cases of latent TB infection (LTBI) have been shown to reduce the development of active TB by 60% and up to 90% if the prophylaxis was completed among HCWs (4–7).

TST has long been used as a diagnostic tool for LTBI, given its ready availability and low cost. However, its limitations include false reactivity from the BCG vac-

cine and non-tuberculous mycobacterial (NTM) infection, administrative and interpretative errors, and the requirement of 2 clinic visits (8). A blood-based assay, IGRA, that detects the interferon (IFN)- γ level, after in vitro stimulation of a subject's white blood cells with specific *M. tuberculosis* antigens, has been developed in the past decade (9). The advantages of IGRA over TST are its higher sensitivity and specificity, no cross reaction with prior BCG vaccination or other NTM, single visit testing, and a more objective result (8). Nonetheless, IGRAs are more expensive than TST and are not available in all settings, especially in TB-endemic resource-limited settings.

Thailand is a TB-endemic region and has an estimated TB prevalence of 149 cases per 100,000 population (10). The country's national guidelines have not been established for LTBI screening among Thai HCWs given the concern about TST limitations (8). Comparative data on the performance of TST and IGRA in LTBI detection is largely from low TB prevalence settings (8). Among Asian countries (Table 1), the overall agreement between TST and IGRA results was poor to fair and depended on the cut-offs for TST reactivity used (11–23). The main factor reported to be associated with poor agreement between the 2 tests was prior BCG vaccination, which resulted in false reactivity of TST (23). The higher rates of TST reactivity compared to the rates of IGRA positivity in most studies suggest the false reactivity of TST among HCWs. Using the lower cut-off level (i.e., 10 mm as recommended by the CDC for employees working in TB high-risk settings) (2) would increase the rate of TST false reactivity in settings with high rates of BCG vaccination, while using very high cut-off level (i.e., 15 or 18 mm) would falsely increase the rate of TST non-reactivity, and may not be ap-

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Table 1. Summary of studies comparing tuberculin skin test (TST) and interferon-gamma release assay (IGRA) for diagnosis of latent tuberculosis infection among healthcare workers in Asian countries

Study year	Ref. (No.)	Country	TB prevalence (cases/100,000) ¹⁾	Sample size (No.)	Type of IGRA	TST reactivity rate (%) (cut-off used in mm)	IGRA positivity rate (%)	Concordance between TST and IGRA (kappa, TST cut-off used in mm)	Rate of indeterminate IGRA result (%)
Tuberculosis high prevalence countries									
2004	(11)	India	211	726	IFN-G	41 (≥ 10); 23 (≥ 15)	40	0.61 (≥ 10); 0.51 (≥ 15)	0
2004	(12)	India	211	216	QFT	22 (≥ 10)	18	0.57 (≥ 10)	0
2006	(13)	South Korea	143	84	QFT	43 (≥ 10)	20	0.31 (≥ 10); 0.33 (≥ 15)	0
2007	(14)	Vietnam	209	300	QFT-IT	66 (≥ 10); 30 (≥ 15)	47	0.44 (≥ 10); 0.50 (≥ 11) 0.46 (≥ 13); 0.39 (≥ 15)	0
2009	(15)	China	94	210	QFT-IT	98 (≥ 10)	77	0.05 (≥ 10)	4
2009–2010	(16)	South Korea	143	82	QFT-IT	38 (≥ 10)	23	0.05 (≥ 10)	0
2010	(17)	South Korea	143	173	QFT-IT	33 (≥ 10); 19 (≥ 15)	21	0.23 (≥ 10); 0.28 (≥ 15)	0
2010	(18)	China	94	999	QFT-IT	69 (≥ 5); 54 (≥ 10); 25 (≥ 15)	68	0.22 (≥ 5); 0.19 (≥ 10) 0.08 (≥ 15)	0
2012	(19)	South Korea	143	82	QFT-IT	37 (≥ 10)	17	0.22 (≥ 10)	0
2014	Our study	Thailand	149	260	QFT-IT	55 (≥ 10); 38 (≥ 15)	20	0.20 (≥ 10); 0.31 (≥ 13)	0
Tuberculosis low prevalence countries									
2004	(20)	Taiwan	No data	39	QFT	85 (≥ 10)	10	0.03 (≥ 10); 0.04 (≥ 15) 0.12 (≥ 18)	0
2005	(21)	Turkey	23	76	QFT	54 (≥ 15)	86	0.22 (≥ 15)	0
2005	(22)	Turkey	23	78	QFT-IT	44 (≥ 10)	73	0.35 (≥ 10 , BCG-vaccinated HCW); 0.35 (≥ 15 , BCG- non-vaccinated HCW)	0
2009	(23)	Israel	7	100	QFT	34 (≥ 10)	17	0.19 (≥ 10)	9

¹⁾: Based on the World Health Organization tuberculosis country profiles (10).

TB, tuberculosis; IFN-G, interferon gamma; QFT, QuantiFERON[®]-TB Gold Test; QFT-IT, QuantiFERON[®]-TB Gold In-Tube Test; BCG, Bacillus Calmette-Guérin.

appropriate in settings with a low rate of BCG vaccination and/or HCWs with decreasing immunity after a long duration from the last BCG vaccination. The appropriate cut-off for TST reactivity among HCWs in Thailand is unknown, and factors associated with discordant results between the TST and IGRA have rarely been described. We conducted a study to evaluate the characteristics of Thai HCWs associated with LTBI, compare the performance of TST and IGRA in diagnosing LTBI among Thai HCWs, and determine factors associated with the discordant results between these 2 tests.

MATERIALS AND METHODS

Study design and setting: A cross-sectional study was conducted at Thammasat University Hospital, a 600-bed tertiary-care center in central Thailand. The hospital has approximately 1,250 HCWs and 120 hospitalized patients with TB per year. It has two negative pressure rooms for hospitalized patients requiring airborne isolation, but no specific and designated wards for TB patients. The study population included the hospital's HCWs aged ≥ 18 years. The study period was from January 2, 2014 to January 31, 2014 during the annual health screening for HCW at the hospital. This study was conducted in accordance with the amended Declaration of Helsinki and was approved by the Faculty of Medicine, Thammasat University Ethics Committee.

Study population and study definitions: All HCWs attending the hospital's annual health screening were screened for eligibility during the 1-month study period.

Exclusion criteria were HCWs with prior or current TB, TST receipt within the prior 12-month period, and HCWs who declined study participation. Those who met the inclusion criteria were interviewed for demographics, comorbidities, working history, history of BCG vaccination, TB contact, a previous TST, LTBI, and LTBI treatment. Medical record review was performed for additional clinical data. Long-term tobacco smoking was defined as smoking everyday for at least 1 year prior to enrollment. Screening for active TB was performed based on symptoms and a chest radiograph as recommended by the WHO (24). Informed consent was obtained from the eligible HCWs before study participation.

IFN- γ release assay and tuberculin skin test protocol: The IGRA used was the QuantiFERON[®]-TB Gold In-Tube Test (QFT-IT) (Qiagen, Gaithersburg, MD, USA). A whole blood sample was collected and transported within the same day to the National Institute of Health, Department of Medical Sciences, Ministry of Public Health of Thailand. Test procedures and interpretation of the results were conducted according to the manufacturer's standard guidelines (25). After collection of the blood sample, TST was performed. All HCWs received inner forearm, intradermal 0.1 ml (5 tuberculin units) of purified protein derivative RT23 (Tubersol; Connaught Laboratories, Toronto, Canada). The results were determined 48–72 h later through the use of the ballpoint pen method. TSTs were performed and read dually and blindly by 2 nurses who were trained and had previous experience on TST procedure. We searched for the best cut-off of skin induration.

tion size to define TST reactivity using the results of IGRA as a reference standard in this study.

Statistical analysis: A sample size of 170 subjects was estimated to detect a 12% difference between IGRA and TST in regard to the rates of LTBI diagnosis, with a significance level of 0.05 and 80% power. This estimate was based on the LTBI detection rate of 14.3% via the IGRA and 2.3% via the TST as reported in a meta-analysis (26). All analyses were performed using SPSS version 15.0 (SPSS, Chicago, IL, USA). The agreement between TST and QFT-IT was determined using the kappa coefficient. A kappa coefficient ≥ 0.81 was considered as very good agreement, 0.61–0.80 as good agreement, 0.41–0.60 as moderate agreement, 0.21–0.40 as fair agreement, and ≤ 0.20 as poor agreement. Correlation between test values and HCWs' continuous variables were evaluated by the Pearson's correlation test. An r value between 0–0.19 was considered very weak correlation, 0.20–0.39 as weak correlation, 0.40–0.59 as moderate correlation, 0.60–0.79 as strong correlation, and 0.80–1.00 as very strong correlation. The performance of TST in comparison with QFT-IT was evaluated by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristics (ROC) curve analysis. Categorical variables were compared using the Pearson's χ^2 or Fisher's exact test as appropriate. Continuous variables were compared using Mann-Whitney U Test. P values < 0.05 were considered statistically significant. An adjusted odd ratio (aOR) and 95% confidence interval (CI) was calculated in the multivariable logistic regression analysis to determine the factors associated with the discordant results between the two tests.

RESULTS

Baseline characteristics of the study patients: We screened 285 HCWs during the study period. Eighteen (6%) who declined participation and 7 (3%) who had a history of TB were excluded (Fig. 1). None of the patients had current active TB. The characteristics of the eligible 260 HCWs are shown in Table 2. All of the HCWs returned for follow-up TST interpretation of the results. The cohort had a median age of 30 years (range, 19–60 years), a median working duration of 5 years (range, 1–39 years), and 240 (92%) were women. Most of the HCWs were either nurses (39%), nurse assistants (25%), or clerks (23%), and 78% reported prior BCG vaccination. History of TB contact was reported in 57% of the HCWs with the median duration since last contact being at 12 months (range, 1–270 months). Ninety-seven HCWs (37%) had previously undergone the TSTs, all of which were performed more than 1 year ago. Of the 22 HCWs who previously had a reactive TST, 7 (32%) received INH prophylaxis and 4/7 (57%) completed the therapy. Using IGRA positivity as a standard reference for LTBI diagnosis, the characteristics associated with LTBI included older age, longer working duration, and receipt of a previous TST (Table 2).

Correlation and agreement between the variables: The TST reaction size weakly correlated with the IFN- γ level ($r = 0.29$, $P < 0.001$) (Fig. 2A), but moderately inversely-correlated with the duration since the diagnosis of LTBI ($r = -0.46$, $P = 0.03$). The TST reaction size did not correlate with age, working duration, duration since the last TST, and duration since the last TB contact. The IFN- γ level very weakly correlated with age

Fig. 1. Study patient flow chart.

LTBI, latent tuberculosis infection; QFT-IT, QuantiFERON®-TB Gold In-Tube Test; TST, tuberculin skin test.

Table 2. Baseline characteristics of the 260 healthcare workers stratified by detection of latent tuberculosis infection (LTBI) defined as positive QuantiFERON®-TB Gold In-Tube test

Characteristic	All <i>n</i> = 260 (%)	LTBI <i>n</i> = 52 (%)	Non-LTBI <i>n</i> = 208 (%)	<i>P</i> ¹⁾
Demographic				
Age; year, median (range)	30 (19–60)	35 (21–60)	29 (19–58)	0.006*
Sex/women	240 (92) ²⁾	47 (90)	193 (93)	0.56
Occupation				
Nurse	102 (39)	16 (31)	86 (41)	0.39
Nurse assistant	66 (25)	16 (31)	50 (24)	
Clerk	58 (23)	17 (33)	41 (20)	
Physical therapist	21 (8)	0 (0)	21 (10)	
Housekeeper	7 (3)	1 (2)	6 (3)	
Forensic personnel	4 (2)	2 (2)	3 (1)	
Physician	2 (1)	1 (2)	1 (1)	
Working duration; year, median (range)	5 (1–39)	9 (1–39)	5 (1–37)	0.02*
Tuberculosis history				
Prior BCG vaccination	203 (78)	40 (79)	163 (78)	0.82
History of tuberculosis contact	147 (57)	29 (56)	118 (57)	1.00
Duration since last tuberculosis contact; month, median (range)	12 (1–270)	12 (1–270)	12 (1–216)	0.88
Previous tuberculin skin test	97 (37)	27 (52)	70 (34)	0.02*
History of positive tuberculin skin test	22 (9)	5 (10)	17 (8)	0.74
Receipt of LTBI treatment	7/22 (32)	1/5 (20)	6/17 (35)	1.00
Completed LTBI treatment	4/7 (57)	1/1 (100)	3/6 (50)	1.00
Comorbidities				
History of long-term tobacco smoking	2 (1)	1 (2)	1 (1)	0.36
Having diabetes mellitus	1 (0.4)	0 (0)	1 (0.5)	1.00
Receipt of chemotherapy within 1 month	2 (1)	0 (0)	2 (1)	1.00

¹⁾: Comparison between LTBI group and non-LTBI group.

²⁾: Data are in numbers (%) unless otherwise indicated. *, statistically significant (<0.05).

and working duration ($r = 0.18$, $P = 0.004$ and $r = 0.16$, $P = 0.01$, respectively) but did not correlate with the duration since last TST, duration since the diagnosis of LTBI, and duration since last TB contact. The agreement between TST and QFT-IT results using different cut-offs for TST reactivity are shown in Fig. 2B. The cut-off of ≥ 13 mm had the best agreement (kappa 0.31) between the two tests' results, while the commonly used cut-offs of ≥ 15 mm and ≥ 10 mm had a fair agreement (0.30 and 0.20, respectively) among all HCWs in this study. The cut-off of ≥ 13 mm also had the best agreement between the two tests among HCWs with and without a previous TST (kappa 0.35 and 0.21) and with and without a history of BCG vaccination (kappa 0.35 and 0.30). This cut-off for TST reactivity was then used in the further analyses.

Latent tuberculosis infection test results: When using the cut-off of ≥ 13 mm for TST reactivity, 114 HCWs were identified with LTBI by either TST or QFT-IT (Fig. 1). Among these 114 HCWs, 62 were TST reactive and QFT-IT negative, 15 were TST non-reactive and QFT-IT positive, and 37 were TST reactive and QFT-IT positive. No HCW had an indeterminate result for QFT-IT. Among the 99 TST-reactive HCWs, the median reaction size was 16 mm (range, 13–27 mm). The group of HCWs who were both TST reactive and QFT-IT positive had TST median reaction sizes larger than the group who was TST reactive and QFT-IT negative (18 mm vs. 16 mm; $P = 0.04$). Among the 52 patients with a positive QFT-IT, the median IFN- γ level was 0.71 IU/ml (range, 0.35–8.51 IU/ml), with no signifi-

Table 3. Multivariable logistic regression analysis for factors associated with concordant and discordant results between tuberculin skin test (TST) and QuantiFERON®-TB Gold In-Tube Test (QFT-IT)

Result		No.	Factor	Adjusted odds ratio (95% confidence interval)	<i>P</i>
TST	QFT-IT				
Reactive	Positive	37	Previous TST	3.53 (1.60–7.80)	0.002
			Age	1.12 (1.02–1.23)	0.01
Reactive	Any	99	Previous TST	3.19 (1.83–5.56)	<0.001
			Age	1.07 (1.00–1.15)	0.04
Any	Positive	52	Being a ward clerk	3.85 (1.54–9.67)	0.004
Reactive	Negative	62	Previous TST	1.83 (1.03–3.27)	0.04
Non-reactive	Positive	15	None	—	—

cant difference in the median IFN- γ level found when the results were stratified by TST reactive (0.71 IU/ml) and non-reactive subjects (0.71 IU/ml).

In the multivariable logistic regression analyses (Table 3), the factor associated with a positive QFT-IT result was being a ward clerk (aOR, 3.85; 95% CI, 1.54–9.67; $P = 0.004$) while, previous TST (aOR, 3.19; 95% CI, 1.83–5.56; $P < 0.001$) and age (aOR, 1.07; 95% CI, 1.00–1.15; $P = 0.04$) were independently associated with TST reactivity. Among the 77 HCWs with discordant results between the 2 tests, the independent factors associated with TST reactivity and a negative

Fig. 2. (A) Correlations between tuberculin skin test (TST) reaction size and interferon-gamma level. (B) The kappa coefficient for agreement between results of TST and QuantiFERON®-TB Gold In-Tube Test (QFT-IT) at different reaction size cut-offs for TST reactivity. (C) Receiver operating characteristics curve analysis of TST using QFT-IT results as standard for diagnosis of latent tuberculosis infection. ^aTST reaction size of at least equal or larger than each cut-off was considered TST reactivity. AUC, area under the curve.

QFT-IT was previous TST (aOR, 1.83; 95% CI, 1.03–3.27; $P = 0.04$), while no factor was identified to be associated with a non-reactive TST and positive QFT-IT.

Performance of TST compared to QFT-IT: When using QFT-IT result as the reference standard for LTBI diagnosis and the cut-off of ≥ 13 mm for TST reactivity, TST sensitivity, specificity, PPV, and NPV were 71%, 70%, 37%, and 91%, respectively (Table 4). False positive and false negative rates for TST were 30% and 29%, respectively. The ROC curve analysis of the TST indicated an area under the curve of 0.73 (95% CI,

Table 4. Performance of tuberculin skin test (TST) with varied cut-offs for reactivity using QuantiFERON®-TB Gold In-Tube Test as reference standard

Parameter	TST cut-off for reactivity (mm)		
	≥ 10	≥ 13	≥ 15
Sensitivity	81 (67–90) ¹⁾	71 (56–82)	62 (47–75)
Specificity	52 (45–59)	70 (63–76)	76 (70–82)
Positive predictive value	30 (22–38)	37 (28–48)	39 (28–50)
Negative predictive value	92 (85–96)	91 (89–95)	38 (83–93)

¹⁾: Data are in percent (95% confidence interval).

0.66–0.81; $P < 0.001$) and indicated that the best performance of TST occurred when using the cut-off of ≥ 13 mm (Fig. 2C). The other cut-offs for TST reactivity had a poorer performance in comparison to this cut-off as shown in Table 4.

DISCUSSION

Our study demonstrated a fair agreement between the TST and QFT-IT results depending on the cut-off for TST reactivity used, which is consistent with the results from other studies conducted in Asian countries (Table 1). In our setting with the high rate of BCG vaccination (78%) among HCWs, and a median duration from the latest BCG vaccination of 30 years, the TST reaction cut-off of ≥ 13 mm had the best agreement with the IGRA results. In contrast, other studies in Table 1 reported the best agreement using different cut-off levels from ≥ 10 mm to ≥ 18 mm. These findings suggest that the appropriate cut-off for TST reactivity among HCWs needs to be studied in each setting and determined based on the influence of BCG vaccination.

We identified a prior TST as an independent factor associated with false reactivity of TST consistent with reports from previous studies (27,28). However, we did not find a significant correlation between the TST reaction size and the duration since the last performed TST. These findings may be explained by the booster phenomenon after receiving a repeated TST as observed in the two-step TST procedure (29) and/or the persistent immunological responses to tuberculin overtime. These findings also imply that HCWs who underwent a prior TST may benefit from IGRA testing. However, if the IGRA is not available, repeated or serial TSTs among previous TST-nonreactive HCWs may be performed at intervals based on the risk classification of the facility (3); however, this should not be performed more frequently than every year. The TST results should be interpreted with caution taking into account the potential of false reactivity, which may lead to unnecessary INH chemoprophylaxis and subsequent risk for adverse drug reactions, especially liver toxicity.

The HCWs with positive QFT-IT and TST reactivity had a significantly larger TST reaction size than those with a reactive TST alone, while patients with a positive QFT-IT and reactive TST did not have significantly higher IFN- γ levels than those with positive QFT-IT alone. These findings suggest the higher sensitivity of QFT-IT than of TST for LTBI diagnosis among HCWs and are consistent with the results from a previous meta-analysis demonstrating a sensitivity of 76% for QFT-IT vs. 70% for TST when using the history of active TB contact as a reference for LTBI diagnosis (30). In addition, studies from low TB prevalence countries demonstrated the superior performance of IGRA as a LTBI screening test for BCG-vaccinated HCWs and immigrants from TB-endemic areas (31,32). However, QFT-IT was costlier than TST (US \$120 vs. US \$18 per test per HCW) in our setting.

We further analyzed the results of QFT-IT with the HCWs' characteristics. The IFN- γ level was found to very weakly correlate with age and working duration. This finding may be due to the accumulative risk of TB exposure and acquisition in older HCWs and in those

who had been working in the hospital for a long period of time. It should be noted that being a ward clerk was a risk factor for IGRA positivity. This higher risk of LTBI acquisition among ward clerks may be explained by the proximity between ward clerks' working areas and patient care areas and their work duration of 6 to 8-h of in those areas in our hospital. In addition, all ward clerks do not wear appropriate protection masks (such as N95 masks) to prevent TB acquisition during their work period. Although this has not been previously reported, this finding suggests ward clerks to be targets for TB screening and prevention in addition to HCWs who closely contact with patients, such as physicians, nurses, and nurse assistants. Providing designated working spaces with good ventilation distant from patient care areas, education on TB prevention for the ward clerks, and strict airborne isolation measures in the wards would be important strategies to prevent TB infection among the ward clerks.

The strengths of our study include the relatively large sample size, complete data for TST reaction size for all enrolled HCWs, the exclusion of HCWs with prior or current TB to minimize the falsely high level of concordance between TST and IGRA, and thorough assessment of factors associated with discordant results between the two tests. However, there are notable limitations. First, we could not assess whether sex had an influence on the results of the tests given the high proportion of women (92%) in our study. Second, given that there was no recommended reference standard for LTBI diagnosis and the limitations of the TST, we used QFT-IT as the reference standard test to assess the diagnostic test utility of TST. Thus, this assessment may not be entirely accurate; however, the findings could potentially suggest the performance of TST in comparison to IGRA and how to better use TST if IGRA is not available. Third, since most of the HCWs in our study were nurses and nurse assistants in early adulthood with a median working duration of 5 years, and that most had a history of previous TB contact, the results may not be generalizable to other settings with differences in HCWs' characteristics. Lastly, there might be recall biases in regards to the history of BCG vaccination and TB contact.

In conclusion, IGRA may be a preferred LTBI diagnostic test for HCWs in TB-endemic regions given its higher sensitivity, and the results are independent of the BCG vaccination effect. In settings where IGRA is not available, TST remains the LTBI diagnostic test of choice for HCWs. However, the cut-off for reactivity needs to be adjusted according to results from locally conducted studies. In settings where IGRA is available but the cost of the screening tests is of concern, our findings suggest that HCWs with a prior non-reactive TST should receive repeated TSTs but if the subsequent result is reactive, they should undergo an additional IGRA to rule out false TST reactivity. Further prospective studies will be needed to evaluate the efficacy of LTBI treatment guided by the results of mono- or sequential testing by TST and IGRA for TB prevention among HCWs.

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Conflict of interest None to declare.

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